The Utility of Immunohistochemistry in the Diagnosis of Breast Lesions

Nour Sneige, M.D.

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Diagnostic Problems in Mammary Gland Tumor Pathology

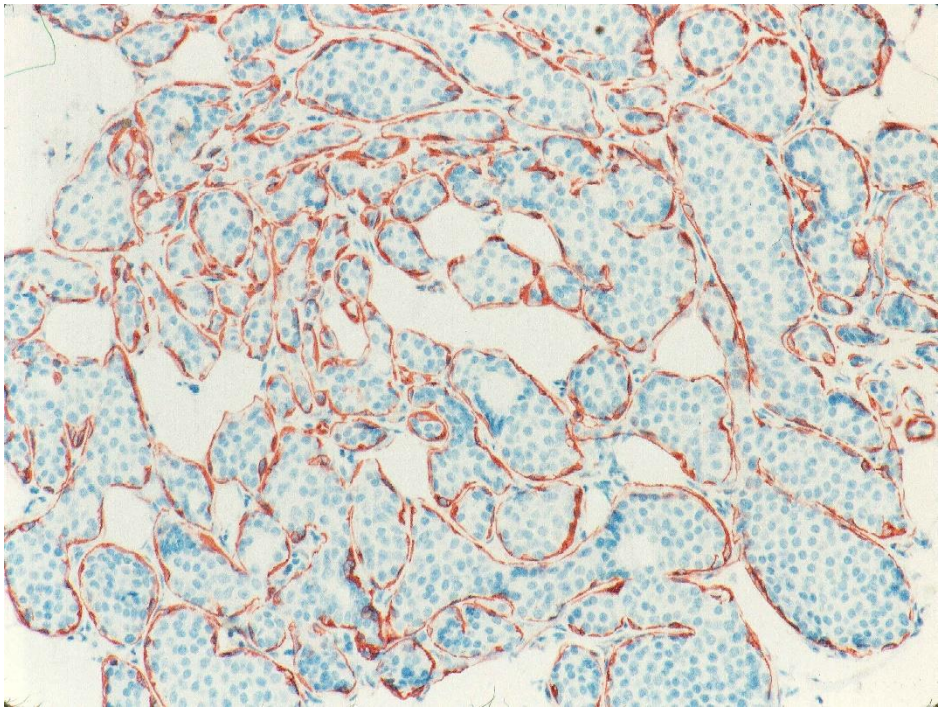
1. Distinguishing *in situ* from invasive carcinoma
2. The differential diagnosis of various types of benign and malignant lesions
3. Confirming the breast as the primary site in metastatic carcinoma

In Situ vs Invasive Carcinoma

Myoepithelial cells (MEC)

An intact layer of MEC surrounding epithelial structures →

benign and in situ proliferation



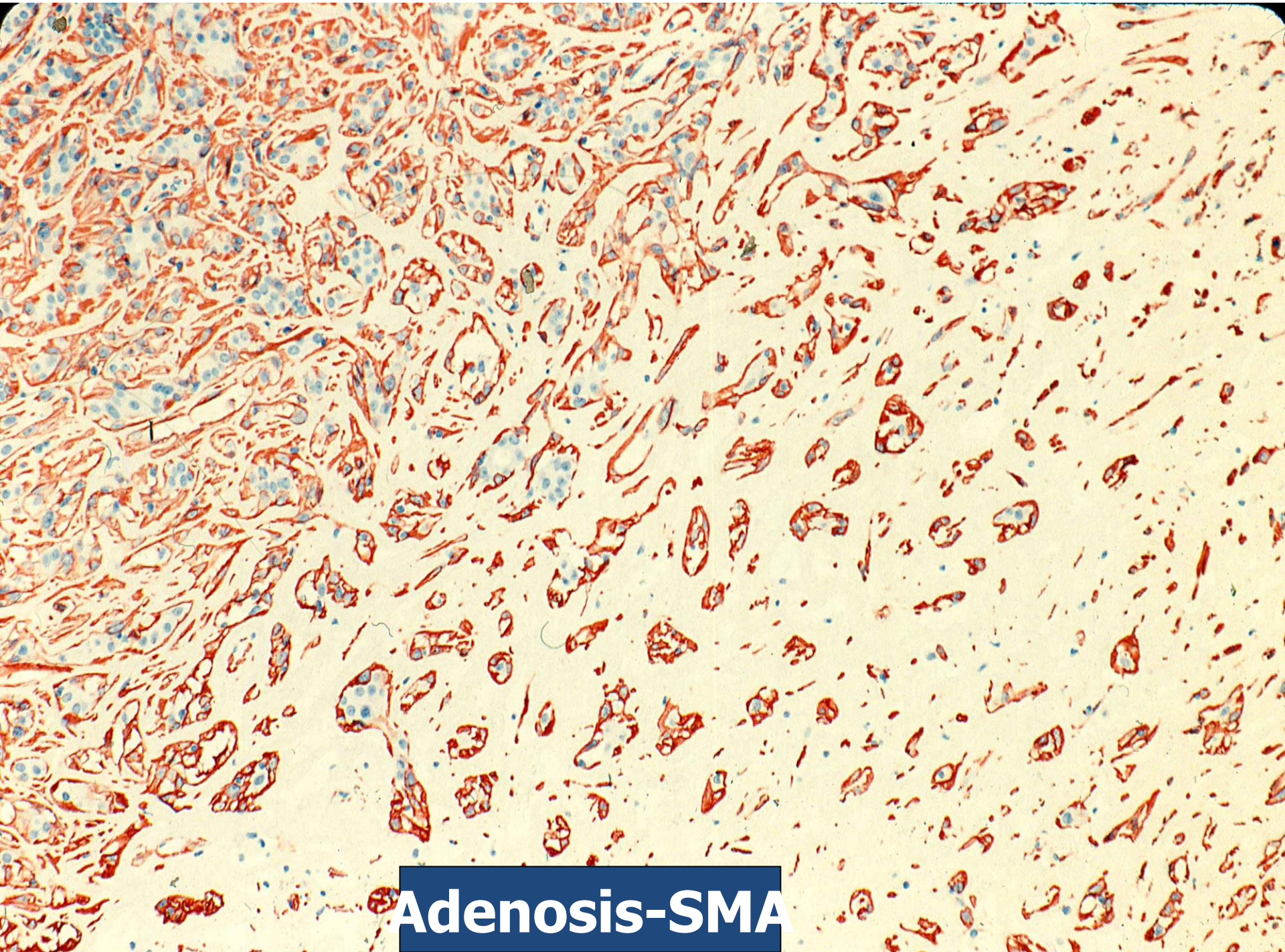
MEC markers

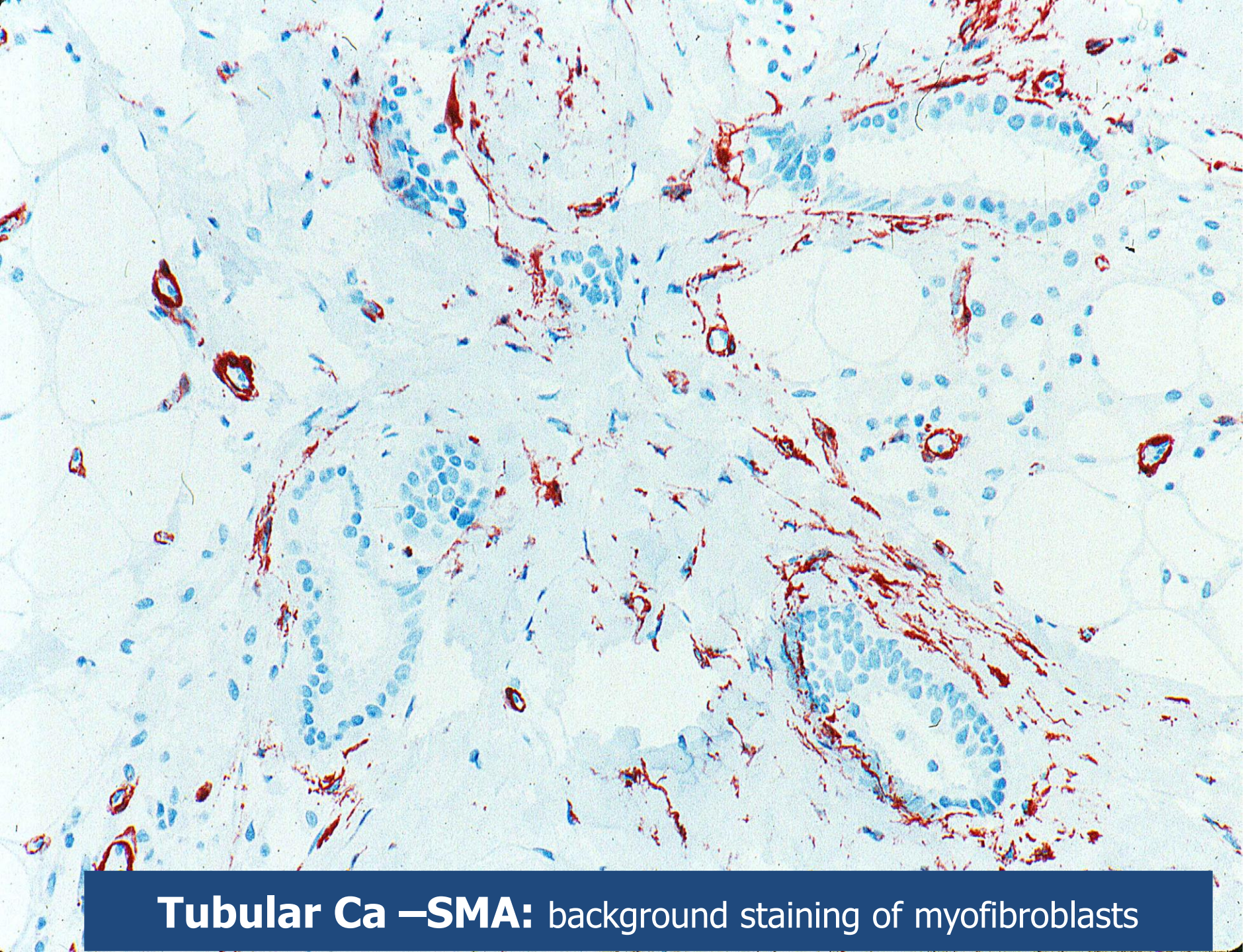
Most commonly used:

- Smooth muscle actin (SMA)
- Smooth muscle myosin heavy chain (SMMHC)
- Calponin
- p63

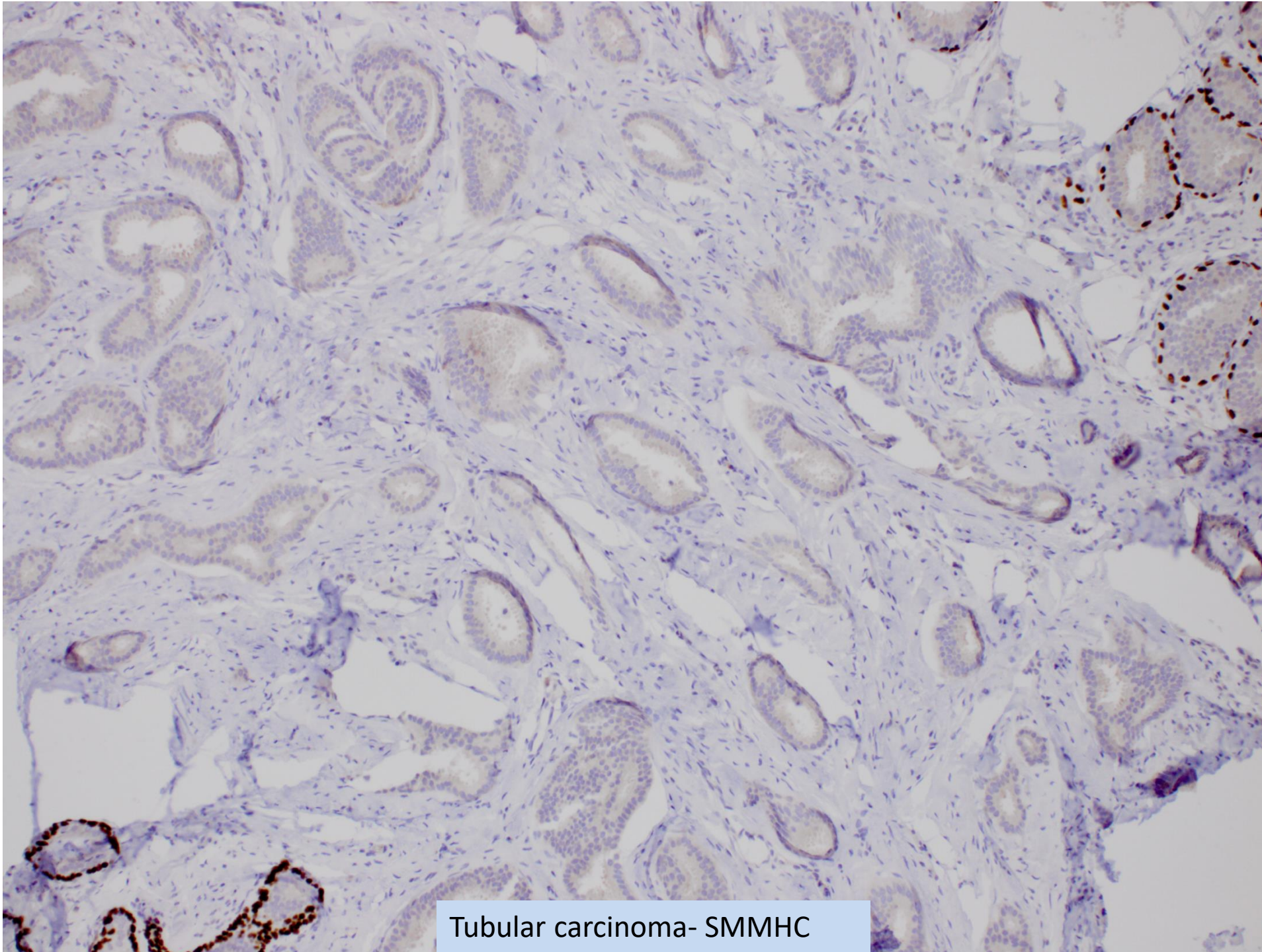
Markers	Localization (staining pattern)	Sensitivity	Myofibroblasts	Vessels
SMA	Cytoplasmic (small arches bulging towards luminal cells)	Most sensitive	Strong	Yes
Calponin		Similar to SMA	Less than SMA	Yes
SMMHC			Less than SMA and calponin	
P63	Nuclear (dotted line)	Slightly less sensitive than SMA	No	No

P63 may stain epithelial cells


Adenosis-SMA

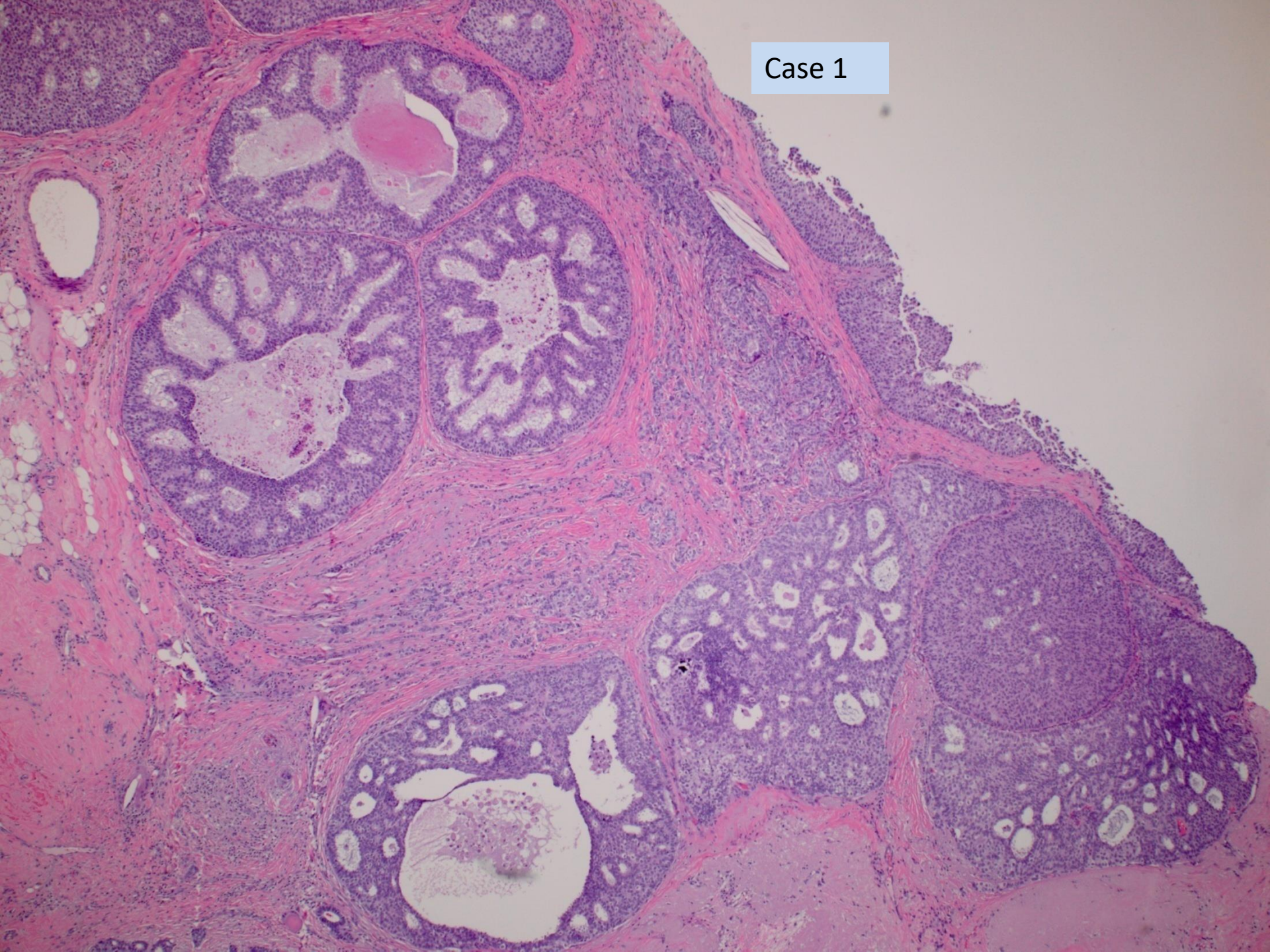


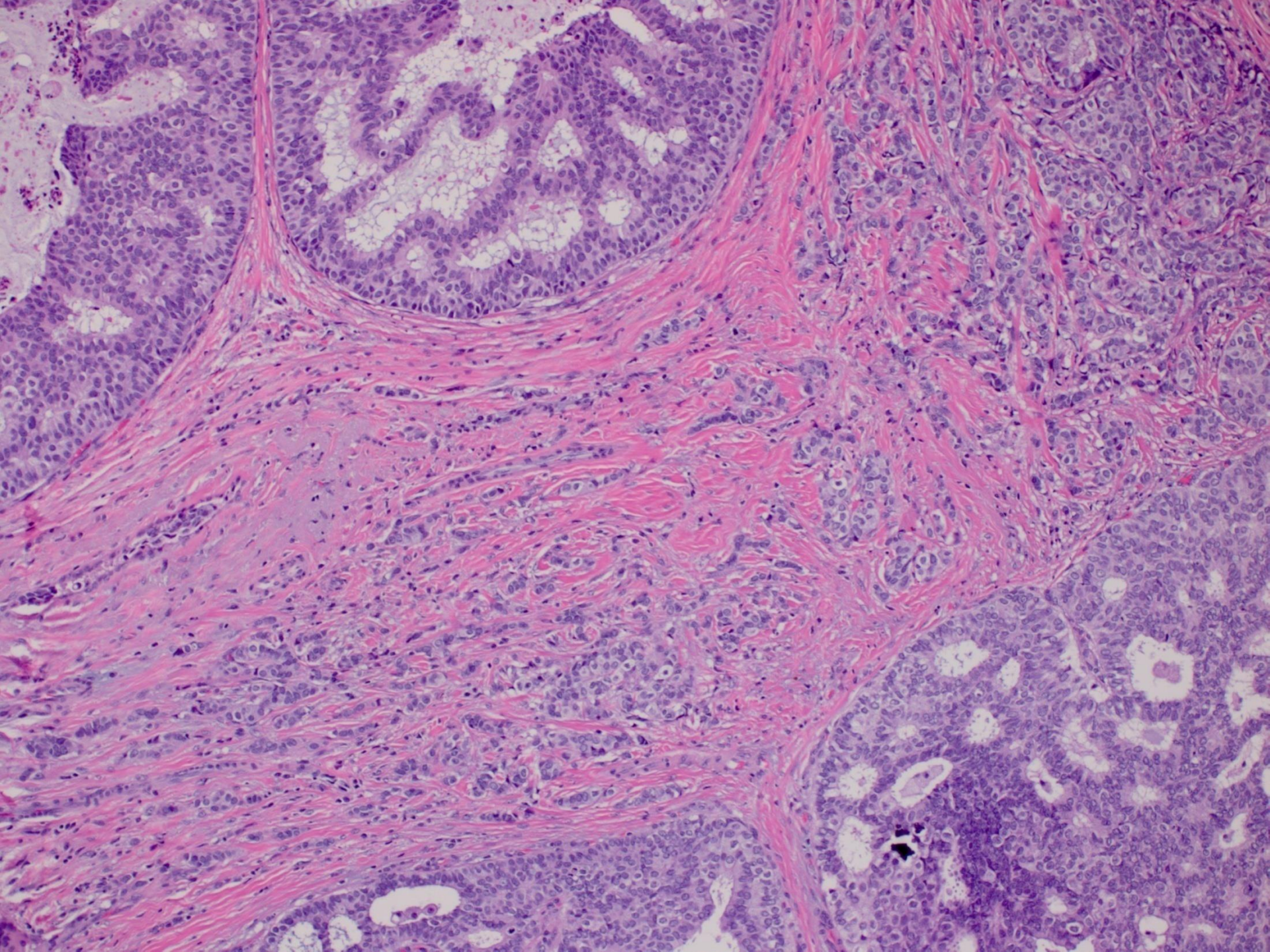
Tubular Ca –SMA: background staining of myofibroblasts

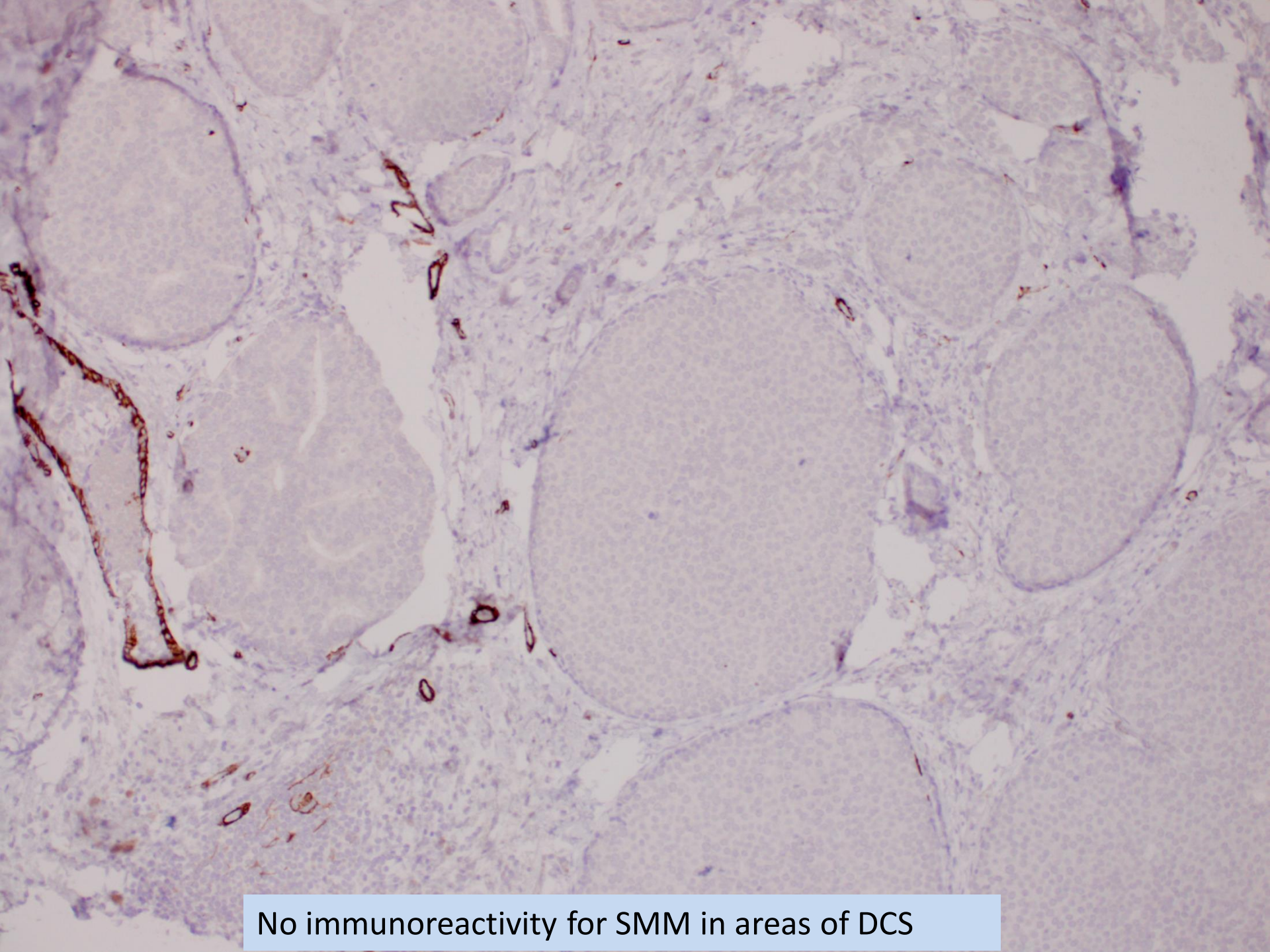

Tubular carcinoma- SMMHC

Myoepithelial Cell Markers

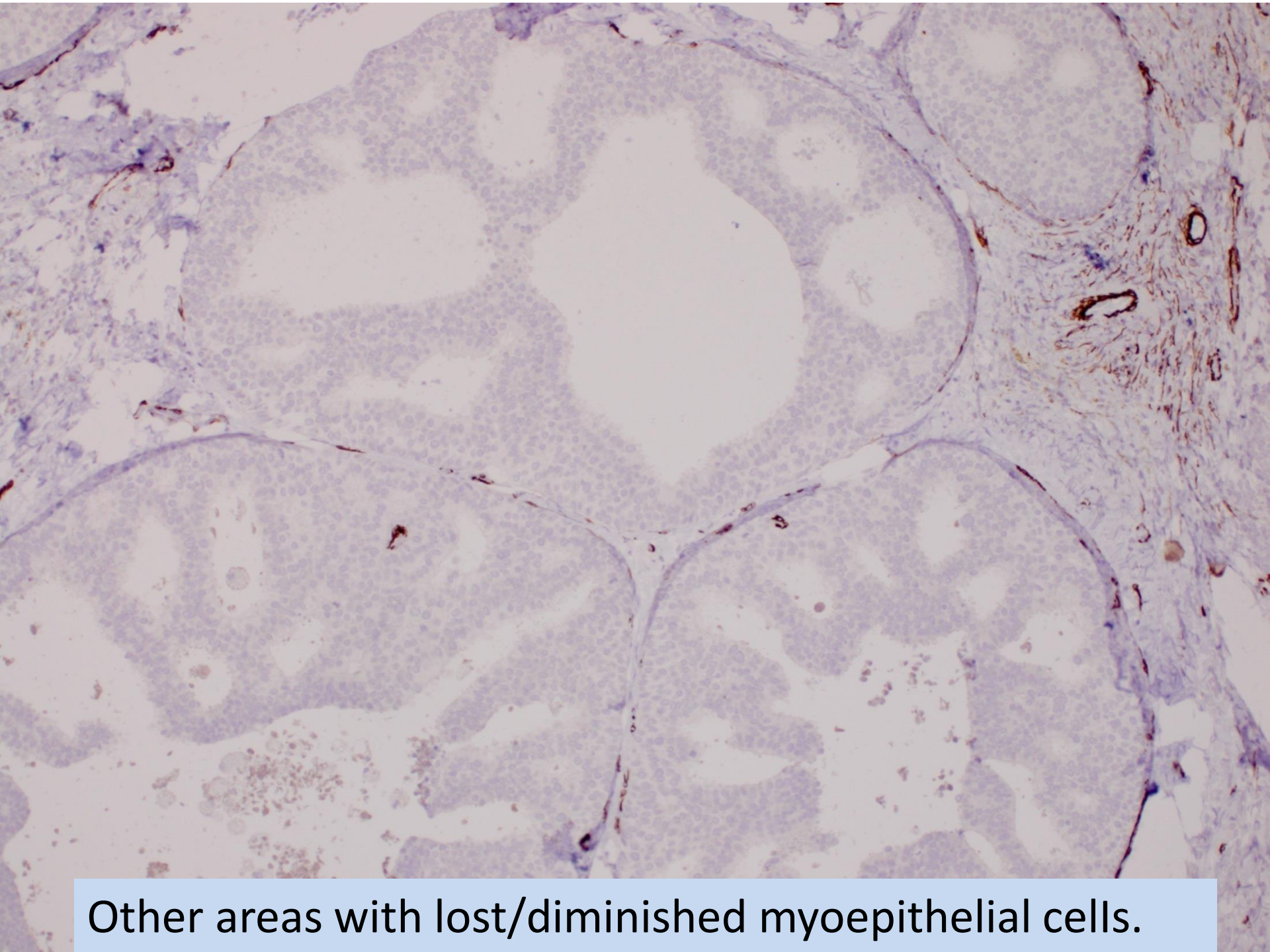
Caveats?


Case 1

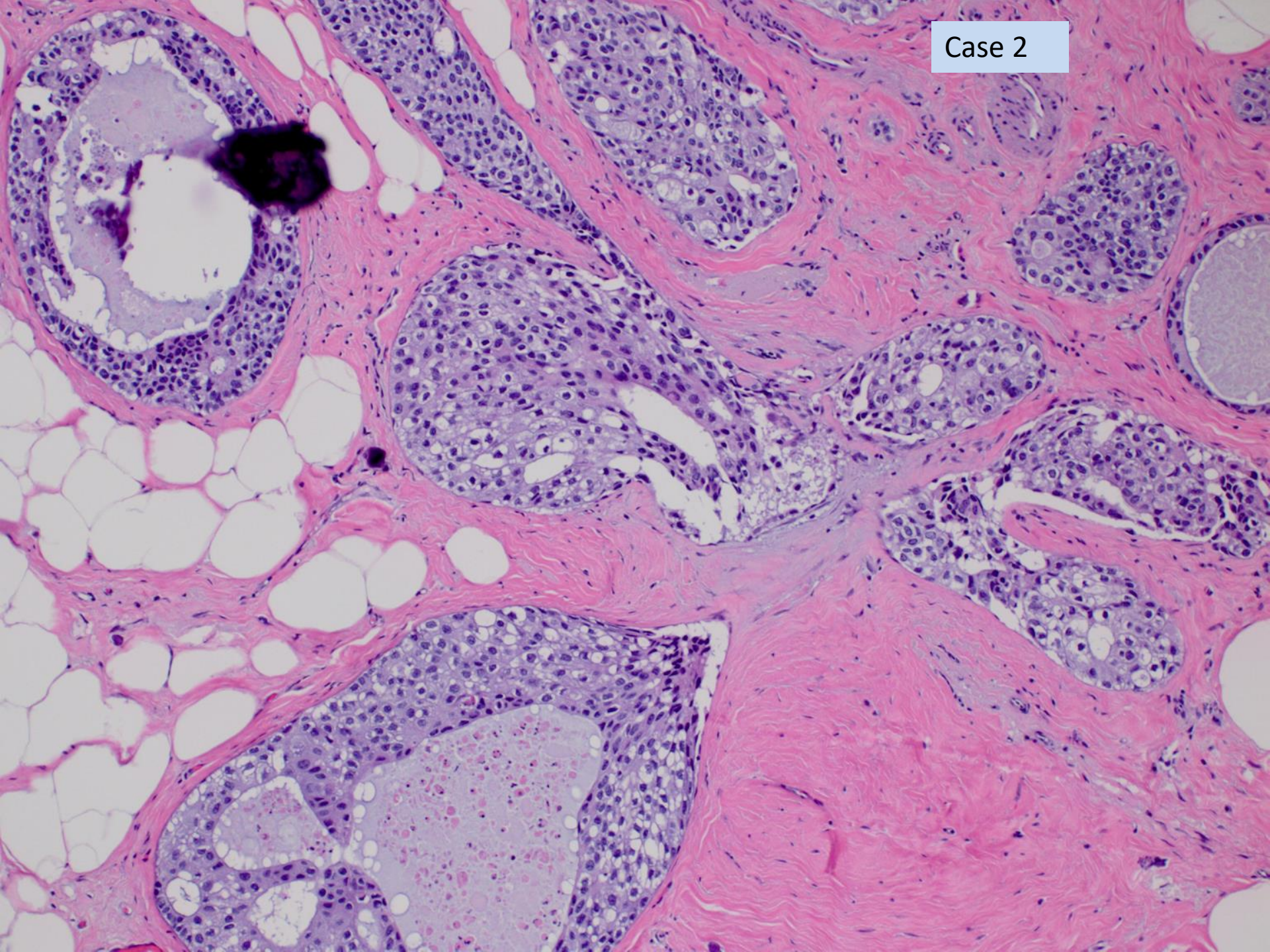


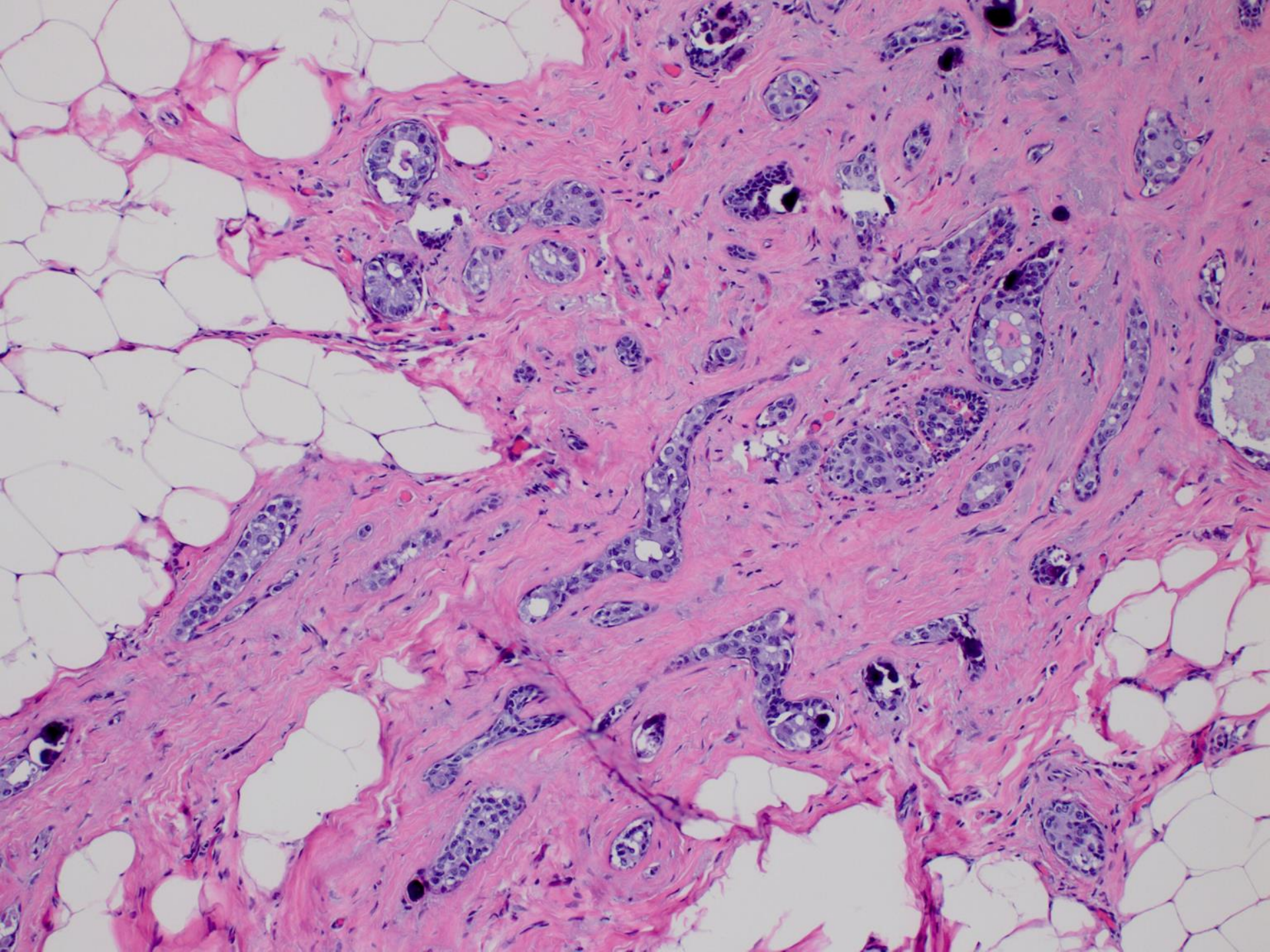


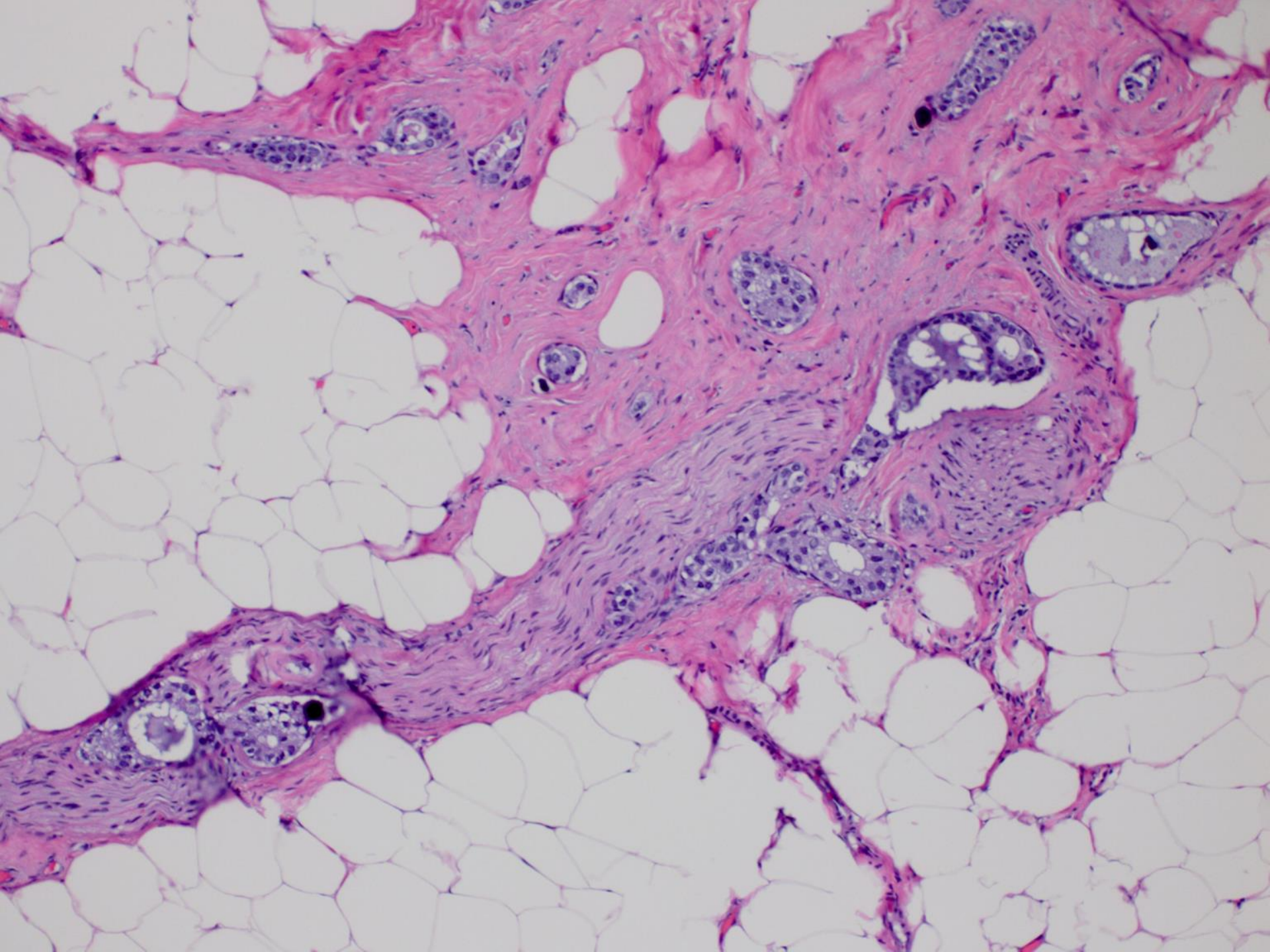
No immunoreactivity for SMM in areas of DCS

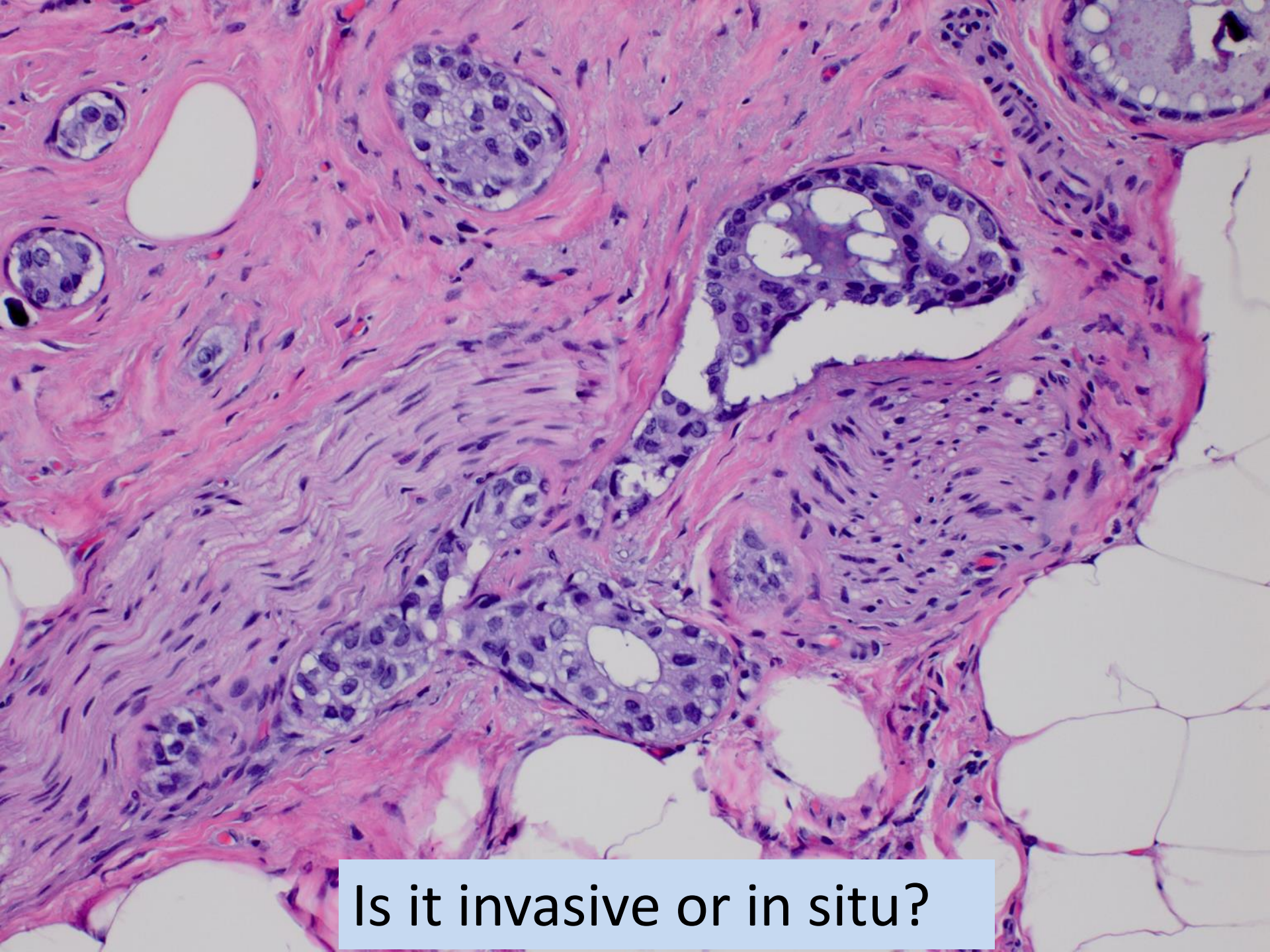


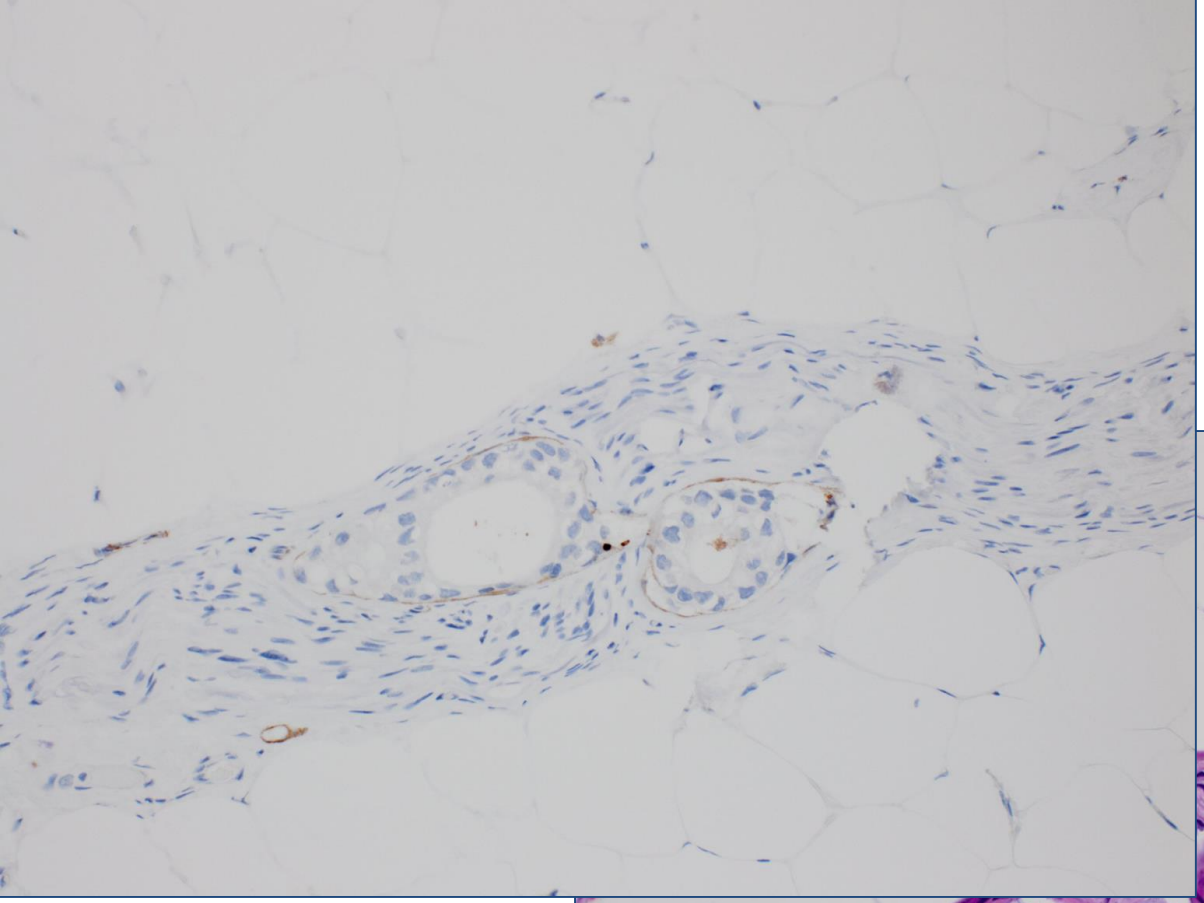
Other areas with lost/diminished myoepithelial cells.

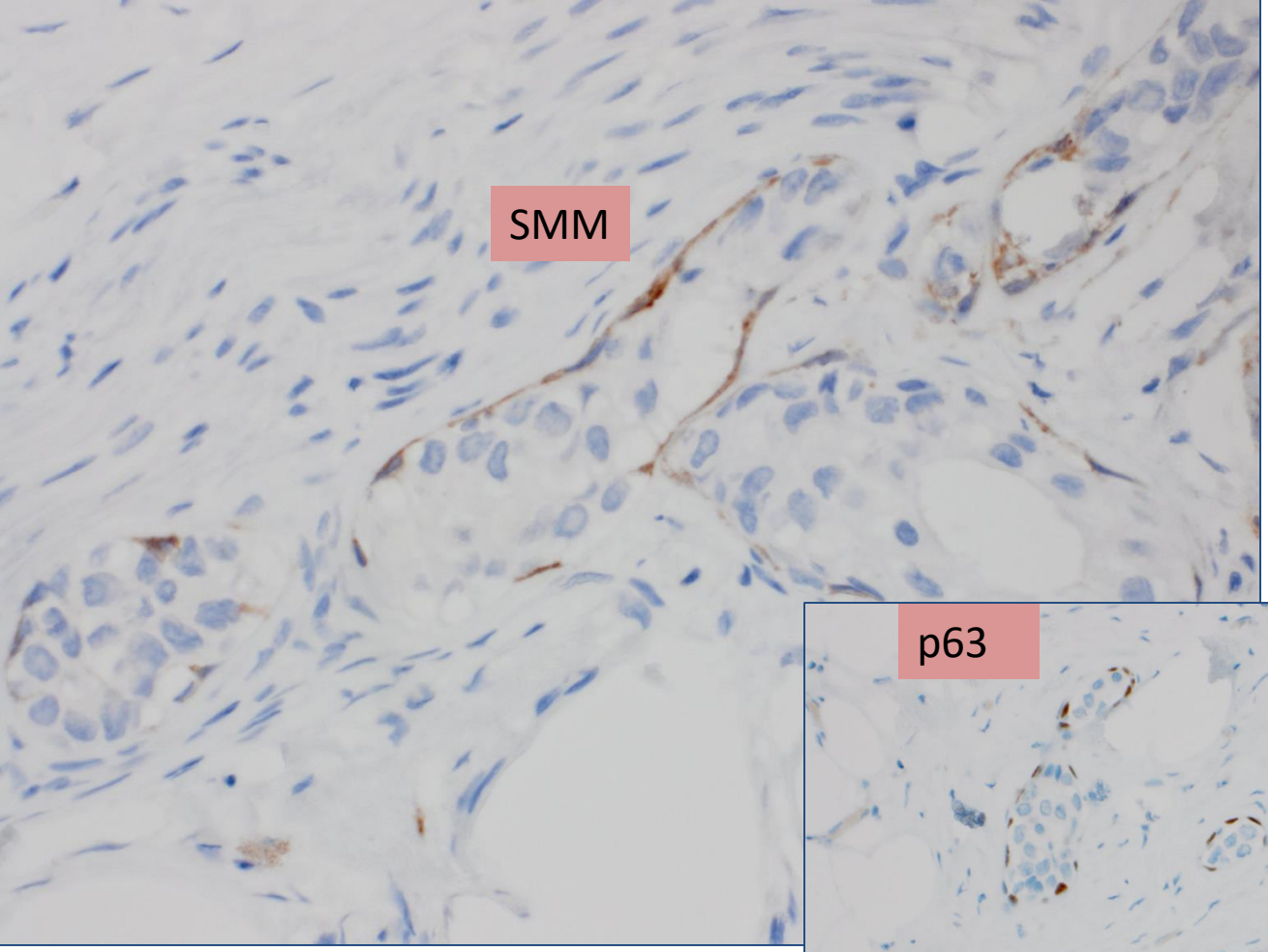

Case 2

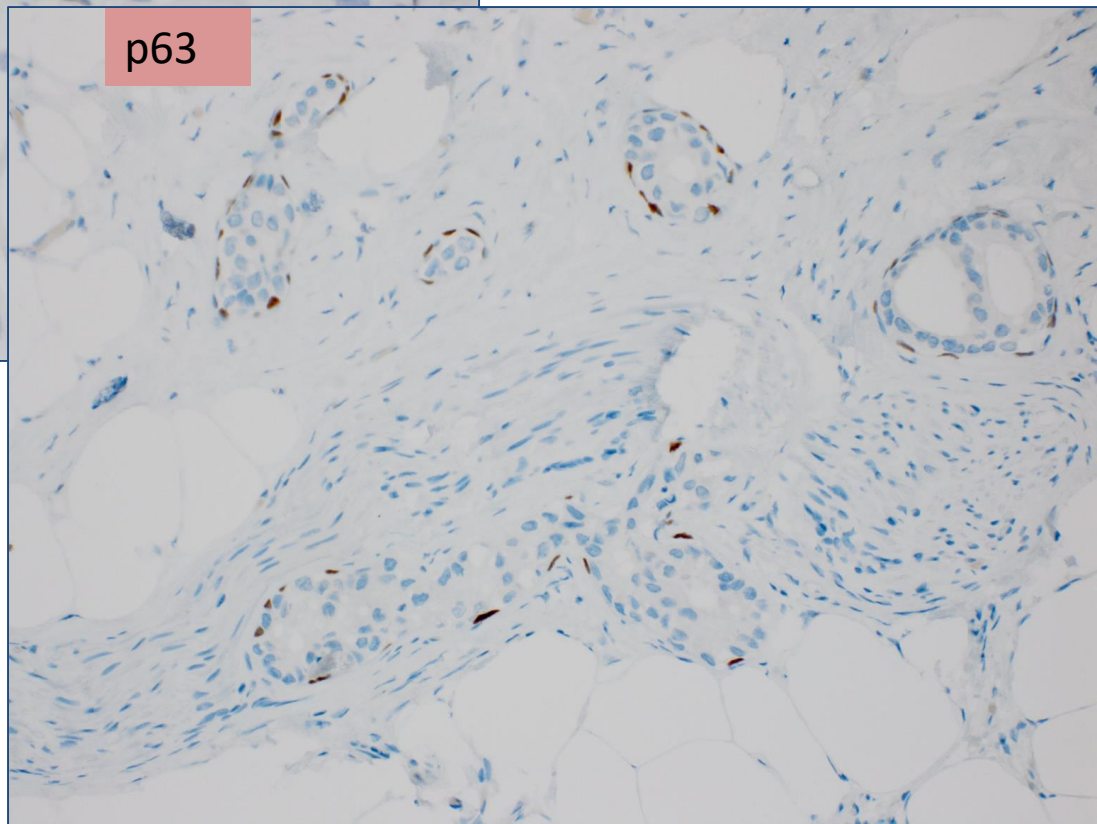


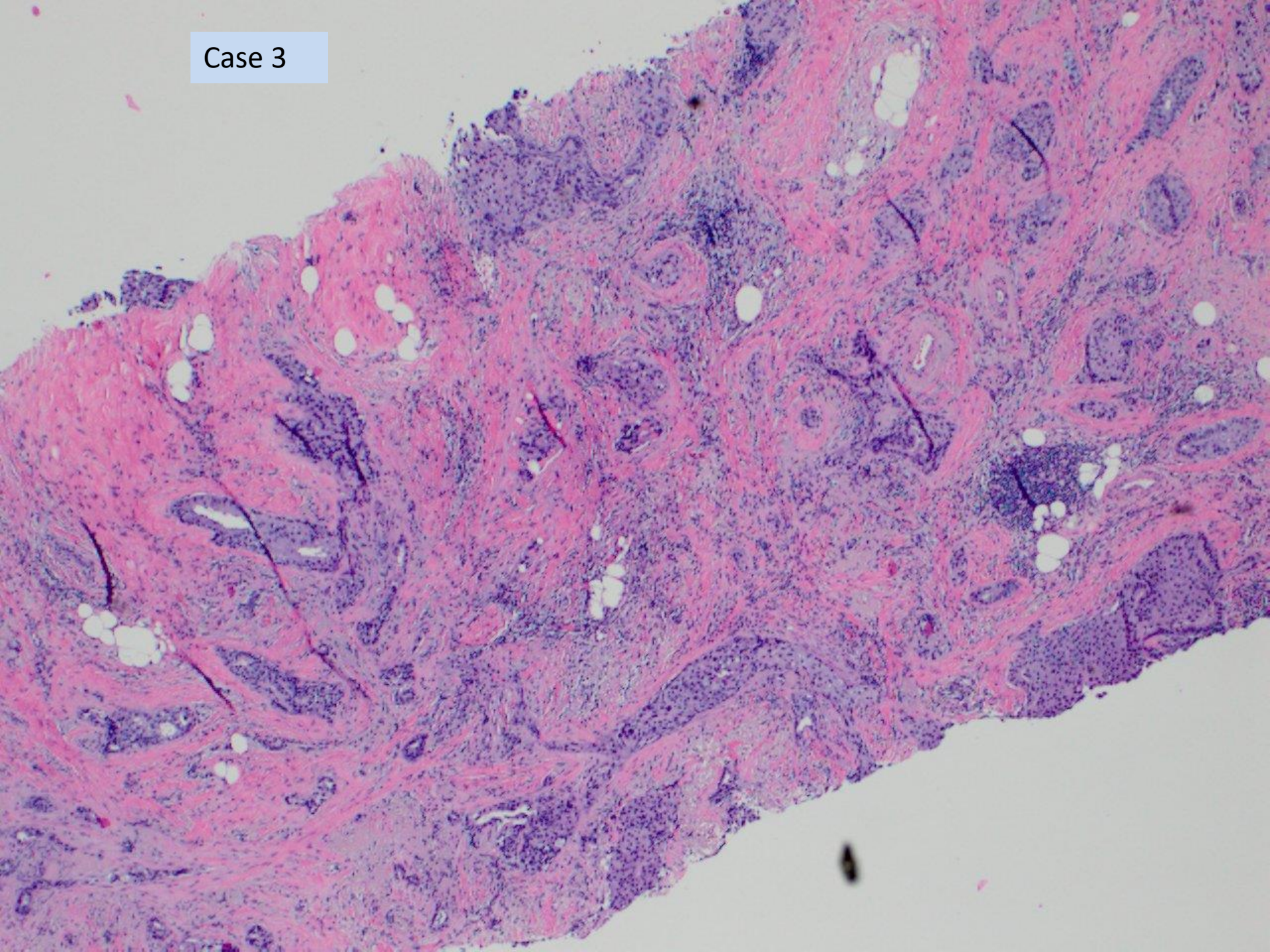


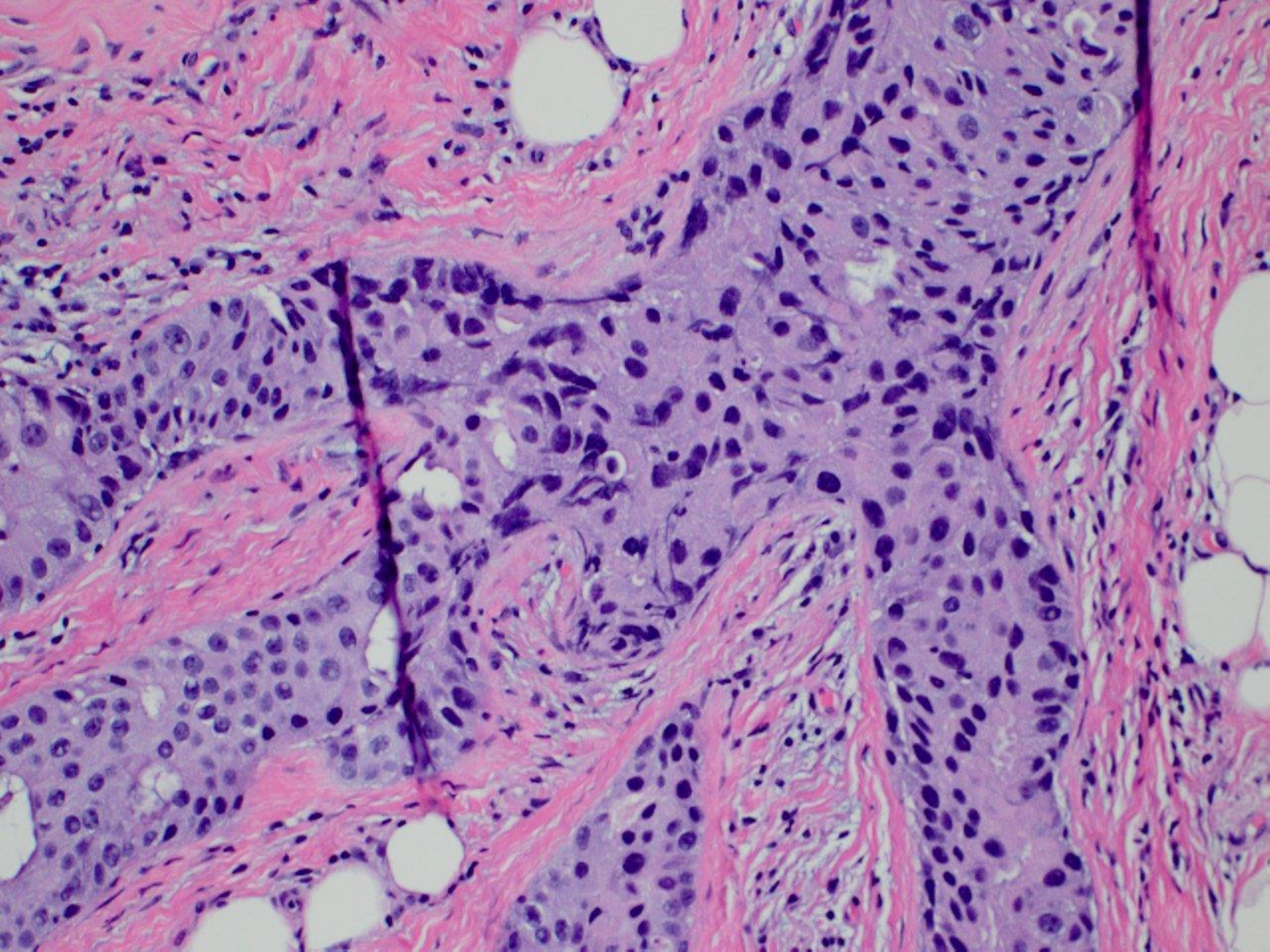

Is it invasive or in situ?

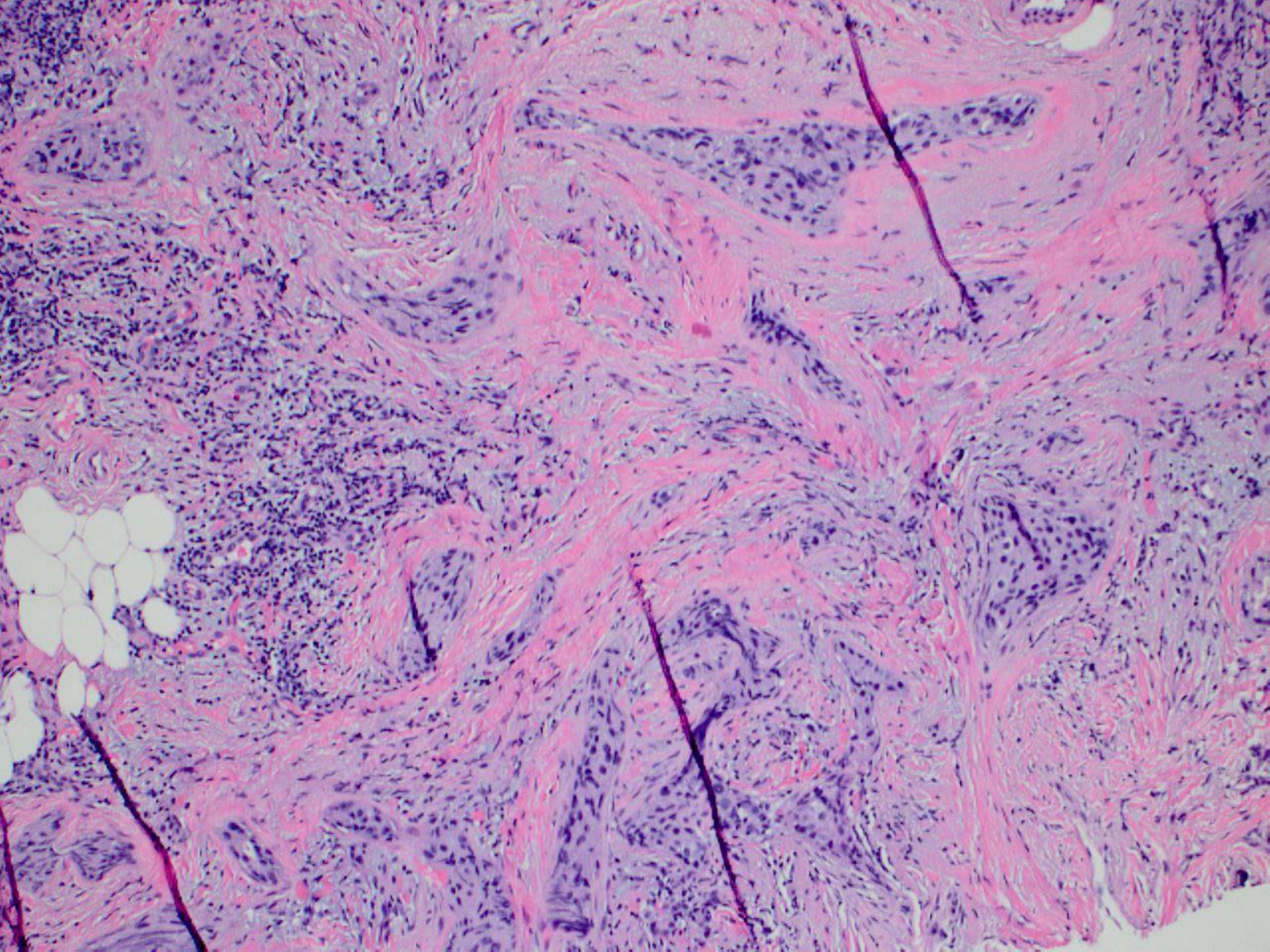


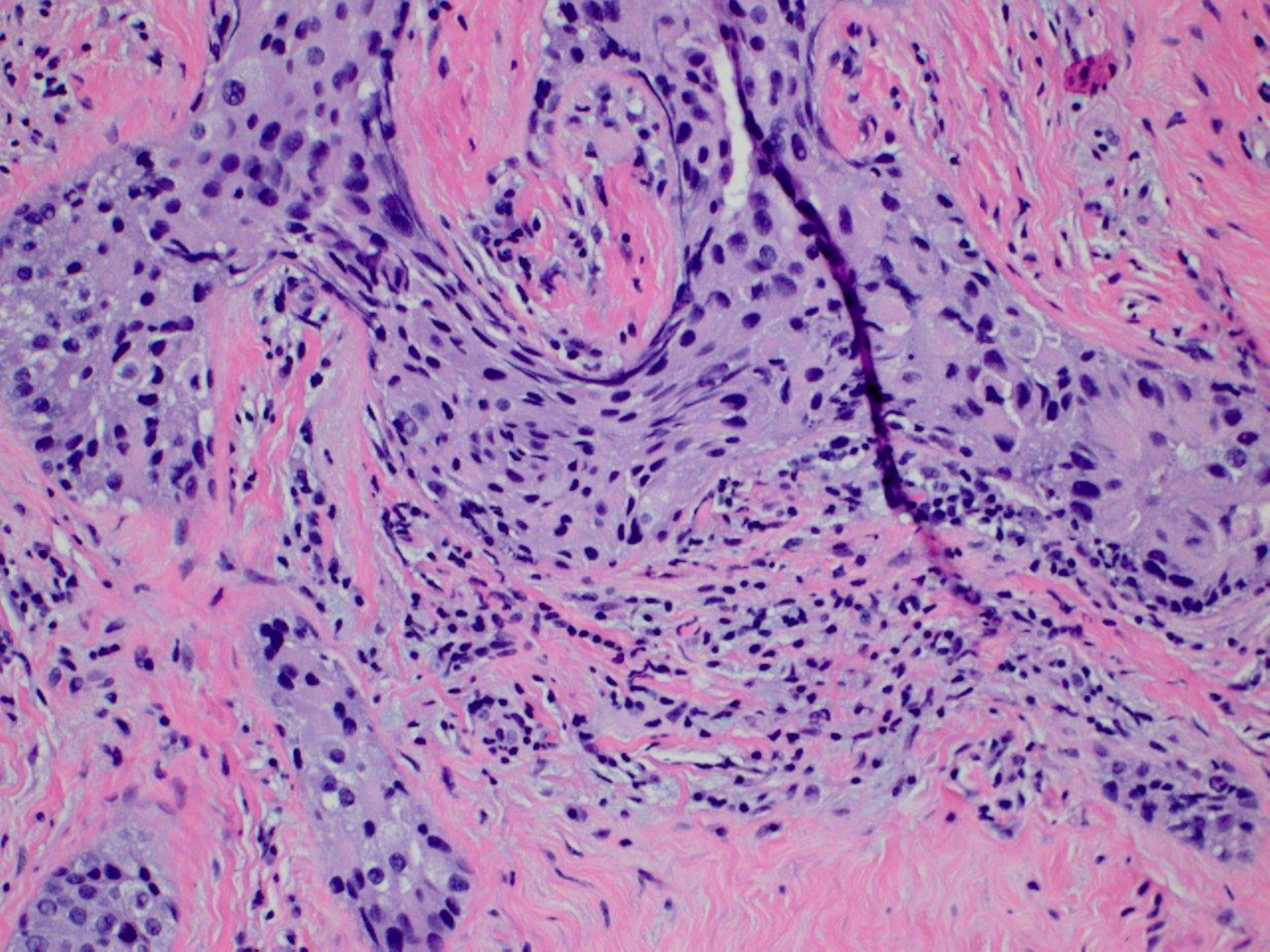

SMM

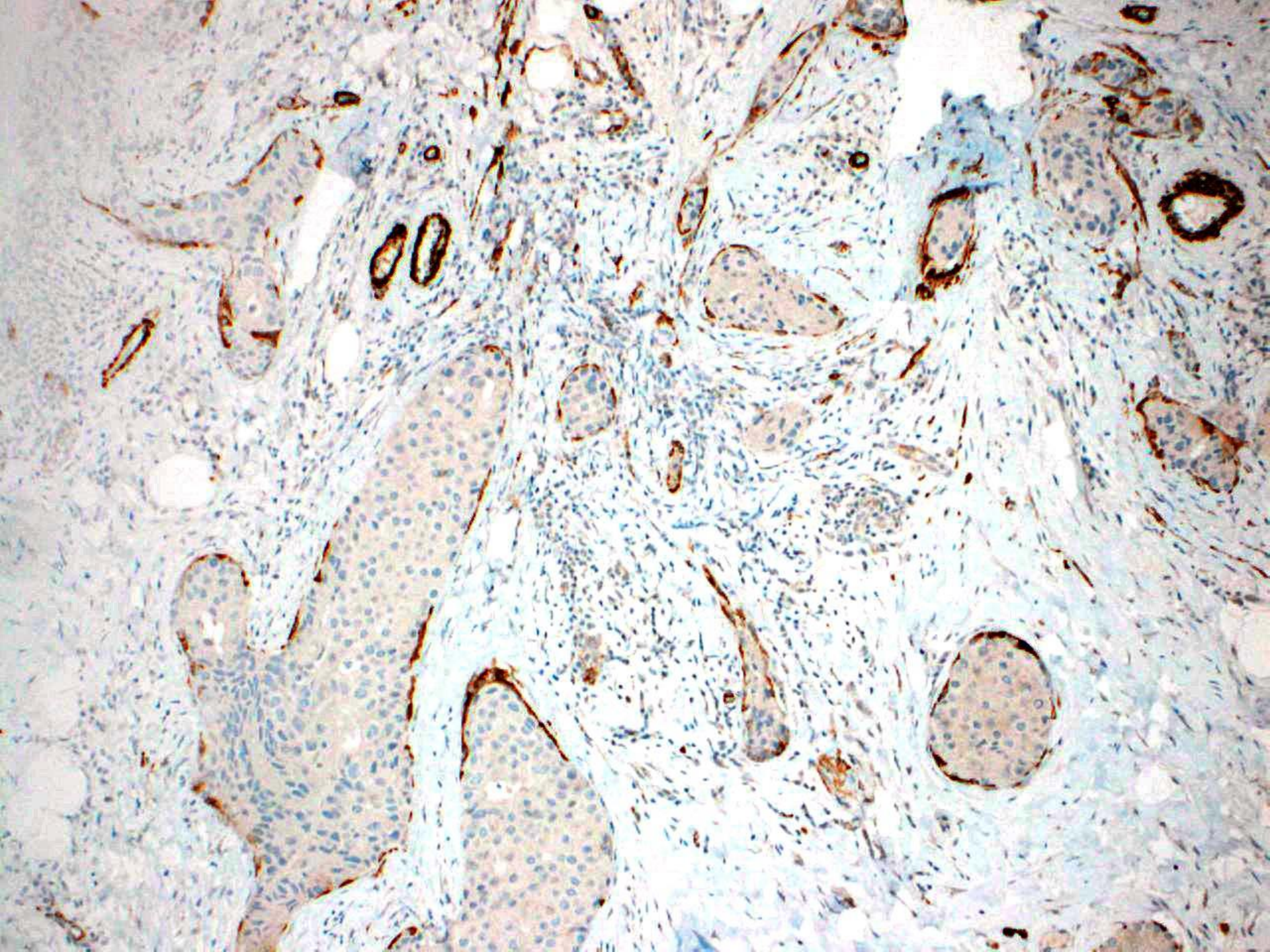

p63

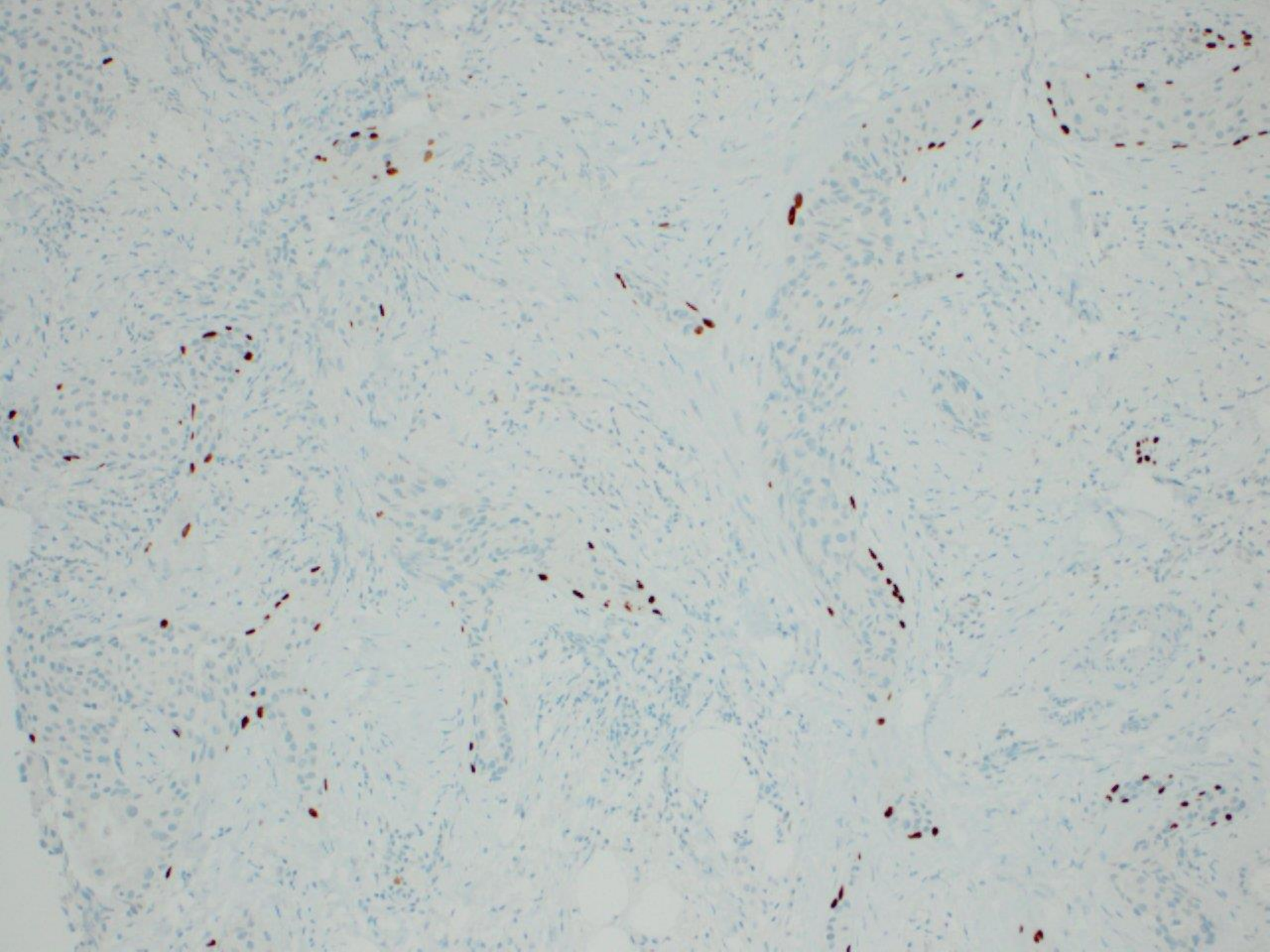

Case 3

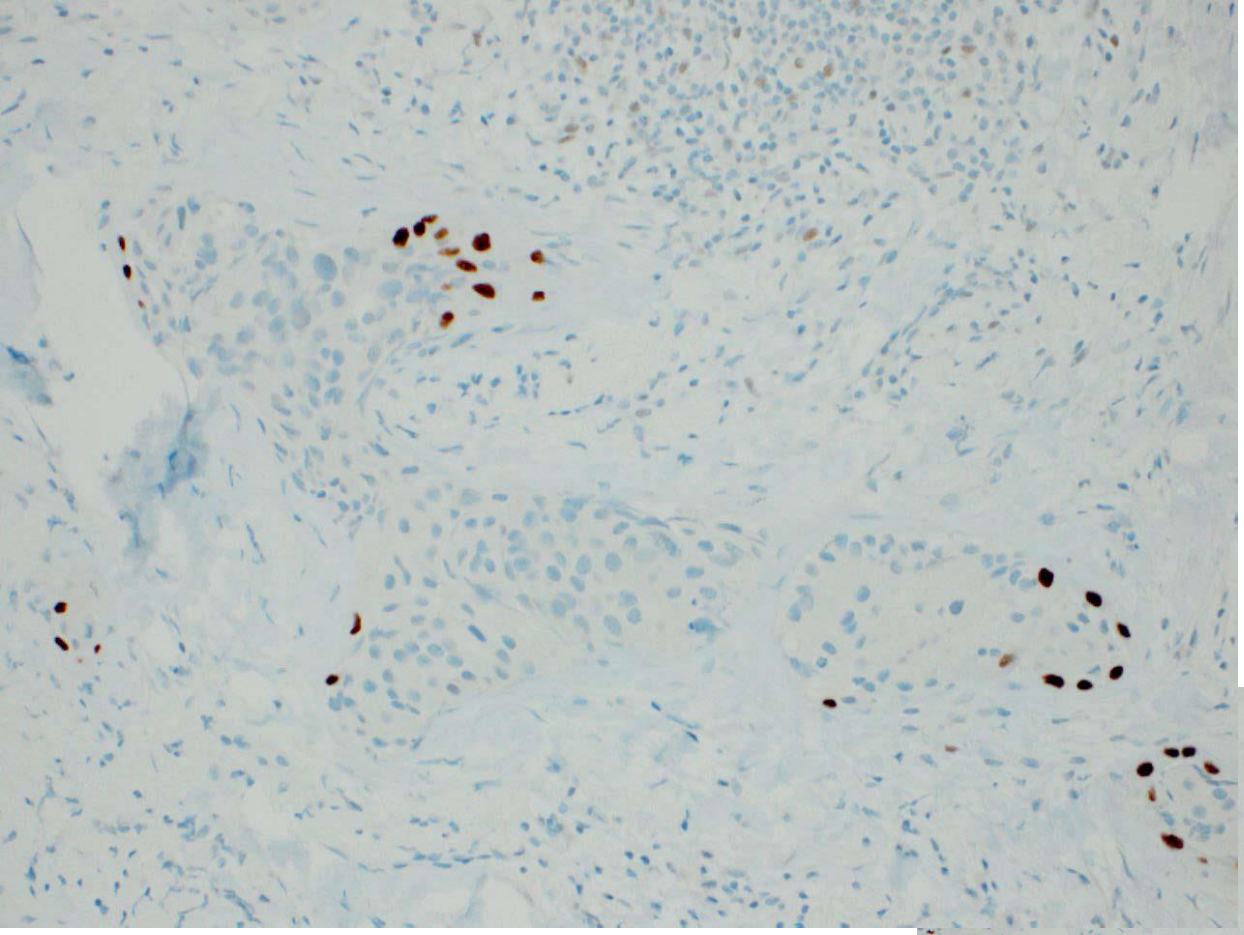


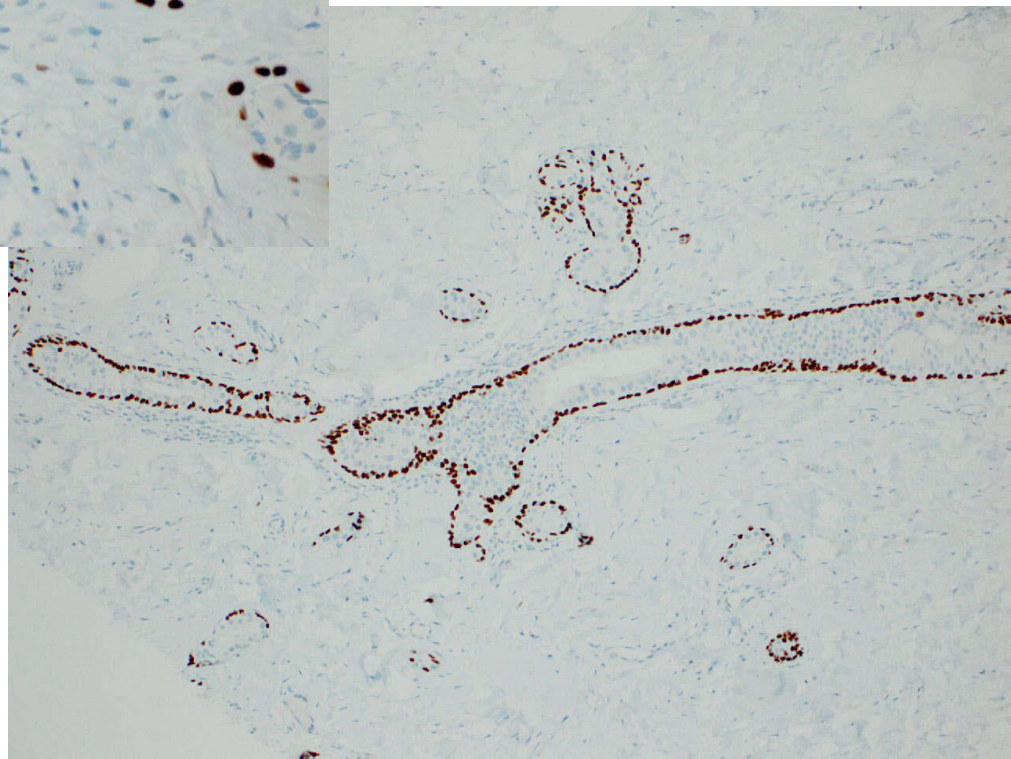






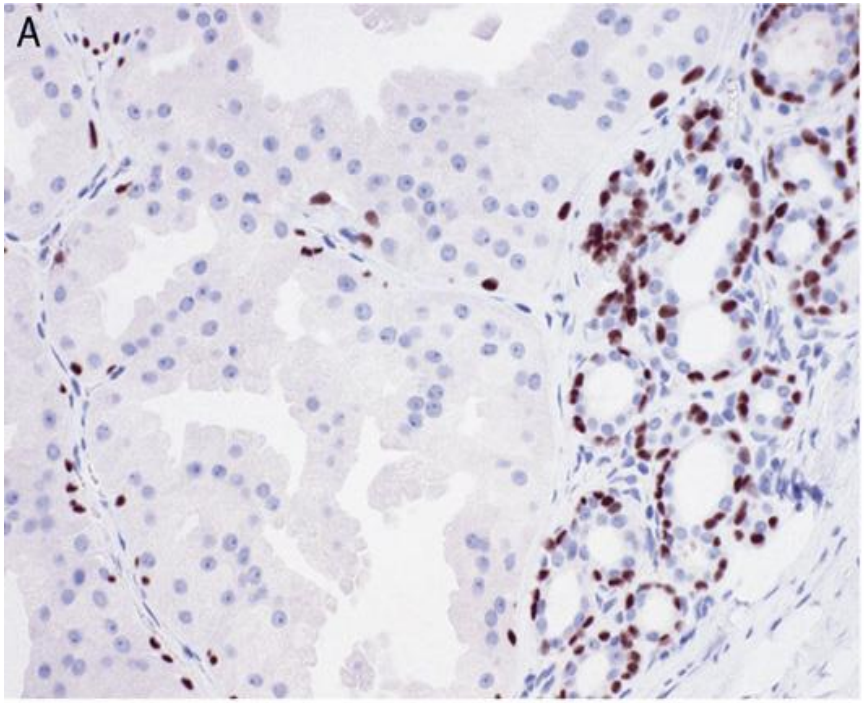




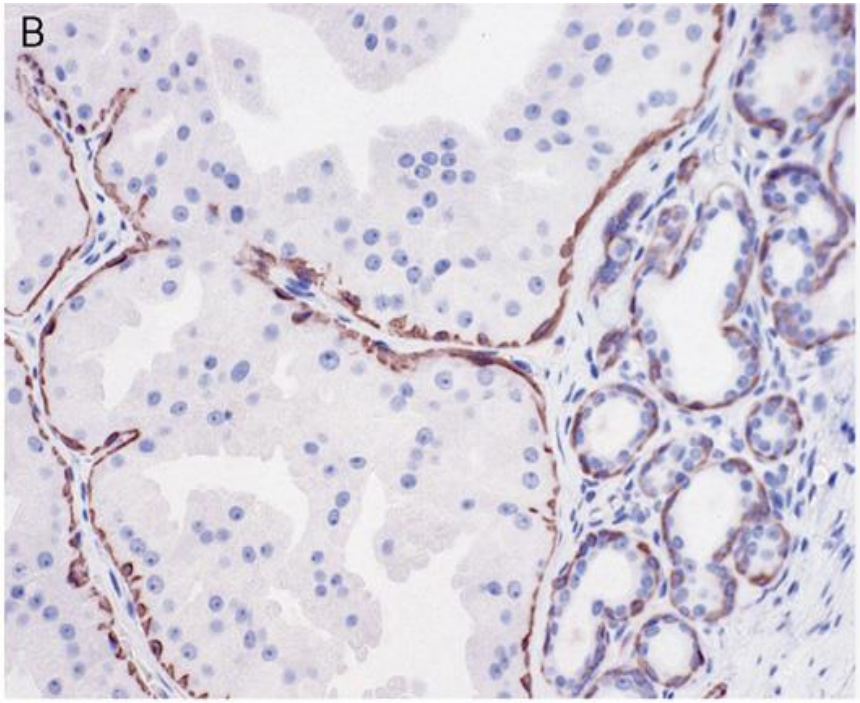


Reduced MECs in DCIS when compared with normal ducts

Diminished Number or Complete Loss of Myoepithelial Cells Associated with Metaplastic and Neoplastic Apocrine Lesions



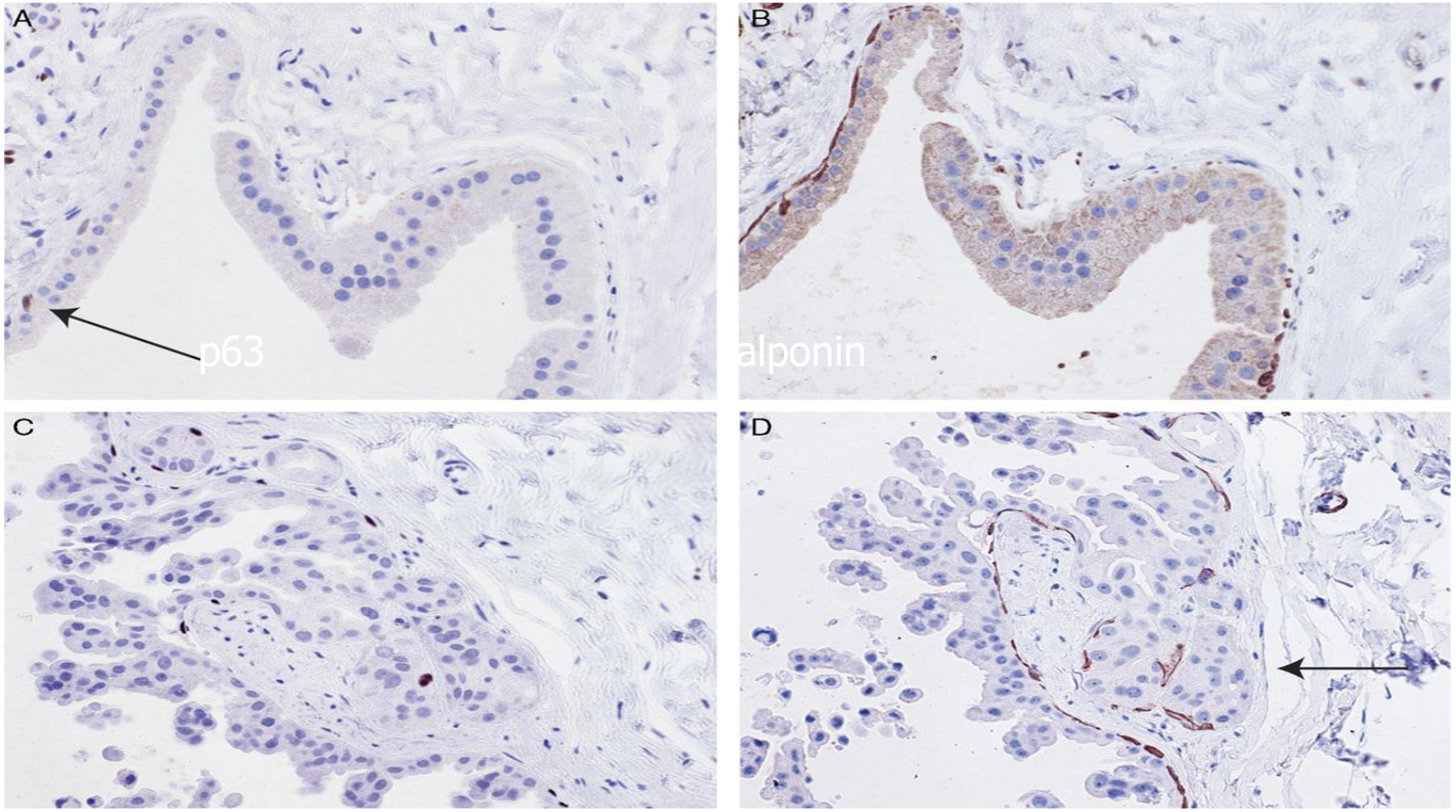
Apocrine proliferation with sparse nuclear p63 compared with the normal glands on the right



The same ducts showing a continuous layer of cytoplasmic positivity with calponin

Tramm, Kim and Tavassoli: Am J Surg Pathol 2011;35;202-211

Diminished Number or Complete Loss of Myoepithelial Cells Associated with Metaplastic and Neoplastic Apocrine Lesions



Tramm, Kim and Tavassoli: Am J Surg Pathol 2011;35;202-211

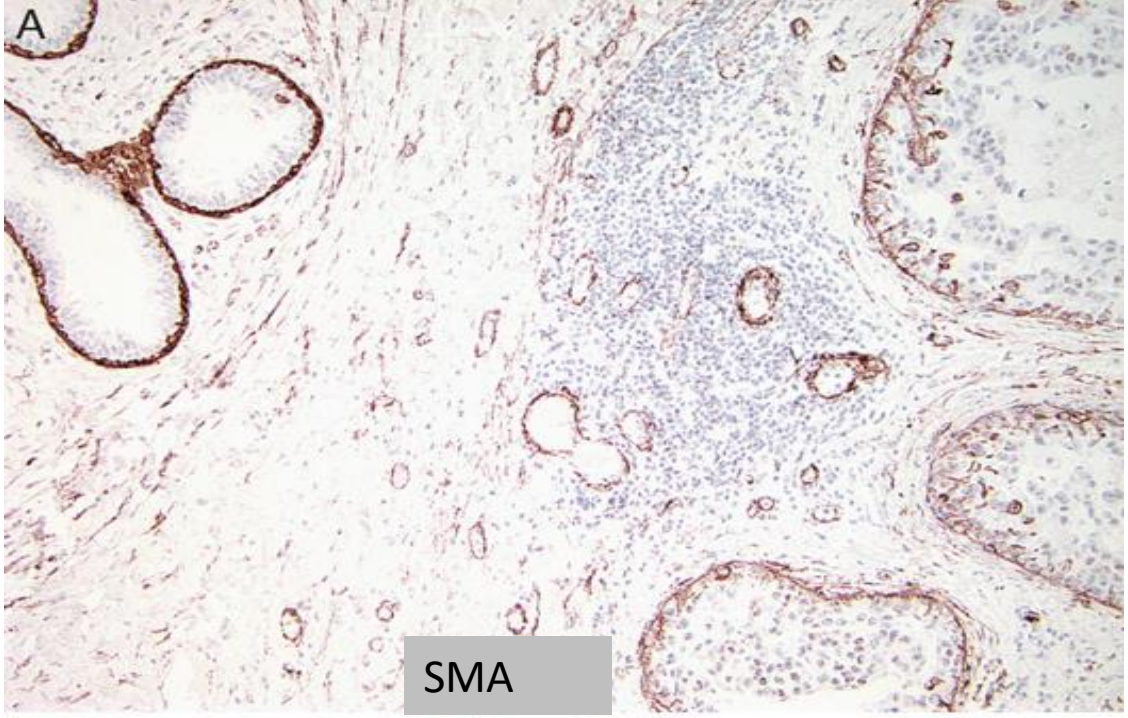
Phenotypic Alterations in DCIS-associated Myoepithelial Cells

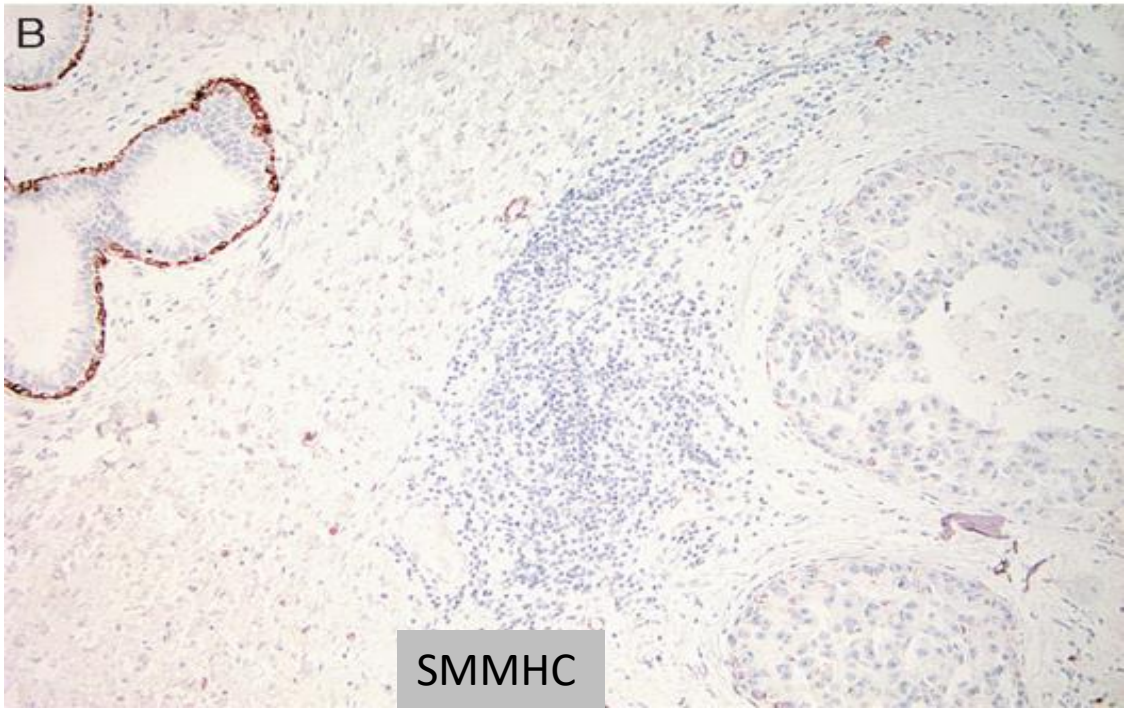
101 cases of DCIS (56 without invasion and 45 with associated inv ca) immunostained for 7 MEC markers: SMA, SMMHC, calponin, p63, CK5/6, CD10 and p75.

DCIS associated MECs showed **decreased expression** (when compared with normal MECs): 76.5% for SMMHC, 34% for CD10, 30% for CK5/6, 17% for calponin, 12.6% for p63, 4% for p75, and 1% for SMA.

Reduced MEC expression of SMMHC more frequent in HG than in non-HG DCIS (84.8% vs 61.5%) and completely absent in 54.7%.

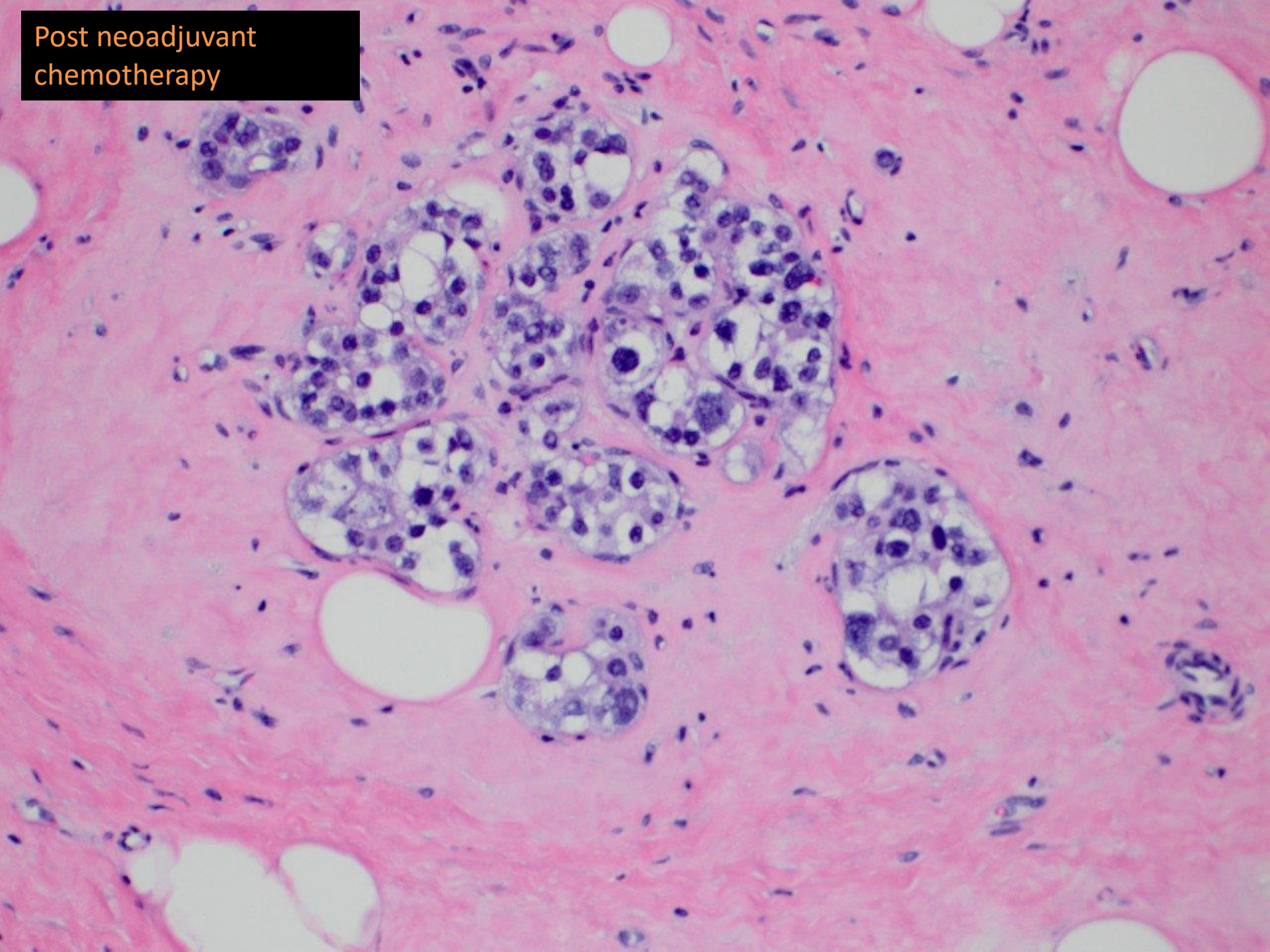
Hilson, Schnitt, and Collins: Am j Surg Pathol 2009;33:227-232

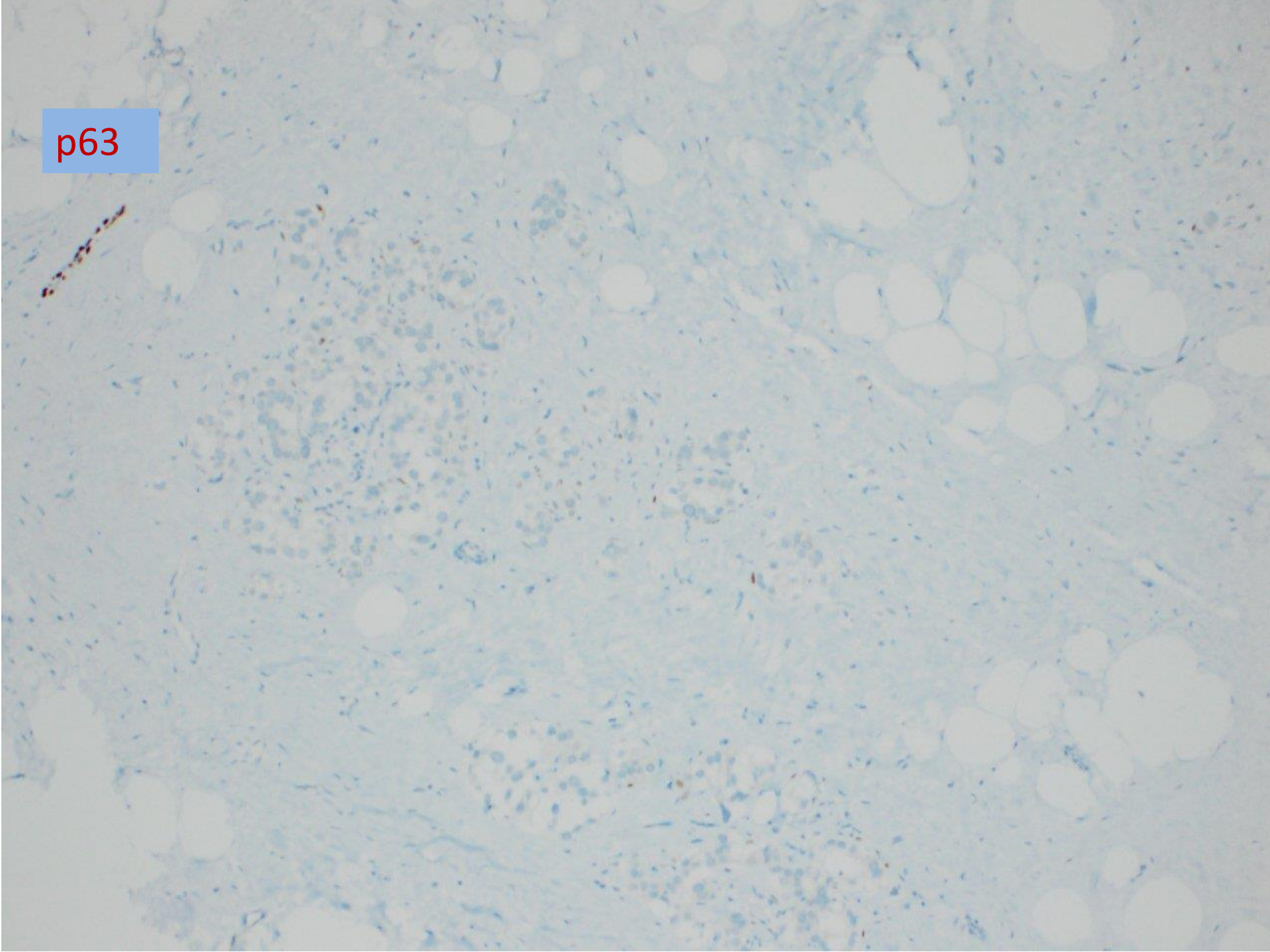


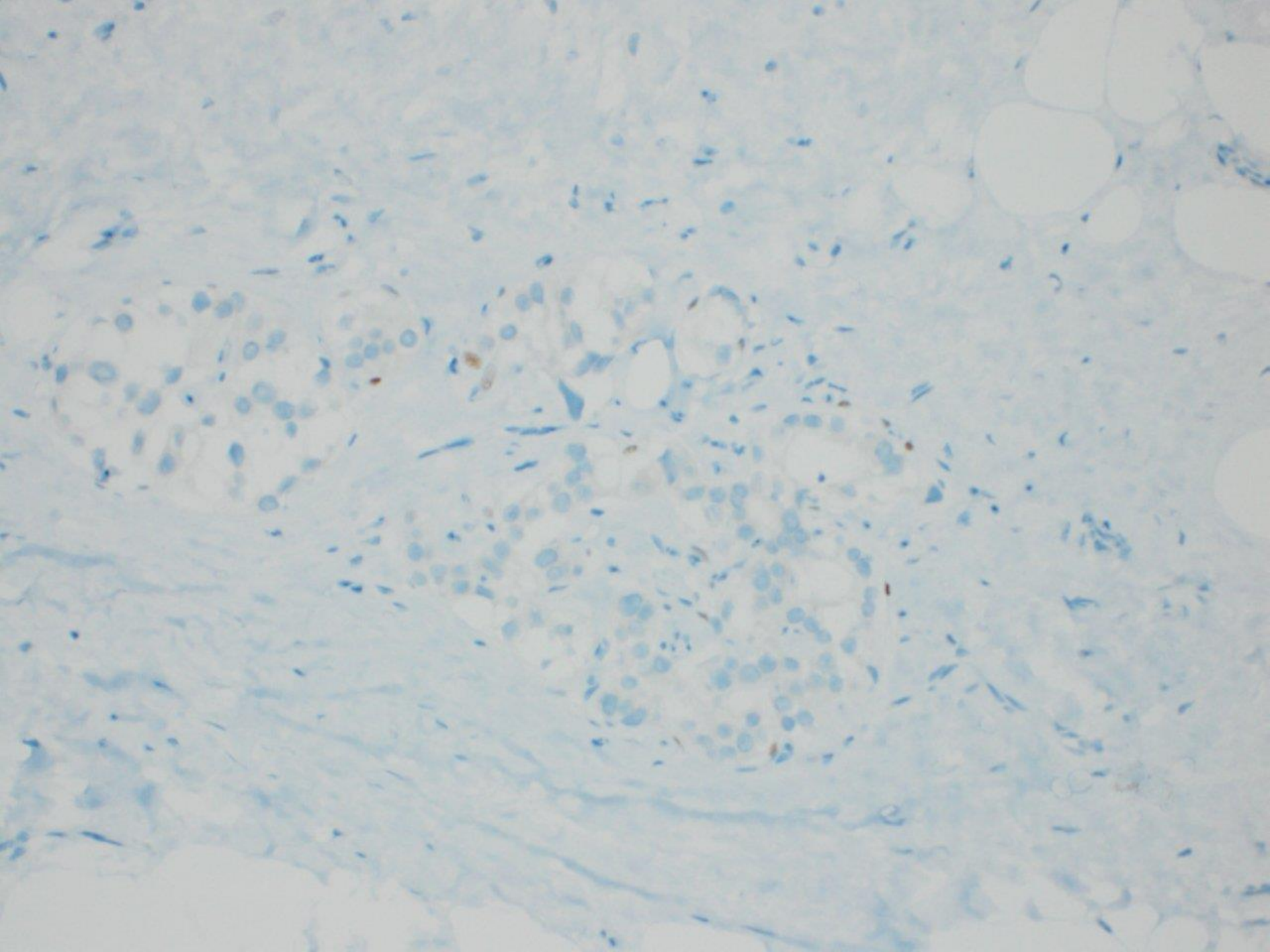


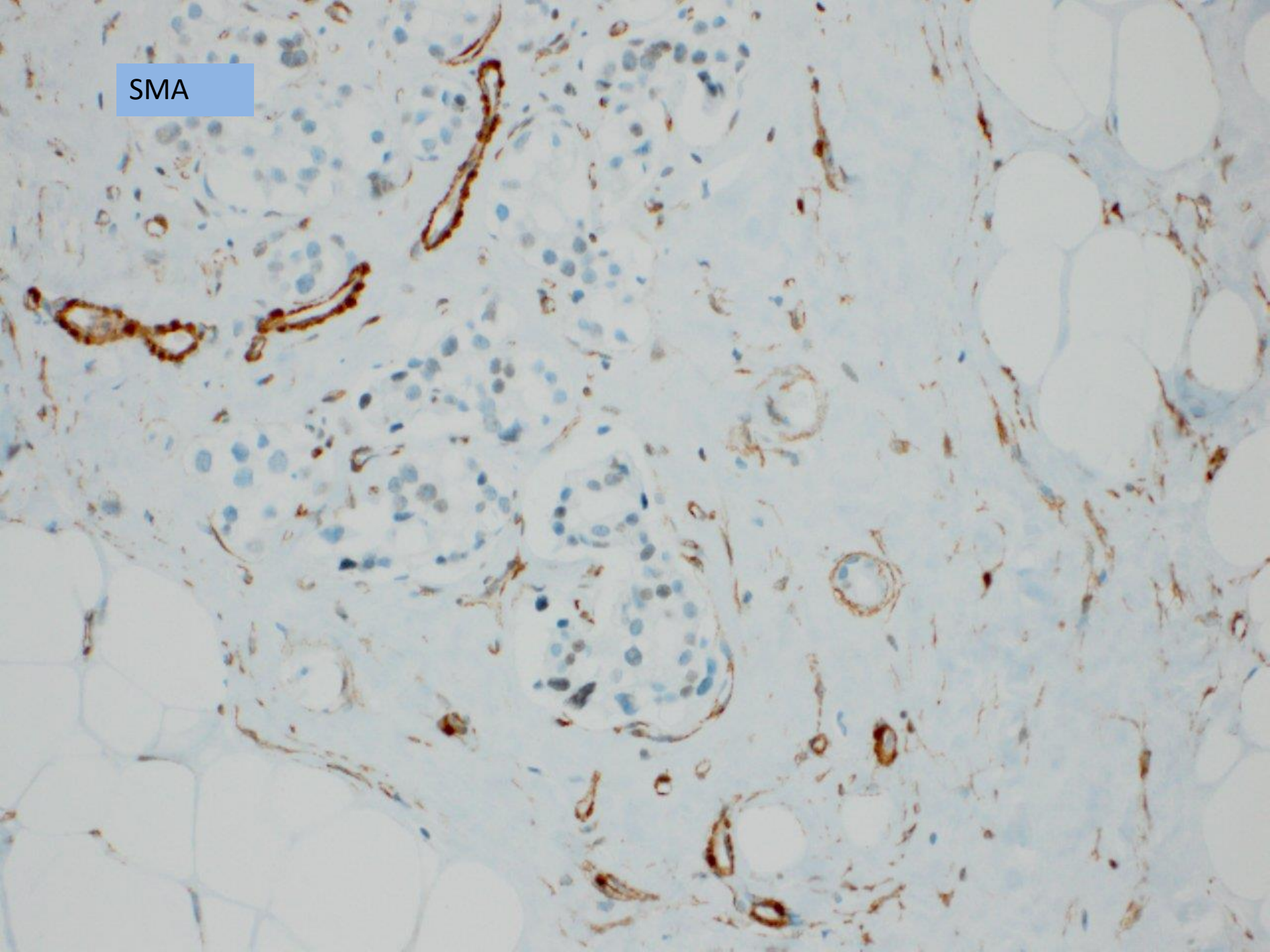
DCIS immunostained for SMA (A) and SMMHC (B)

Hilson et al. Am J Surg Pathol 33, 227-232, 2009


Post neoadjuvant
chemotherapy


p63




SMA

Phenotypic Alterations in Myoepithelial Cells Associated with Benign Sclerosing Lesions of the Breast

48 BSL were evaluated using 7 myoepithelial markers.

- MEC associated with BSL showed **reduced expression** of CK5/6 (31.8%), SMMHC (20.9%), CD10 (15%), p63 (9%) and calponin (6.4%)
- In 15.9% of cases, **complete absence of staining for CK 5/6**. None of the cases showed reduced expression for SMA or p75.

- The proportion of radial scars/complex sclerosing lesions and sclerosing adenosis with reduced expression was significantly different for CD10 (26.9% vs 0%), and p63

(17.4% and 0%).

Conclusion: myoepithelial cells associated with BSL may show immunophenotypic differences from normal myoepithelial cells.

Hilson, Schnitt and Collins: Am J Surg Pathol 2010;34:896-900

Benign Sclerosing lesion on CNB, negative for SMA/p63

Sclerosing lesion, favor benign/indeterminate

Recommend excision for a definitive Dx

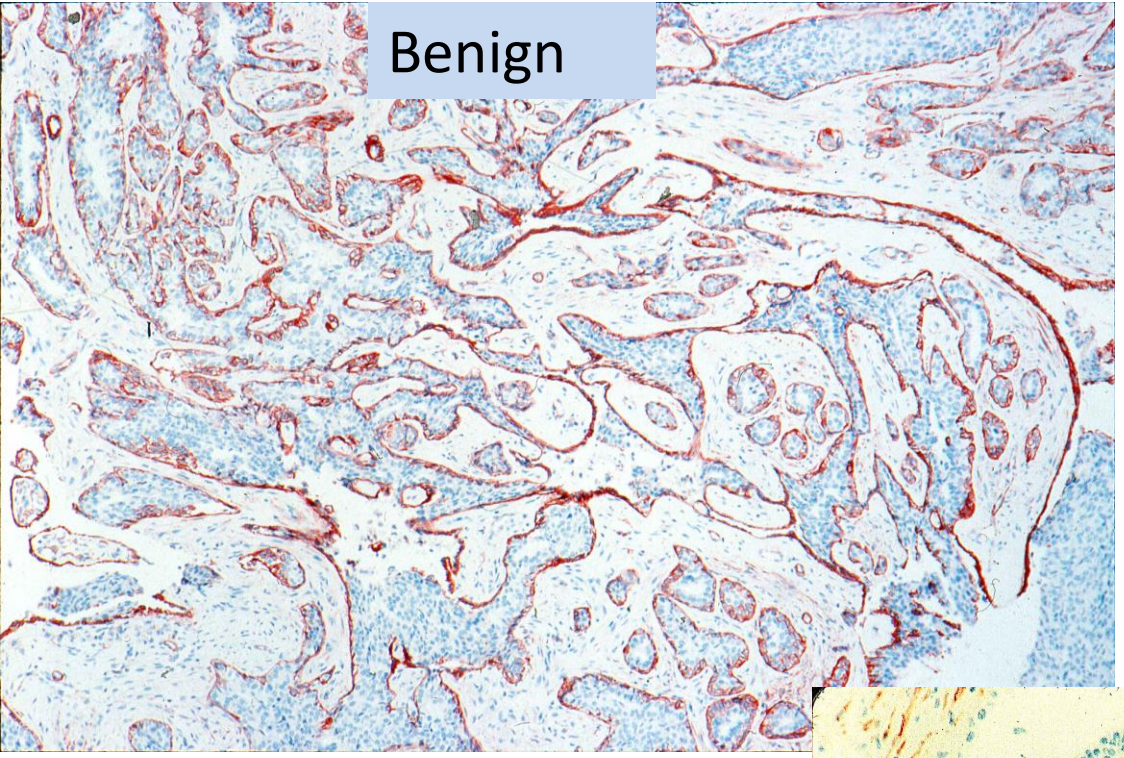
Myoepithelial Cell Markers

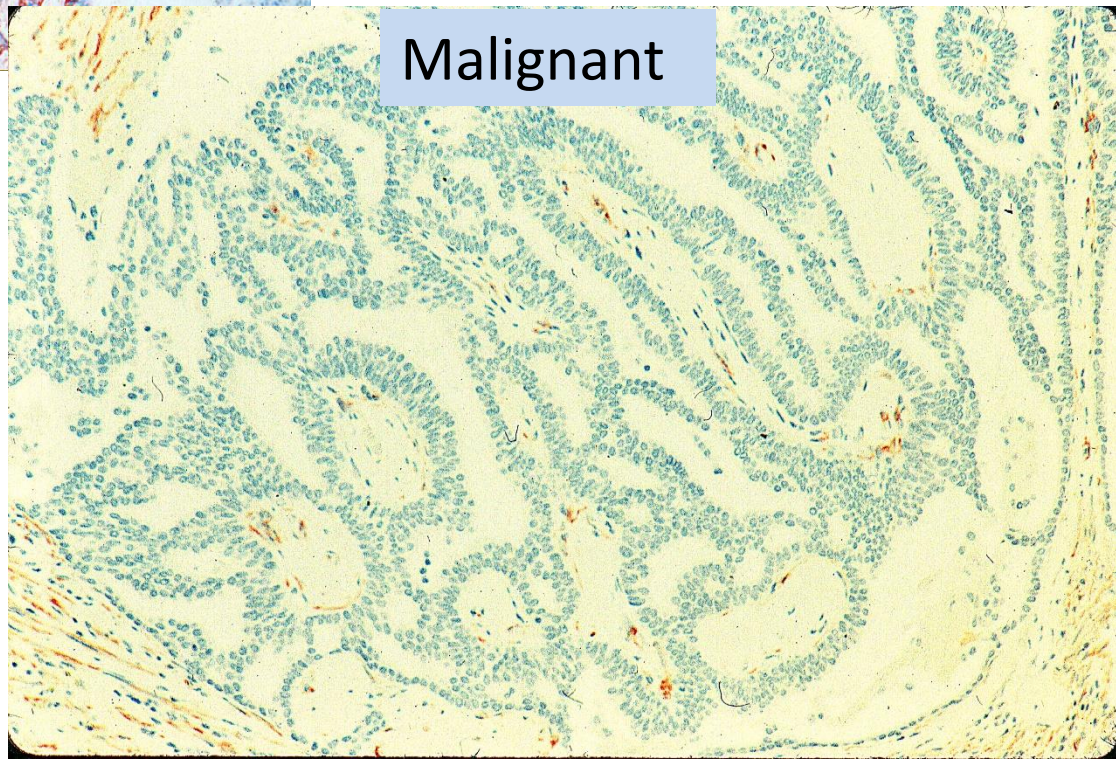
Caveats:

- MECs may be attenuated in distended benign ducts and in large ducts of in situ ca
- Sensitivity of some MEC markers is lower/absent in DCIS-associated MECs and benign sclerosing than in normal MECs.
- Any positivity for MEC favors in situ ca.

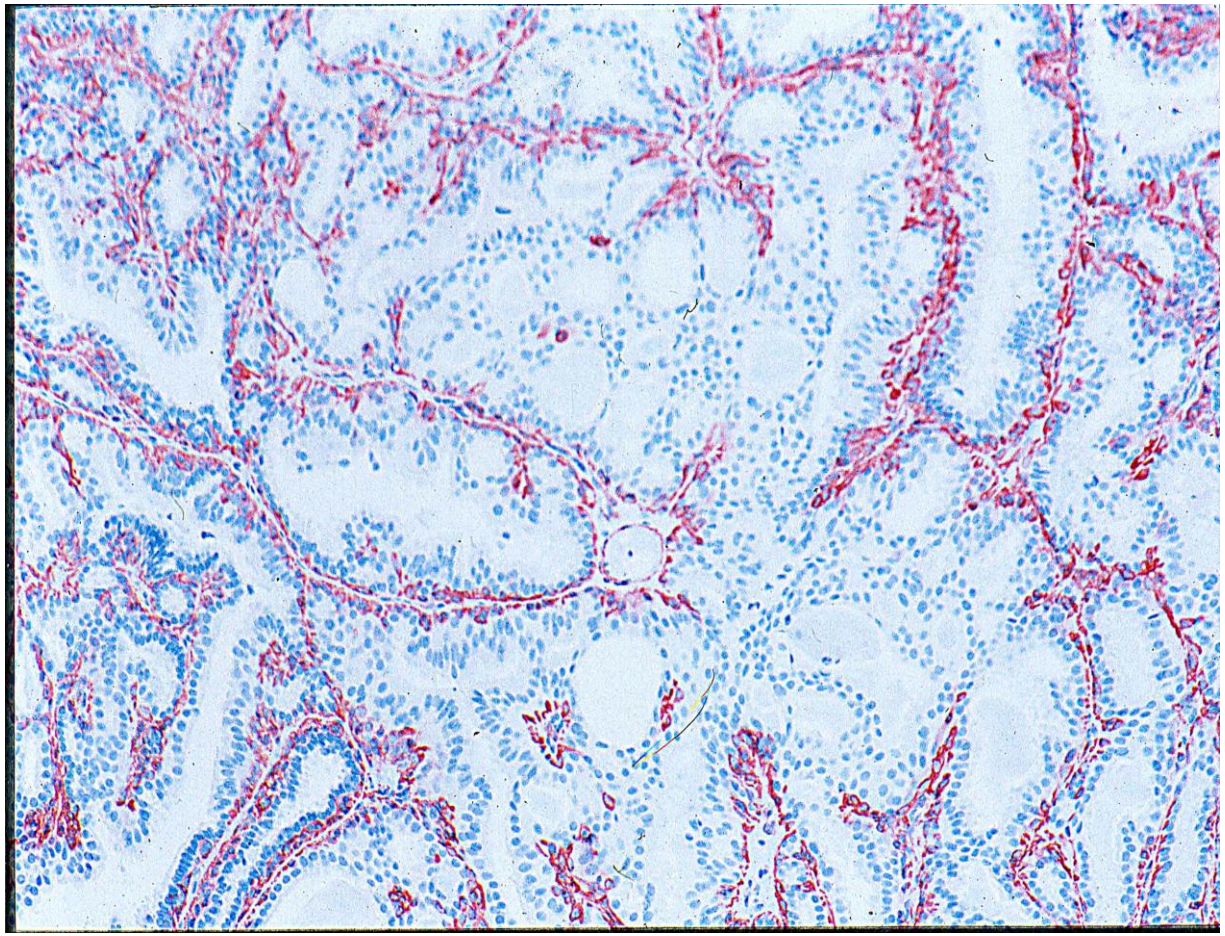
MEC in The Evaluation of Papillary Lesions

- Papilloma
- Atypical papilloma
- Papillary carcinoma in situ
- Solid papillary carcinoma
- Encapsulated papillary carcinoma

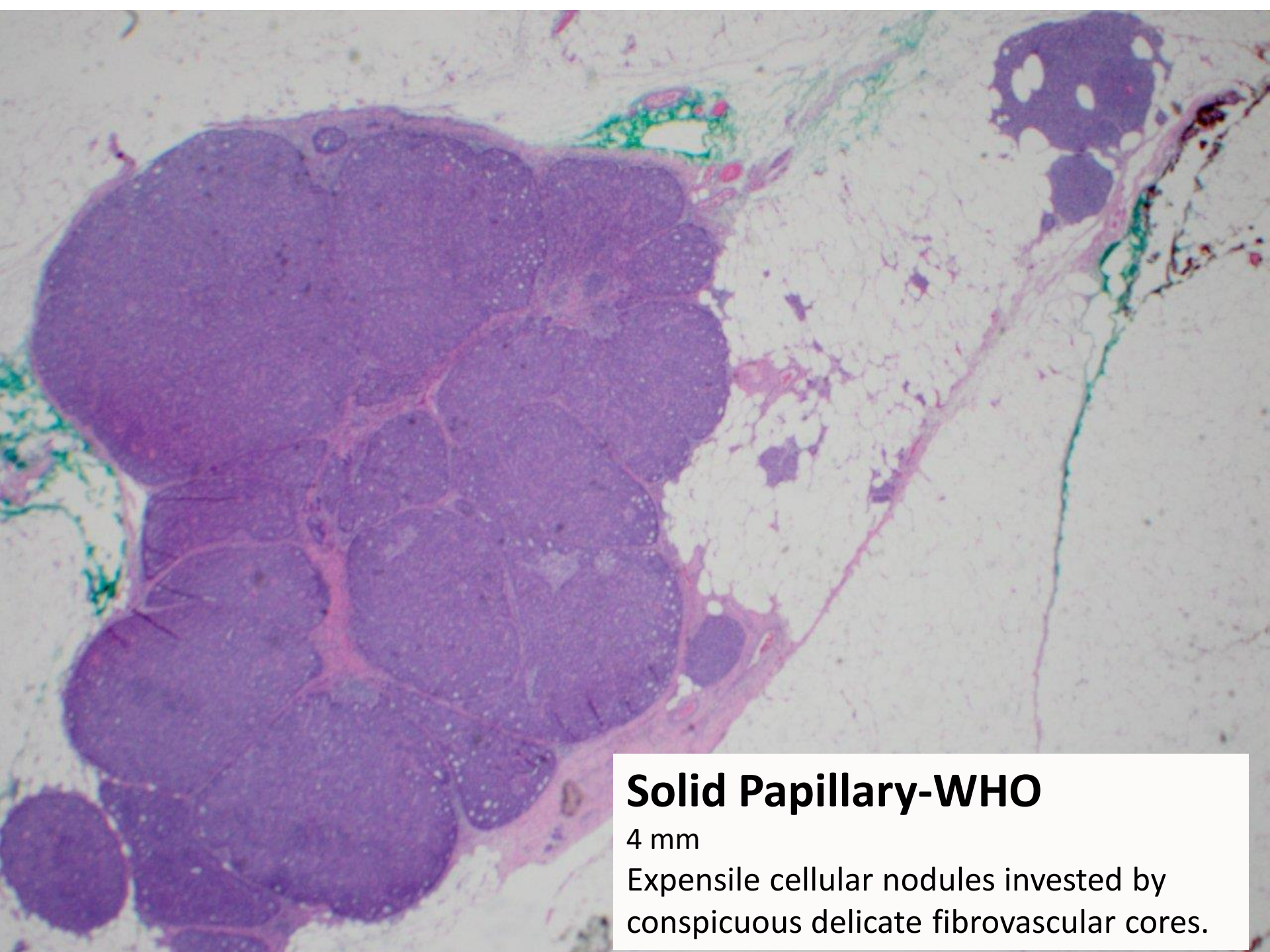

Benign


Malignant

Atypia in a Papilloma



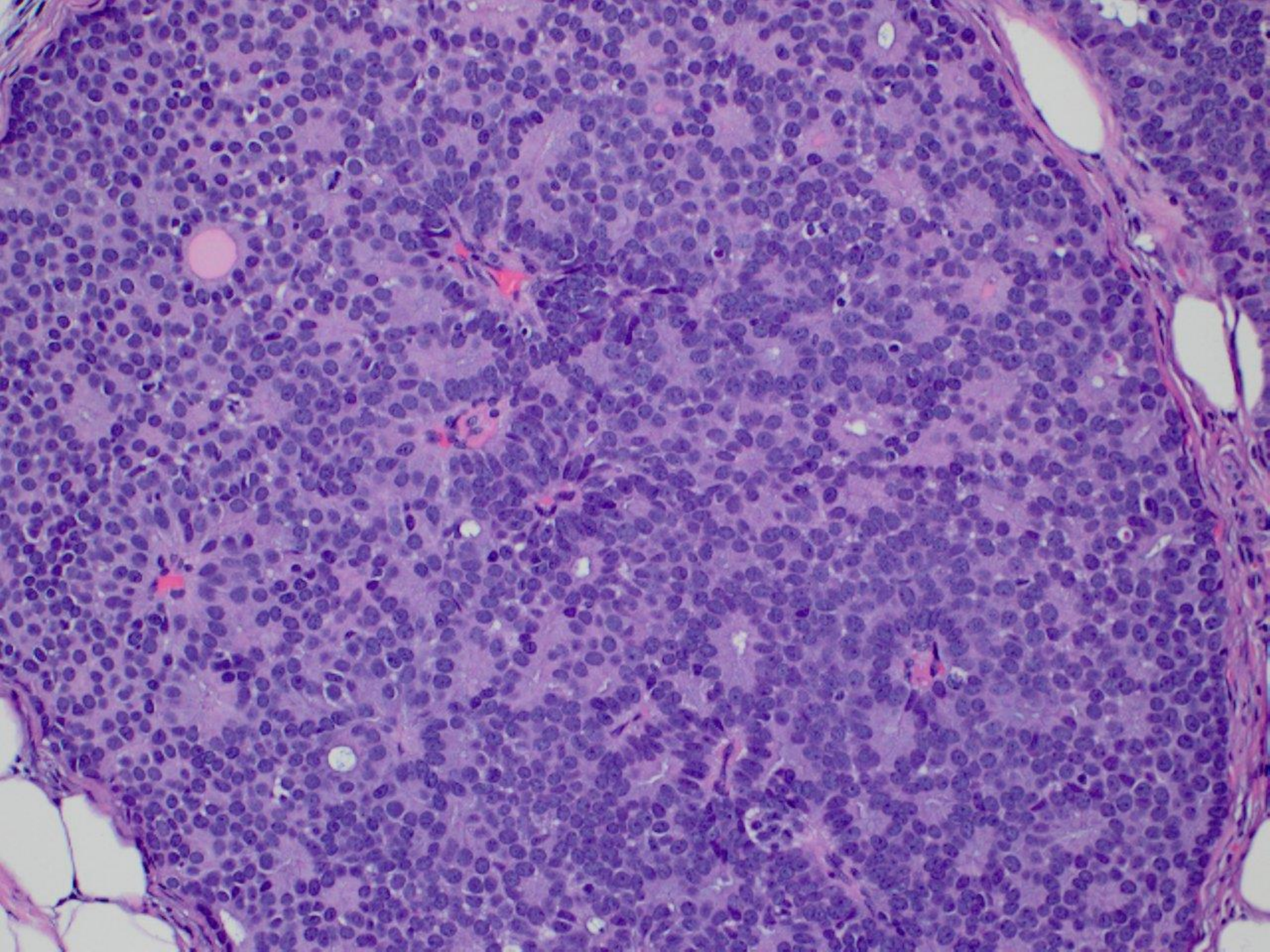
ADH/DCIS area up to 3 mm (criteria of Page)



Solid Papillary-WHO

4 mm

Expensile cellular nodules invested by conspicuous delicate fibrovascular cores.



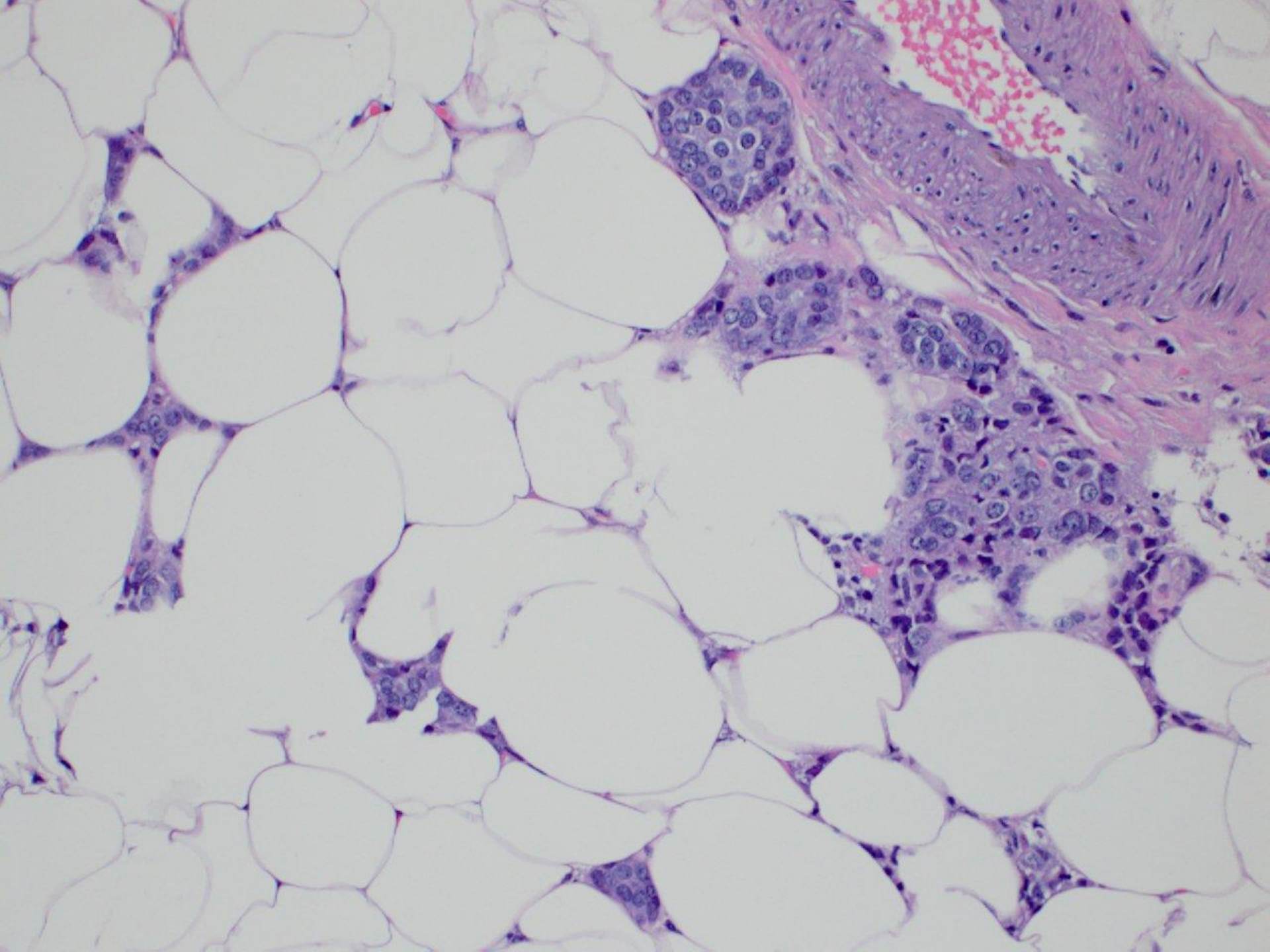
Solid papillary-WHO

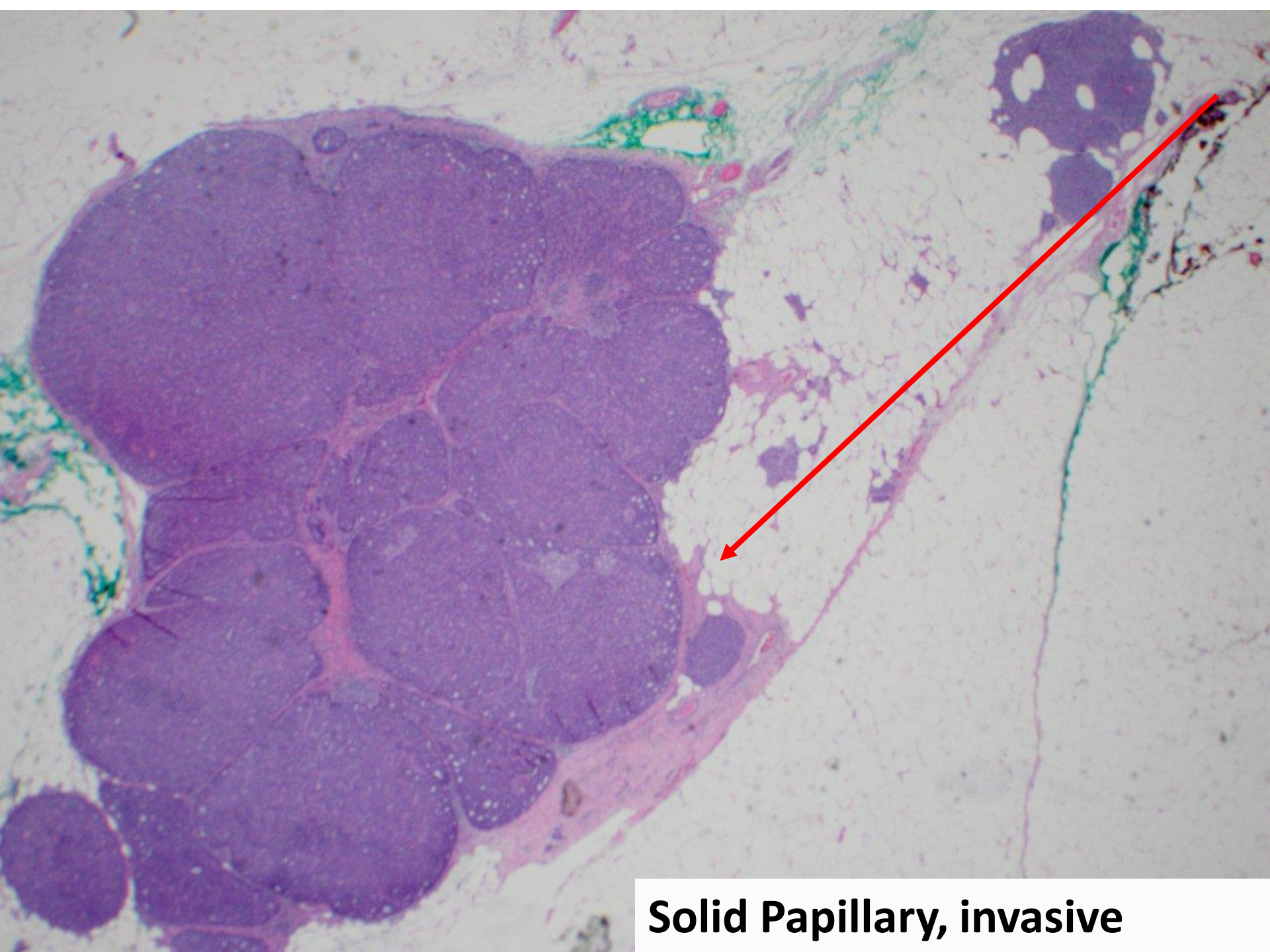
Assess for Myoepithelial Cells

1. Present: around the solid nodules = variants of DCIS

2. Absent, rounded nodules: stage as in situ but consider as a special rounded form of invasive disease with indolent behavior and extremely favorable prognosis

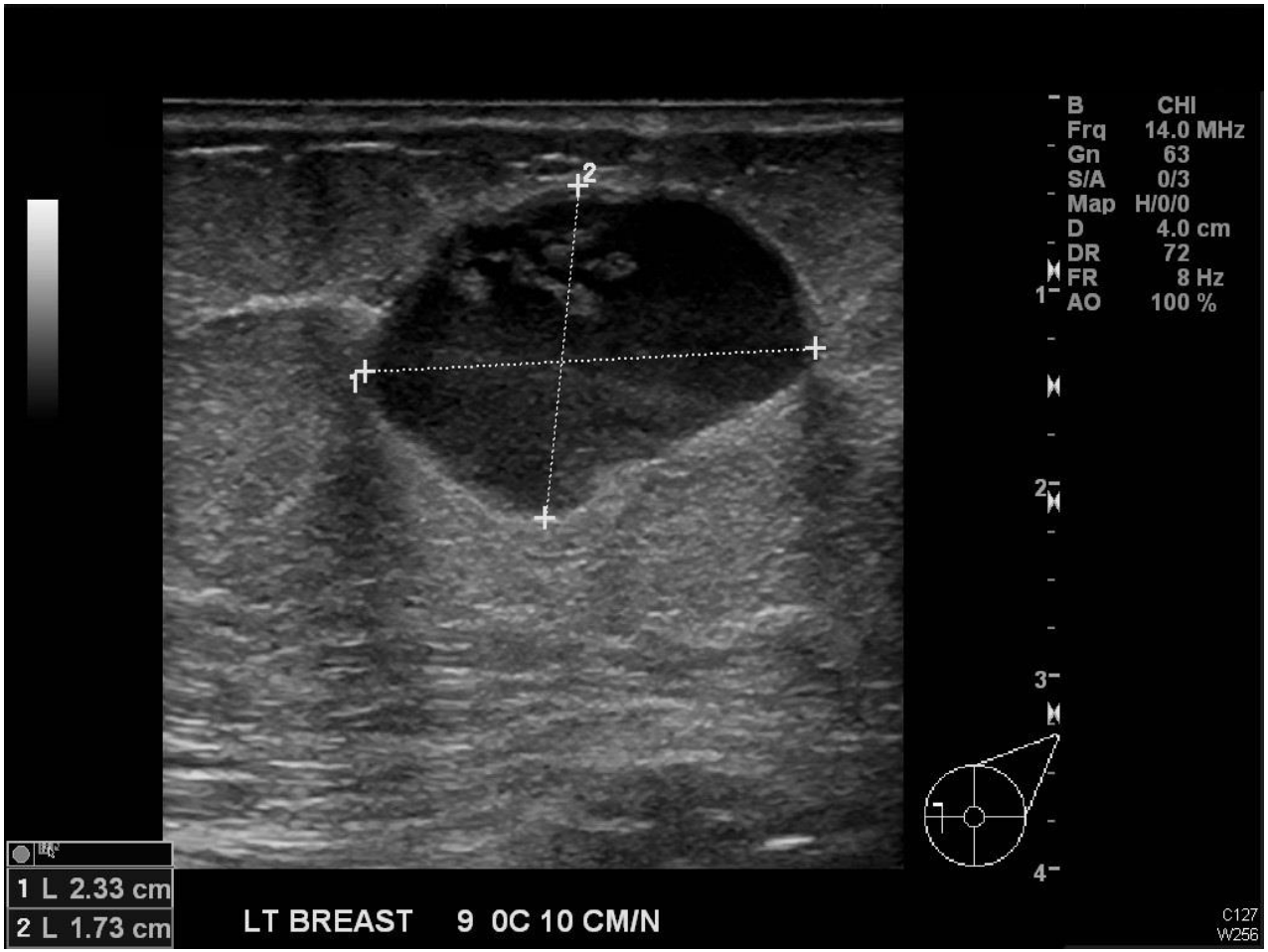
3: Invasive solid papillary ca.= irregularly shaped epithelial islands with jagged contours arranged in jig-saw pattern set within a desmoplastic stroma, or cells infiltrating into adjacent fat

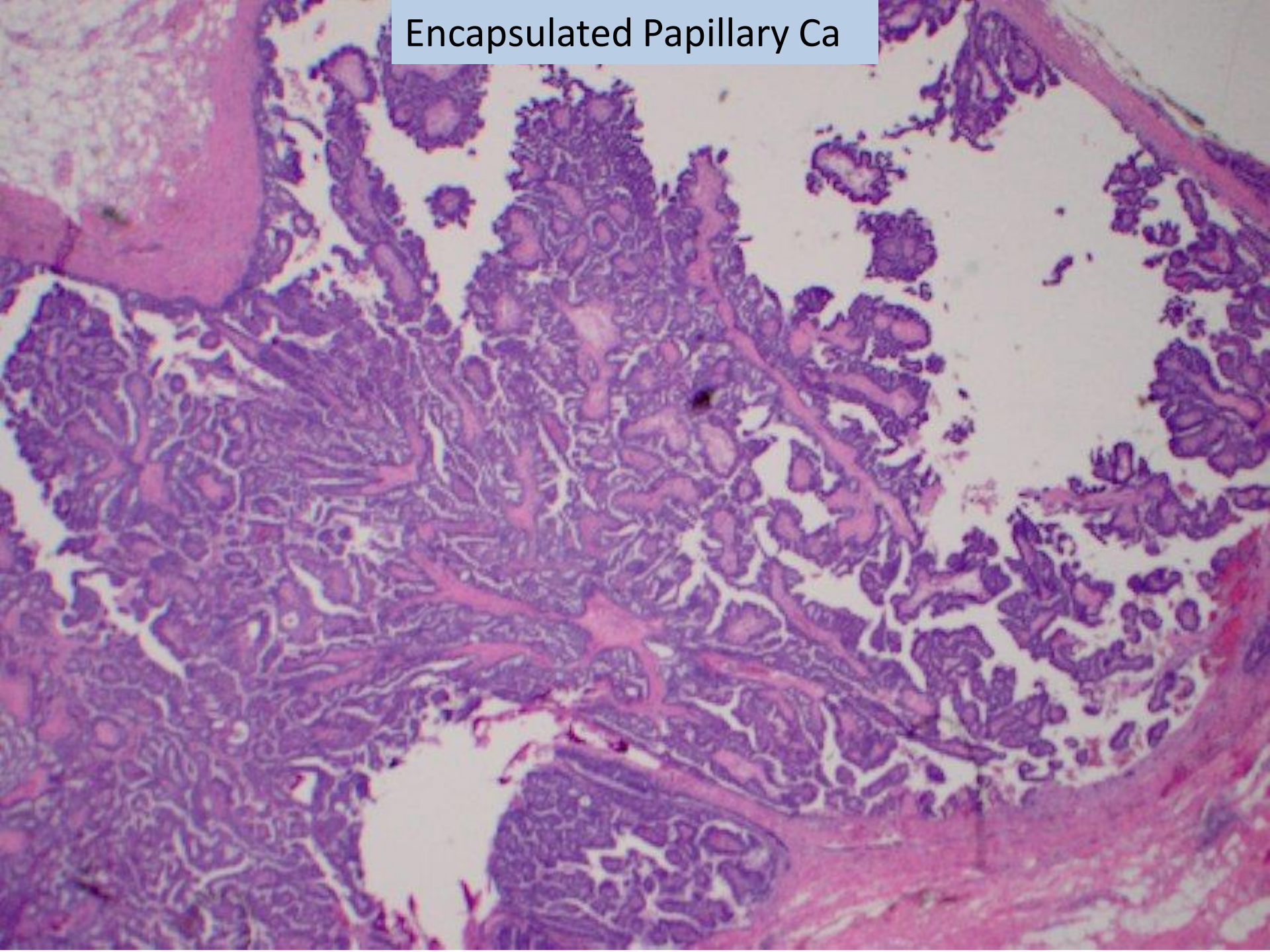


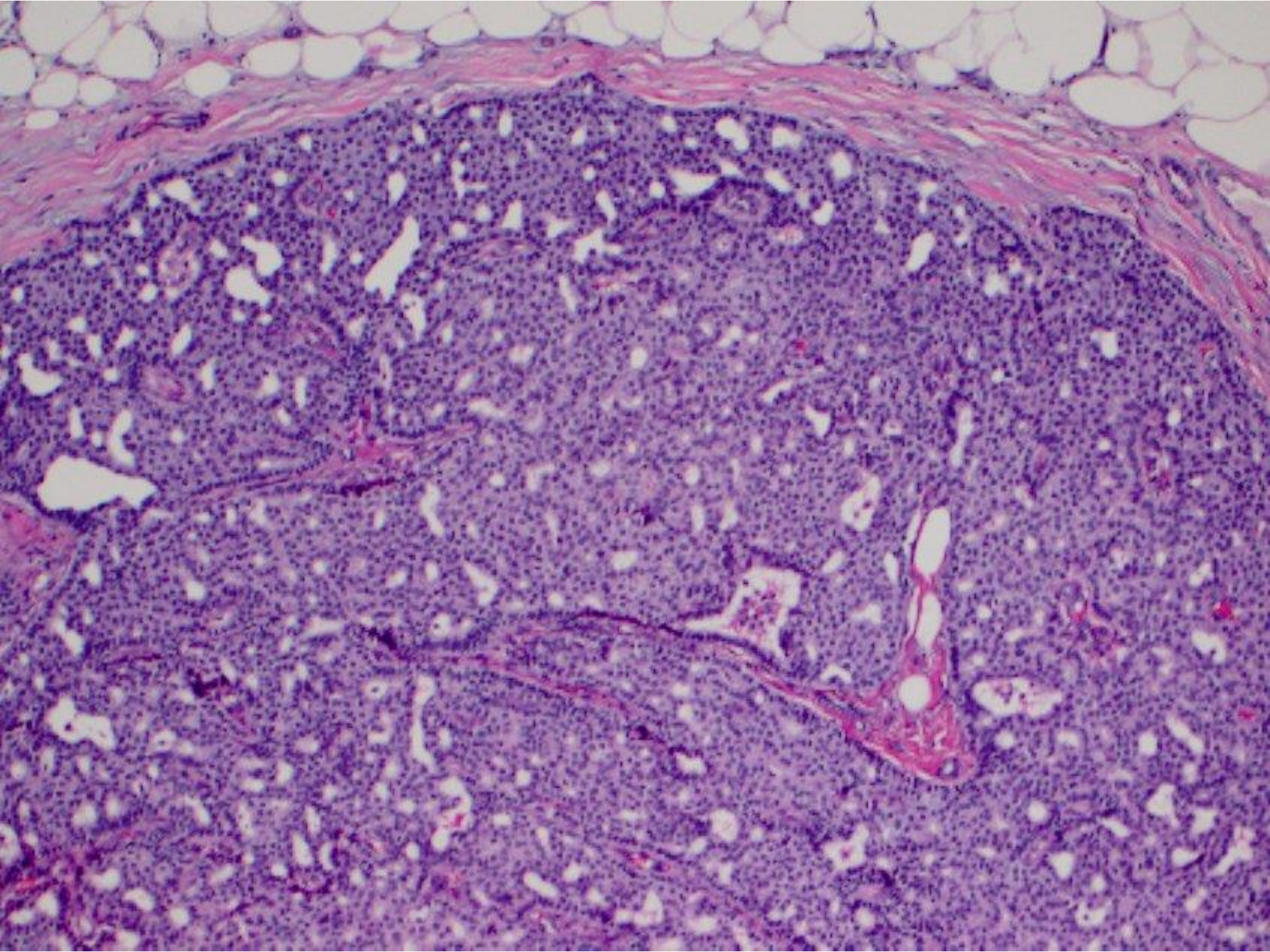


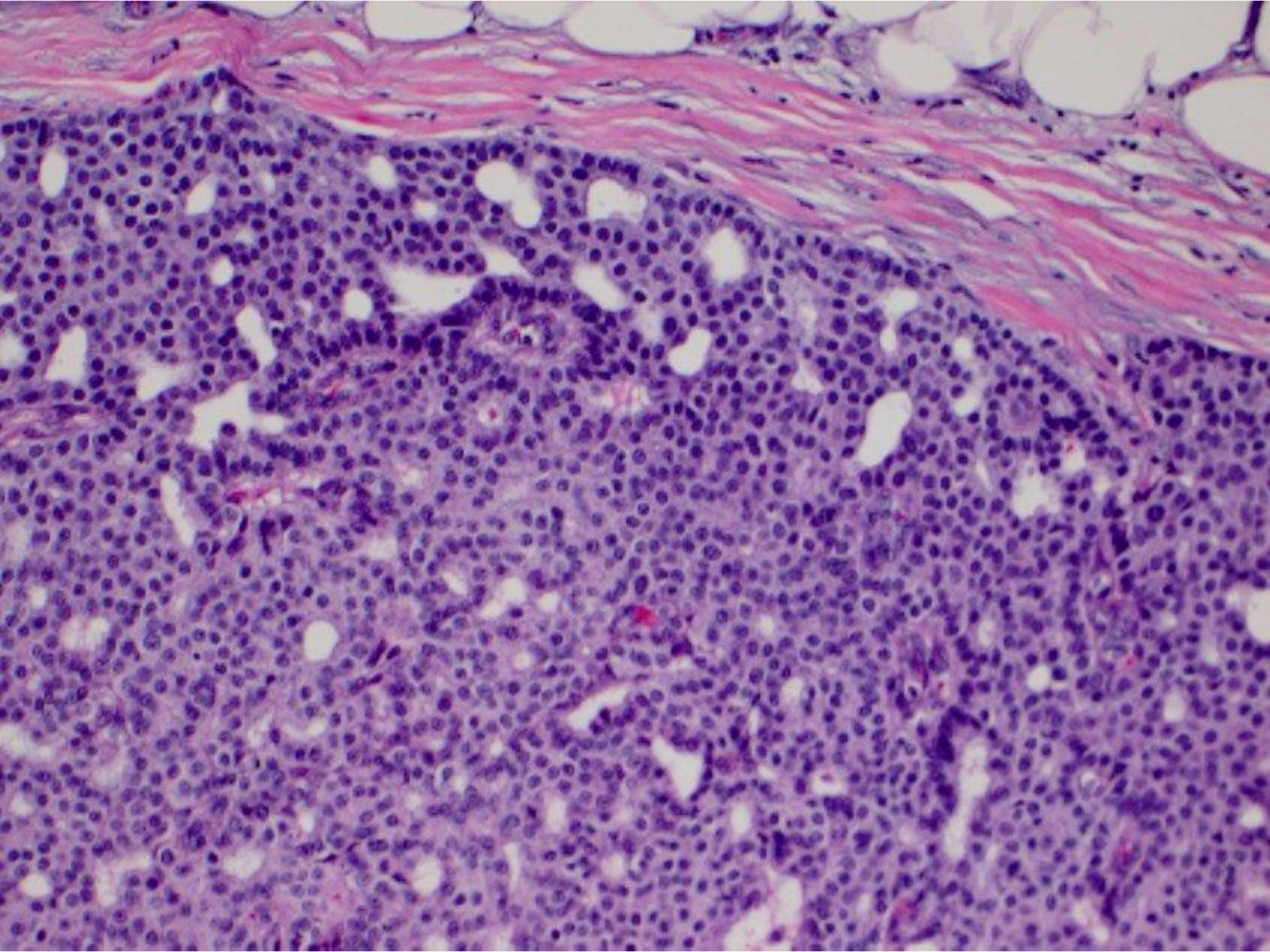
Solid Papillary, invasive

3 cm mass


B CHI
Frq 14.0 MHz
Gn 63
S/A 0/3
Map H/0/0
D 4.0 cm
DR 72
FR 8 Hz
AO 100 %
1 L 2.33 cm
2 L 1.73 cm
LT BREAST 9 0C 10 CM/N
C127
W256


Encapsulated Papillary Ca





Encapsulated papillary carcinoma- WHO

Staged as Tis (in situ)

True invasion should only be rendered when there are permeative epithelial islands extending beyond the fibrous capsule (NOS).

Size of invasion: largest extent of the frankly invasive component without including the size of EPC.

Entrapped epithelial cells subsequent to needling procedures can mimic invasion and have to be distinguished from true invasion

Diagnostic Problems in Mammary Gland Tumor Pathology

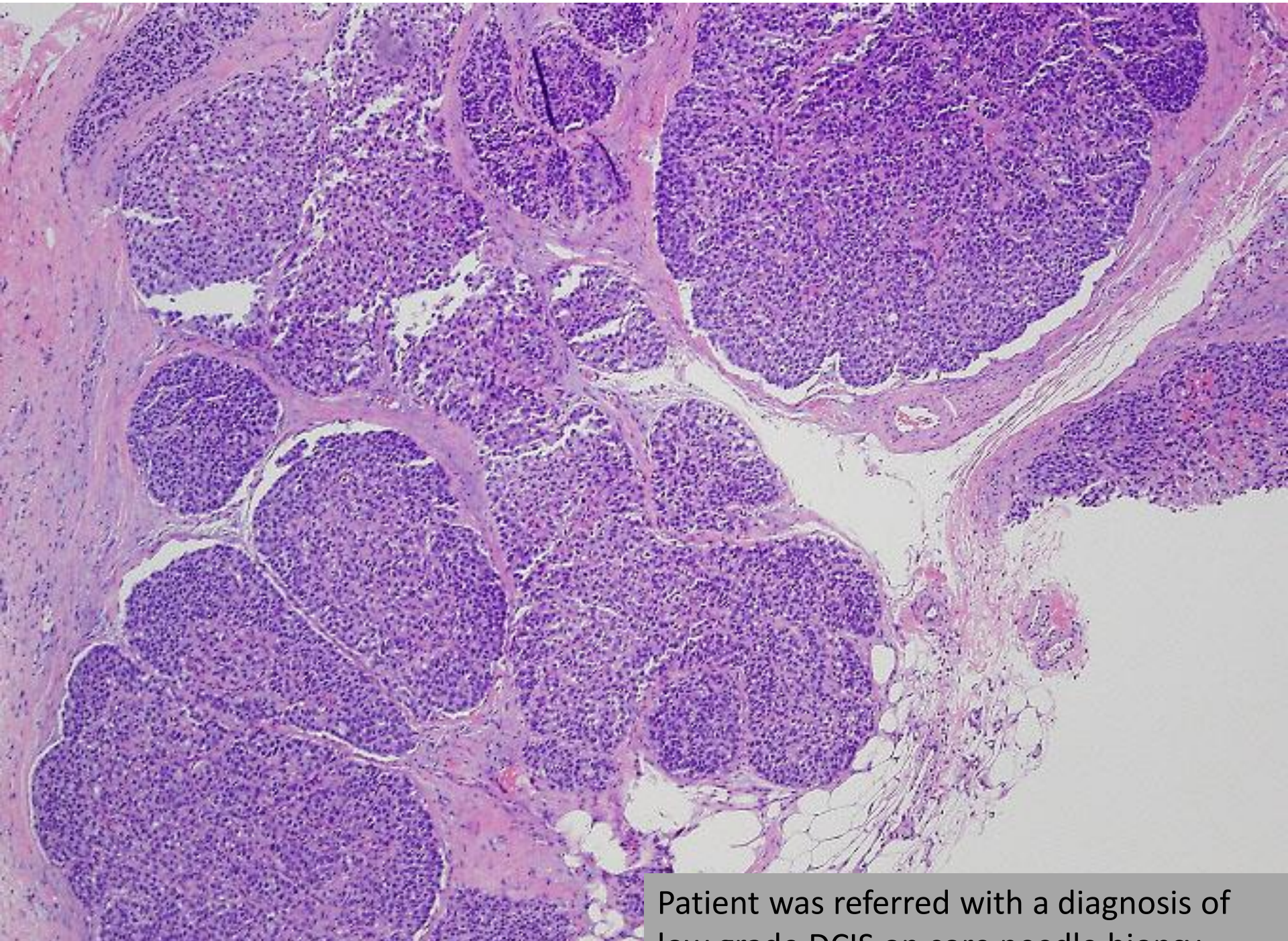
1. Distinguishing *in situ* from invasive carcinoma
2. **The differential diagnosis of various types of benign and malignant lesions**
3. Confirming the breast as the prim ary site in metastatic carcinoma

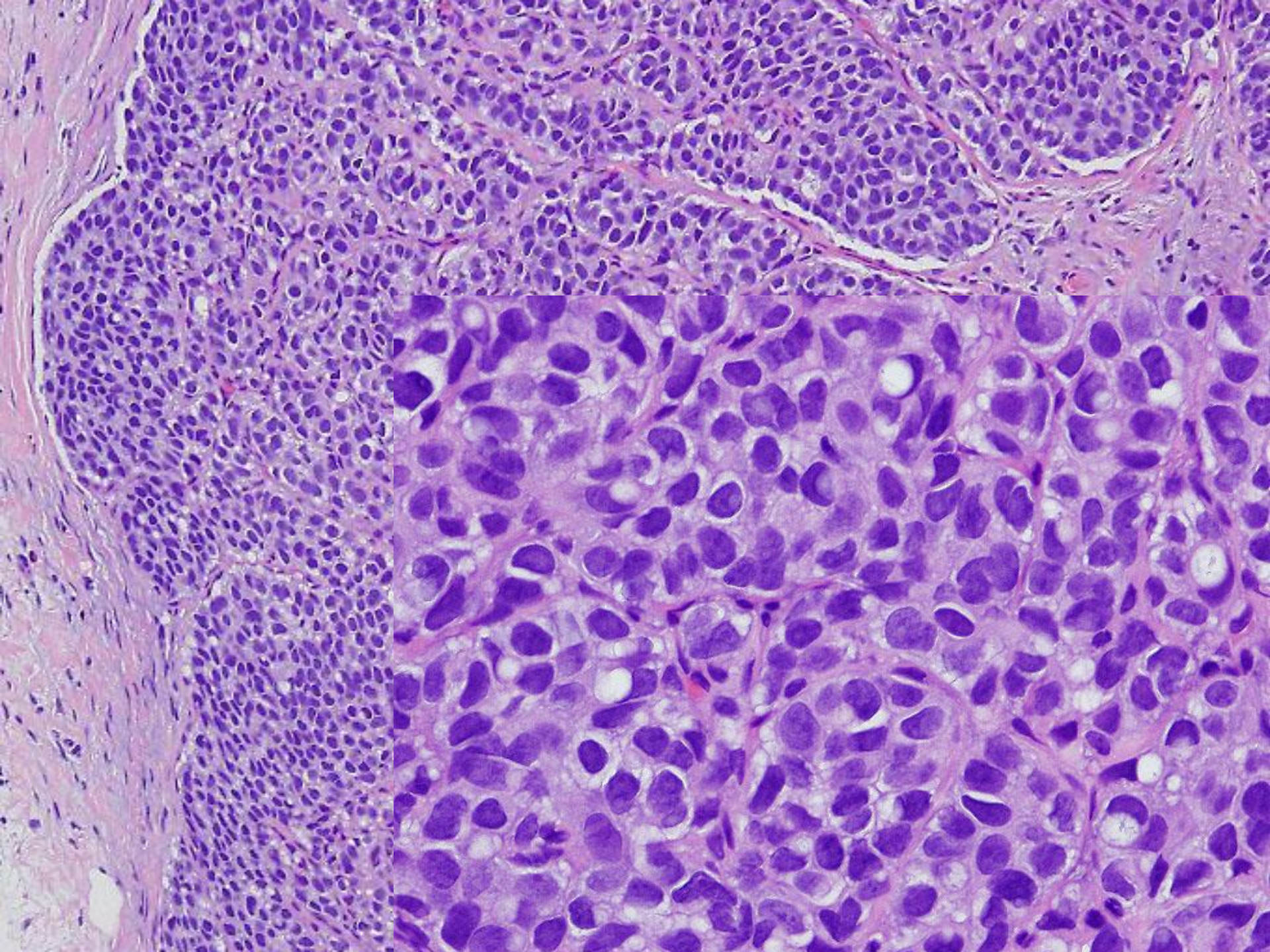
Immunohistochemistry in the Differential Diagnosis of:

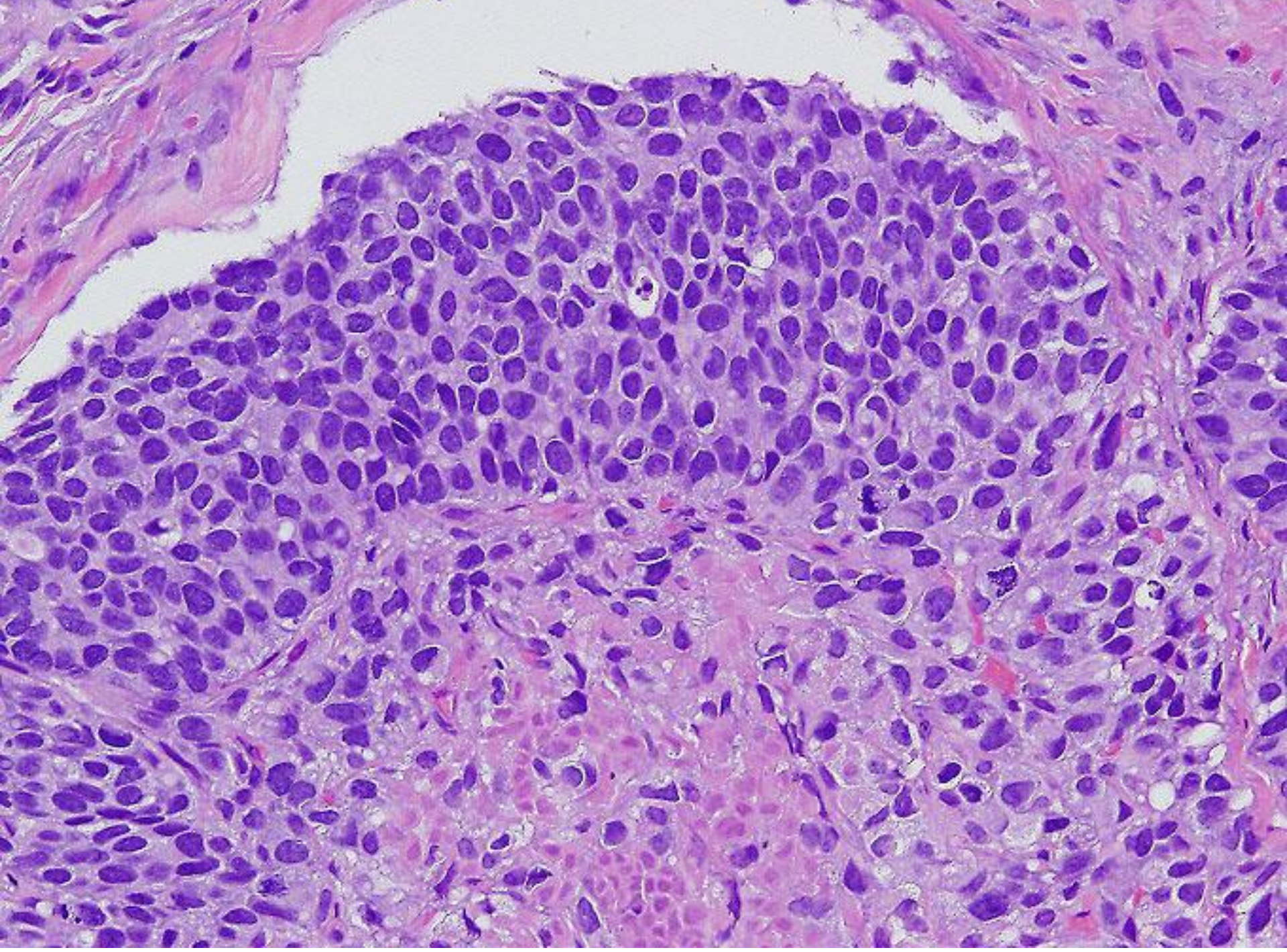
1. Lobular vs Ductal (especially in situ ca.)

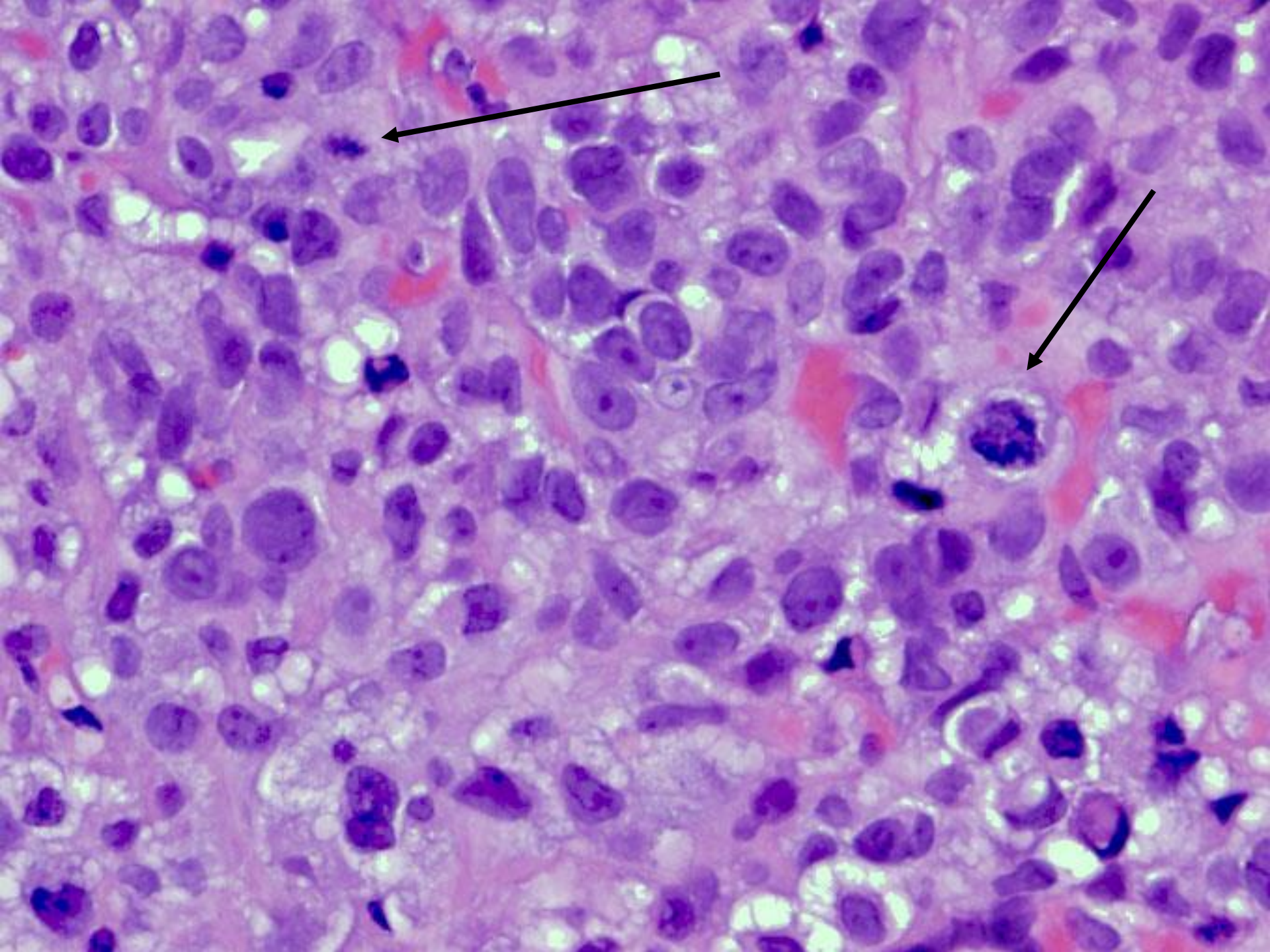
2. Adenoid cystic vs Cribriform ca vs
   Collagenous spherulosis

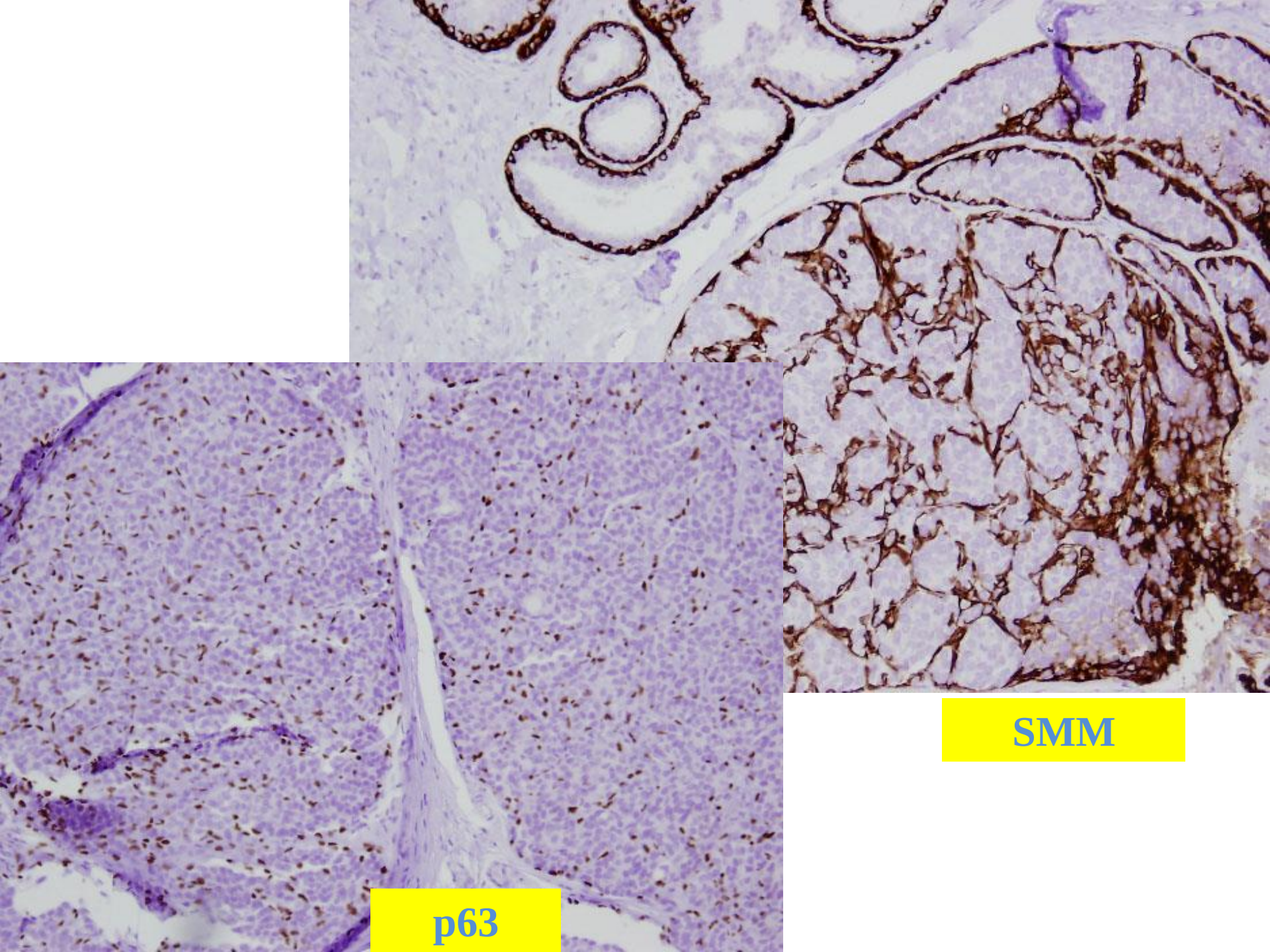
3. Spindle cell and Fibromatosis
   like metaplastic carcinomas vs
   other spindle cell lesions

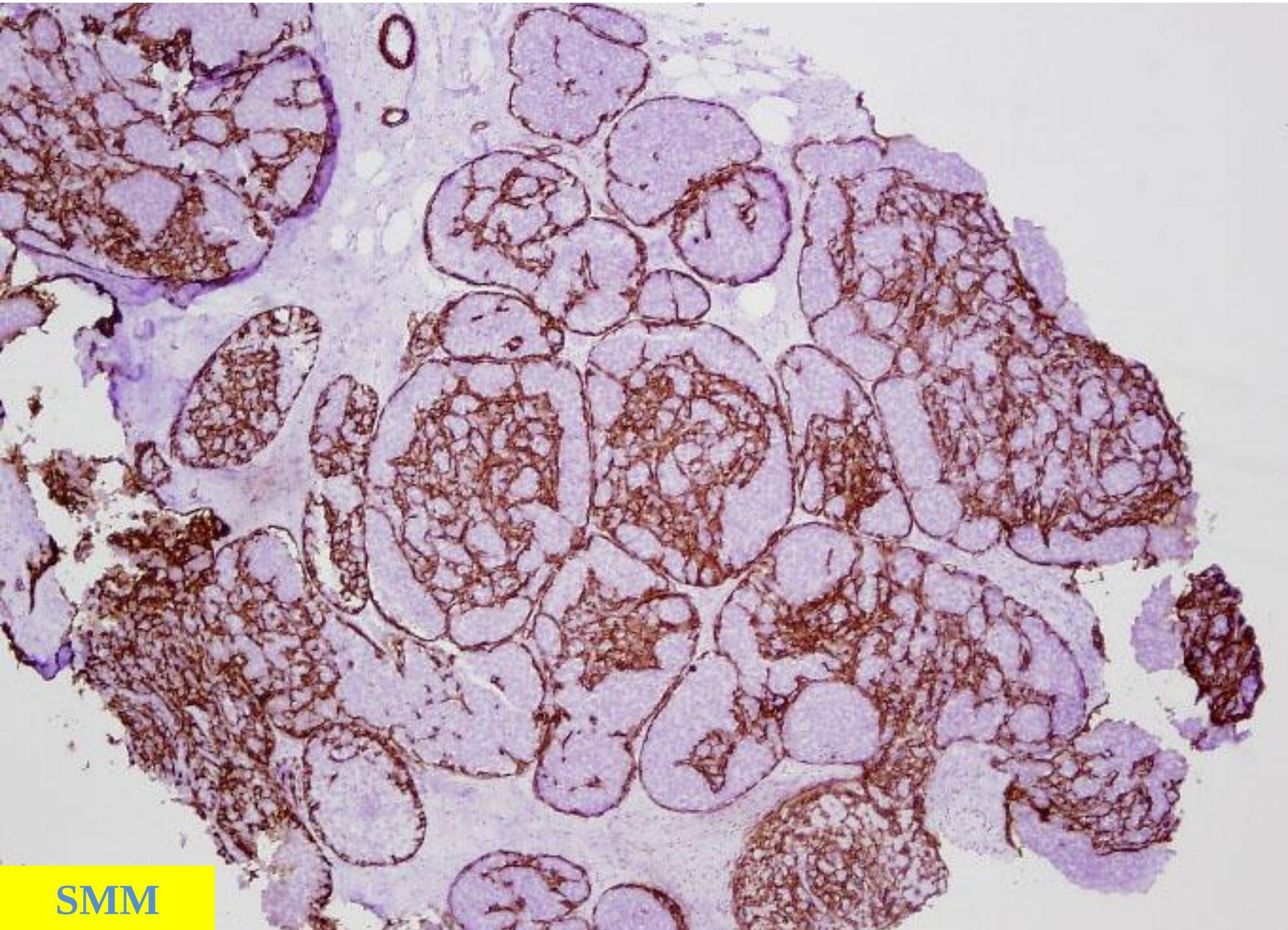

Patient was referred with a diagnosis of

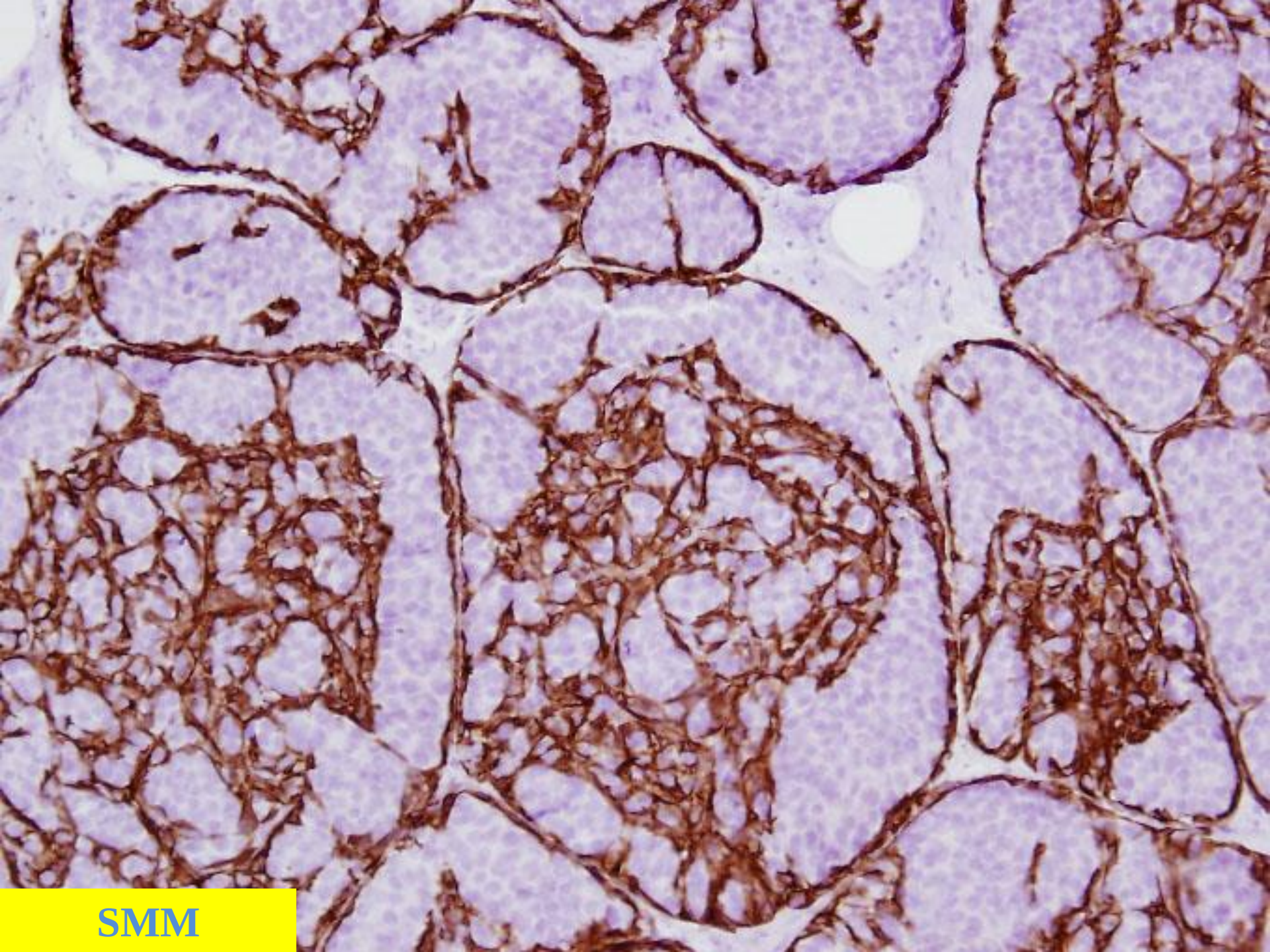


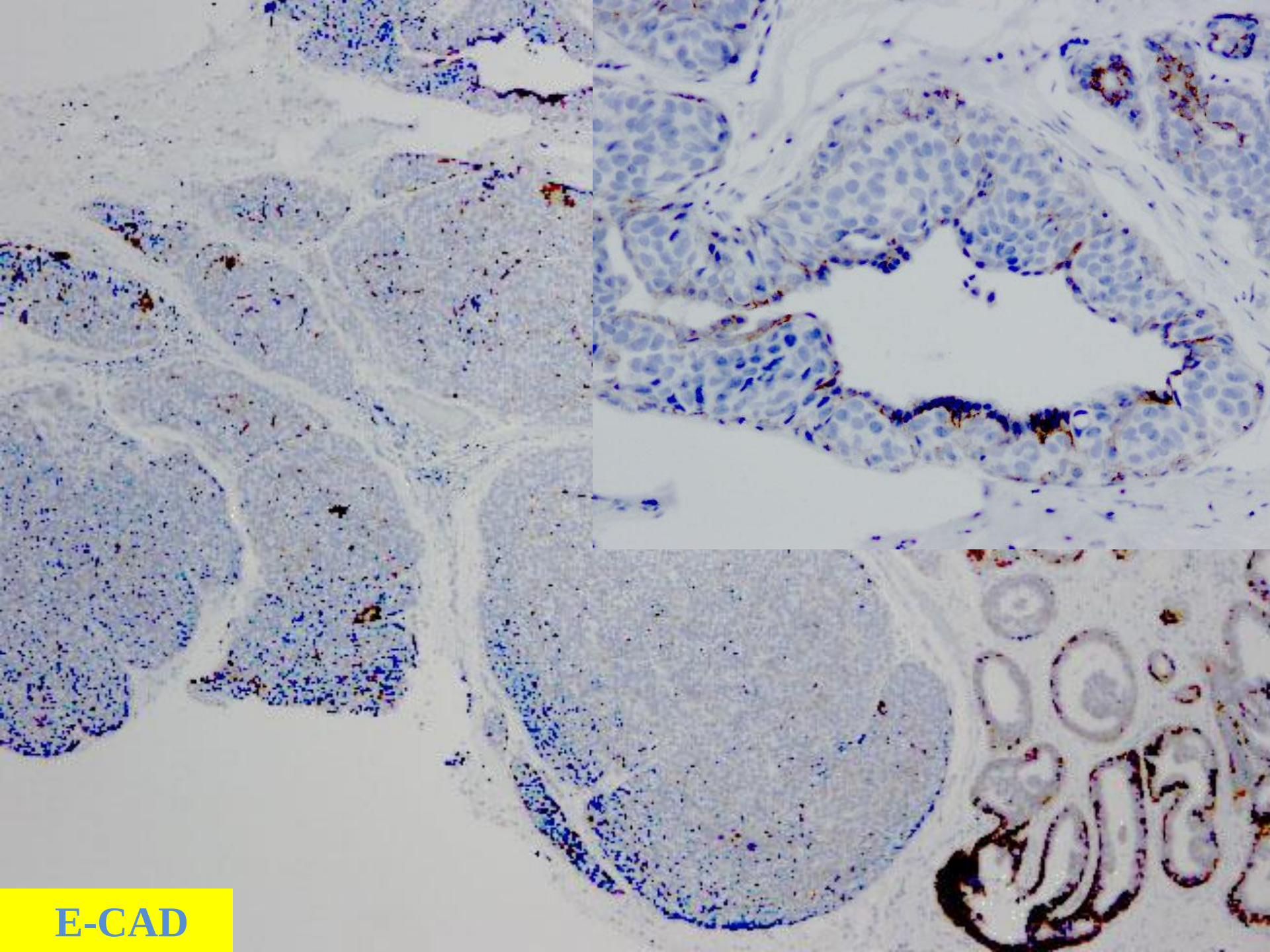


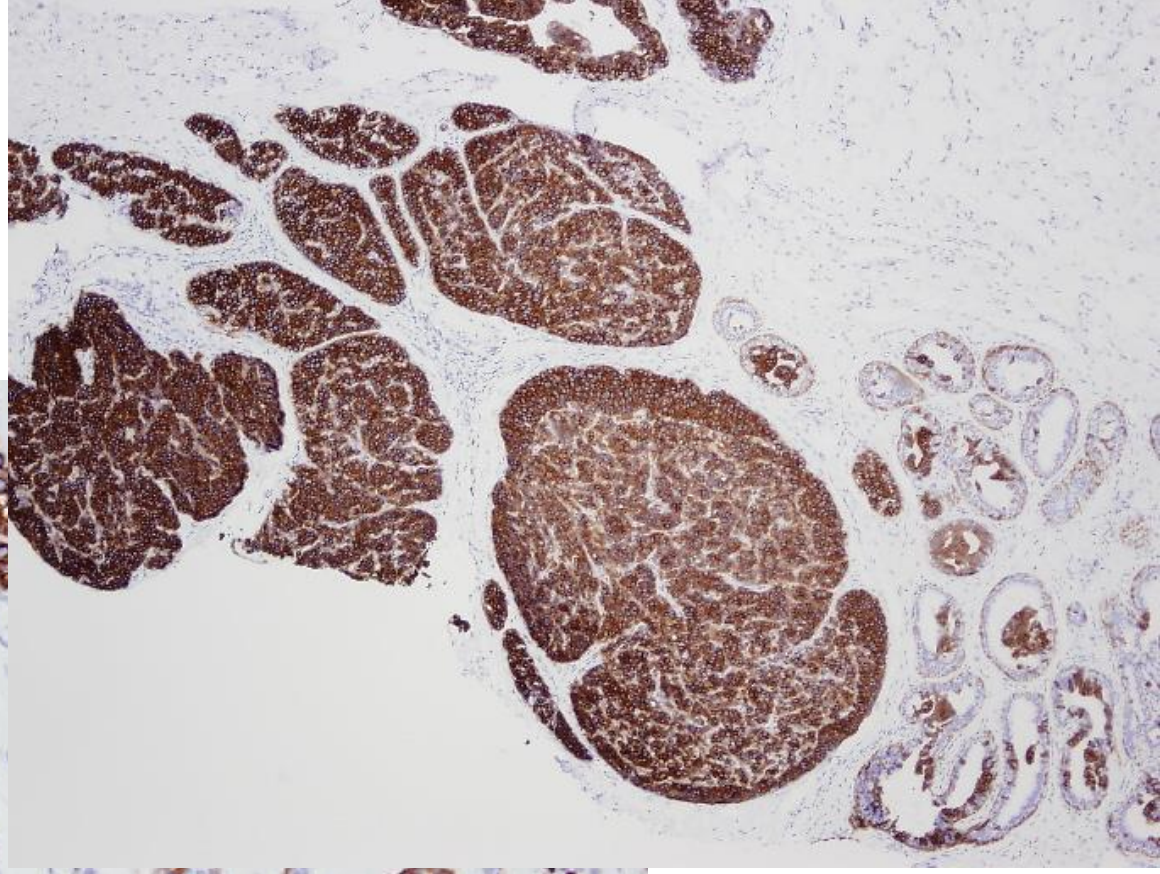


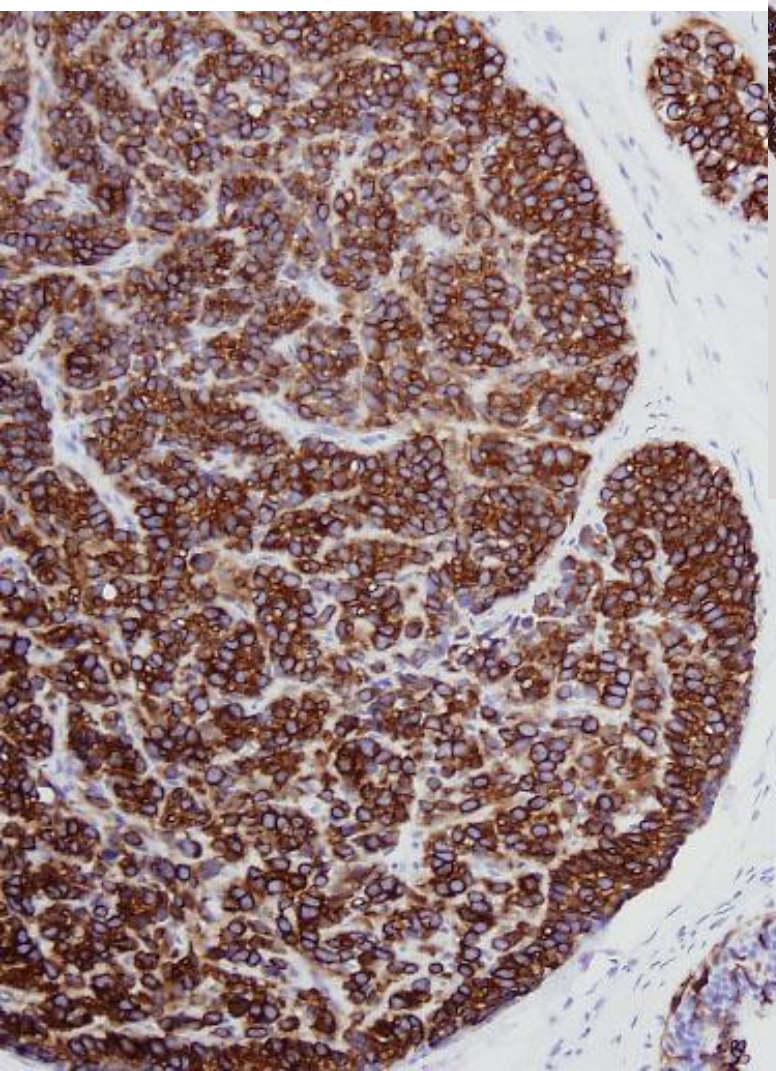

SMM
p63

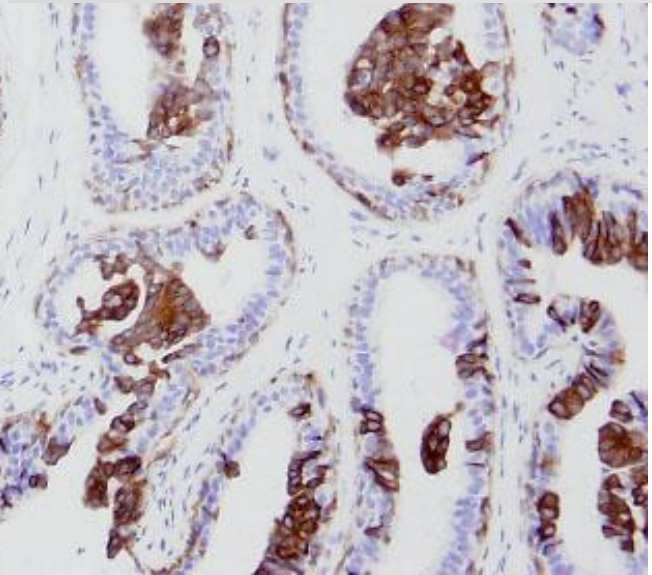

SMM


SMM

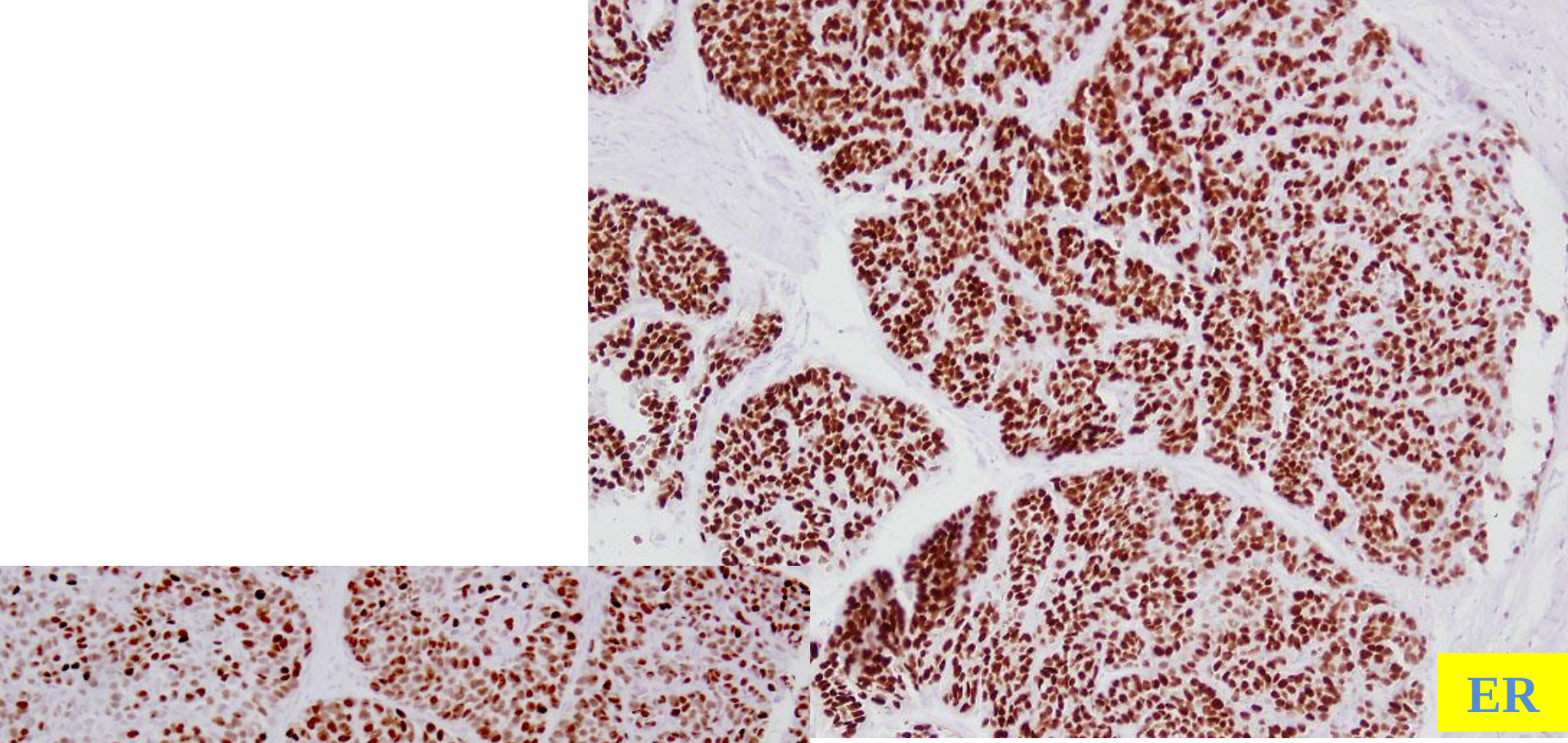

E-CAD

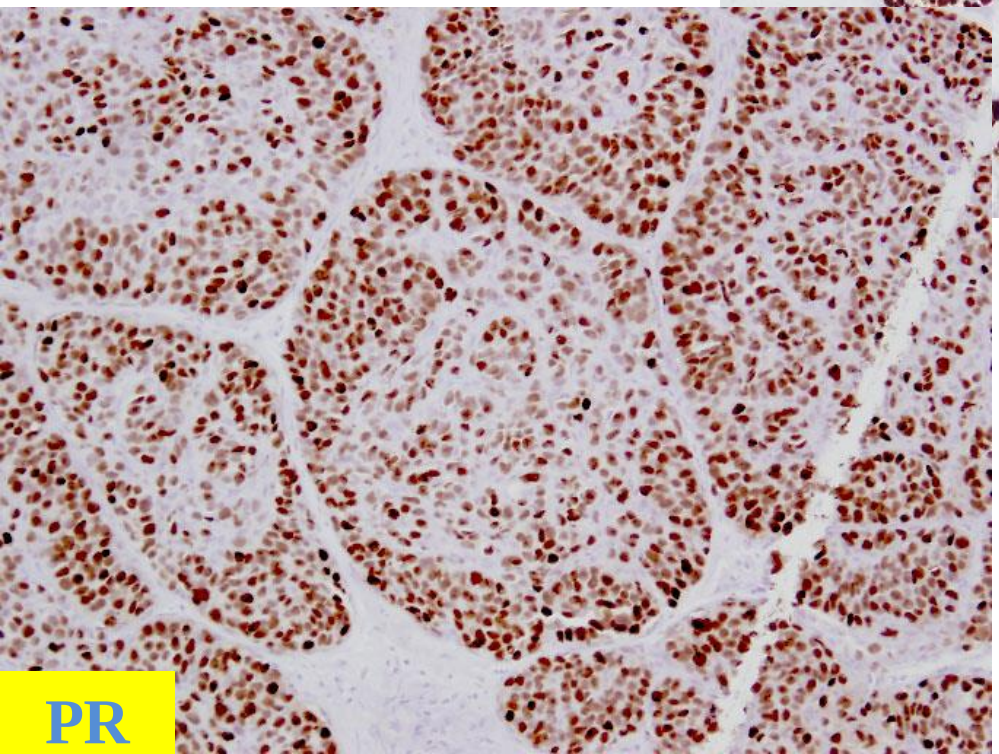






CK903

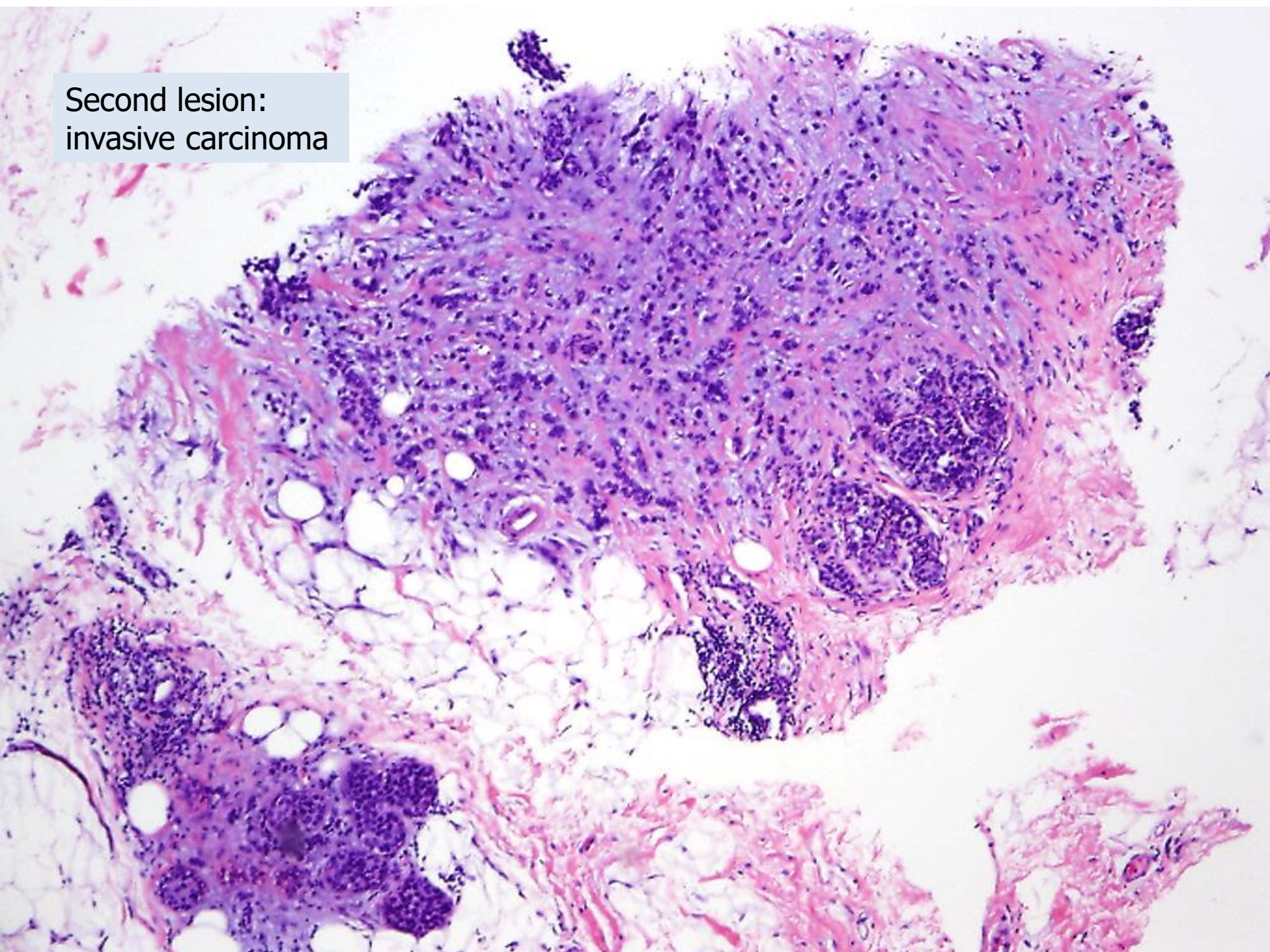


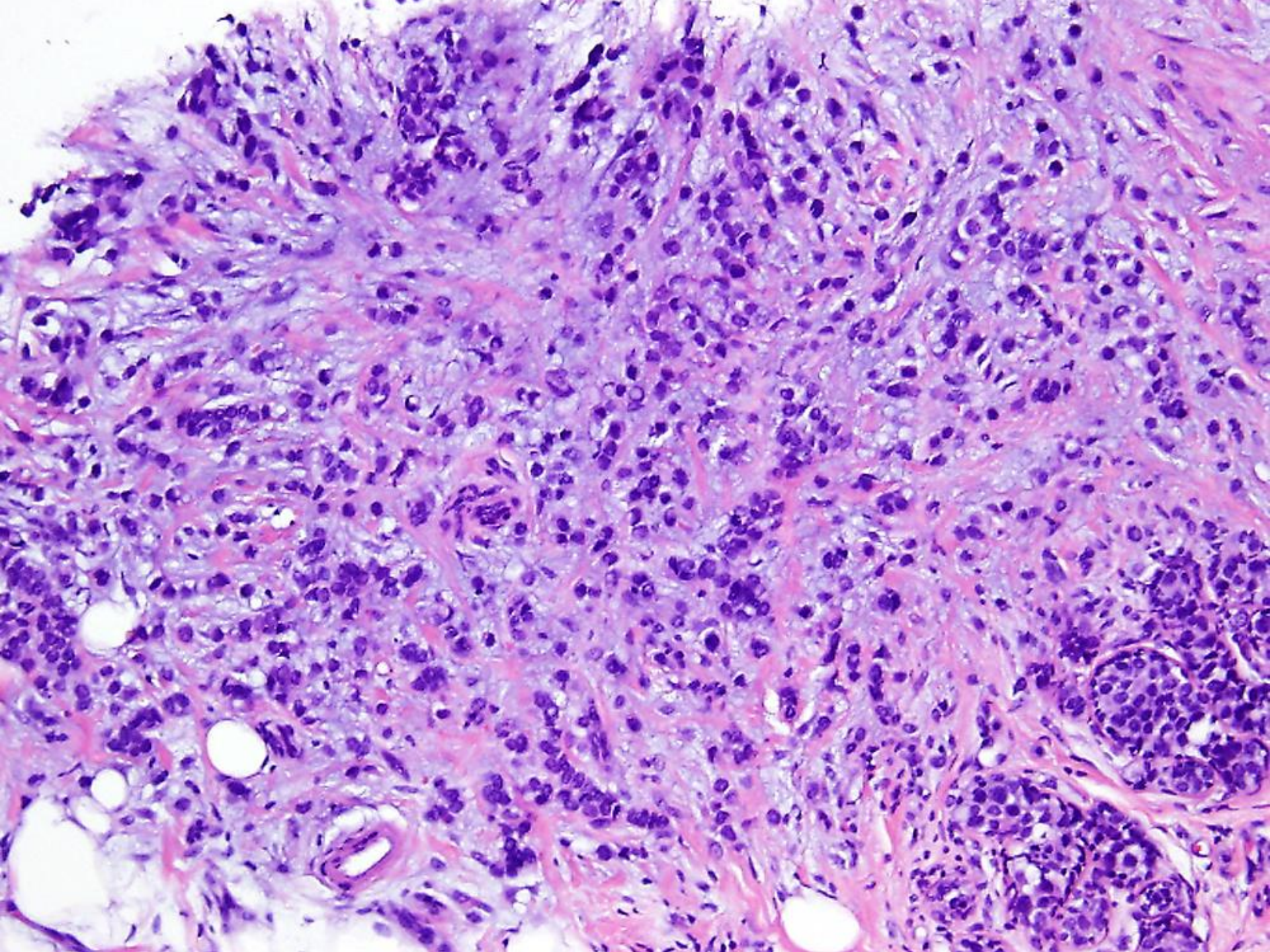


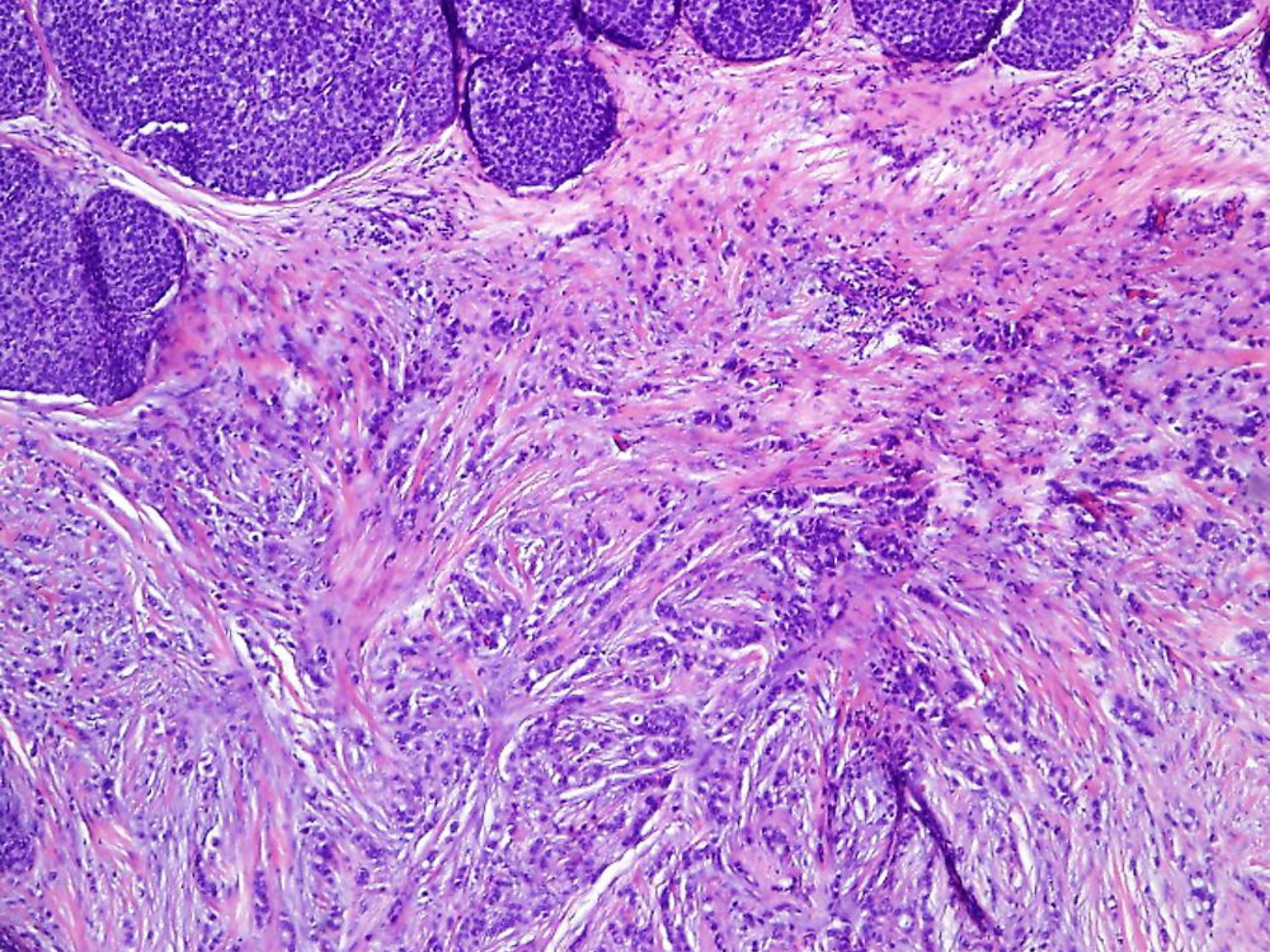
Dx: LCIS, variant

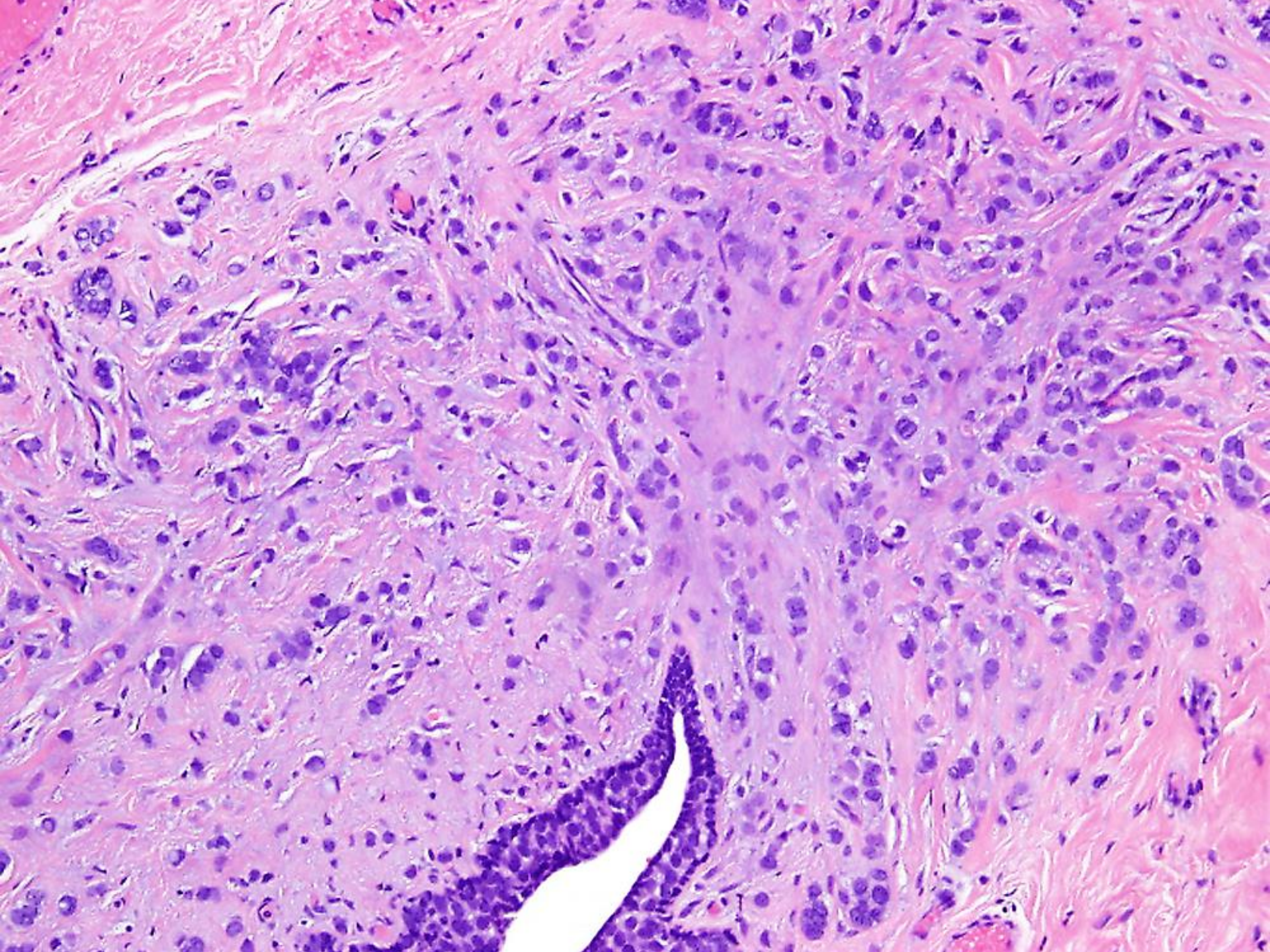
MRI was followed.
A second lesion in
a different clock position noted.

MRI guided bx was performed.


Second lesion:
invasive carcinoma







E-Cadherin

(diagnostic challenges)

- E-cadherin gene (*CDH1*) located on the long arm of Ch16 (16q22.1) encodes a transmembrane protein involved in intercellular adhesion.
- Cell-to-cell adhesion through E-cad is also dependent on the sub plasmalemmal cytoplasmic catenin complexes (α, β, γ, and p120 isoforms) that link E-cad to the actin cytoskeleton of the cell.
- Abnormalities of the catenins or E-cad gene expression: → a complete absence or abnormal localization (apical or perinuclear) of the E-cad protein.

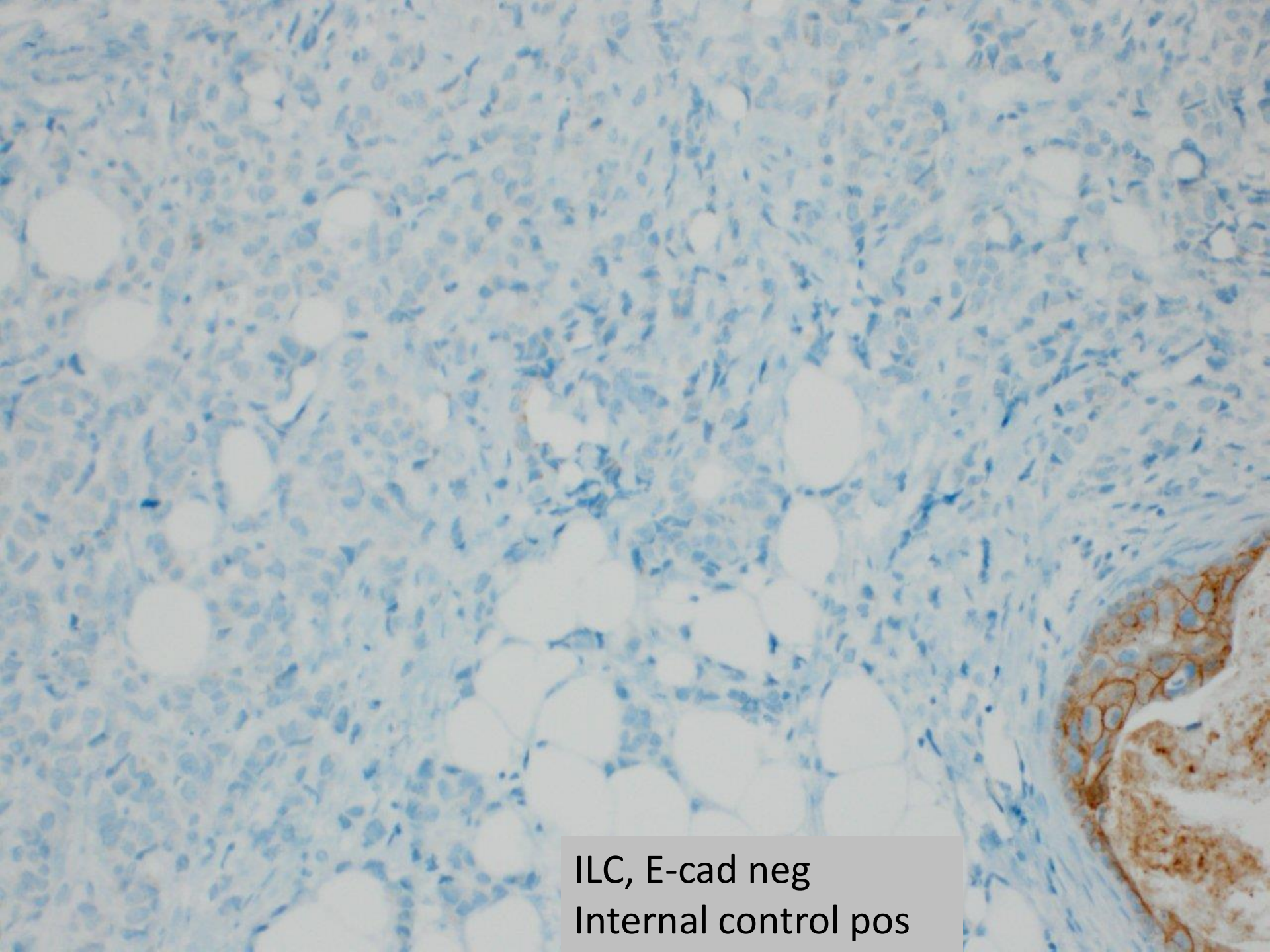
E- Cadherin and P120

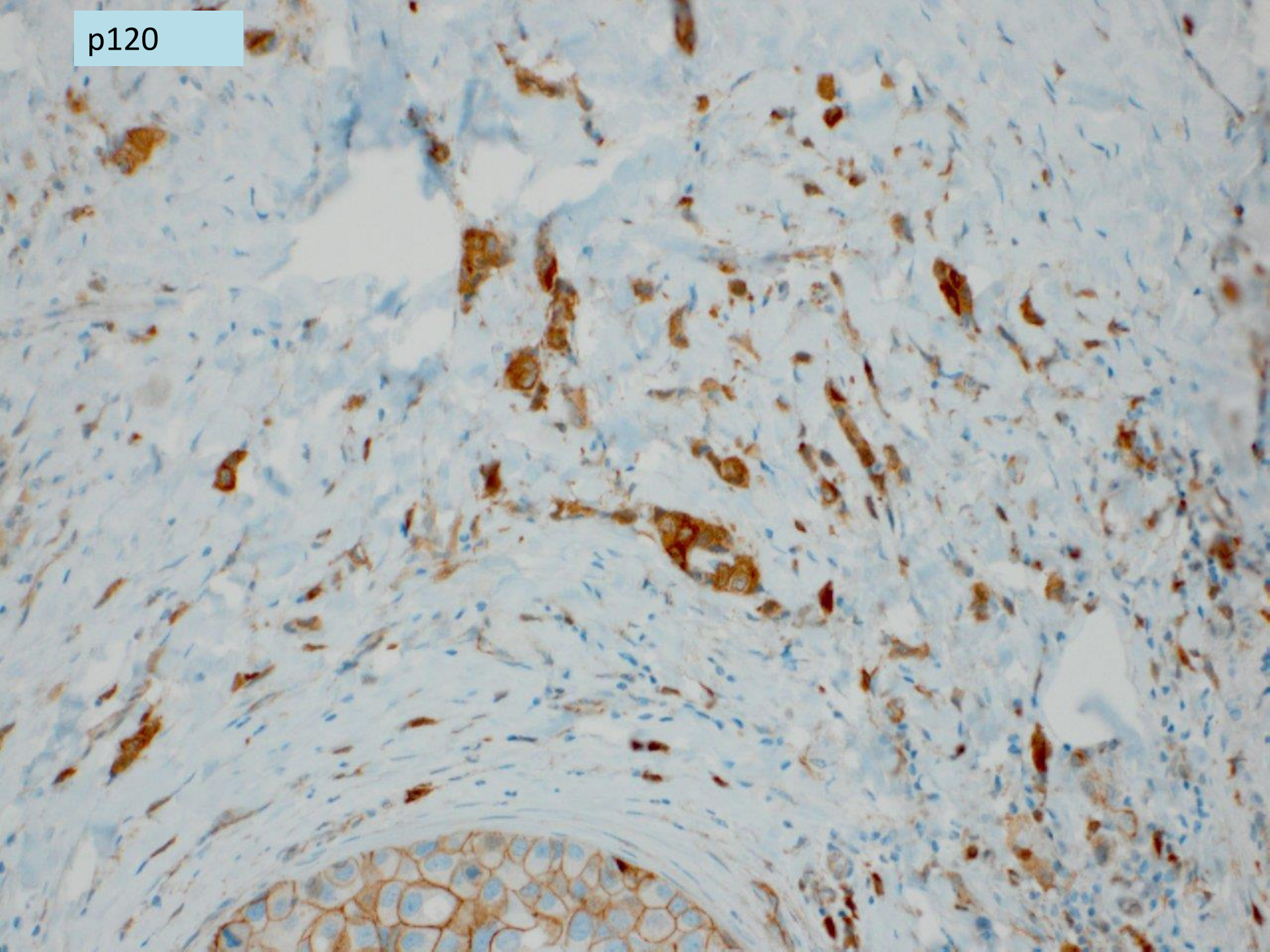
- Majority of cases: E-Cad staining unequivocal (pos or neg)
- Minority (~15%) of cases, stain difficult to interpret. Another stain (p120) could be used
- P120 immunoreactivity:

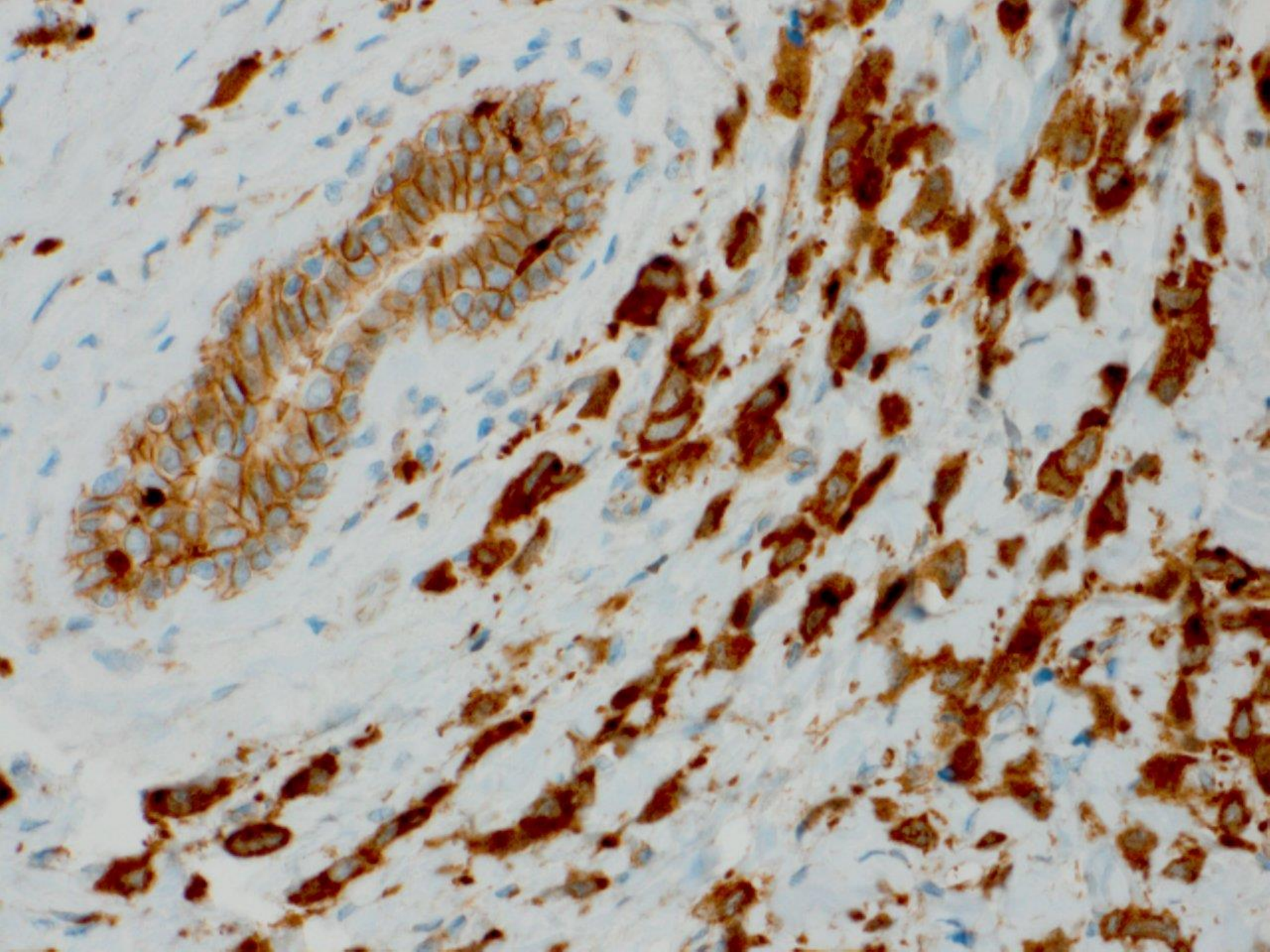
  Membranous in normal ducts and ductal ca

  Strong cytoplasmic: Lobular ca

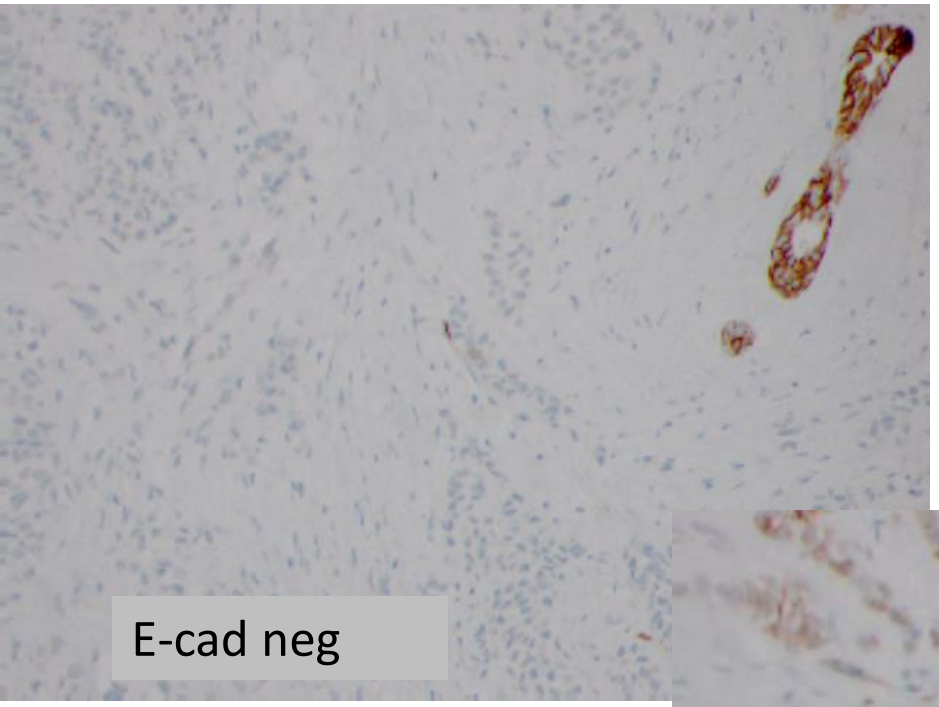
A combination of E-cad and p120 reduces the number of ambiguous diagnoses

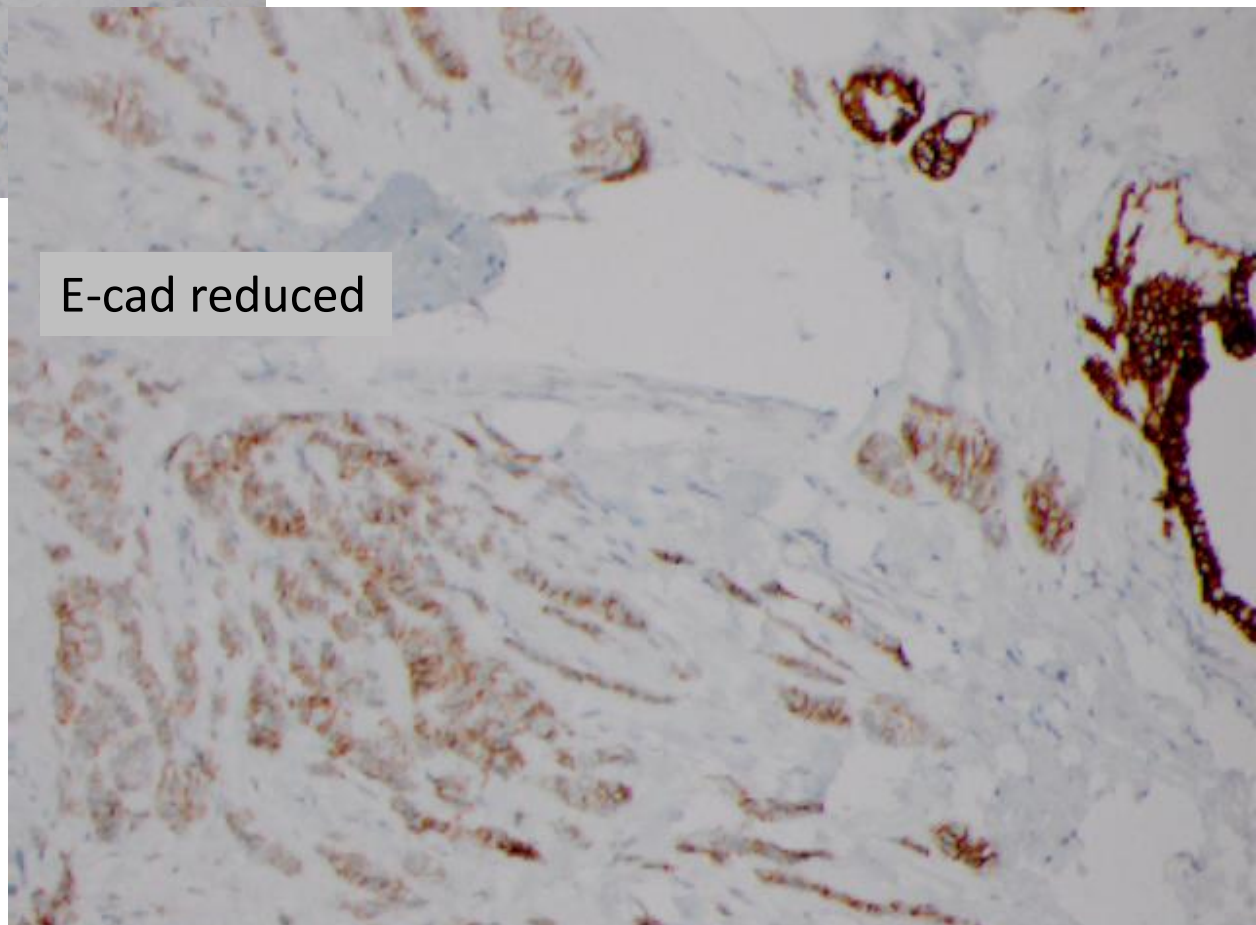

ILC, E-cad neg
Internal control pos

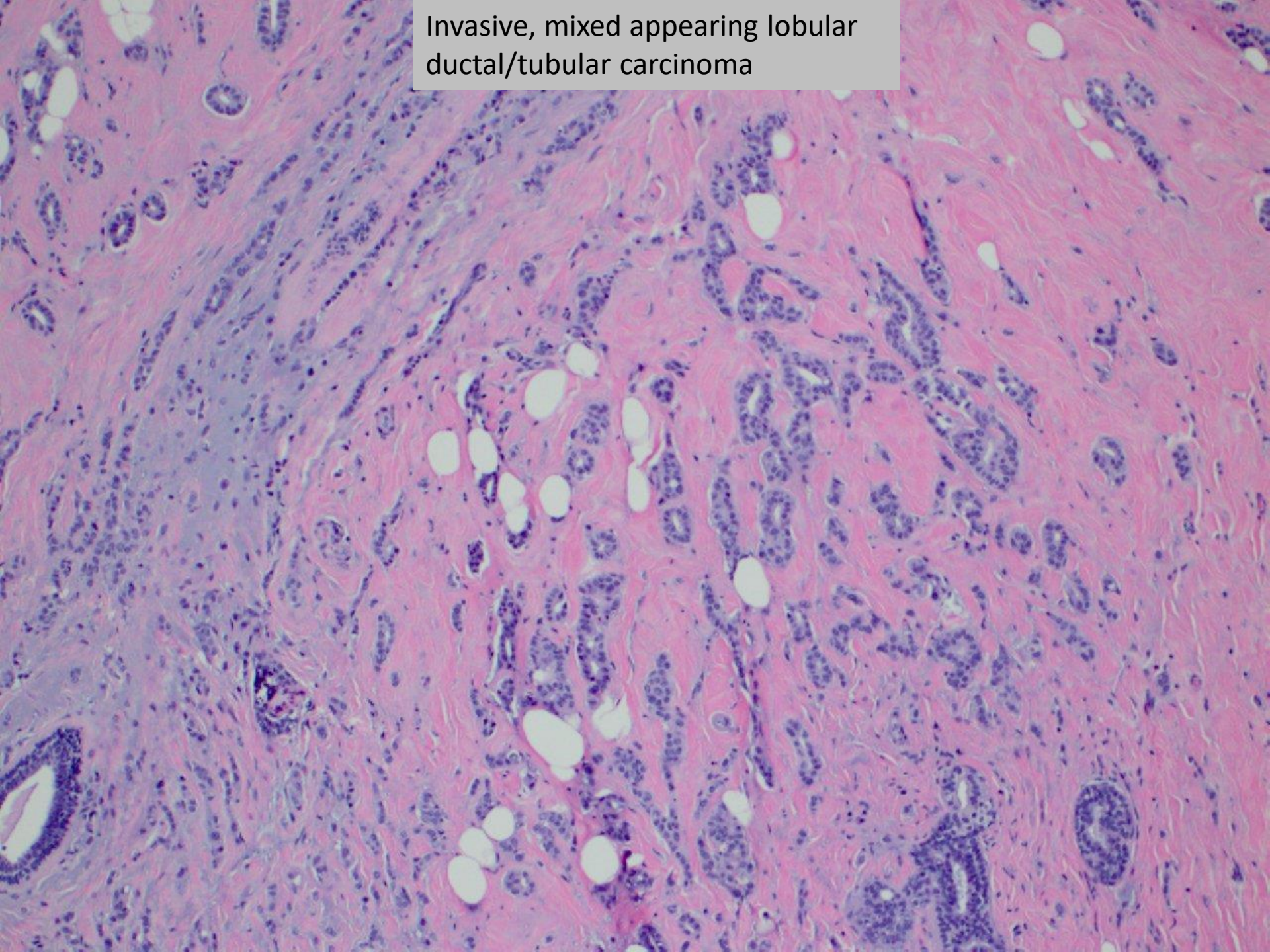

p120

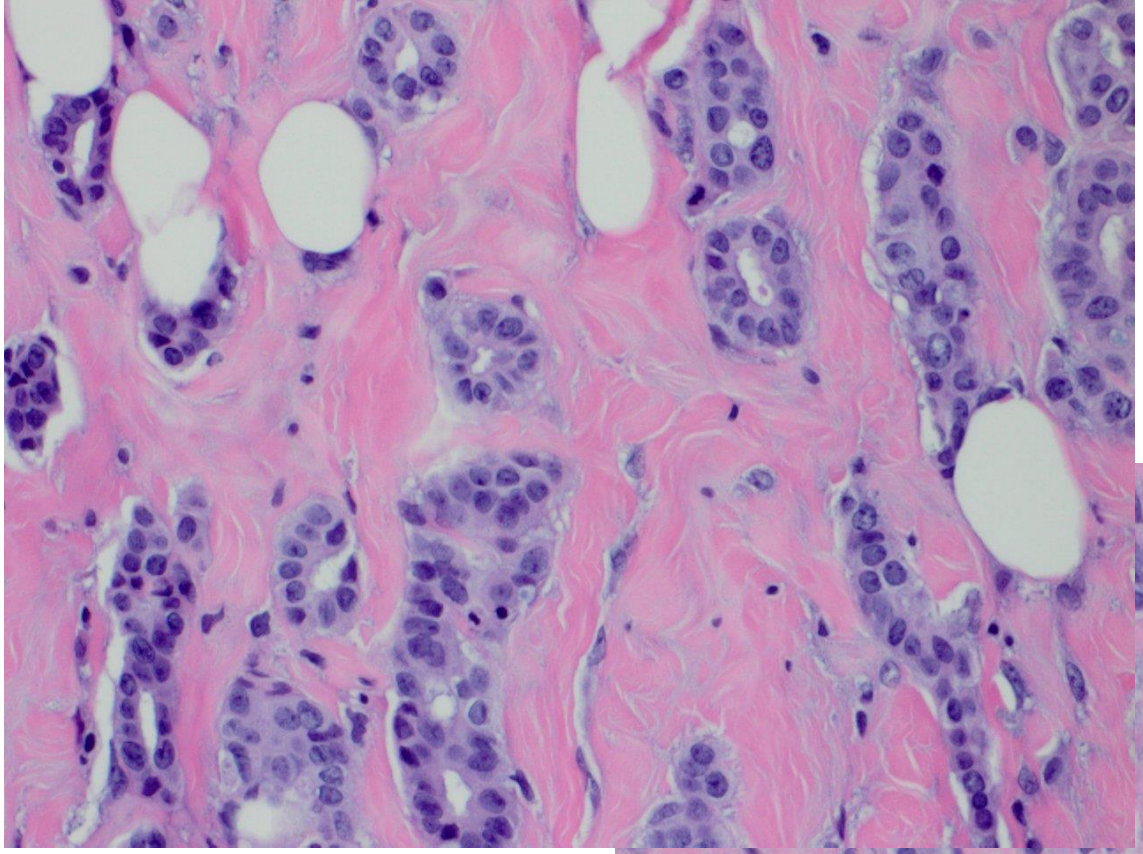
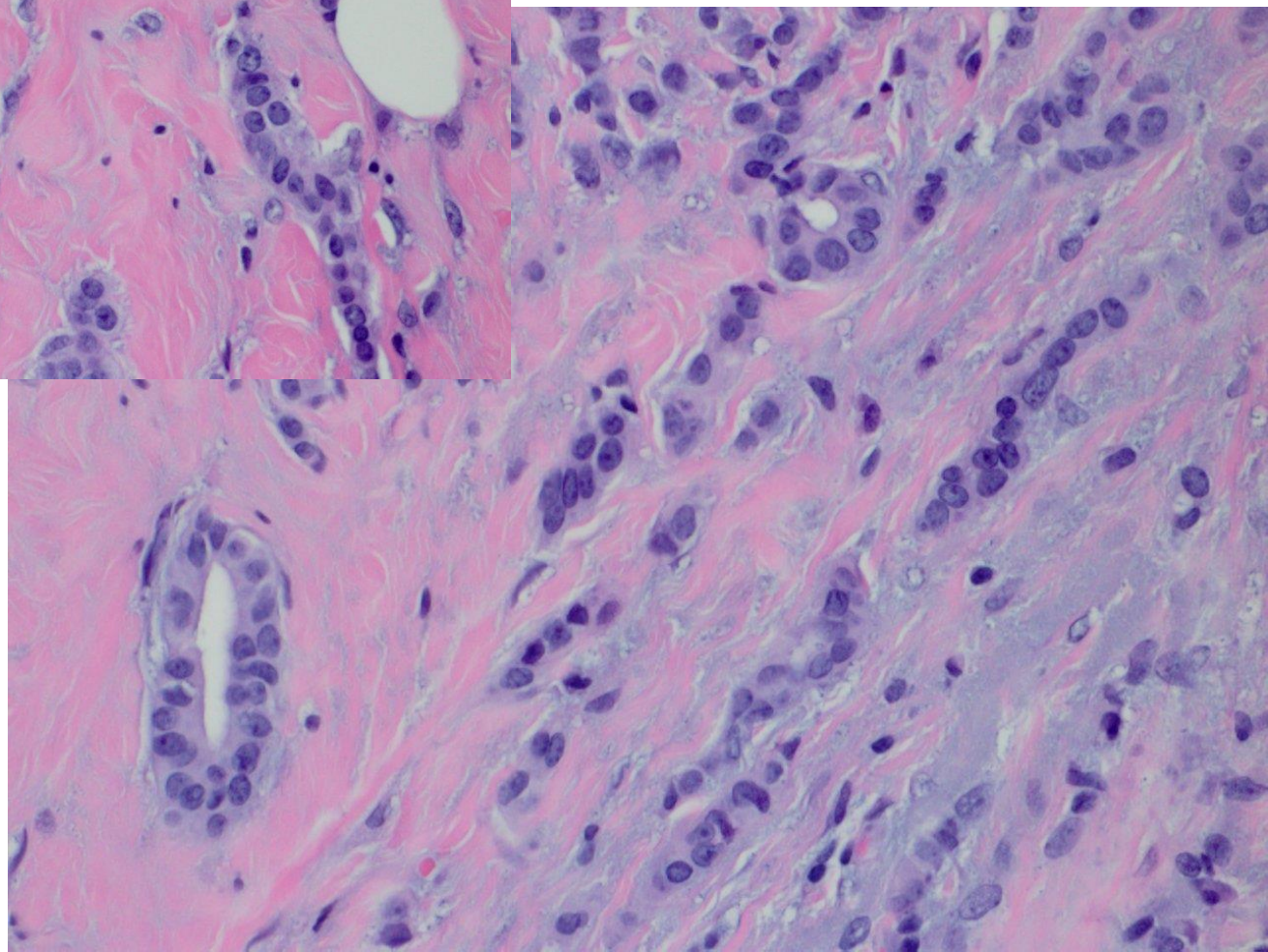


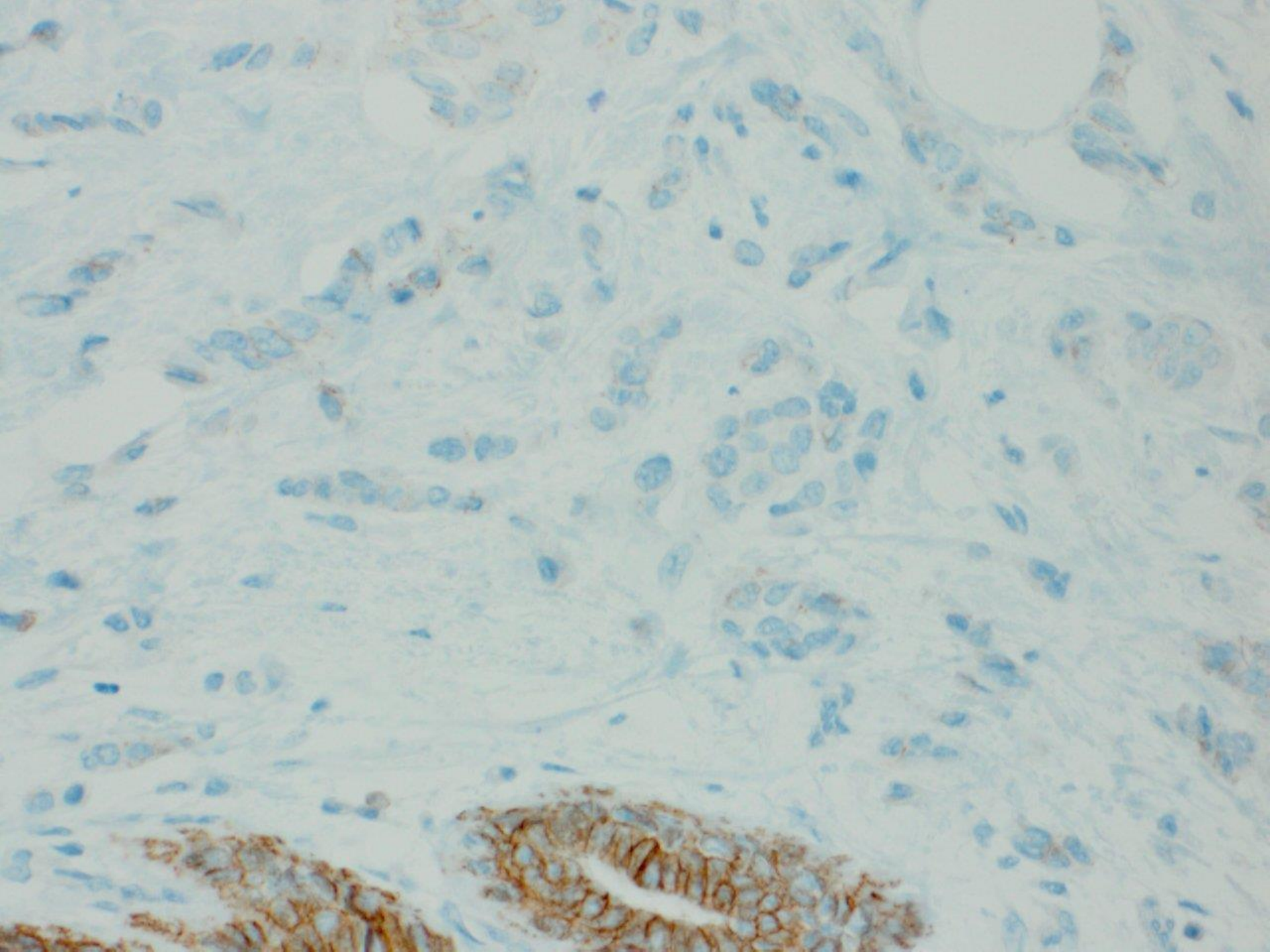
E-cad: other patterns (compared to normal ducts)

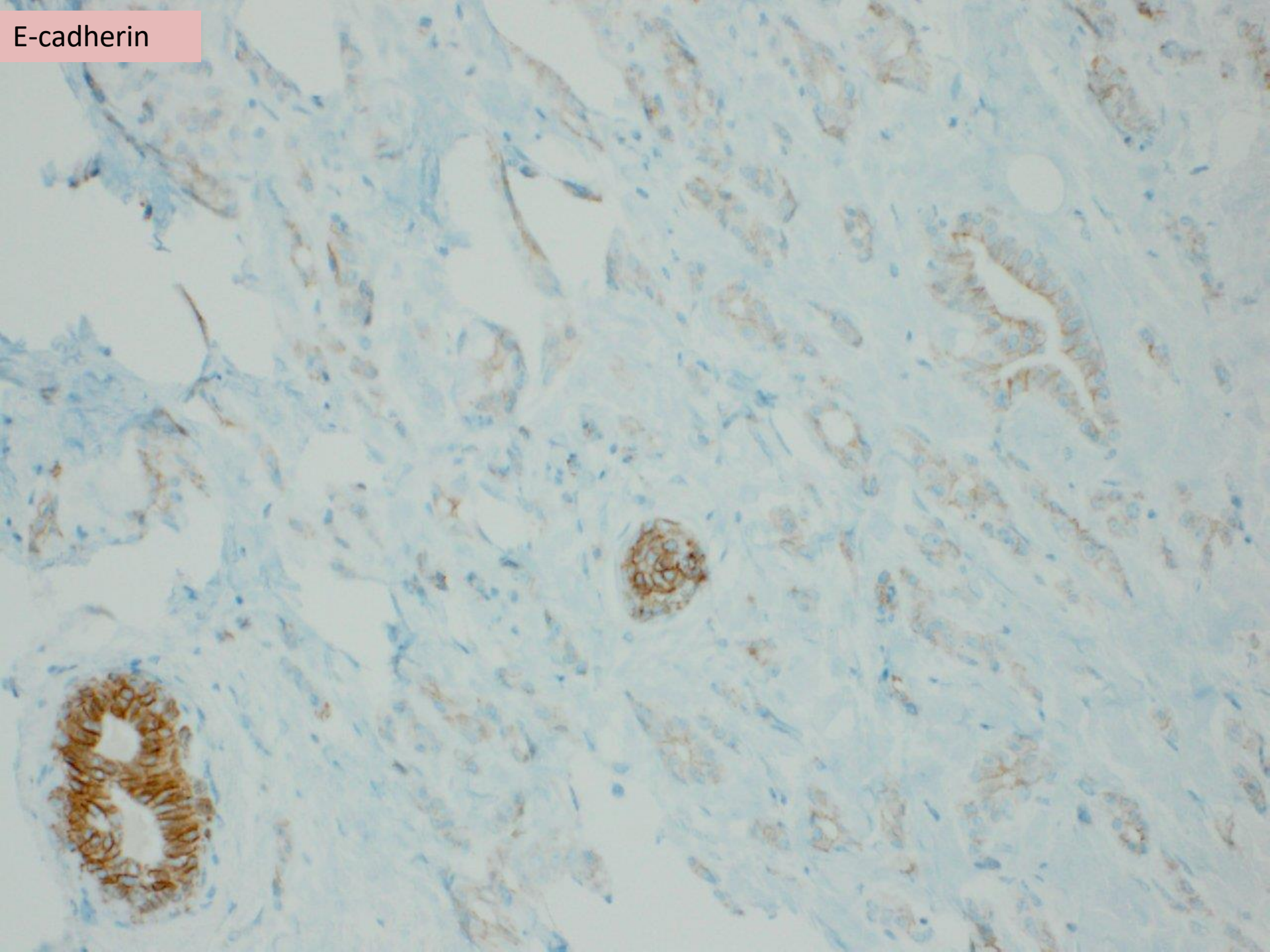


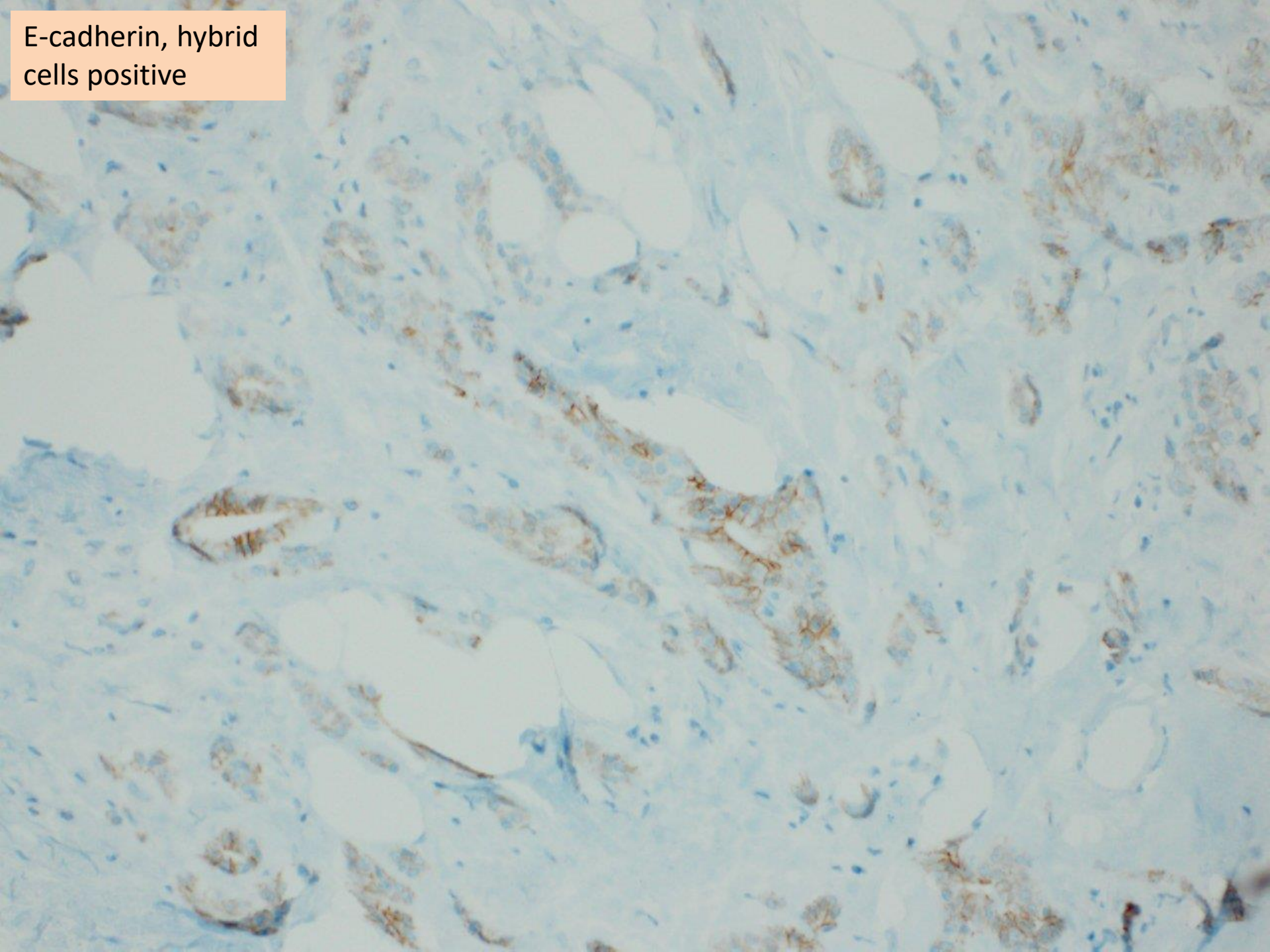


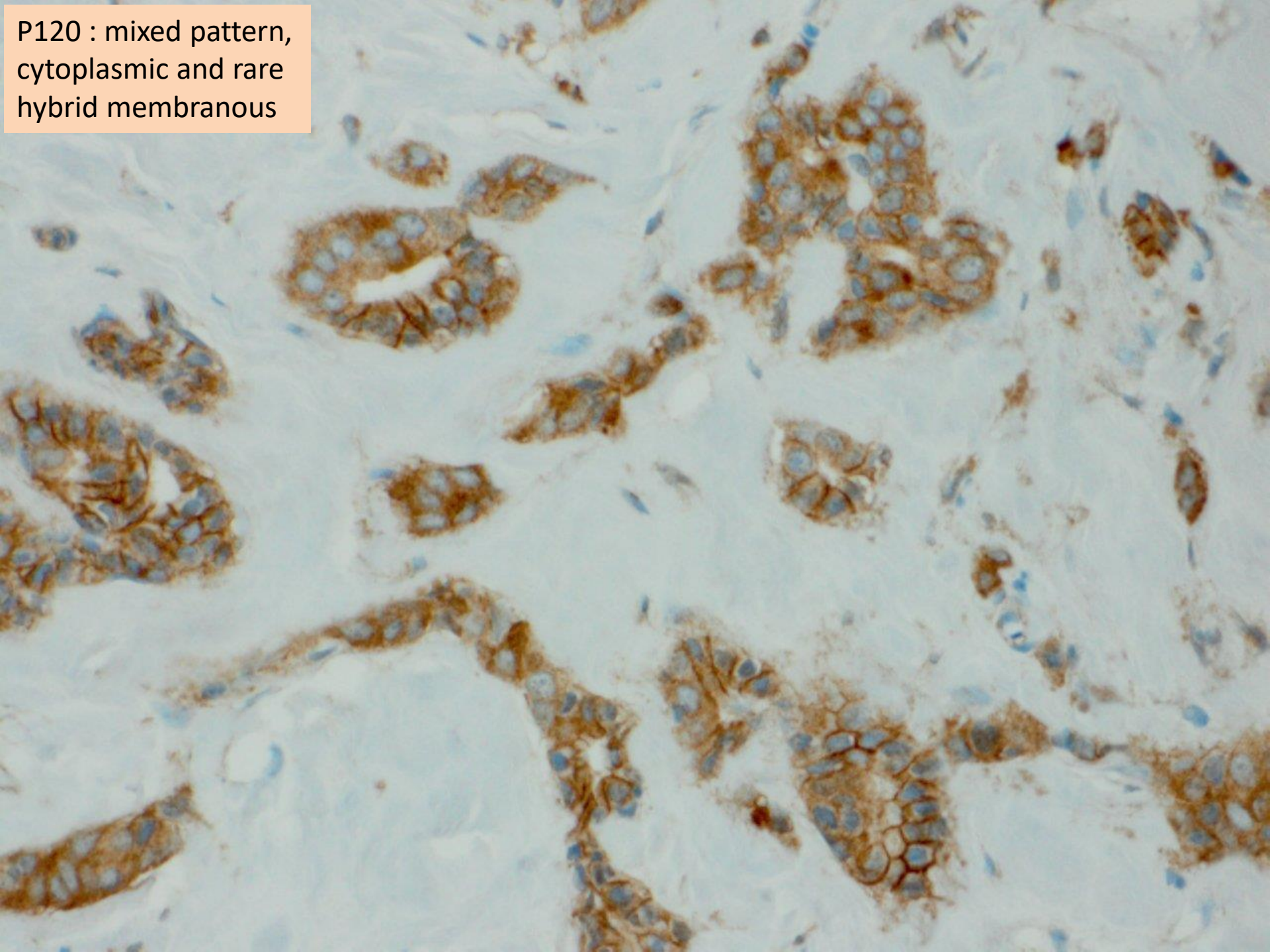

Invasive, mixed appearing lobular ductal/tubular carcinoma




E-cadherin


E-cadherin, hybrid cells positive


P120 : mixed pattern,
cytoplasmic and rare
hybrid membranous

E-cadherin /p120 Expression in LCIS

- Uncertain pattern: In situ carcinoma with mixed DL features/undeterminate

E-cadherin negative IDC

- 7.2% of cases
- **Associated significantly with larger tumor size and higher grade.**
- **More frequent in basal-like and triple-negative phenotypes**

Expression of E-cadherin, P120 catenin, and β-catenin

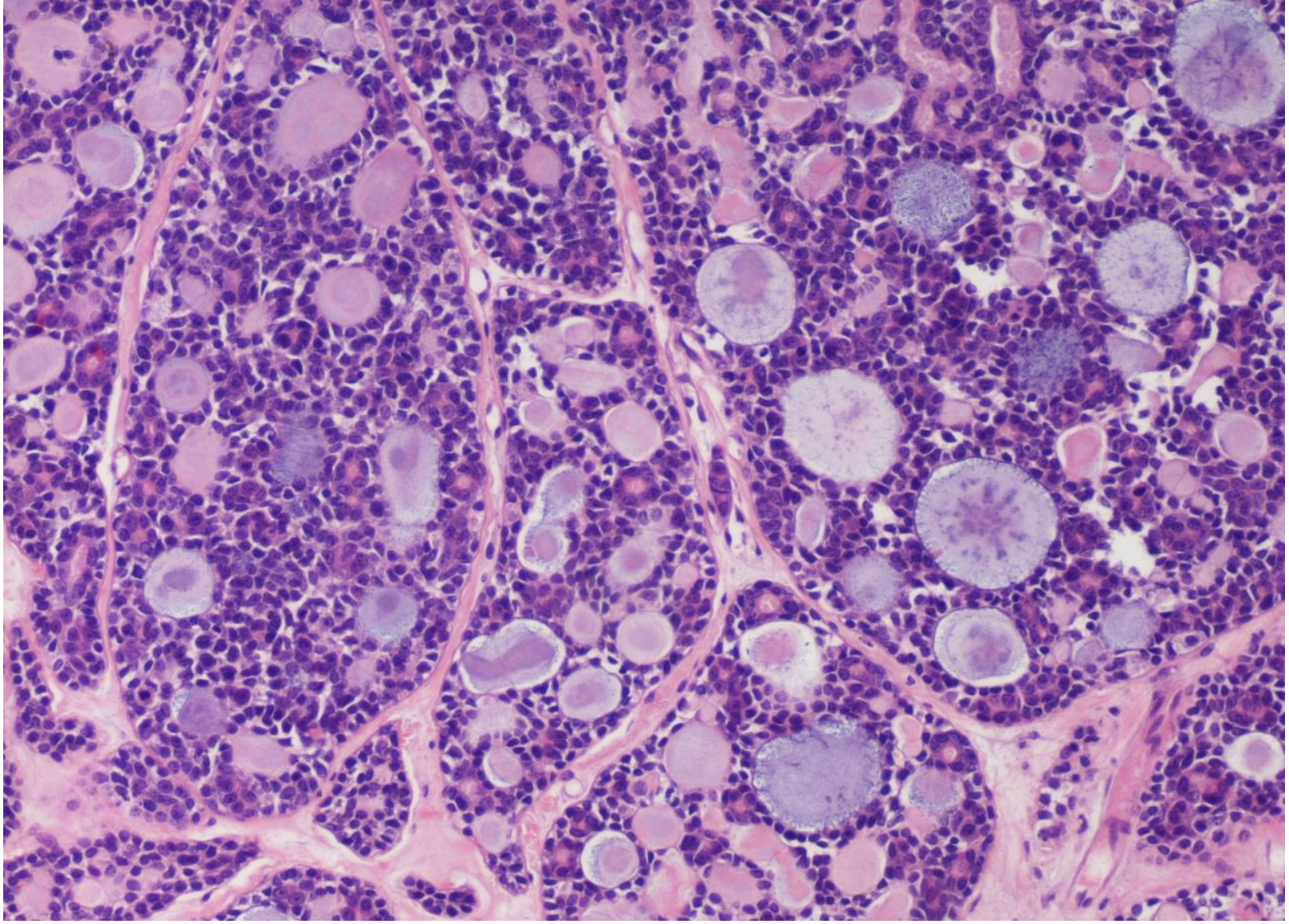
	Normal epithelium	Lobular carcinoma	Ductal carcinoma
E-cadherin	Membranous	Absence of M	Membranous
P120 catenin	Membranous	Cytoplasmic	Membranous
B-catenin	Membranous	Absence of M	Membranous

Immunohistochemistry in the Differential Diagnosis of:

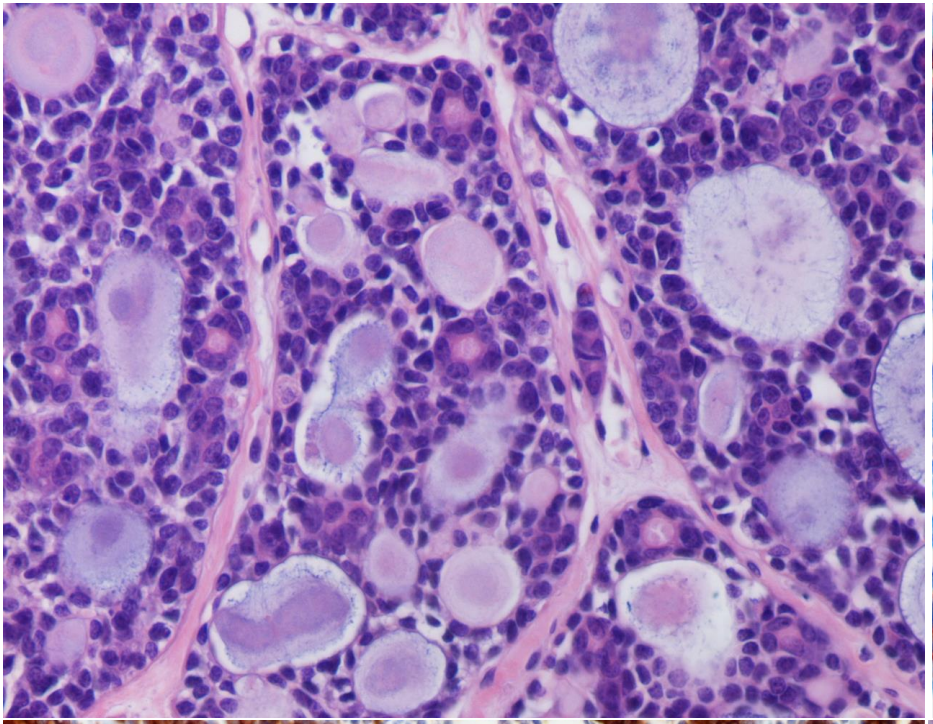
1. Lobular vs Ductal (especially in situ ca.)

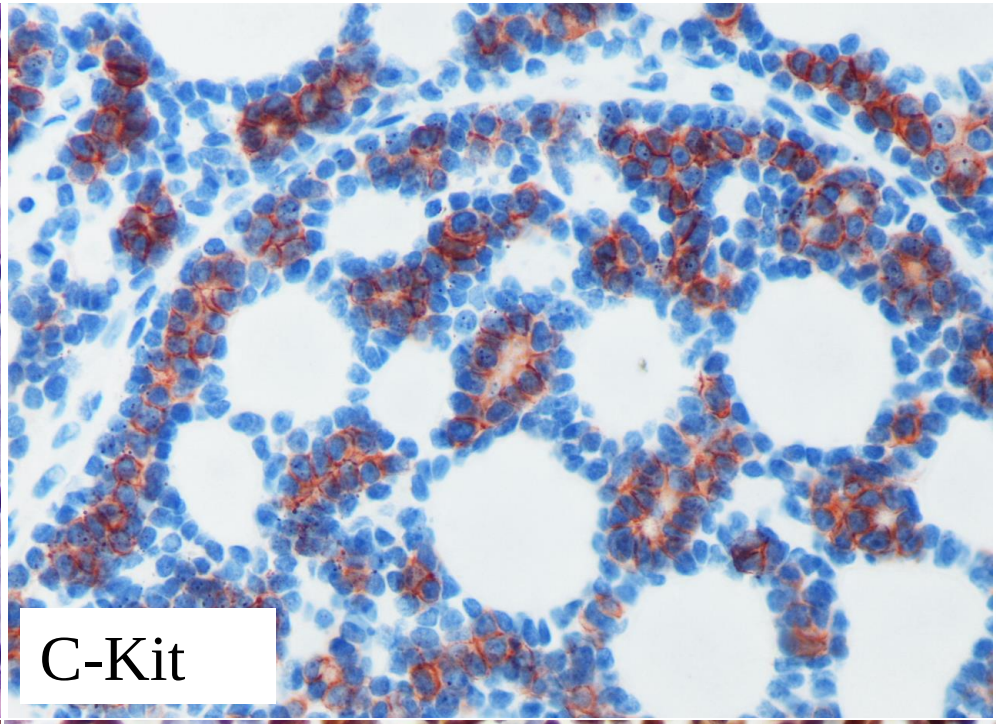
2. Adenoid cystic vs Cribriform ca vs Collagenous spherulosis

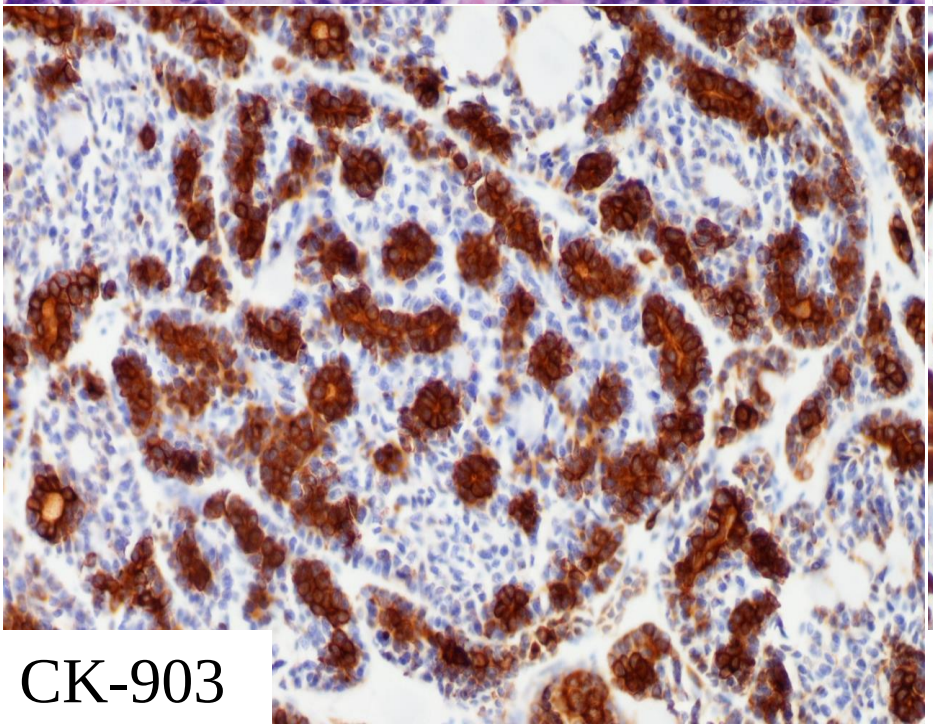
3. Spindle cell and Fibromatosis like metaplastic carcinomas vs other spindle cell lesions

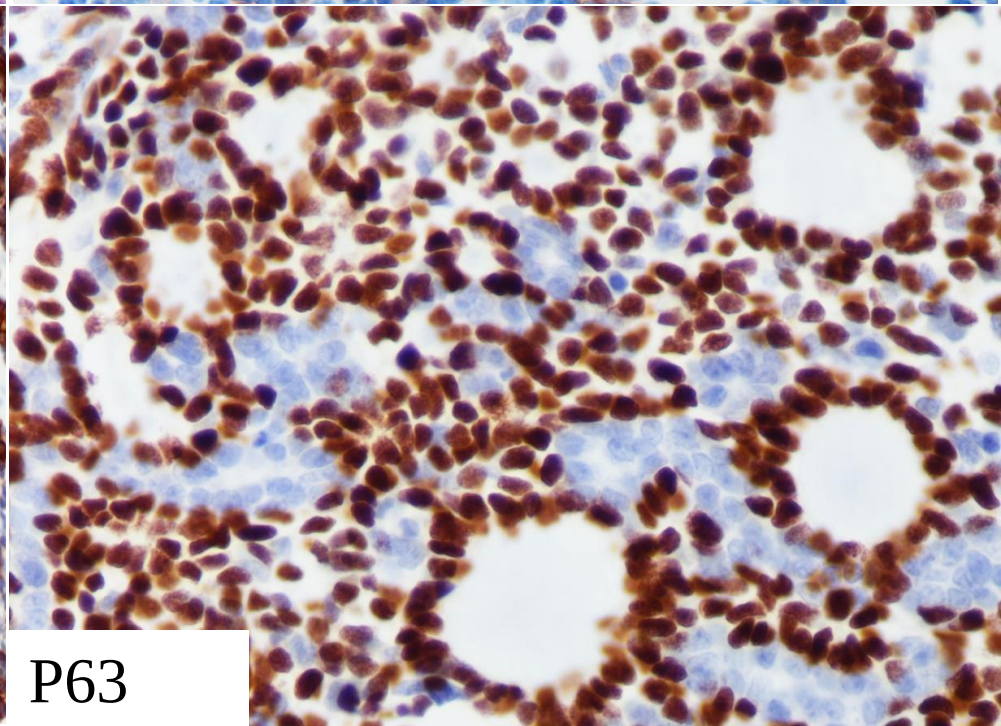


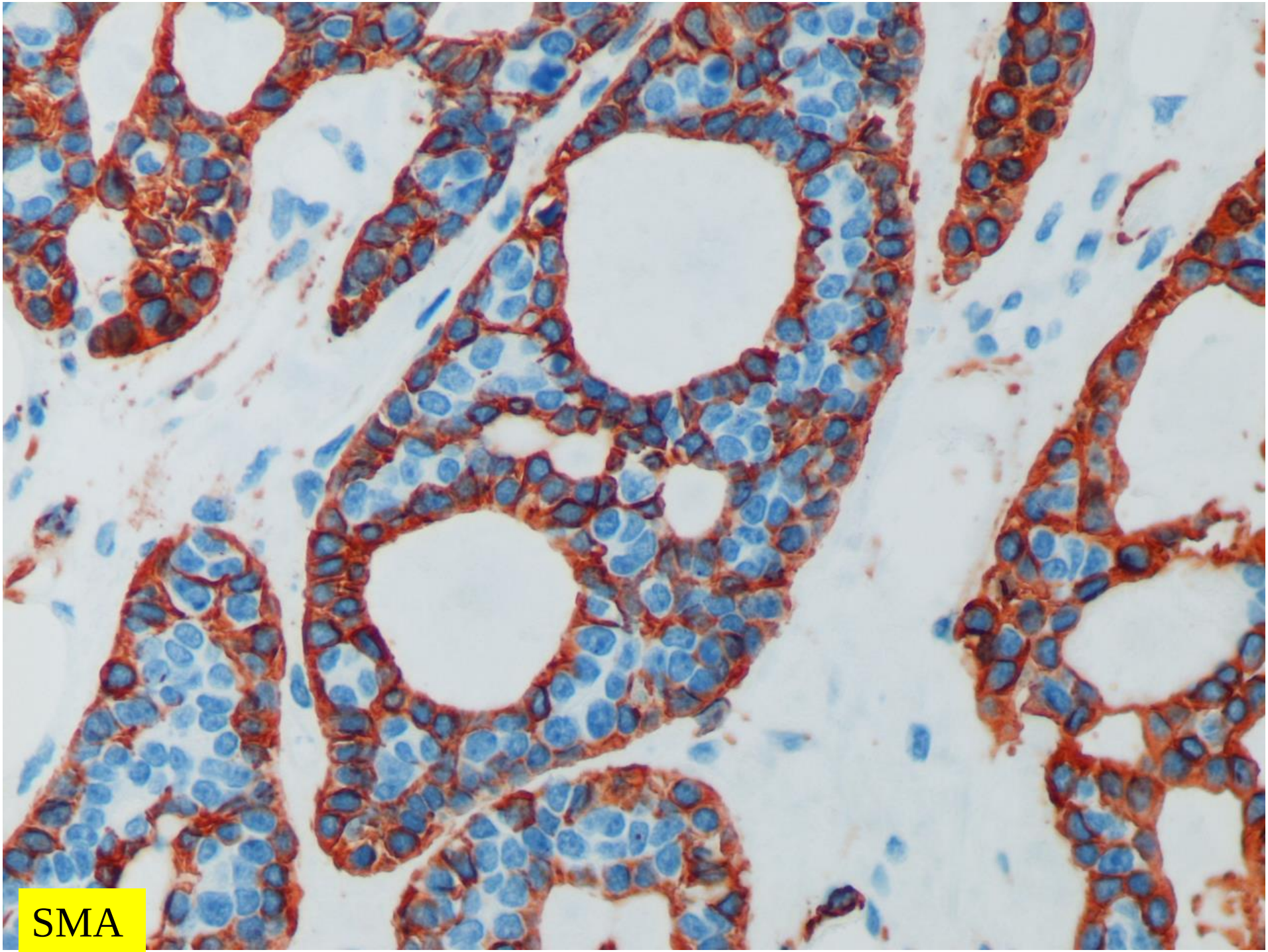
Two cell types: cuboidal epithelial cells lining tubular duct-like structures (PAS and mucin+) and myoepithelial-like cells that elaborate acid mucopolysaccharides and abundant basal lamina material (alcian blue+)

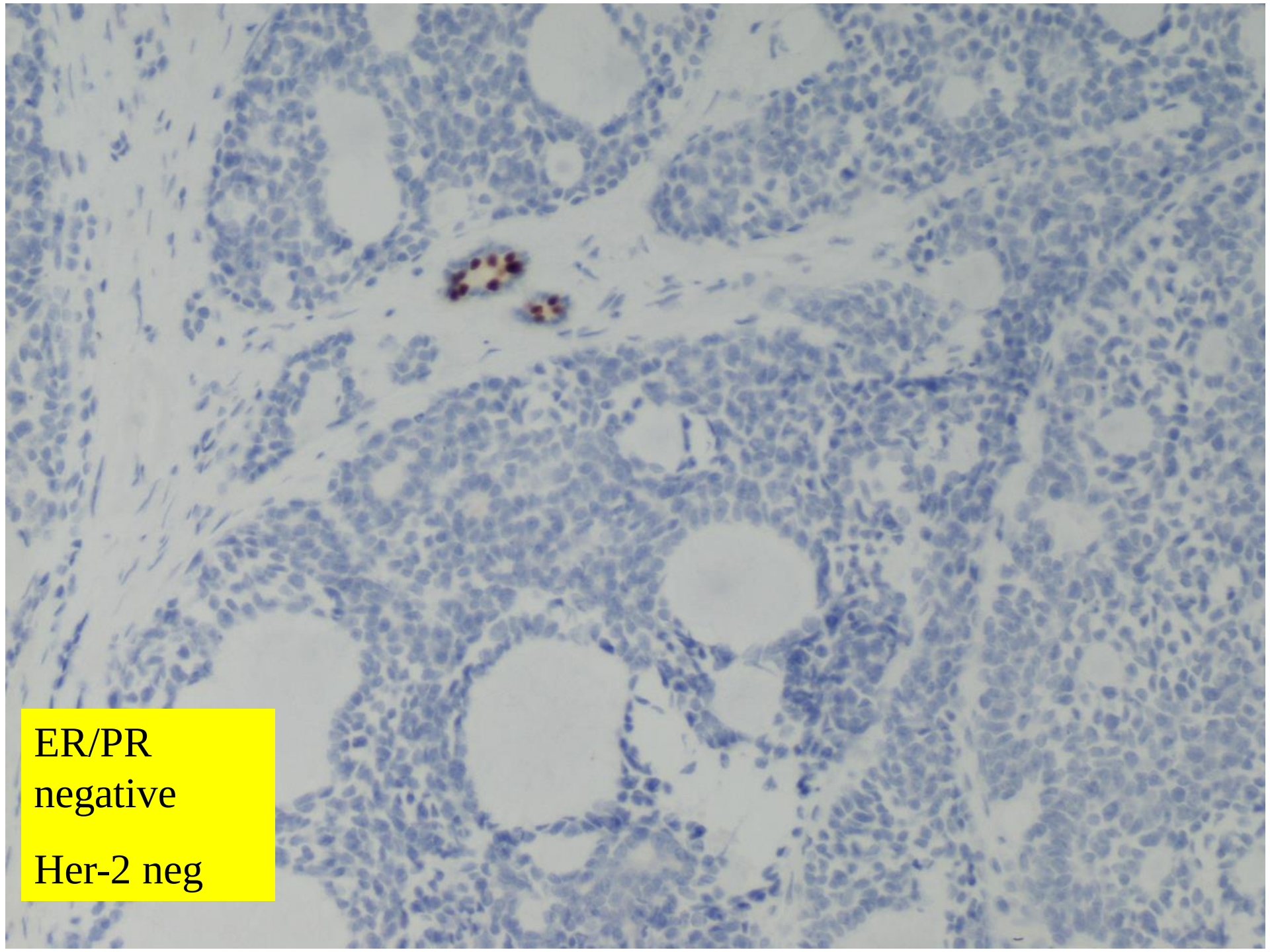



C-Kit


CK-903


P63


SMA


ER/PR
negative
Her-2 neg

IHC - adenoid cystic

- Myoepithelial cells: SMA, S100, SMMHC, HMW-ck and p63 positive

  (CD 10 neg)
- Lumen of pseudocyst: BM component,

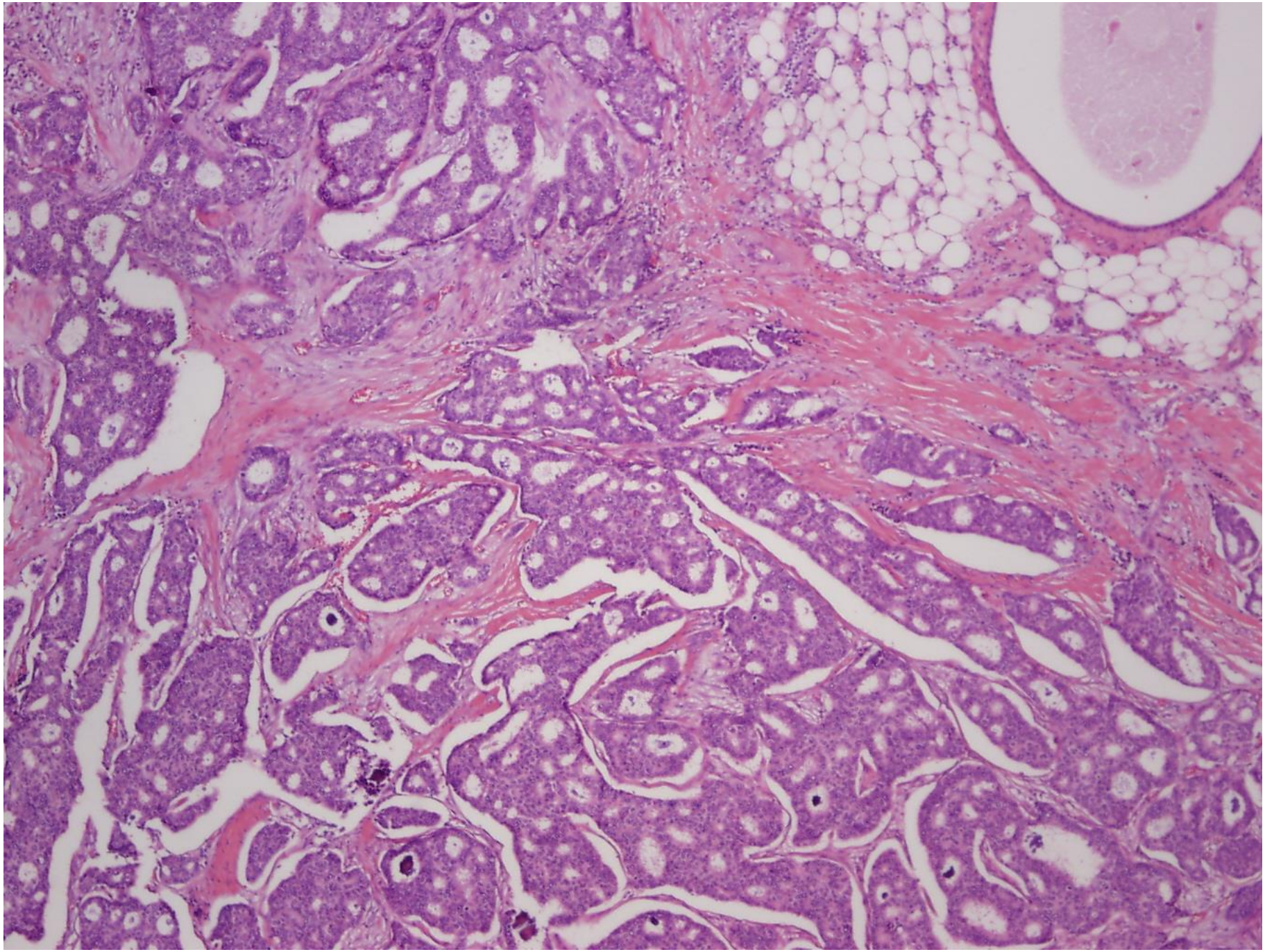
  IV collagen and laminin
- Epithelial cells: CK 8/18, and CK 903 pos.
- C-KIT (CD117): pos in all neoplastic cells regardless of grade
- ER/PR (0-46%)

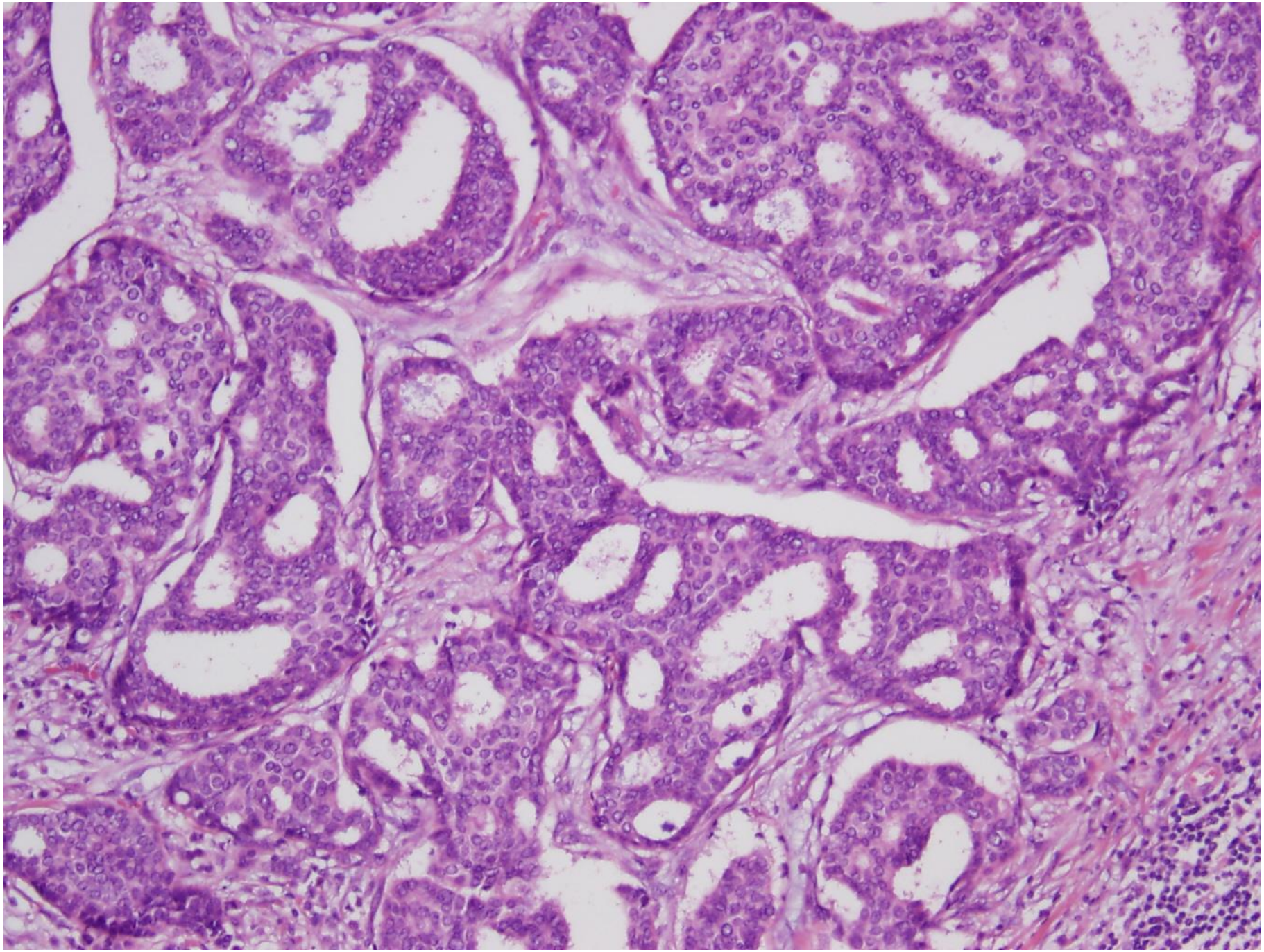
Genetics

similar to salivary gland ACCs

Recurrent chromosomal translocation t(6;9)(q22-23;p23-24)

fusion transcripts involving the genes MYB and NFIB





Cribriform Carcinoma

One cell type: Epithelial

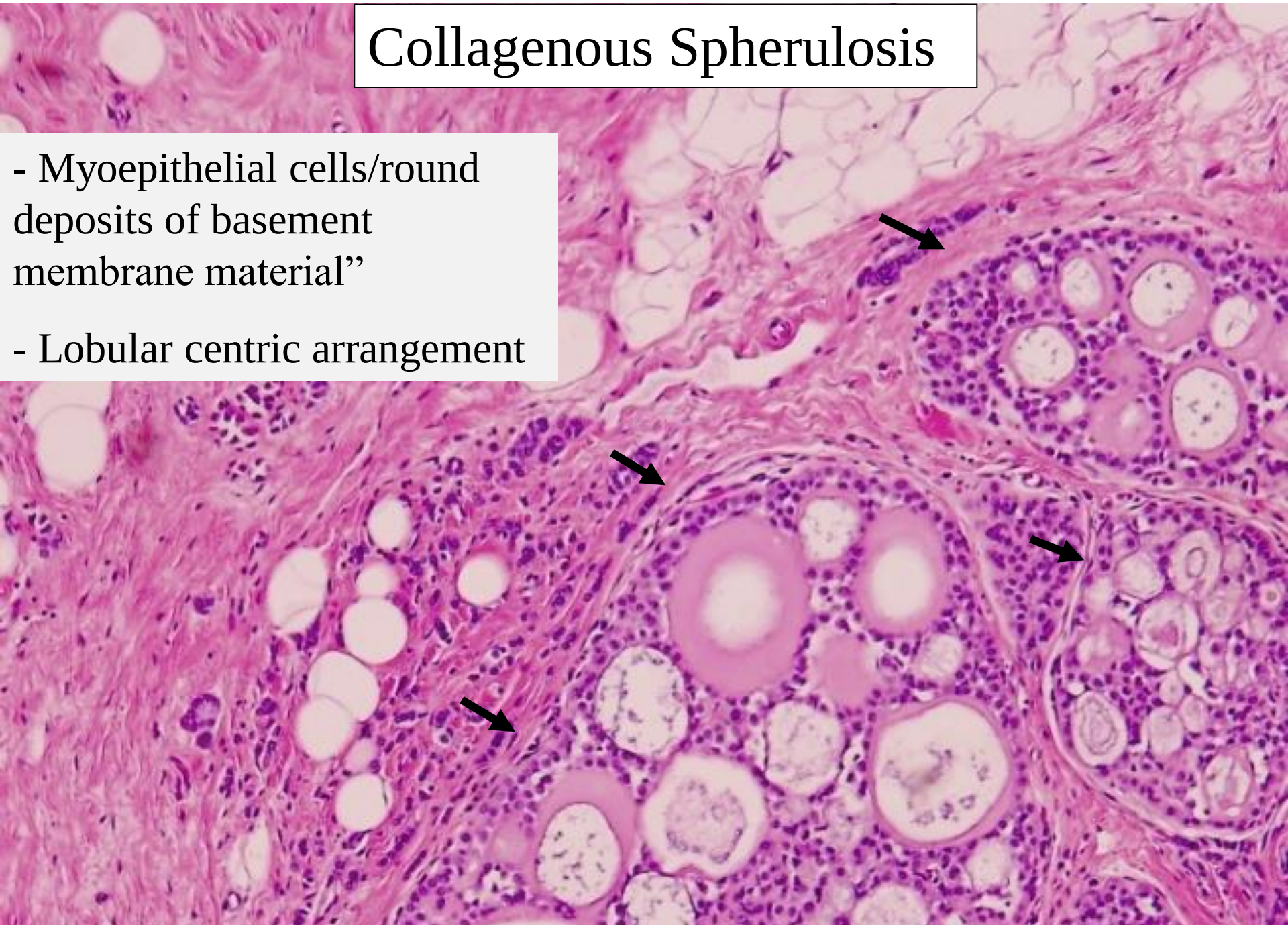
ER/PR abundant

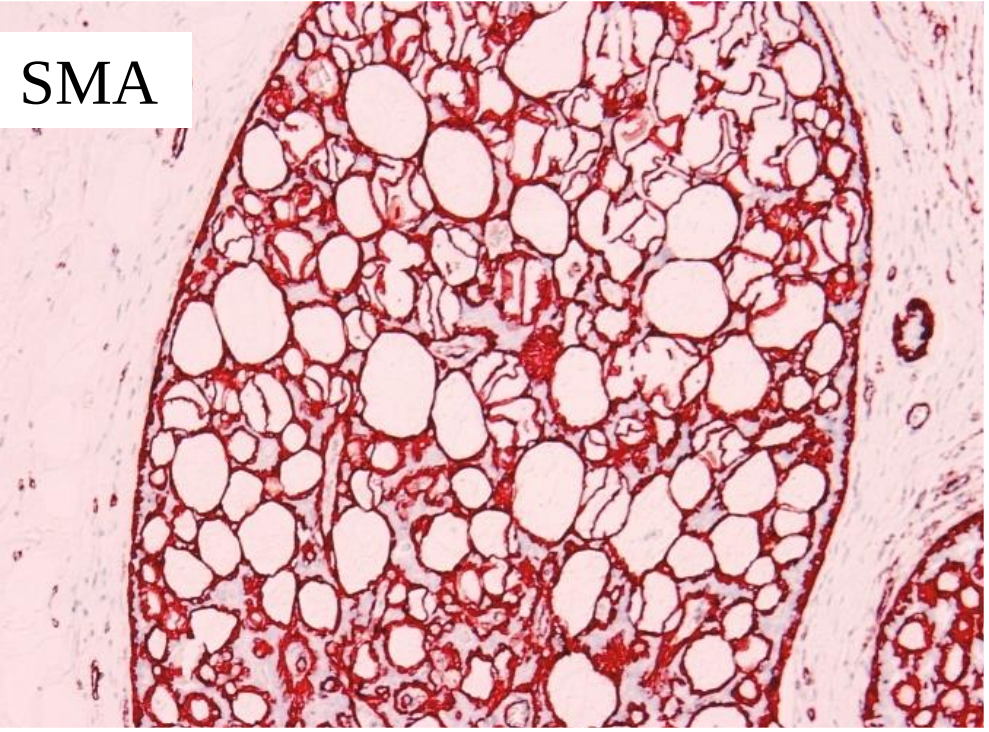
No myoepithelial cells (p63 and C-kit neg)

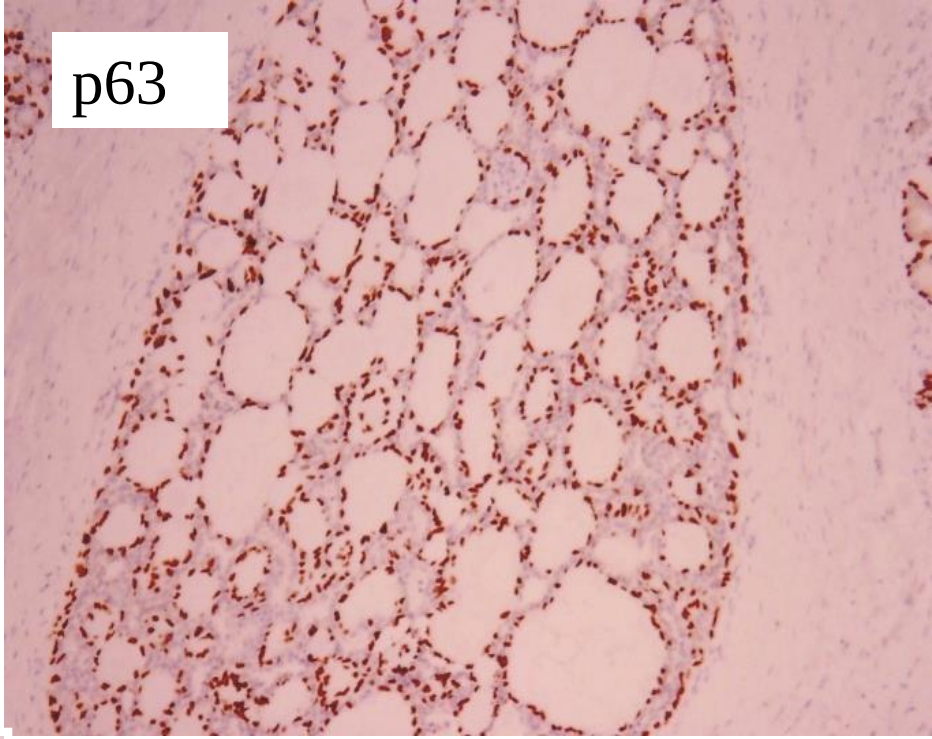
Collagenous Spherulosis

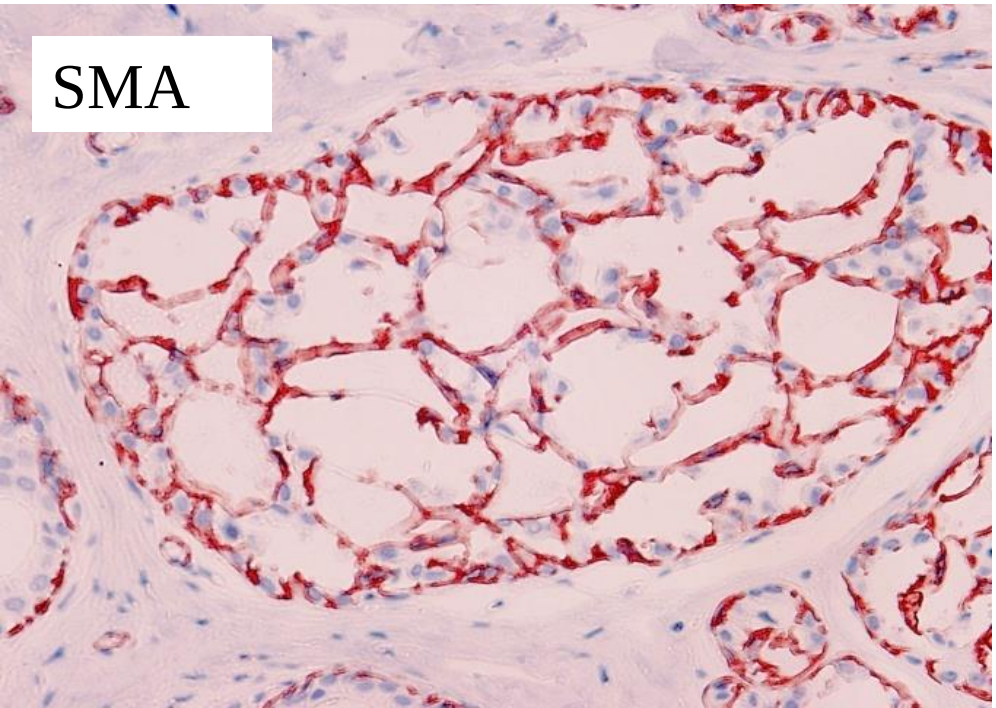
- Myoepithelial cells/round deposits of basement membrane material”

- Lobular centric arrangement

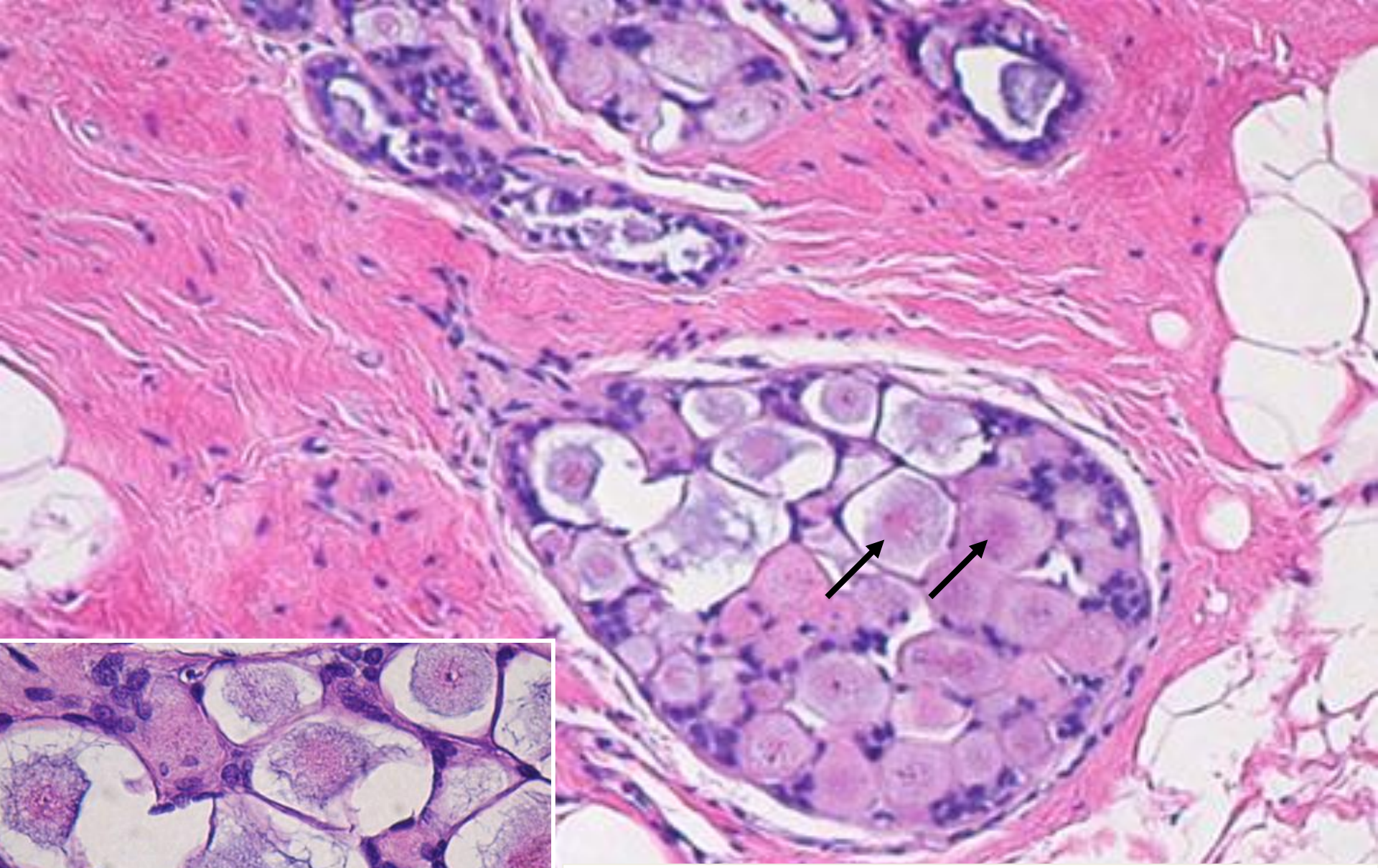




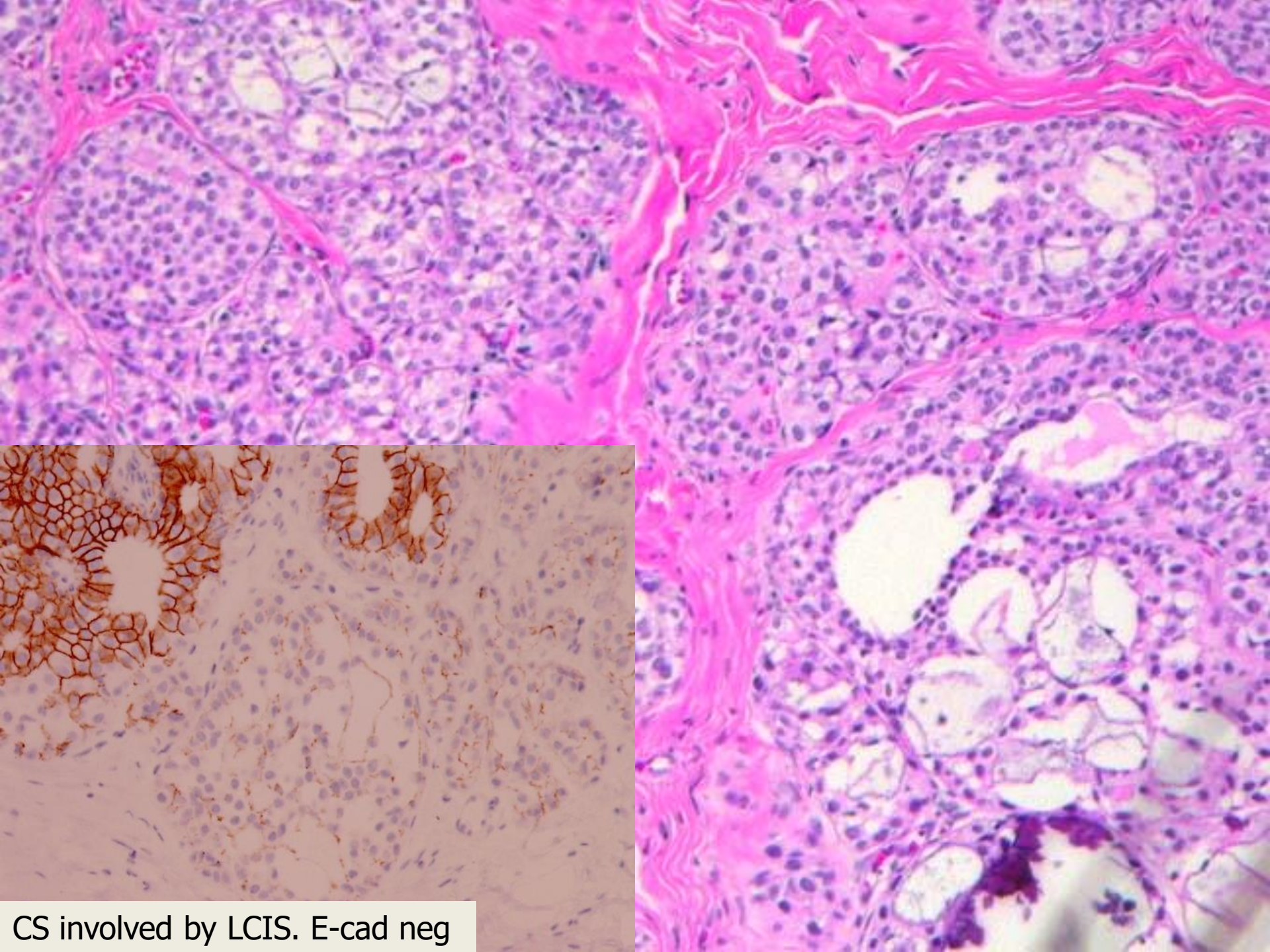




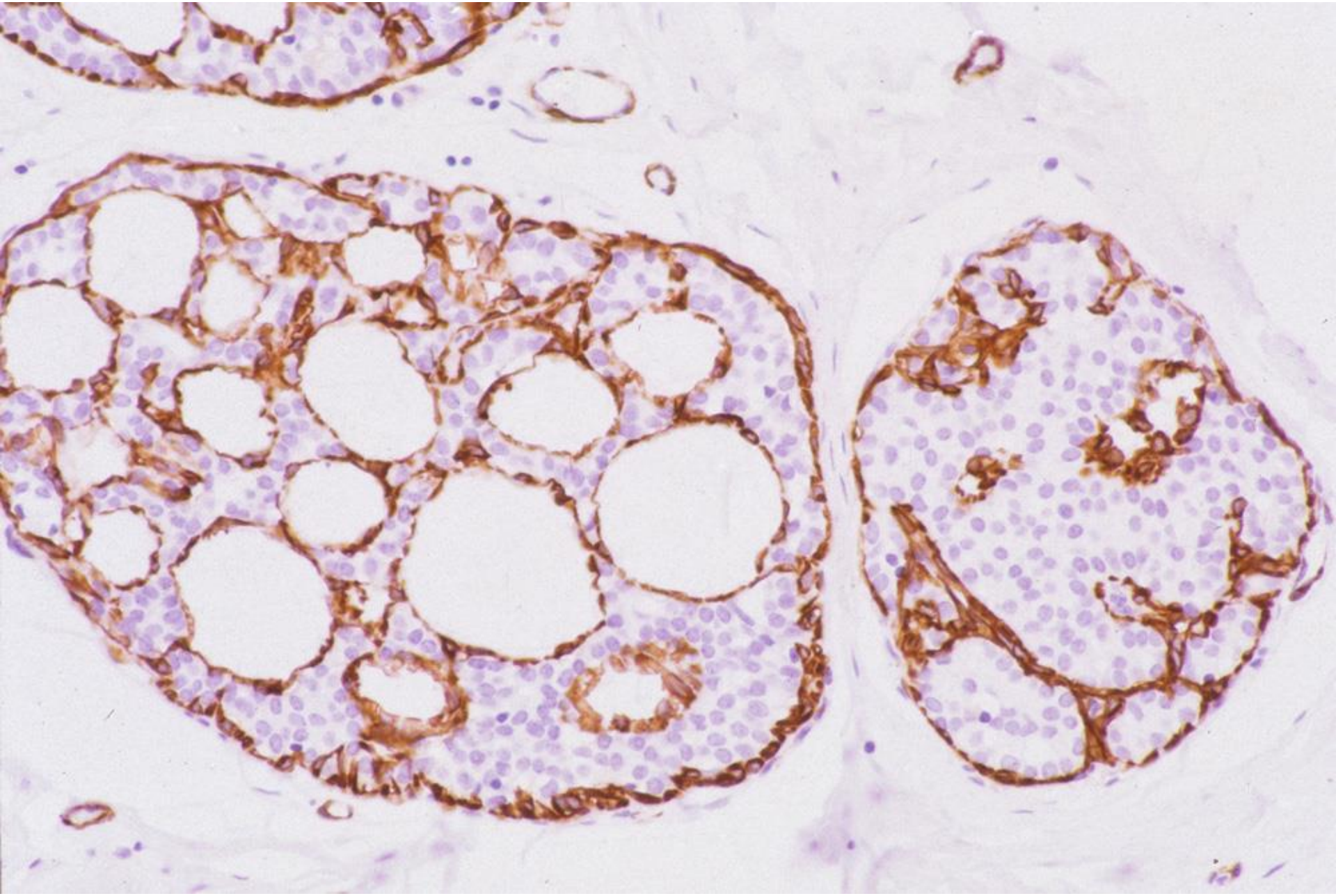
Collagenous spherulosis



Collagenous Spherulosis: densley packed membrane-like material and stellate fibrils radiating from central nidus



CS involved by LCIS. E-cad neg



Immunohistochemistry in the Differential Diagnosis of:

1. Lobular vs Ductal (especially in situ ca.)

2. Adenoid cystic vs Cribriform ca vs Collagenous spherulosis

3. Spindle cell and Fibromatosis-like metaplastic carcinomas vs other spindle cell lesions

Metaplastic carcinoma

1. Low-grade adenosquamous carcinoma
2. Fibromatosis-like metaplastic carcinoma
3. Spindle cell carcinoma
4. Squamous cell carcinoma
5. Metaplastic carcinoma with mesenchymal differentiation
6. Mixed metaplastic carcinoma

WHO Definition: Differentiation of the neoplastic epithelium into squamous and/or mesenchymal elements (spindle, chondroid, osseous and rhabdomyoid cells)

Immunoprofile of Metaplastic Carcinomas of the Breast

Rakha et al, 2017, 975-985, Histopathology

AE1/AE3 and MNF116 80%
Basal CK (34bE12, CK5/6,CK14, and CK17) 70 %
Luminal CK (CK8/18,CK7 and CK19) 30-60%
P63 75% (SCC) and 94% (FLSSC)

CD34 consistently neg (positive in PT)

Overlapping features with myoepithelial ca (strong HMW ck and nuclear p63, and weak LMW ck). Current recommendation is consider these tumors excluding adenomyoepithelioma as MBC. No internationally accepted definition of the morphological and immunpphenotypical characteristics of myoepithelial carcinoma.

Immunoprofile of metaplastic carcinomas of the breast

Emad A Rakha et al. Histopathology, December 2016

A cut-off of ≥50% metaplastic elements was used in this study

Although several cut-offs have been used in the literature (<10%, >10%, ≥20% or ≥50%), there is no international consensus on the percentage of metaplastic component within a tumor to define MBC

Immunoprofile of MBC

Emad Rakha et al. Histopathology, December 2016

- 172 local cases (1/2 spindle cells):

57 spindle cell MBC

36 matrix-producing MBC

30 squamous cell carcinomas (SCC)

23 fibromatosis-like MBC

3 low-grade adenosquamous carcinoma

and 23 tumours of mixed type

Simplified approach to spindle cell lesions of the breast

Low grade/Bland

vs

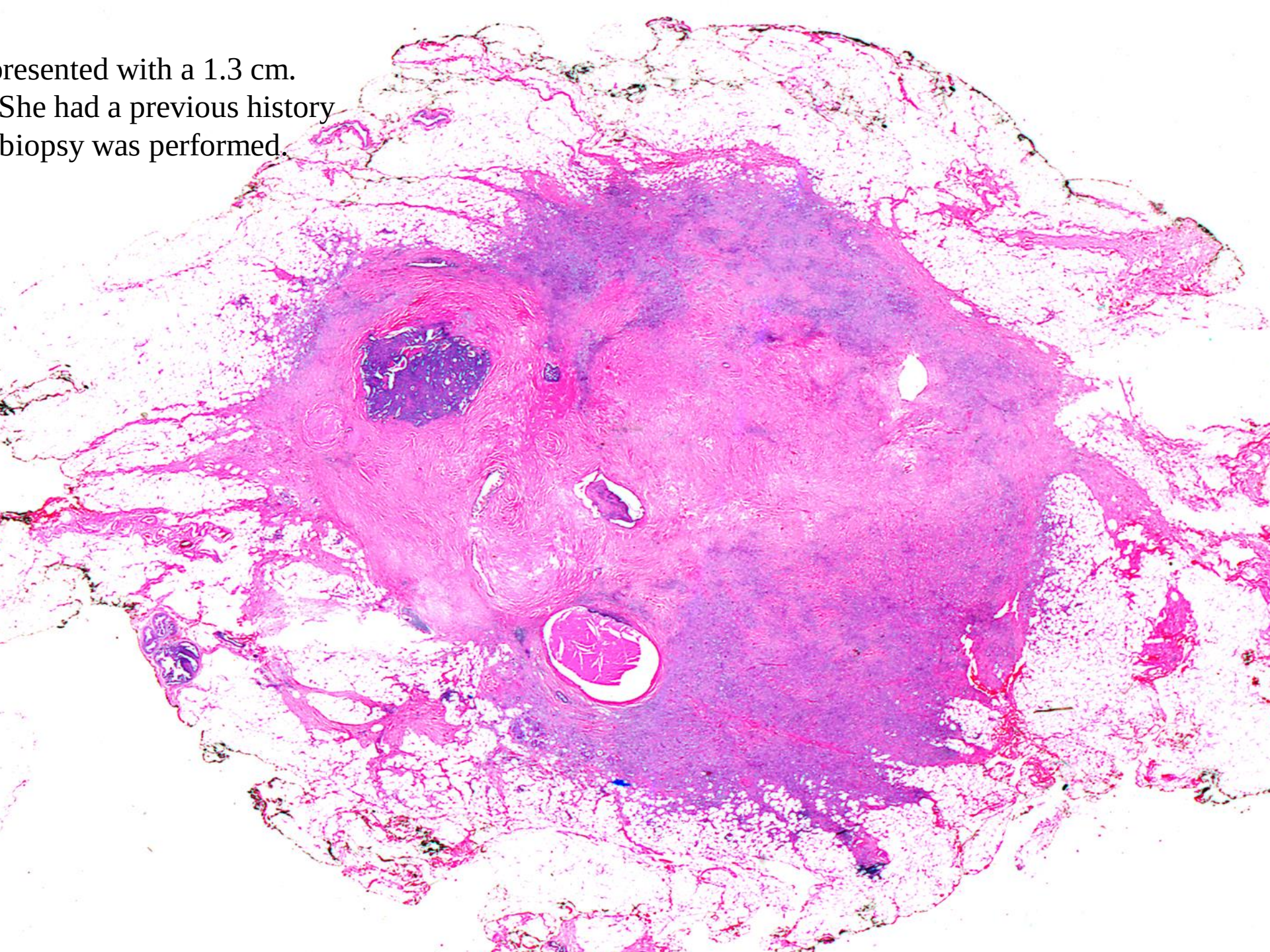
High grade /malignant appearing

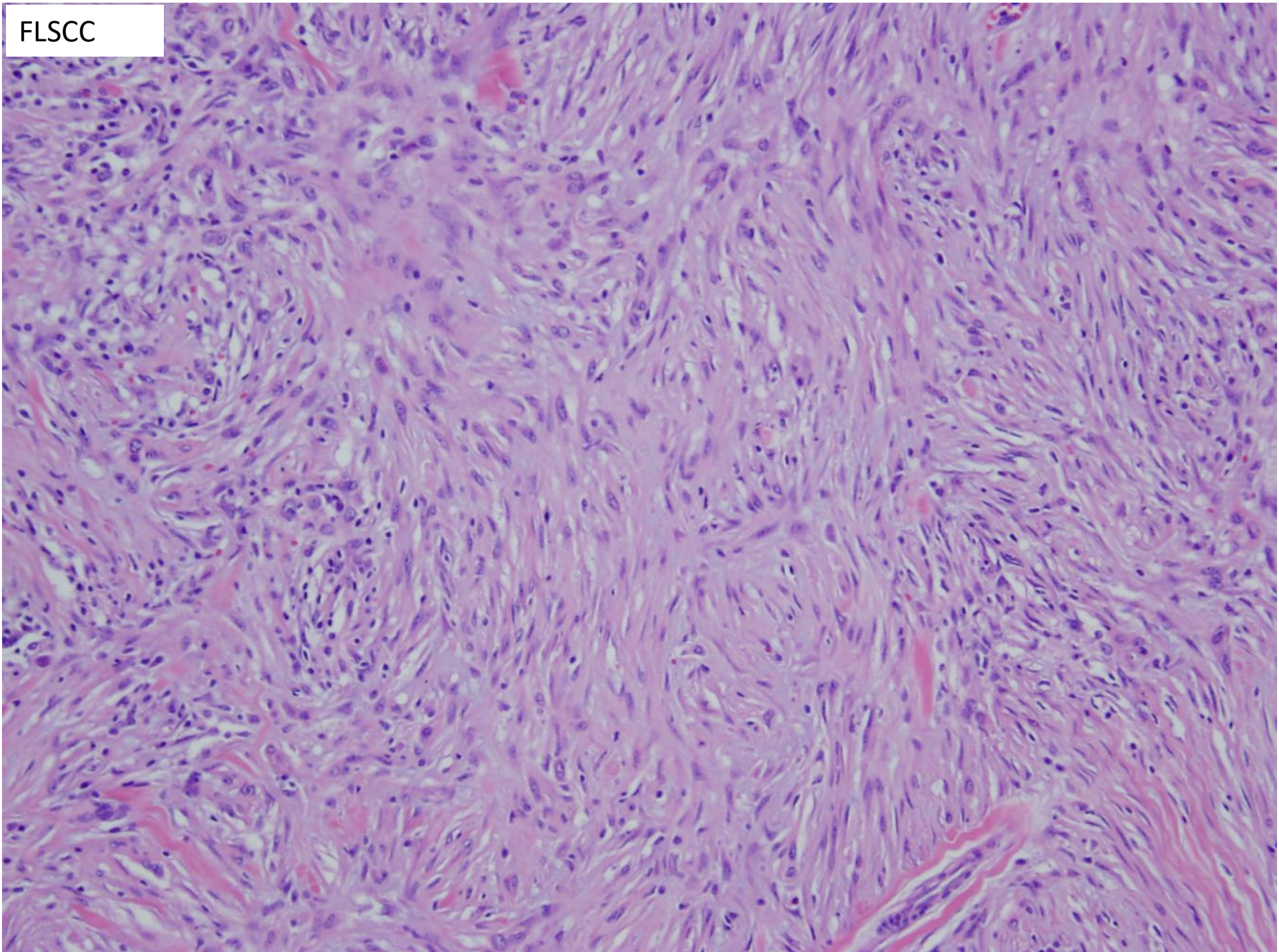
Bland-Looking Spindle Cell Lesions of the Breast

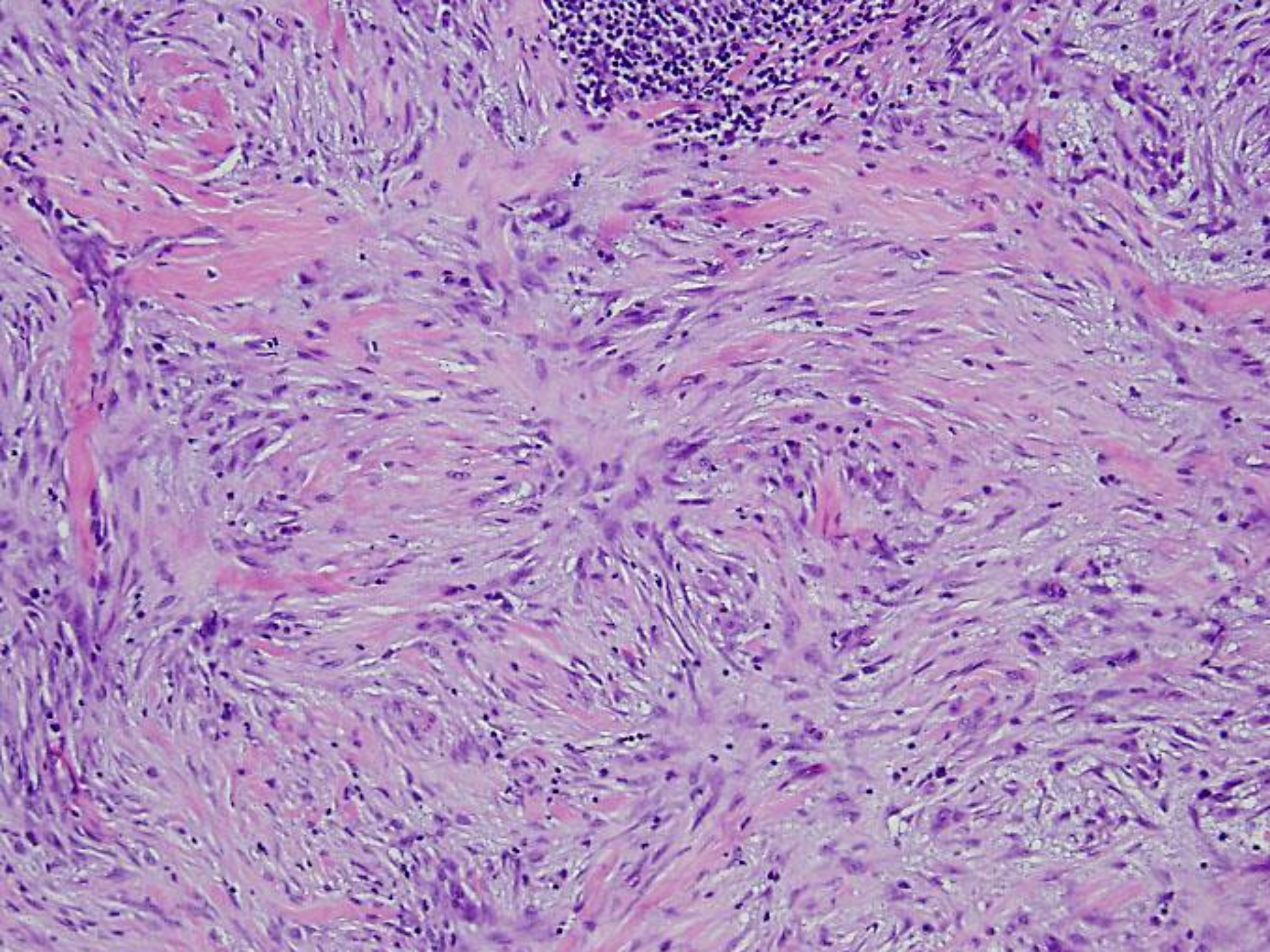
- Fibromatosis like spindle cell carcinoma

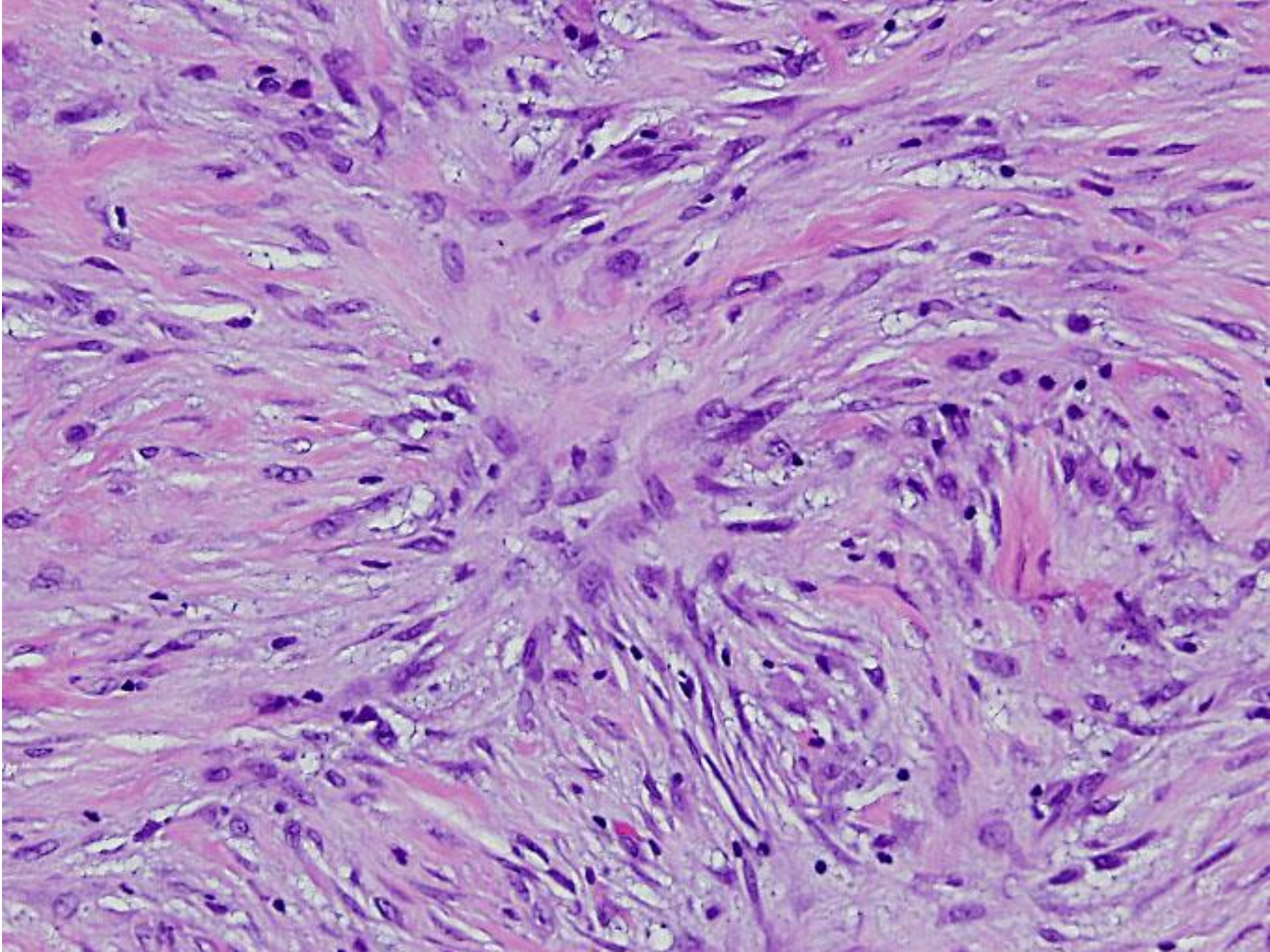
  Almost all positive for at least one CK
- Reactive spindle cell nodules after CNB
- Nodular fasciitis
- Inflammatory myofibroblastic tumors
- Myofibroblastoma
- Fibromatosis
- Pseudoangiomatous hyperplasia (PASH)

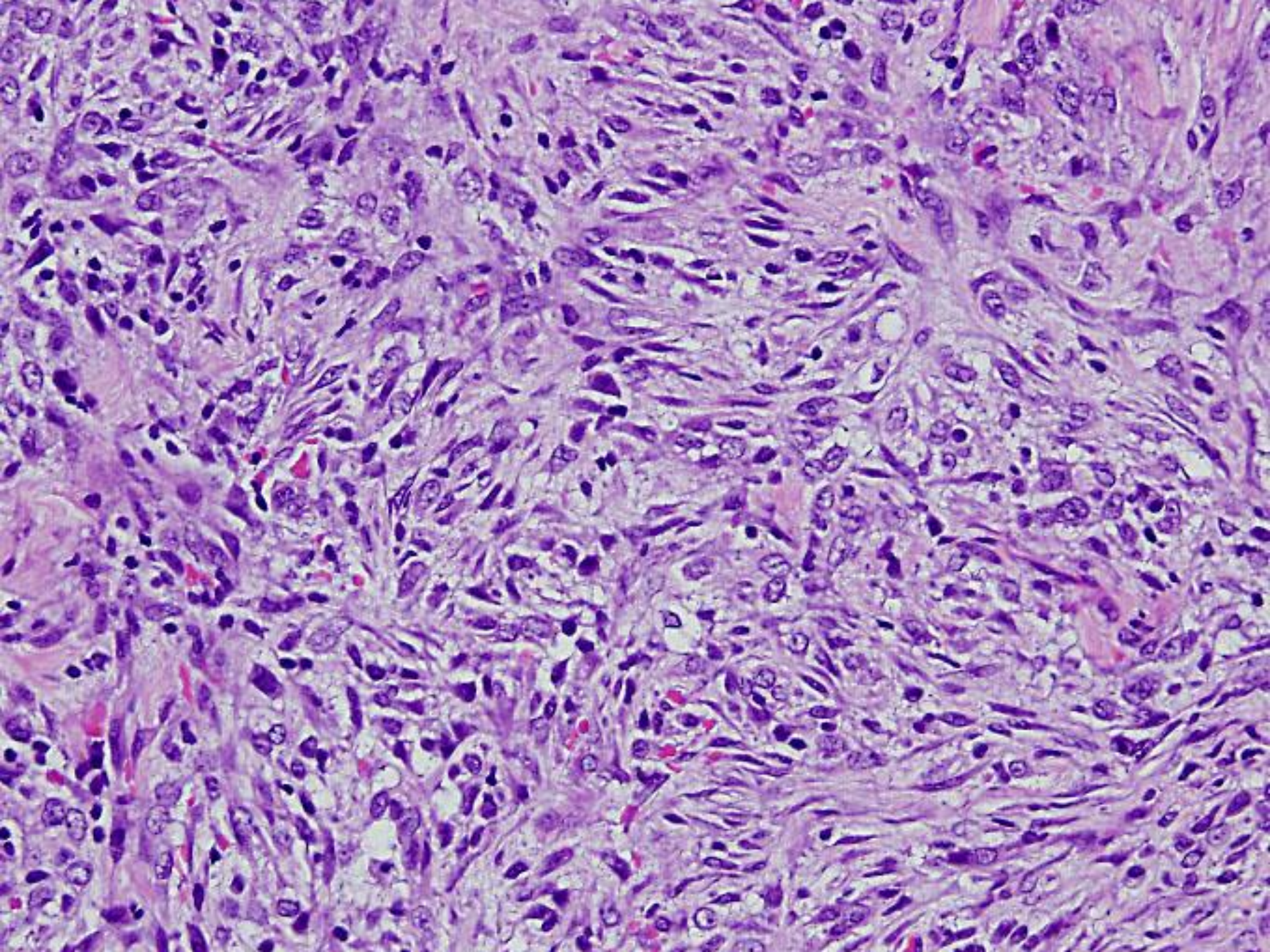
resented with a 1.3 cm.
She had a previous history
biopsy was performed.




FLSCC





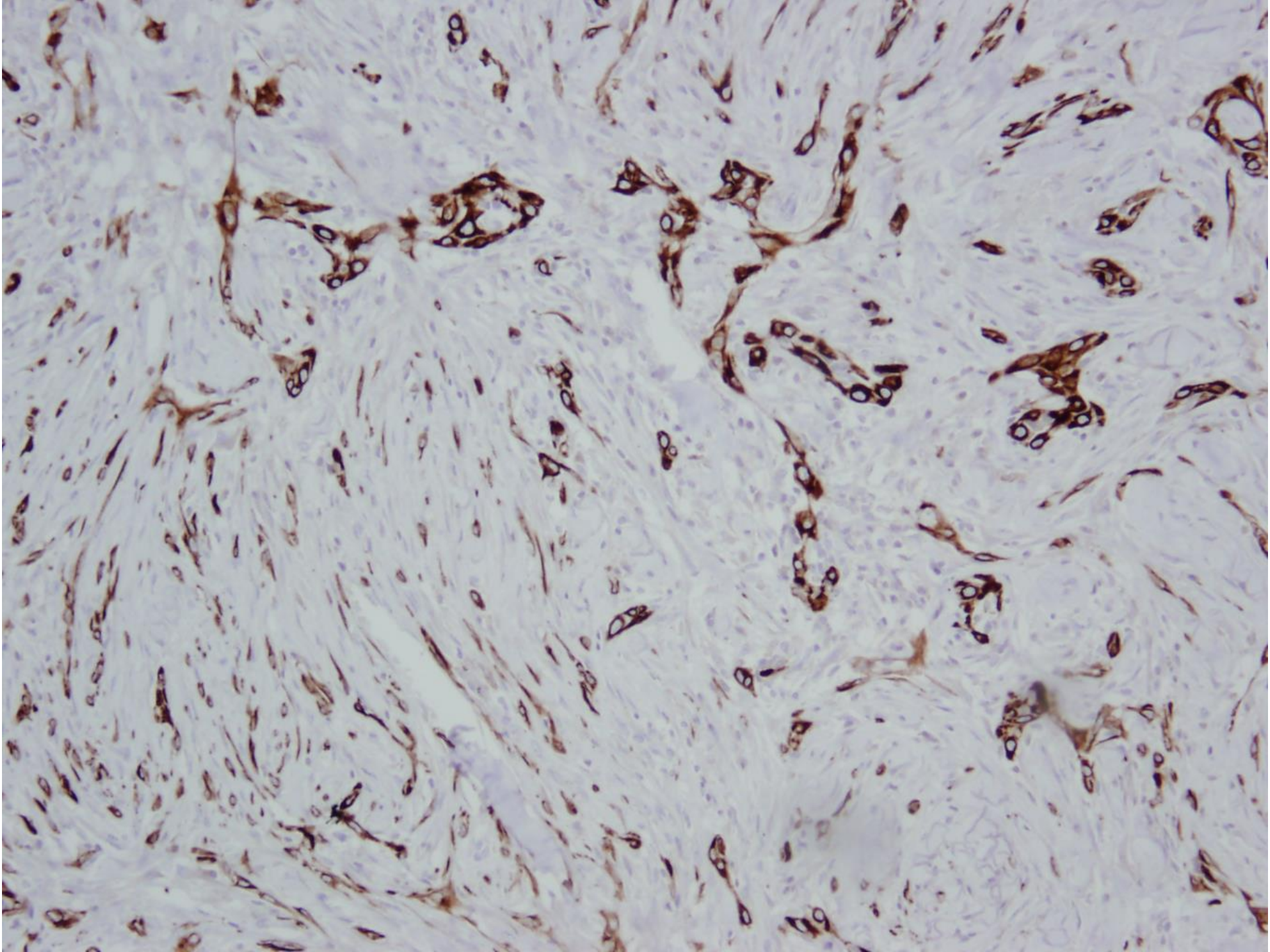


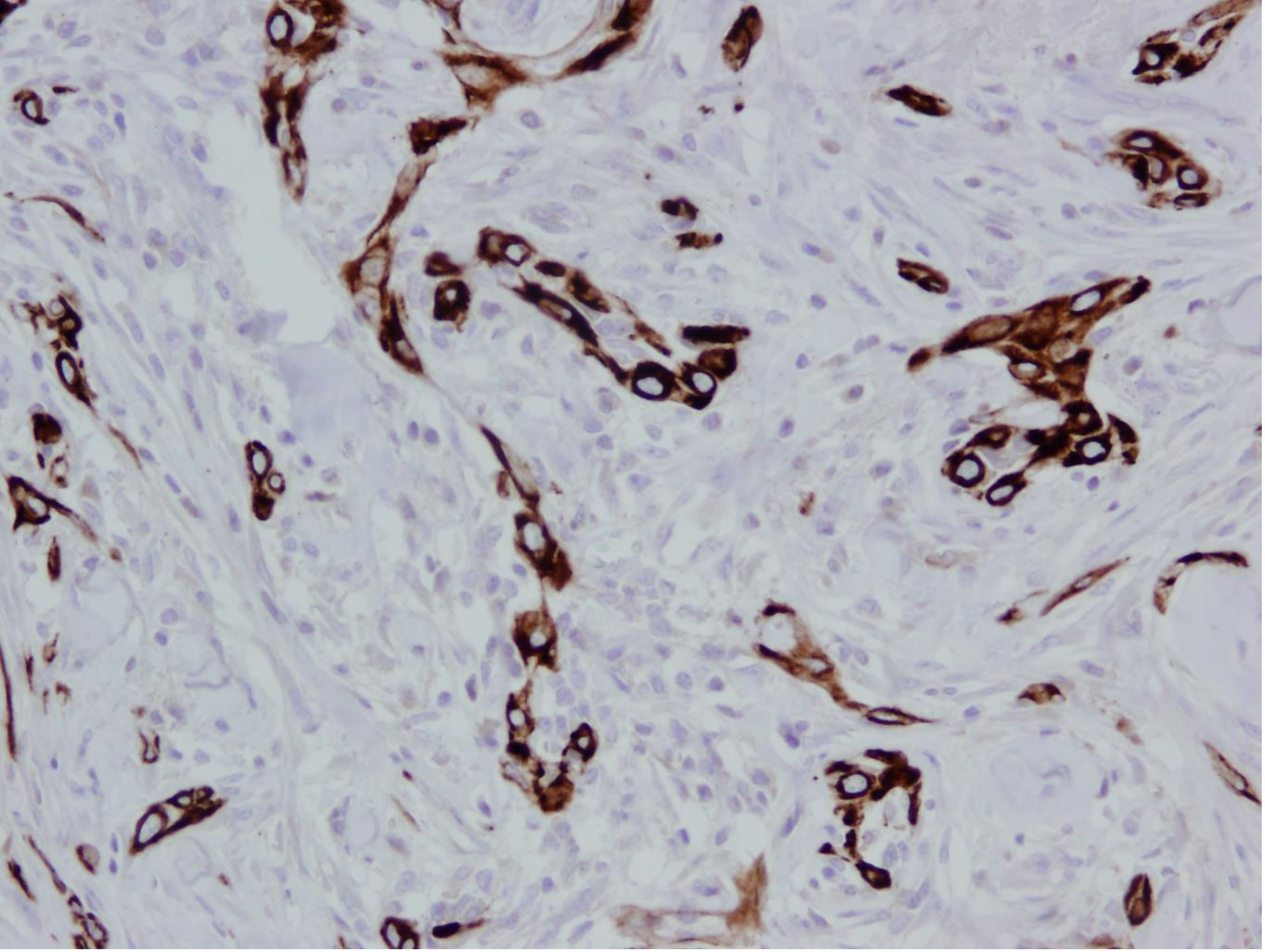
CK in Spindle Cell Carcinoma of the Breast

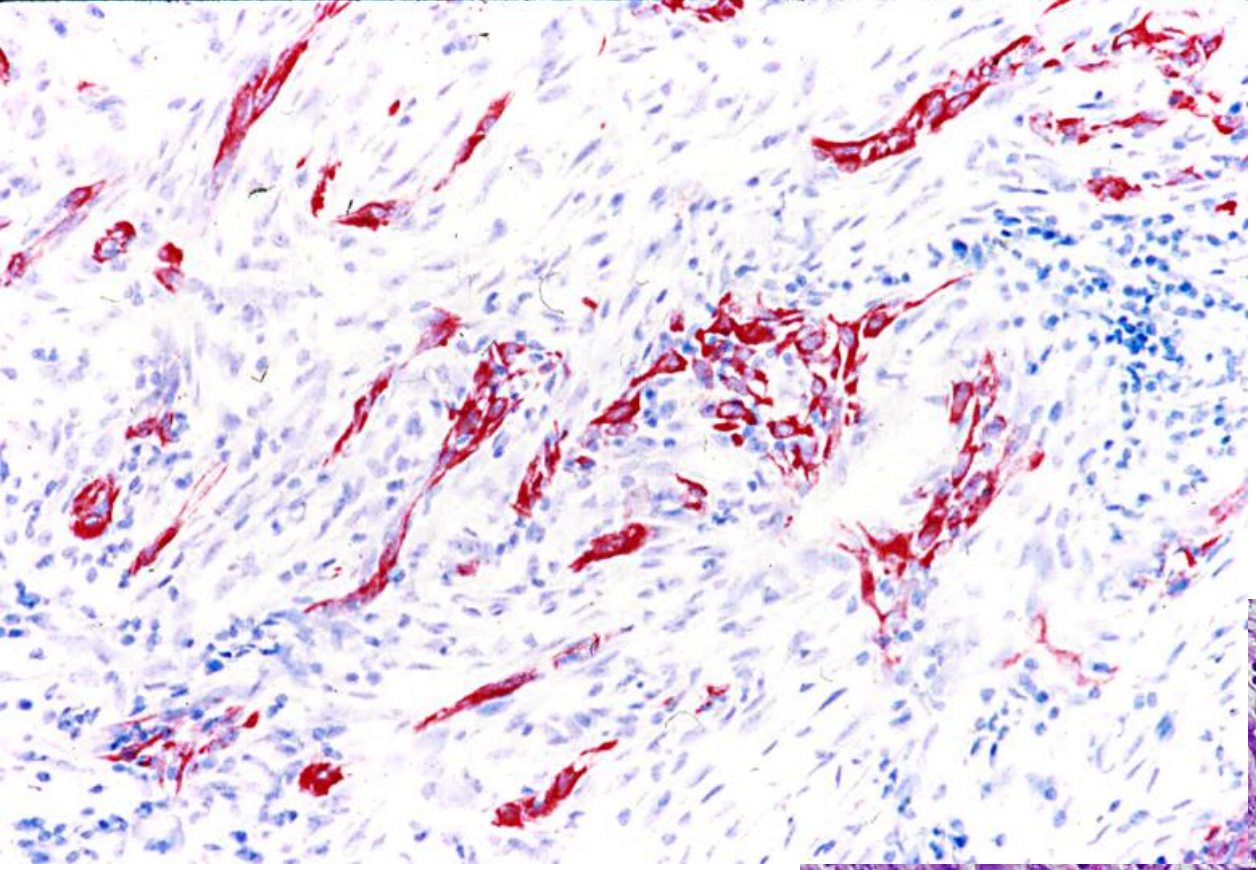
- Wide spectrum polyclonal anti CK antibody or enhanced CK immunostain
- Sensitivity AE1/AE3 improved with antigen retrieval but 20% of tumors still immunonegative (Adem et. al. 2002)
- Pankeratin (MNF116) most sensitive (93%), CK 14 (90%), AE1/AE3 (41%) (Carter et. al. (2006)

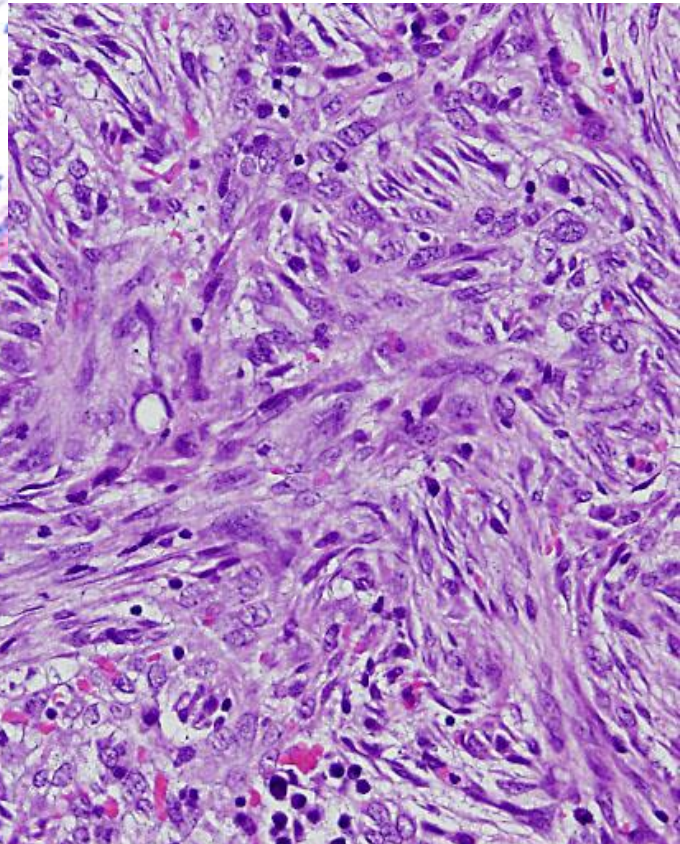
Our CK cocktail :

AE1/AE3, CAM5.2, CK8/18, and MNF116



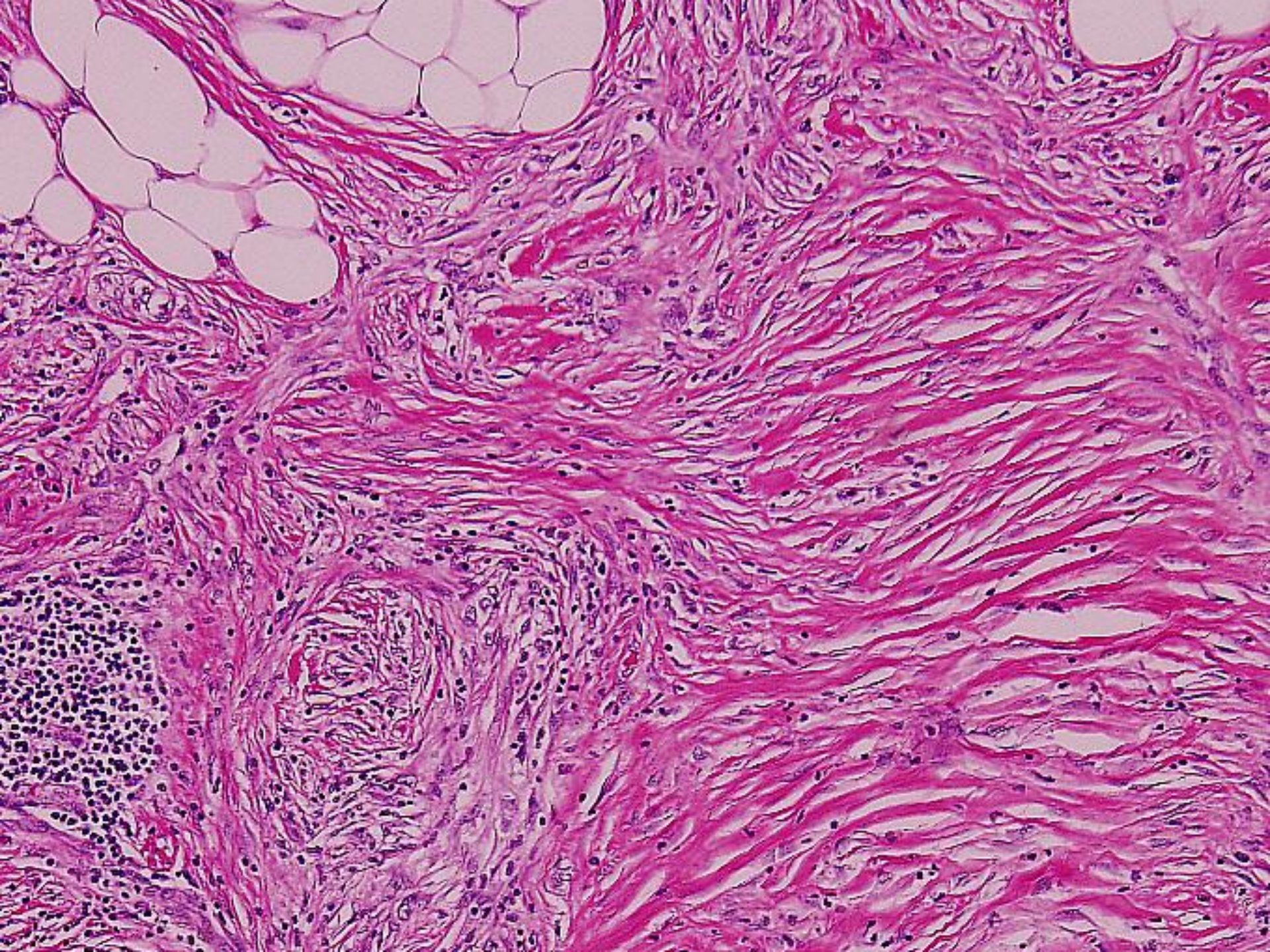


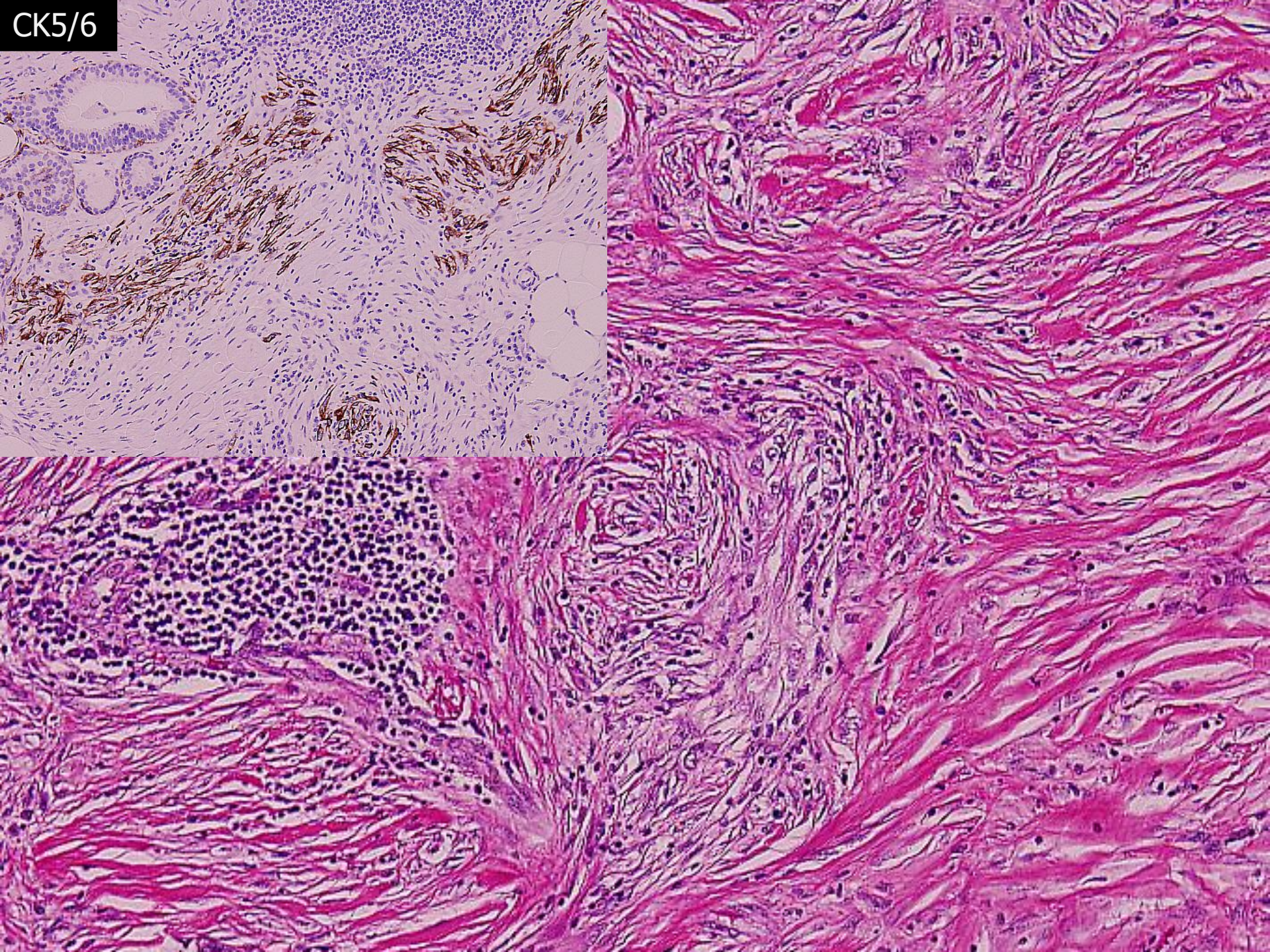


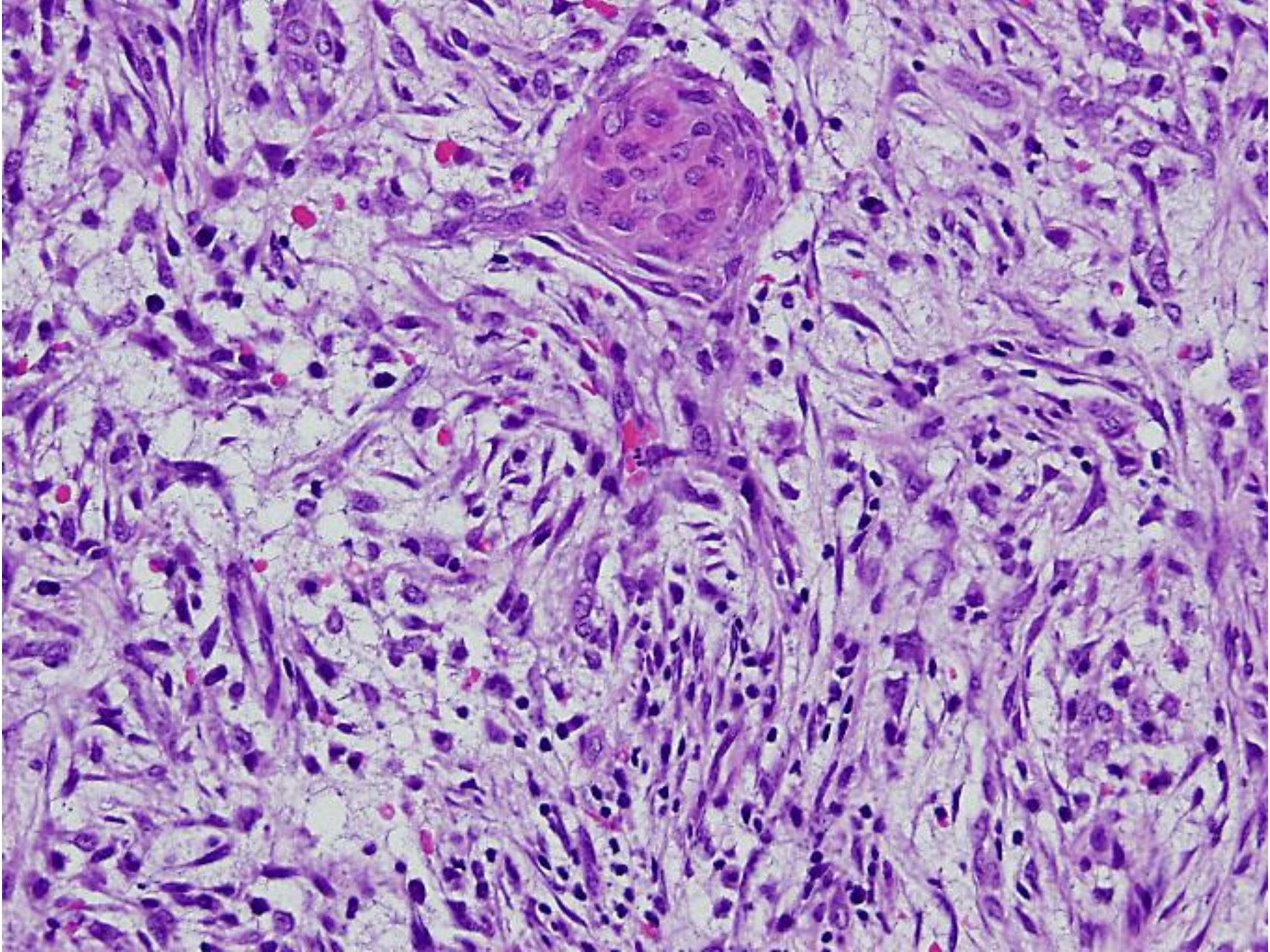


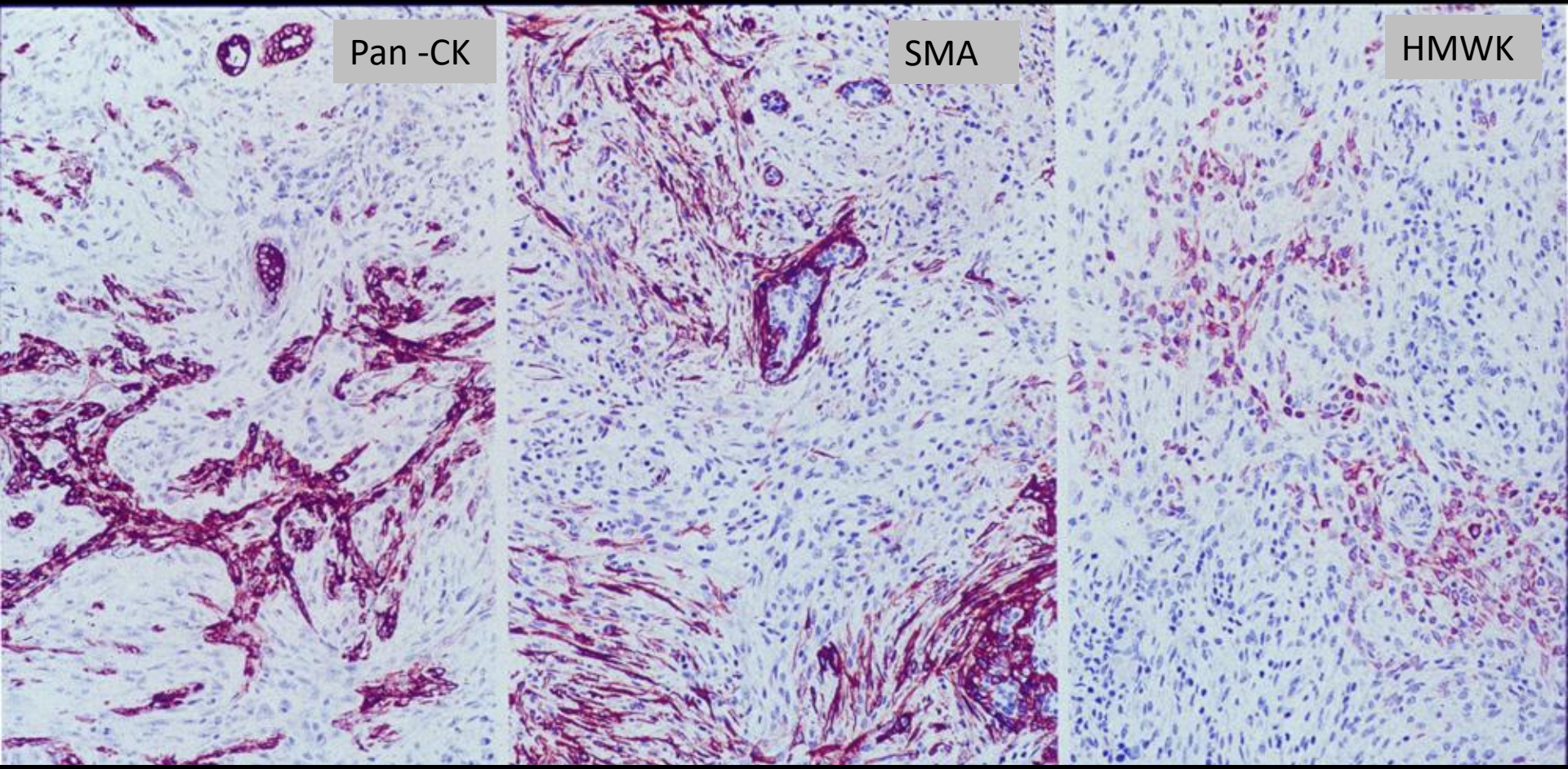
Cytokeratin

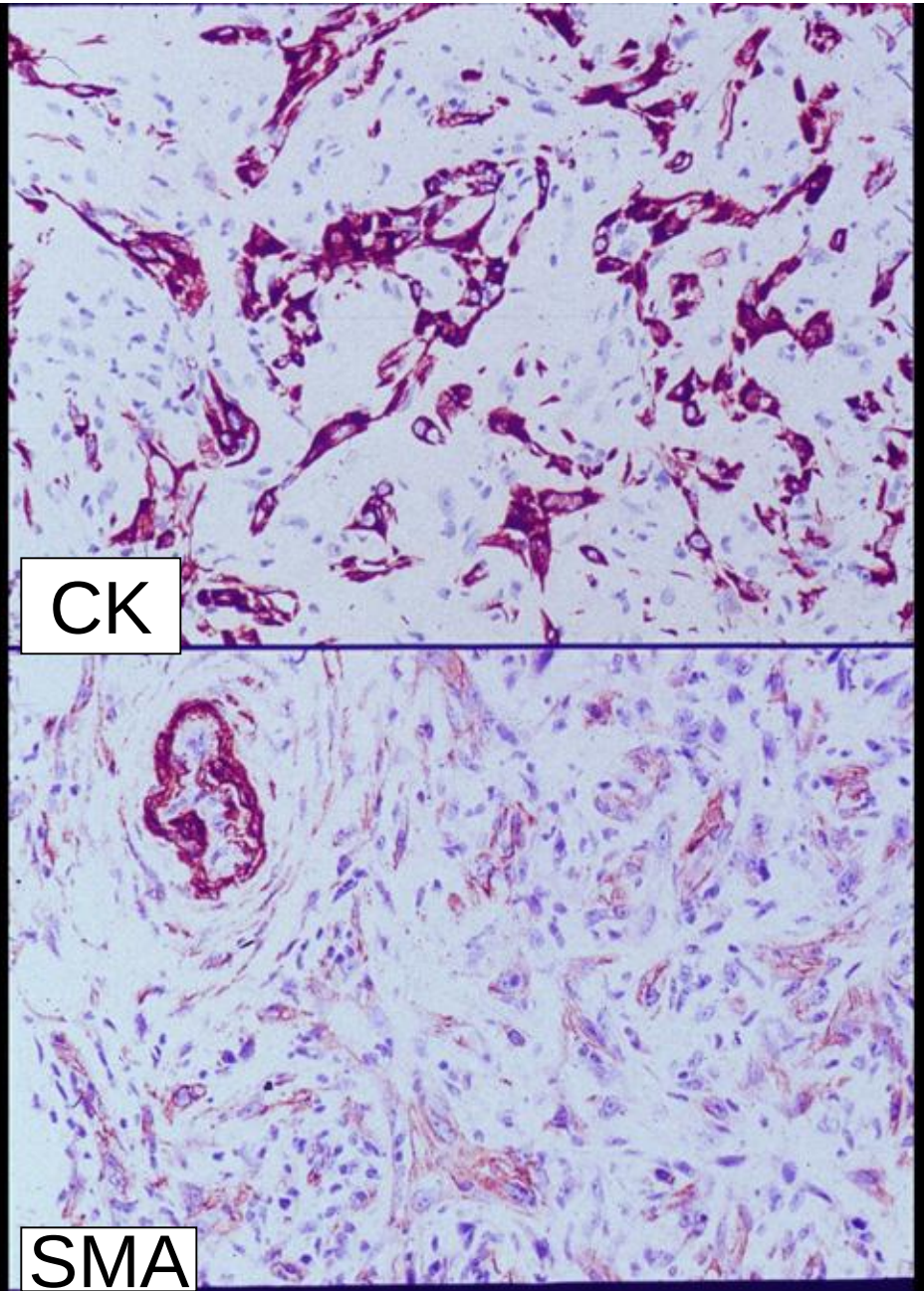
Immunoreactivity for CK range from 20-80% of cells




CK5/6




Pan -CK
SMA
HMWK

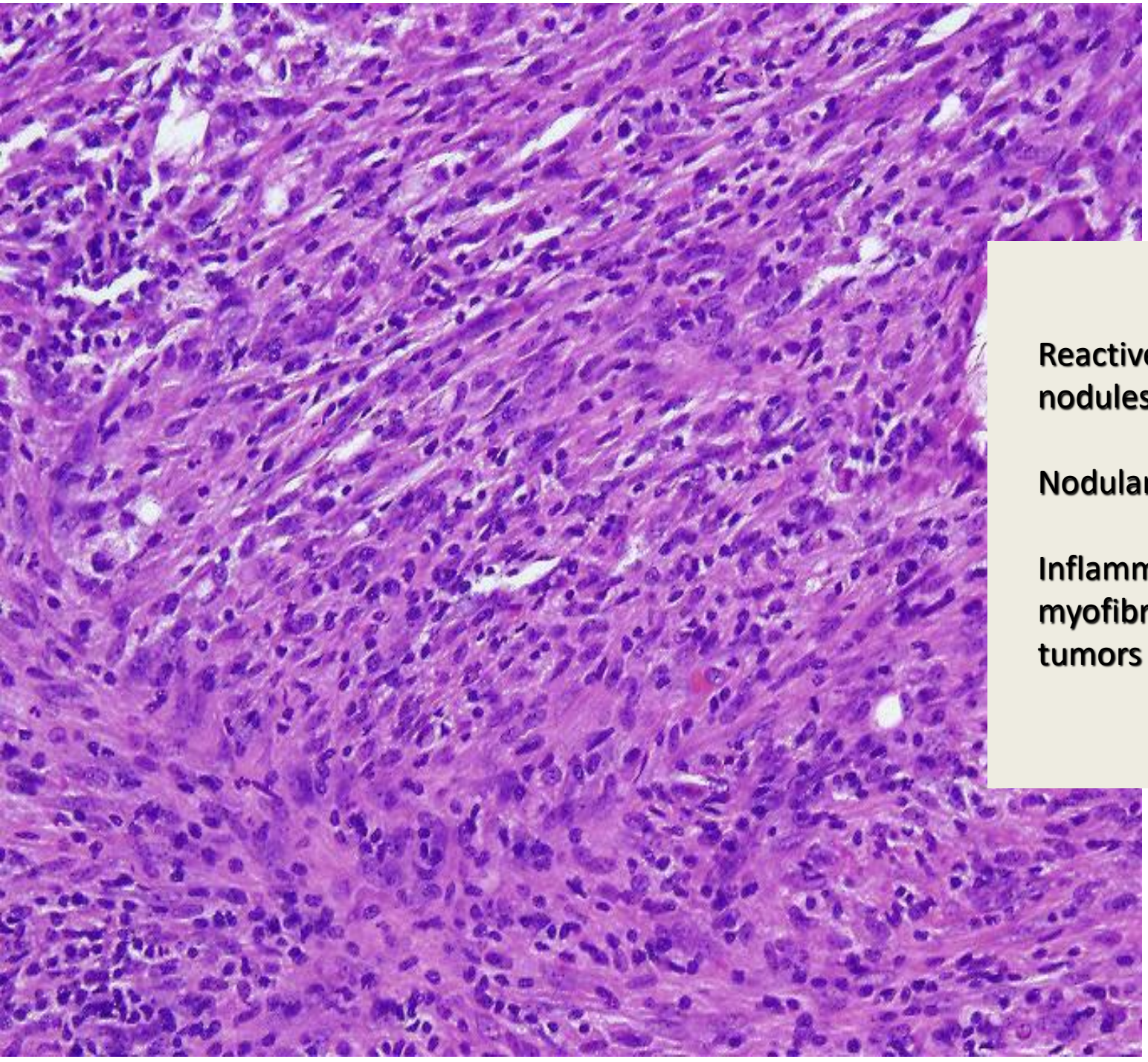

CK
SMA

Fibromatosis-like spindle cell carcinoma

- AE1/AE3, MNF116, 34βE12, CK5/6, CK14 (100%)
- p63 (94%), SMA (83%) and CK8/18 (79%)
- CK7 and CK19 (17% and 18%, respectively).
- All tumours were triple-negative (ER, PR and HER2)

Bland-Looking Spindle Cell Lesions of the Breast

- Fibromatosis like spindle cell carcinoma
- Reactive spindle cell nodules after CNB
- Nodular fasciitis
- Inflammatory myofibroblastic tumors
- Myofibroblastoma
- Fibromatosis
- Pseudoangiomatous hyperplasia (PASH)



Reactive spindle cell nodules after CNB

Nodular Fasciitis

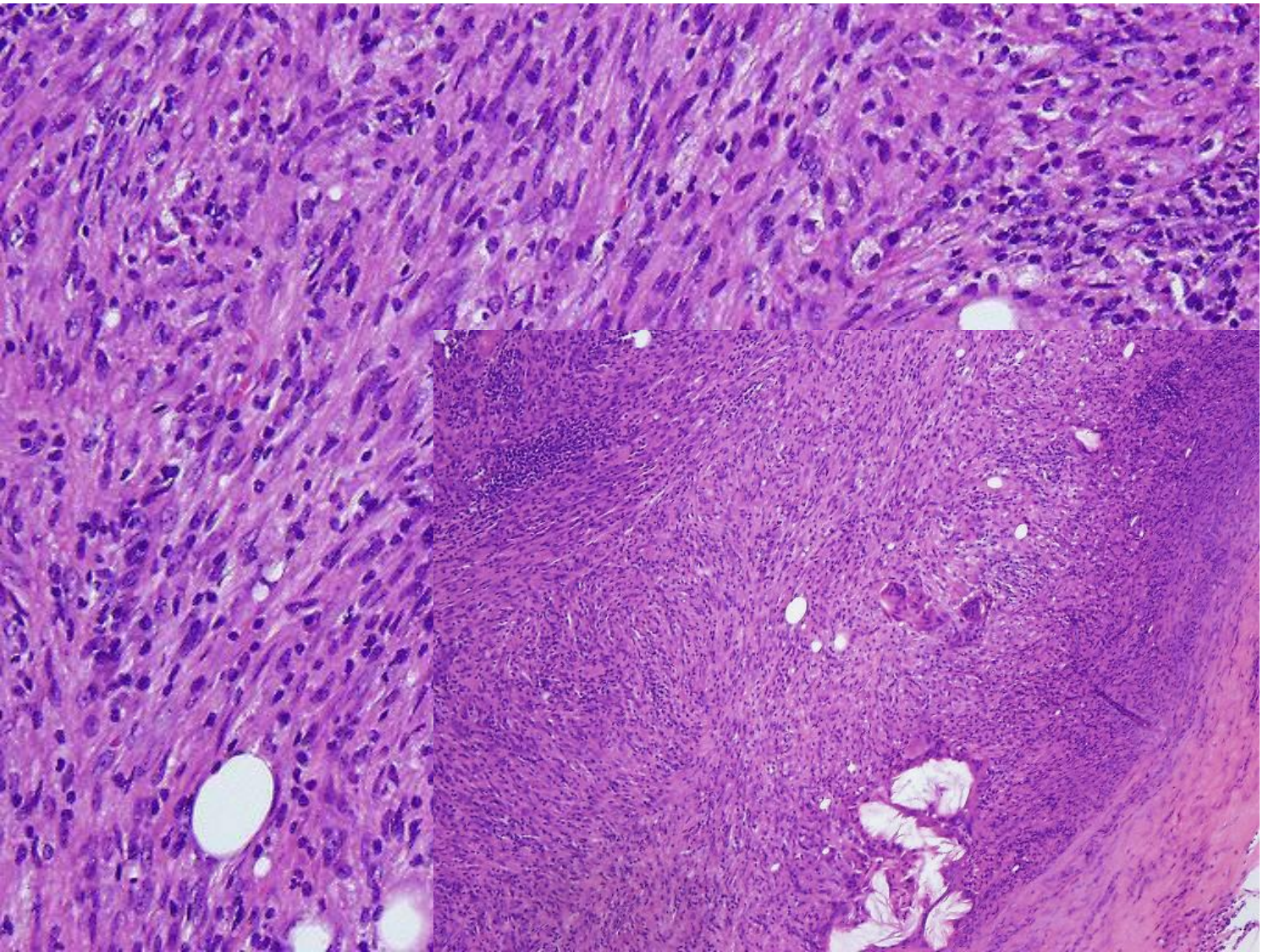
Inflammatory myofibroblastic tumors

Reactive spindle Cell Nodule of the Breast After CNB/FNA

- 18 cases after CNB/FNA (interval 6-38 days, av. 16.4 days)
- Associated with papilloma or CS lesions (15 cases)
- Non encapsulated 1.5-9 mm
- Interlacing fascicles of plump spindle cells, small blood vessels, inflammatory cells
- Negative for AE1/AE3 and HMW keratin but expressed SMA

Gobbi et. Al, Am J Clin Pathol 2000; 113: 288-294

Inflammatory Myofibroblastic Tumor



Rare

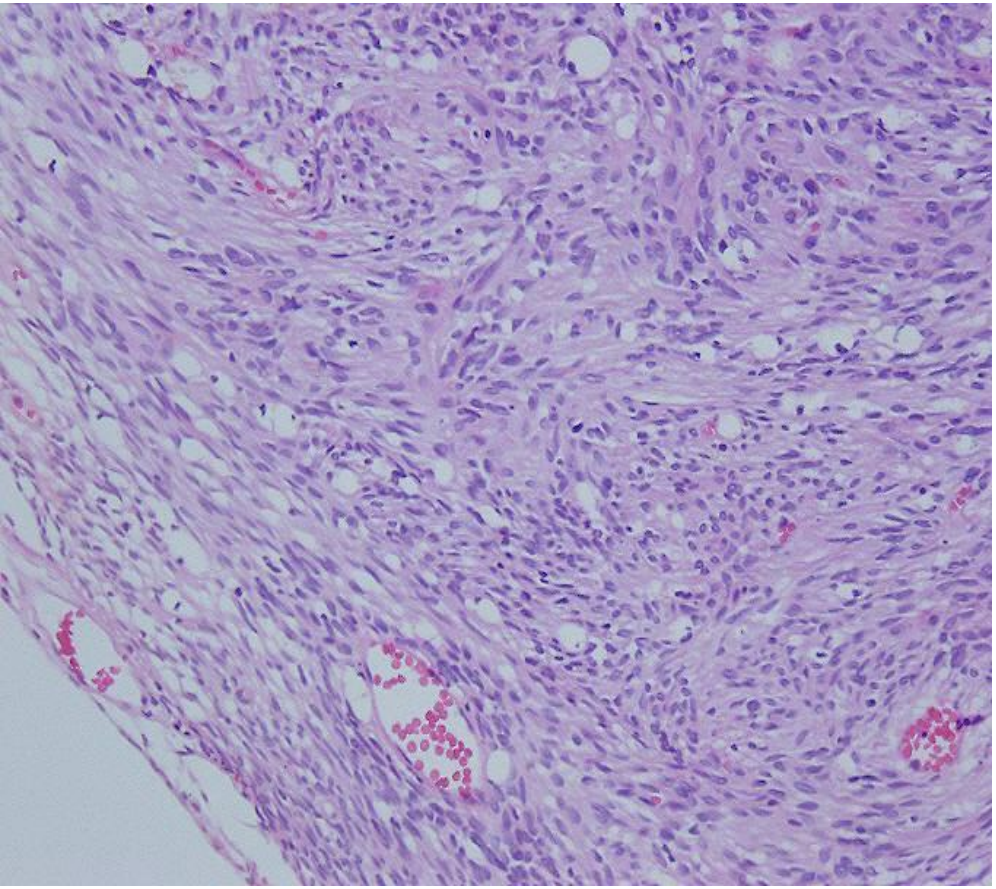
Well defined

Clonal

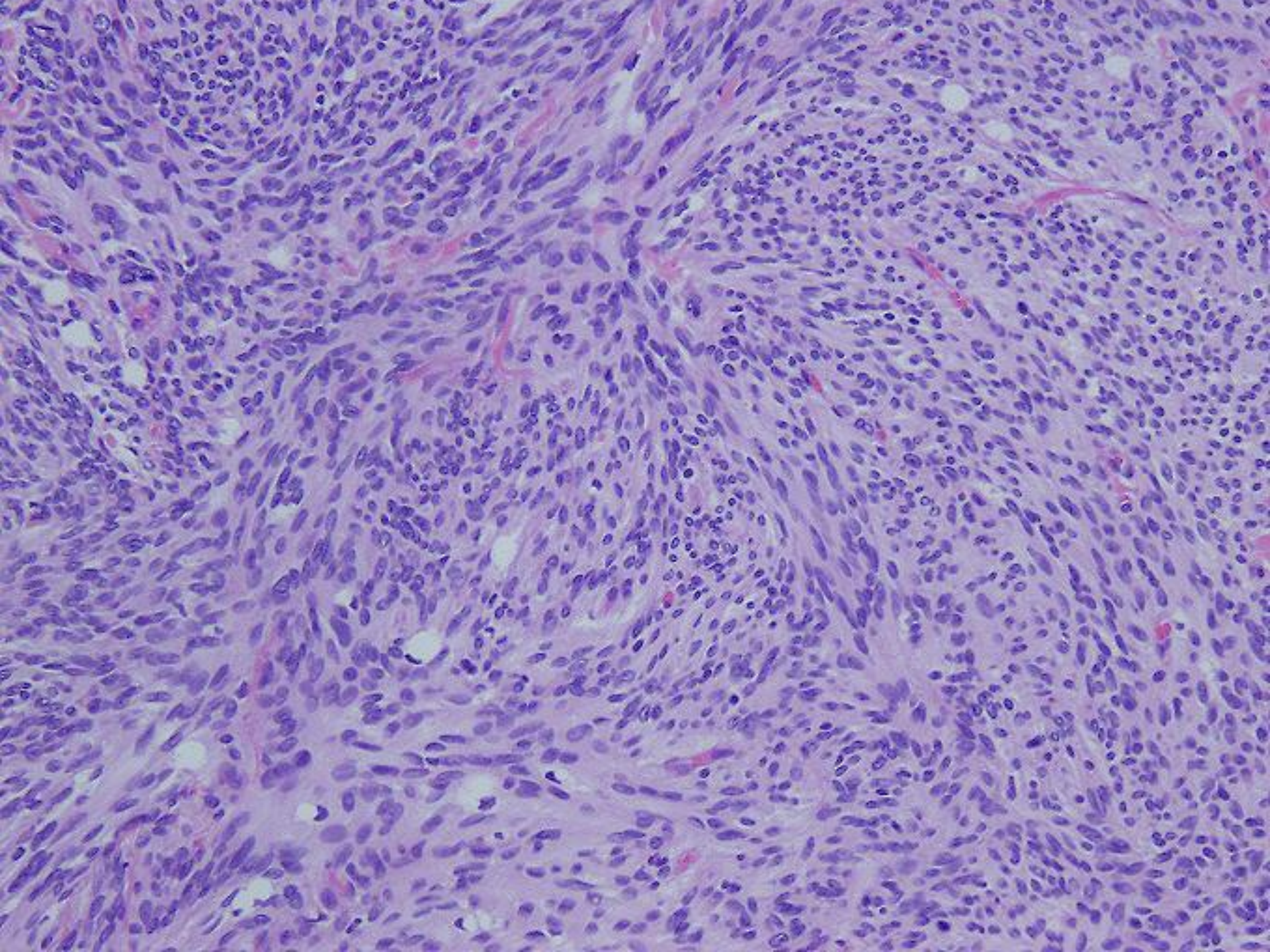
Bland-Looking Spindle Cell Lesions of the Breast

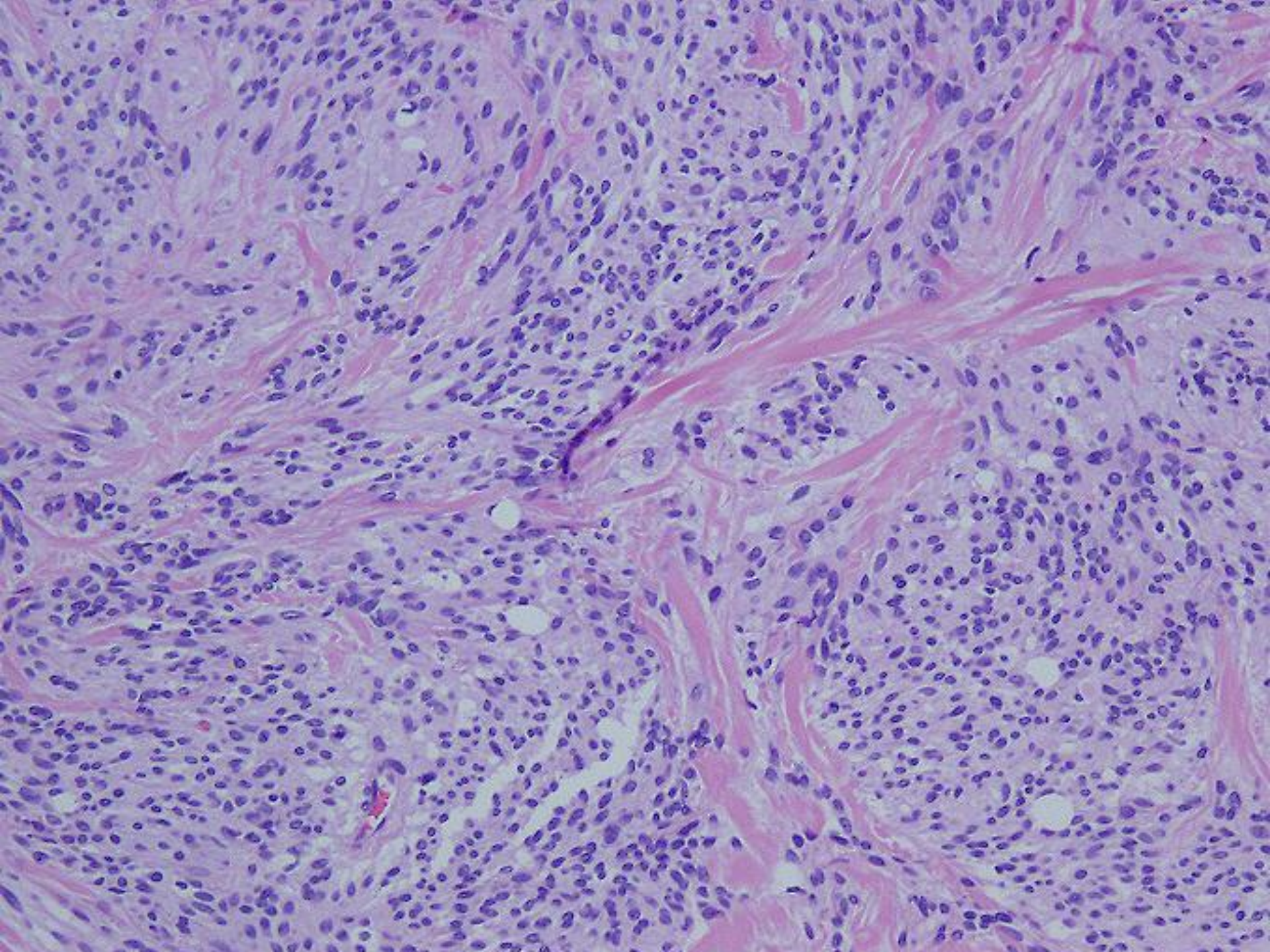
- Fibromatosis-like spindle cell carcinoma
- Reactive spindle cell nodules after CNB
- Nodular Fasciitis
- Inflammatory myofibroblastic tumors
- Myofibroblastoma
- Fibromatosis
- Pseudoangiomatous hyperplasia (PASH)

Myofibroblastoma



- Most often men > 40 yr
- Sharply circumscribed
- Fascicles of spindle cells
- Bands of hyaline collagen





Variations:

infiltrative margins

Prominent epithelioid component

Mono or multinucleated giant cells with atypia and myxoid hyaline change

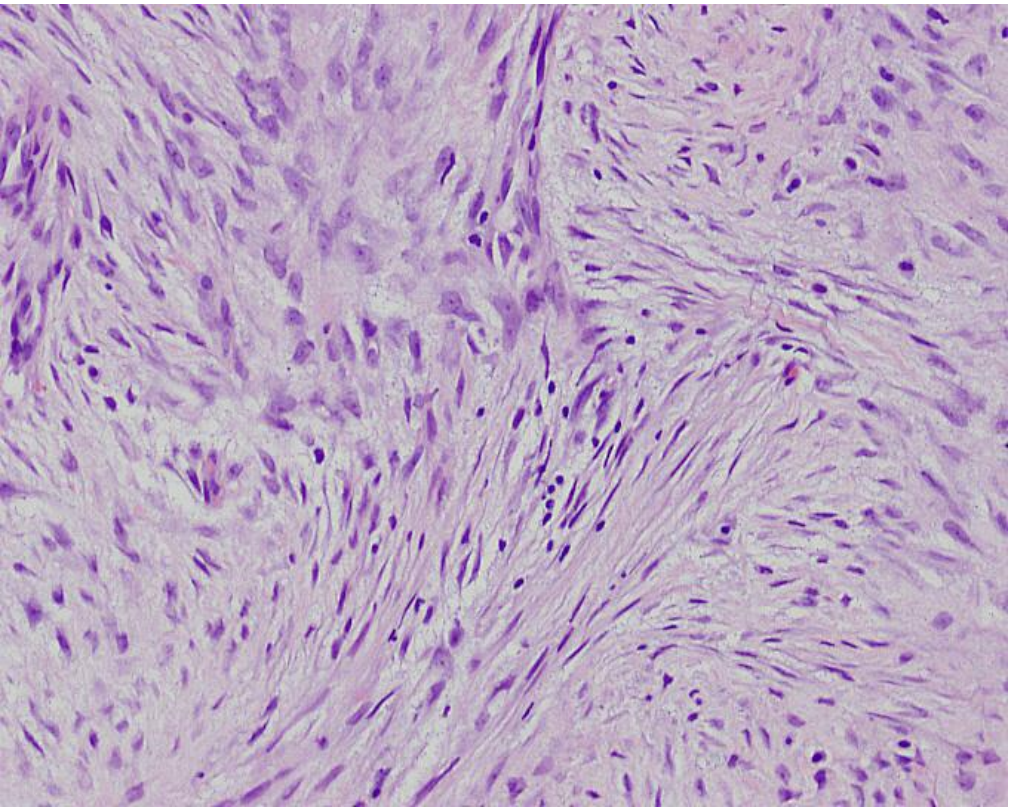
Immunoprofile: CD34 in at least 50% of cells, variable reactivity for actin, desmin and ER/PR

Molecular: partial monosomy of 13 q and 16 p with deletion of the region 13 q 14 in greater than 50% of cases (likely related to spindle cell lipoma)

Monophasic Bland-Looking Spindle Cell Lesions of the Breast

- Fibromatosis-like spindle cell carcinoma
- Reactive spindle cell nodules after CNB
- Nodular Fasciitis
- Inflammatory myofibroblastic tumors
- Myofibroblastoma
- Fibromatosis
- Pseudoangiomatous hyperplasia (PASH)

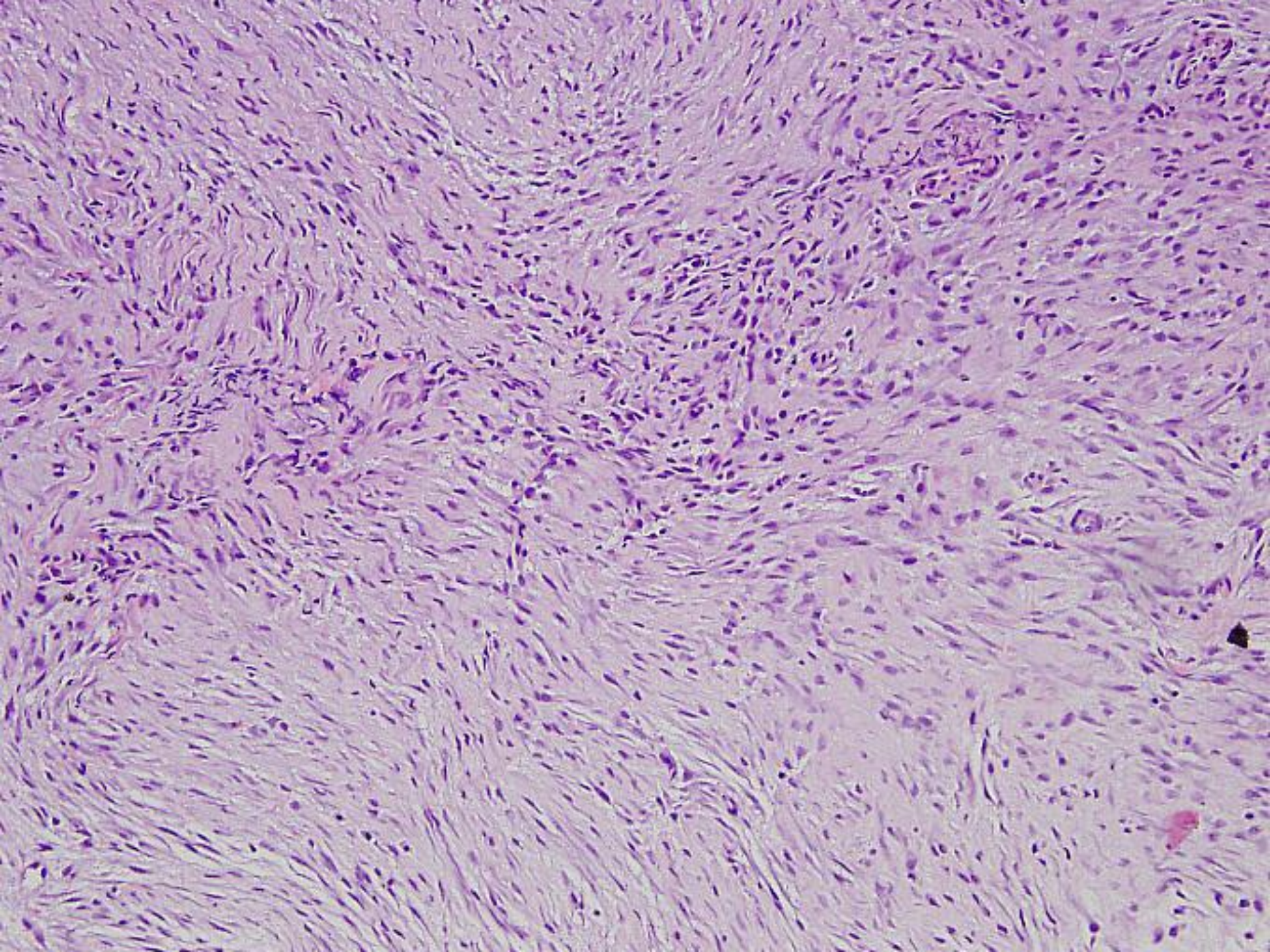
Fibromatosis of the Breast

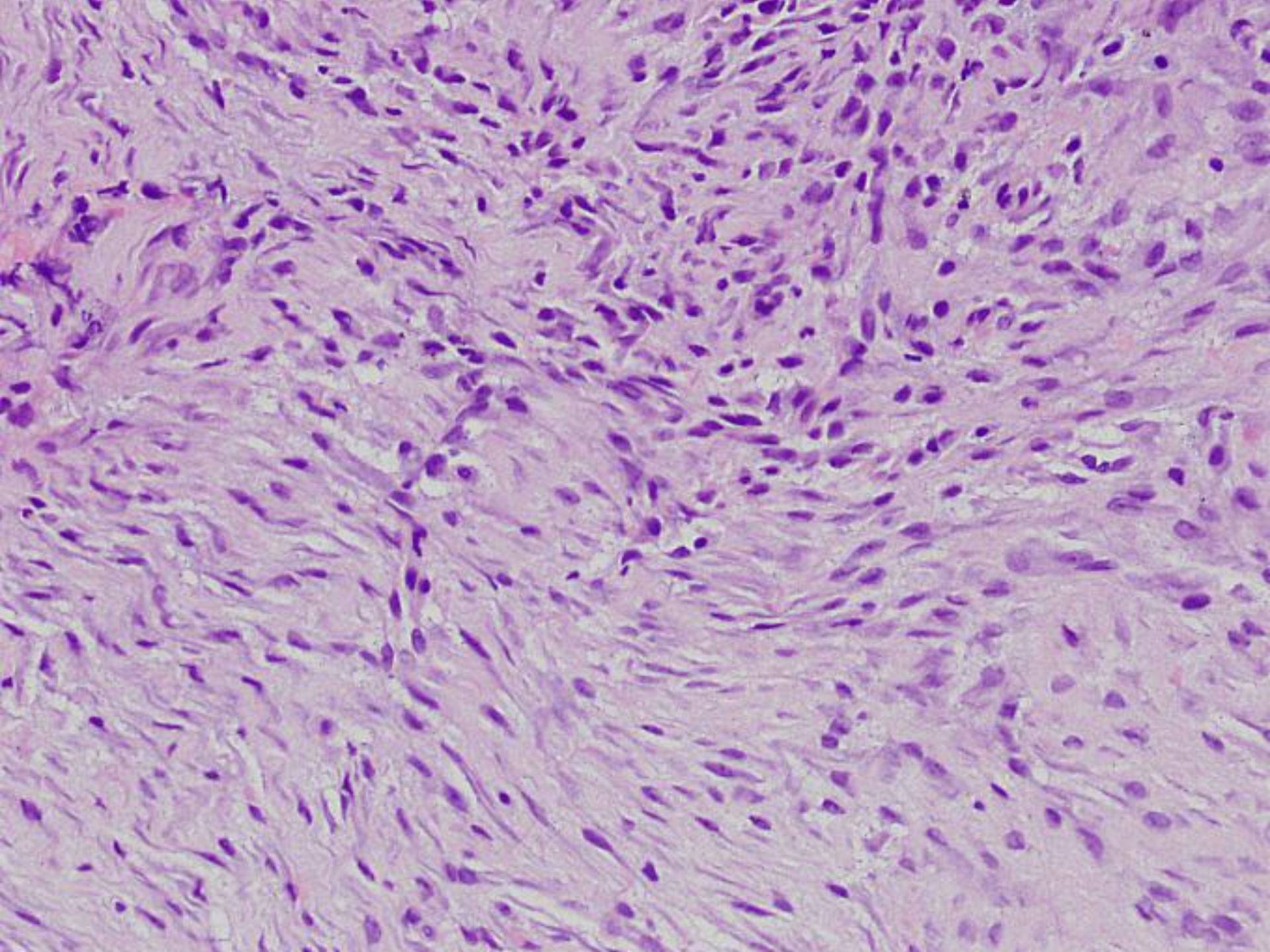


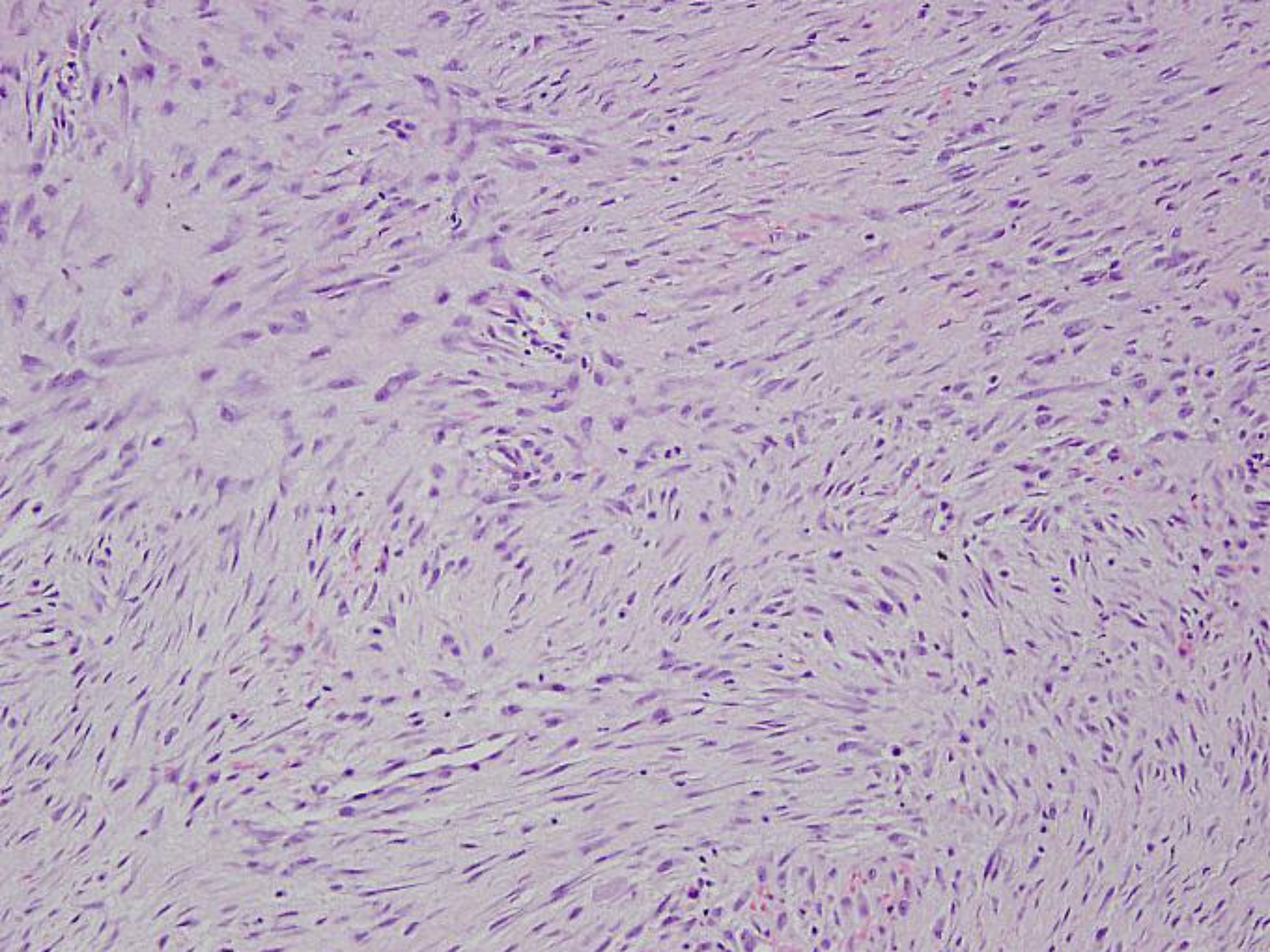
- Rare, locally aggressive
- Women 13-80 yrs

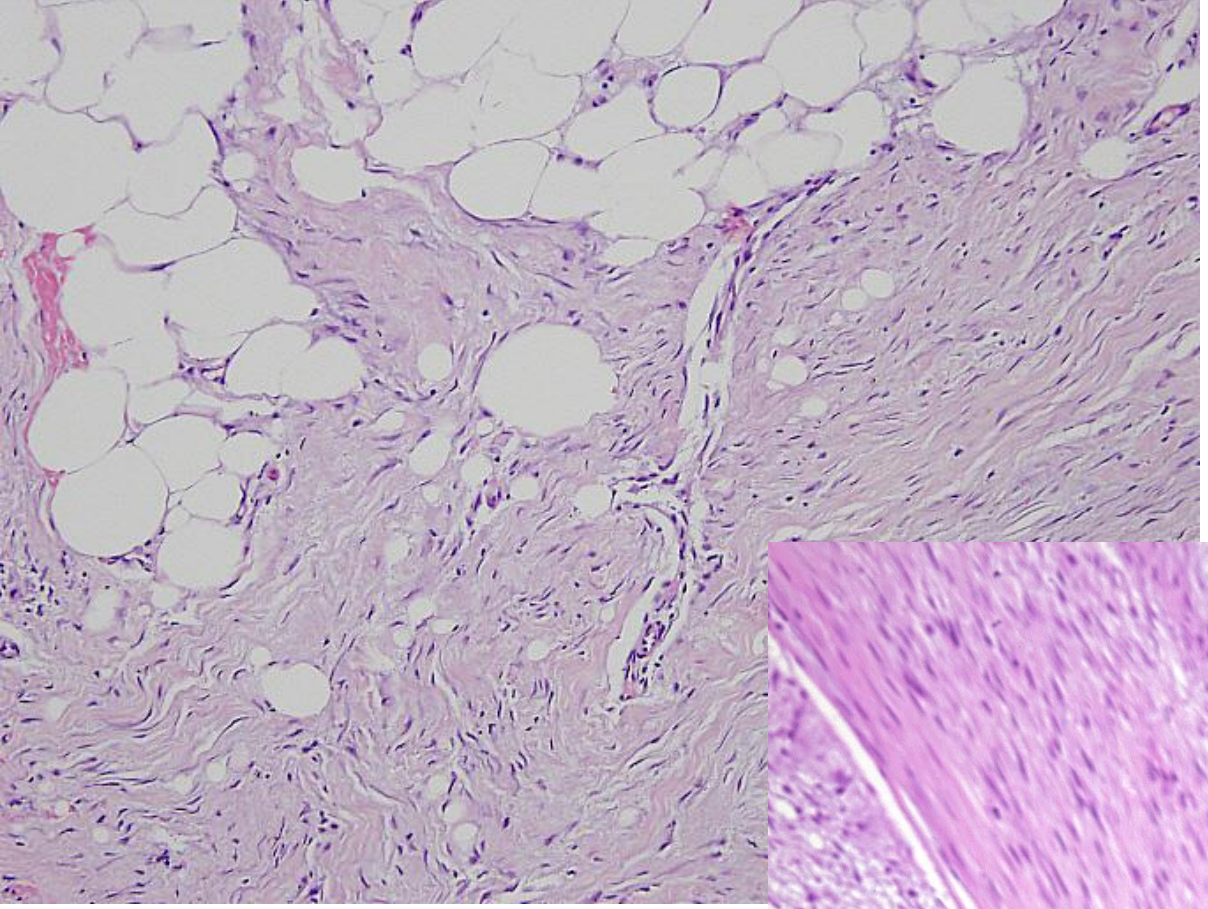
(mostly child bearing)

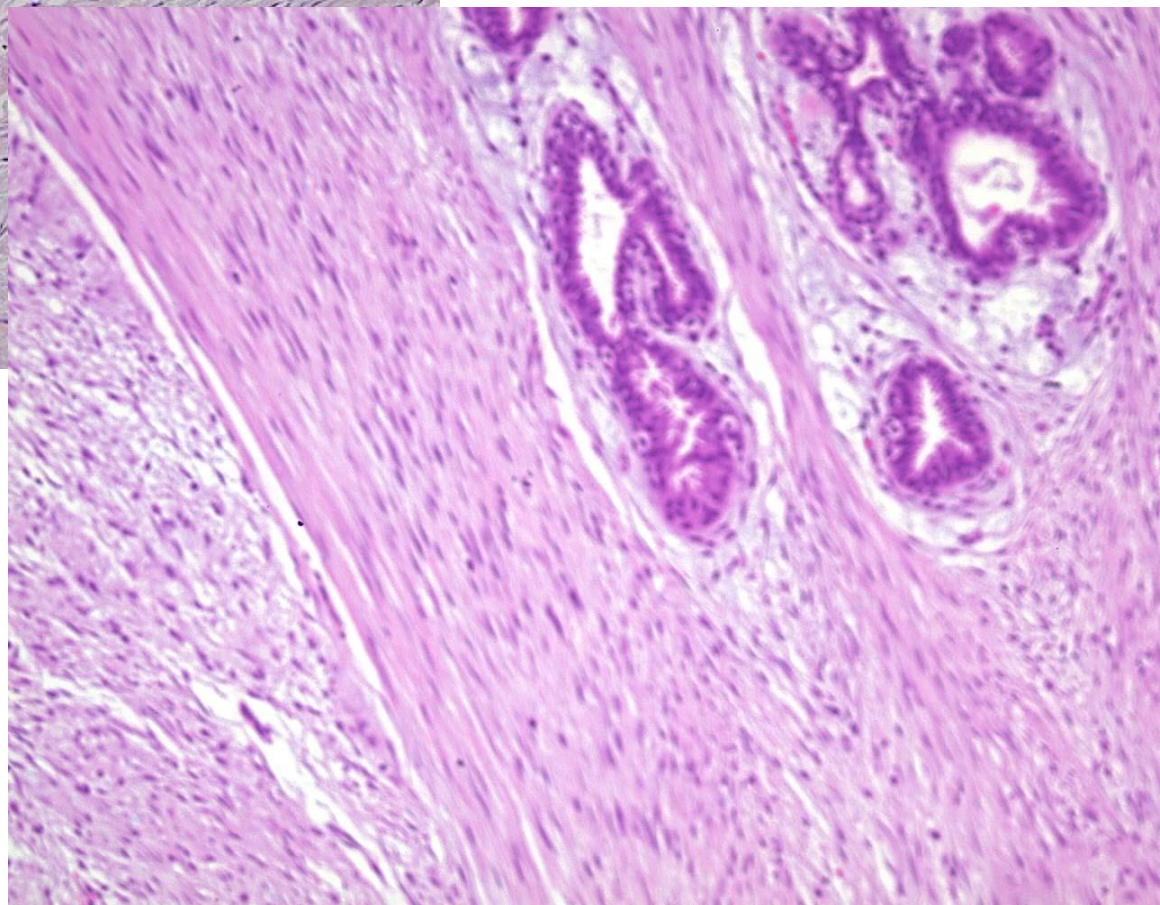
- Solitary firm suspicious mass
- Poorly demarcated, 0.5-10 cm (av. 2.5 cm)



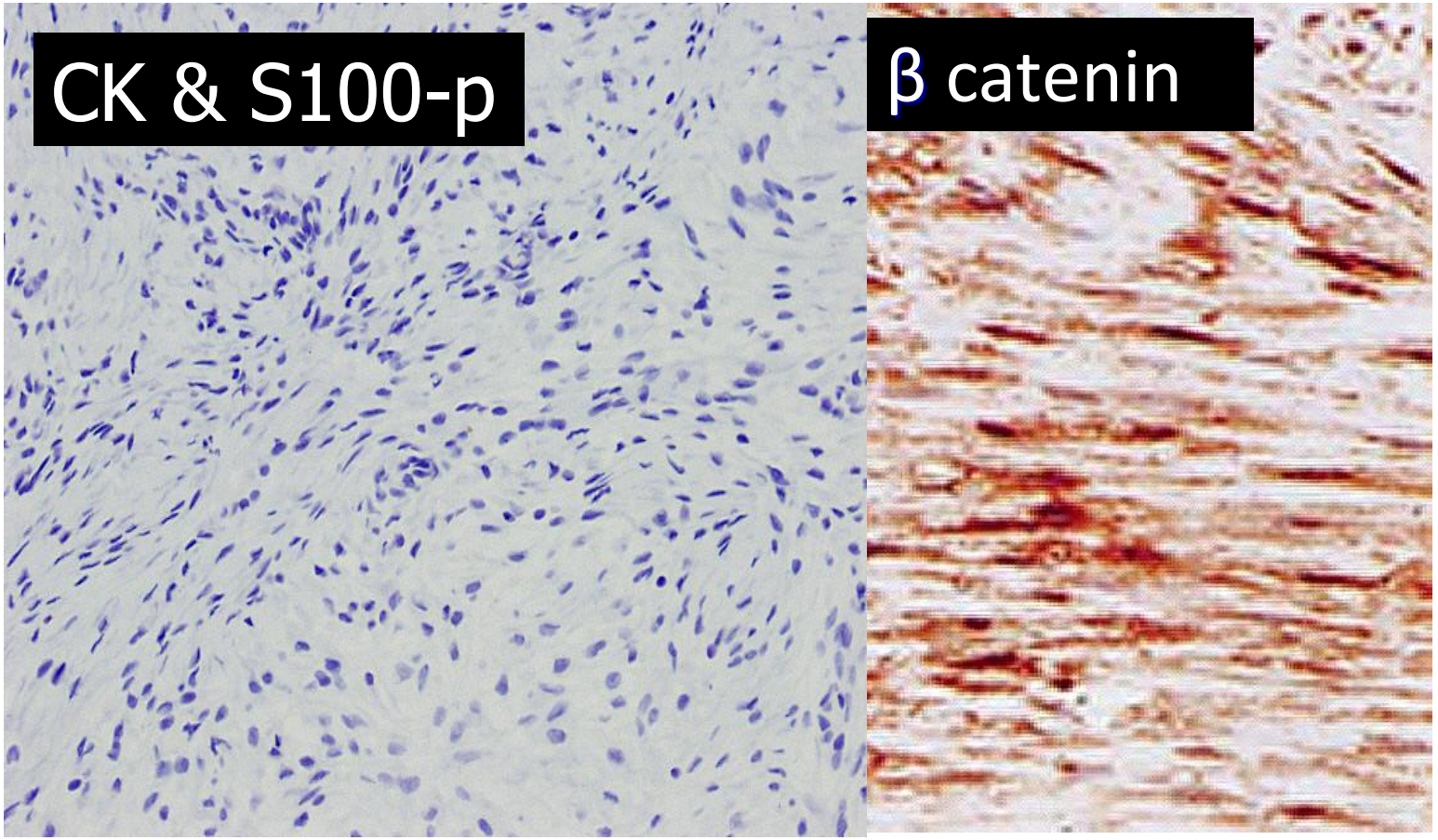








Fibromatosis of the Breast- Immunoprofile



ER, PR, AR and pS2 neg

Monophasic Bland-Looking Spindle Cell Lesions of the Breast

- Fibromatosis-like spindle cell carcinoma
- Reactive spindle cell nodules after CNB
- Nodular Fasciitis
- Inflammatory myofibroblastic tumors
- Myofibroblastoma
- Fibromatosis
- Pseudoangiomatous hyperplasia (PASH)

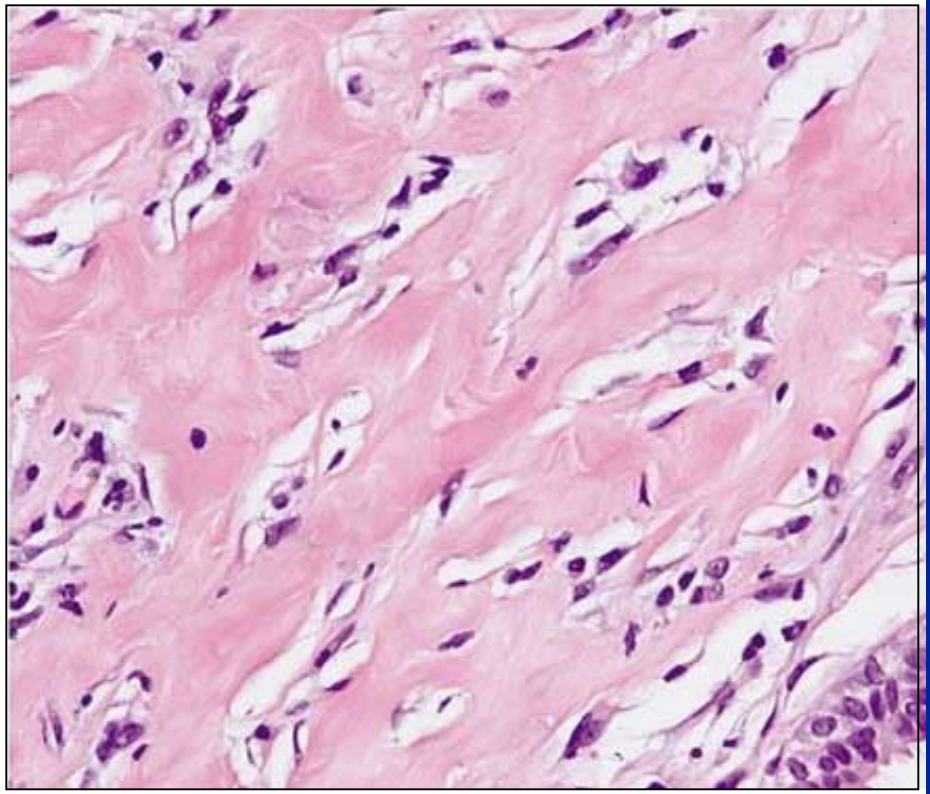
PASH

- Incidental microscopic findings (23% of bx), often associated with a benign or malignant condition
- Diffuse involvement or localized palpable or nonpalpable mass (0.4% of bx)
- Gynecomastia (25% of cases)

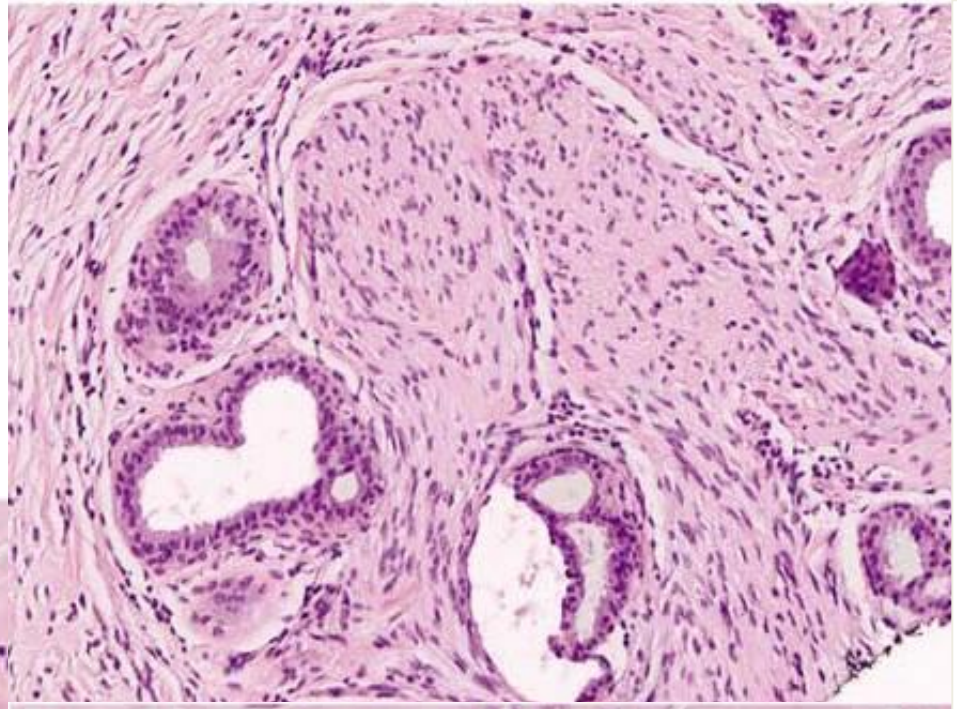
Symptomatic: Firm, non tender mass/ FA like, 1-15 cm

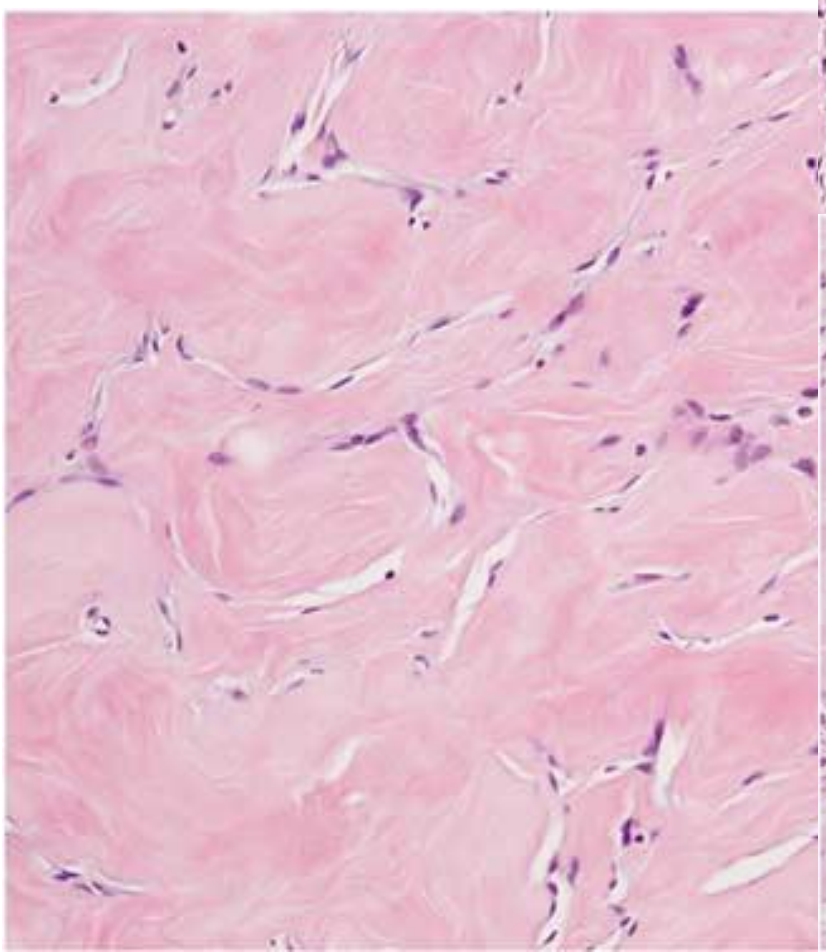
PASH

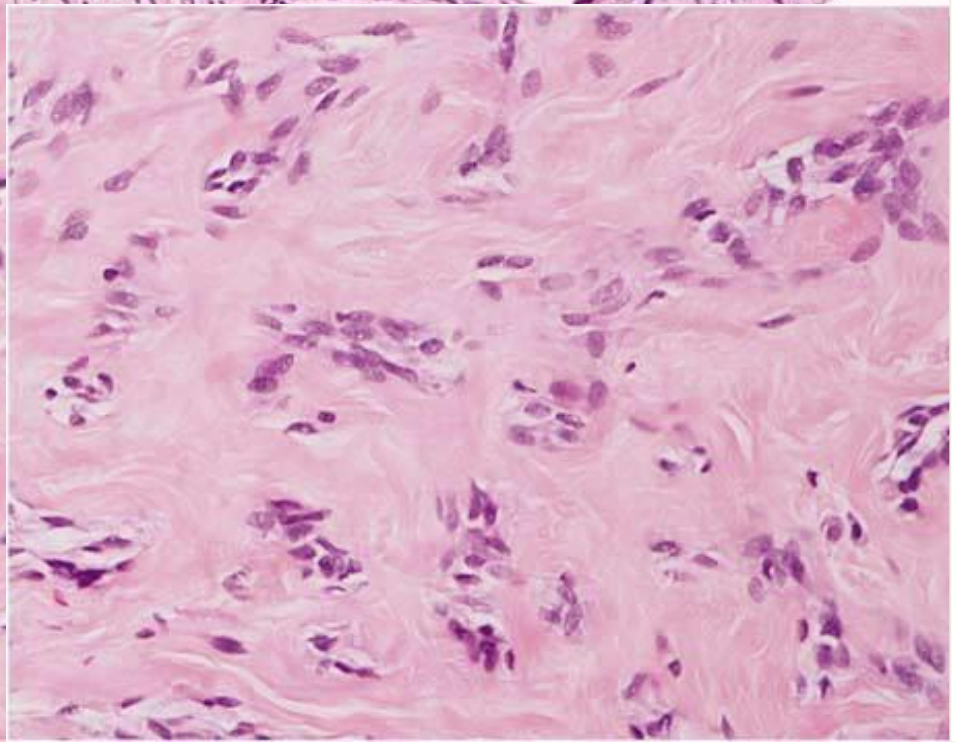
- Slit like spaces lined by myofibroblasts separated by bands of hyalinized tissue
- No atypia, no mitotic activity
- CD34+, Vim+, SMA + (CD31 and vascular markers neg)

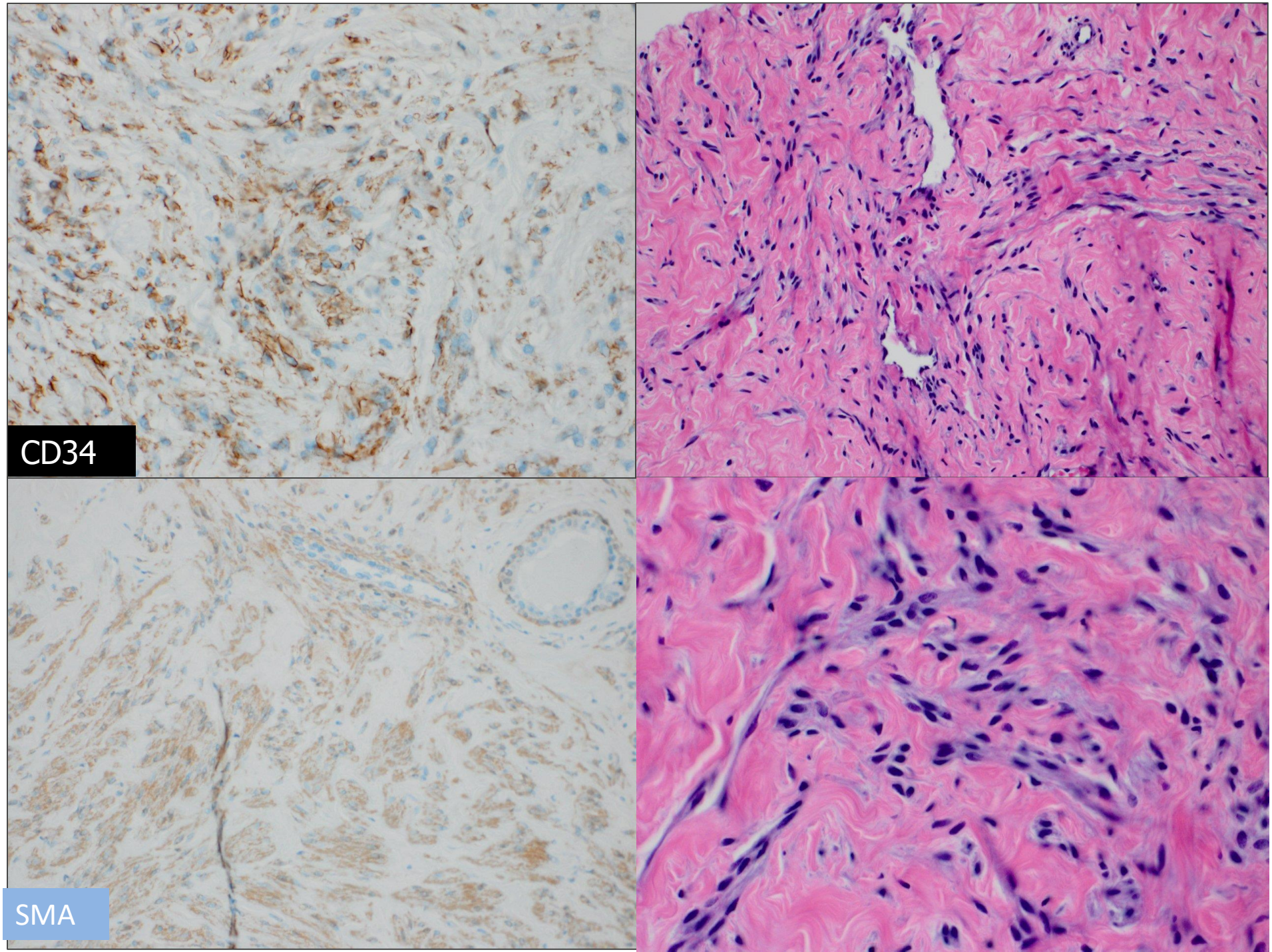


PASH with increased cellularity, small bundles or fascicles of myofibroblasts








CD34
SMA

Other bland spindle cell lesions

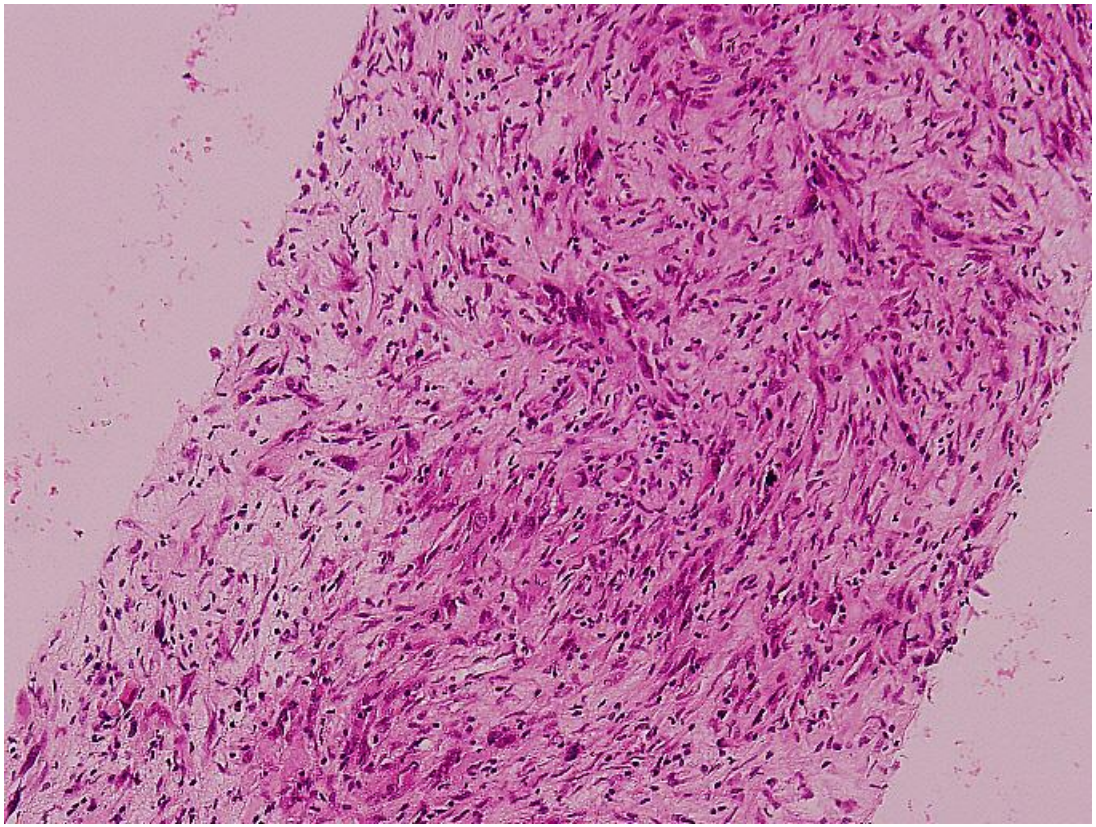
- Solitary fibrous tumor: STAT 6
- Leimyoma: actin, desmin and caldesmon
- Myxofibrosarcoma/myxoid MFH low to intermediate

	Nodular fasciitis	Myofibroblastoma	Fibromatosis	PASH
SMA	+	V +	+	+
Desmin	-	+	V +	+/-
S100	-		-	
CD34	-	+	-	+
Beta-catenin			+ nuclear Can be + in metaplastic and PT	
		V + ER, PR, CD99, bcl2, CD10	Variably +	+ Bcl2, PR, less for ER
Molecular	FISH USP6 rearrangement	Loss of nuclear reactivity for RB due to Ch13 rearrangement	Mutation CTNNB1gene encoding B-catenin	Neg for CD31, ERG

High grade spindle cell lesions

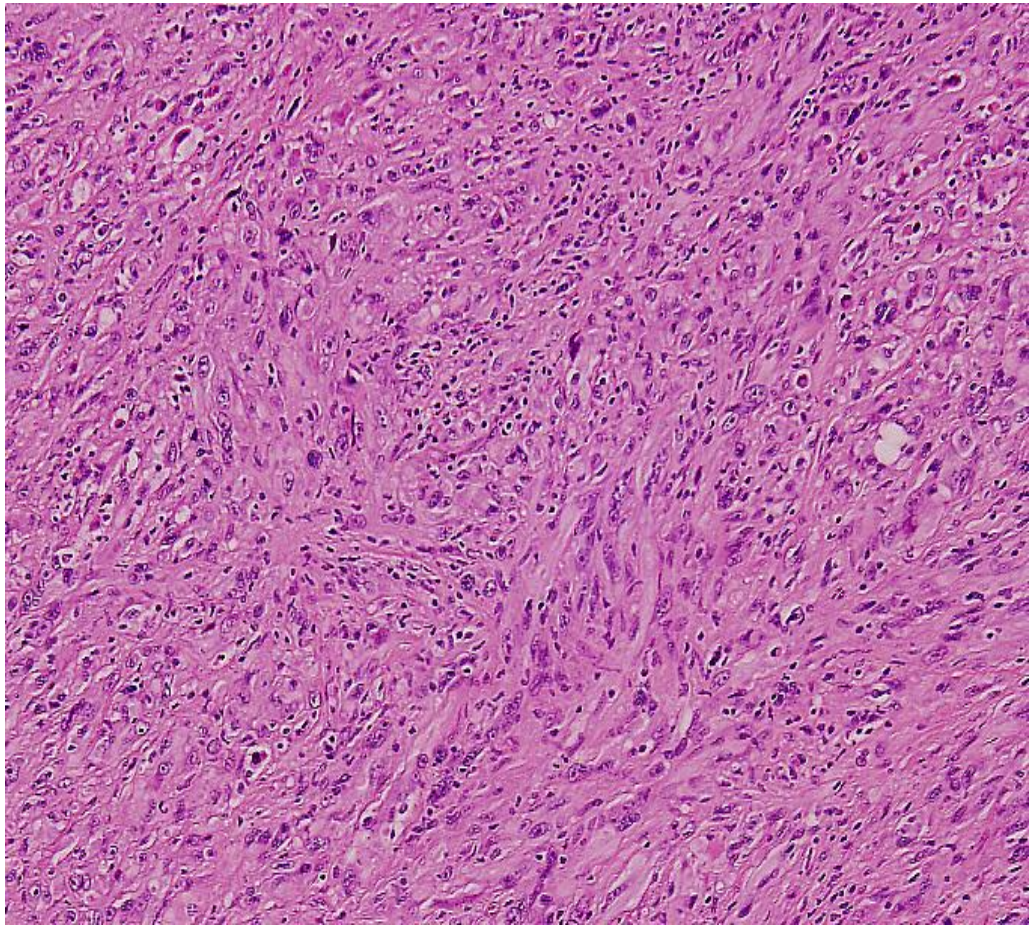
- Spindle cell metaplastic carcinoma
- Metastasis
- Melanoma
- Primary sarcoma including angiosarcoma
- Stromal component of phyllodes

Metastatic Spindle Cell Melanoma



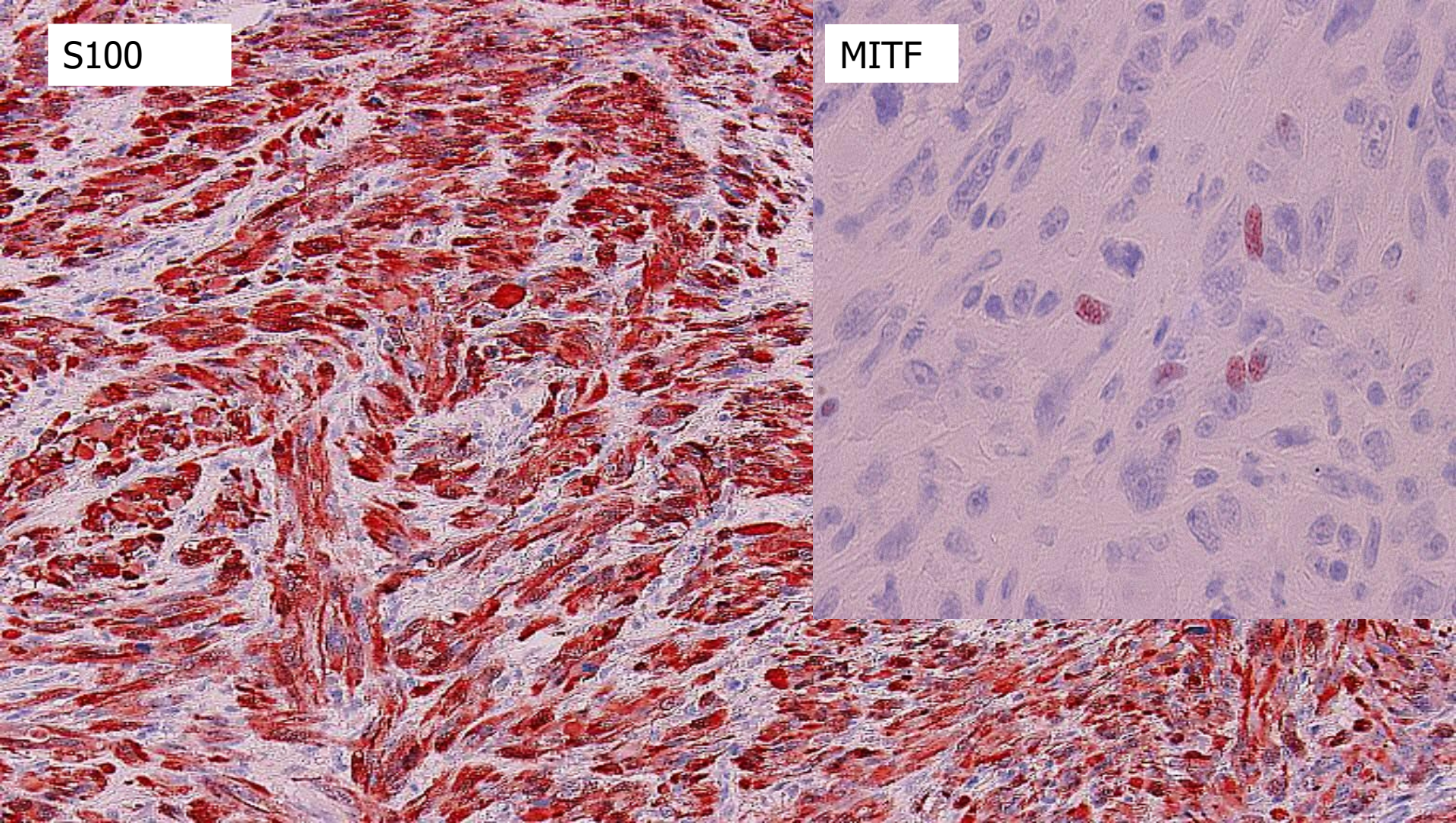
25 yrs old woman with axillary mass misdiagnosed as metaplastic breast carcinoma

Metastatic Spindle Cell Tumors-Melanoma



HMB-45 and Melan A can be neg

Strong S100-protein would support melanoma over carcinoma



Misdiagnosed as: Metaplastic Carcinoma

S100 +, CK focally +

Melan A and HMB 45 neg

Spindle Cell Sarcoma

Primary sarcoma (very rare-dx by exclusion)

- Leiomyosarcoma: SMA and Actin (strong diffuse reactivity)
- Fibrosarcoma: herringbone growth
- Follicular dentritic cell tumors: CD 35 & CD 21+
- Angiosarcoma: vascular markers, D2-40, FLI-1---

Periductal stromal tumor/phyllodes

Most Important Diagnostic Problems in Mammary Gland Tumor Pathology

1. Distinguishing *in situ* from invasive carcinoma
2. The differential diagnosis of various types of benign lesions and carcinoma
3. **Confirming the breast as the primary site in metastatic carcinoma**

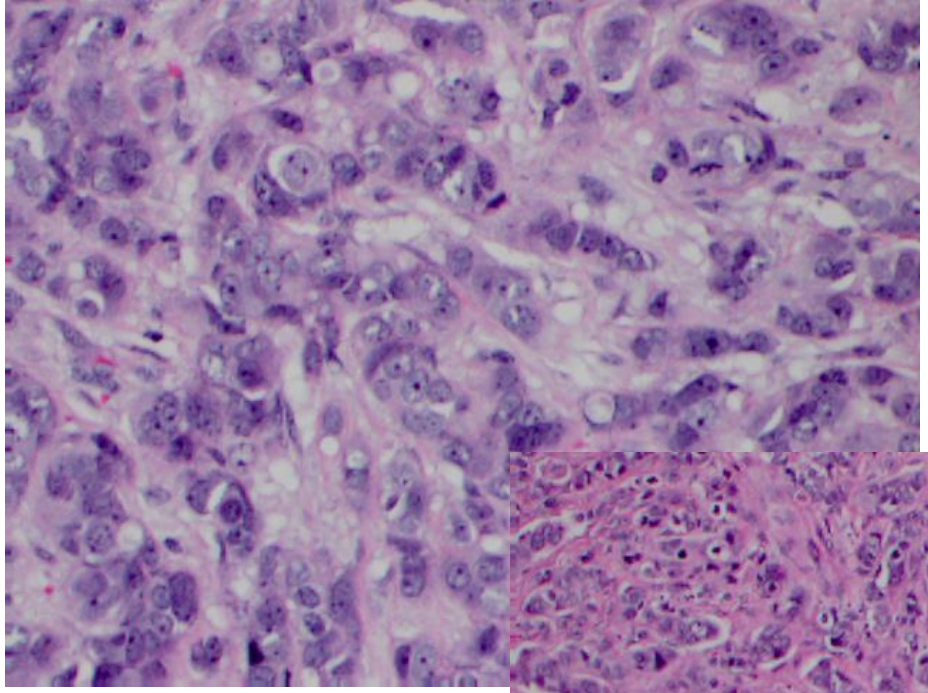
Metastatic Breast Carcinoma

- Usual breast carcinoma immunoprofile: CK7+, GATA3+, GCDFP-15+, mammaglobin+, ER+
- Negative for CK20, TTF-1, WT1, and PAX8.

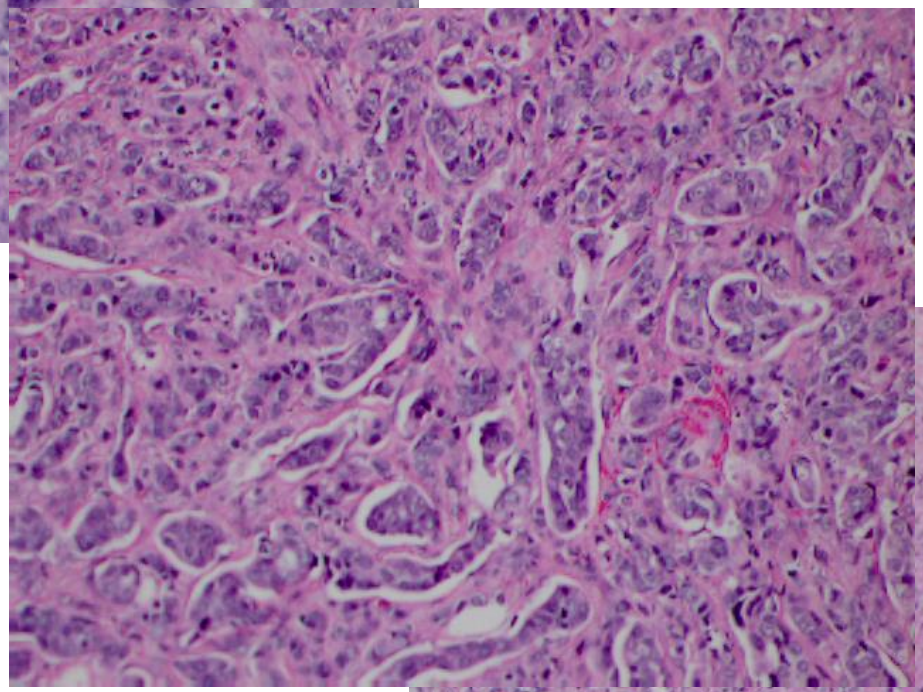
- GCDFP-15 is the most specific marker of breast ca.
- GATA3 is the most sensitive marker of breast ca.

- Mammaglobin also stains endometrioid adenocarcinomas (up to 40% cases) and rare melanomas.
- Up to 30% of breast ca may be negative for both GCDFP-15 and mammaglobin.
- Salivary gland carcinomas and skin adnexal carcinomas have immunoprofile similar to breast carcinomas.

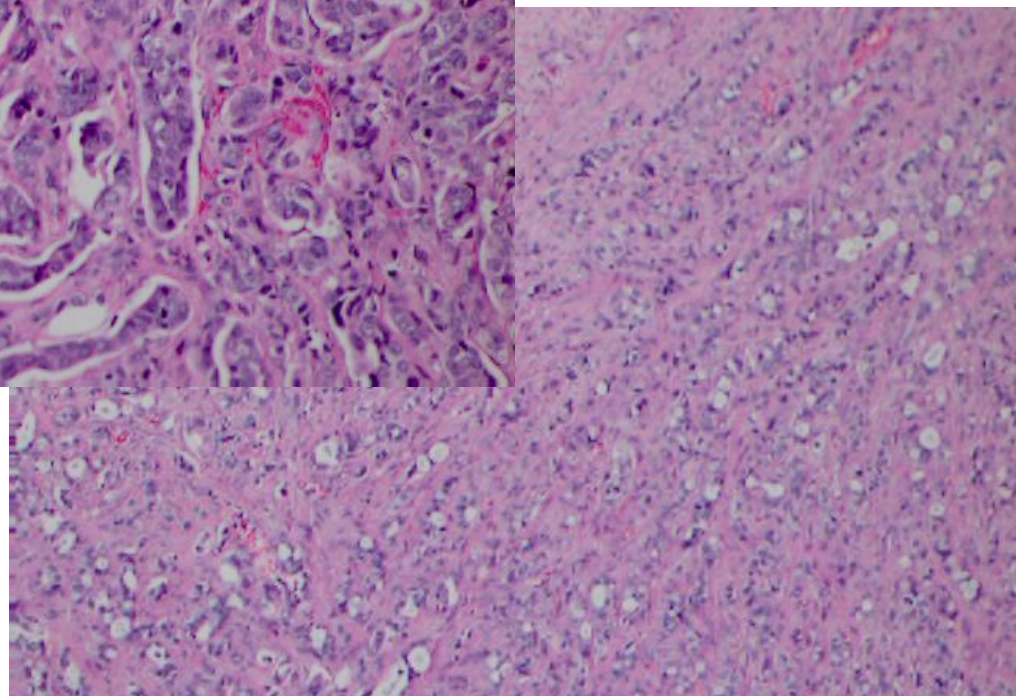
37 yrs old
Primary breast ca 2013
Bilateral ovarian masses in 2017

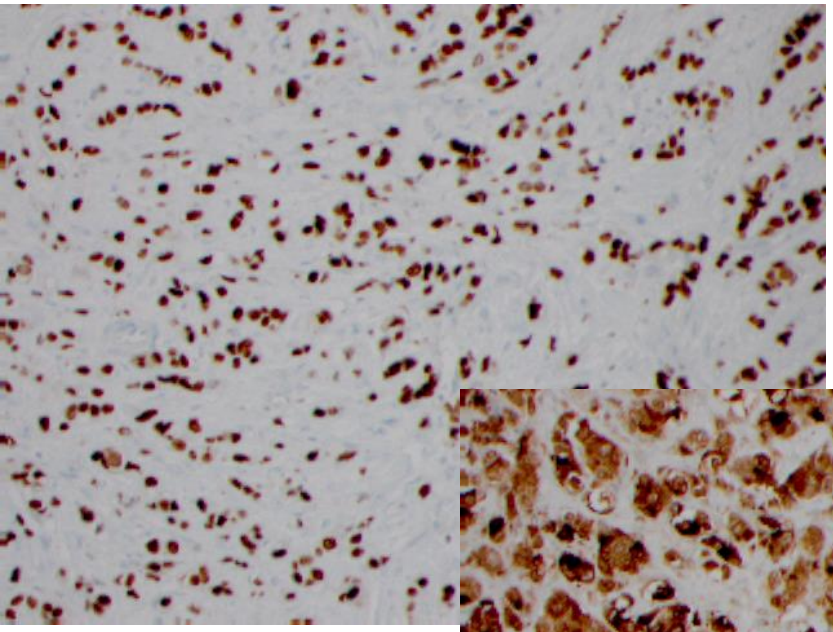


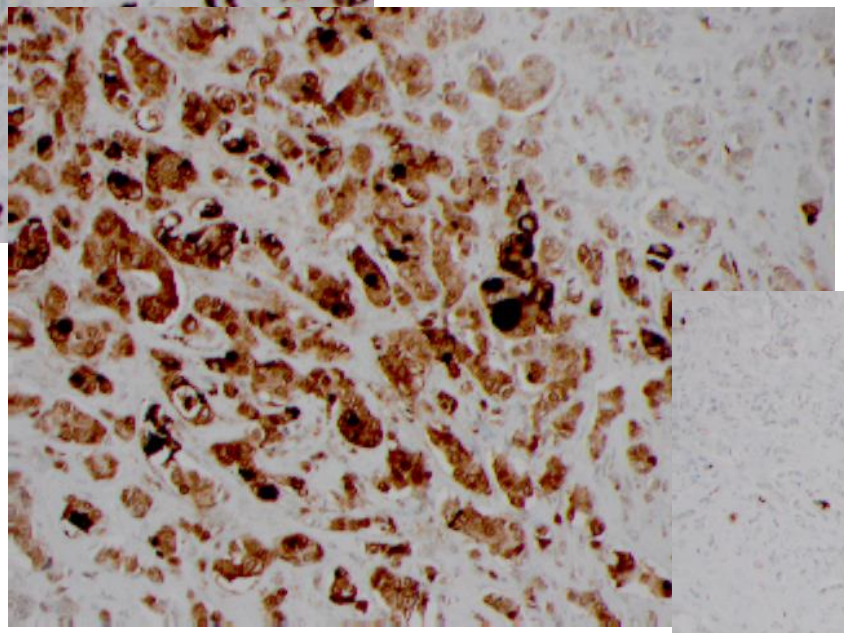
Ovarian tumor

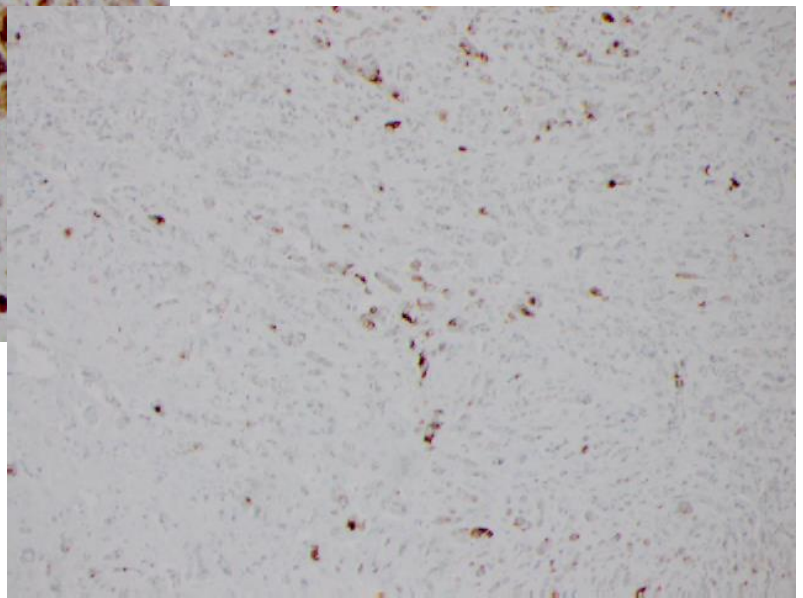


Breast primary









GATA3 100%

Mammaglobin 60%

BRST2/ GCDFP-15 10%

Primary breast ca metastatic to ovary

GATA 3 – A MULTISPECIFIC BUT POTENTIALLY USEFUL MARKER IN SURGICAL PATHOLOGY – A SYSTEMATIC ANALYSIS OF 2500 EPITHELIAL AND NON-EPITHELIAL TUMORS

Miettinen et al, *Am J Surg Pathol*. 2014; 38(1): 13–22.

- GATA3, a transcription factor important in the differentiation of breast epithelia, urothelia, and subsets of T-lymphocytes. (study material 2040 epithelial and 460 mesenchymal or neuroectodermal neoplasms).
- GATA3 expression in epithelial neoplasms: >90% of primary and metastatic ductal and lobular carcinomas of the breast, urothelial, and cutaneous basal cell carcinomas, and trophoblastic and endodermal sinus tumors.
- In metastatic breast carcinomas, it was more sensitive than GCDFP.

GATA 3 –continue

- Among squamous cell carcinomas, the expression was highest in the skin (81%) and lower in cervical (33%), laryngeal (16%) and pulmonary tumors (12%).
- Common positivity: skin adnexal tumors (100%), mesothelioma (58%), salivary gland (43%) and pancreatic (37%) ductal carcinomas.

  Frequency of expression in adenocarcinomas of lung, stomach, colon, endometrium, ovary, and prostate <10%.
- Chromophobe renal cell carcinoma: frequent positivity (51%), whereas oncocytomas were positive in 17% of cases but other types only rarely.
- Among mesenchymal and neuroectodermal tumors, paragangliomas were usually positive, which sets these tumors apart from epithelial neuroendocrine tumors. Mesenchymal tumors were only sporadically positive, except epithelia of biphasic synovial sarcomas. GATA3 is a useful marker in characterization not only mammary and urothelial but also for renal and germ cell tumors, mesotheliomas, and paragangliomas.

Primary vs Metastasis

Breast vs lung

- Breast: GCDFP-15 (up to 5% of lung ca +), and mammaglobin
- Lung: TTF-1 (2.4% of breast ca pos)

Breast vs serous

Serous: pax 8 and WT1 (WT1 pos in 2%)

- Always correlate with clinical, radiologic and histologic characteristics