WORKSHOP

06 GIUGNO 2025

CRPT- PROGRAMMA REGIONALE DI SCREENING
PREVENZIONE SERENA
AGLI ESTREMI DELLO SCREENING MAMMOGRAFICO

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Lesioni B3 della mammella: to B or not to B – ted?

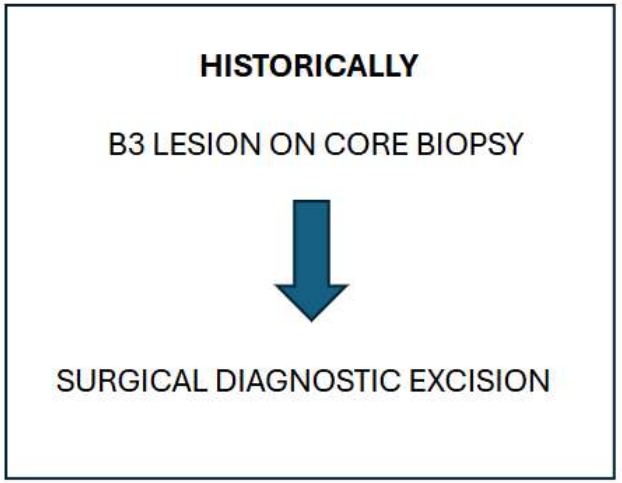
B3 lesions of the breast

Lesions of uncertain malignant potential
3-21% incidence on biotical material
Higher rate in screening population

Heterogeneous group of lesions that can be associated with
- Atypia
- Malignancy

Broad spectrum of lesions:

- **Atypical ductal epithelial hyperplasia (AIDEP)**
- **Flat epithelial atypia (FEA)**
- **Lobular neoplasia**
- **Papillomatous lesions**
- **Radial scar/complex sclerosing lesions**
- **Cellular fibroepithelial lesions**
- **Mucocele-like lesions**
- **Miscellaneous uncommon lesions**



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NOW

B3 LESION ON CORE BIOPSY OR VABB

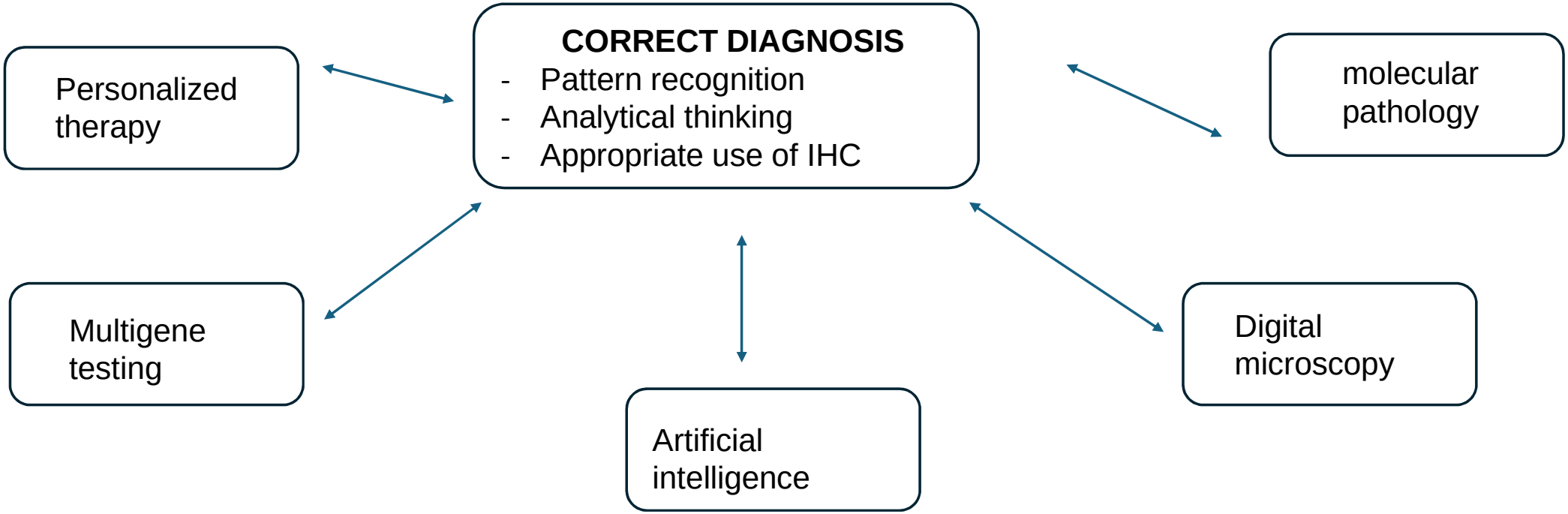
TUMOR BOARD

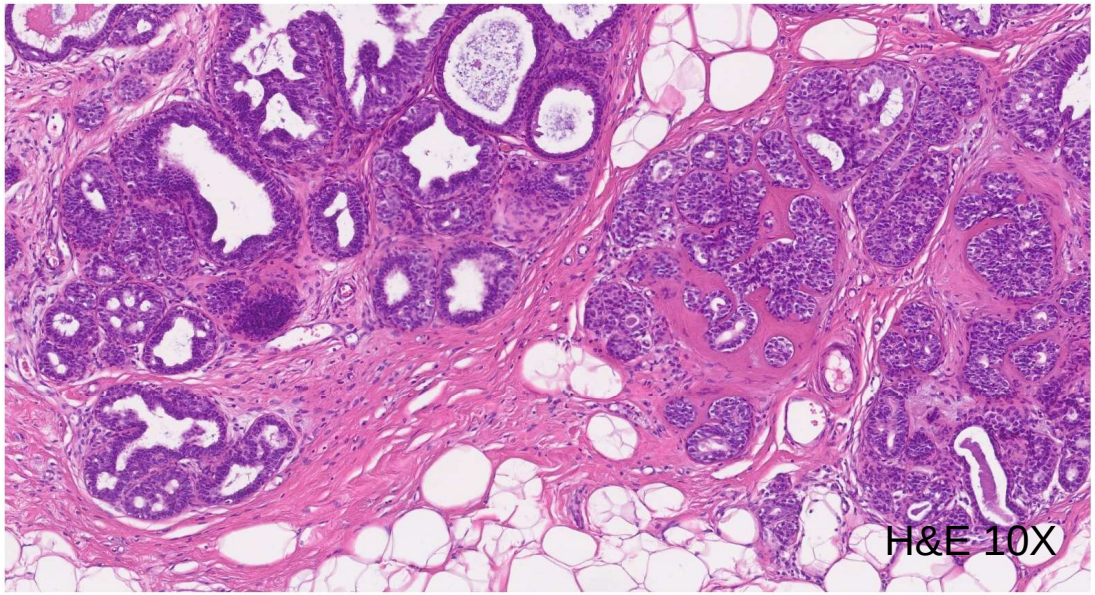
- SURGICAL DIAGNOSTIC EXCISION
- VAE
- FOLLOW UP

- Radiological findings
- Lesion size
- Nature of the lesion
- Patient factors

“Overdiagnosis is more common than underdiagnosis, especially by pathologist with less than 10 years experience"
"never use a microscope without a low power view"

"Problems in breast pathology" Azzoppardi, 1979

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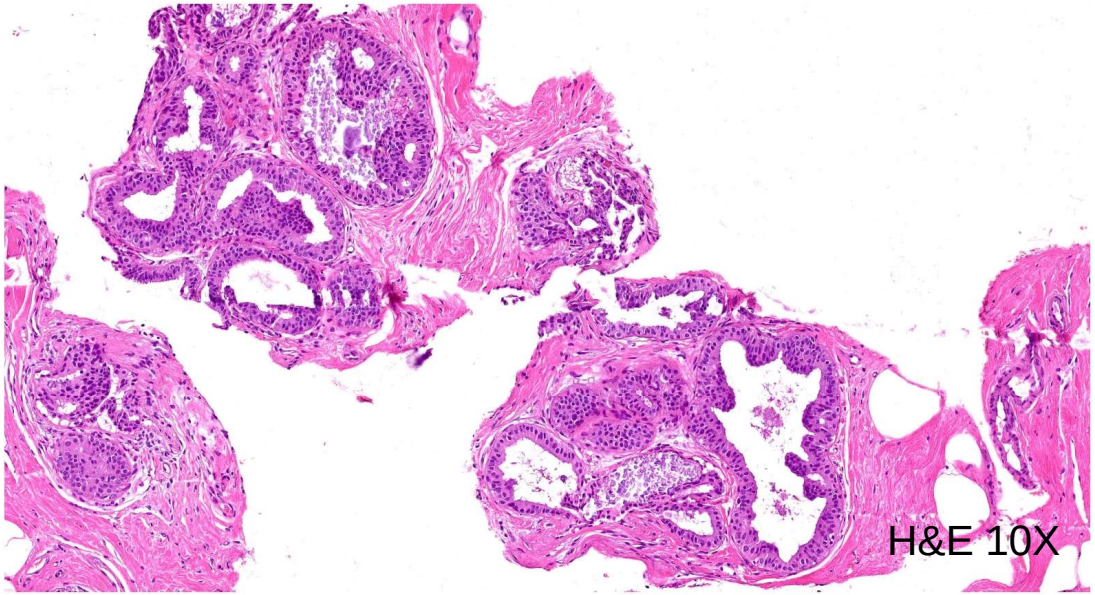
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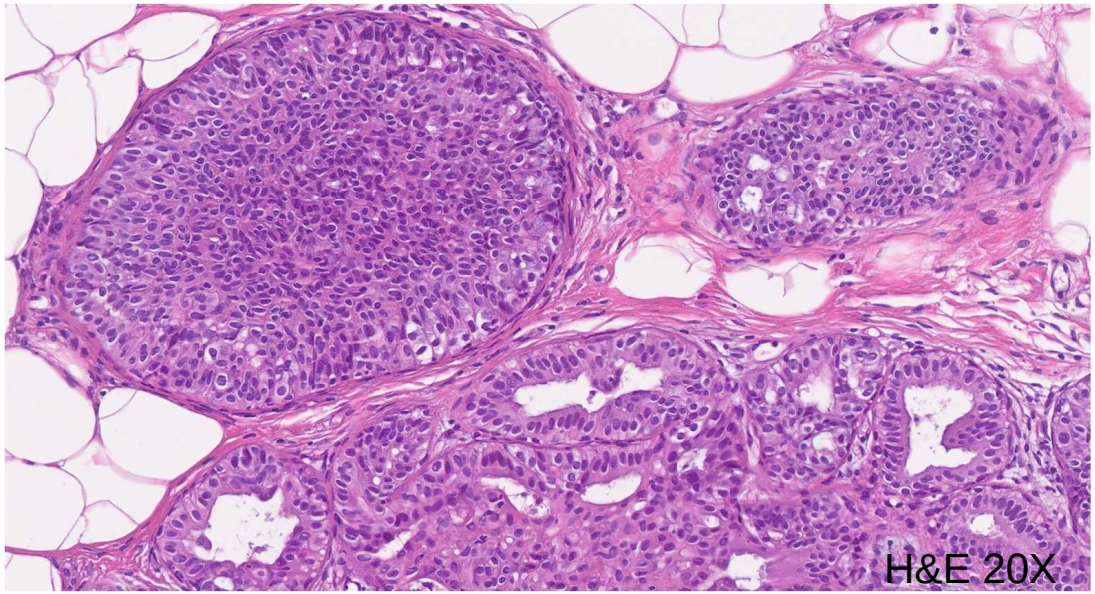
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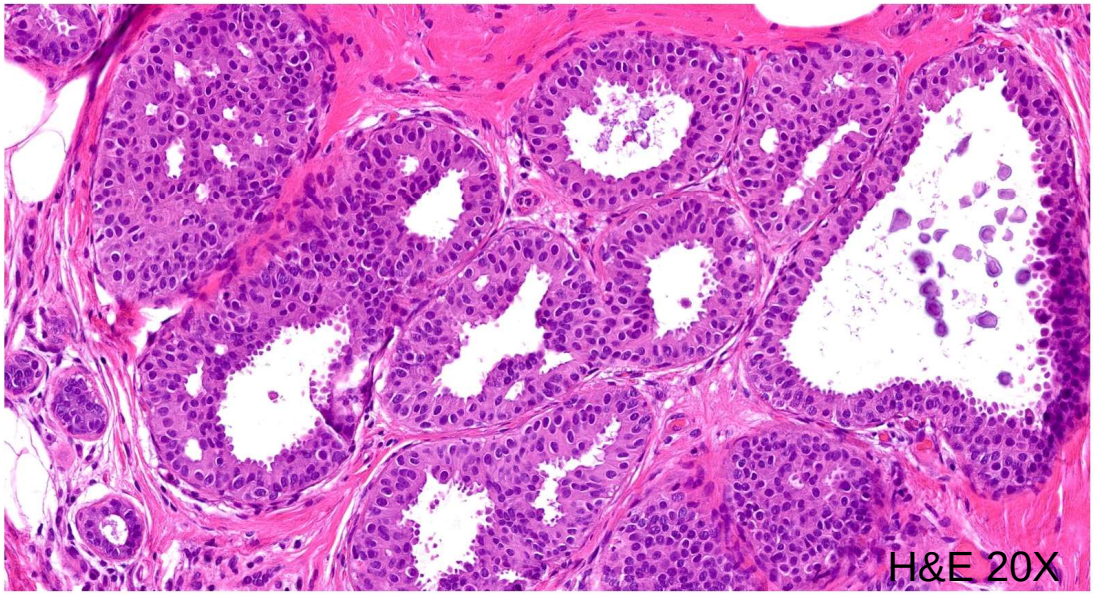
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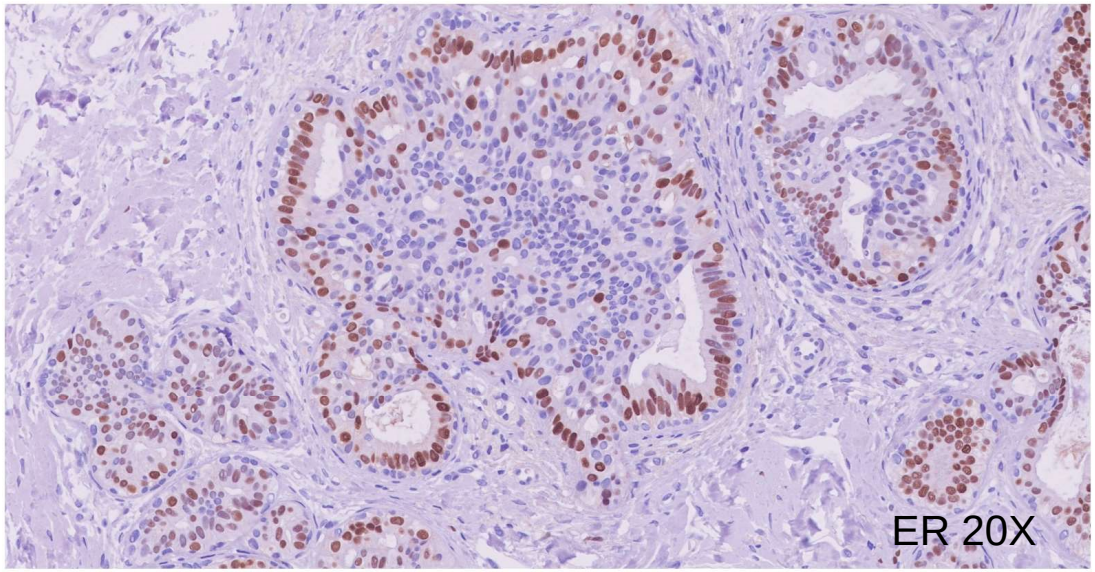
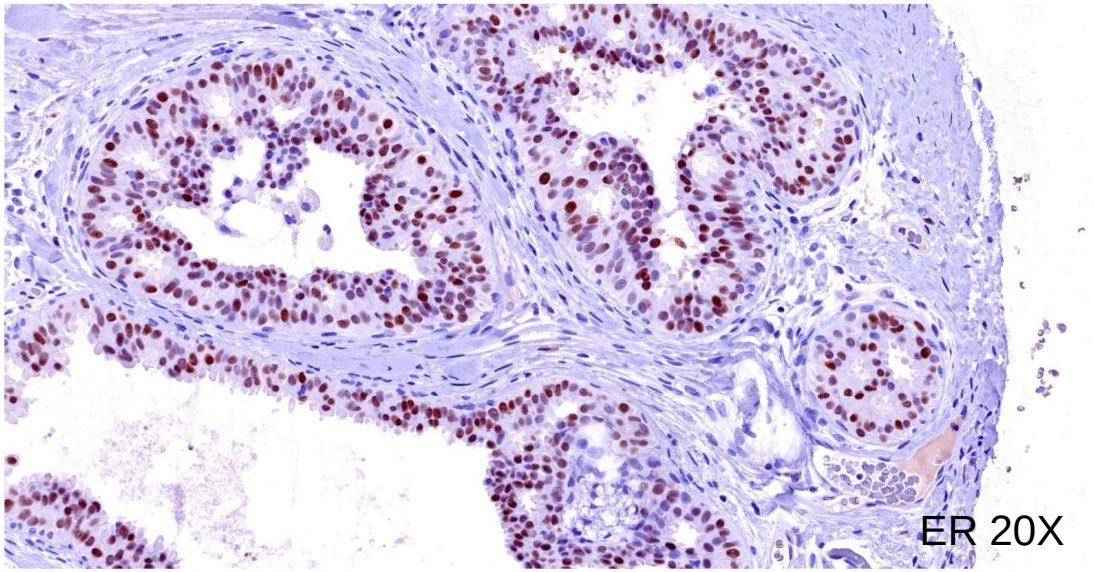
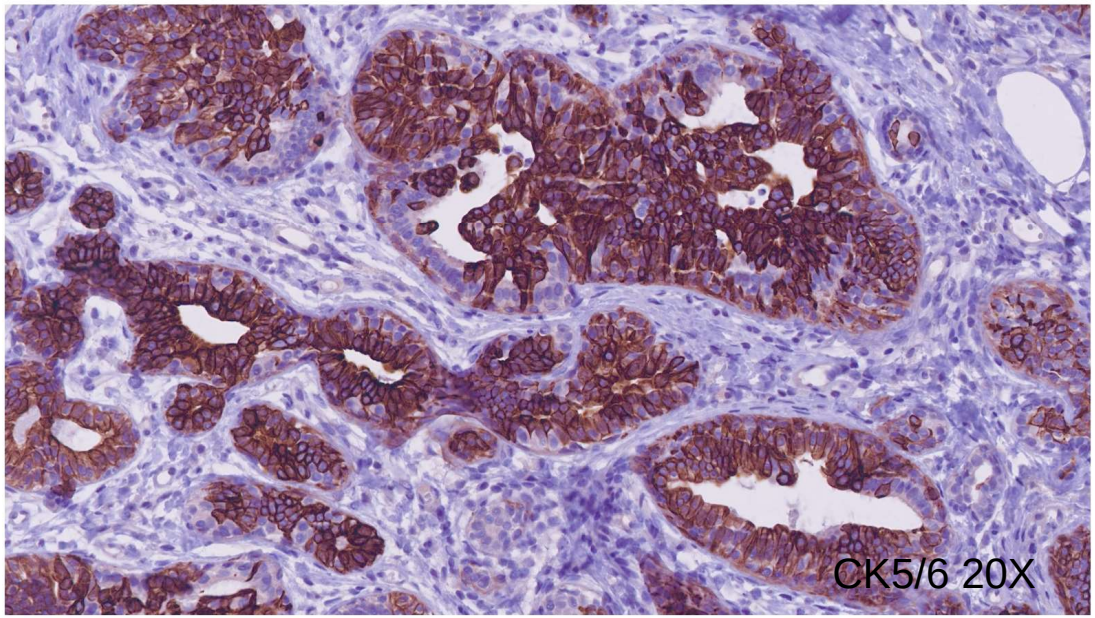
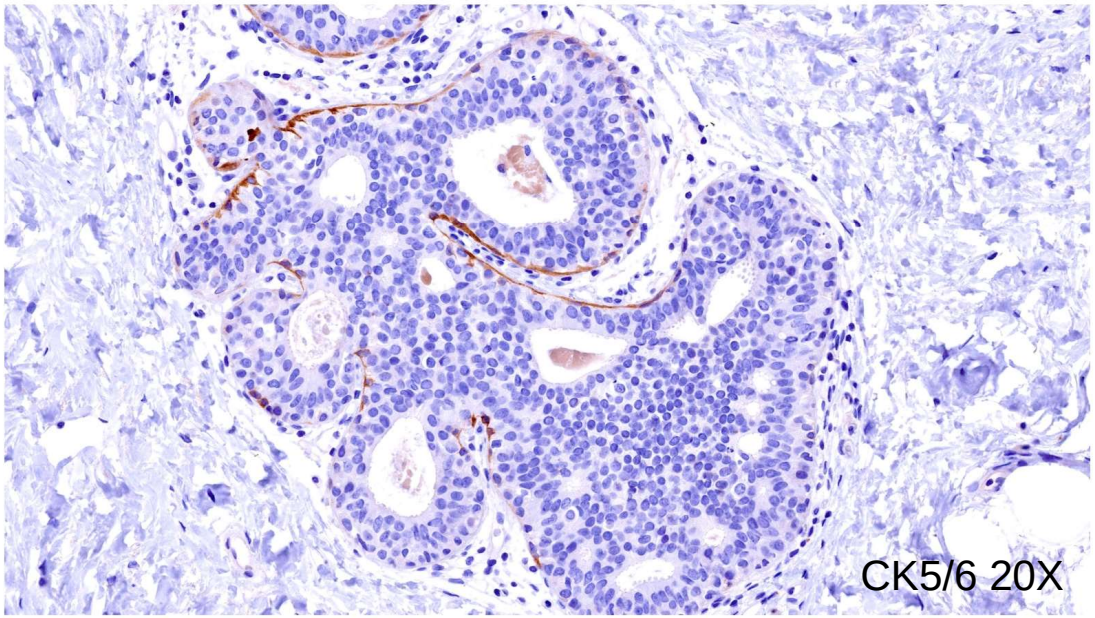
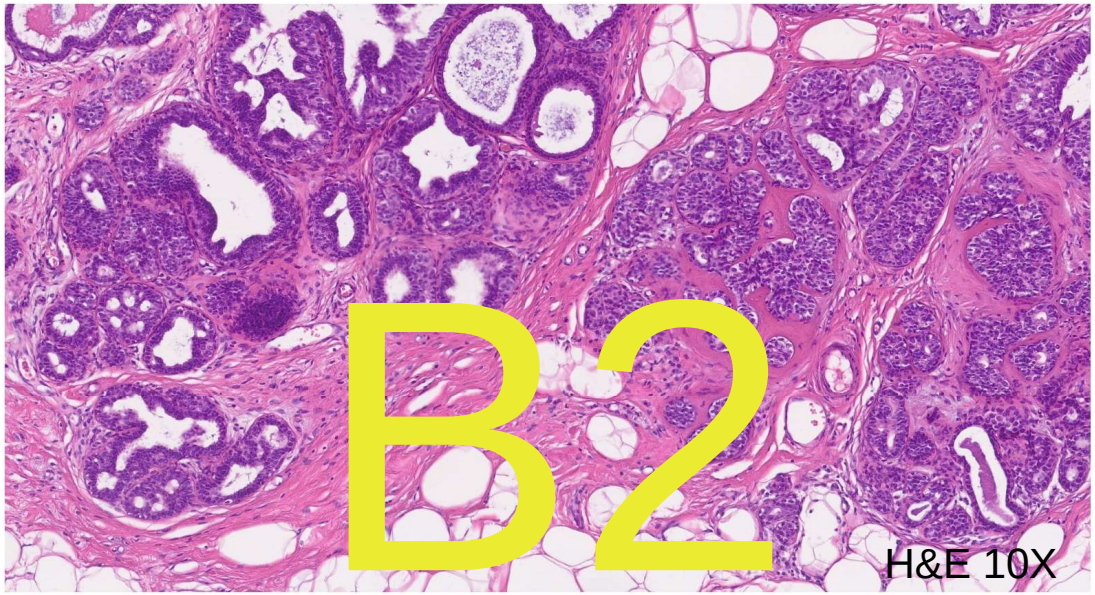
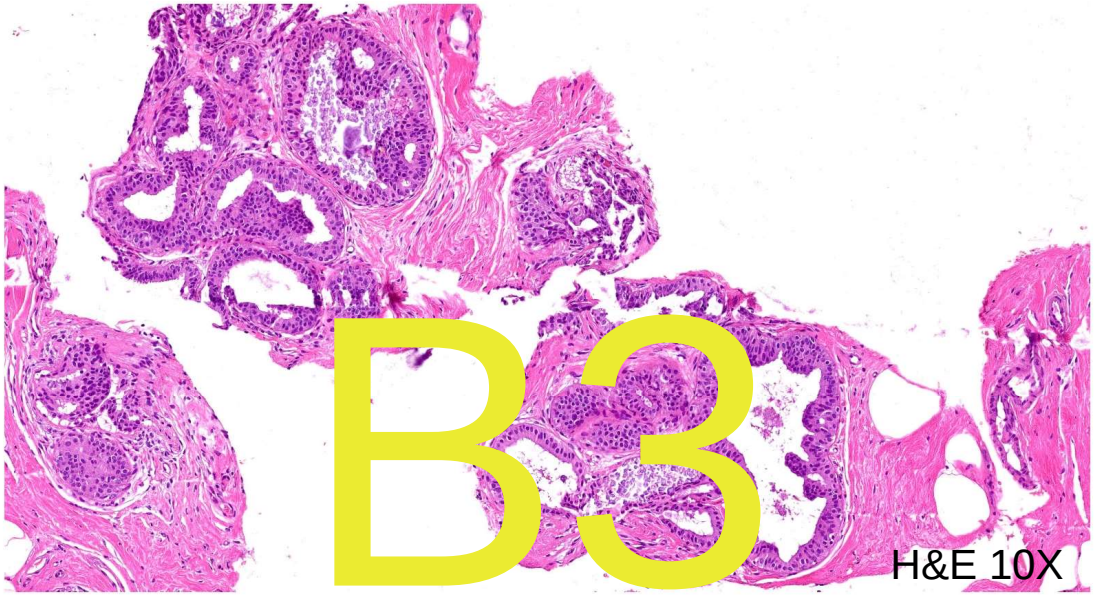

ER 20X

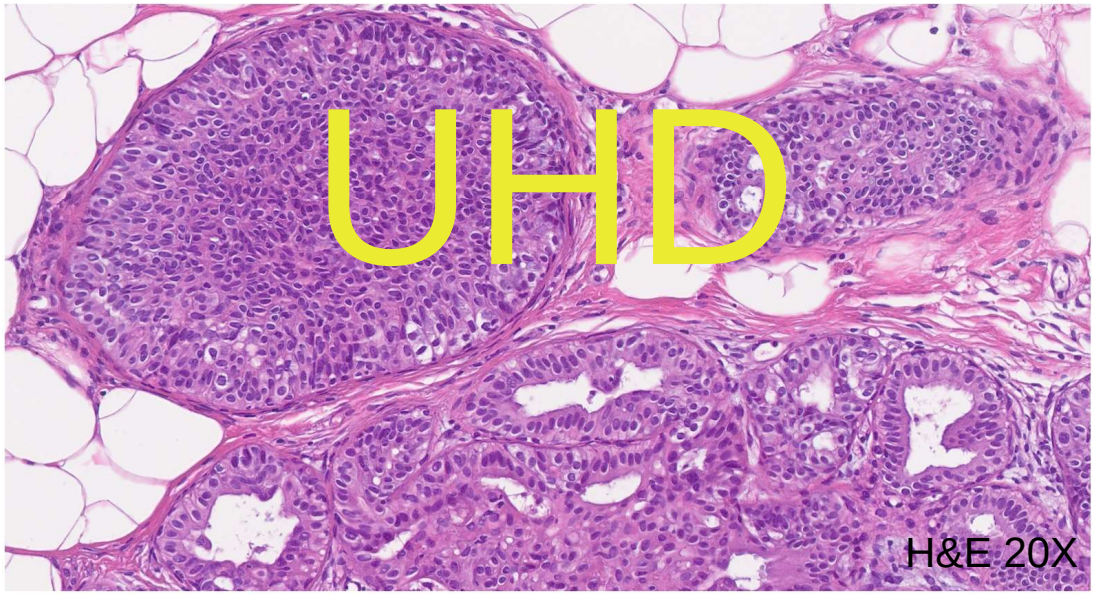

ER 20X

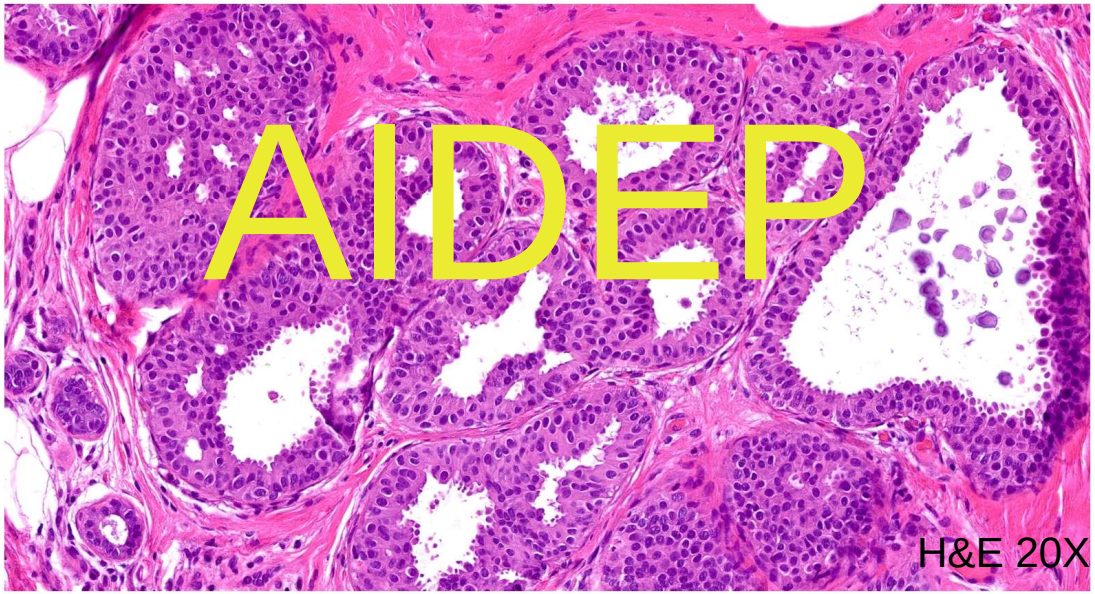

CK5/6 20X


CK5/6 20X

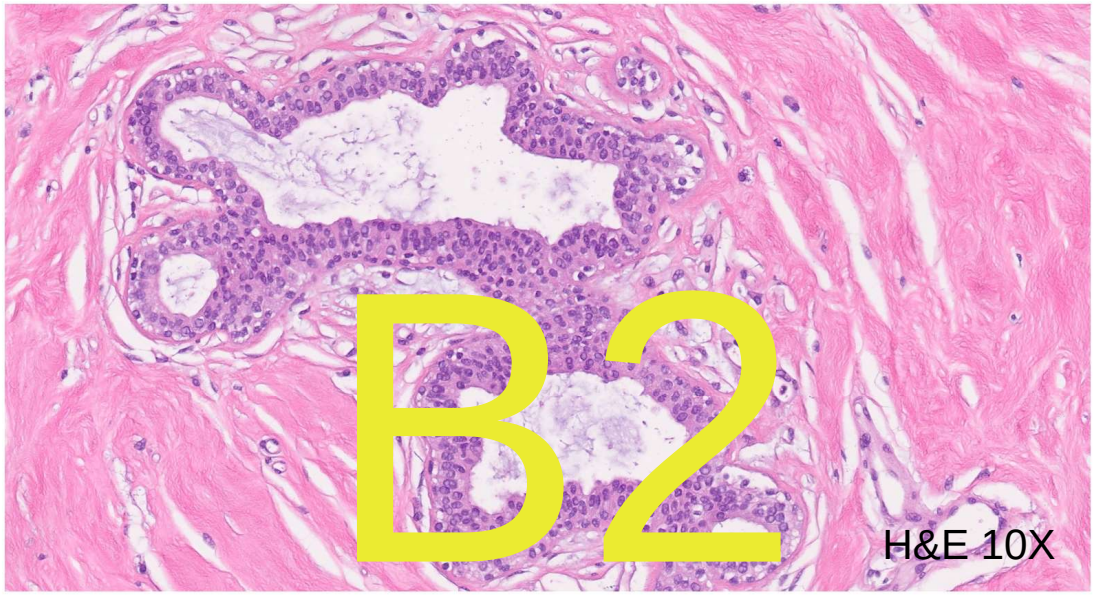

B2
H&E 10X

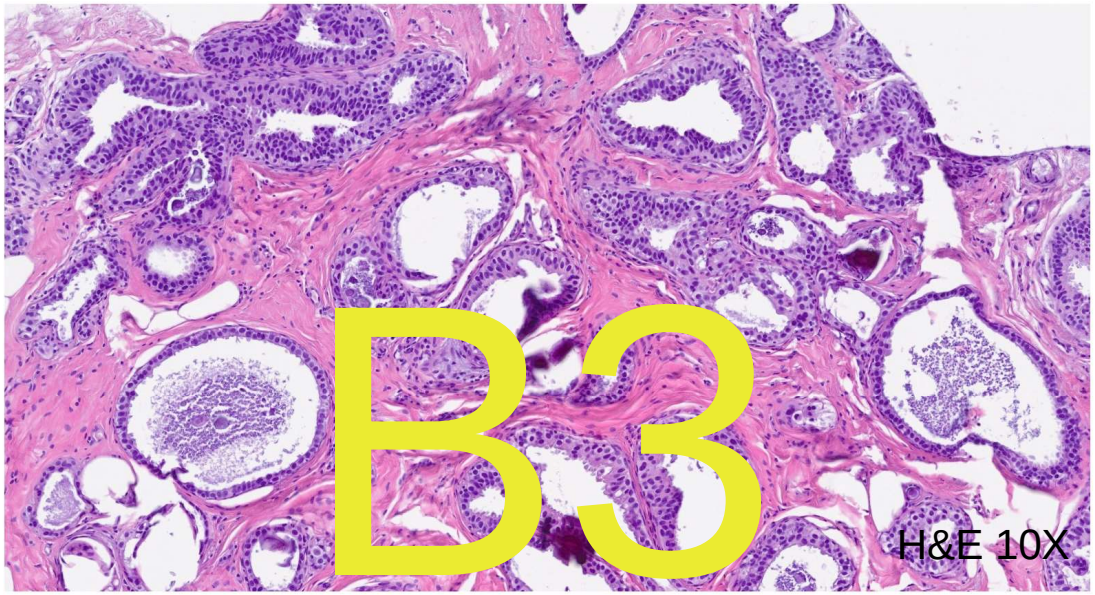

B3
H&E 10X

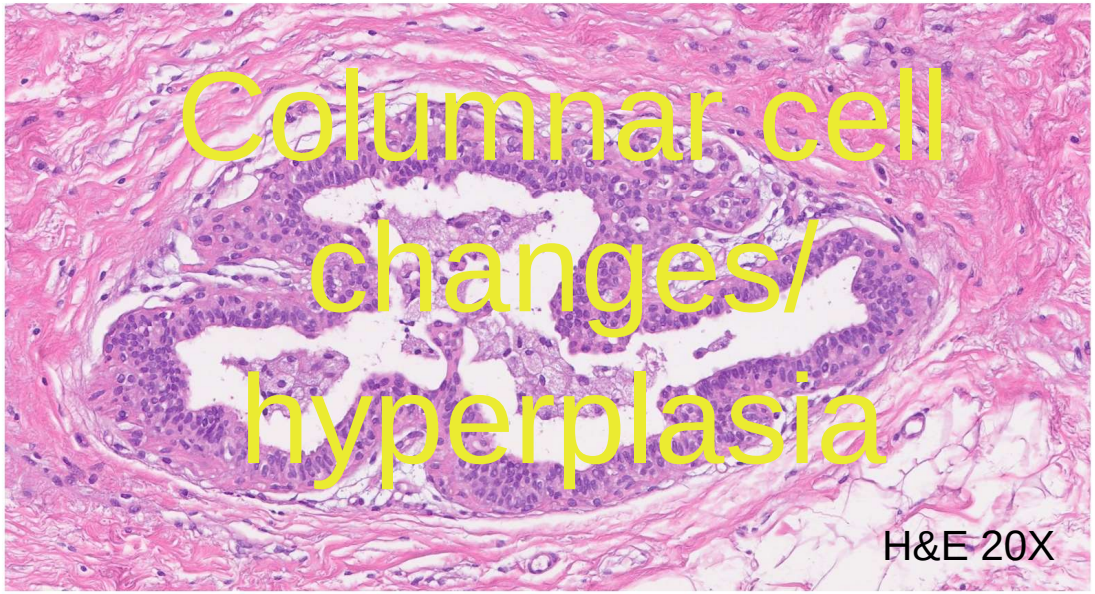

UHD
H&E 20X

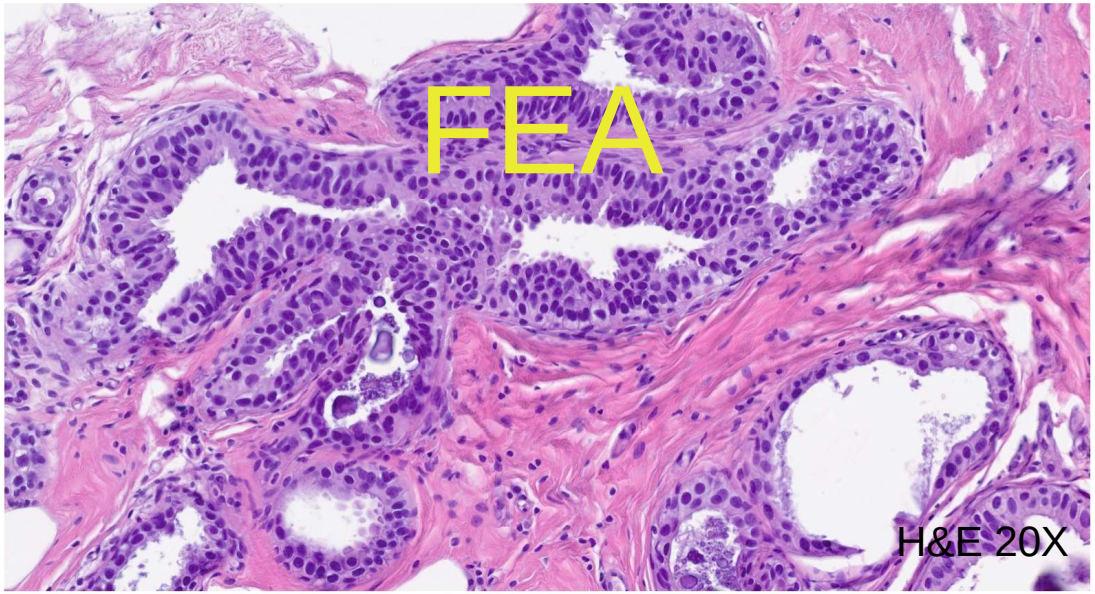

AIDEP
H&E 20X

	B2	**B3**
	Usual / florid ductal hyperplasia	**AIDEP** **Atypical intraductal epithelial proliferation**
Architectural features	Solid, fenestrated, or micropapillary Lumens irregular, variable in size and shape, often slit-like and displaced to periphery without polarization of surrounding cells Bridges stretched or twisted with central attenuation	Rigid bridges -arcades of uniform thickness, micropapillations, cribriform and solid pattern Partial involvement of one or more spaces; complete involvement of fewer than two spaces or <2 mm in extent
Cytological features	Heterogeneous cell population Variation in cell size, shape, and orientation Cell borders poorly defined	Atypical cell population similar to that of low-grade ductal carcinoma *in situ* (small, uniform cells
Immunistochemistry	ER scattered and heterogeneous nuclear stain, from weak to strong intensity	ER strong and diffuse nuclear stain CK 56 absent in atypical cells
Upgrade risk		5–50% (22%)


B2
H&E 10X


B3
H&E 10X


Columnar cell changes/ hyperplasia
H&E 20X


FEA
H&E 20X

	B2	**B3**
	Columnar cell changes /hyperplasia	**Atypical flat hyperplasia (FEA)**
Architectural features	Cellular stratification: 2 ore more cell layers of columnar cells, sometimes forming tufts or mounds Complex architectural patterns not present	One to several layers of cuboidal to columnar epithelial cells Complex architectural patterns not present
Cytological features	Columnar cells with uniform ovoid to elongated nuclei oriented perpendicular to basement membrane Nucleoli absent or inconspicuous Hobnail cells may be present	Cuboidal to columnar cells with monomorphic-type cytologic atypia – low grade Cells may resemble those of tubular carcinoma
Immunistochemistry	Not useful	Not useful
Upgrade risk		1-6%

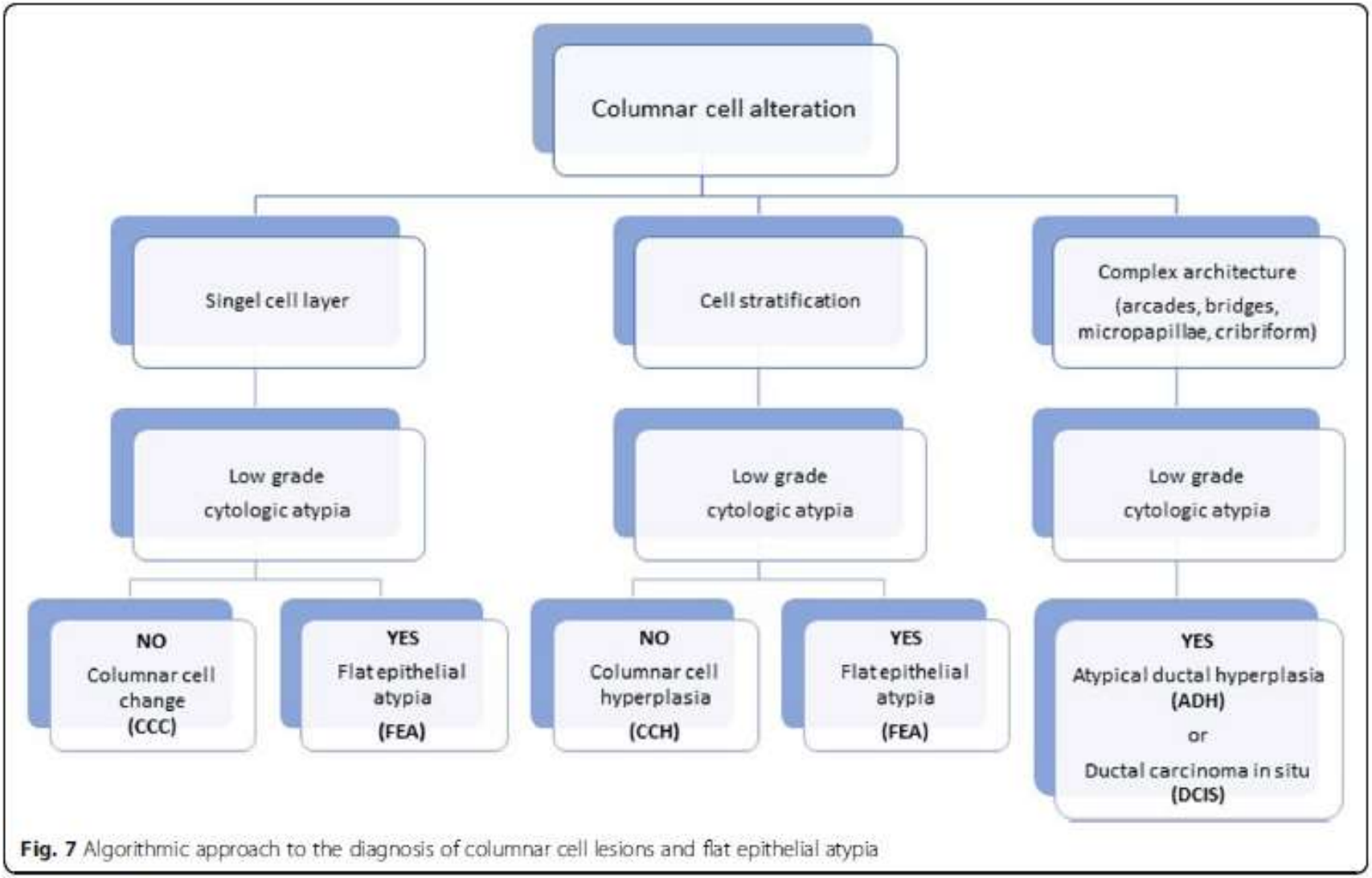
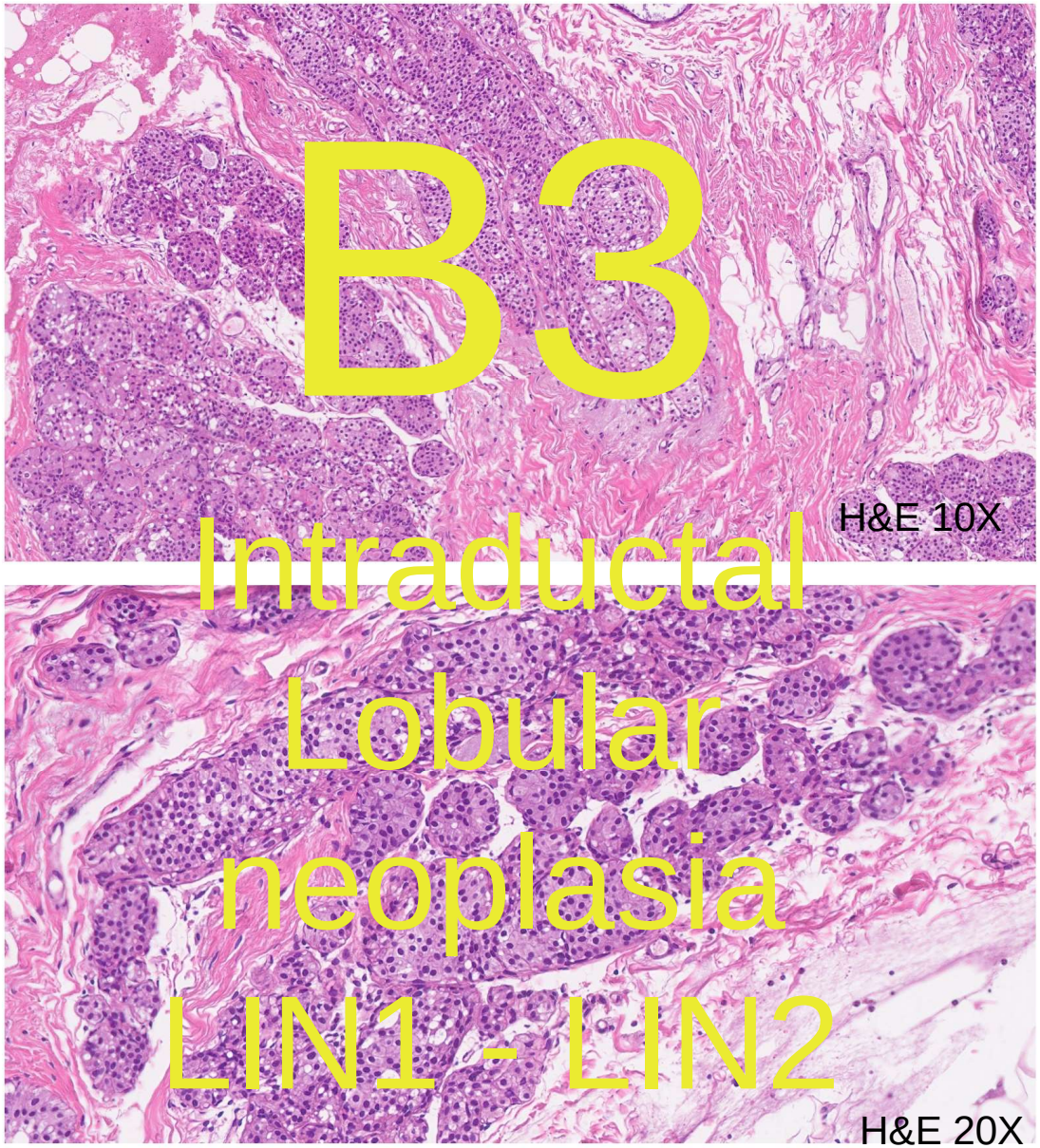
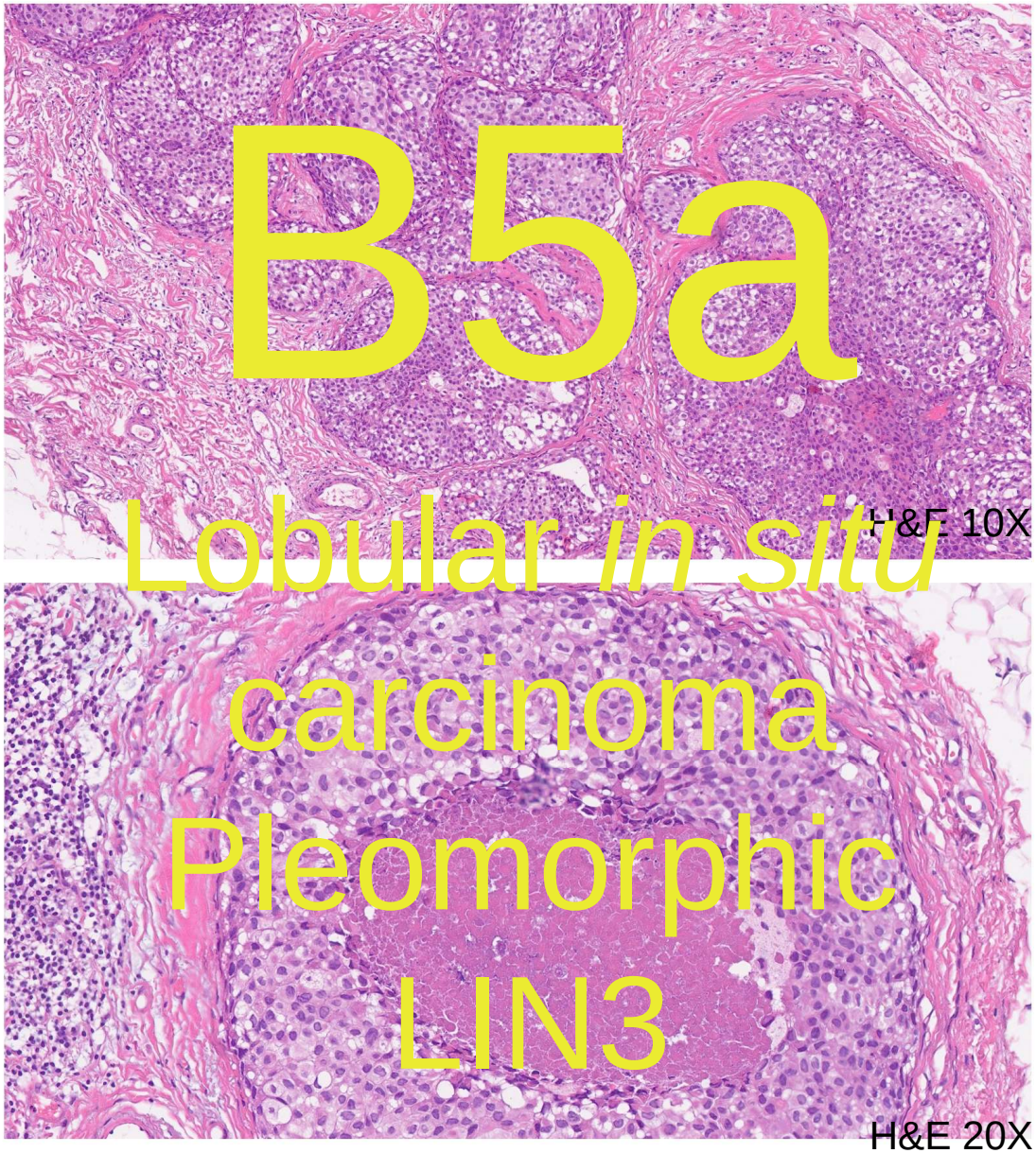
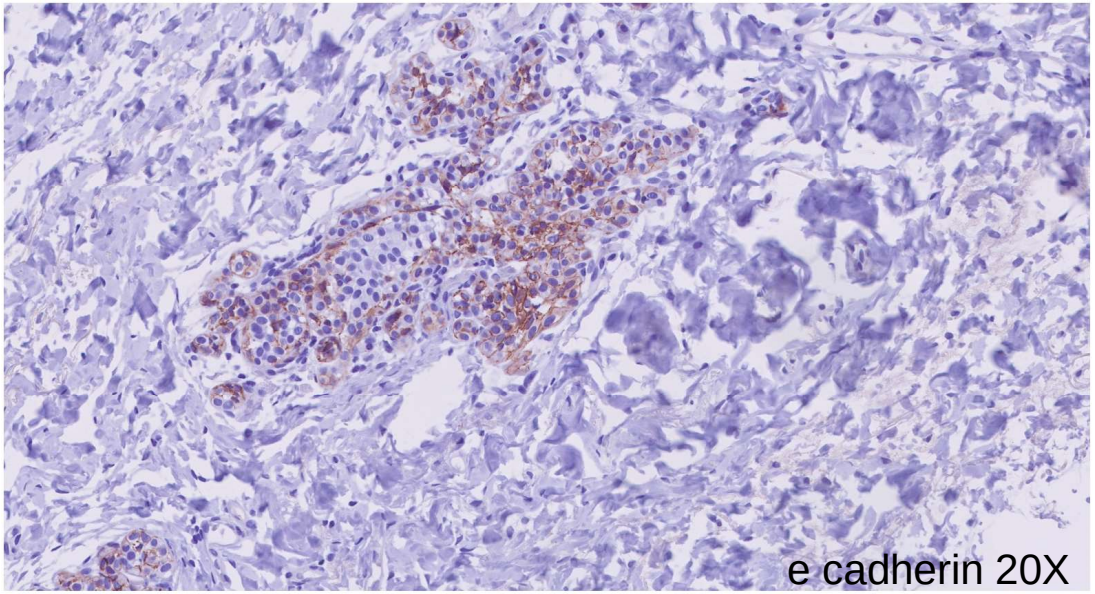


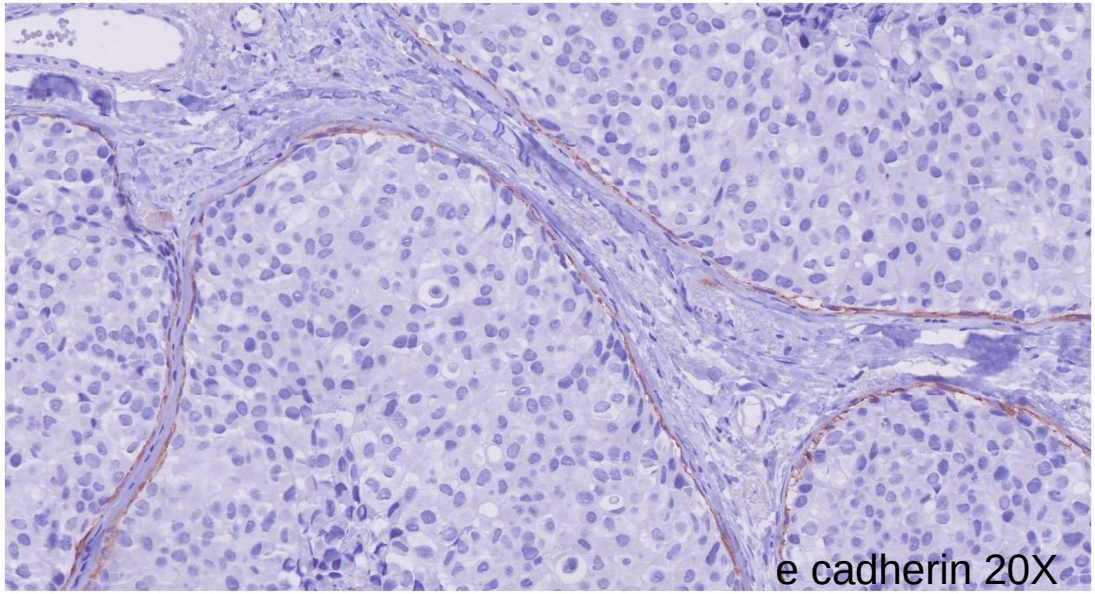
Fig. 7 Algorithmic approach to the diagnosis of columnar cell lesions and flat epithelial atypia

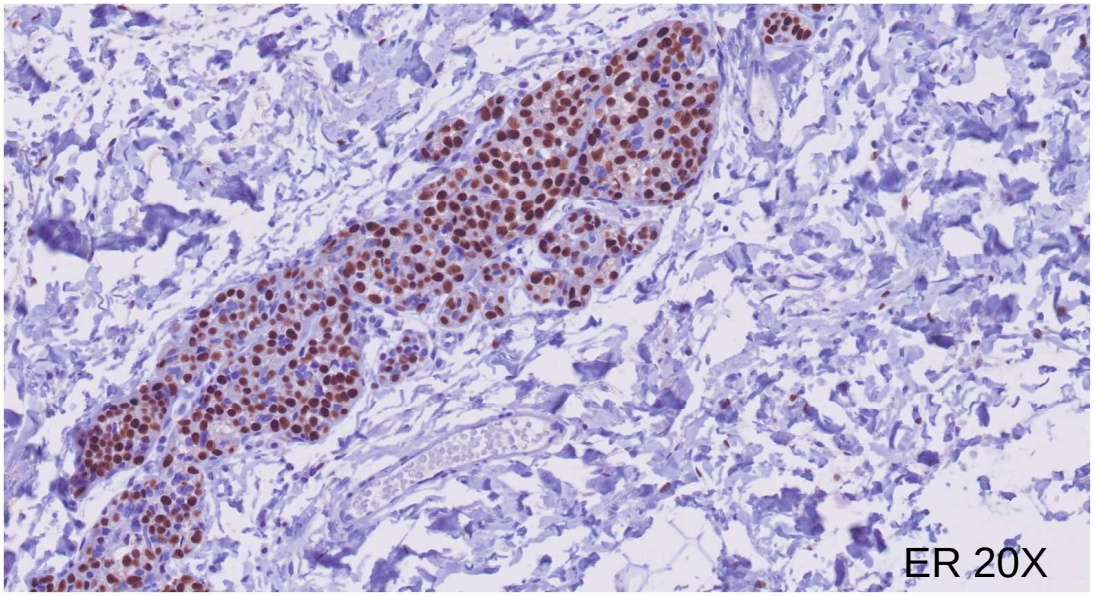
Logullo, A.F., Nimir, C. Columnar cell lesions of the breast: a practical review for the pathologist. *Surg Exp Pathol* **2**, 2 (2019). https://doi.org/10.1186/s42047-018-0027-2

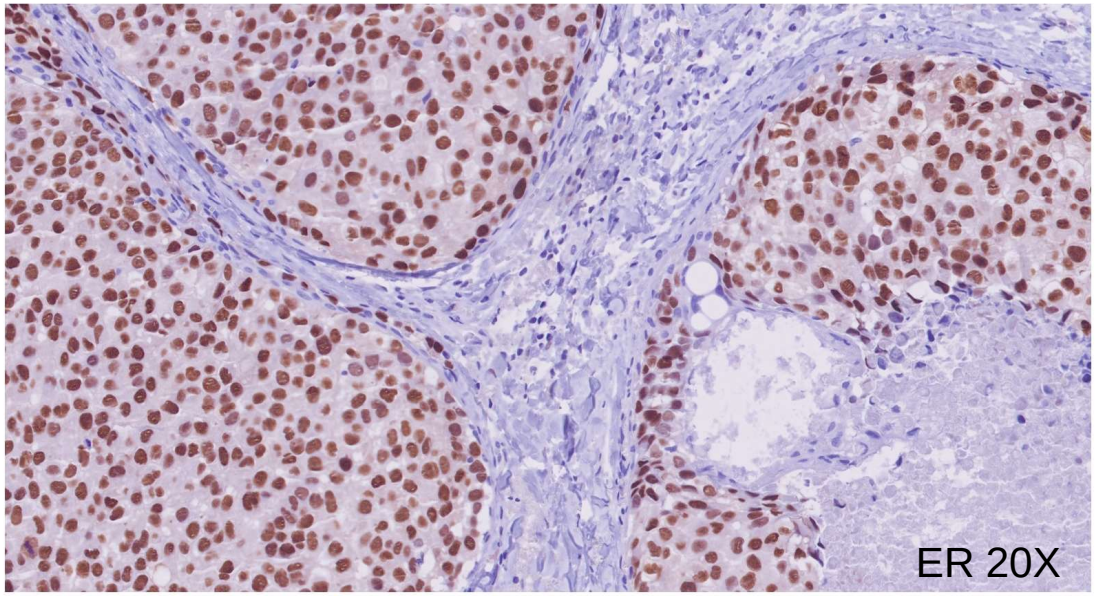

B3
H&E 10X
Intraductal
Lobular
neoplasia
LIN1 - LIN2
H&E 20X


B5a
H&E 10X
Lobular *in situ*
carcinoma
Pleomorphic
LIN3
H&E 20X

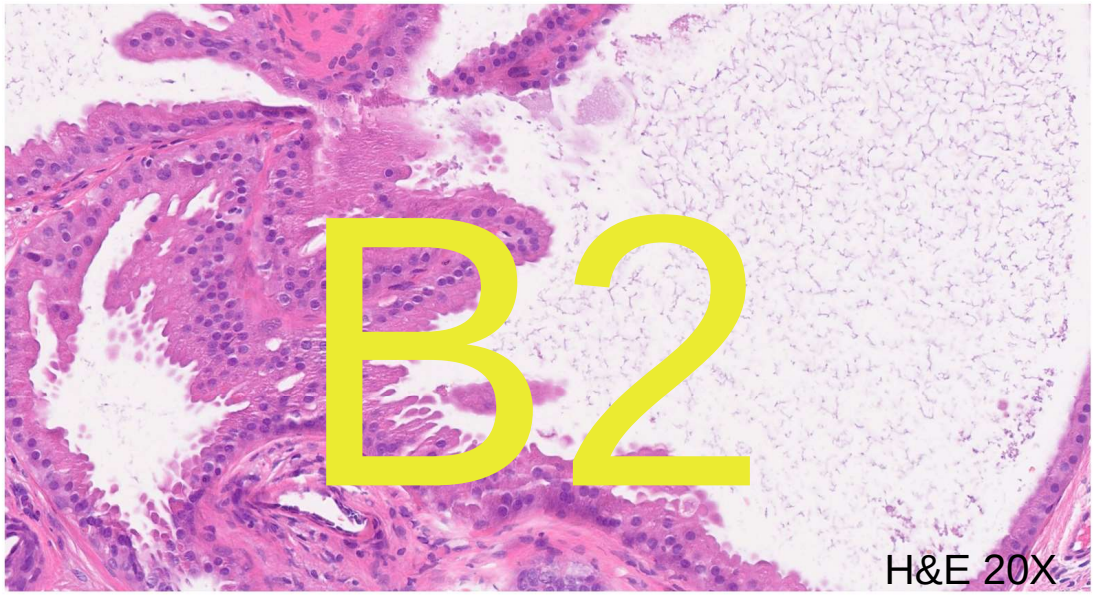

e cadherin 20X

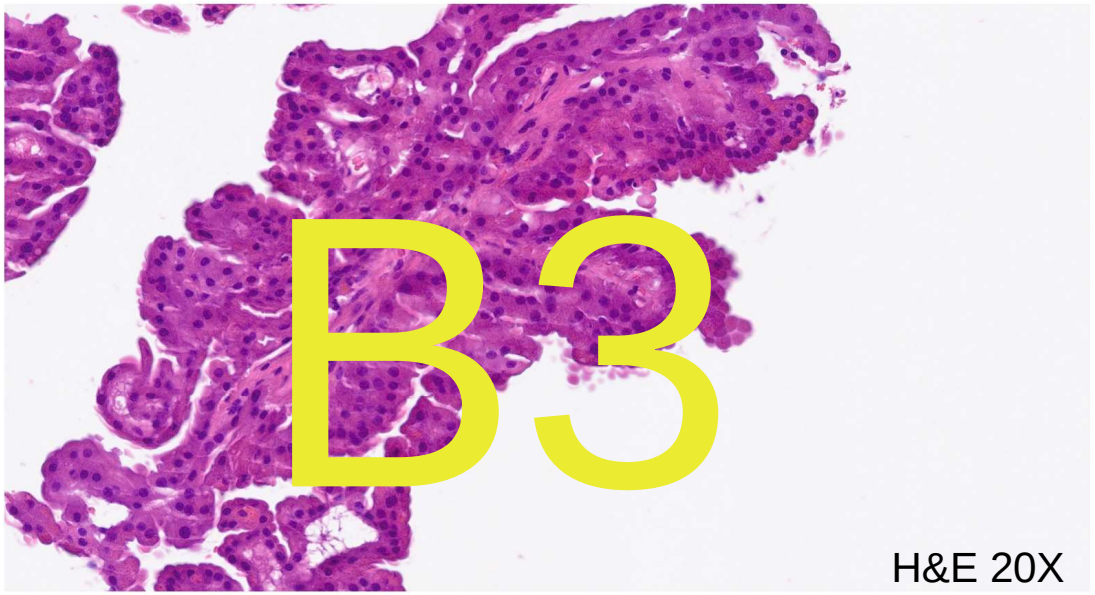

e cadherin 20X

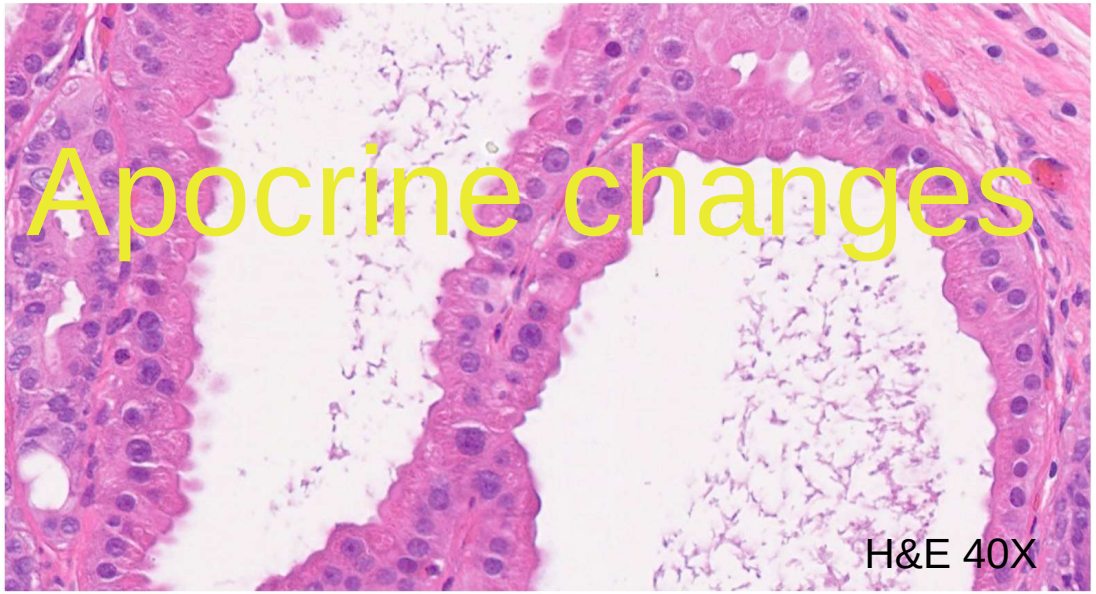

ER 20X


ER 20X

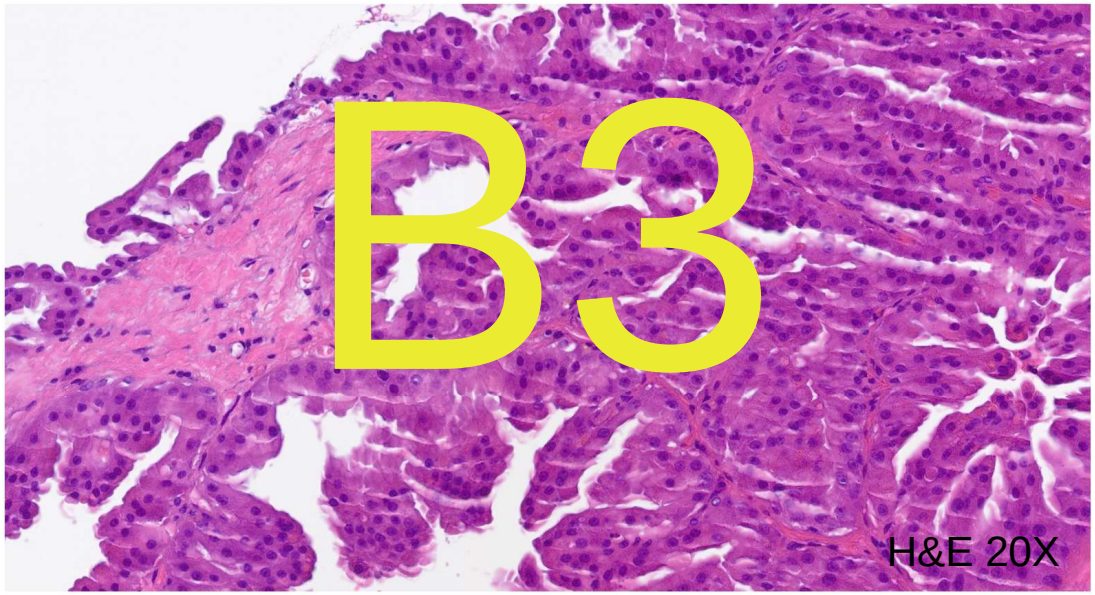
	B3	**B5a**
	Lobular neoplasia LIN1 and LIN2	**Pleomorphic or florid lobular *in situ* carcinoma**
Architectural features	Solid proliferation of dyscohesive monomorphic epithelial cells < 50% of the acini in a TDLU involved, with or without pagetoid involvement of terminal ducts →LIN1 More than 50% of the acini in a TDLU filled →LCIS.	Pleomorphic LCIS → large cells with marked nuclear pleomorphism, > 4 times the size of a lymphocyte with or without apocrine features. Florid LCIS marked distention of TDLUs or ducts, creating a confluent mass-like architecture
Cytological features	Type A cells have scant cytoplasm and uniform, round, small to slightly enlarged nuclei and inconspicuous nucleoli Type B cells have more-abundant cytoplasm and larger nuclei (2 times the size of a lymphocyte nucleus), with more variability in size and shape and more-prominent nucleoli	Two to threefold variation in nuclear size, nuclear membrane irregularity, and variably prominent nucleoli Cells may show prominent apocrine features
Immunistochemistry	Not useful	Not useful

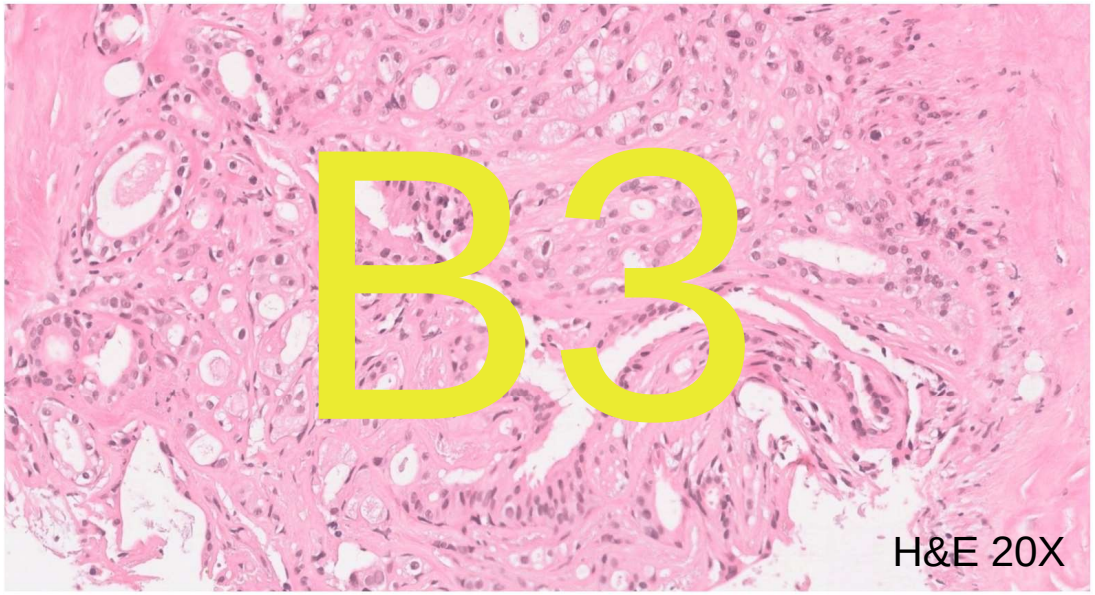

B2
H&E 20X

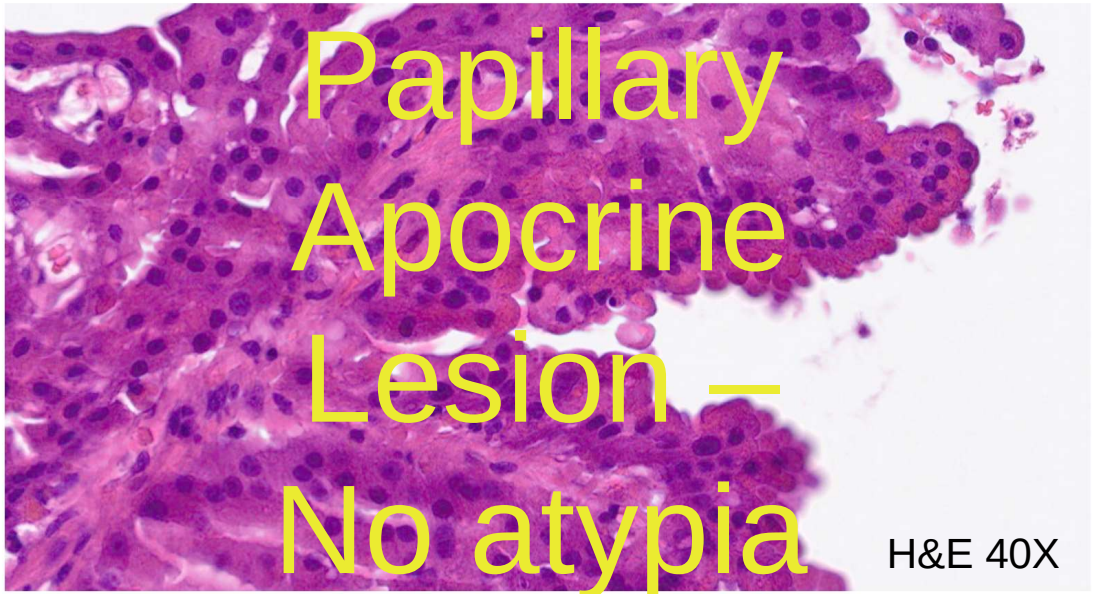

B3
H&E 20X


Apocrine changes
H&E 40X


Papillary Apocrine Lesion – No atypia
H&E 40x

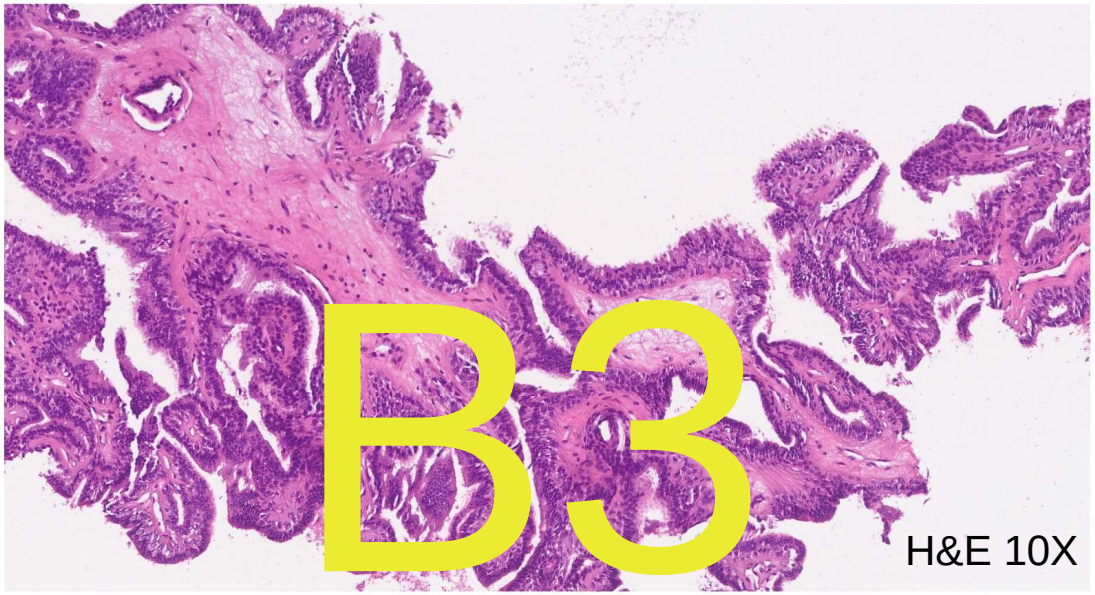

B3
H&E 20X

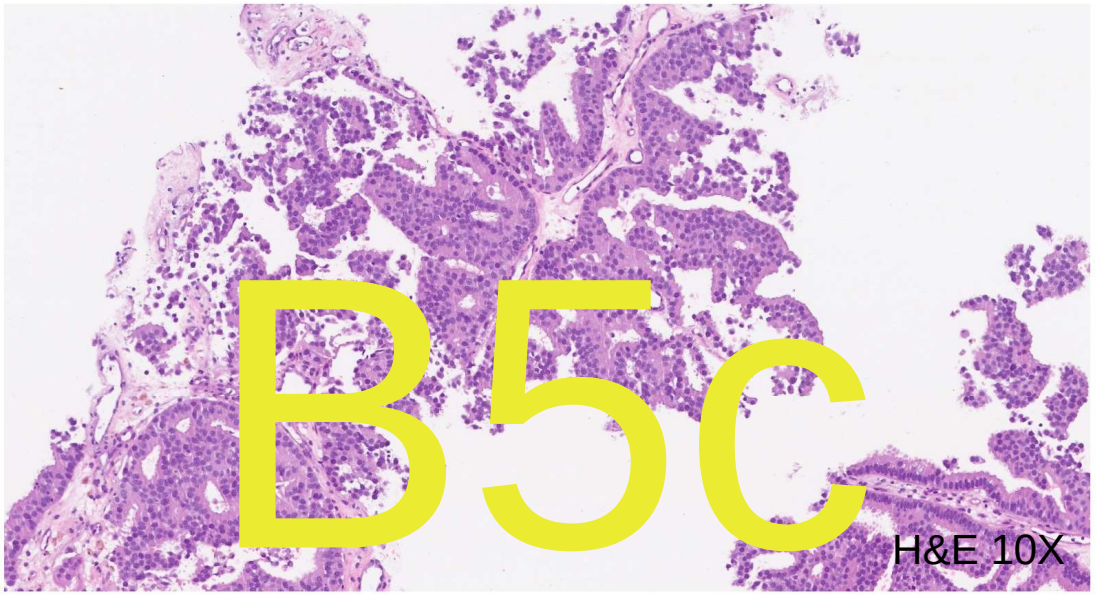

B3
H&E 20X

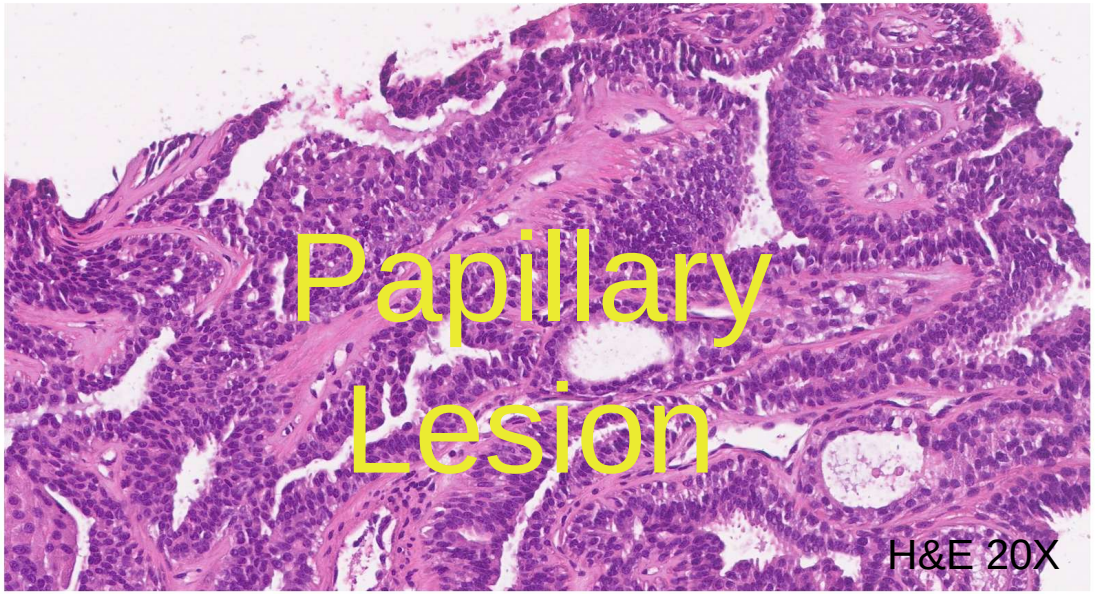

Papillary Apocrine Lesion – No atypia
H&E 40X

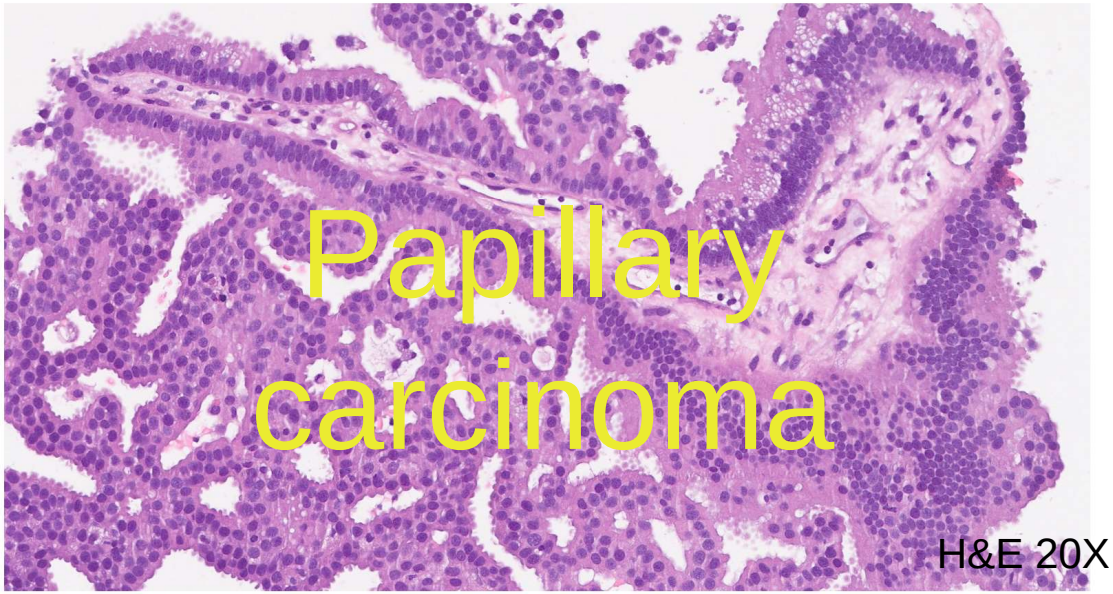

Atypical apocrine adenosis
H&E 40X

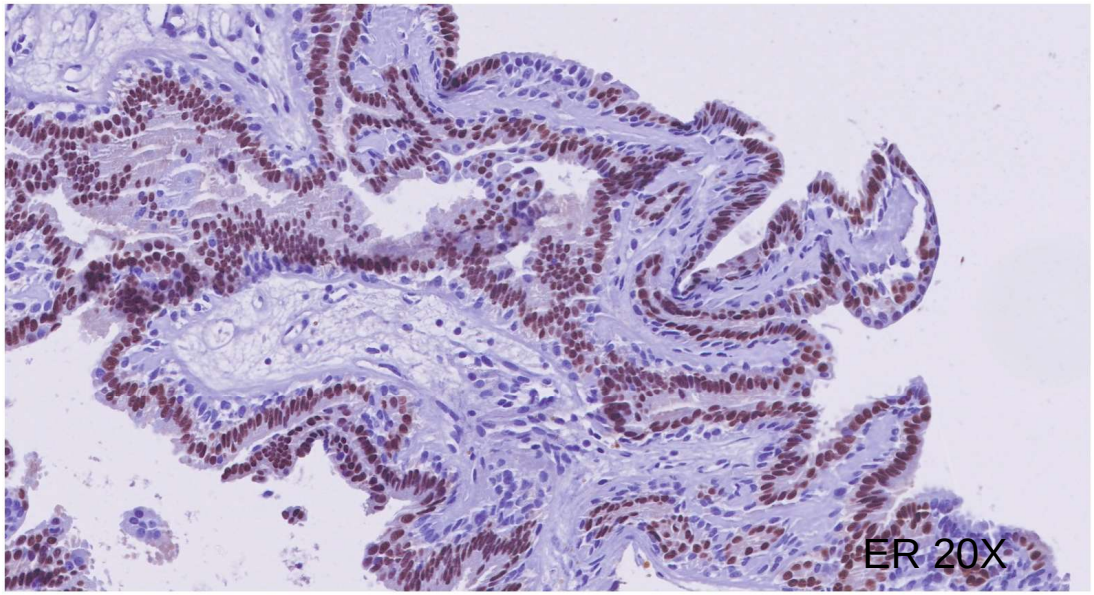
	B2	**B3**	**B3**
	Apocrine changes	**Apocrine papillary lesions**	**Atypical apocrine hyperplasia/adenosis**
Architectural features	Cysts may be lined by a single layer of flat, non-proliferative, apocrine epithelium	Fibrovascular cores covered by epithelial and myoepithelial cells, composed of apocrine cells	No architectural atypia No necrosis Lobulo-centric configuration with glands surrounded by myoepithelium
Cytological features	Variation in nuclear size may be seen - should be less than three-fold	Variation in nuclear size may be seen - should be less than three-fold	Presence of at least a threefold variation in nuclear size
Immunistochemistry	Not useful	Not useful	Not useful
Upgrade risk		<10%	Uncertain – 16.7 to 25 %

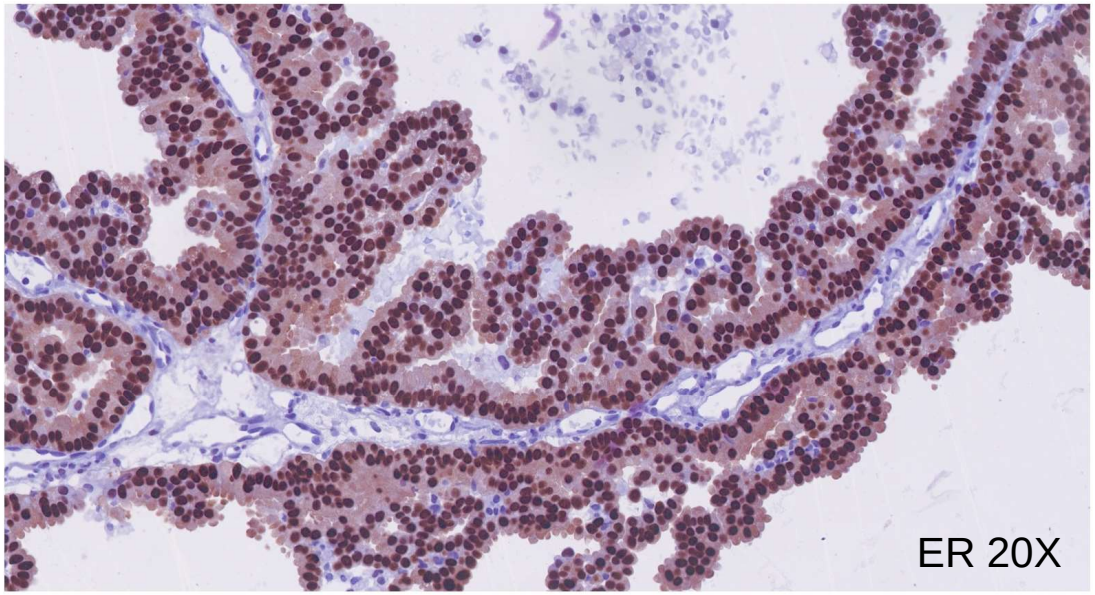

B3
H&E 10X

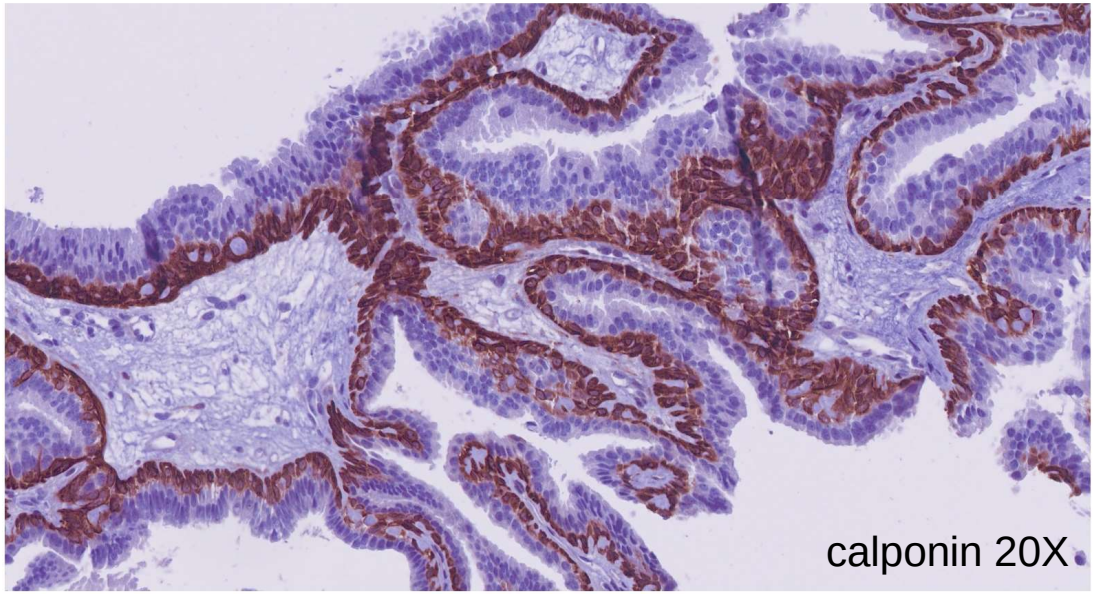

B5c
H&E 10X

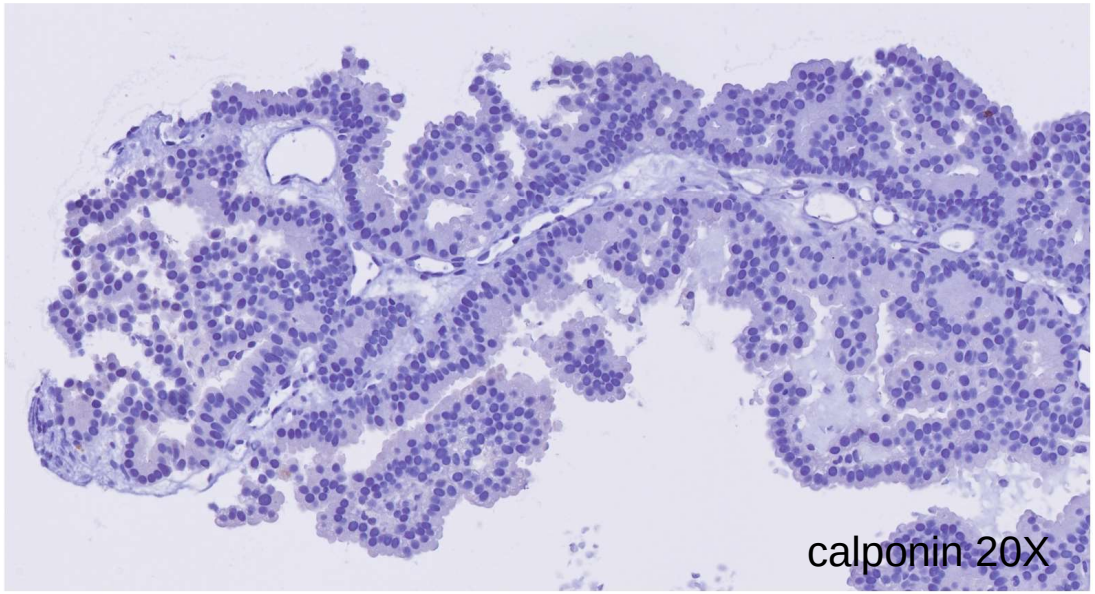

Papillary
Lesion
H&E 20X


Papillary
carcinoma
H&E 20X

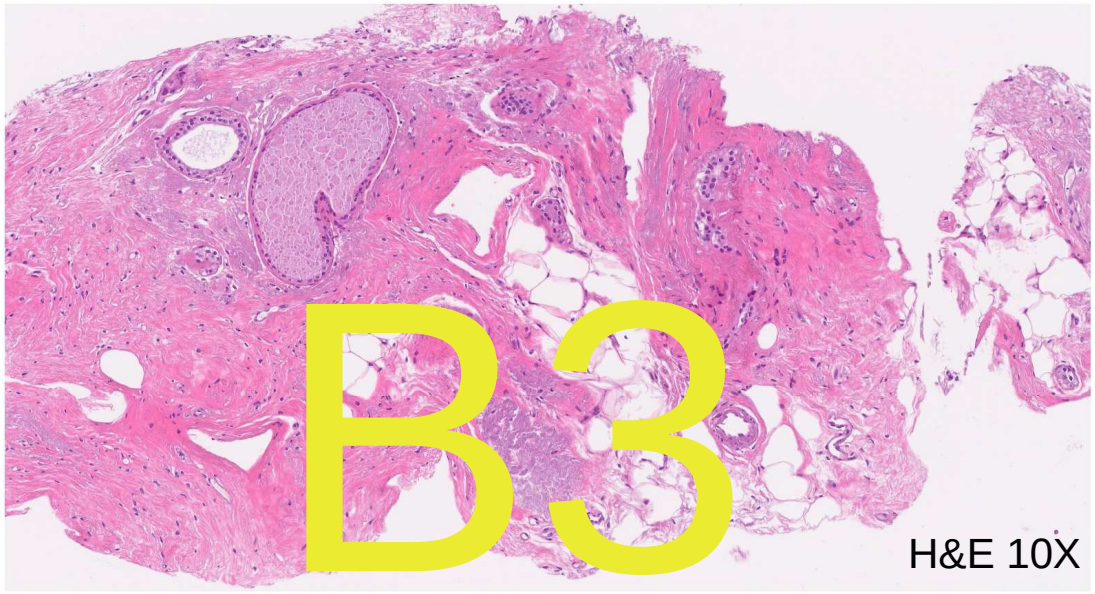

ER 20X

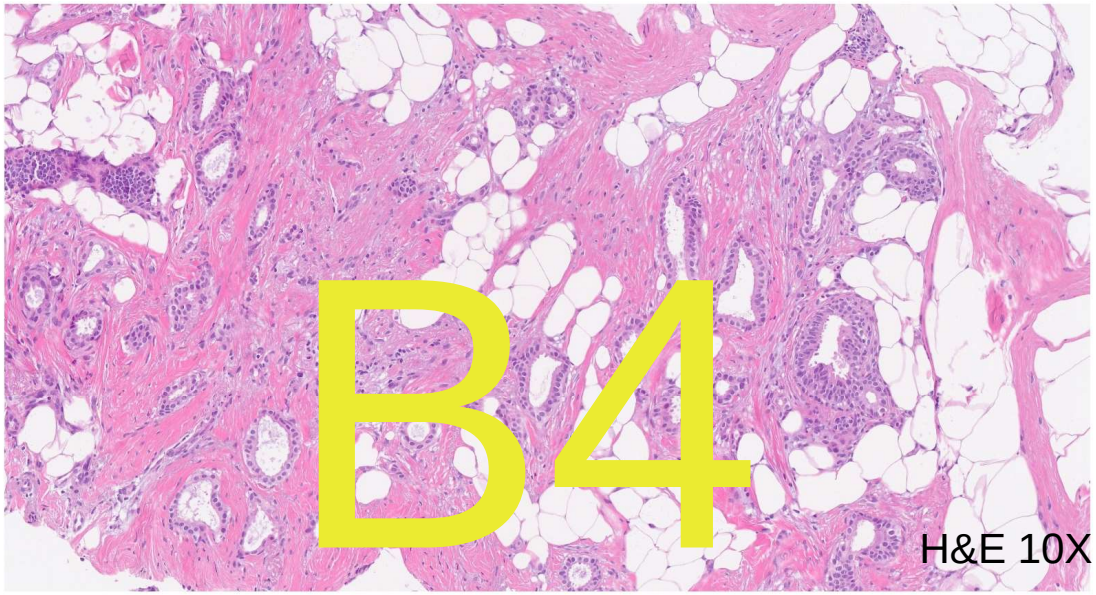

ER 20X

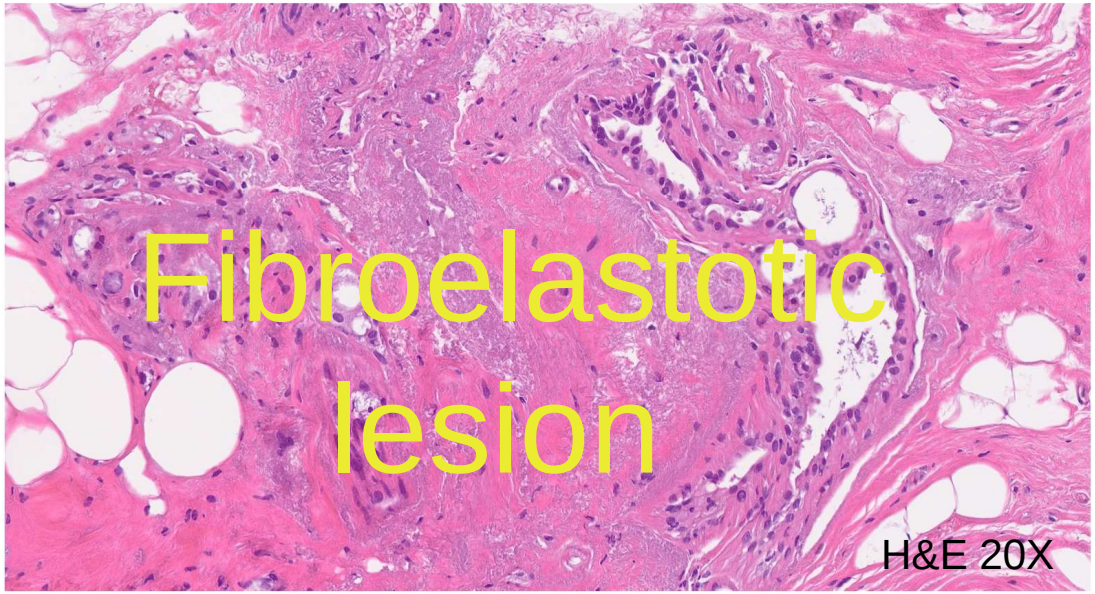

calponin 20X

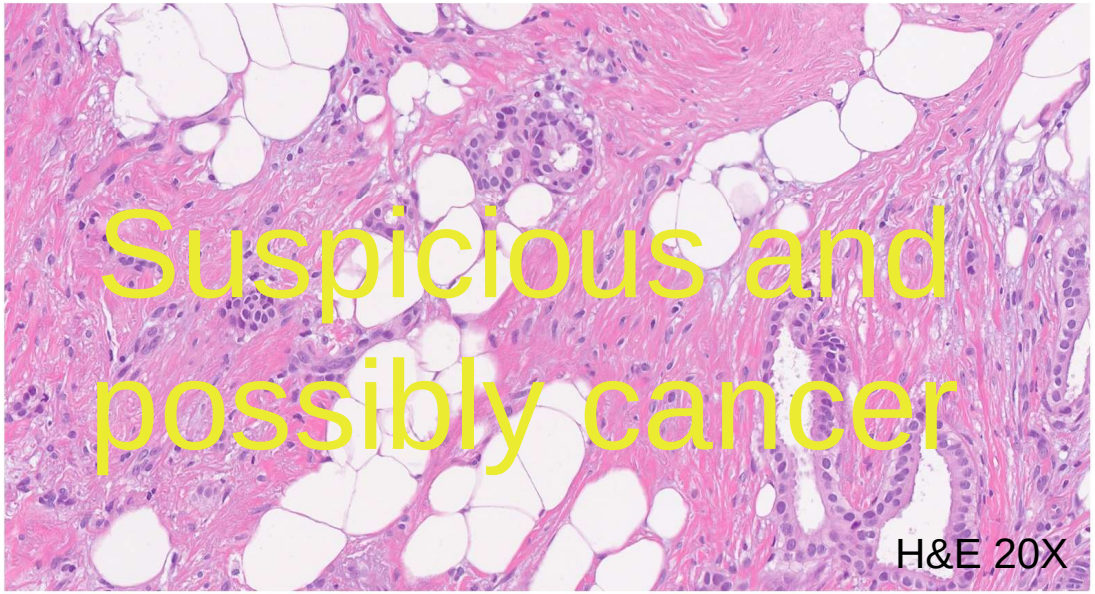

calponin 20X

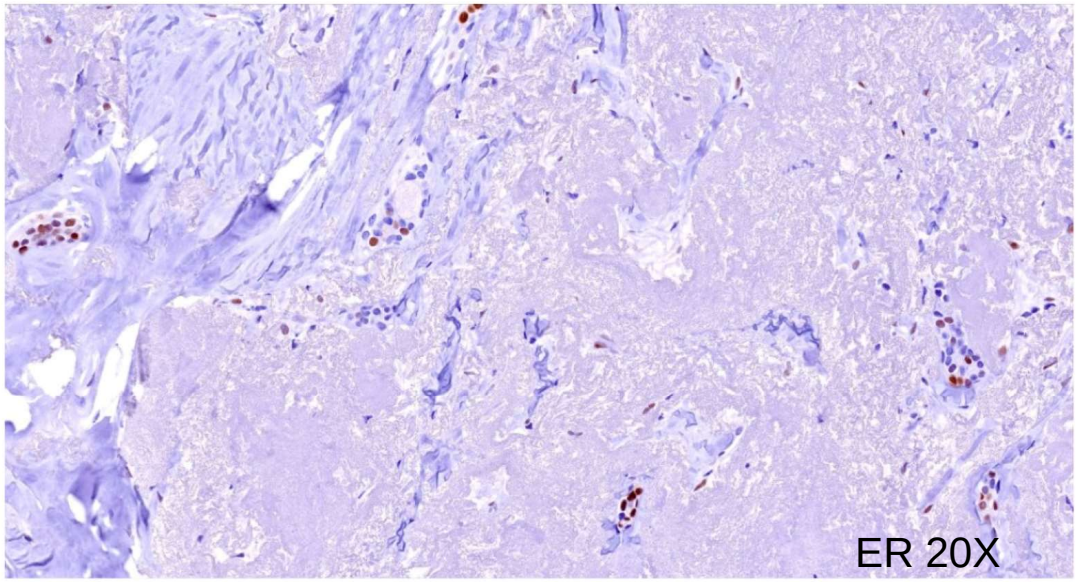
	B3	**B3**	**B5c**
	Papillary lesion	**Papillary lesions with atypia**	**Papillar carcinoma**
Architectural features	Variably fibrotic fibrovascular cores covered by epithelial and myoepithelial cells Epithelium consists of one to several layers of cuboidal to columnar cells Apocrine metaplasia and/or squamous metaplasia may be seen	Fibrovascular cores covered by epithelial and myoepithelial cells Epithelium consists of one to several layers of cuboidal to columnar cells	Fibrovascular cores covered by epithelial cells Absence of myoepithelial component Solid, cribriform and micropapillary pattern are present
Cytological features	No atypia	Areas with low-grade atypia	Atypia present
Immunistochemistry	ER present, scattered; calponin present in fibrovascilar cores	ER present diffuse and strong; calponin present in fibrovascular cores	ER present, diffuse and strong; calponin absent in fibrovascular cores
Upgrade risk	<10%	27-36%	

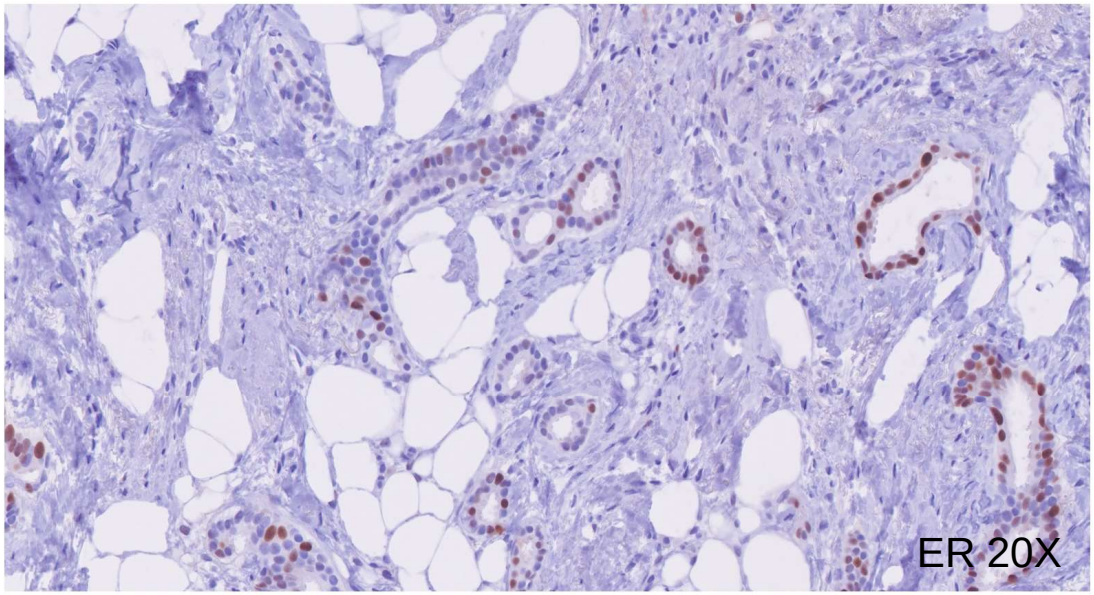

B3
H&E 10X


B4
H&E 10X


Fibroelastotic lesion
H&E 20X


Suspicious and possibly cancer
H&E 20X


ER 20X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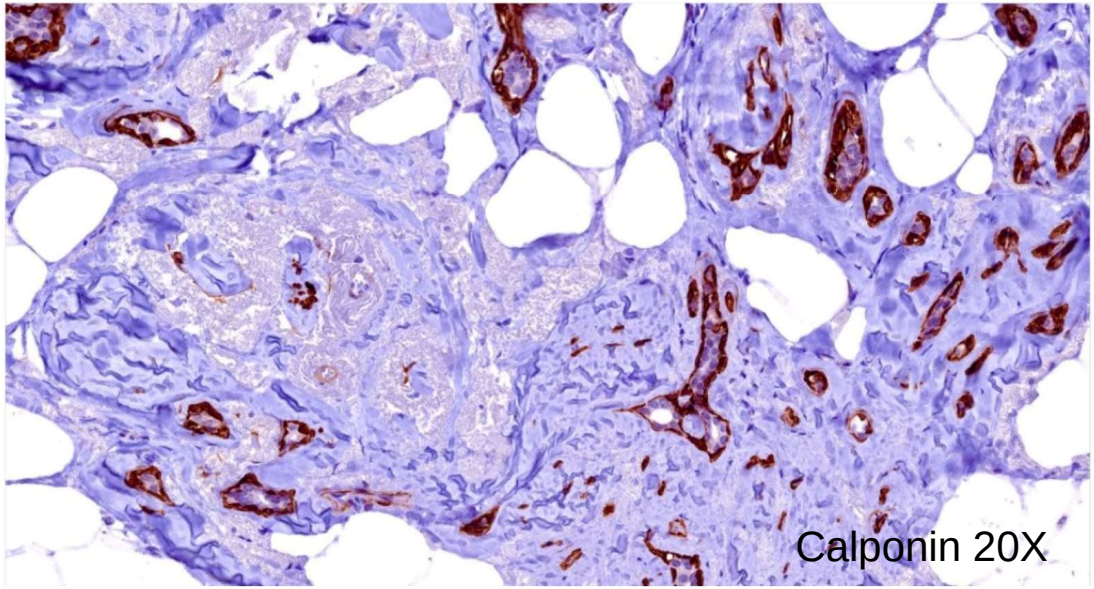
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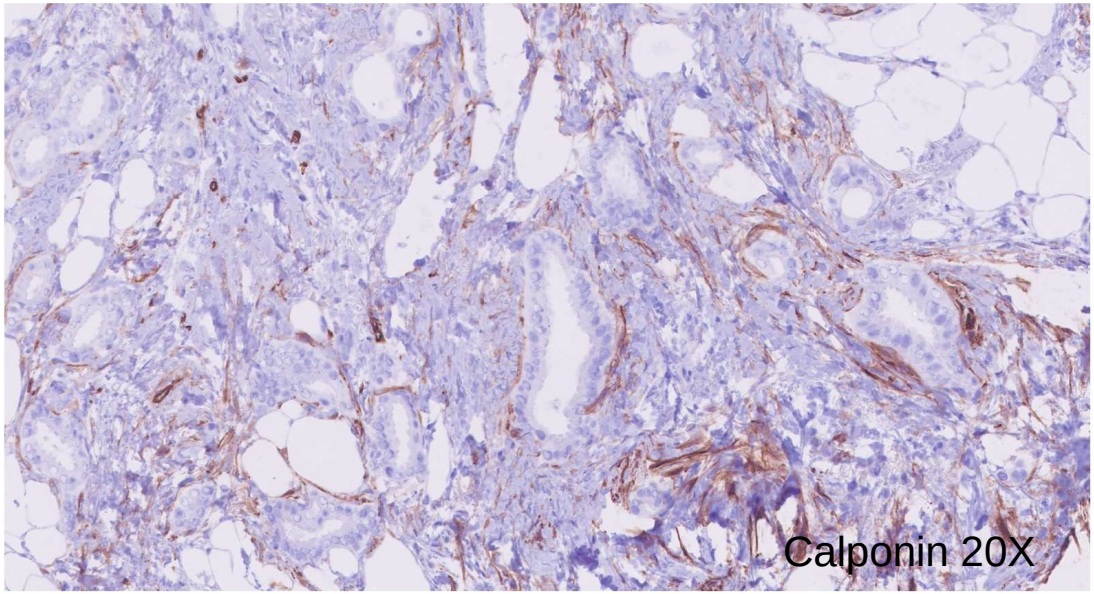
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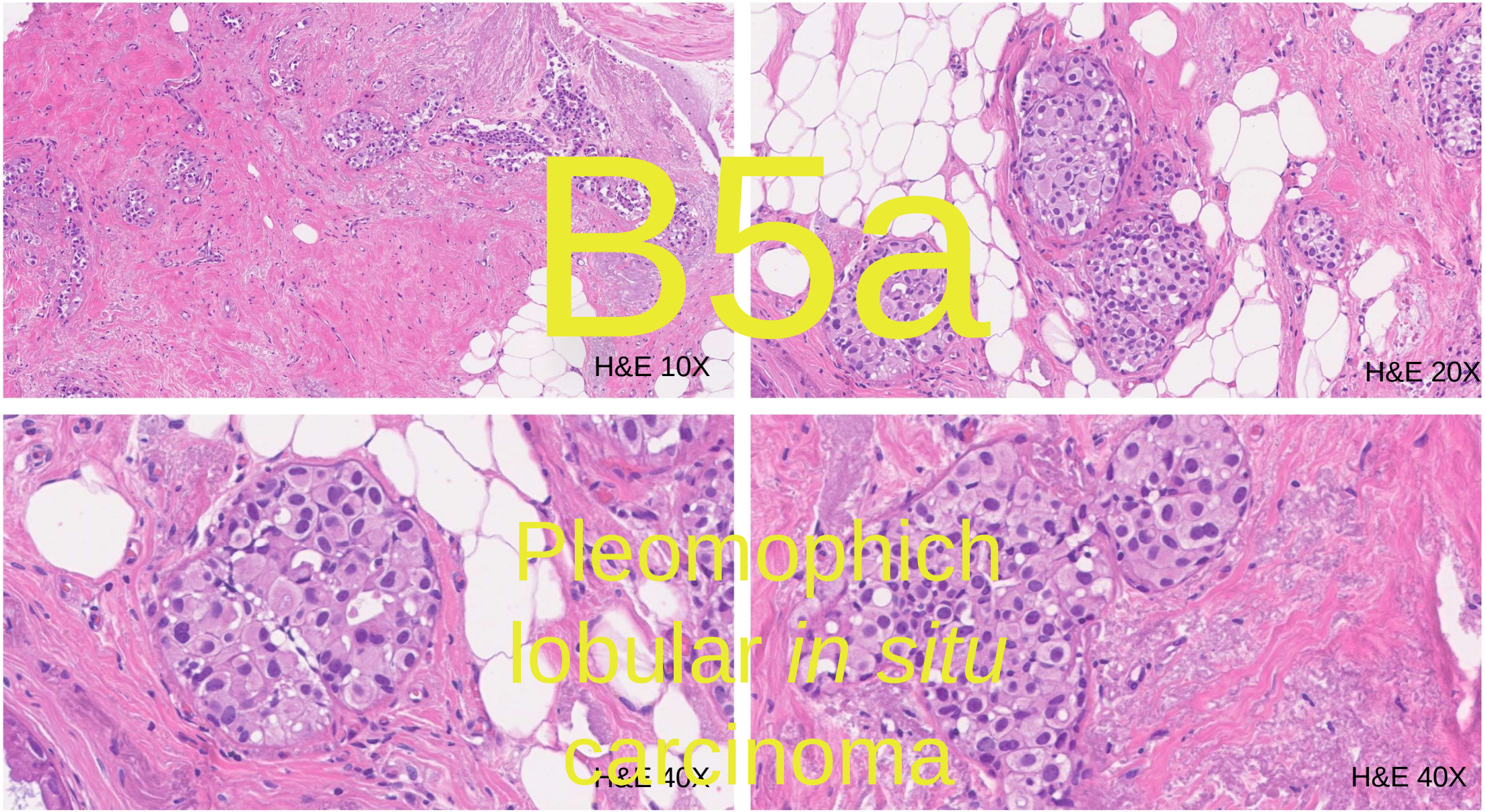
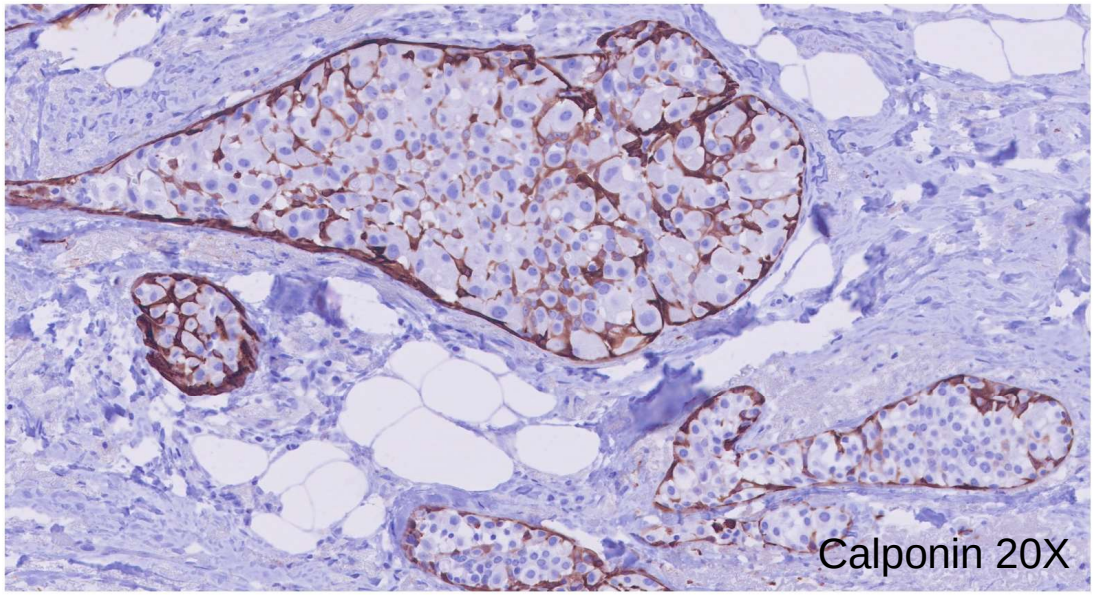

B5a
H&E 10X
H&E 20X
Pleomophich lobular *in situ* carcinoma
H&E 40X
H&E 40X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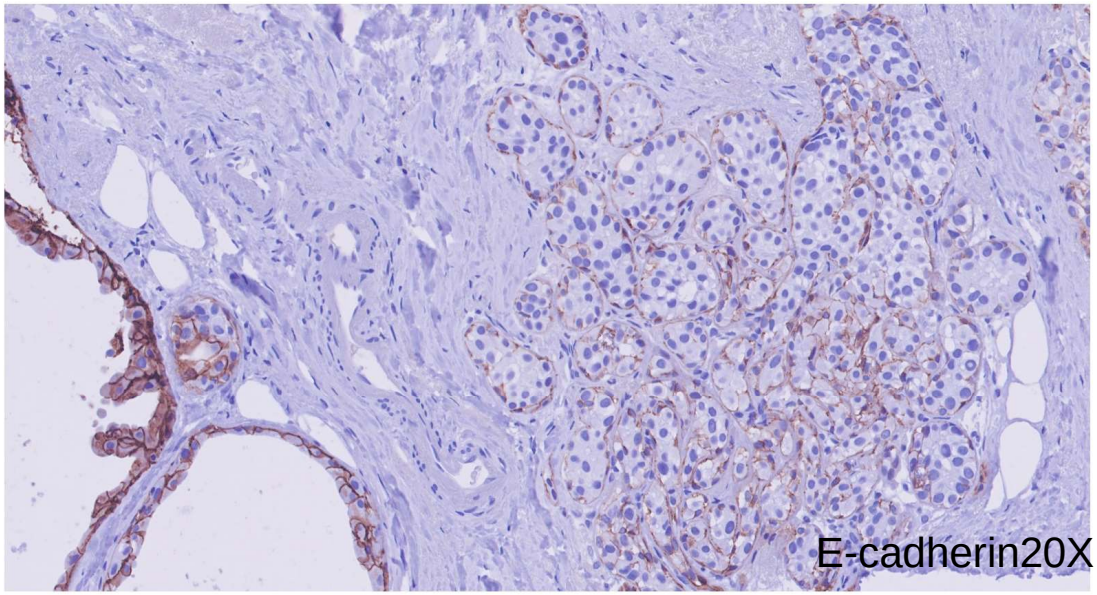
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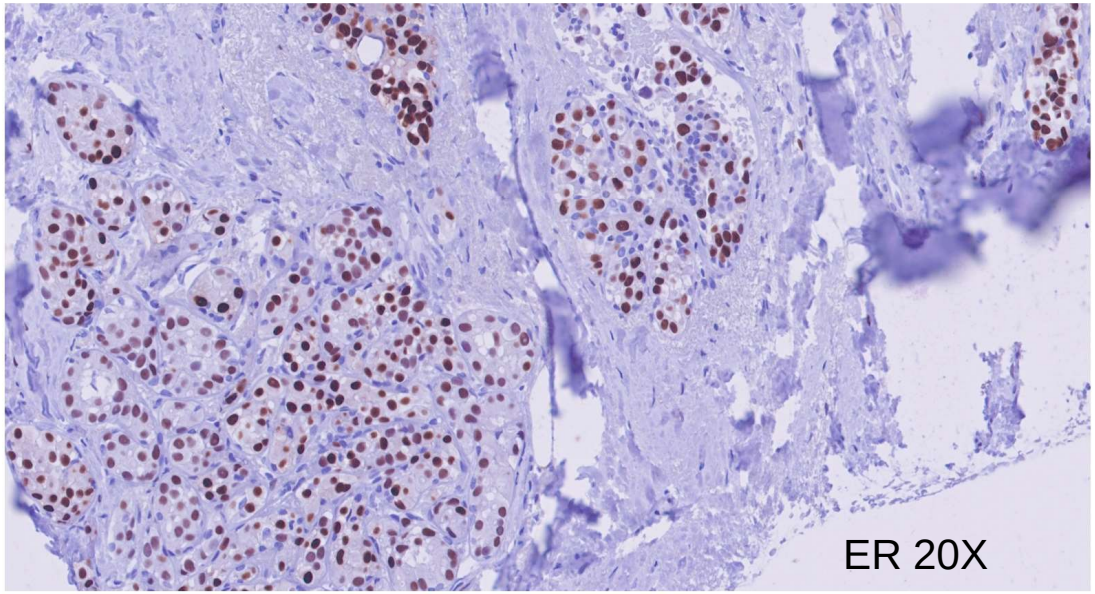
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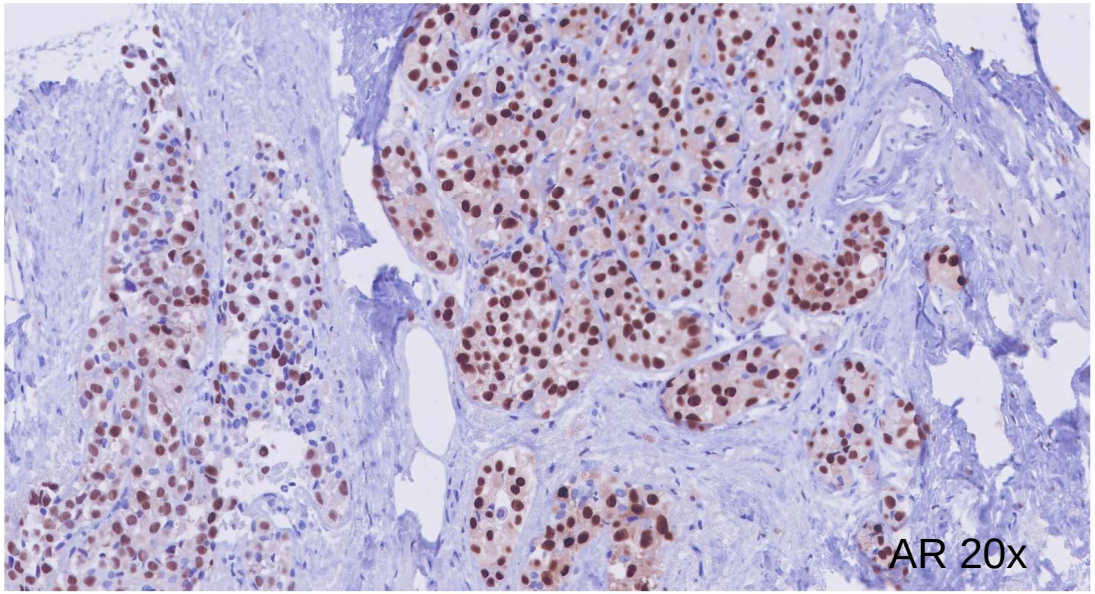
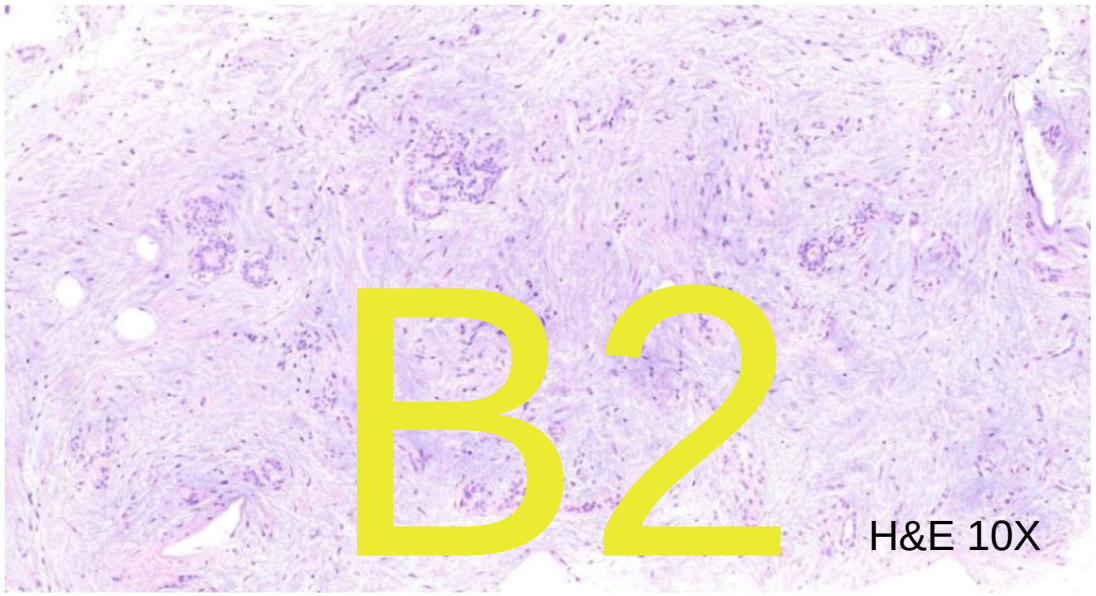
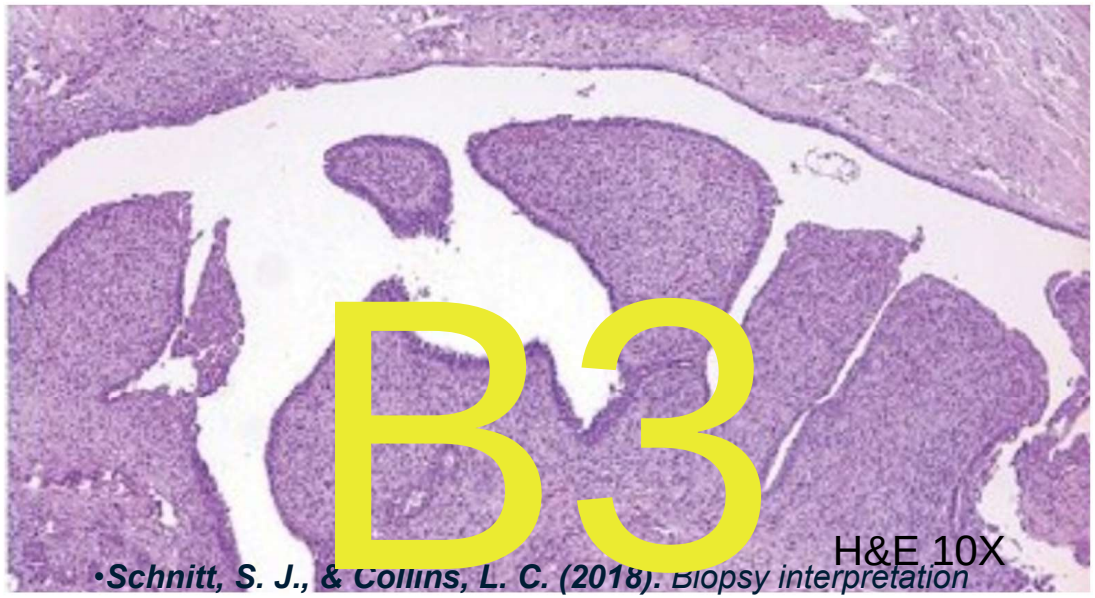
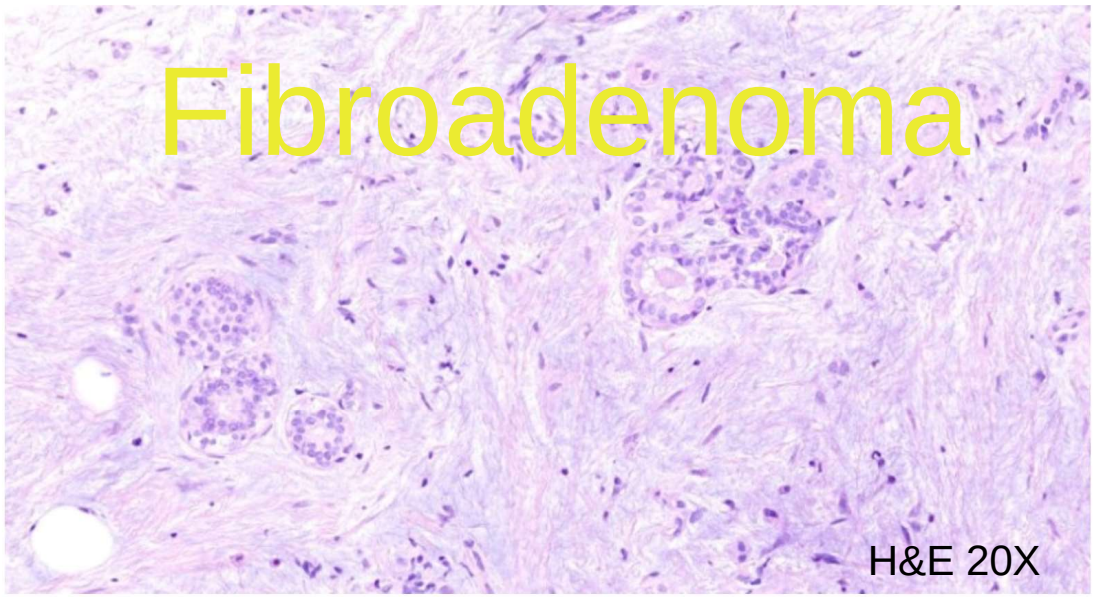

AR 20x

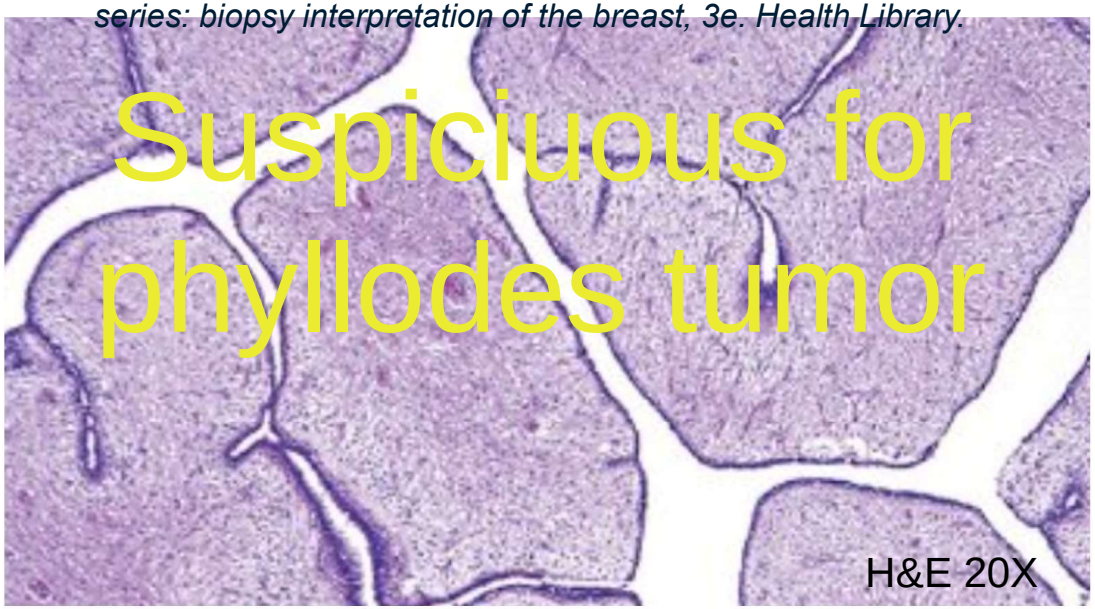
	B3	**B4 – B5a**
	Fibroelastotic lesion	**Mimikers – warning features**
Architectural features	Central fibroelastotic core with entrapped glands Glands surrounded by myoepithelial layer Peripheral ducts/lobules radiate circumferentially from central core and show varying degrees of adenosis, hyperplasia, papillomas, and cysts	Distorted glands Intraductal proliferation
Cytological features	No atypia	Cytological atypia
Immunistochemistry	Calponin positive in myoepithelial cells	Unclear expression of myoepithelial layer
Upgrade risk	If atypia present 36%; no atypia <10%	-



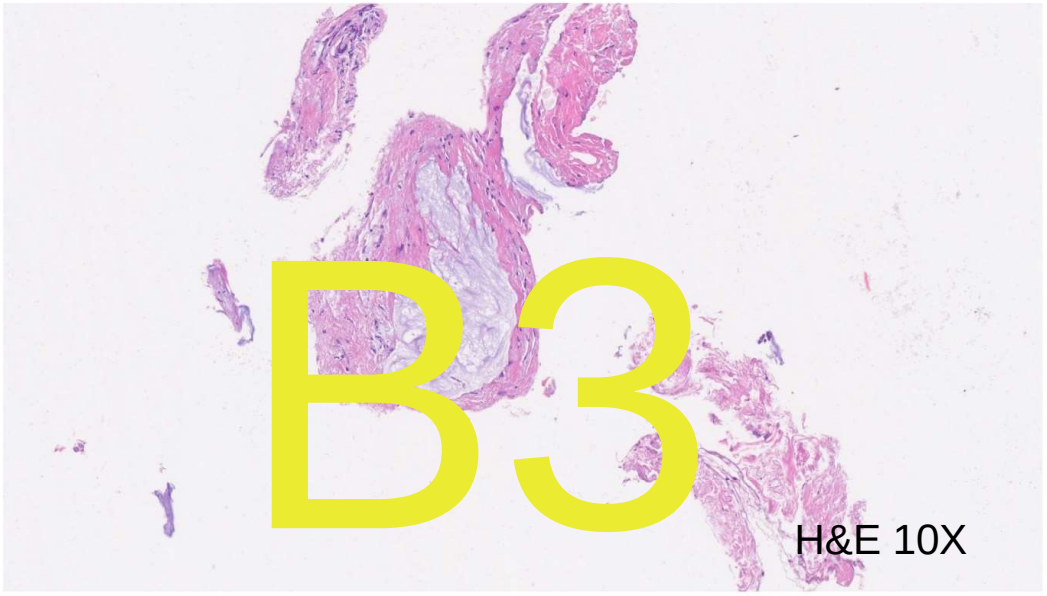


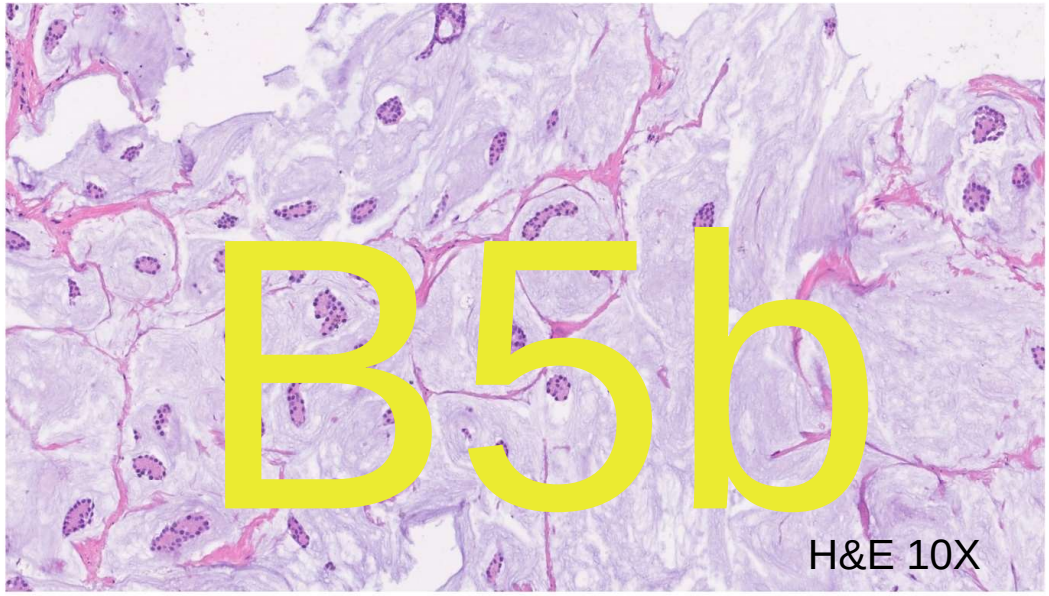
•***Schnitt, S. J., & Collins, L. C. (2018).*** *Biopsy interpretation series: biopsy interpretation of the breast, 3e. Health Library.*

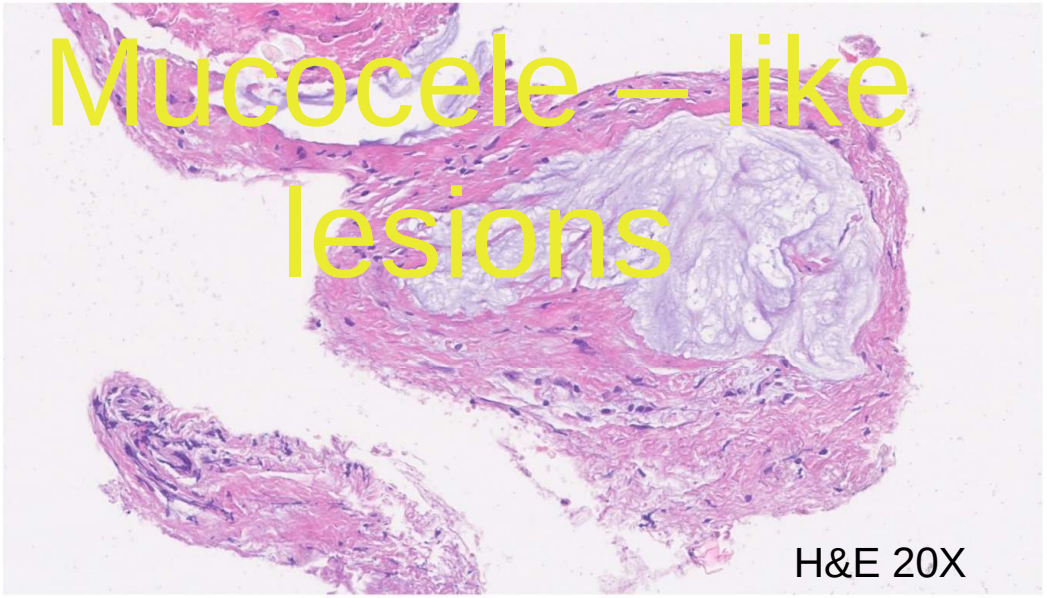


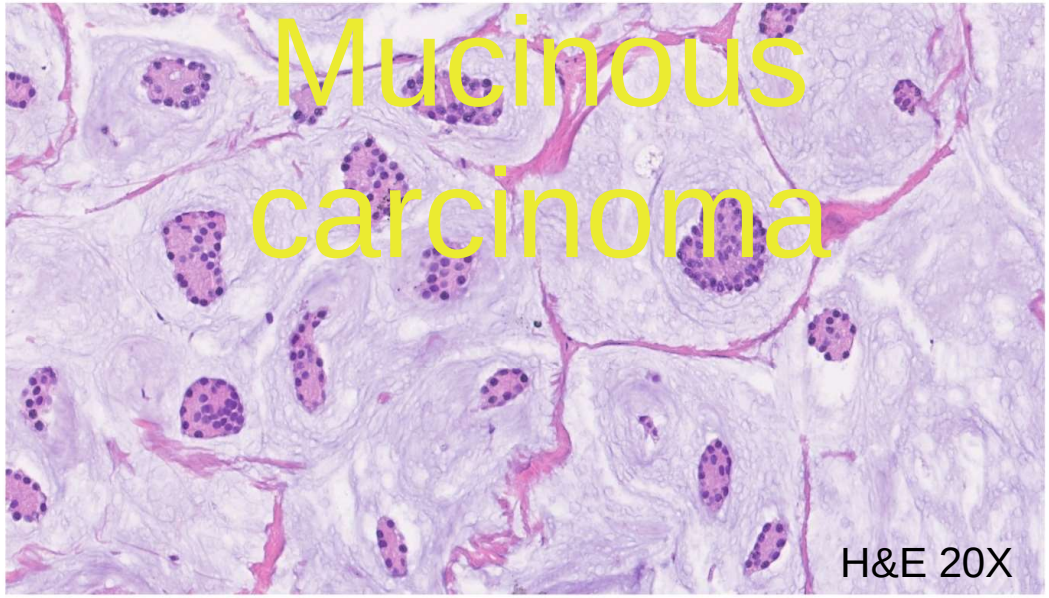


	B2	**B3**
	Fibroepithelial lesion	**Phyllodes tumor can not be ruled out**
Architectural features	Hypocellular or myxoid stromal component Absence of leaf like epithelial structures	Stromal overgrowth: x10 field of stroma with no glandular elements Fragmentation: defined as a stromal fragment with epithelium at one or both ends Leaf-like epithelial spaces
Cytological features	No atypia	Mitoses: one or two per 10 high-power fields favour phyllodes tumour, but can be seen as fibroadenomas; and three or more per 10 high-power fields more strongly favour phyllodes tumour.
Immunistochemistry	Not useful	Not useful
Upgrade risk		uncommon


B3
H&E 10X


B5b
H&E 10X


Mucocele – like lesions
H&E 20X


Mucinous carcinoma
H&E 20X

Mucocele – like lesions

- Mucin in the stroma (a mucoele-like lesion) can be associated with benign cysts, AIDEP/ADH, DCIS and invasive carcinoma, particularly of mucinous type.
- The risk of malignancy appears to be low if there is no atypia on the core biopsy.
- Without epithelial cells within the mucus pools, the upgrade rate is very low (<2%)
- Diagnosis on CNB and no atypia found → VAE
- If atypia is present → surgical diagnostic excision

Miscellaneous uncommon lesions

Adenomyoepithelioma
Microglandular adenosis
Granular cell tumour
Spindle cell lesions such as fibromatosis and myofibroblastoma
Vascular lesions

difficult to classify → B3 on bioptical material
For the majority of them, surgical diagnostic excision

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2020

Should We Ignore, Follow, or Biopsy? Impact of Artificial Intelligence Decision Support on Breast Ultrasound Lesion Assessment

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OBJECTIVE.—The objective of this study was to assess the impact of artificial intelligence (AI)-based decision support (DS) on breast ultrasound (US) lesion assessment.

MATERIALS AND METHODS.—A multicenter retrospective review of 900 breast lesions (470/900 [52.2%] benign; 430/900 [47.8%] malignant) on US by 15 physicians (11 radiologists, two surgeons, two obstetrician/gynecologists). An AI system (Koios DS for Breast, Koios Medical) evaluated images and assigned them to one of four categories: benign, probably benign, suspicious, and probably malignant. Each reader reviewed cases twice: 750 cases with US only or with US plus DS; 4 weeks later, cases were reviewed in the opposite format. One hundred fifty additional cases were presented identically in each session. DS and reader sensitivity, specificity, and positive likelihood ratios (PLRs) were calculated as well as reader AUCs with and without DS. The Kendall τ-b correlation coefficient was used to assess intra- and interreader variability.

RESULTS.—Mean reader AUC for cases reviewed with US only was 0.83 (95% CI, 0.78–0.89); for cases reviewed with US plus DS, mean AUC was 0.87 (95% CI, 0.84–0.90). PLR for the DS system was 1.98 (95% CI, 1.78–2.18) and was higher than the PLR for all readers but one. Fourteen readers had better AUC with US plus DS than with US only. Mean Kendall τ-b for US-only interreader variability was 0.54 (95% CI, 0.53–0.55); for US plus DS, it was 0.68 (95% CI, 0.67–0.69). Intrareader variability improved with DS; class switching (defined as crossing from BI-RADS category 3 to BI-RADS category 4A or above) occurred in 13.6% of cases with US only versus 10.8% of cases with US plus DS ($p = 0.04$).

CONCLUSION.—AI-based DS improves accuracy of sonographic breast lesion assessment while reducing inter- and intraobserver variability.

2023

diagnostics

MDPI

Article

AI: Can It Make a Difference to the Predictive Value of Ultrasound Breast Biopsy?

Abstract: (1) Background: This study aims to compare the ground truth (pathology results) against the BI-RADS classification of images acquired while performing breast ultrasound diagnostic examinations that led to a biopsy and against the result of processing the same images through the AI algorithm KOIOS DS ™ (KOIOS). (2) Methods: All results of biopsies performed with ultrasound guidance during 2019 were recovered from the pathology department. Readers selected the image which better represented the BI-RADS classification, confirmed correlation to the biopsied image, and submitted it to the KOIOS AI software. The results of the BI-RADS classification of the diagnostic study performed at our institution were set against the KOIOS classification and both were compared to the pathology reports. (3) Results: 403 cases were included in this study. Pathology rendered 197 malignant and 206 benign reports. Four biopsies on BI-RADS 0 and two images are included. Of fifty BI-RADS 3 cases biopsied, only seven rendered cancers. All but one had a positive or suspicious cytology; all were classified as suspicious by KOIOS. Using KOIOS, 17 B3 biopsies could have been avoided. Of 347 BI-RADS 4, 5, and 6 cases, 190 were malignant (54.7%). Because only KOIOS suspicious and probably malignant categories should be biopsied, 312 biopsies would have resulted in 187 malignant lesions (60%), but 10 cancers would have been missed. (4) Conclusions: KOIOS had a higher ratio of positive biopsies in this selected case study vis-à-vis the BI-RADS 4, 5 and 6 categories. A large number of biopsies in the BI-RADS 3 category could have been avoided.

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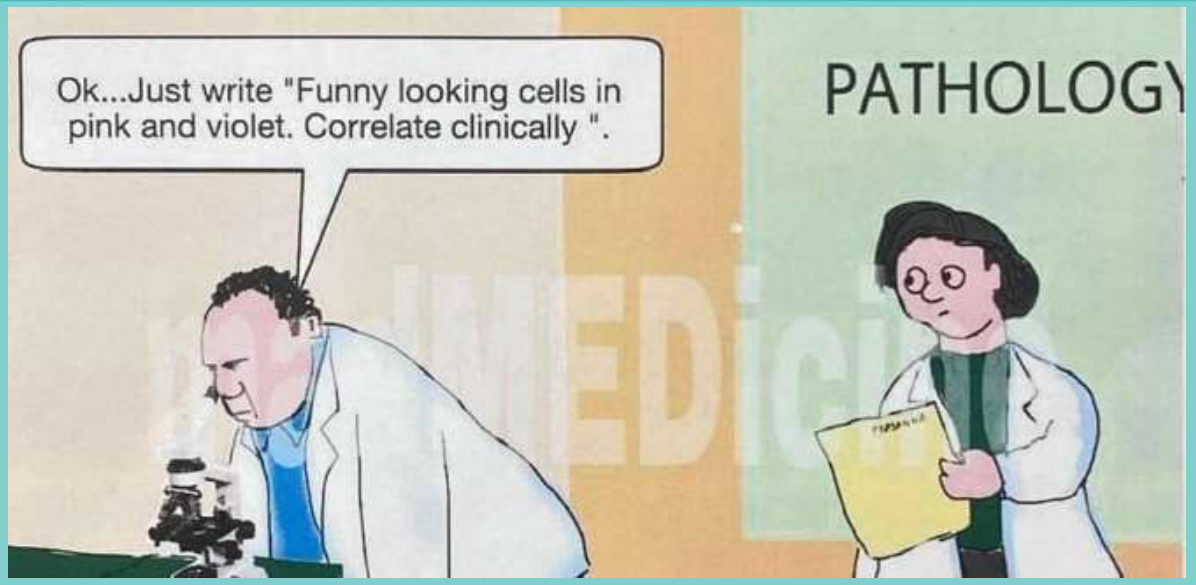
AGLI ESTREMI DELLO SCREENING MAMMOGRAFICO

Dott.ssa Cecilia Taverna



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