



Memorial Sloan Kettering
Cancer Center™

Lobular Carcinoma In situ (LCIS)

Morphologic variants and management implications

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Pezcoller Seminar

September 16, 2022 – Trento, Italy

Lobular Carcinoma In Situ (LCIS)

- Morphology
 - WHO 2019 update
- Differential diagnosis and pitfalls
- E-cadherin and related proteins
- Notes on management





Epithelial Tumours of the Breast

1. Benign epithelial proliferations and precursors
2. Adenosis and benign sclerosing lesion
3. Adenomas
4. Epithelial-myoepithelial tumors
5. Papillary neoplasms

6. Non-invasive lobular neoplasia

7. DCIS
8. Invasive Breast Carcinoma
9. Rare and salivary gland-type tumors
10. Neuroendocrine neoplasms

Atypical Lobular Hyperplasia (ALH)

Lobular Carcinoma In situ (LCIS)

- Classic LCIS

- Florid LCIS

- Pleomorphic LCIS





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Atypical Lobular Hyperplasia (ALH)

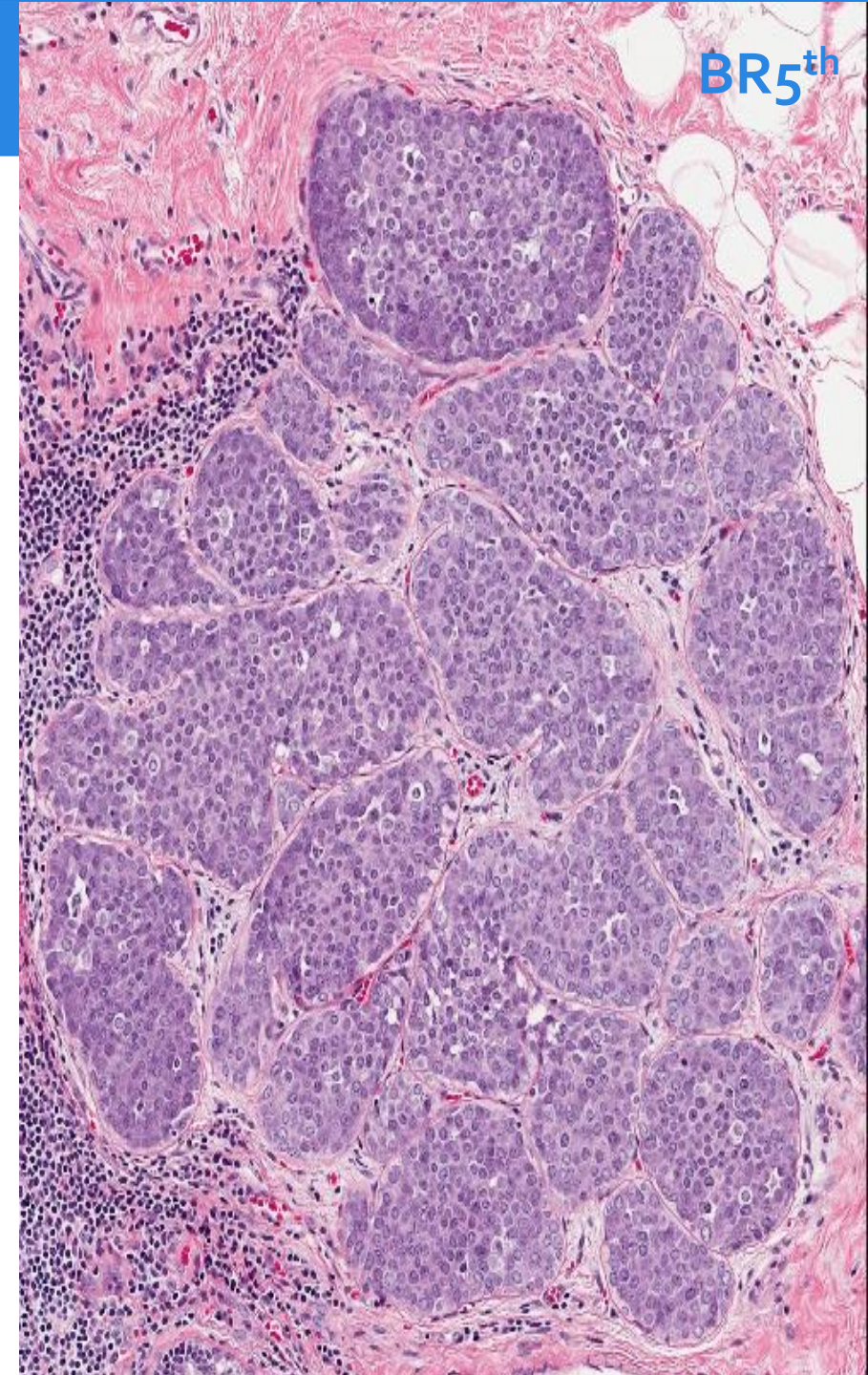
Lobular Carcinoma In situ (LCIS)

- Classic LCIS
- Florid LCIS
- Pleomorphic LCIS



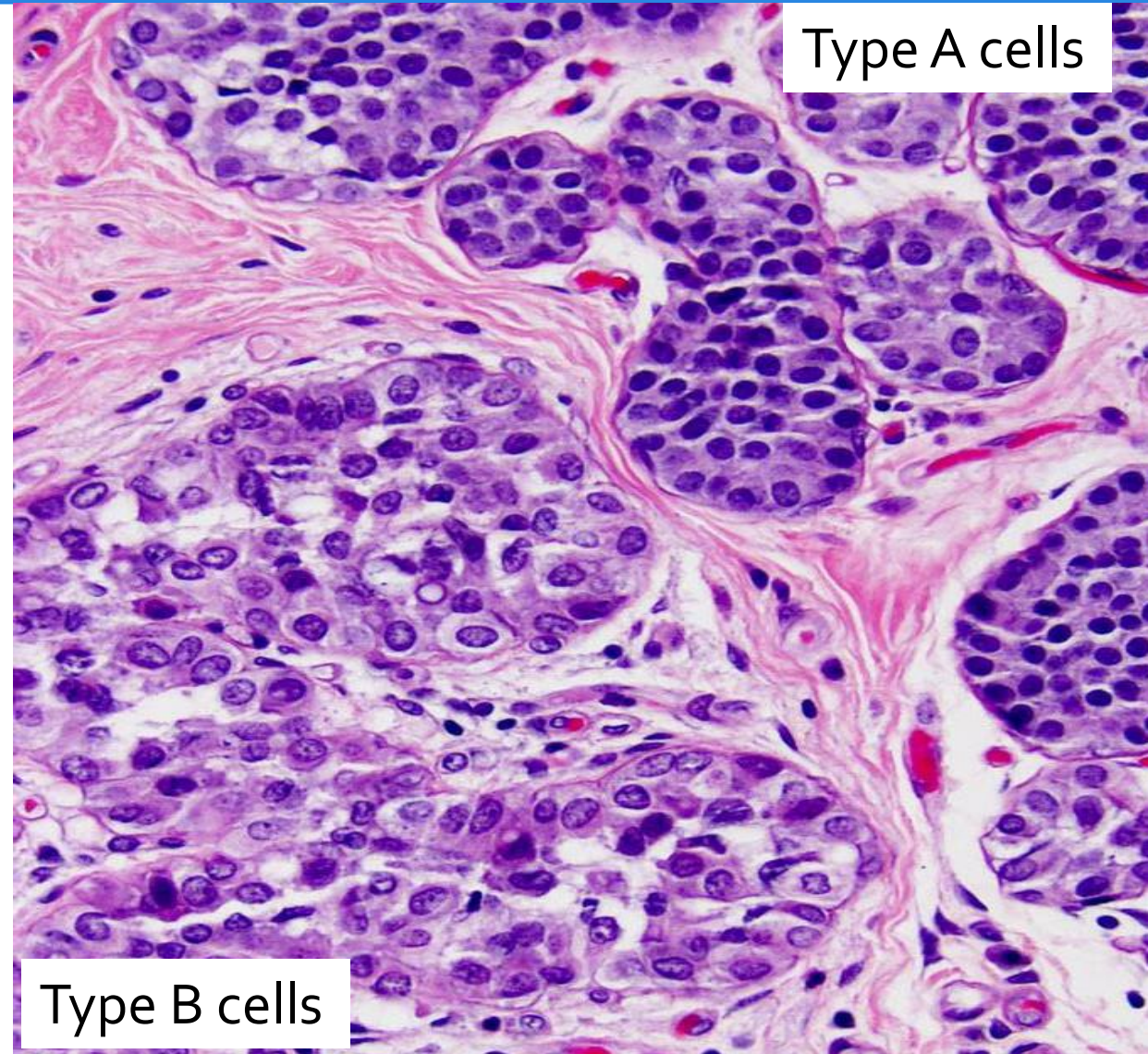
BR5th ed - Classic LCIS definition

- **Dyscohesive proliferation of type A and/or type B epithelial cells.**
- Type A cells are small cells with uniform hyperchromatic nuclei
- Type B cells have slightly larger vesicular nuclei, with mild variability in size and shape and with small nucleoli.
- The cell populations may be mixed in individual proliferations.



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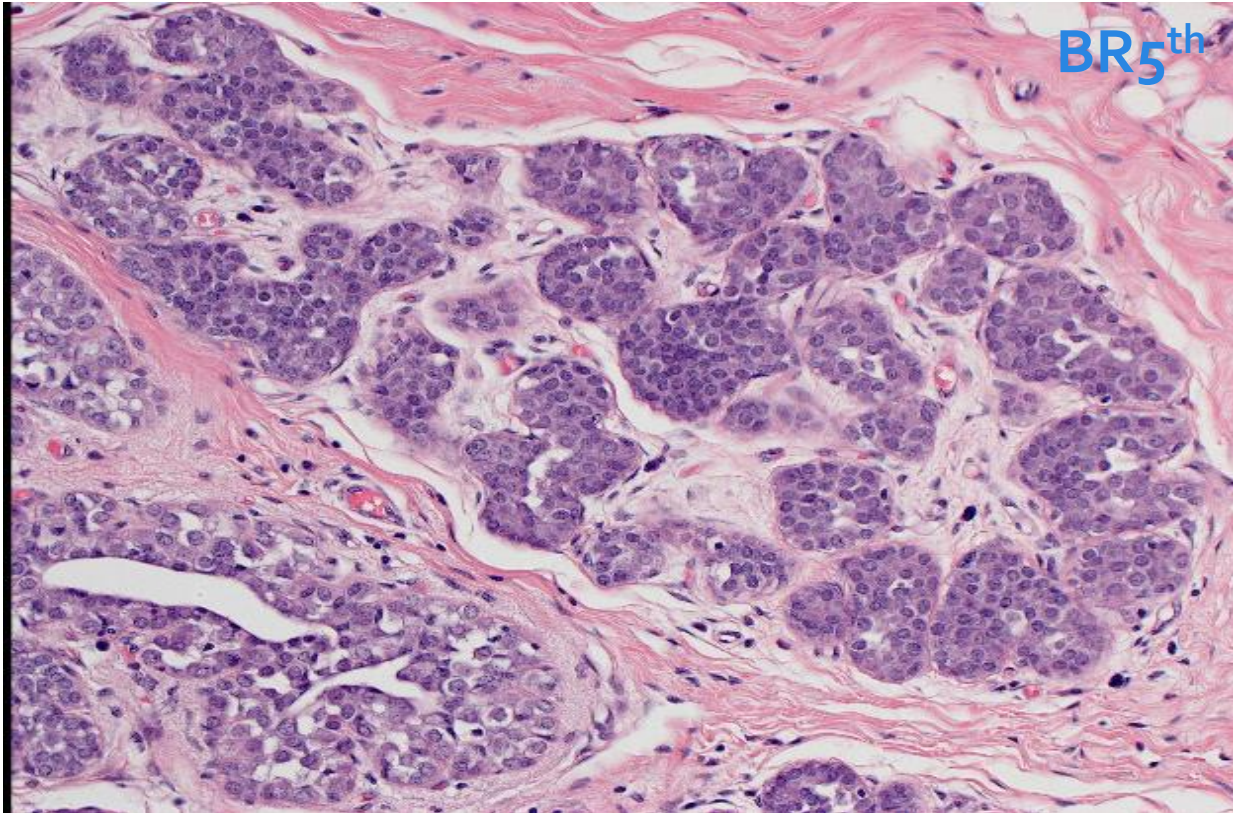
Type A cells

Type B cells



BR 5th - Atypical Lobular Hyperplasia (ALH) definition

<50% acini filled and expanded

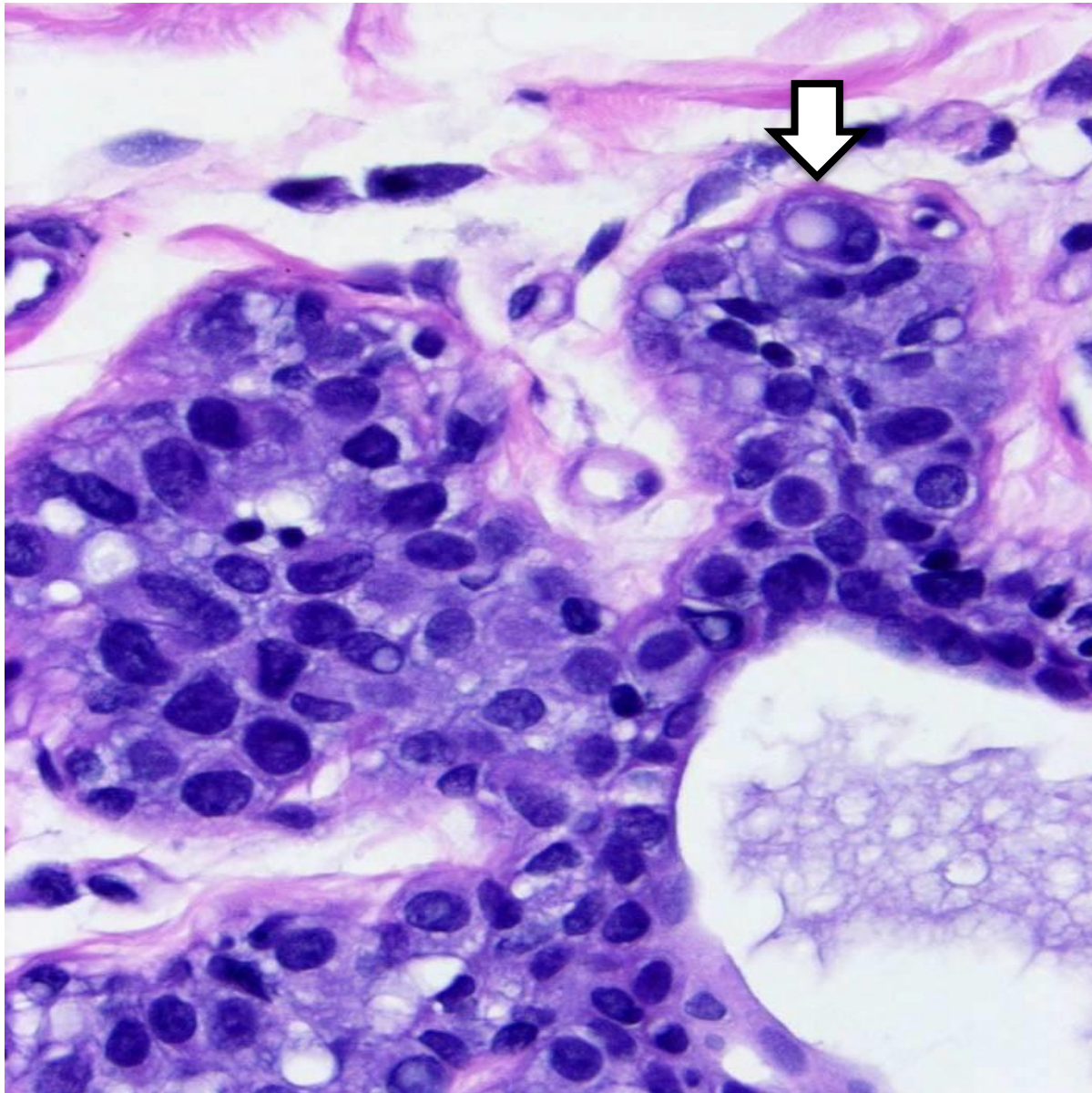


Non-invasive neoplastic proliferation of small, dyscohesive cells, originating in the TDLUs, with or without pagetoid involvement of terminal ducts.

Fewer than half of the acini in a TDLU are filled and expanded by the neoplastic cells.

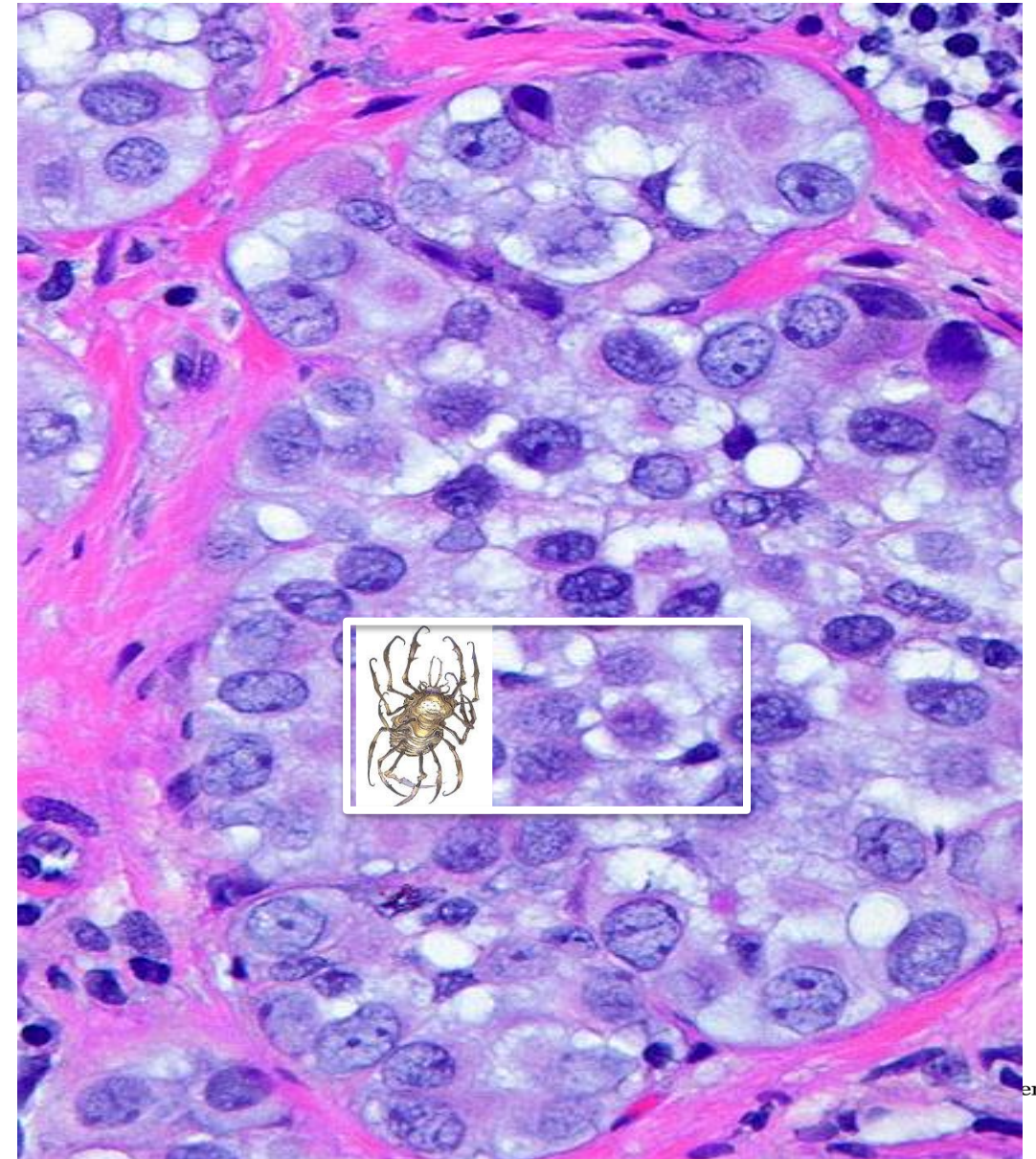
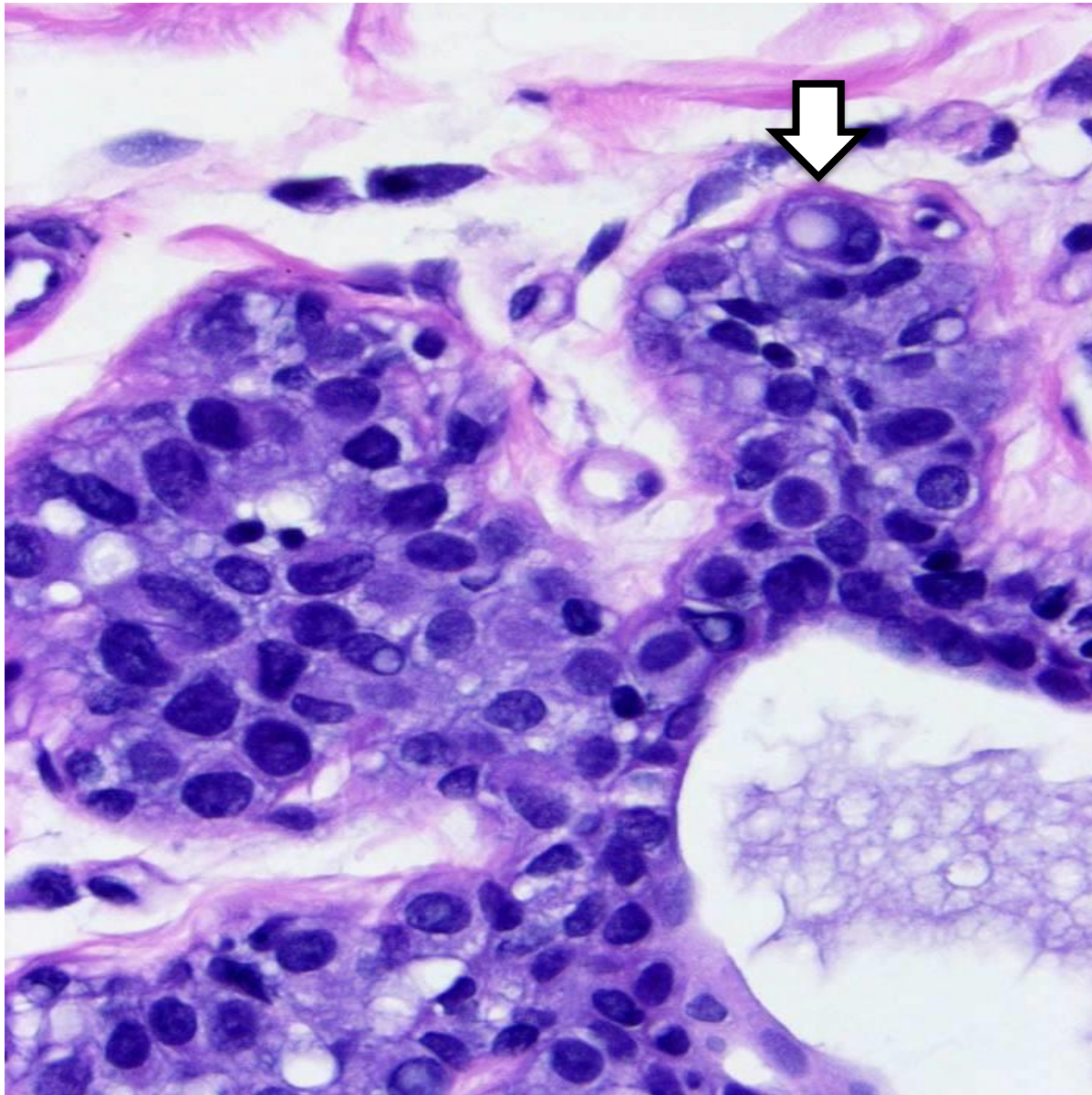


intracytoplasmic vacuoles

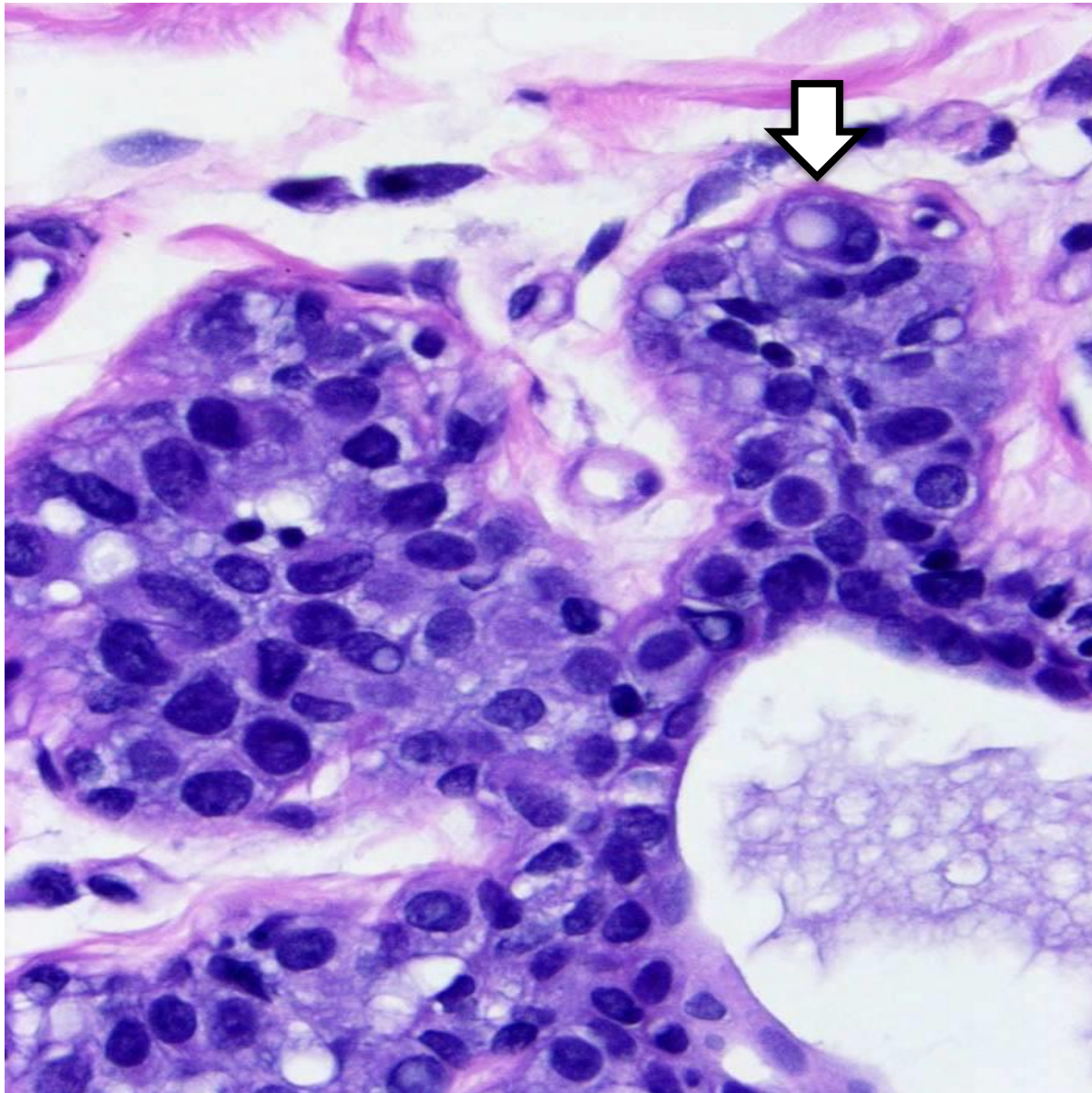


intracytoplasmic vacuoles

“spidery” cells

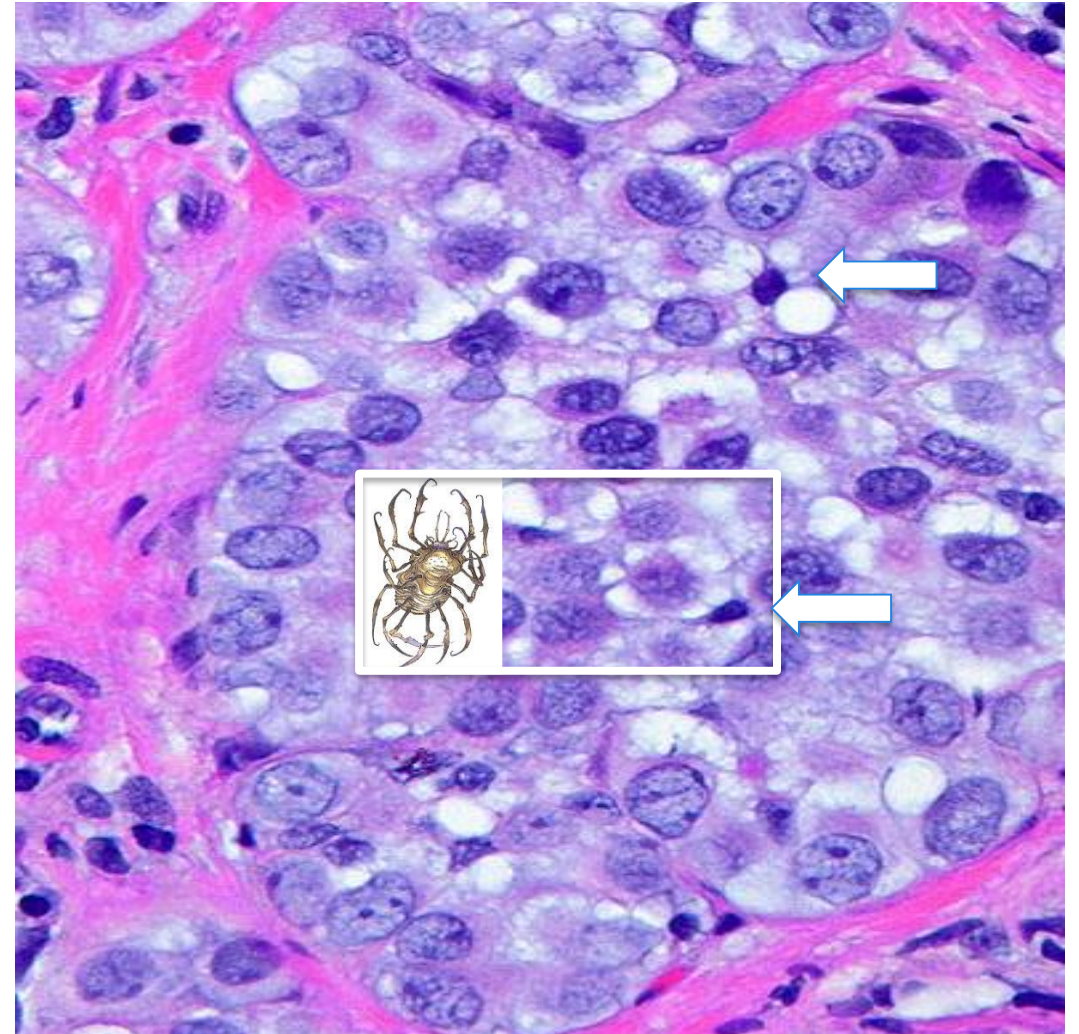


intracytoplasmic vacuoles



"spidery" cells

myoepithelial cell nuclei
admixed with classic LN

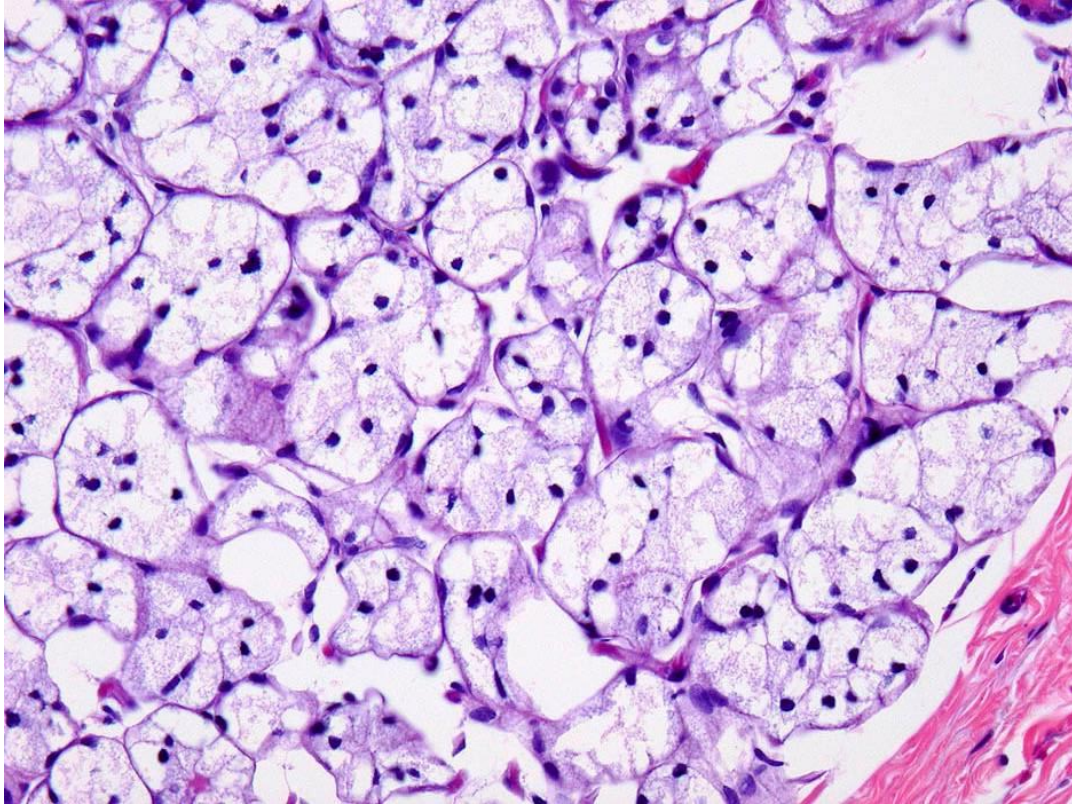


Classic LCIS/ALH - morphology and presentation

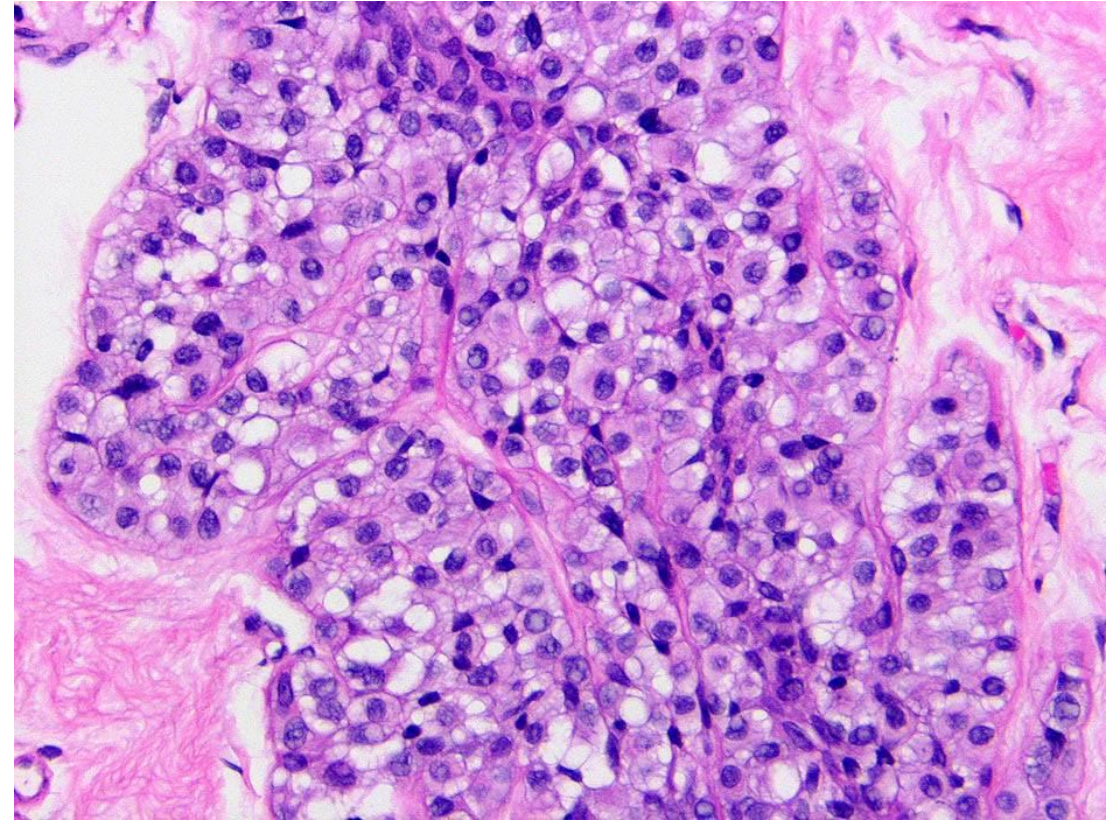
- Lobulocentric lesions
- +/- Pagetoid spread
- dyshesion
- cytomorphology
 - round-oval cells with central nuclei
 - lack cell polarization ("fried egg" appearance)
 - low nuclear grade
 - inconspicuous nucleoli
 - intracytoplasmic vacuoles (signet ring)
- usually no mitotic activity
- BR5th- Single cell necrosis possible
- Ca²⁺ rare and minute
- ALH and classic LCIS usually are incidental findings
 - MRI may detect classic LCIS/ALH
- Multifocal in ~80% cases
- Bilateral in 30-40% cases



Morphologic mimics of classic LCIS/ALH



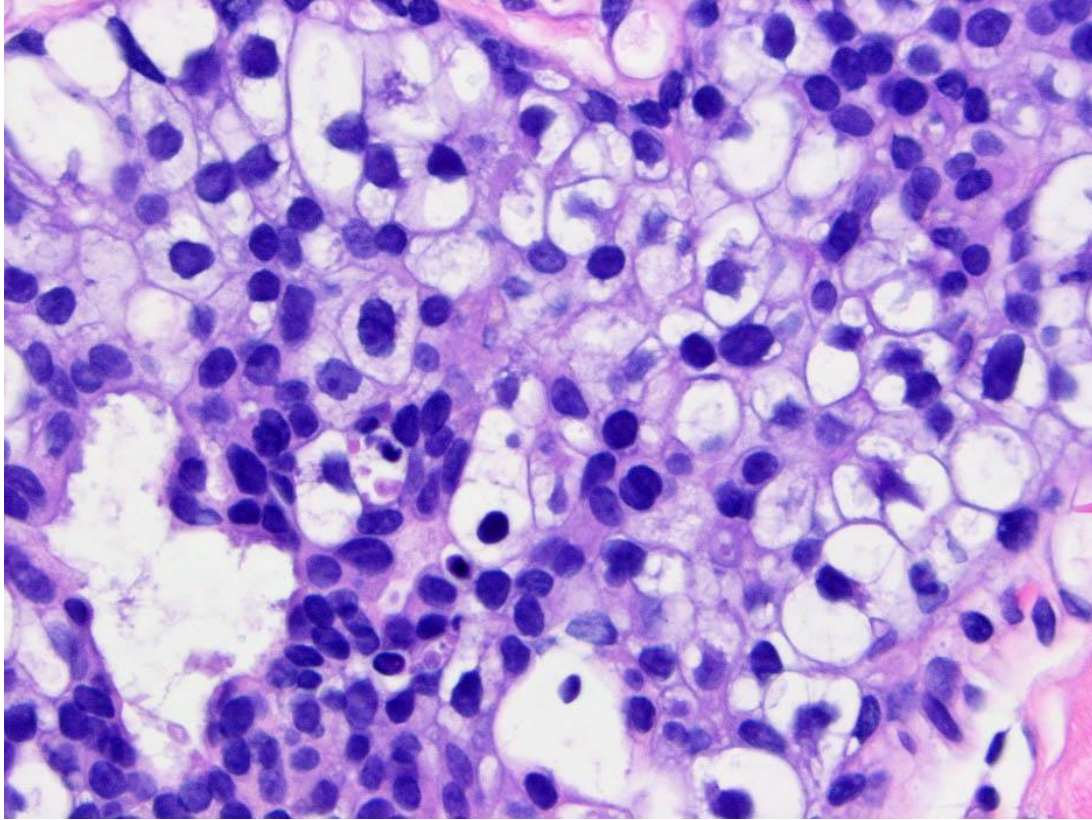
Clear Cell Change



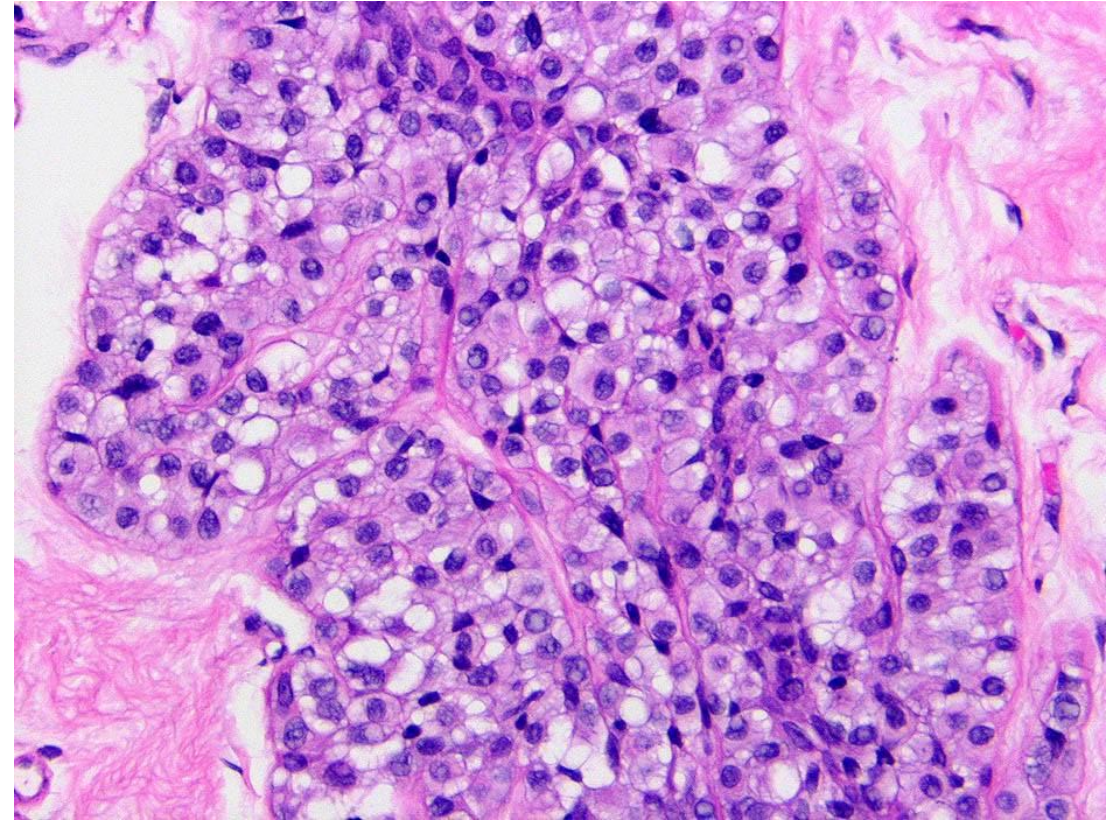
classic LCIS



Morphologic mimics of classic LCIS/ALH



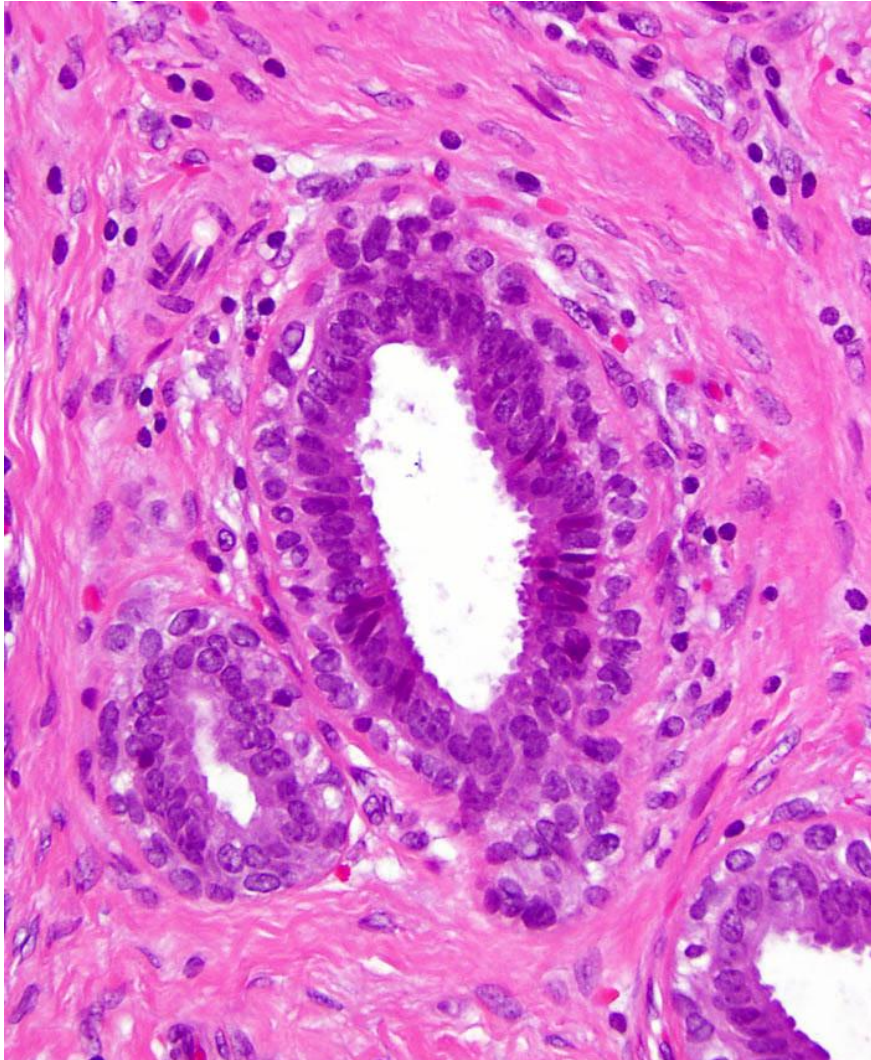
Clear Cell DCIS



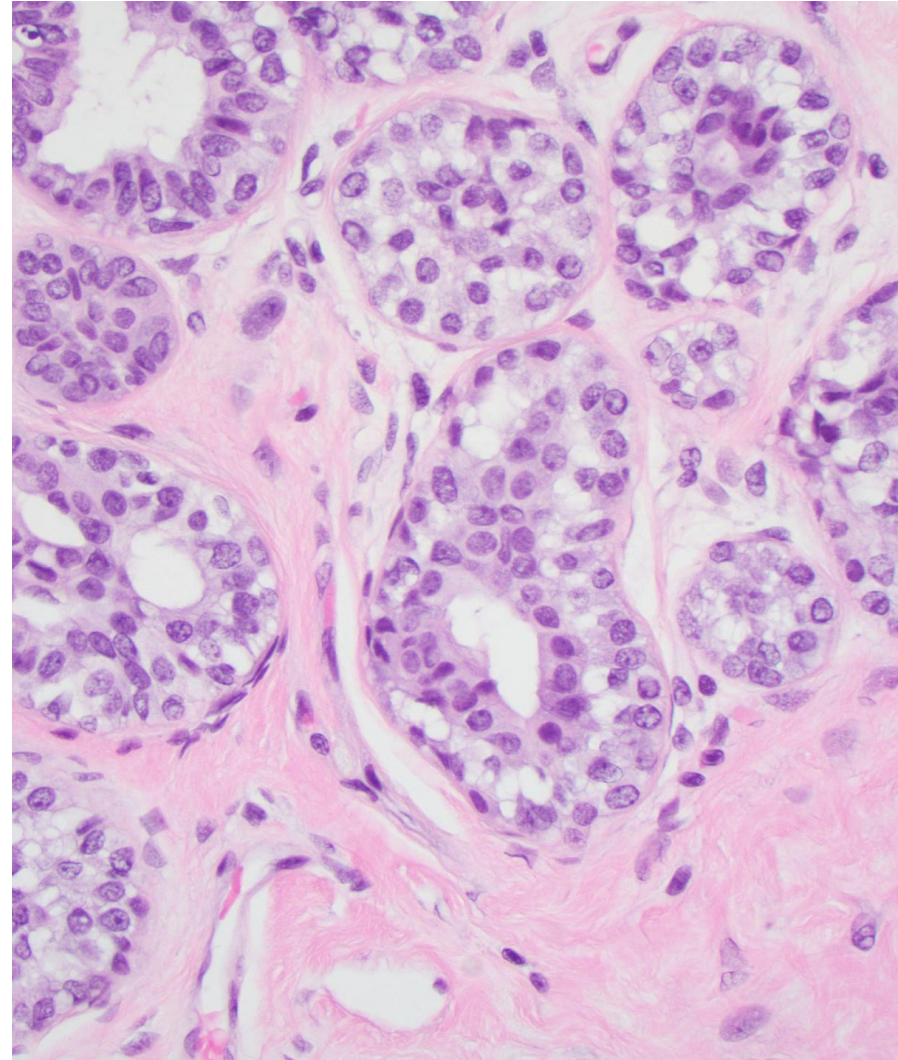
classic LCIS



Myoepithelial cells may mimic ALH



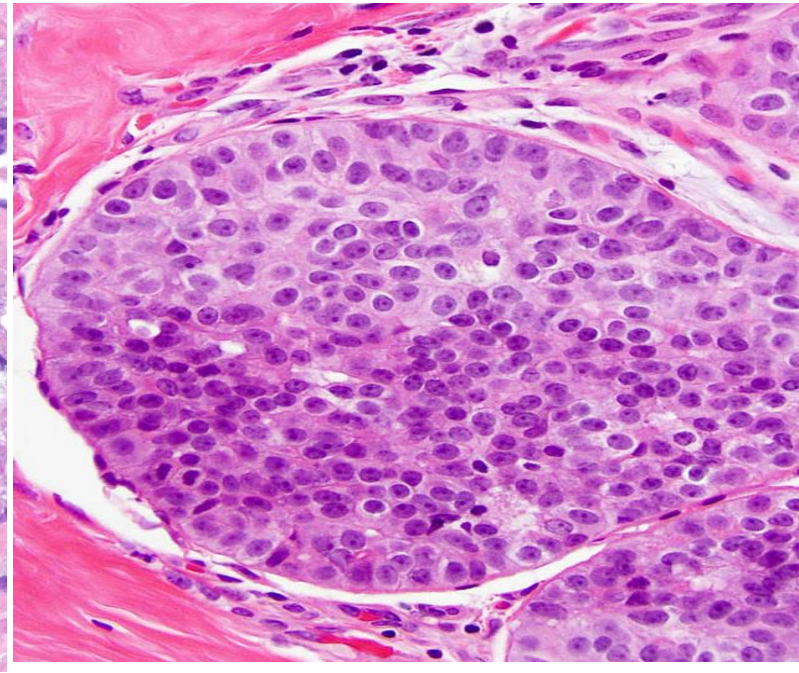
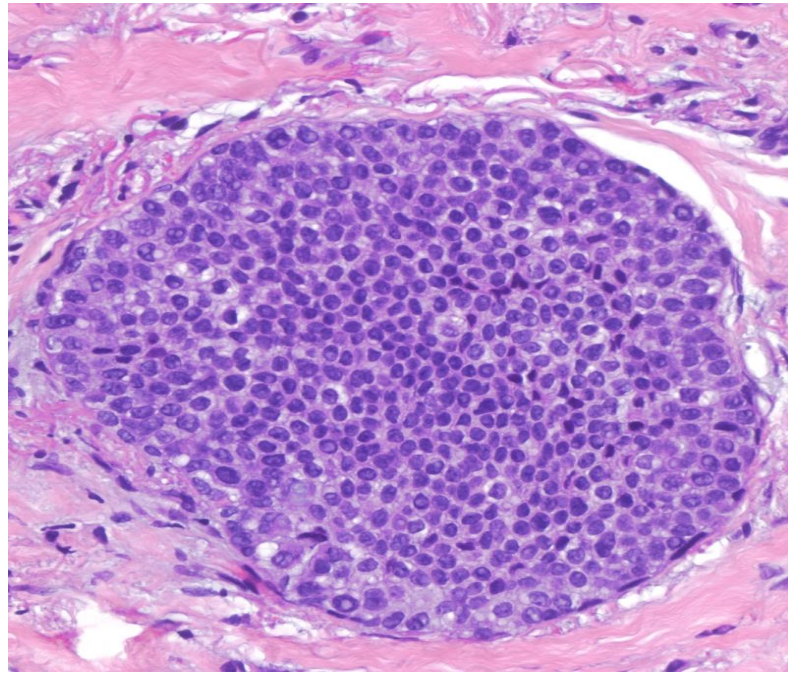
Myoepithelial cells



ALH

Classic LCIS/ ALH may mimic other lesions

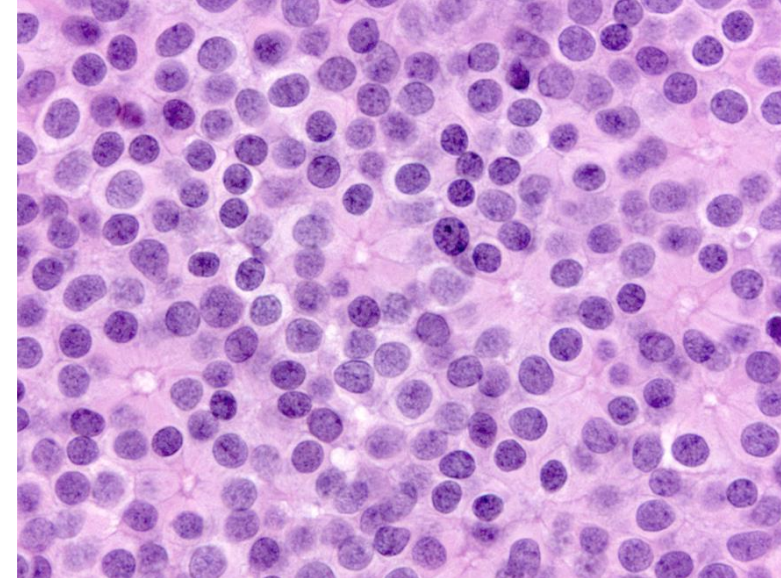
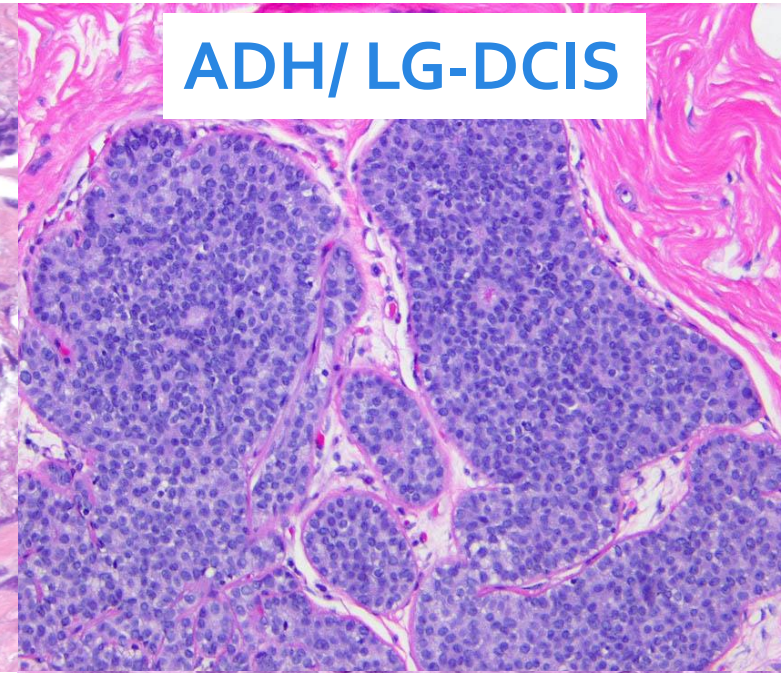
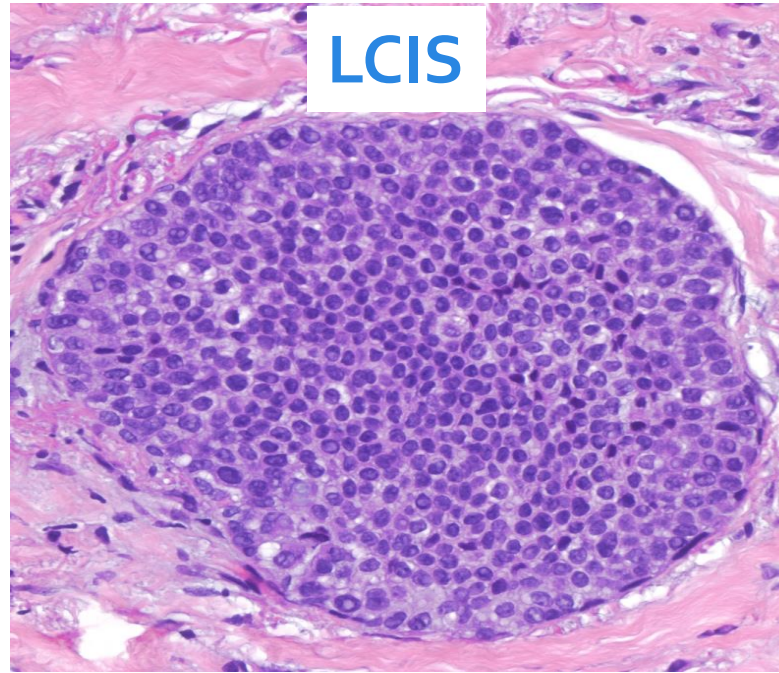
Classic LCIS may mimic
Solid ADH/ Low Grade DCIS



Classic LCIS/ ALH may mimic other lesions

Classic LCIS may mimic
Solid ADH/ Low Grade DCIS

Microacinar arrangement
occurs only in ADH/ LG DCIS



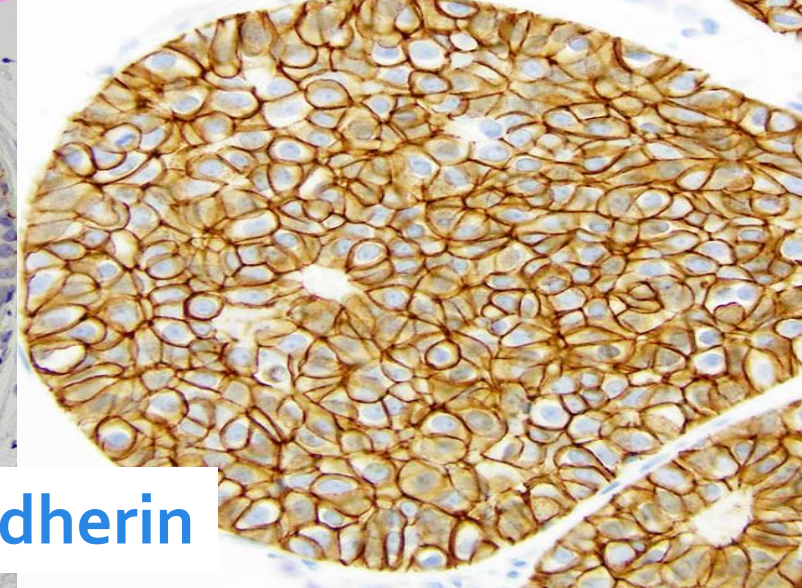
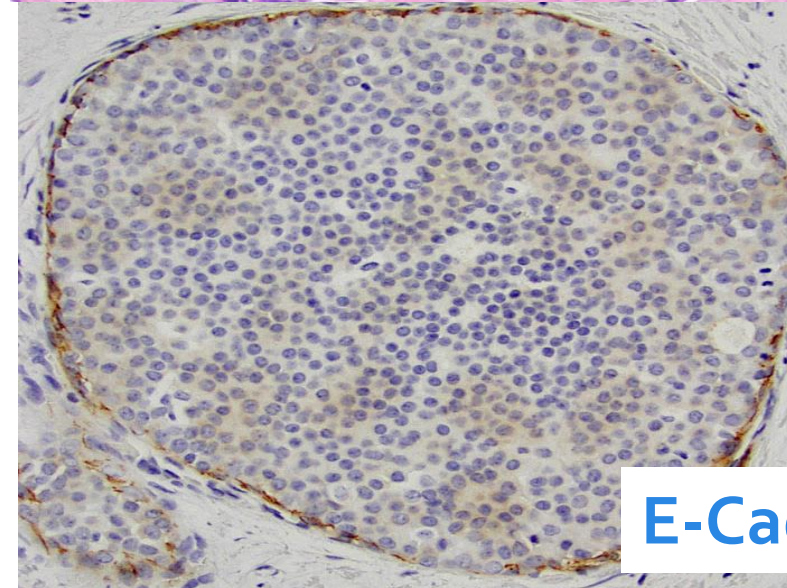
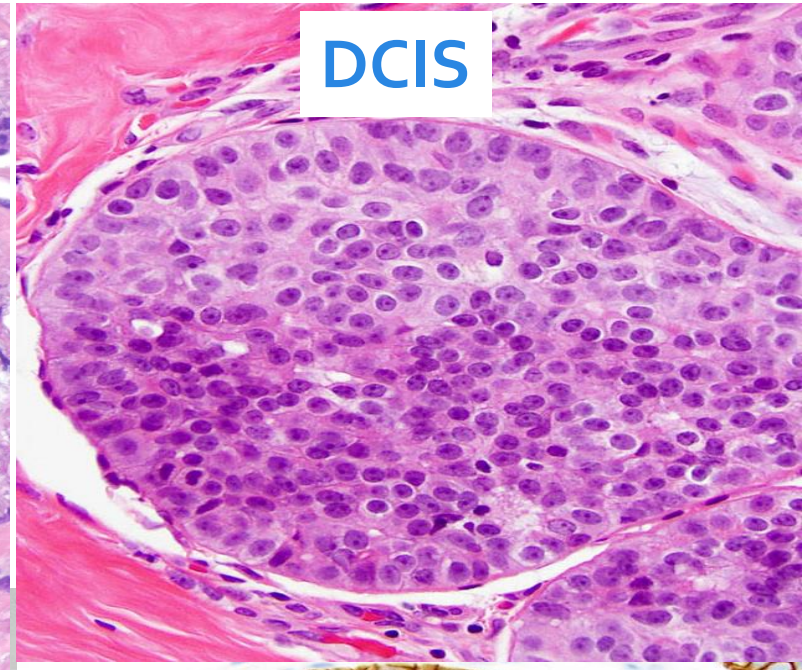
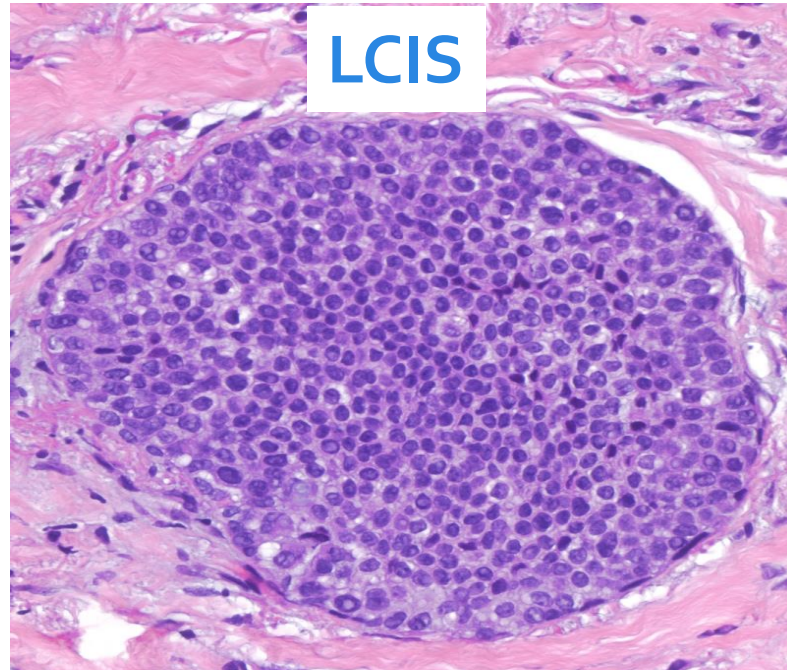
Classic LCIS/ ALH may mimic other lesions

Classic LCIS may mimic
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Immunohistochemistry

LCIS: E-cadherin-negative
B-catenin-negative
cytoplasmic P120

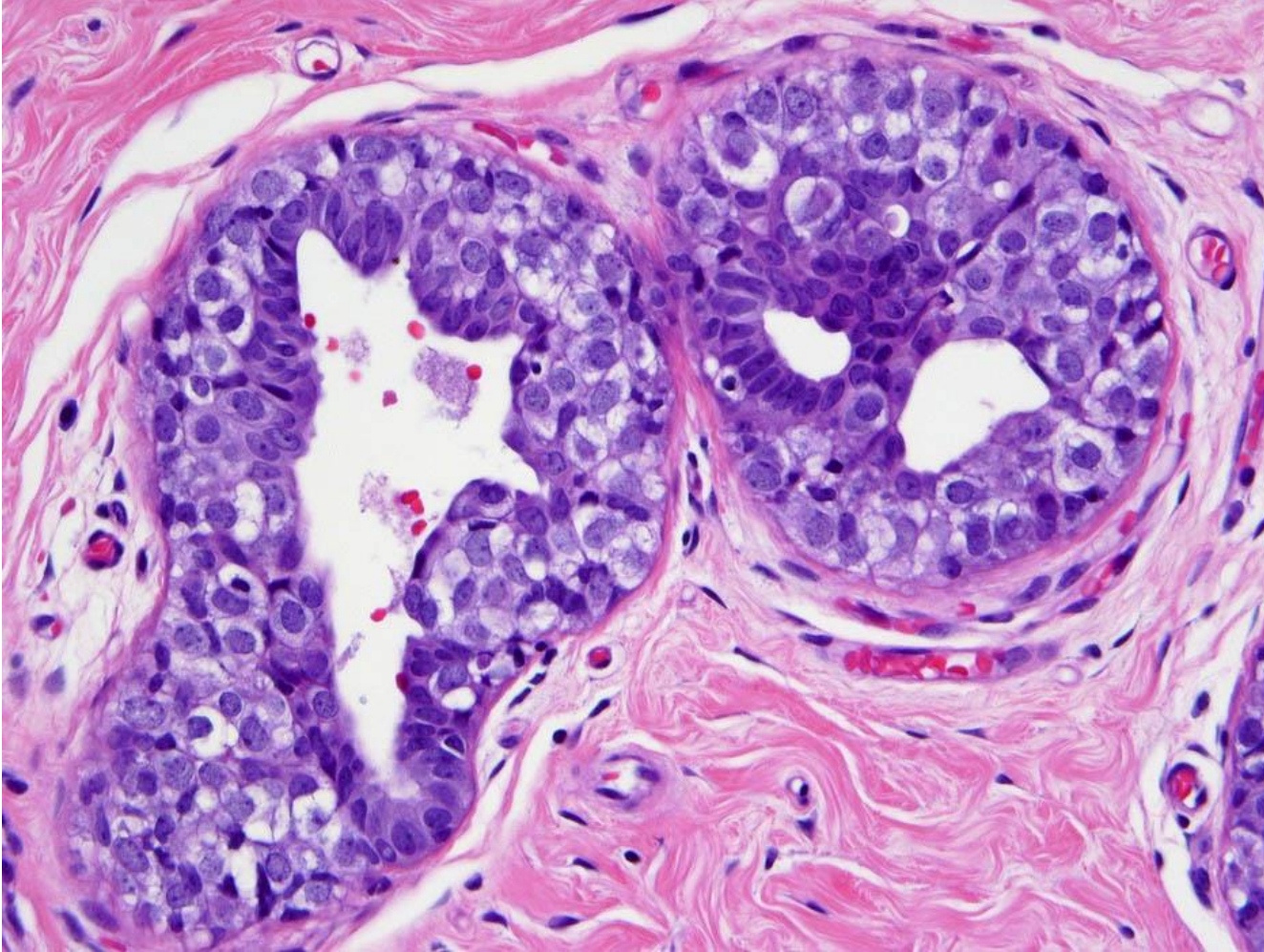


Classic LCIS/ALH + another lesion → few possible scenarios

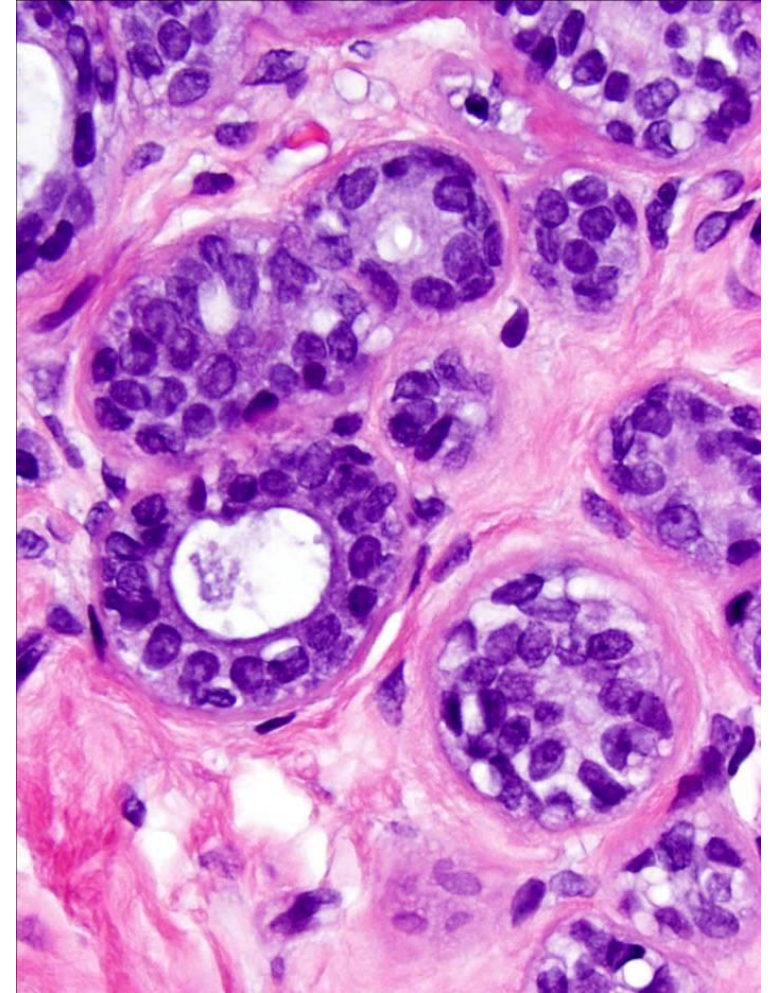
| If ALH/C-LCIS involves... | May mimic.. |
|------------------------------------|---|
| Normal acini (partial involvement) | <ul style="list-style-type: none">• ADH |
| Usual ductal hyperplasia (UDH) | <ul style="list-style-type: none">• UDH• ADH• Low grade DCIS• "mixed" ductal and lobular mammary carcinoma in situ |
| Collagenous spherulosis | <ul style="list-style-type: none">• ADH• Low grade DCIS |
| Sclerosing adenosis | <ul style="list-style-type: none">• Invasive lobular carcinoma |



Classic LN partially involving normal acini

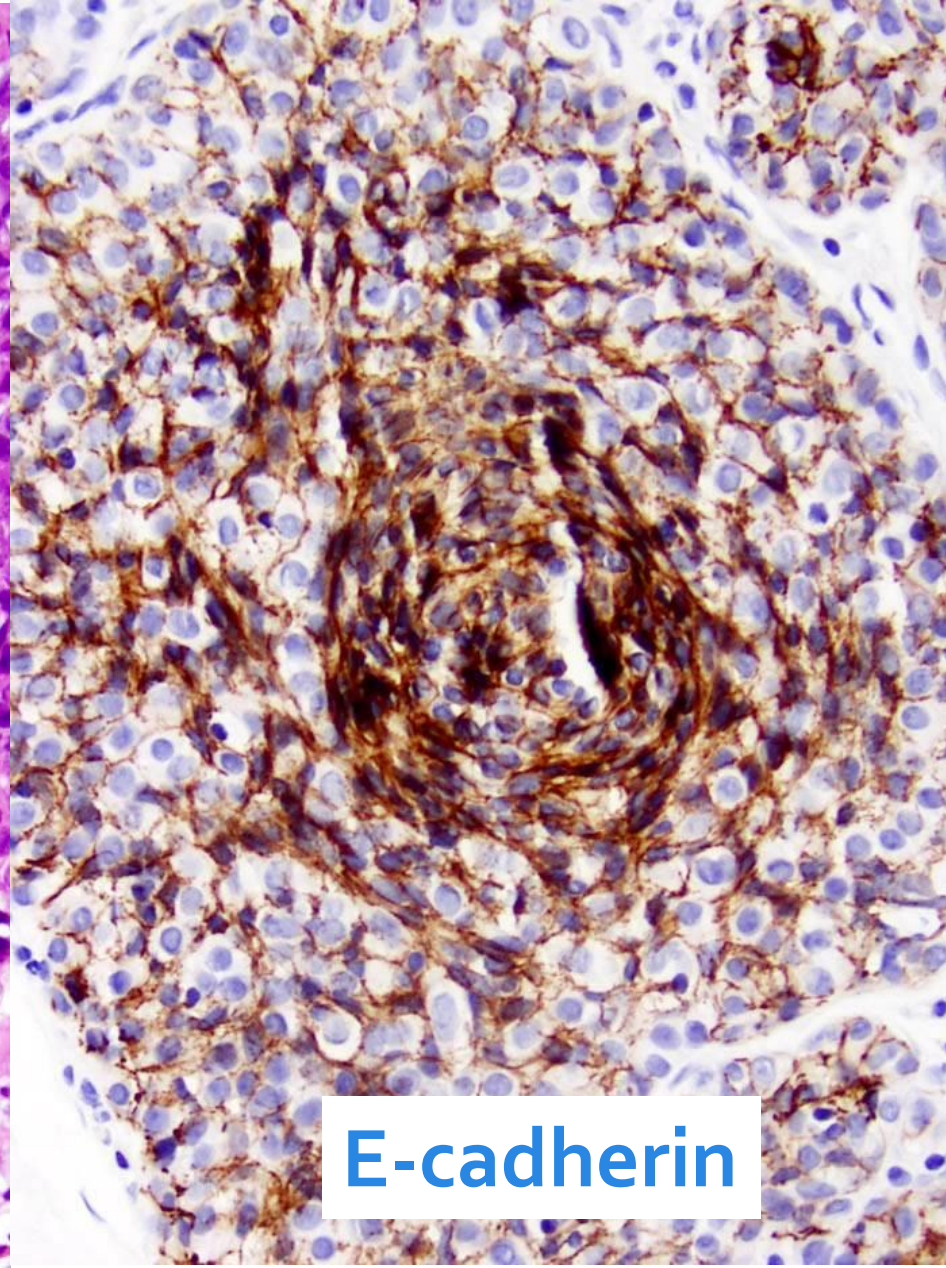
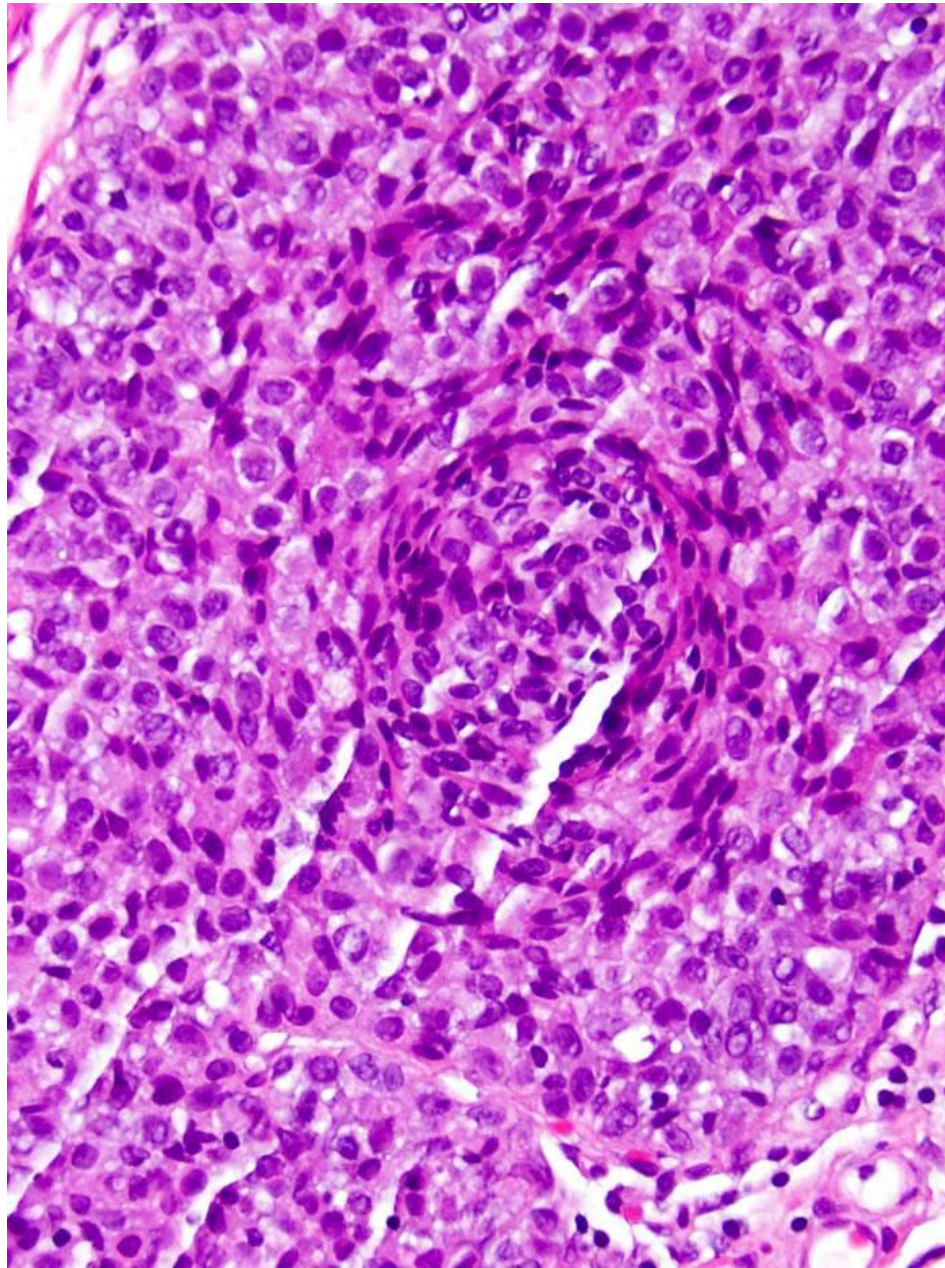


classic LN in normal acini
Luminal cells + myoepith cells + LN cells
3 cell morphologies



normal acini
Luminal cells + myoepith cells
2 cell morphologies

Classic LN Involving Usual Ductal Hyperplasia



E-cadherin

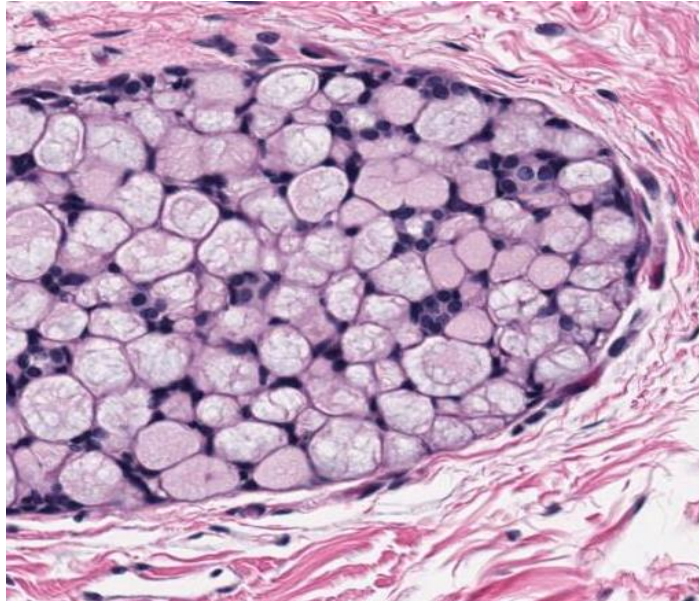
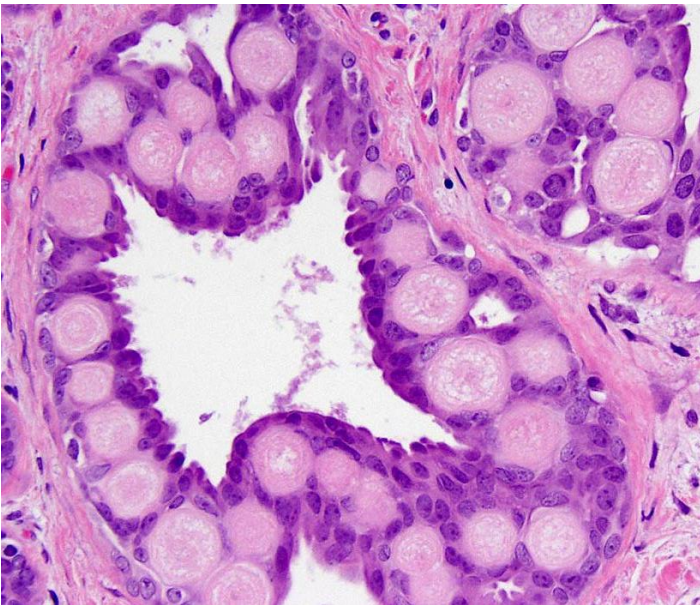
Collagenous Spherulosis (CS)

- Globoid deposits of eosinophilic or myxoid extracellular matrix surrounded by basement membrane and myoepithelium

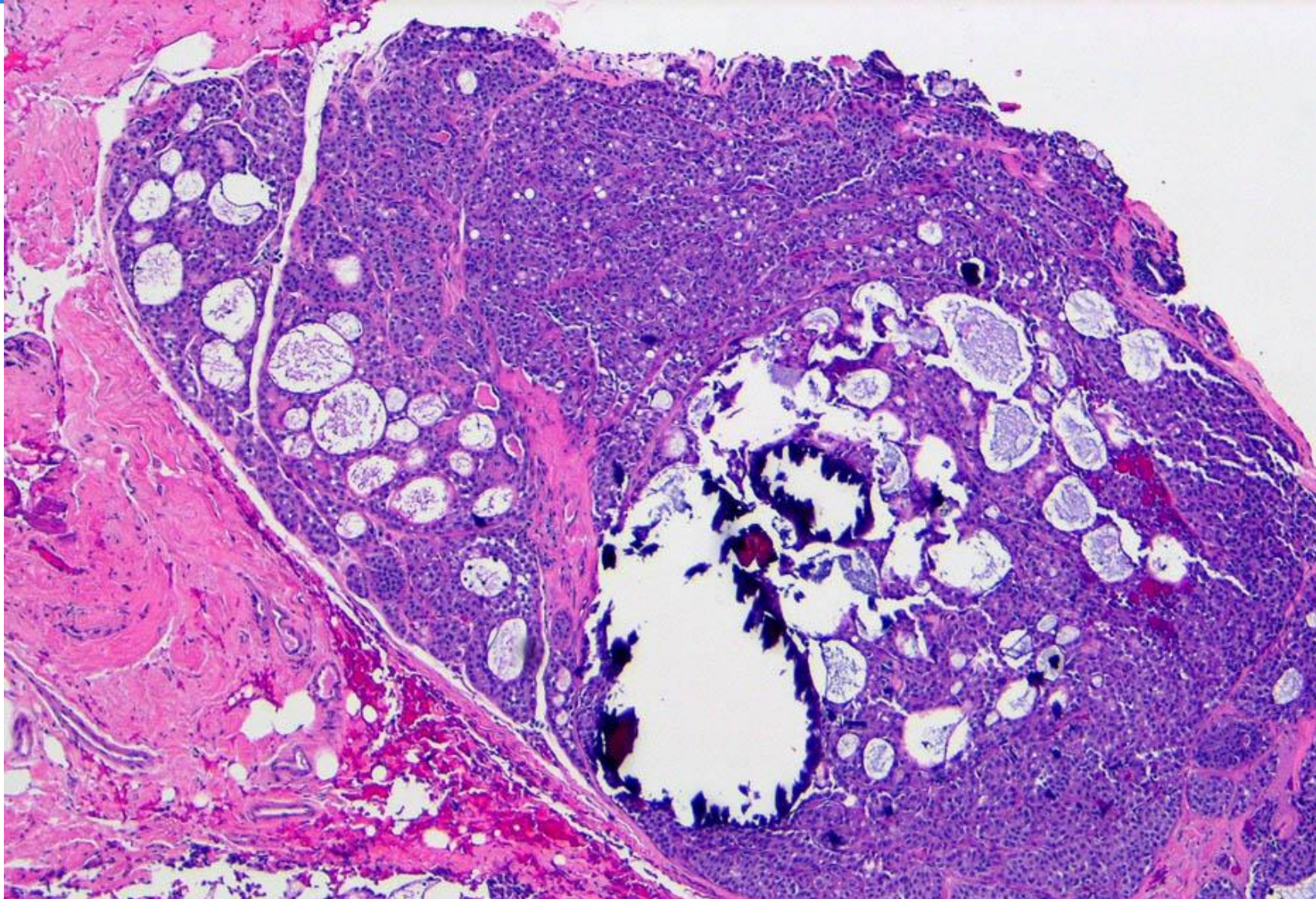
Clement P et al, *AJSP* 1987

- Common in sclerosing lesions
- Can be mass-forming (1-3 mm) or harbor Ca^{2+} → mammographic detection

Resetskova E et al, *AJSP* 2006



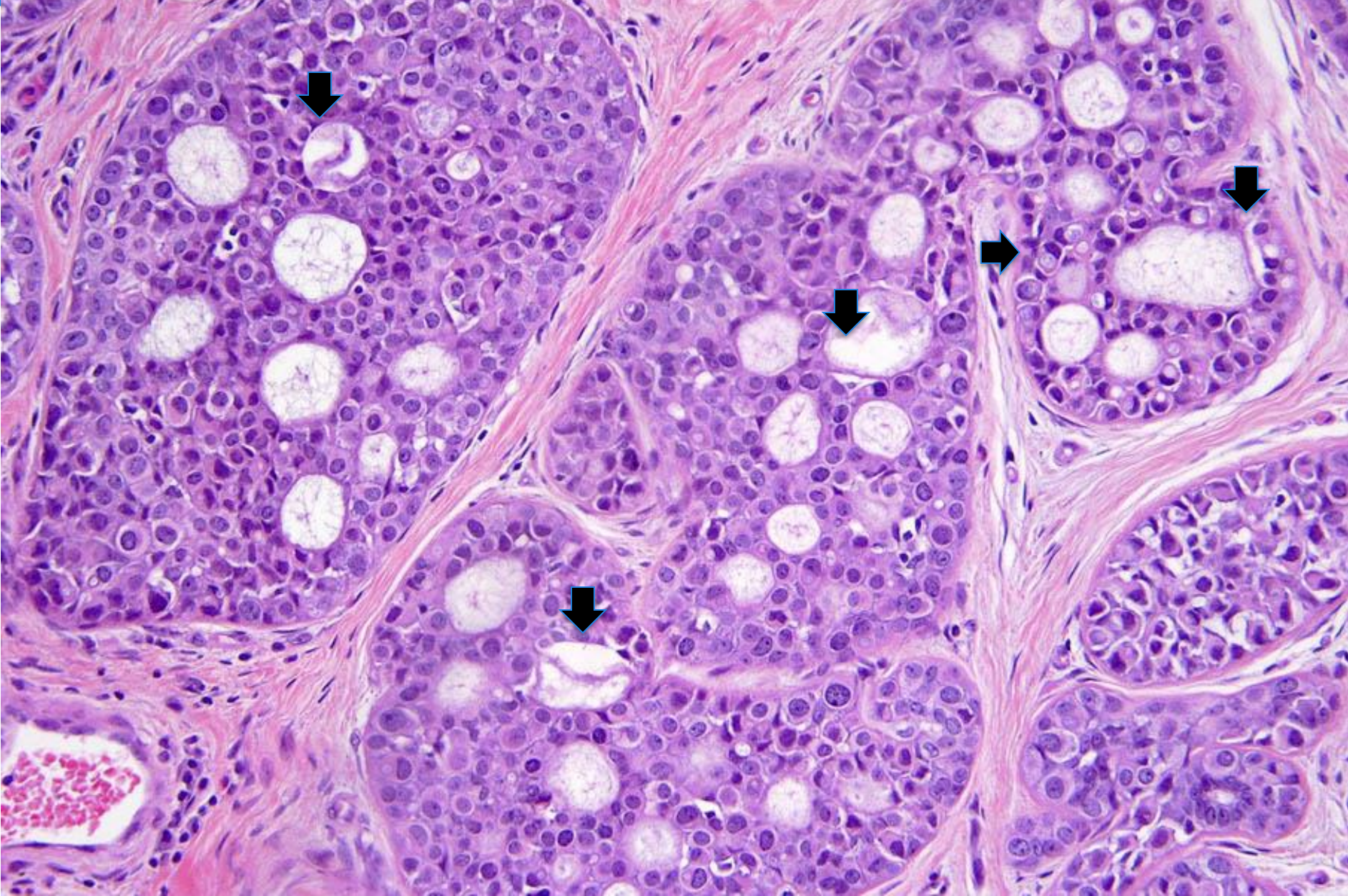
Classic lobular neoplasia in CS may mimic low grade DCIS



CNB imaging target often consists of Ca^{2+}

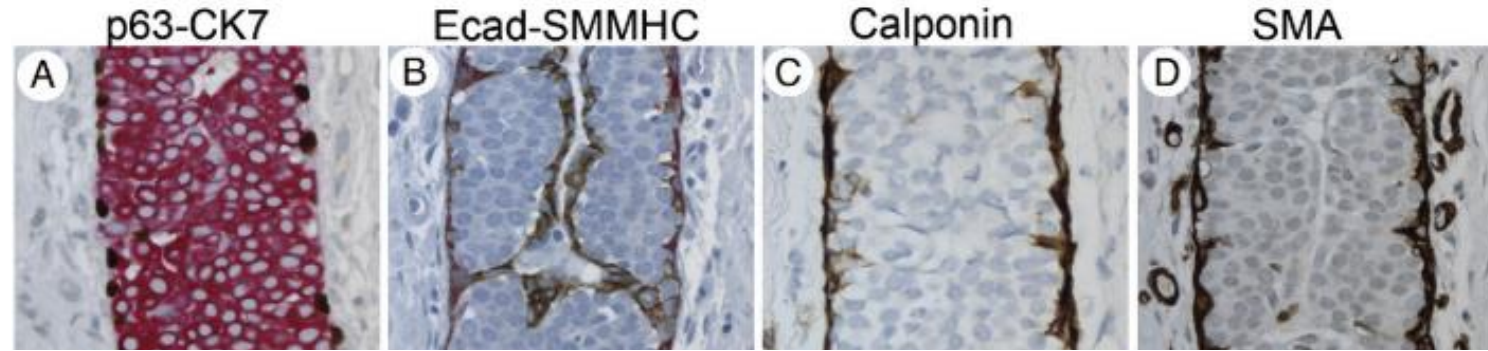
First described by SgROI D and Koerner F, *AJSP* 1995

Lobular neoplasia in CS may mimic DCIS



Myoepithelium and LCIS: 3 patterns

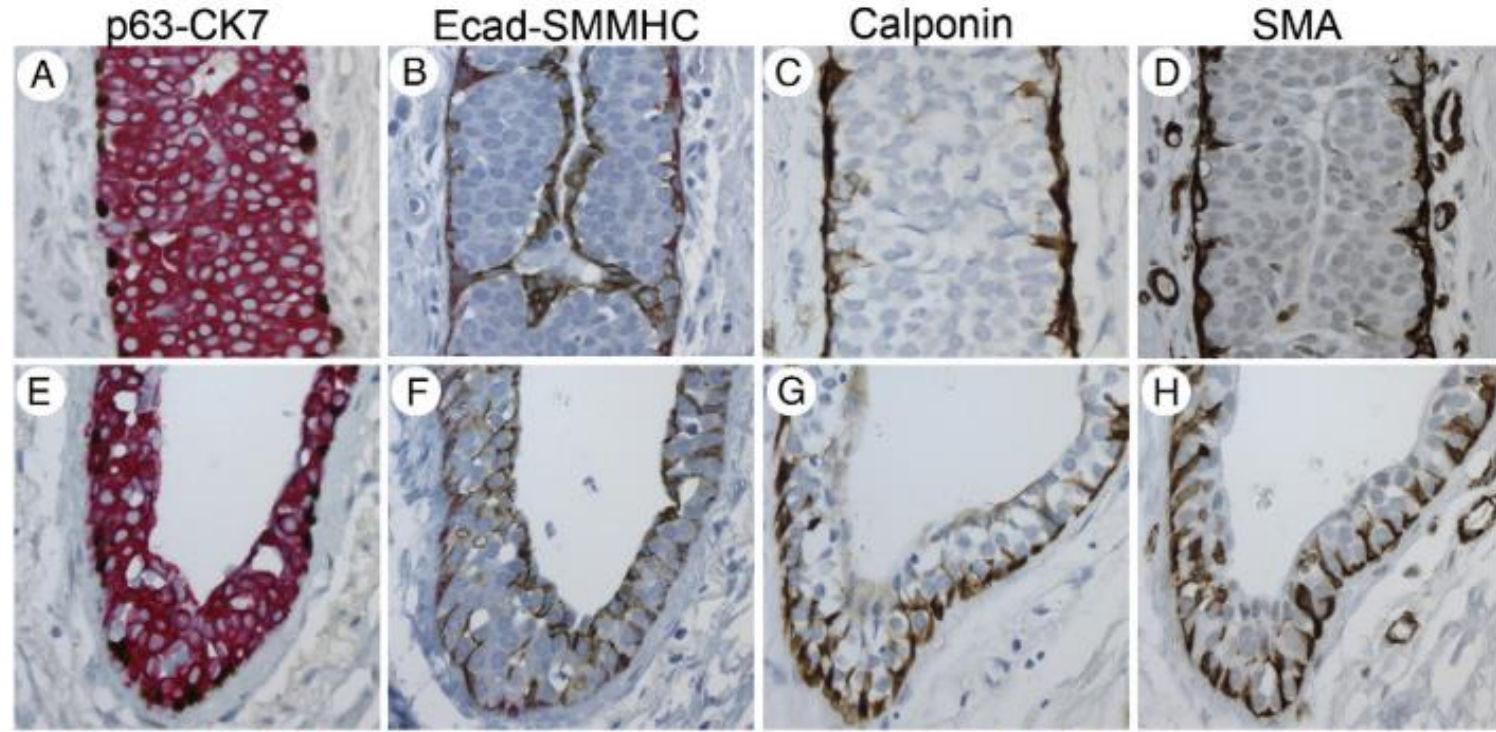
Normal
MECs lie flat on BM



Myoepithelium and LCIS: 3 patterns

Normal
MECs lie flat on BM

Perpendicular
MECs perpendicular to BM
(some Pagetoid growth)

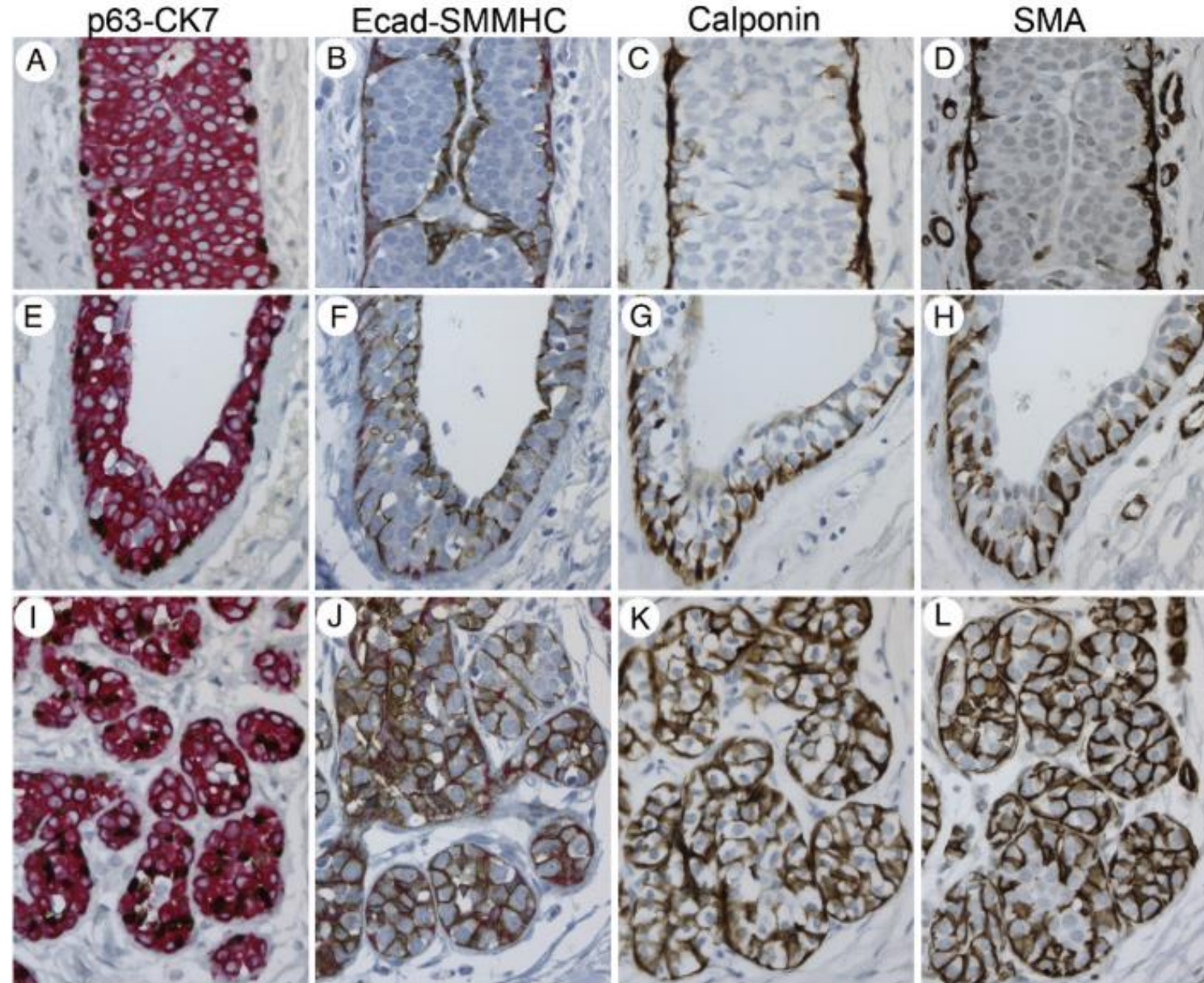


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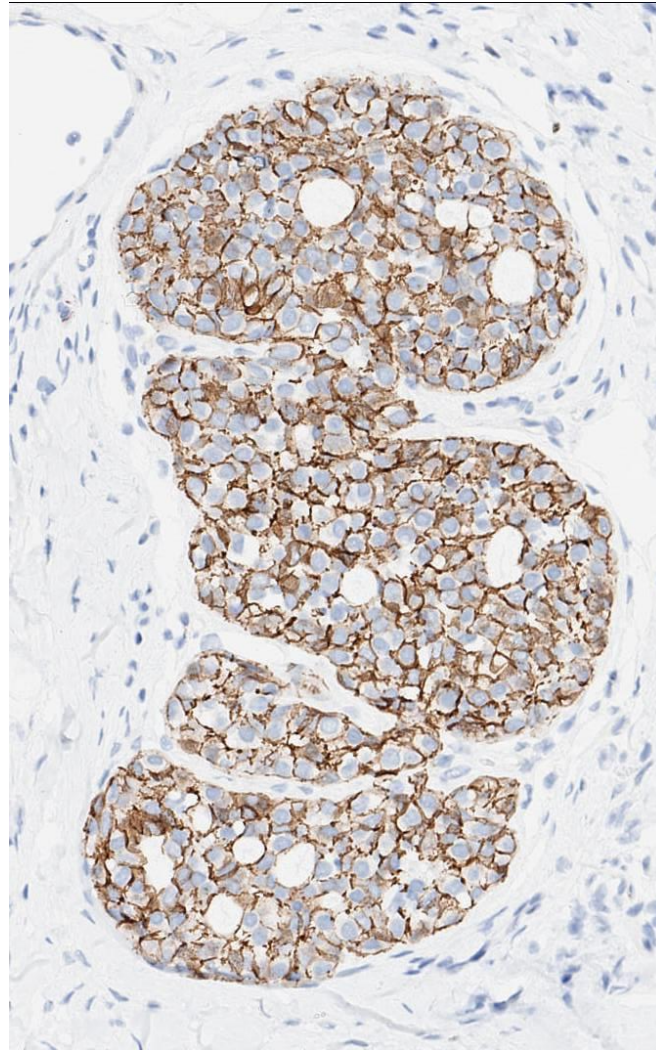
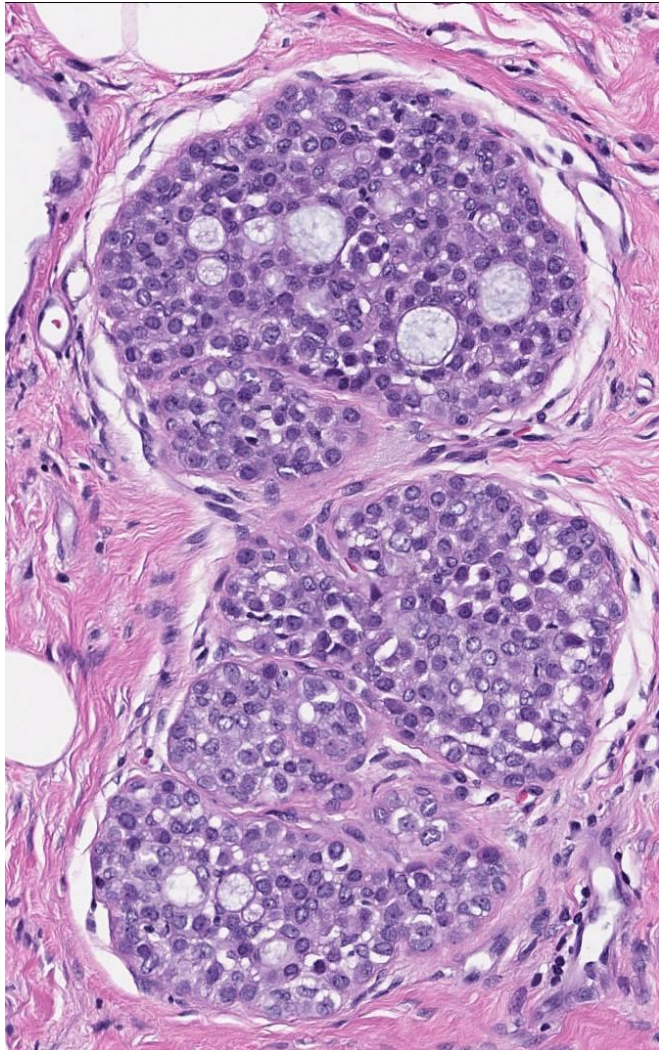
Normal
MECs lie flat on BM

Perpendicular
MECs perpendicular to BM
(some Pagetoid growth)

Central
MECs interdigitate with LCIS
in the center of the acini

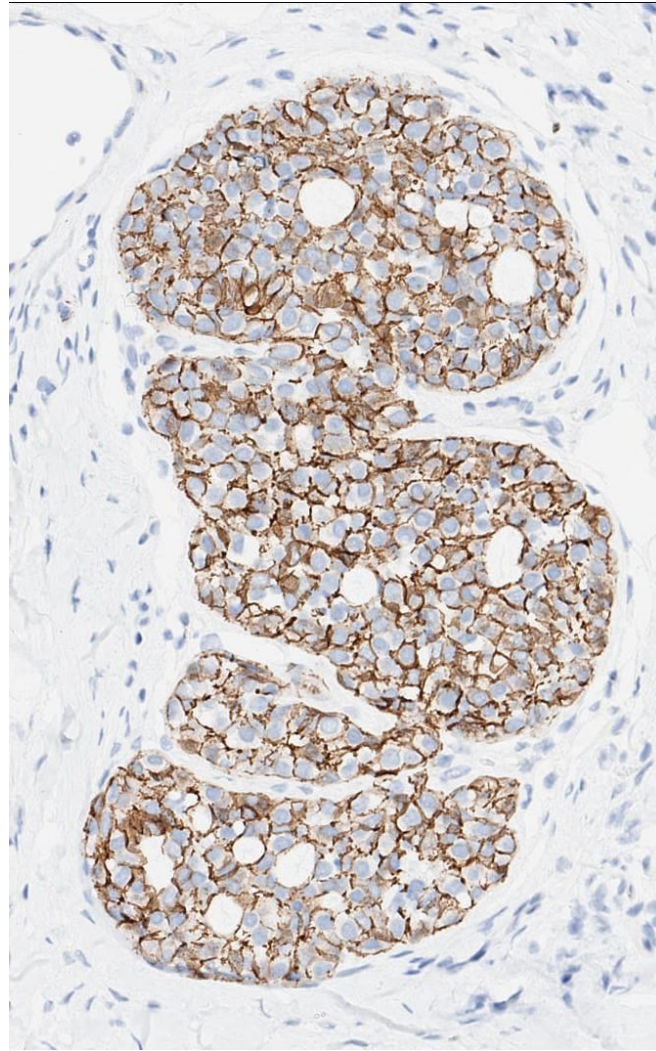
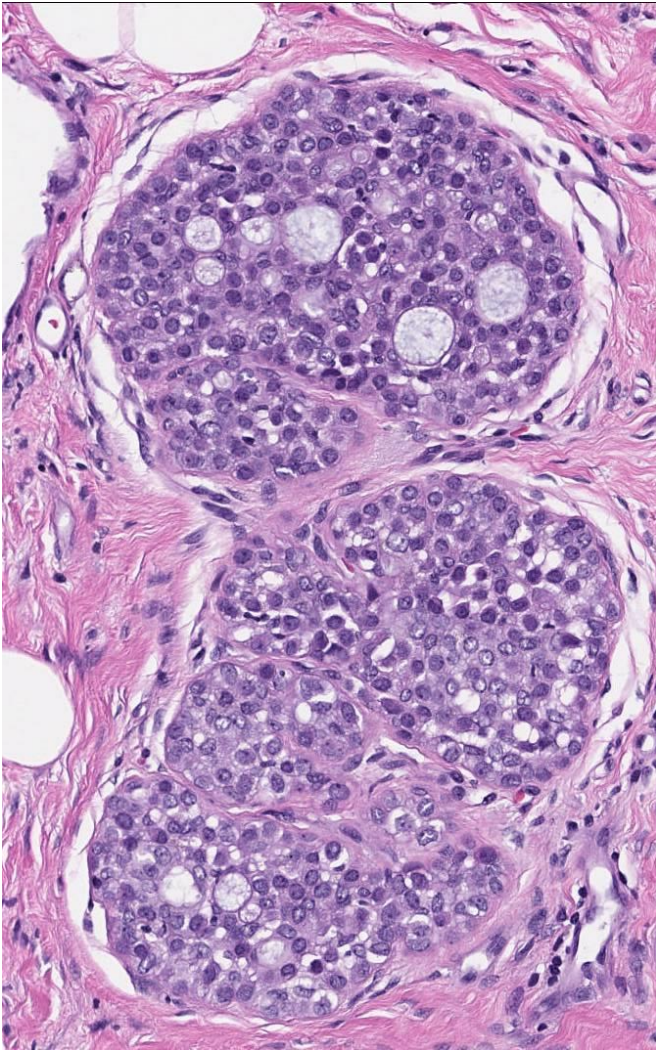


MECs are E-cadherin(+)

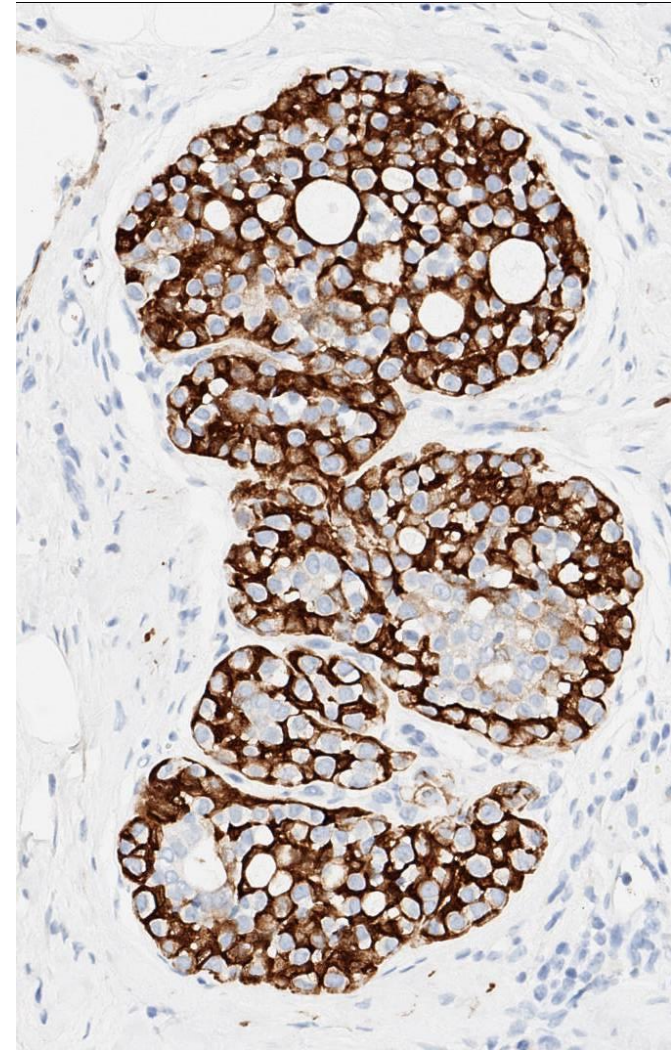


E-cadherin

MECs are E-cadherin(+)

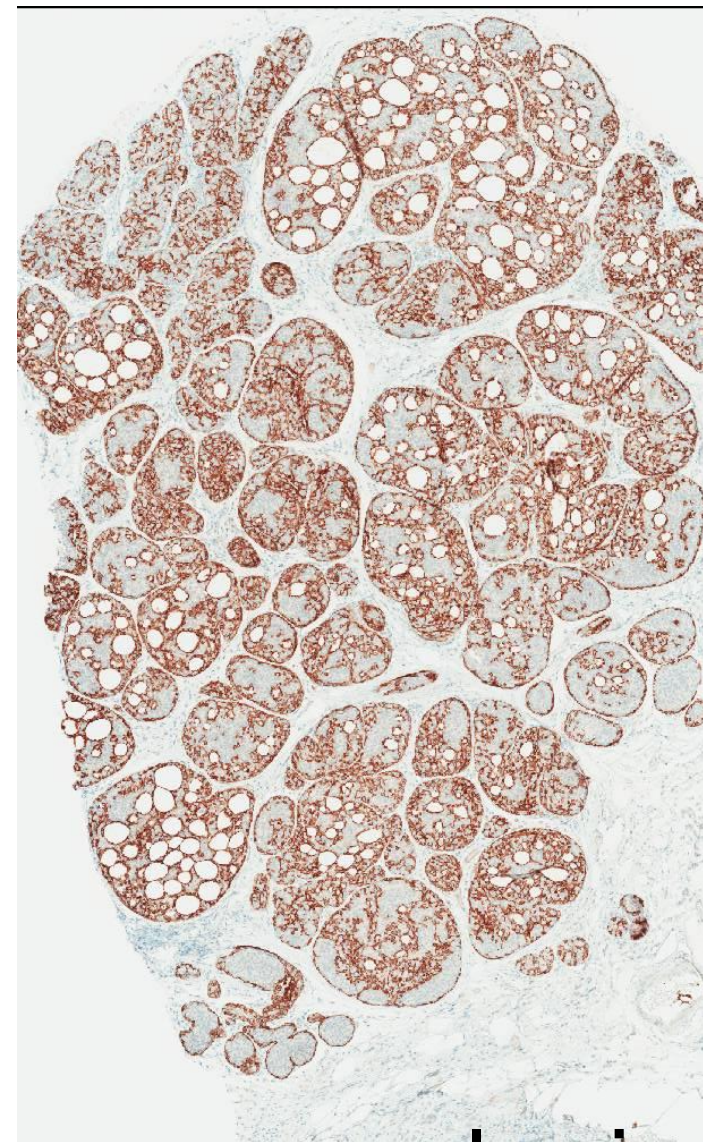
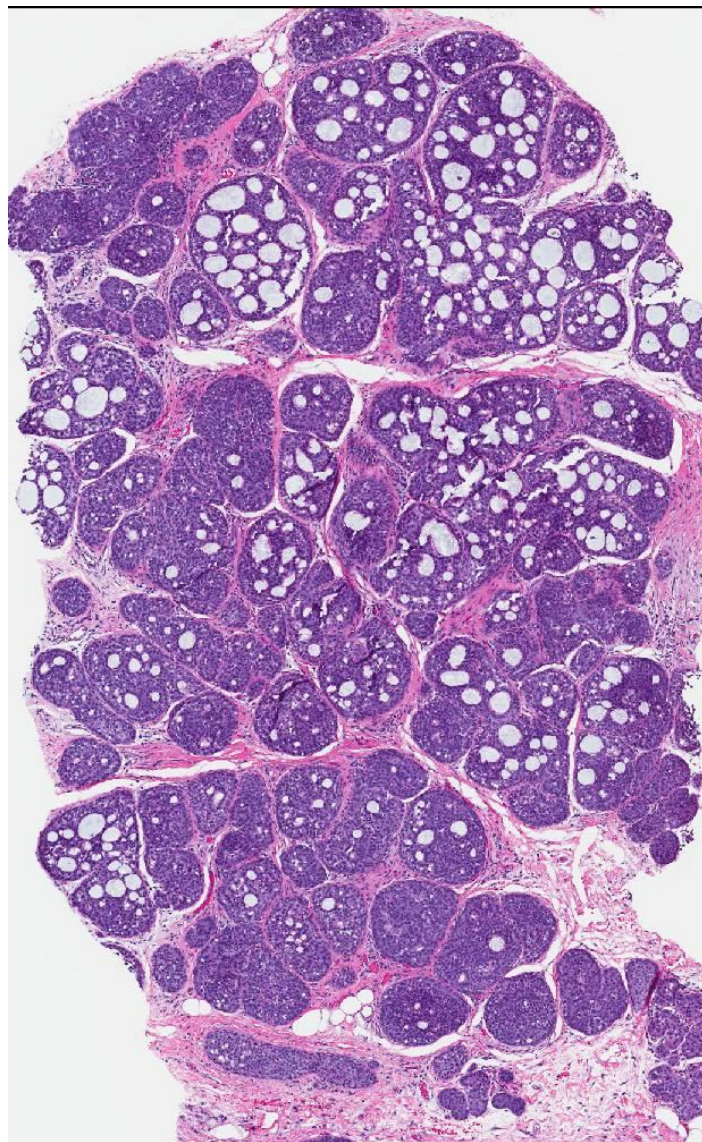


E-cadherin



calponin

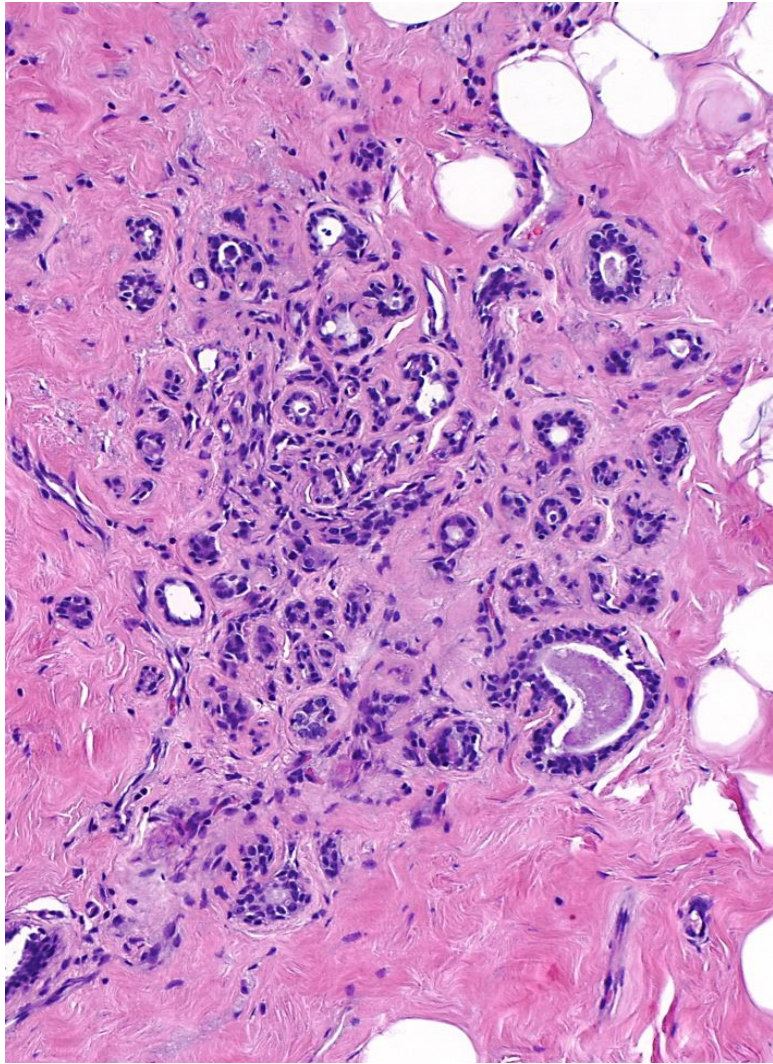
Classic lobular neoplasia in CS may mimic low grade DCIS



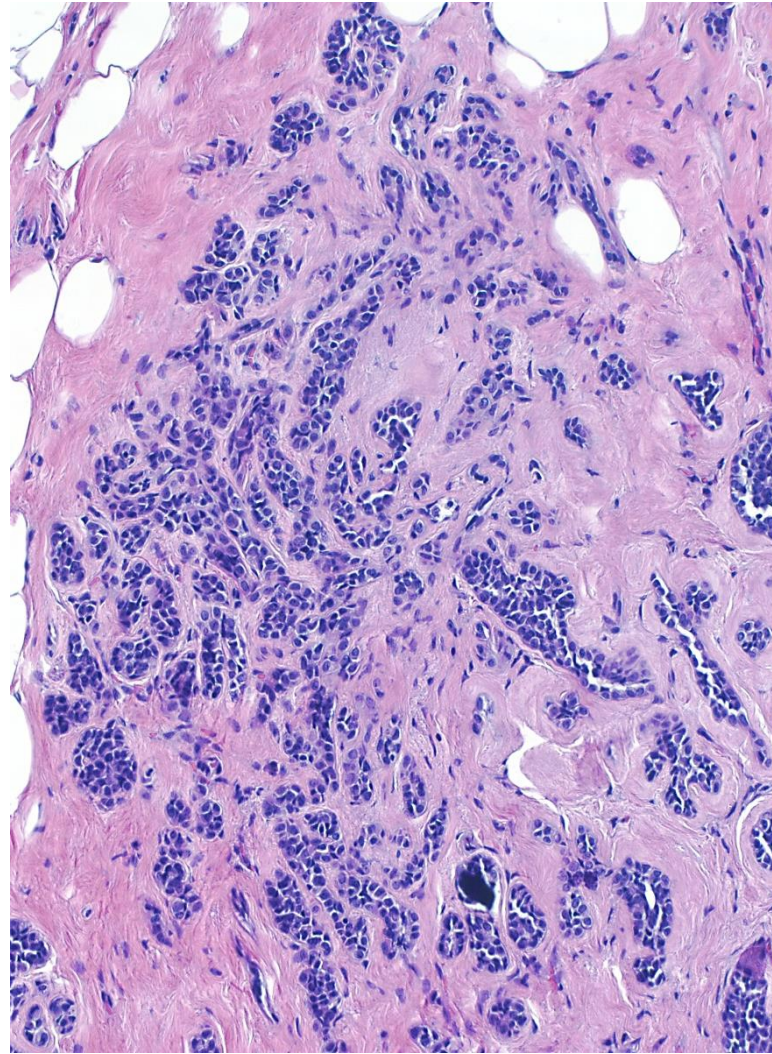
calponin



Sclerosing Adenosis (SA) and classic LN



sclerosing adenosis

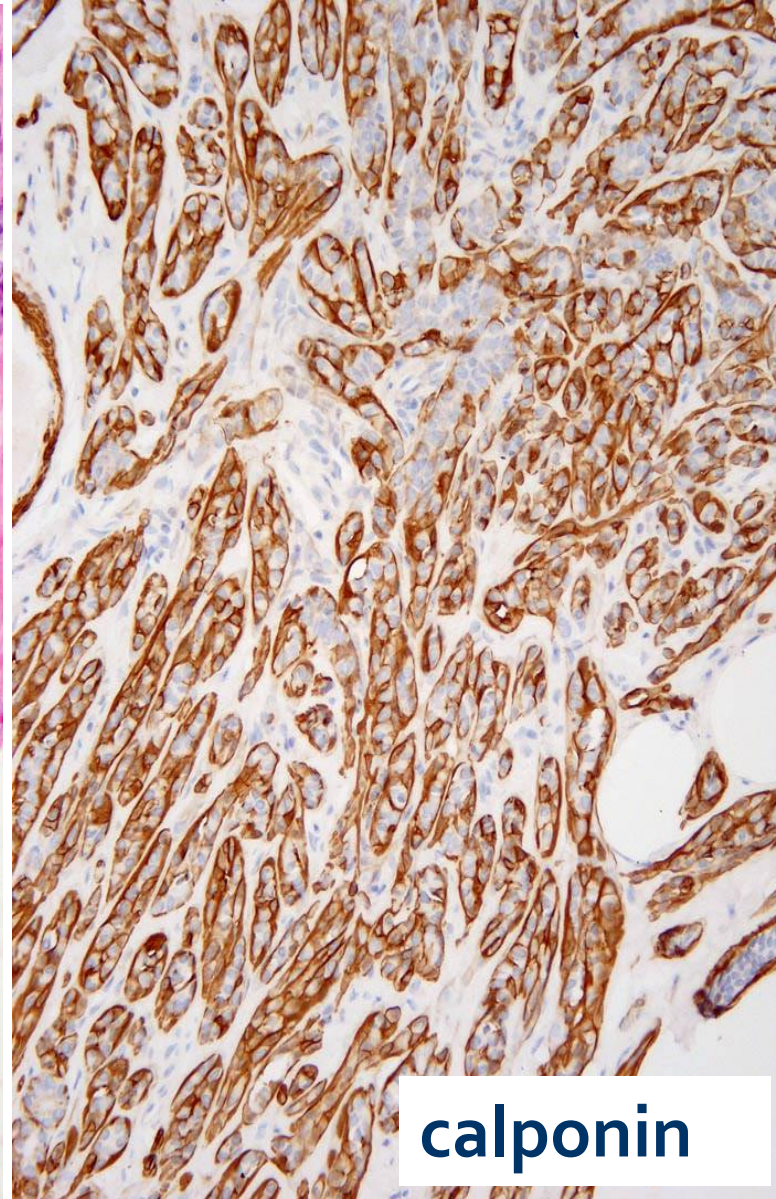
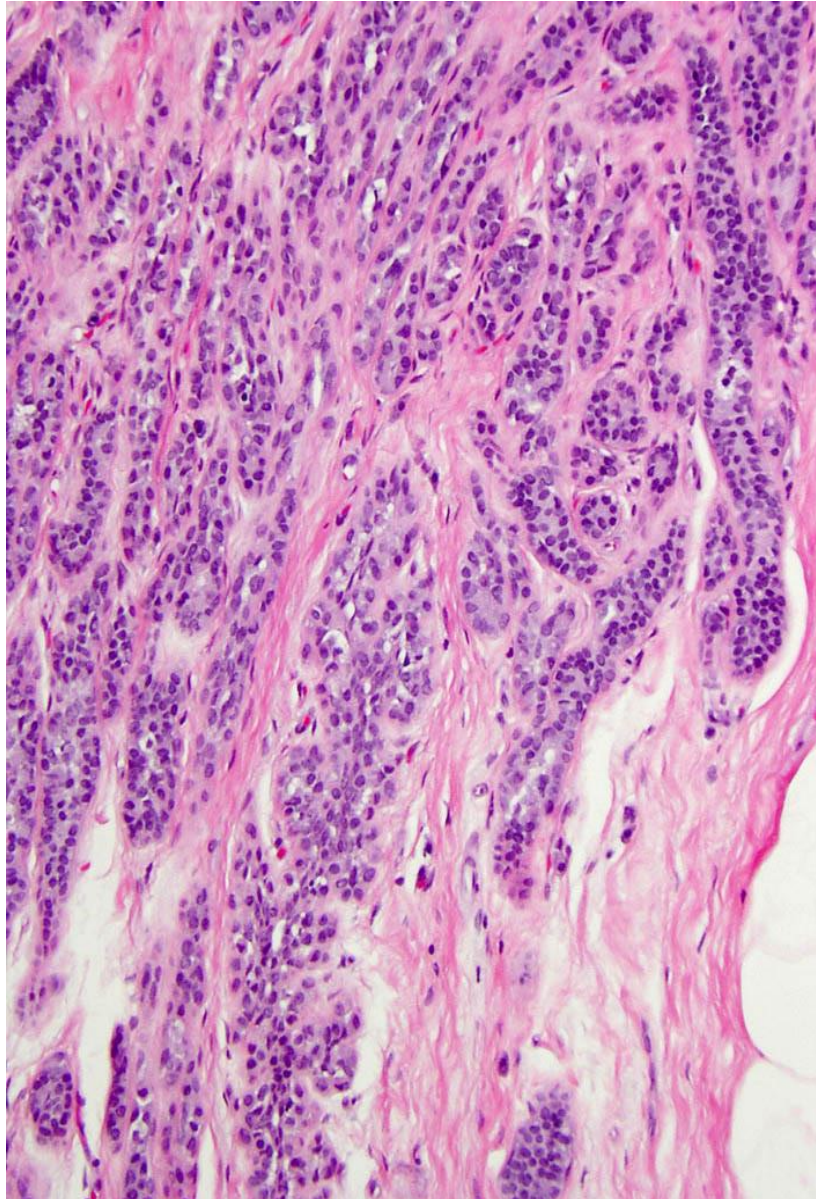


ALH in sclerosing adenosis

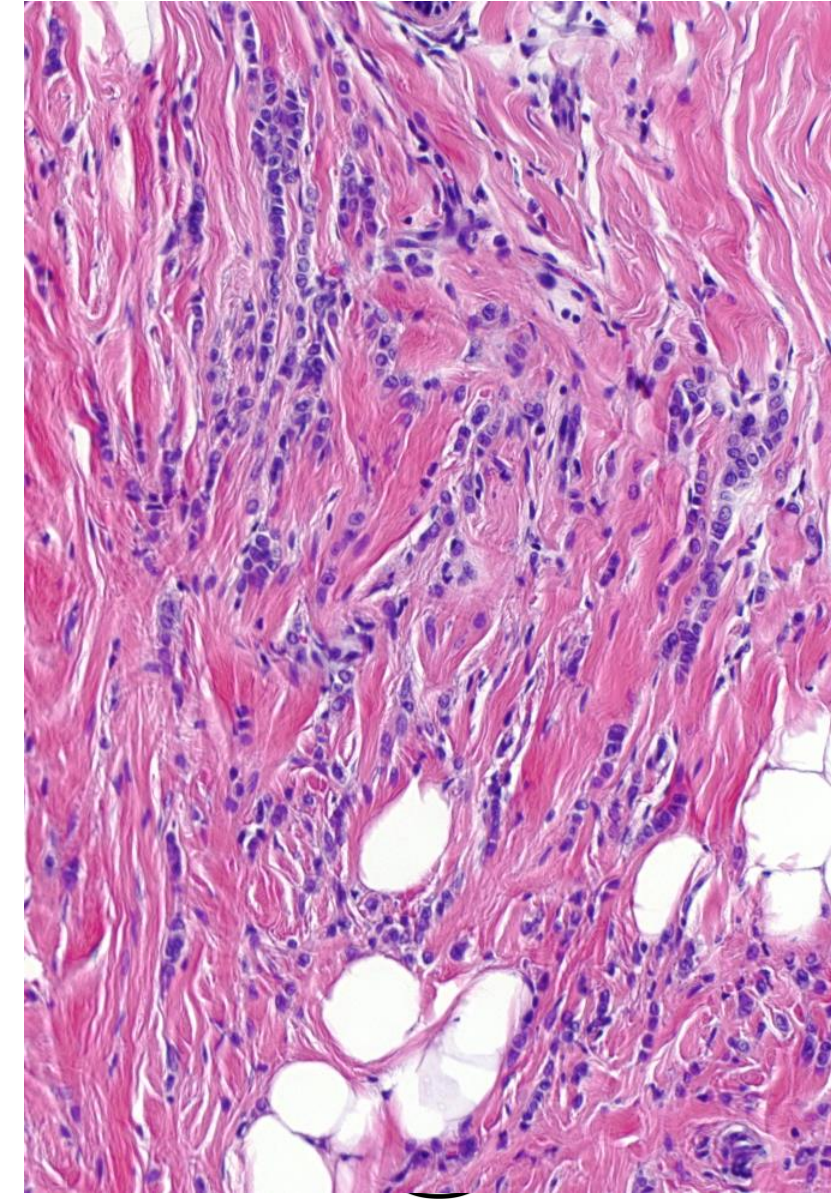


Classic LN in sclerosing adenosis

carcinoma



Invasive lobular

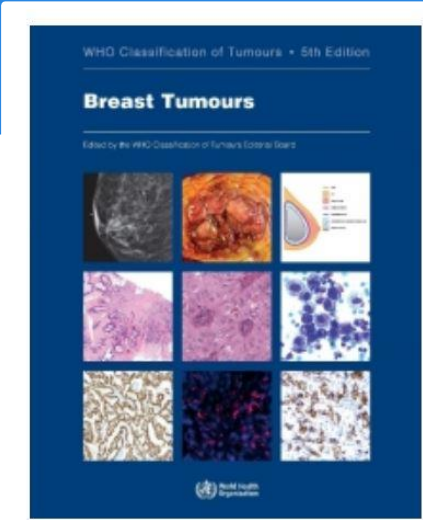


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Lobular Carcinoma In situ (LCIS)

- Classic LCIS

- **Florid LCIS**

- **Pleomorphic LCIS**



BR 5th ed: Florid LCIS - Definition

The LCIS cells show the cytological features of classic LCIS, but there is marked distention of TDLUs or ducts, creating a confluent mass-like architecture.

- Florid LCIS should have at least one of two ARCHITECTURAL features:
 - little to no intervening stroma between markedly distended acini of involved TDLUs and a
 - size cut-off point at which an expanded acinus or duct fills an area equivalent to ~40–50 cells in diameter

Alvarado-Cabrero | *Arch Med Res* 41(6):436-41. 2010.

Shamir ER *Am J Surg Pathol* 43(3):399-408, 2019

Shin SJ *Hum Pathol* 44(10):1998-2009, 2013.

Wen HY and Brogi E *Surg Pathol Clin* 11(1):123-145, 2018 (review)



BR 5th ed: Florid LCIS

Florid LCIS has cytological features similar to those of classic LCIS (type A and/or type B cells) but is distinguished by marked expansion of TDLUs with little to no intervening stroma between markedly distended acini of involved TDLUs.



BR 5th ed: Florid LCIS definition

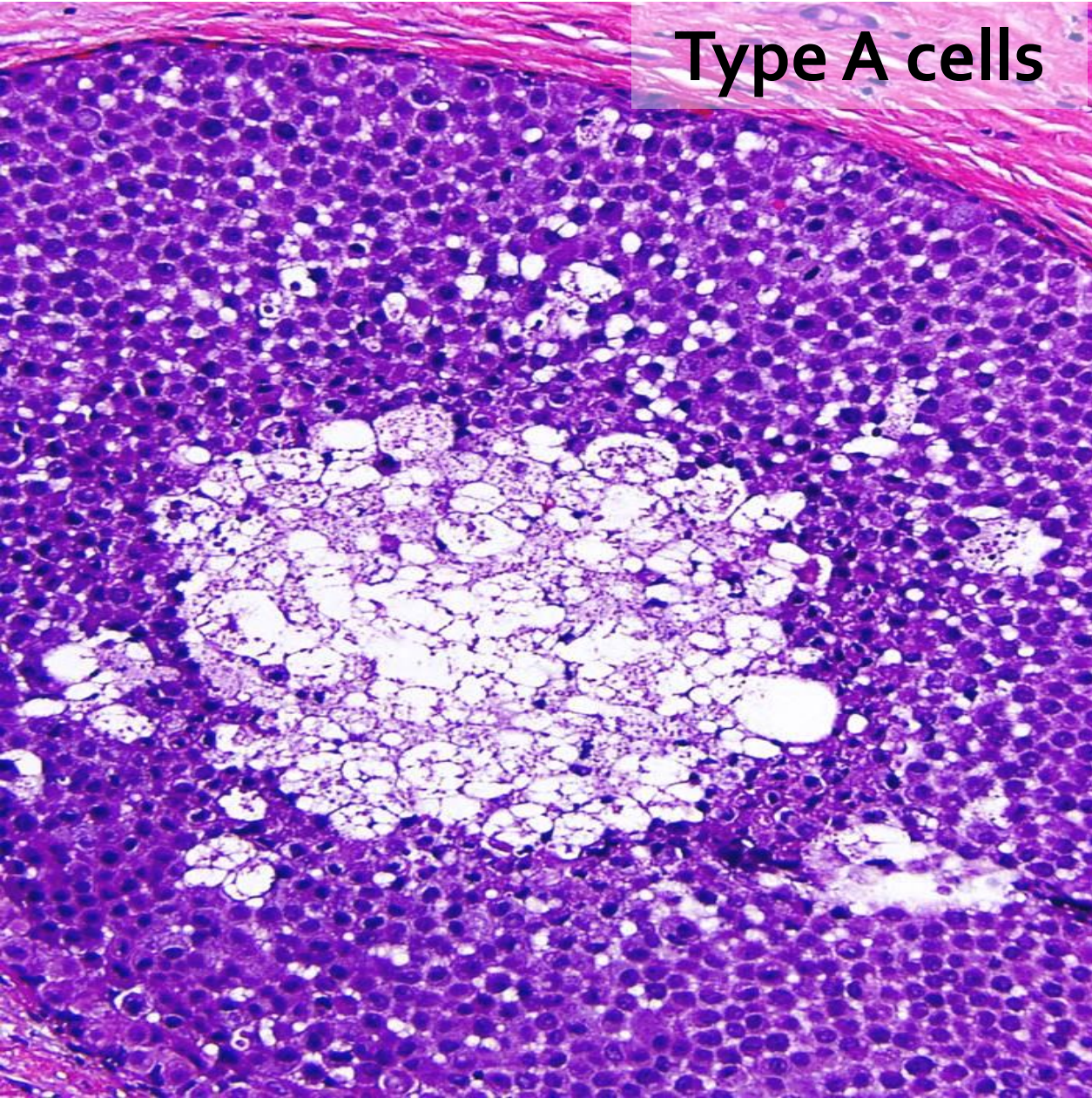
In florid LCIS, the acini or ducts are markedly expanded (filling at least one high power field, equivalent to >40–50 cells in diameter) and often associated with central necrosis.

*Necrosis and/or Ca²⁺
NOT required for diagnosis of
Florid LCIS*

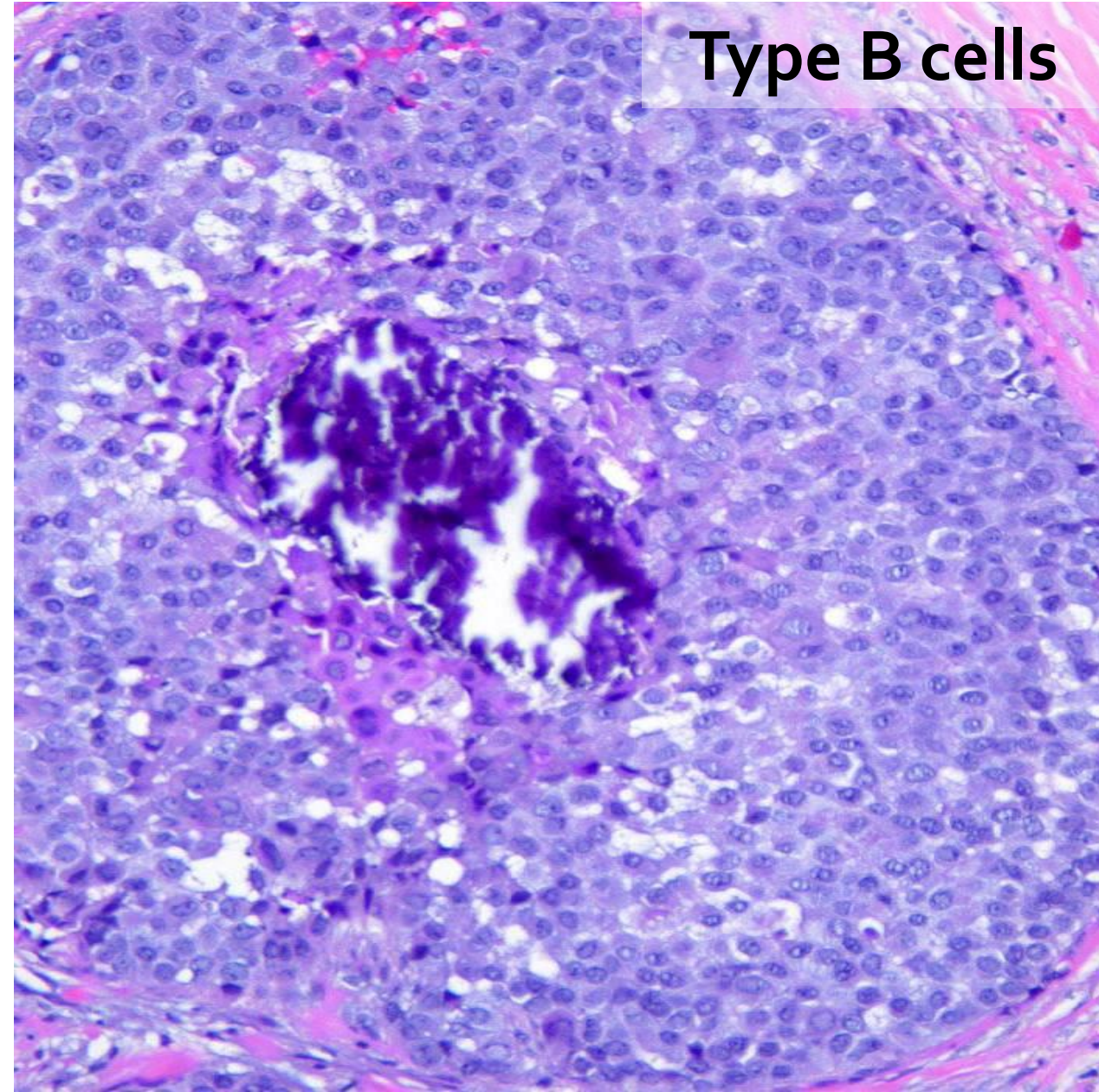


Florid LCIS

Type A cells

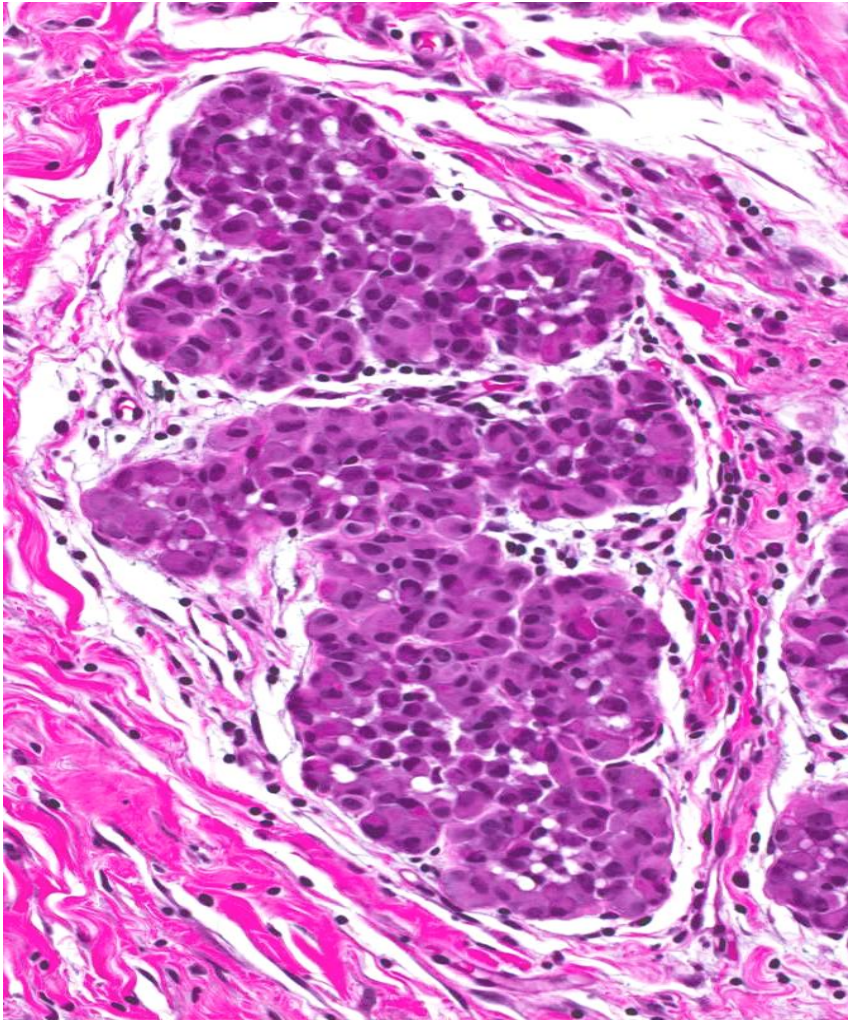


Type B cells

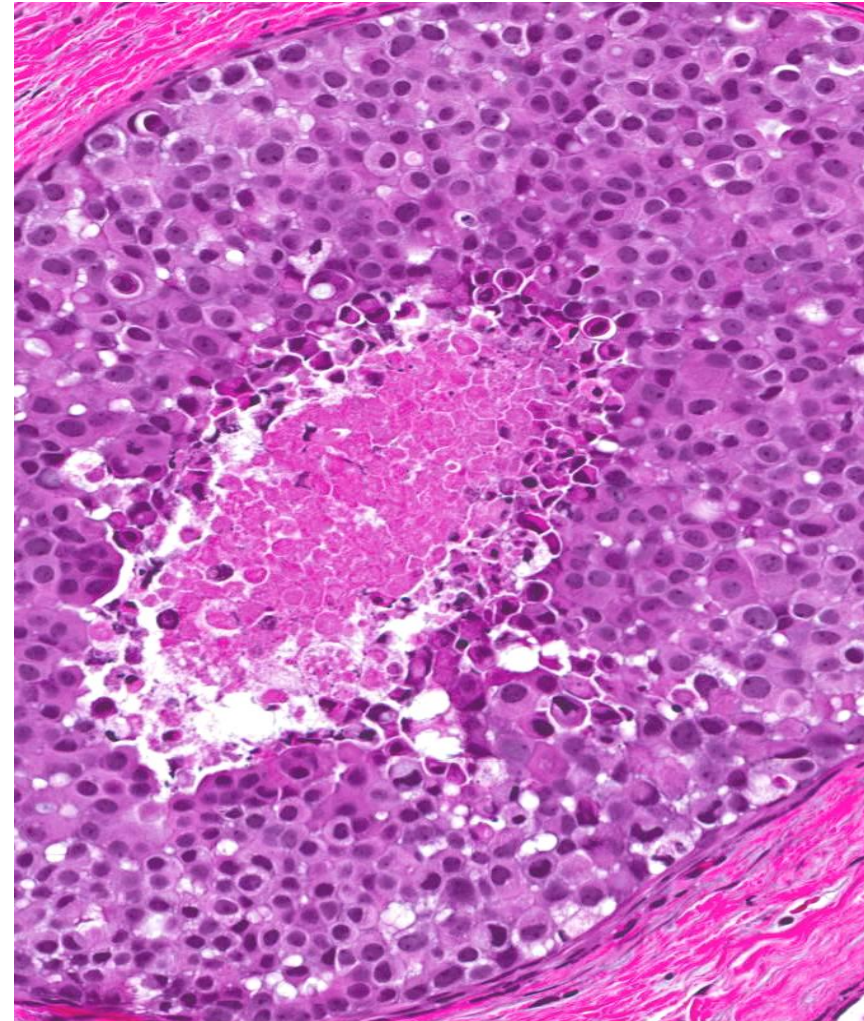


Florid LCIS

Classic LCIS cytomorphology, exaggerated architecture



classic LCIS



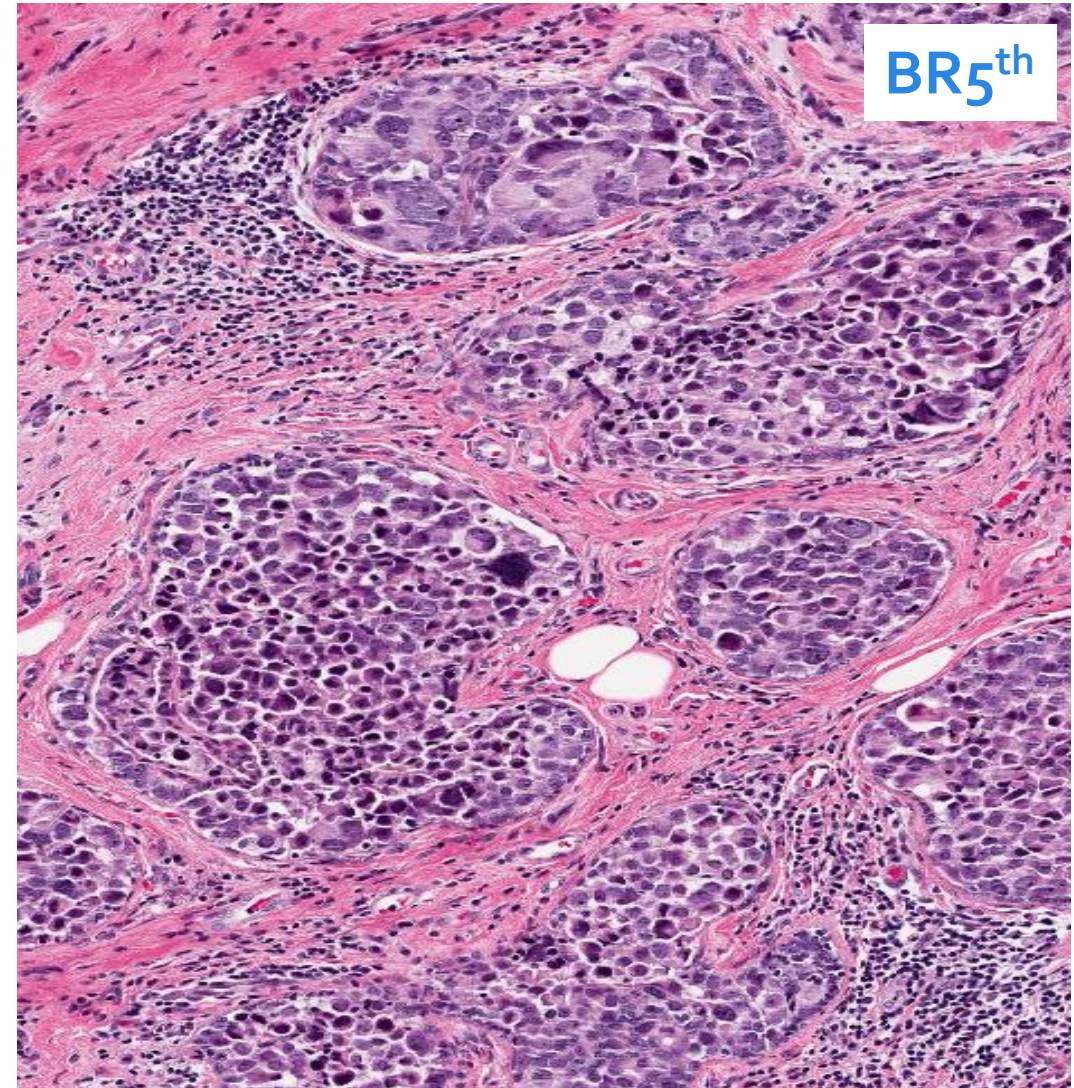
florid LCIS

(two images of the same case, same magnification)

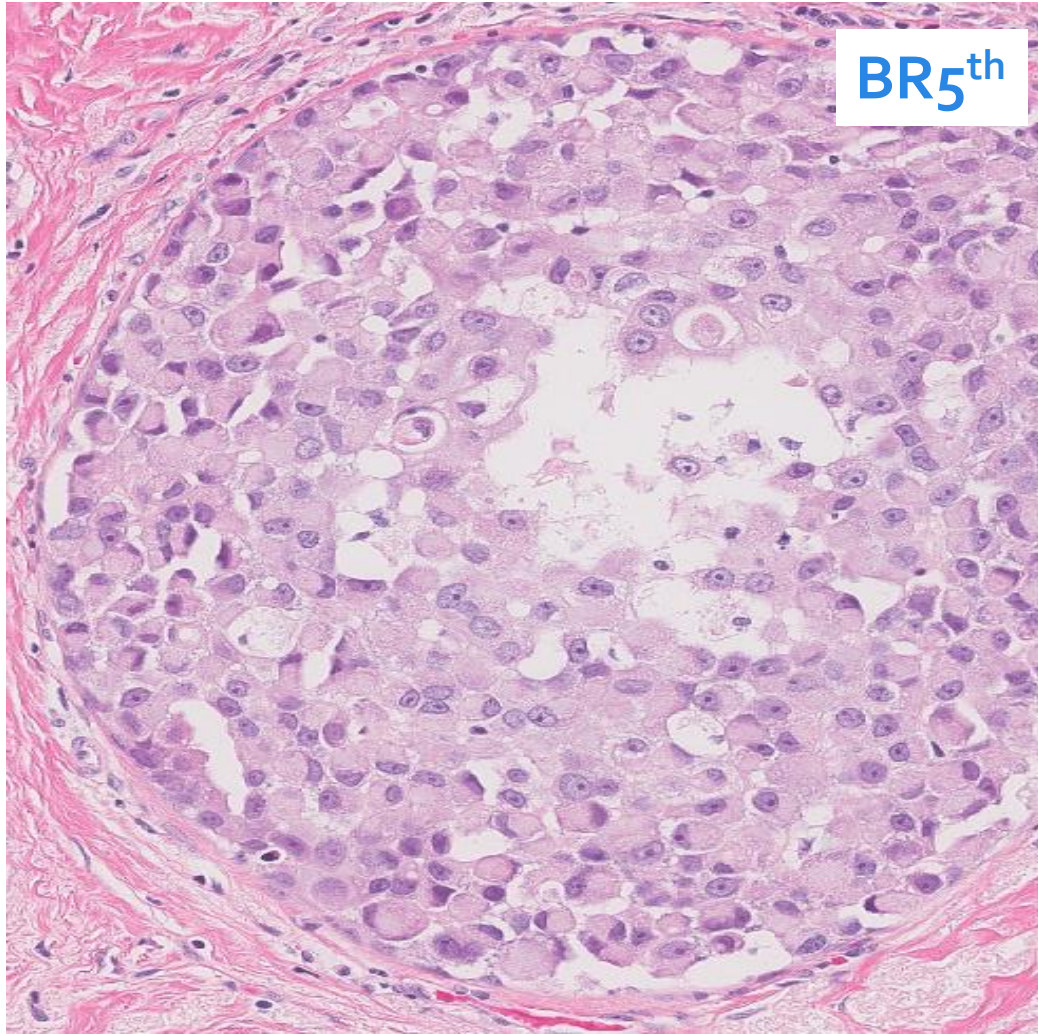


BR 5th ed: Pleomorphic LCIS – definition

- Pleomorphic LCIS is composed of **larger cells** with **marked nuclear pleomorphism**,
- **(some nuclei) are >4 times (the size) of lymphocytes**
- **nuclei equivalent to those of high-grade DCIS**, with or without apocrine features



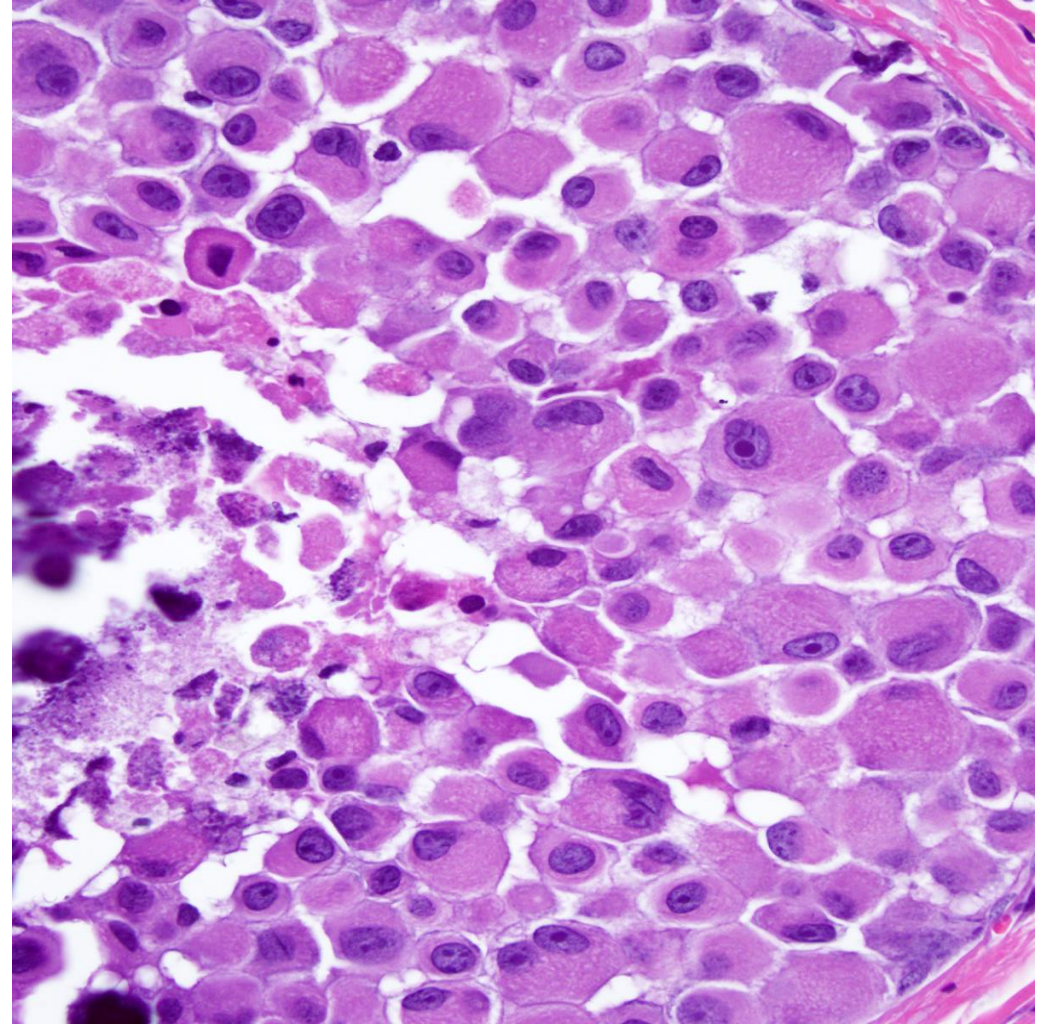
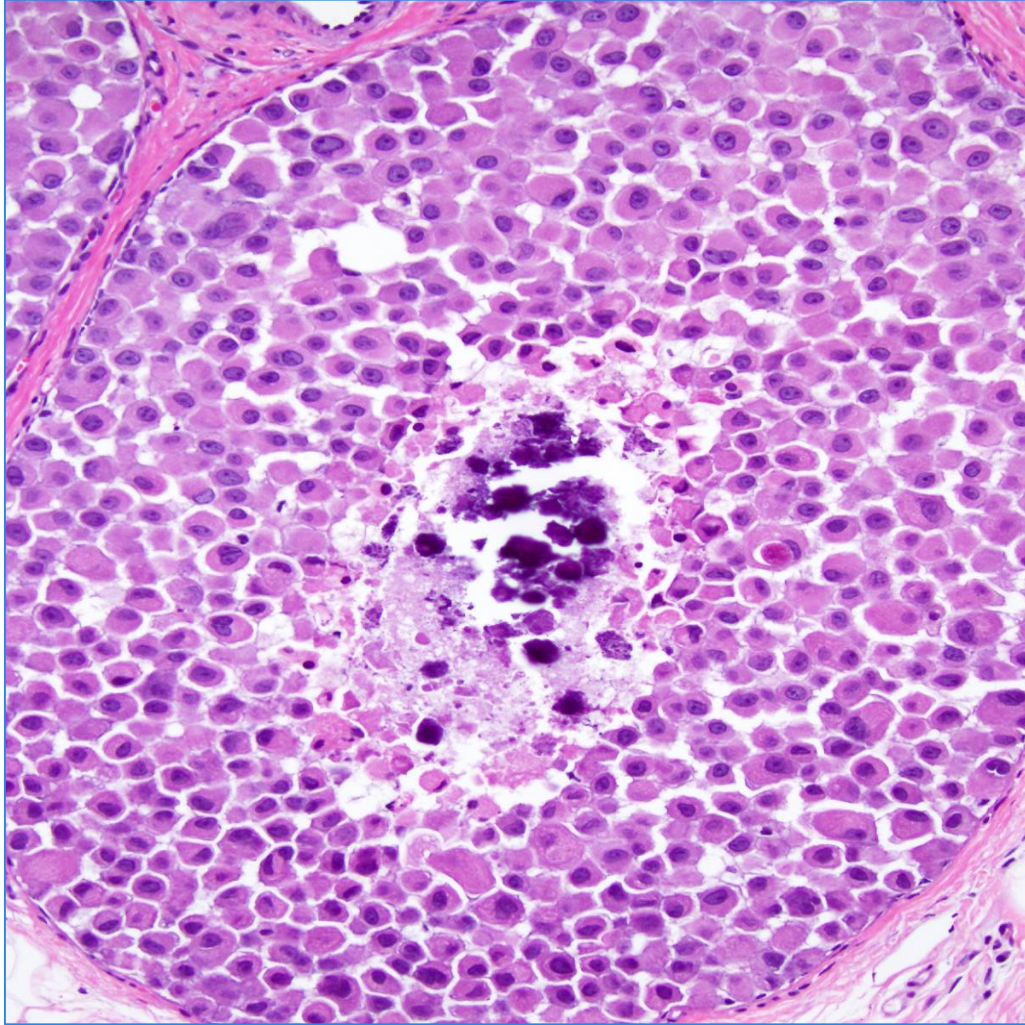
BR 5th ed: Pleomorphic LCIS, apocrine type



A **subset of pleomorphic LCIS** is further categorized as **apocrine type**, based on large cells with abundant eosinophilic granular cytoplasm and round to oval nuclei containing prominent nucleoli.



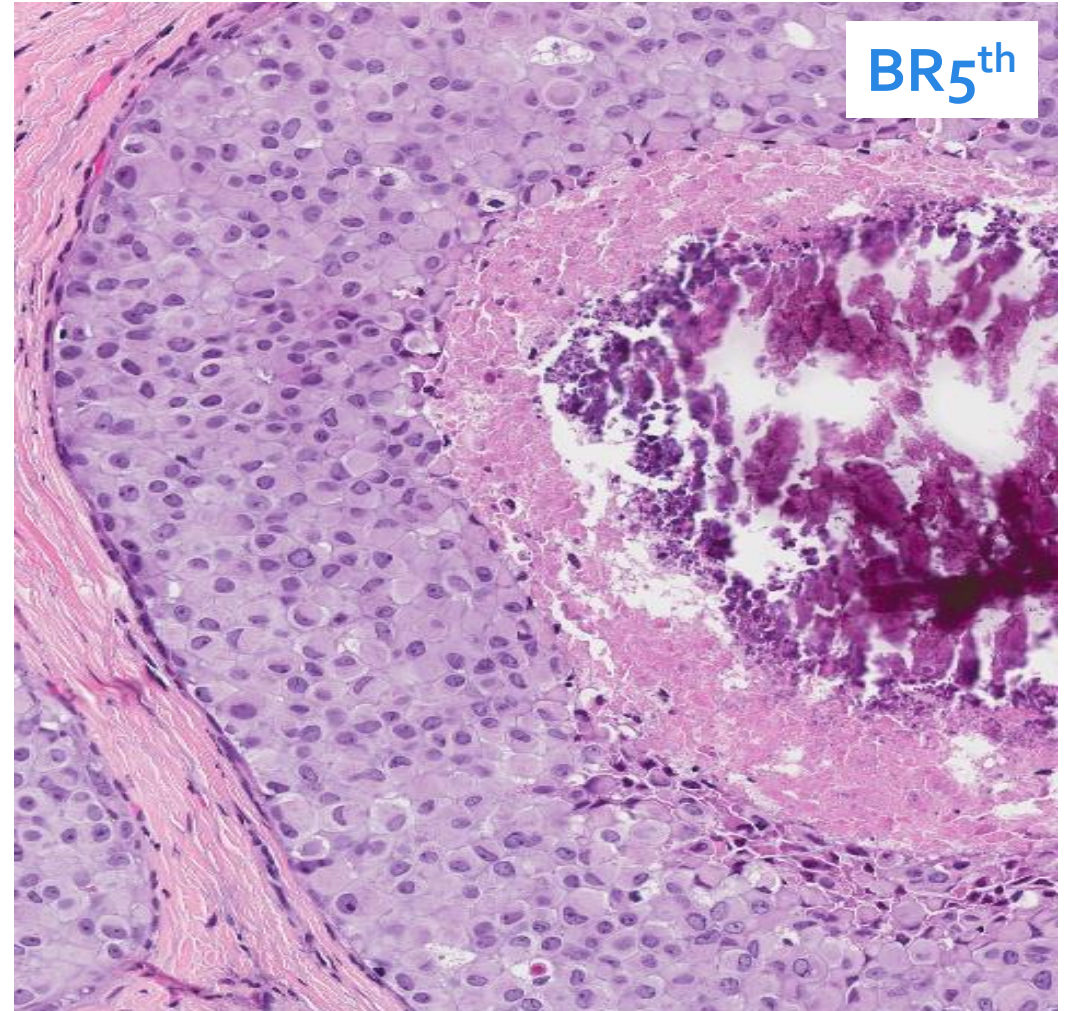
Pleomorphic LCIS Apocrine Type



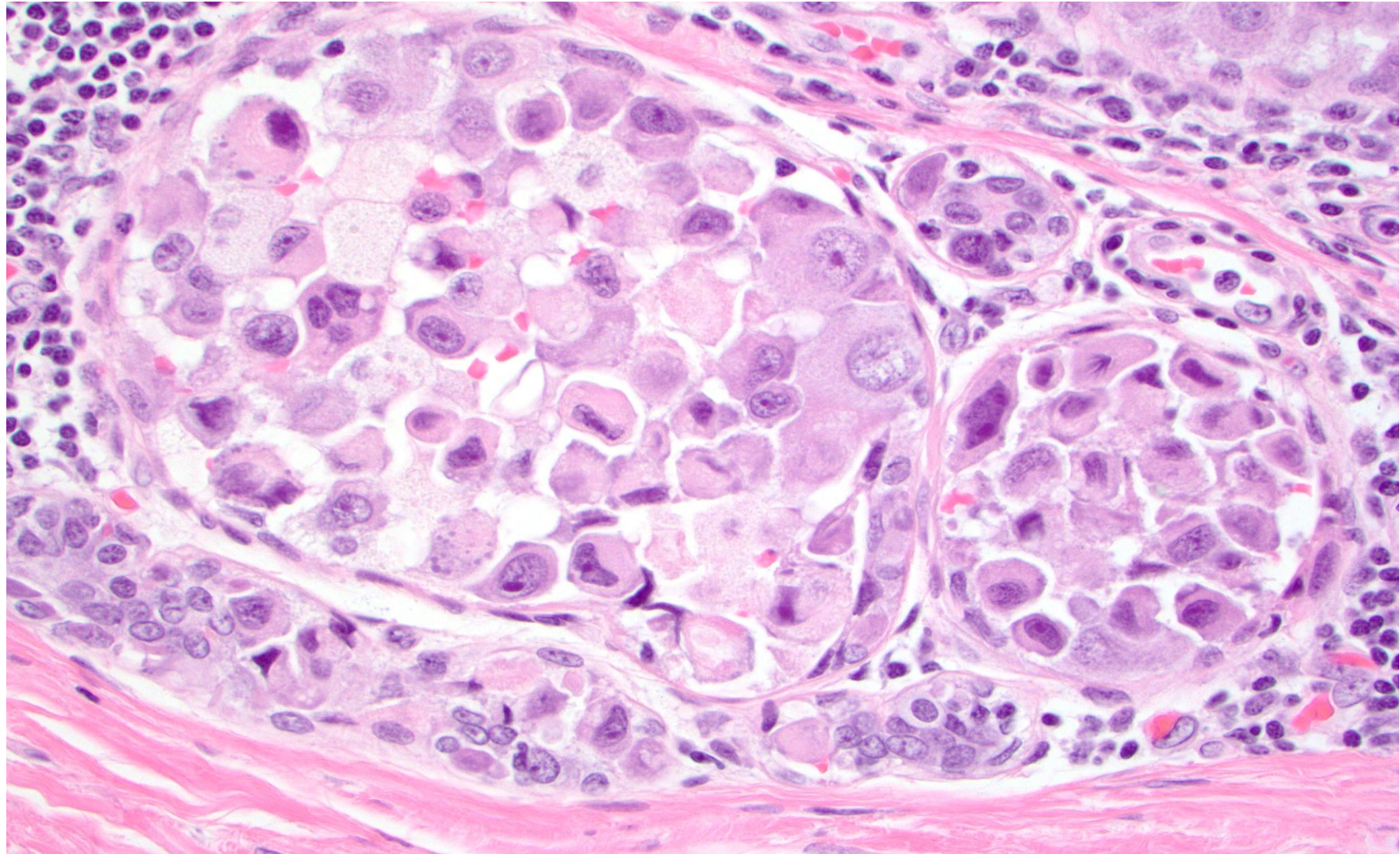
BR 5th ed: Pleomorphic LCIS

Pleomorphic LCIS is often associated with comedo necrosis and calcifications, leading to mammographic detection.

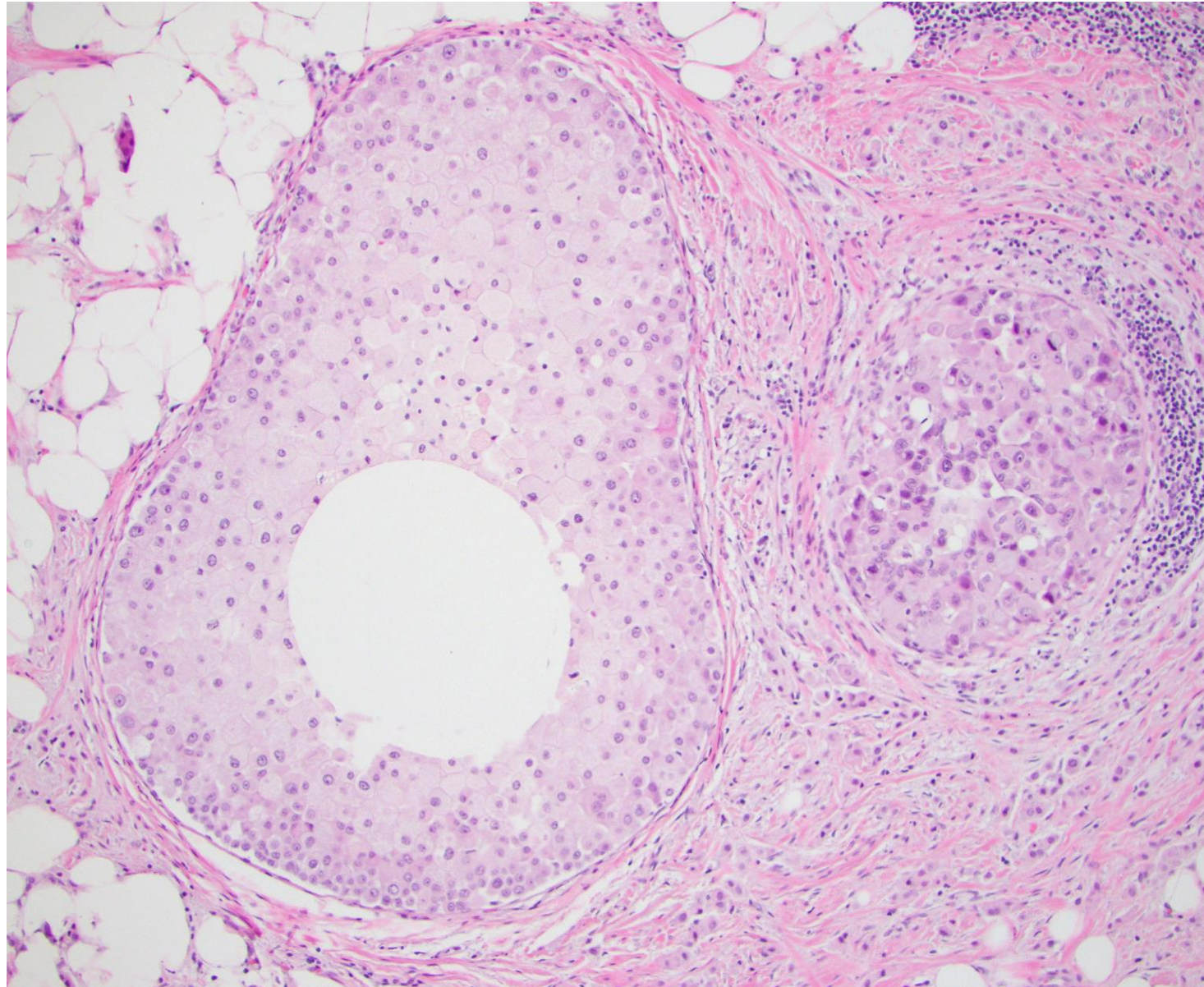
*Necrosis and/or Ca^{2+}
NOT required for diagnosis of
Pleomorphic LCIS*



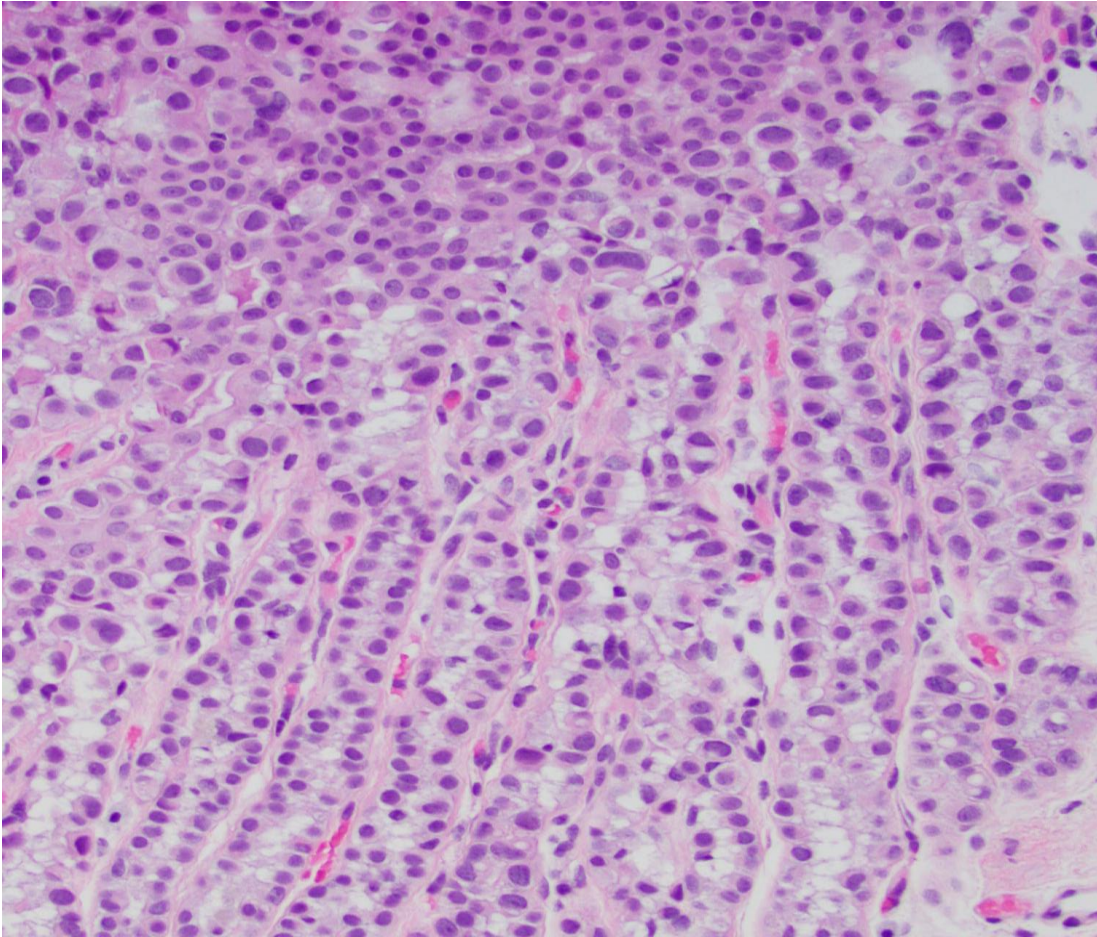
P-LCIS: acinar expansion may be less conspicuous than in F-



Florid LCIS and Pleomorphic LCIS may coexist



BR 5th ed: mix of type B + pleomorphic cells → classic LCIS



- LCIS lesions that are borderline between classic LCIS composed of type B cells and pleomorphic LCIS should be categorized as classic LCIS composed of type B cells.

- *Guideline very useful for excision specimens*
- *Is it also applicable to CNBs?*
limited data

4 rad-path concordant CNBs → no upgrade

Kuba MG et al. *Mod Pathol.* 2021 Aug;34(8):1495-1506.



P-LCIS and F-LCIS – clinical presentation

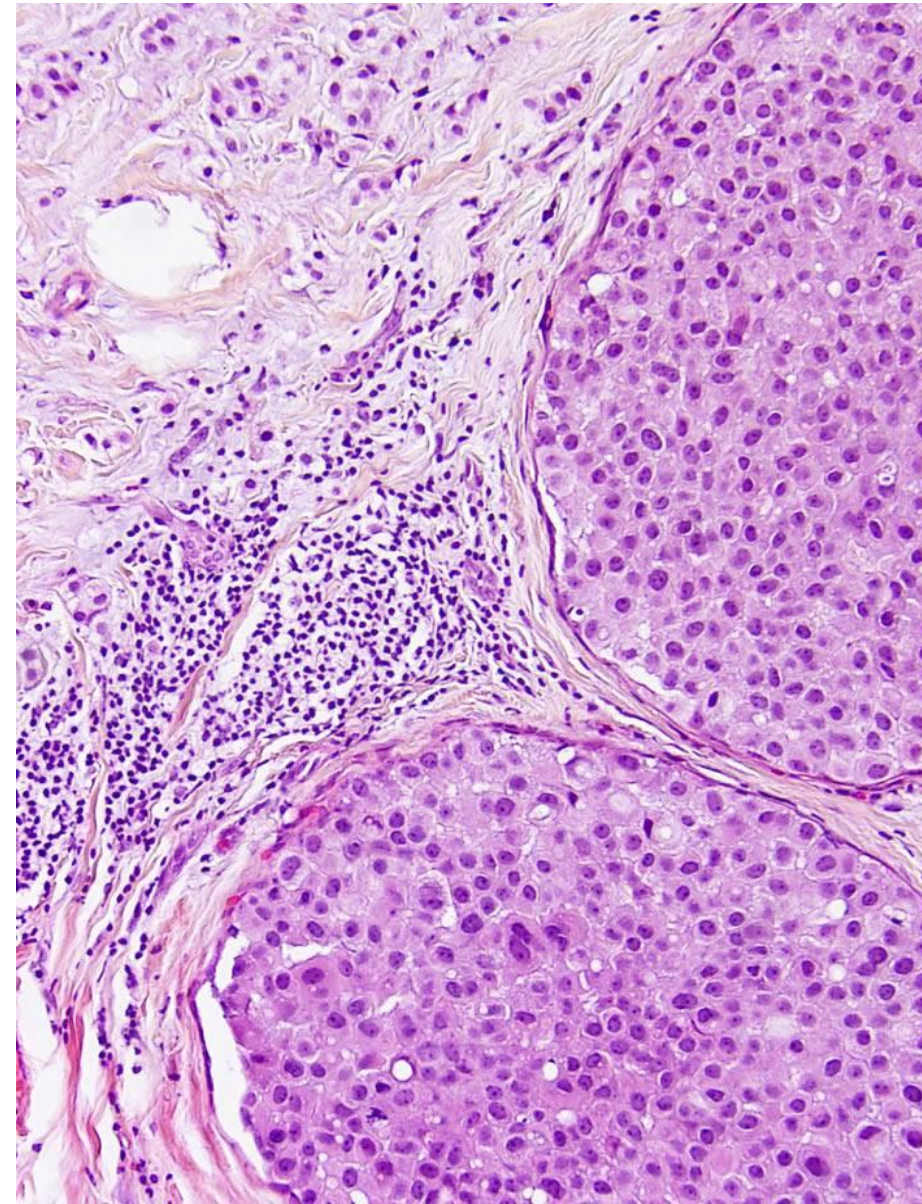
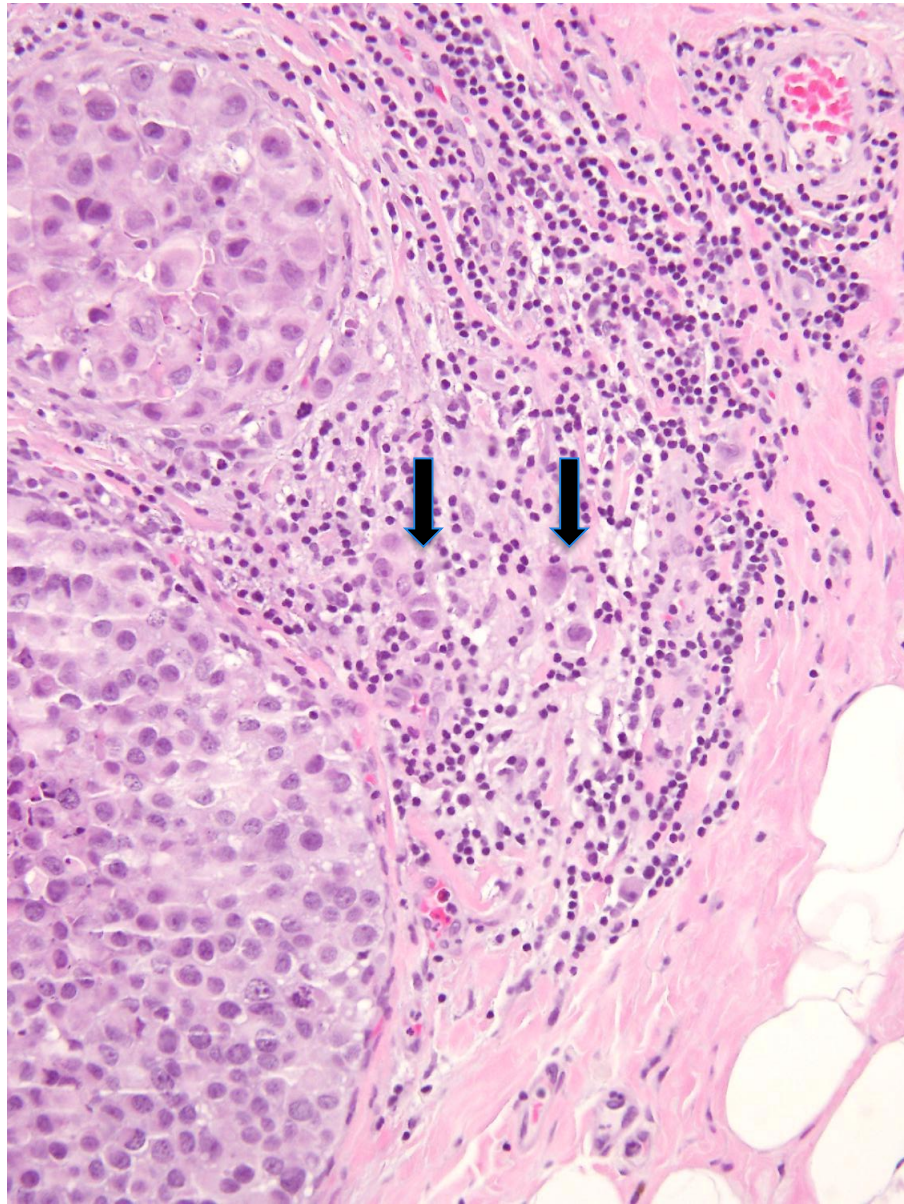
- mammographic Ca²⁺
about 80% of cases
- mass lesion +/- Ca²⁺

Sneige, *Mod Pathol* 2002;15:1044-50
Fadare, *Am J Surg Pathol* 2006;30:1445-53
Sapino, *Virchows Arch* 2000; 436:421-30
Chen *Am J Surg Pathol* 2009;33:1683-94
Shin, *Human Pathol* 2013;44:1998-2009
Flanagan, *Ann Surg Oncol* 2015;22:4263-9
Khoury, *Histopathology* 2014, 64:981-993
Susnik B et al. 2016,
Fasola, *Breast J* 2017 DeBrot, *Breast Cancer Res Treat*,
2017,165:411-420
Foschini MP et al *Am J Surg Pathol* 2019
Harrison B, *Mod Pathol* 2020;33(7):1287-1297
Shamir E, *Mod Pathol* 2020;33:1078–1091
Kuba MG et al. *Mod Pathol*. 2021 Aug;34(8):1495-1506.

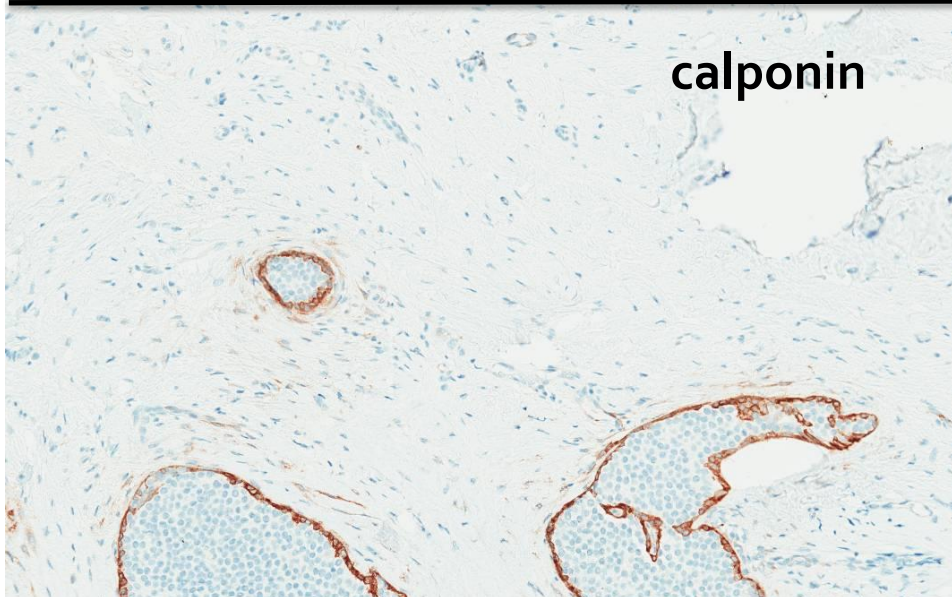
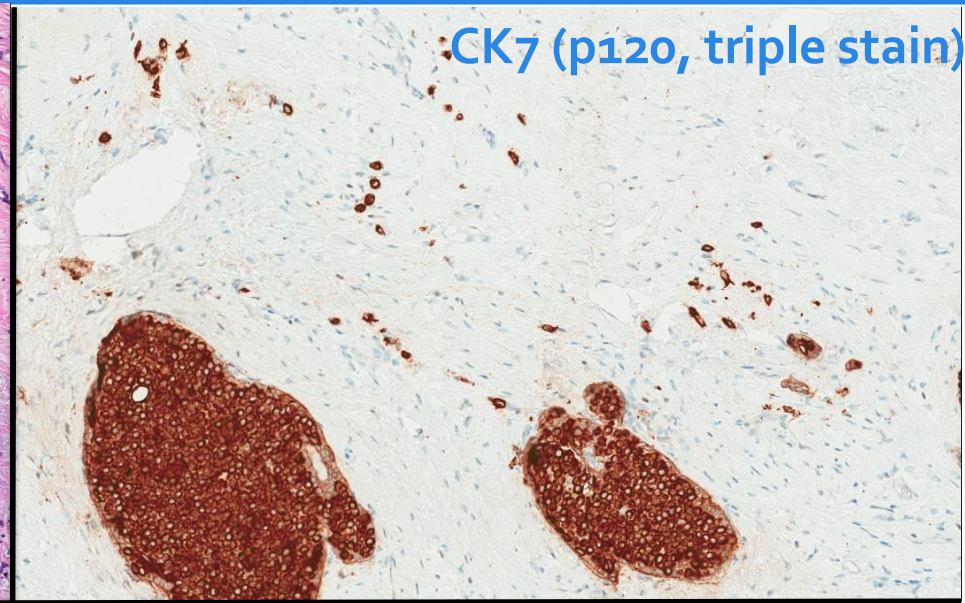
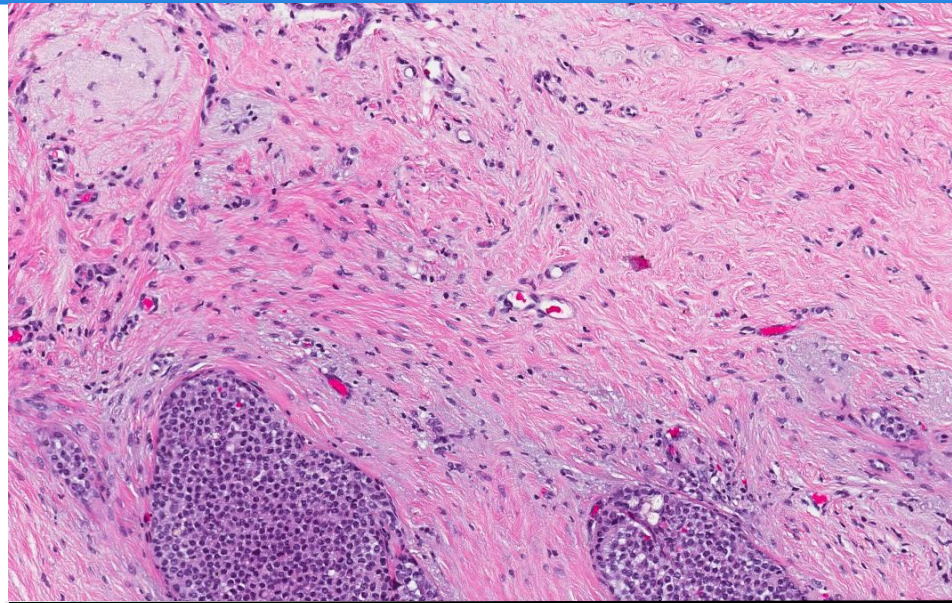
- Often associated with invasive carcinoma
 - 4/10 (40%) cases
Sapino, *Virchows Arch* 2000; 436:421-30
 - 10/24 (42%) cases
Sneige, *Mod Pathol* 2002;15:1044-50
 - 12/18 (67%) cases
including 10 ILCs
Fadare, *Am J Surg Pathol* 2006;30:1445-53
 - 47/78 (60%) cases
44 ILCs
Fasola, *Breast J*. 2018;24:66-69
 - 62/85 (73%) cases
including 27 P-ILCs and 19 ILC
Shamir E, *Mod Pathol* 2020;33:1078–1091



Inflamed/ reactive stroma near F-LCIS/ P-LCIS: rule out (micro)invasive lobular carcinoma



Microinvasive Lobular Carcinoma: use "positive" IHC



Non-invasive lobular neoplasia

| ALH | CLASSIC LCIS | F-LCIS* | P-LCIS* |
|-----|--|--|-----------------------|
| | Type A cells and/or Type B cells | Type A cells and/or Type B cells | Pleomorphic nuclei |

*molecular alterations support lobular genotype, with higher number of genomic alterations

- Palacios, J et al. Mod Pathol, 2003
- Simpson PT et al. J Pathol, 2008
- Reis-Filho JS et al. J Pathol, 2008
- Chen YY et al. Am J Surg Pathol. 2009

- Bolt V et al. Gene Chromosomes Cancer 2010
- Shin, *Human Pathol* 2013
- Shamir, Am J Surg Pathol 2019
- Harrison, Mod Pathol 2020



E-CADHERIN

transmembrane glycoprotein involved in cell-to-cell adhesion

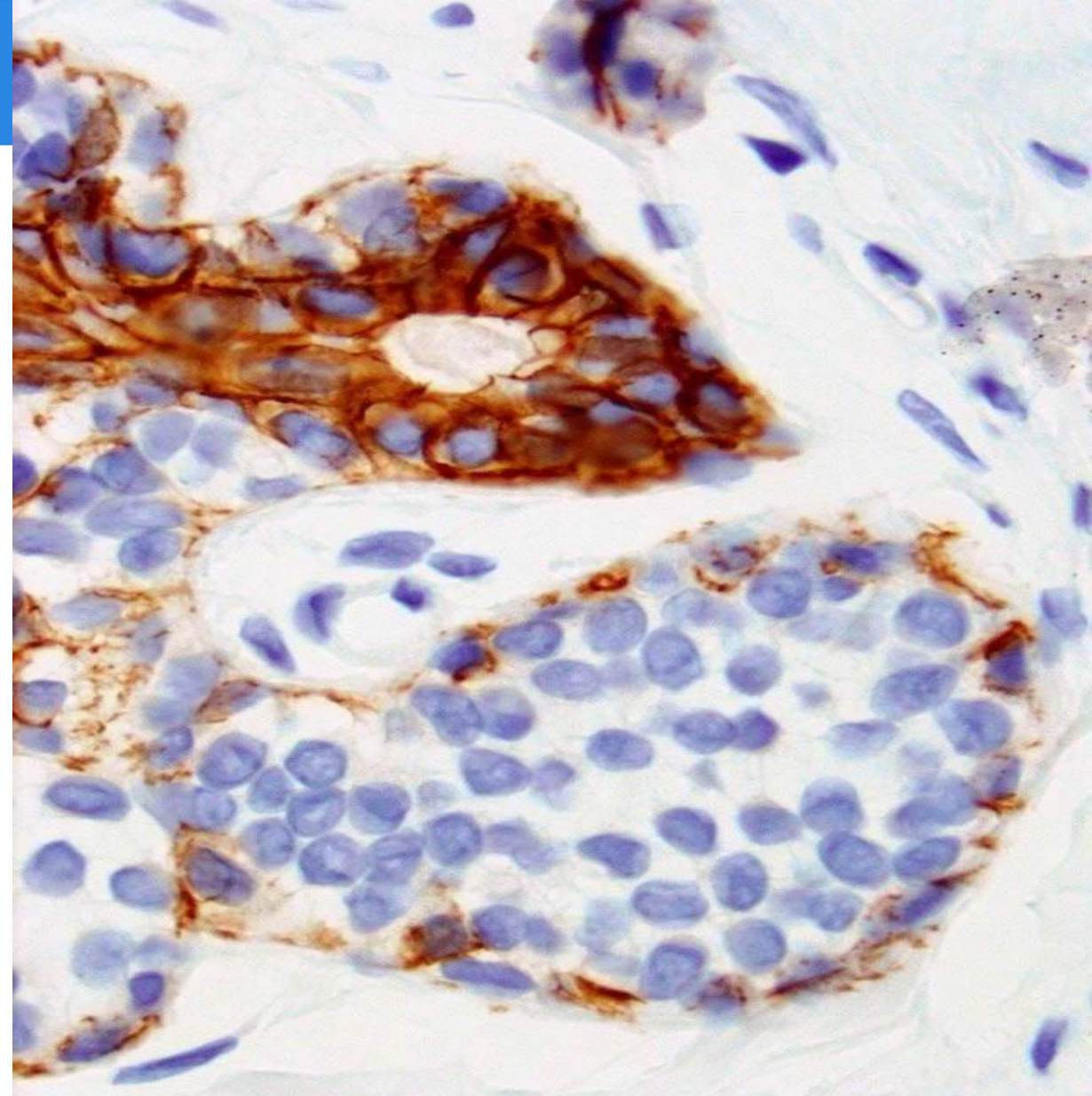
CDH1 on chromosome 16q22.1

Ductal epithelium: (+) cell membrane; continuous linear stain

Myoepithelium: (+) cell membrane facing the epithelium; “dot-like”/granular linear stain

Lobular neoplasia: loss of E-cadherin

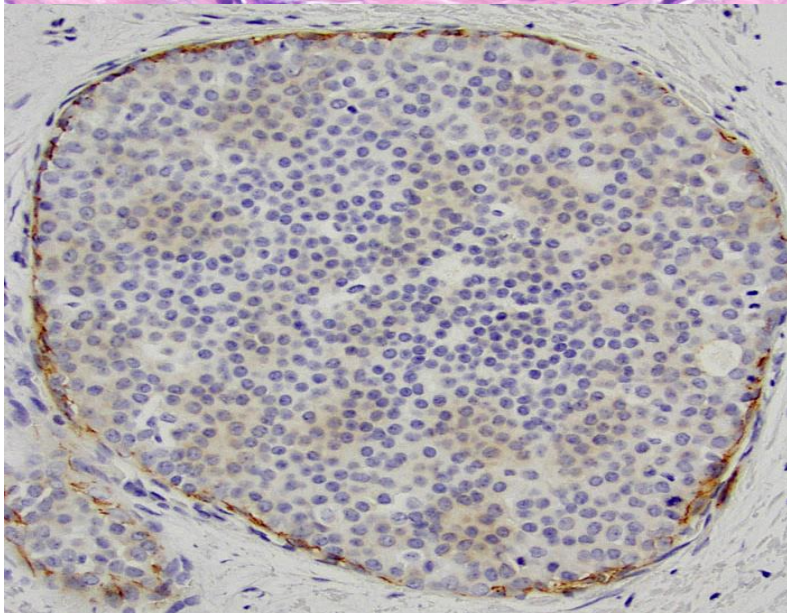
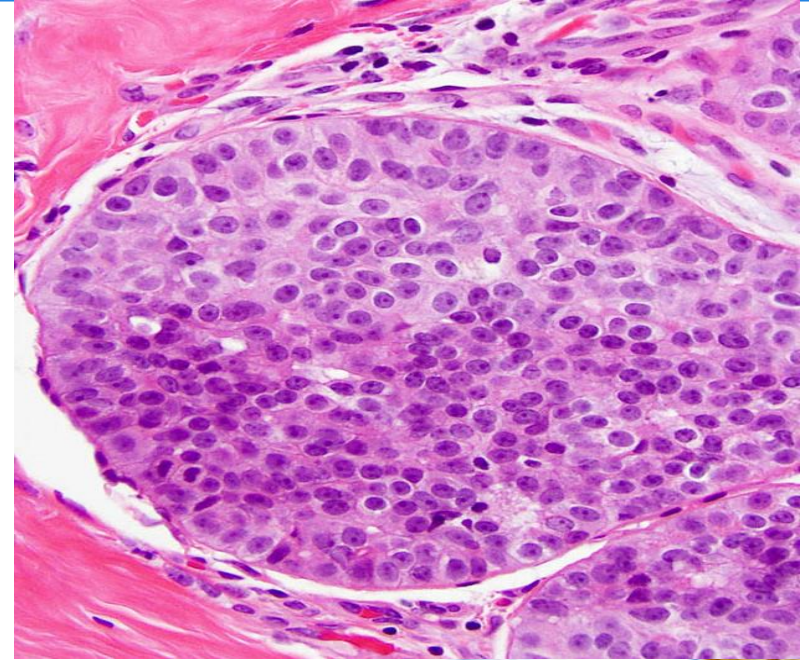
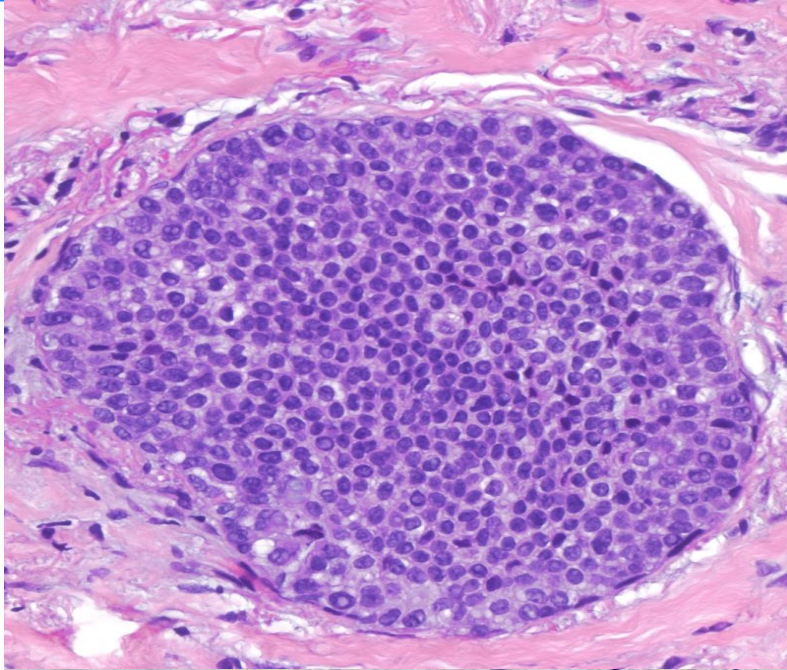
Endothelium may be weakly positive



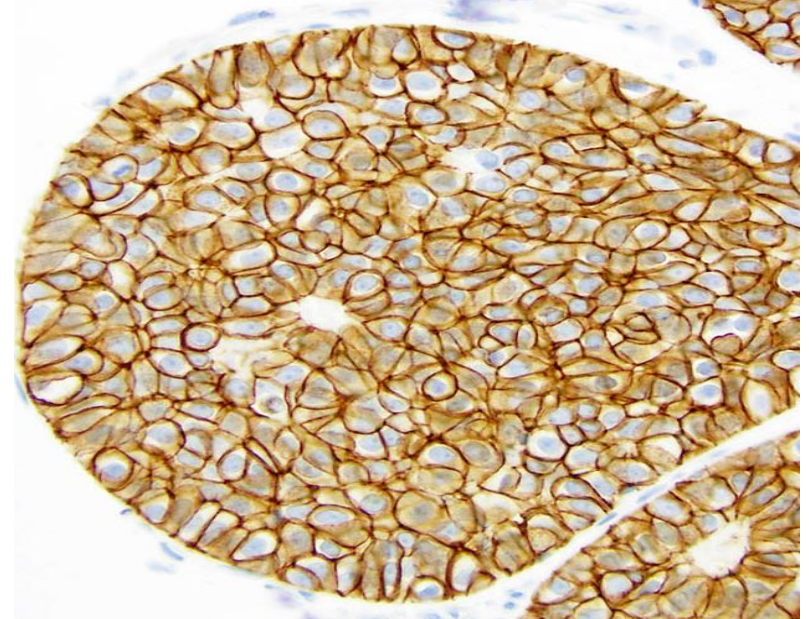
Classic LCIS

VS

Low Grade DCIS



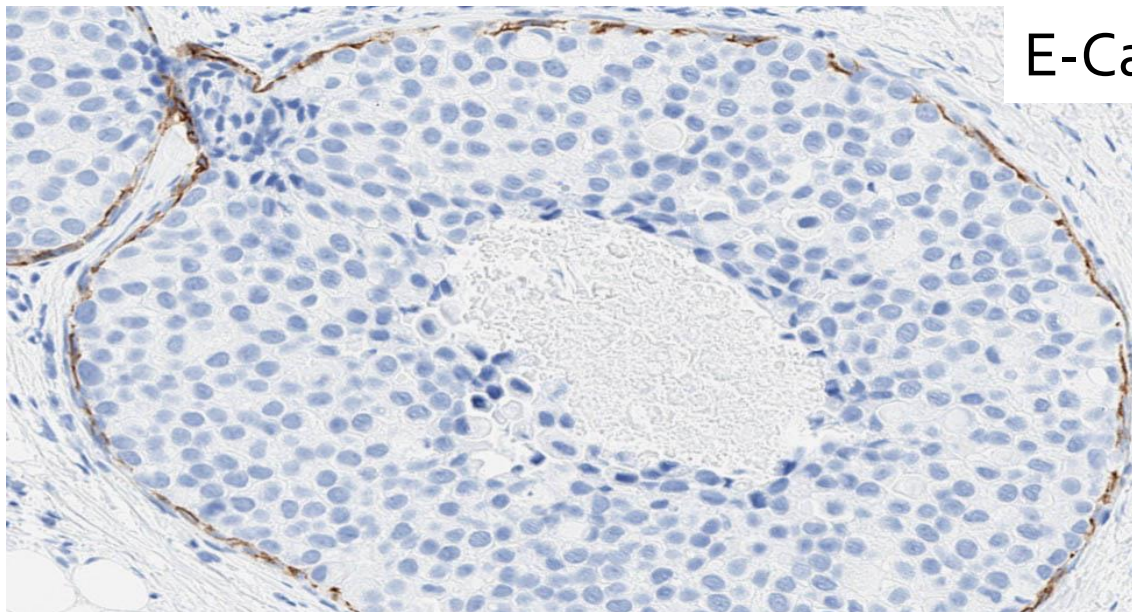
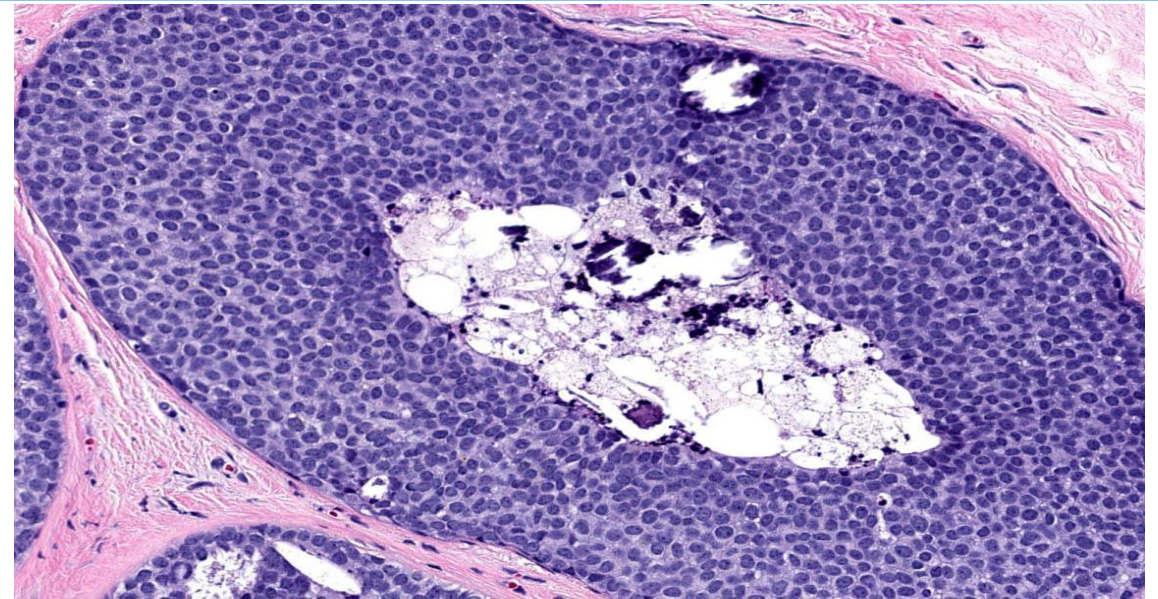
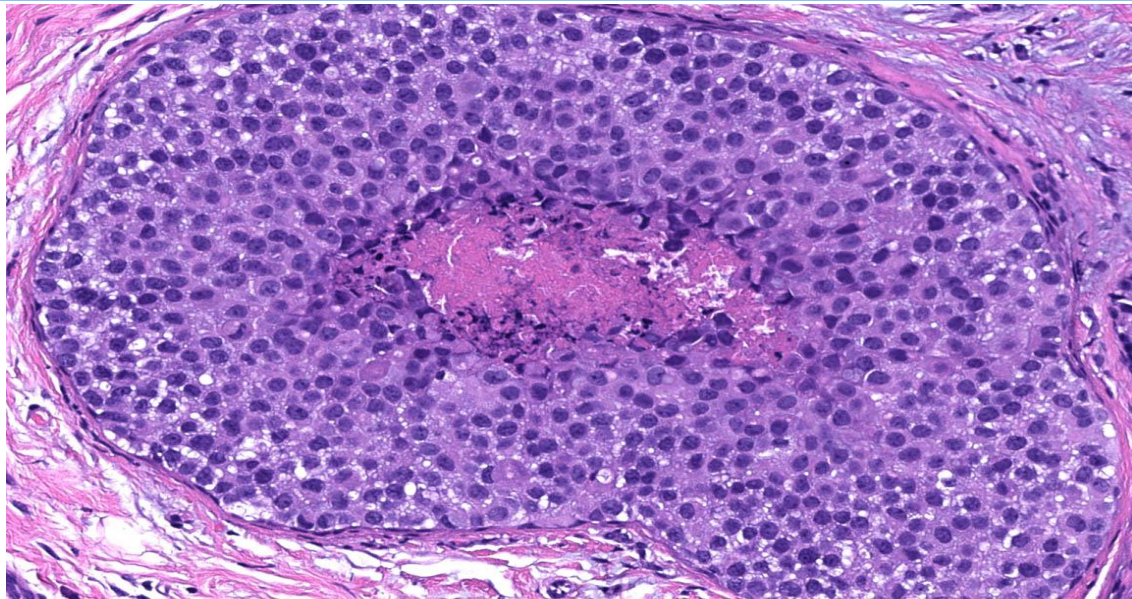
E-Cadherin



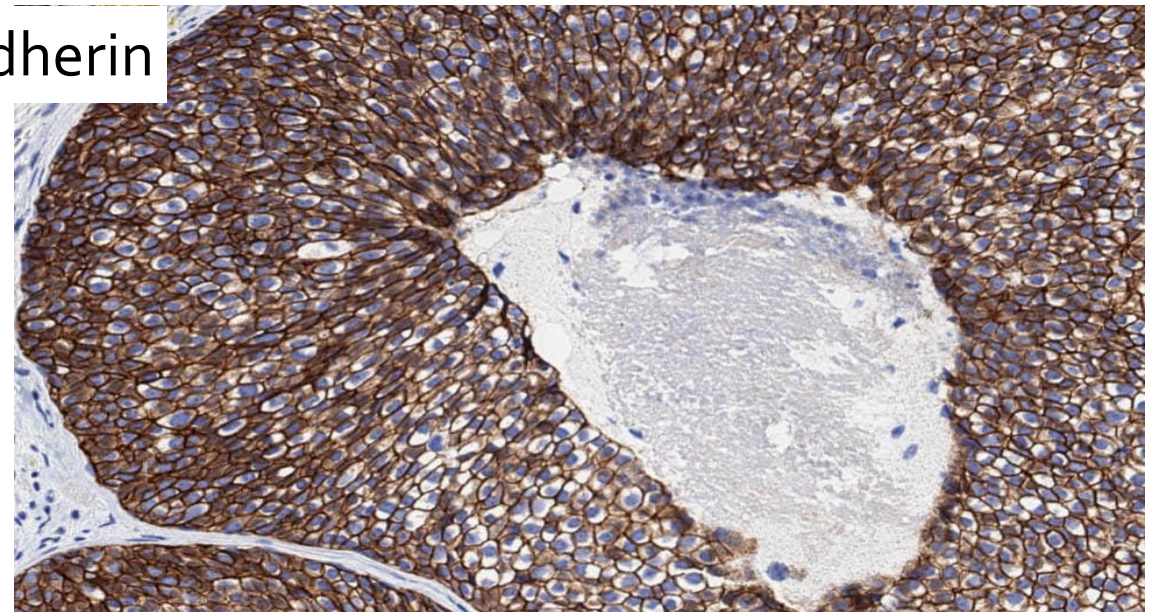
F-LCIS and P-LCIS

vs

Solid DCIS



E-Cadherin



Aberrant expression of E-Cadherin in ILC and LCIS

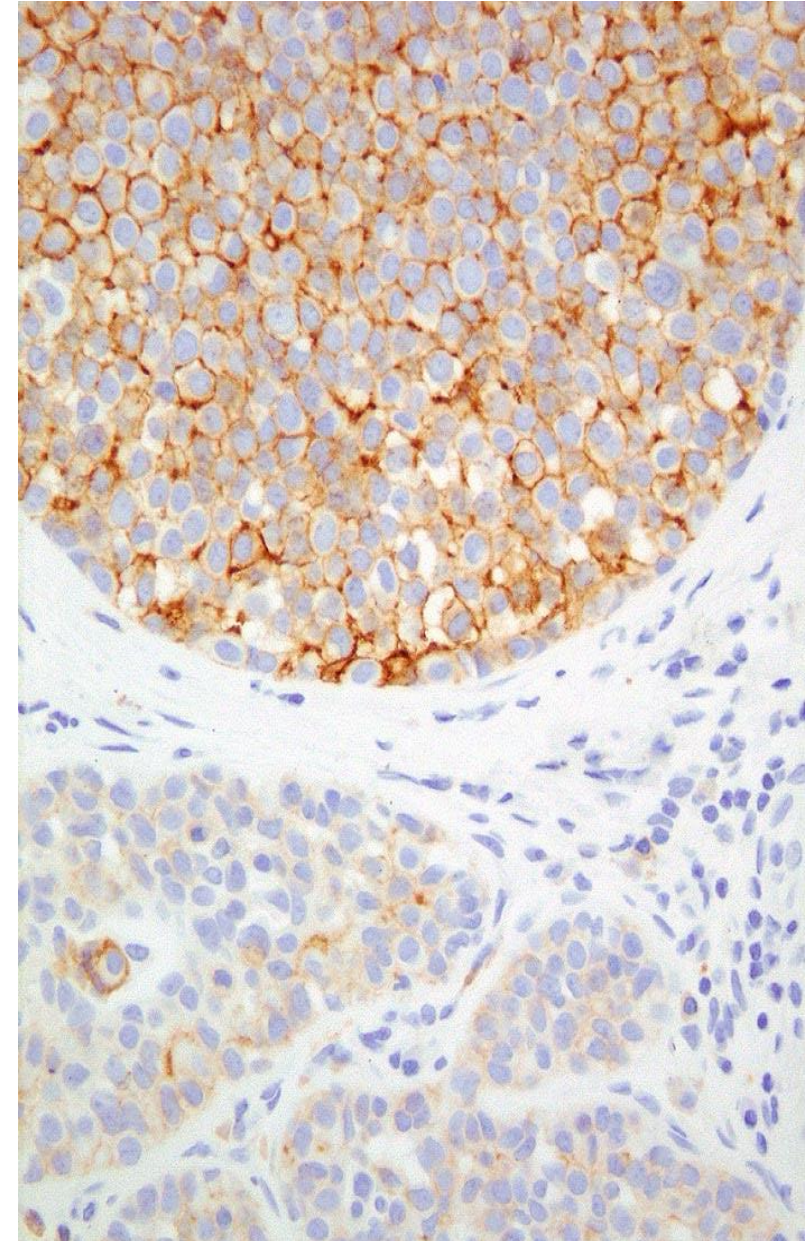
- E-cadherin expression retained in some invasive lobular carcinomas (ILCs)

Da Silva L. et al, *Am J Surg Pathol* 2008 32(5):773-83

E-cadherin expression in ILCs correlates with CDH1 somatic alterations

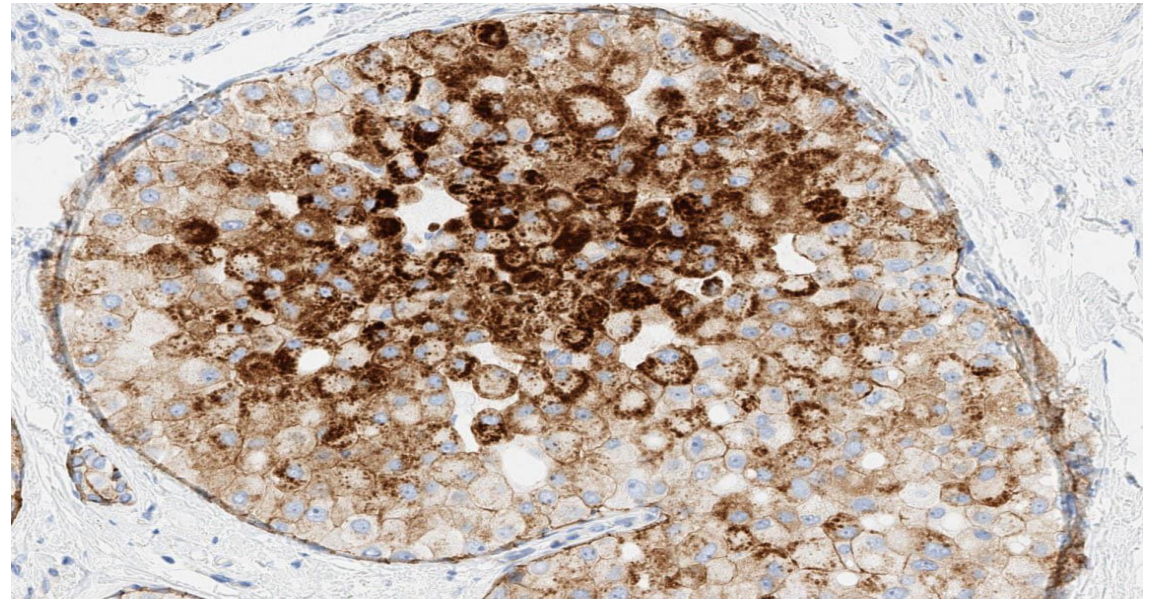
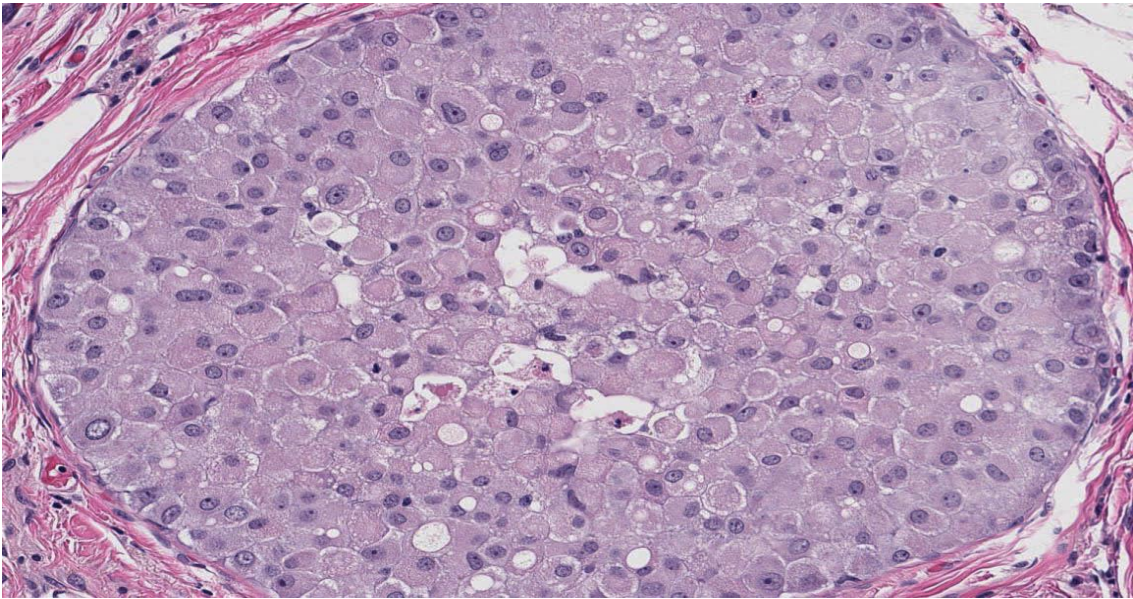
Grabenstetter A. et al. *Hum Pathol* 2020 Aug;102:44-5

Possible pitfall: LCIS with aberrant E-cadherin expression misdiagnosed as DCIS



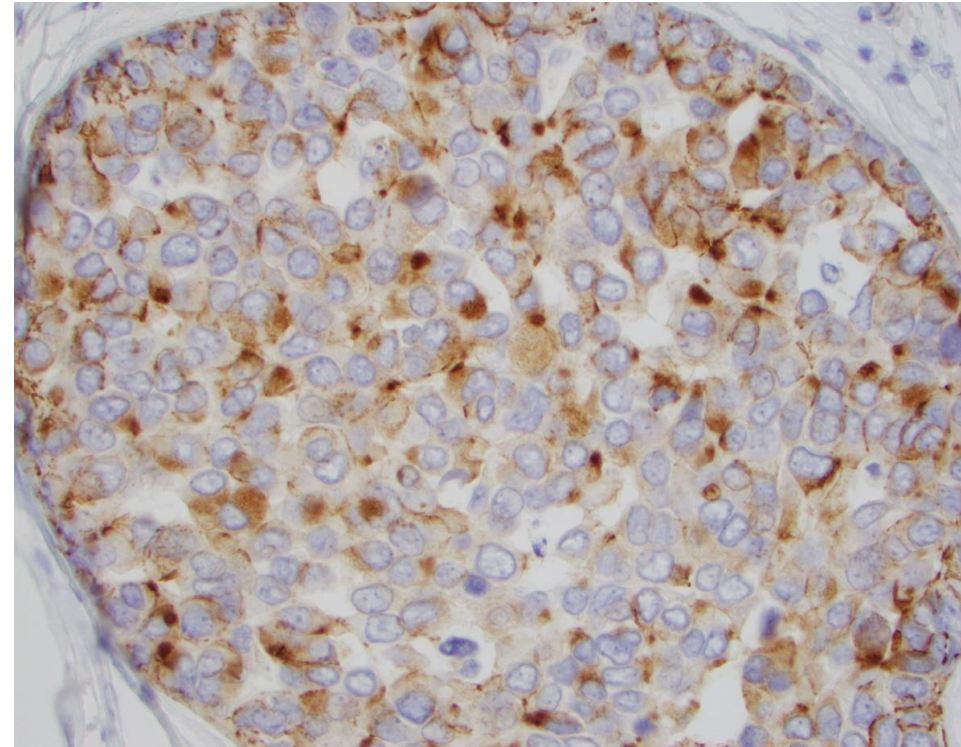
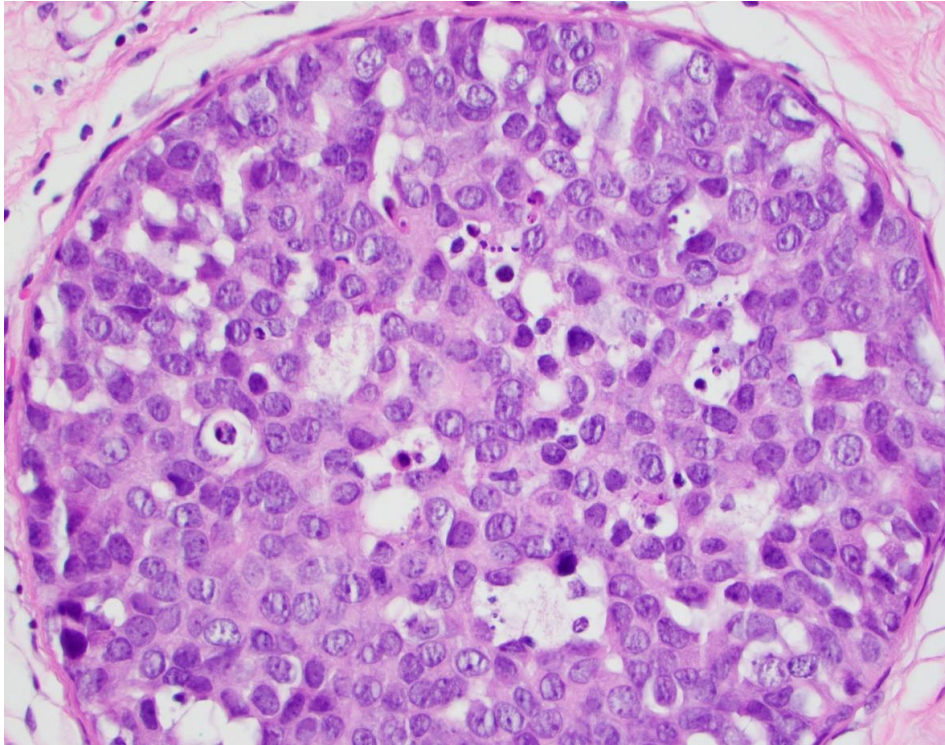
E-cadherin expression patterns in F-LCIS and P-LCIS

- Granular cytoplasmic staining



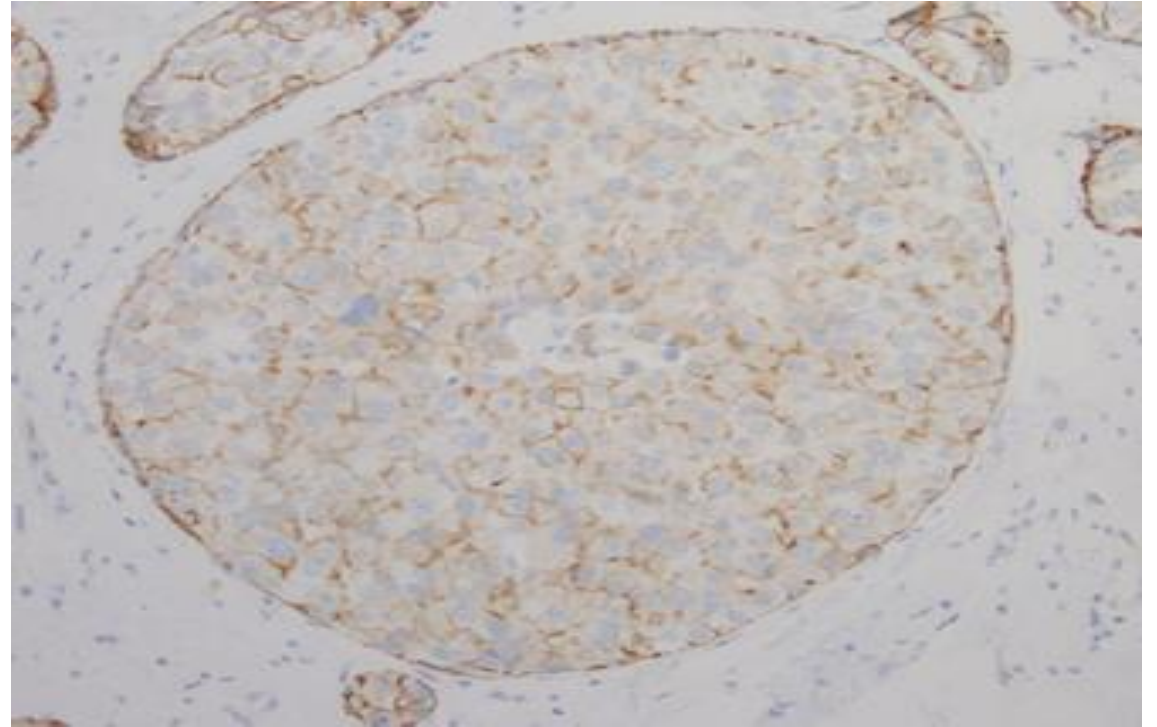
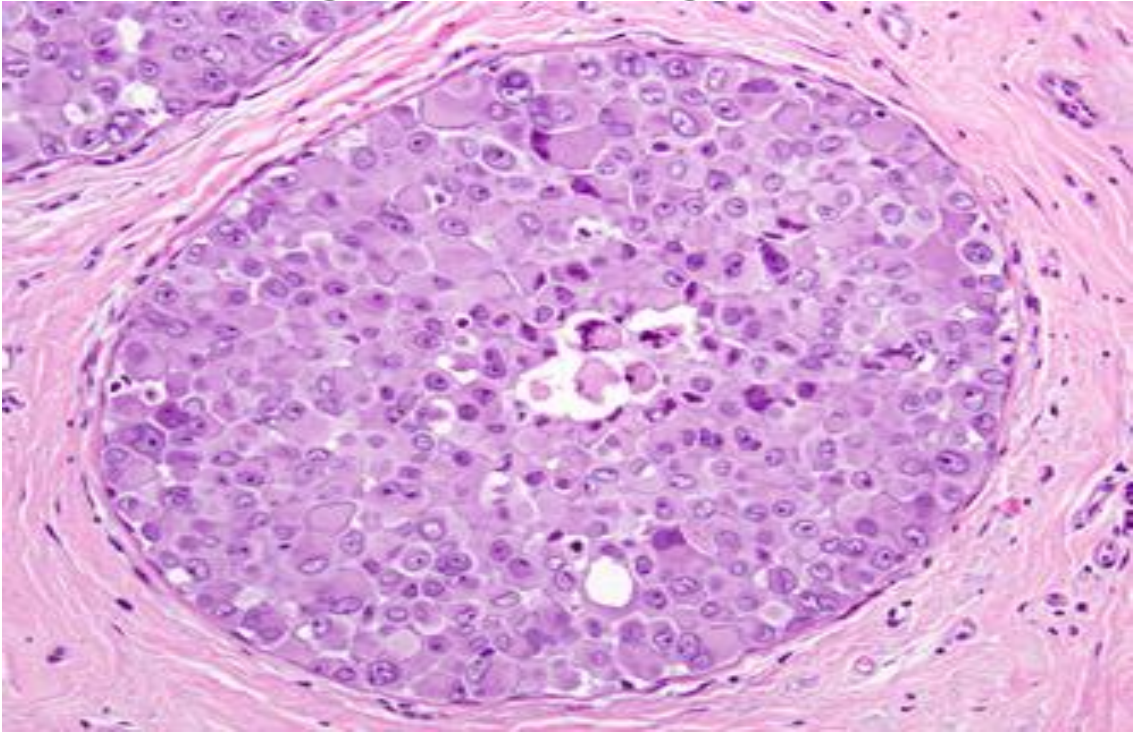
E-cadherin expression patterns in F-LCIS and P-LCIS

- Punctate/ Golgi apparatus distribution



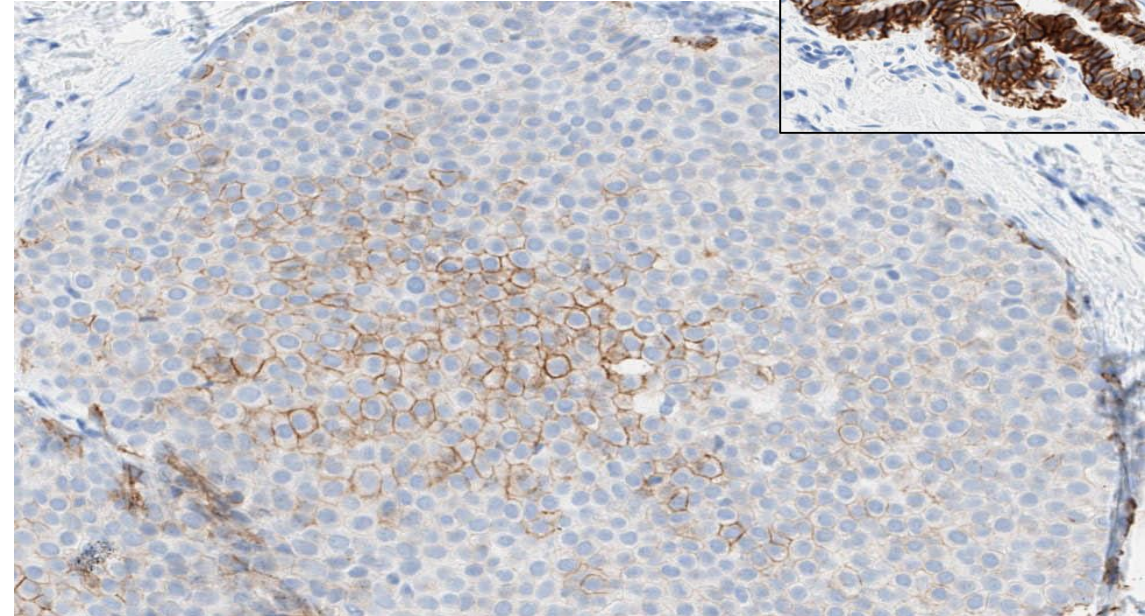
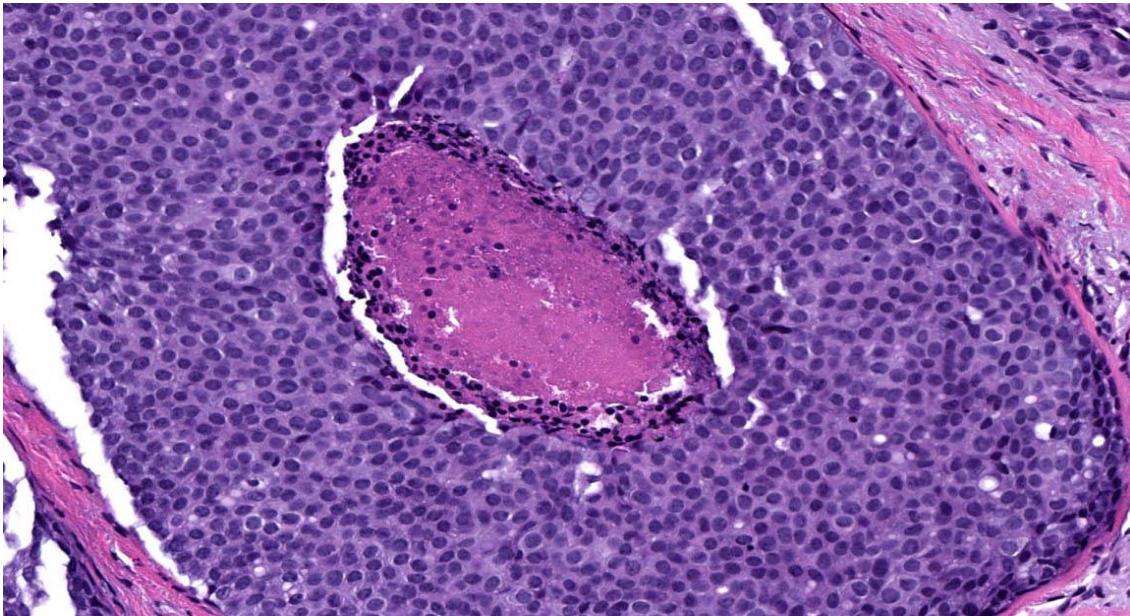
E-cadherin expression patterns in F-LCIS and P-LCIS

- Partial, fragmented, granular, membrane stain

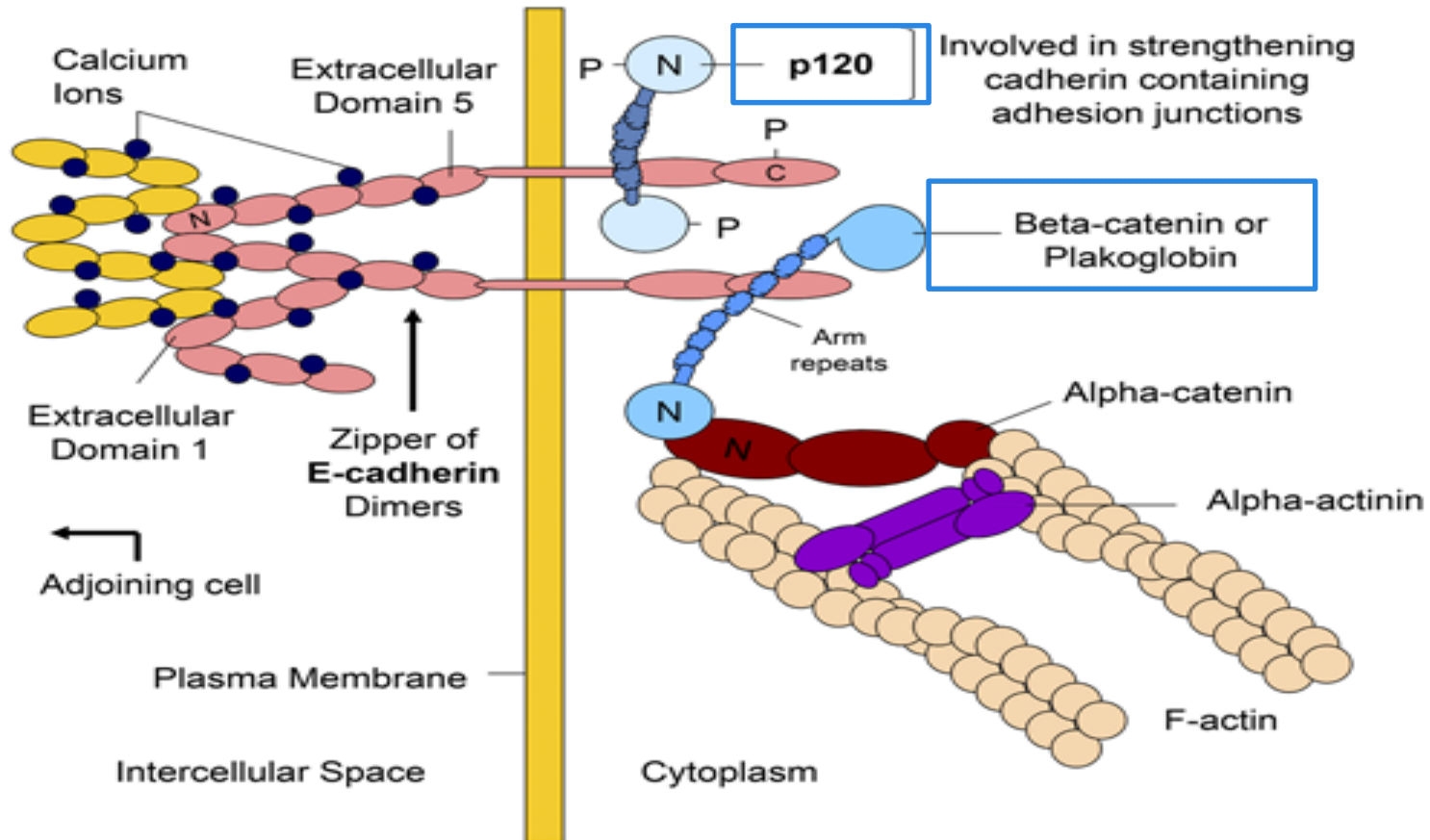


E-cadherin expression patterns in F-LCIS and P-LCIS

- Circumferential membrane stain, but with reduced intensity compared with adjacent ductal cells



E-cadherin and *wnt*-related proteins



E-cadherin
intracytoplasmic domain
binds
p120/ beta-catenin
binds
actin cytoskeleton

Dabbs AJ et al. *AJSP* 2013;37:e1-e11

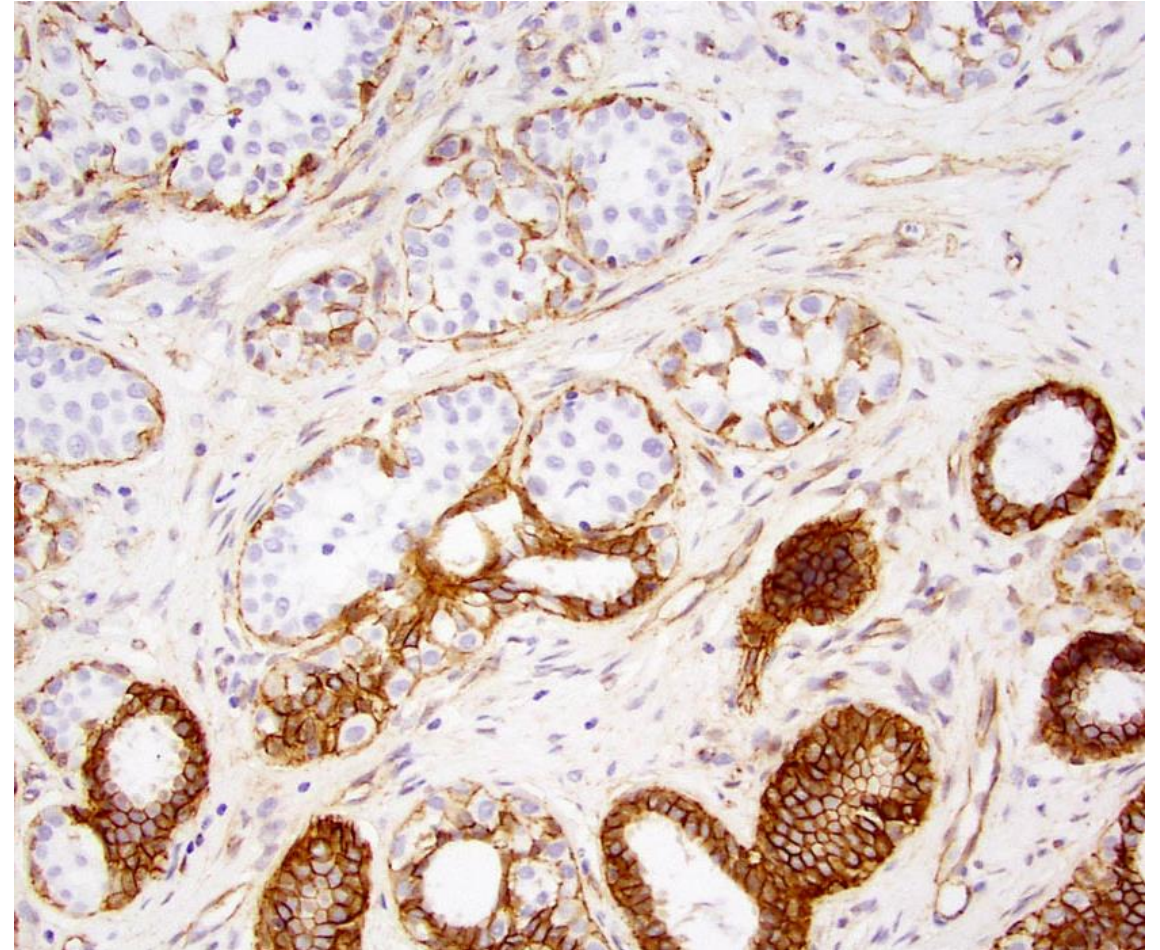
β -catenin

Loss in lobular neoplasia

Ductal epithelium: (+) cell membrane;
continuous linear stain

Myoepithelium: (+) cell membrane facing
the epithelium; "dot-like"/granular linear
stain

Endothelium may be weakly positive



De Leeuw WJ et al. *J Pathol.* 1997 Dec;183(4):404-11

Dabbs AJ et al. *AJSP* 2013;37:e1-e11

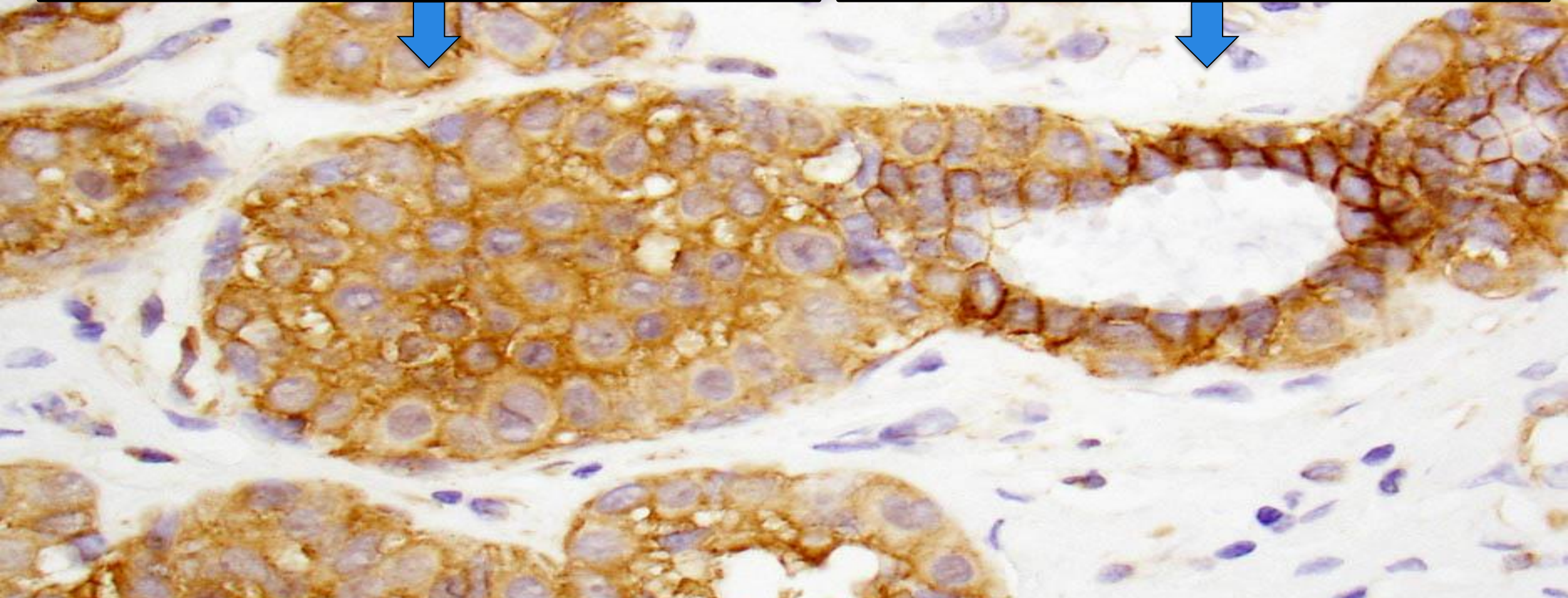


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P120

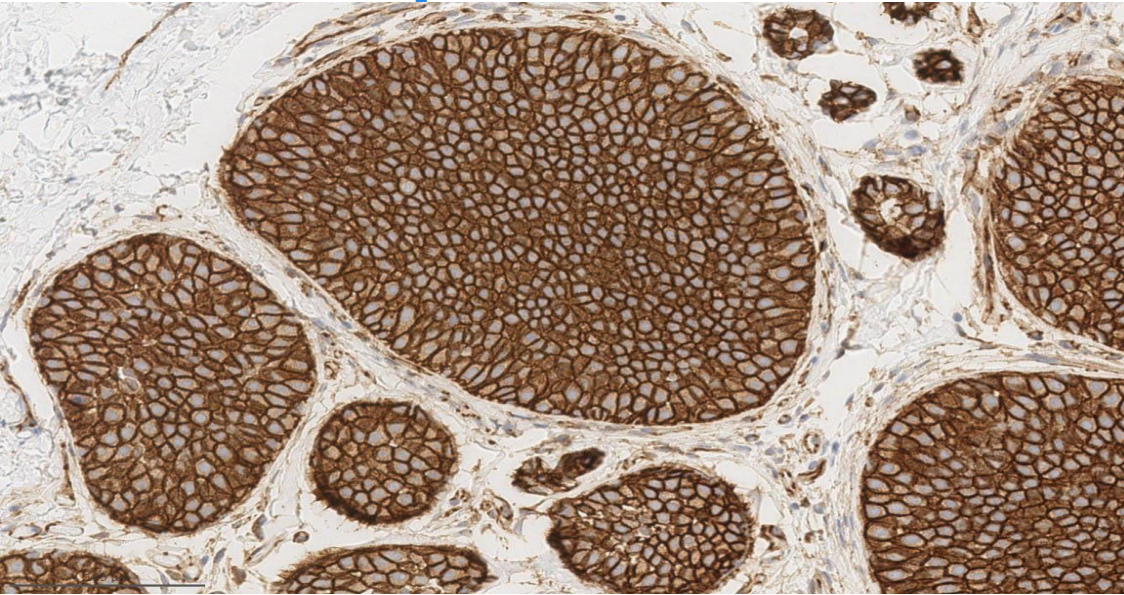
**Diffuse cytoplasmic staining
in lobular neoplasia**

**Linear membrane
staining in ductal cells**

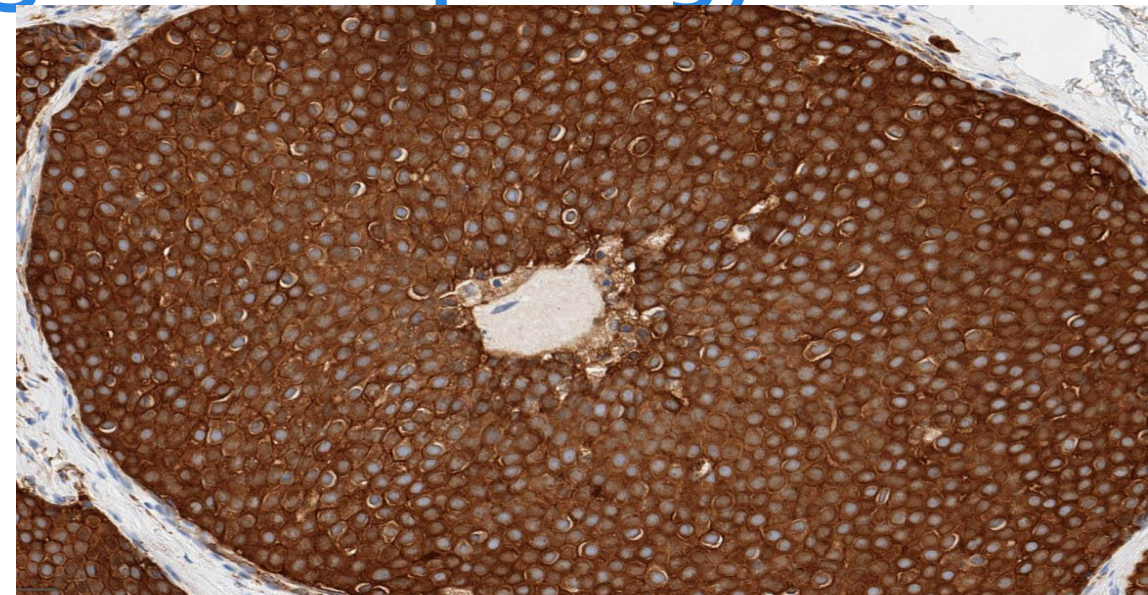


P120

useful to evaluate solid intraductal epithelial proliferations with ambiguous morphology



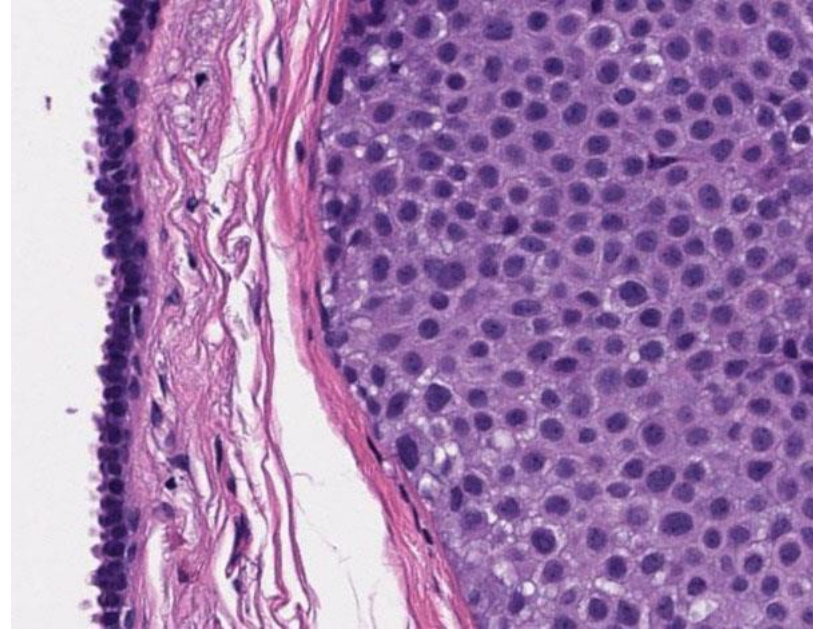
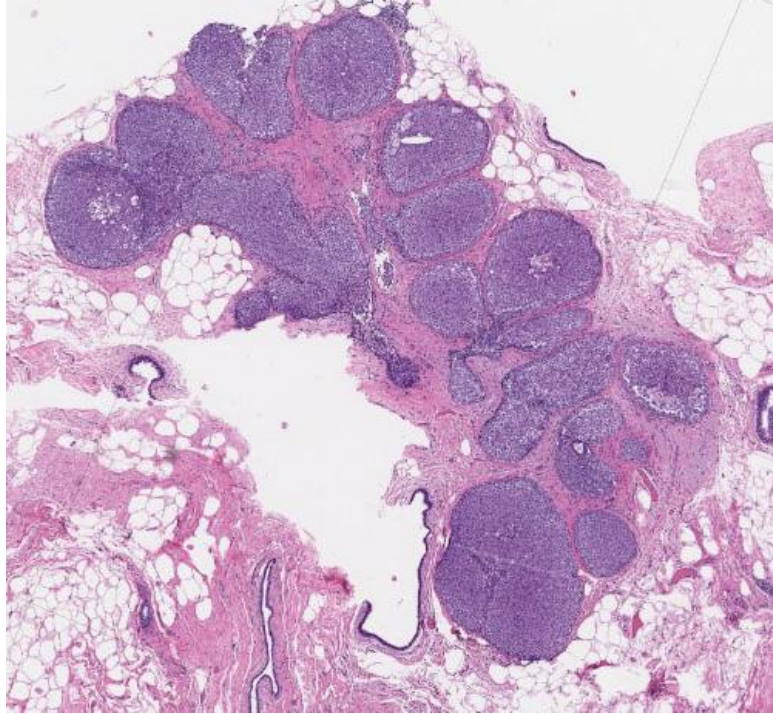
- DCIS: (+) cell membrane stain



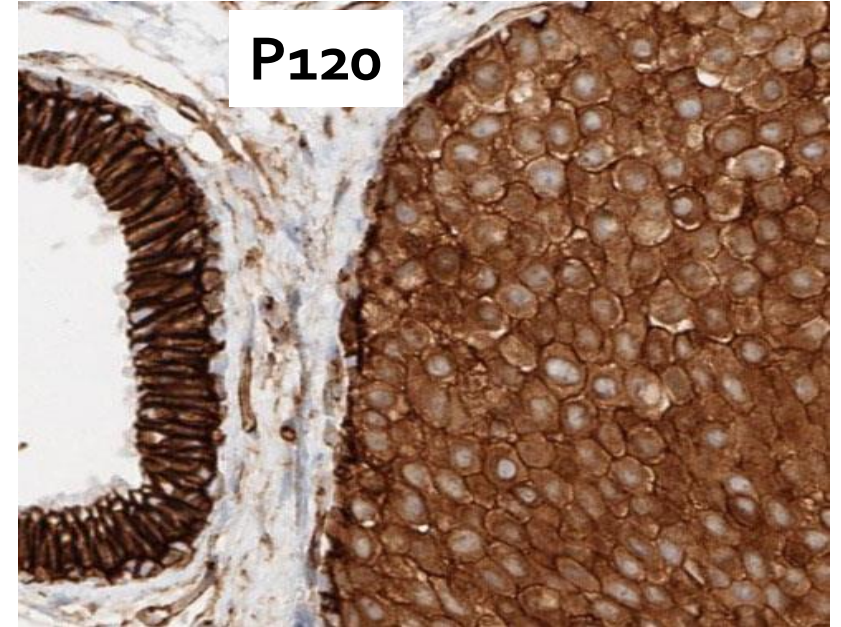
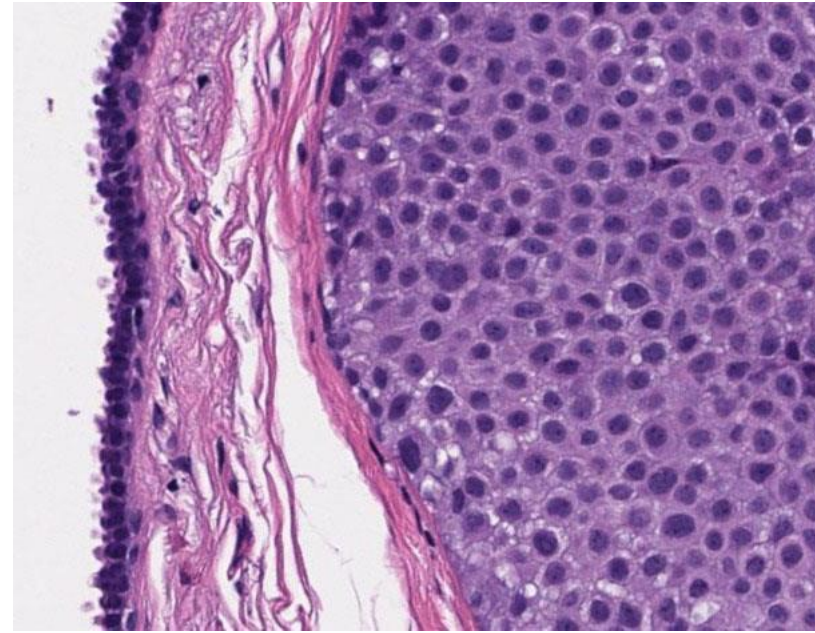
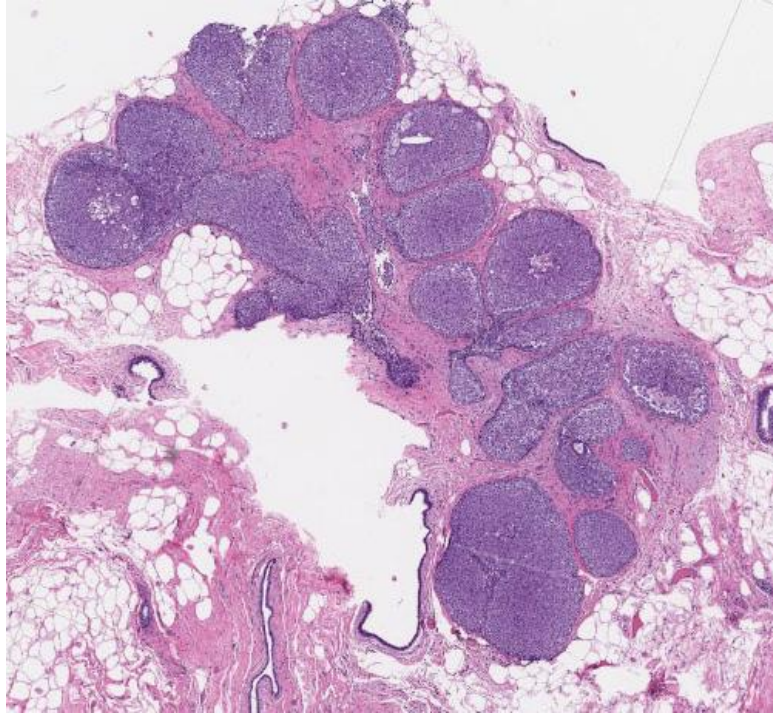
- LCIS: (+) cytoplasmic stain



Aberrant E-cadherin in Florid (or Pleomorphic) LCIS: utility of p120



Aberrant E-cadherin in Florid (or Pleomorphic) LCIS: utility of p120



IHC in the DDX of Lobular vs Ductal epithelial proliferations

| Antigen | Pattern of Staining | | |
|------------------|-------------------------------------|---|---|
| | Ductal epithelium | Lobular Neoplasia | <i>Myoepithelium</i> |
| E-cadherin | continuous linear cell membrane (+) | absent (aberrant staining of cell membrane, weak linear) | <i>granular/ beaded stain with linear distribution limited to the cell membrane facing the epithelium</i> |
| β -catenin | continuous linear cell membrane (+) | absent | |
| P120* | continuous linear cell membrane (+) | cytoplasm diffusely (+) cell membrane (-) | |

***p120:** Most useful marker in cases with aberrant E-cadherin
Useful in the detection of microinvasive lobular carcinoma (microILC)



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Core Needle Biopsy

ALH and Classic LCIS

Florid LCIS and Pleomorphic LCIS

Range of upgrade rates and management

Rad-Path concordant ALH/classic LCIS @CBX: upgrade @EXC

| Author year | Cases w/ EXC | Invasive | DCIS | Upgrades (%) |
|----------------|-----------------|------------------|------------------|------------------|
| Rendi 2012 | 68 | 0 | 2 | 2(2.9%)* |
| Niell 2012 | 60 | 4 (3 ILC, 1IDC) | 3 | 7(11%) |
| Zhao 2012 | 237 | 4 (2 ILC, 2 TC) | 7 | 11 (4.6%) |
| Shah-Khan 2012 | 91 | 1 | 0 | 1 (1%)* |
| Atkins 2013 | 38 | 0 | 0 | 0 |
| Murray 2013 | 72 | 1 | 1 | 2 (3%) |
| D'Alfonso 2013 | 53 | 1 | 2 | 3(5.6%)* |
| Nakhlis 2016 | 74 | 0 | 1 | 1(1%) |
| Susnik 2016 | 180 | 3 (2 ILC, 1 IDC) | 4 | 7 (3.9%) |
| Sen 2016 | 442 | 8 (6 ILC, 2 TC) | 9 | 17 (3.8%)* |
| Holbrook 2018 | 55 | 0 | 0 | 0 |
| Total | 1370 | 22 (1.6%) | 29 (2.1%) | 51 (3.7%) |

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| Holbrook 2018 | 55 | 0 | 0 | 0 |
| Total | 1370 | 22 (1.6%) | 29 (2.1%) | 51 (3.7%) |

Classic Lobular Neoplasia @CNB: to excise or not to excise?

USA + Canada

If *classic* LCIS/ ALH is the highest risk lesion in a rad-path concordant CNB, surgical excision can be *safely* spared if the patient can be followed with imaging studies

Excision is warranted if

- Radiologic-pathologic findings are discordant
AND/OR
- Another lesion is present which by itself mandates excision (e.g. ADH)



CNB Dx of P-LCIS/ F-LCIS mandates surgical excision

Table 2 Upgrade rates at excision of florid LCIS and pleomorphic LCIS in CNBs

| Author, Year | Core biopsy | | Carcinoma in excision | | | Upgrade rate (%) |
|----------------------|--------------|----|-----------------------|----------------------------|--------------------------|------------------|
| | Diagnosis | n | DCIS | Invasive | Any carcinoma/ all cases | % |
| Chivukula, 2008 [68] | P-LCIS | 12 | 0 | 3 ILC | 3/12 | 25 |
| Carder, 2010 [70] | P-LCIS | 10 | 0 | 1 mIC; 2 ILC | 3/10 | 30 |
| Sullivan, 2010 [58] | F-LCIS | 11 | 1 | 4 ILC | 5/11 | 45% |
| | P-LCIS | 17 | 2 | 3 ILC | 5/17 | 29% |
| Niell, 2012 [37] | P-LCIS | 4 | 1 | 2 ILC; 1 IDC | 4/4 | 100 |
| D'Alfonso, 2013 [39] | F-LCIS | 8 | 0 | 1 mIC; 1 ILC | 2/8 | 25 |
| Flanagan, 2015 [63] | P-LCIS | 17 | 3 | 5 ILC; 1 IC | 9/17 | 53 |
| Susnik, 2016 [40] | P-LCIS | 15 | 0 | 4 IC | 4/15 | 27 |
| Fasola, 2018 [62] | P-LCIS | 20 | 2 | 4 ILC | 6/20 | 30 |
| Guo, 2018 [69] | P-LCIS | 25 | 0 | 2 mIC; 13 ILC; 1 IDC | 16/25 | 64 |
| Desai, 2018 [66] | P-LCIS | 15 | 0 | 3 IC | 3/15 | 20 |
| Nakhlis, 2019 [67] | Variant LCIS | 76 | 10 | 9 ILC; 5 IDC; 3 IC | 27/76 | 36% |
| Shamir, 2019 [53] | P-LCIS | 8 | 0 | 2 ILC; 1 P-ILC | 3/8 | 38 |
| | F-LCIS | 6 | 1 | 1 ILC | 2/6 | 33 |
| Foschini, 2019 [57] | F/P-LCIS | 70 | 3 | 28 IC | 31/70 | 44 |
| Harrison, 2020 [76] | P-LCIS | 17 | 1 | 5 ILC | 6/17 | 35 |
| Kuba, 2021 (55) | F-LCIS | 2 | 1 | 0 | 1/2 | 50 |
| | P-LCIS | 8 | 0 | 1 ILC; 1 mIC | 2/8 | 25 |
| | F-LCIS | 24 | 0 | 3 mIC; 1 ILC | 4/24 | 17 |

**Upgrade
rate $\geq 17\%$
in all series**

CNB: Core needle biopsy; DCIS; ductal carcinoma in situ; P-LCIS: pleomorphic lobular carcinoma in situ; F-LCIS: florid lobular carcinoma in situ; F/P-LCIS: florid/pleomorphic lobular carcinoma in situ; ILC: invasive lobular carcinoma; IDC: invasive ductal carcinoma; IC: invasive carcinoma; mIC: microinvasive carcinoma; P-ILC: pleomorphic invasive lobular carcinoma

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European perspective on the management of LCIS (all morphologies)

Table 5 Summary of the recent literature on LN since 2015

| Author and year | Number of patients analyzed or type of publication if no patients have been analyzed (e.g., review or comment) | Findings | Conclusions |
|-----------------------------|--|---|--|
| Calhoun et al. 2016 [50] | n = 76 on CNB Upgrade after 15 years follow-up | 10 cases (13%) with upgrade | The extent of LN in CNB may be an indicator of the likelihood of upgrade to carcinoma |
| Donaldson et al. 2018 [15] | n = 393 on CNB with ADH/LN Upgrade rate and follow-up (87 months) | Upgrade in n = 181 (46%) The 7-year cumulative breast cancer incidence was 9.9% | Multiple foci do not influence BC development Close clinical and radiologic follow-up for more than 5 years in this patient population |
| Fives et al. 2016 [51] | n = 25 LN on CNB accompanying fibroadenomas | Upgrade in 1 case (5%) | Rare upgrade |
| King et al. 2015 [40] | n = 1004 with /wo chemoprevention Median follow-up 81 months | 10-Year cumulative risk 7% With chemoprevention 21% (3.2% per year) with no chemoprevention | Chemoprevention reduced BC risk Volume of disease, (ratio of slides with LCIS to total number of slides) was associated with breast cancer development (p = 0.008) |
| Mao et al. 2017 [52] | BC risk in LN -Hormone receptor status -Skin color | | LN was higher in HR positive and in black patients |
| Maxwell et al. 2016 [53] | n = 392 pure LN 326 with OE | Upgrade to pleomorphic LN In 23/326 cases (7%) | Screen detected LN -In younger women -Unilateral -Non-pleomorphic |
| Nakhlis et al. 2016 [54] | n = 77 on CNB | Upgrade in 2 of 77 cases (2%) | Routine excision is not indicated for patients with pure LN on CB and concordant imaging findings |
| Renshaw and Gould, 2016 [4] | n = 69 CNB with LN Upgrade Follow-up | Upgrade in 17 of 69 cases (25.8%) | Immediate BC risk is higher for ADH than LN Long-term BC risk is higher for LN than ADH |
| Schmidt et al. 2018 [55] | n = 178 on CNB 115 OE 54 Surveillance (55 months follow-up) | Upgrade in 13/115 cases (11%) 1/54 Cases developed BC after follow-up (2%) | Low-upgrade rate and low BC risk |
| Sen et al. 2016 [56] | n = 447 (ALH and LCIS) | Upgrade ALH 2.4% Upgrade LCIS 8.4% | Excision is recommended for LCIS on CNB and for ALH surveillance at 6, 12, and 24 months |
| Susnik et al. 2016 [47] | n = 302 of 370 Upgrade after OE | Upgrade In 3.5% (8/228) pure LN lesions In 26.7% in "LCIS variants" (4/15) in 28.3% in LN with ductal atypia (15/53) | LN with non-classic morphology or with associated ductal atypia requires surgical excision, this can be avoided in pure LN |
| Xie et al. 2017 [57] | Survival outcome in SEER database (n = 208 + 5756 cases) Bilateral or partial mastectomy | OS after partial mastectomy without radiotherapy was not inferior to patients who underwent bilateral prophylactic mastectomy | Low breast cancer-specific mortality in patients with LCIS, therefore aggressive prophylactic surgery like bilateral prophylactic mastectomy should not be advocated for most patients with LCIS |

Broad range of upgrade rates at EXC: 2% - 46%

Upgrade rates
Classic LN: 2.4%- 10.4%
Non-classic LCIS: >20%

Rageth C et al *Breast Cancer Research and Treatment* (2019) 174:279–296



Lobular neoplasia (LN)

Consensus recommendation for management of lobular neoplasia by a European multidisciplinary expert panel

A lesion containing **classical LN** which is **visible on imaging should undergo excision with Vacuum Assisted Biopsy (VAB)**. Thereafter surveillance is justified if there is no pathological-radiological discordance and no residual lesion.

In contrast, **morphologic variants of LN** (LIN₃, pleomorphic LCIS, and florid LCIS) which are reported as B5a lesions **should undergo open excision**

Rageth C et al *Breast Cancer Research and Treatment* (2019) 174:279–296

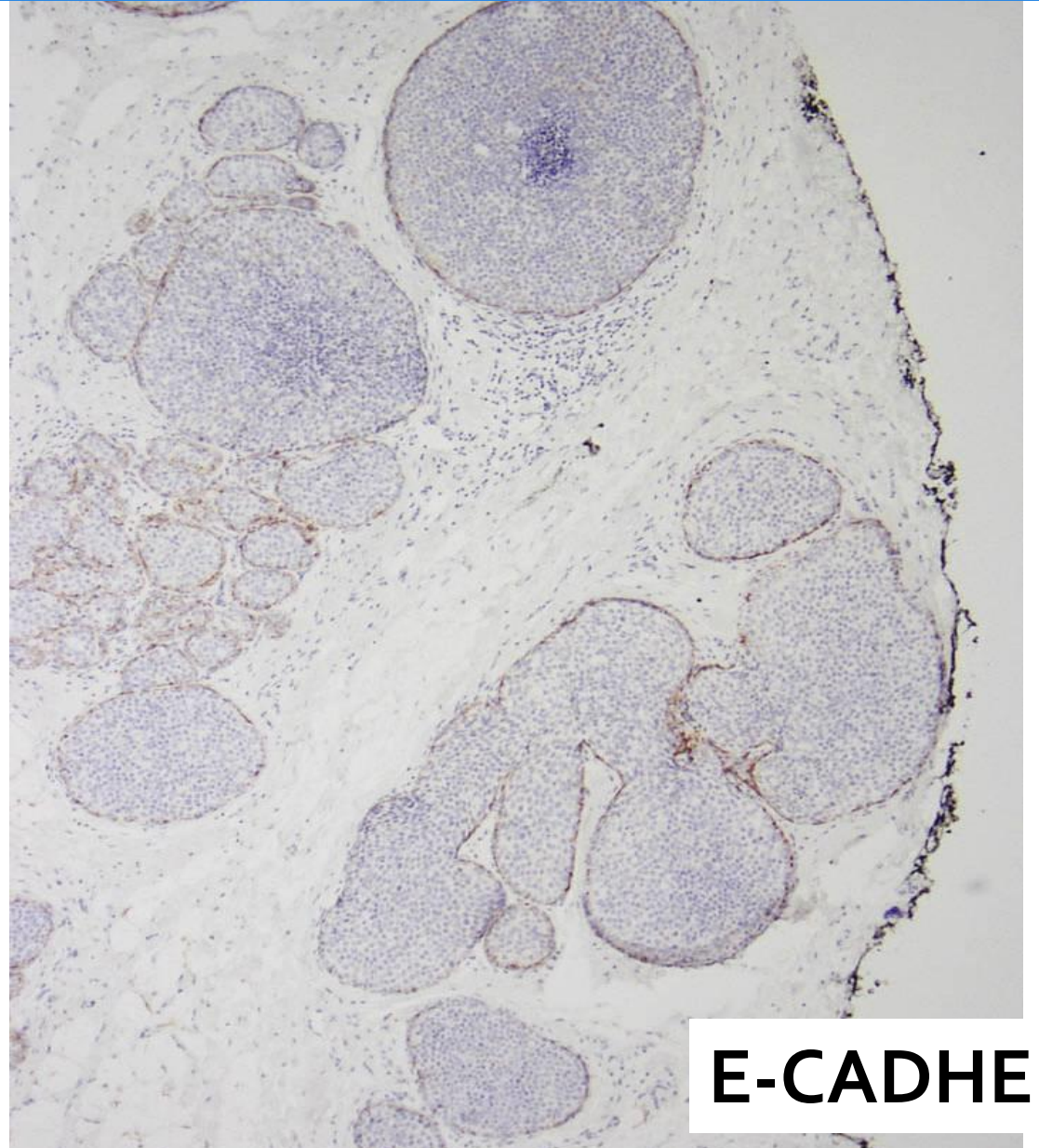
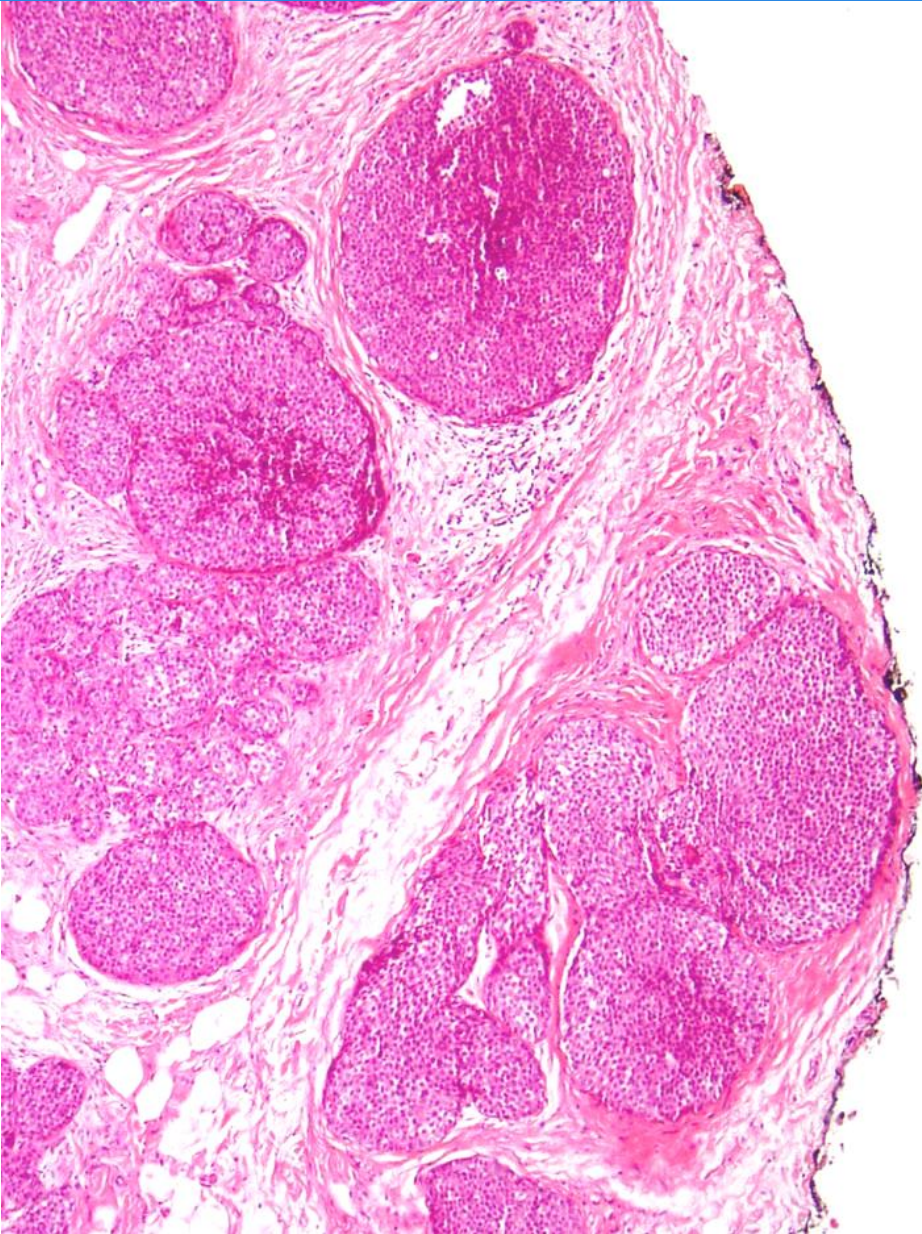


| CNB diagnosis Societies recommendations | Classic lobular neoplasia (ALH/Classic LCIS) | Pleomorphic LCIS | Florid LCIS |
|--|---|--|---|
| NCCN ¹ , 2022 (US) | Surgical excision not required if radiologic pathologic concordant | Surgical excision | Not mentioned |
| American Society of Breast Surgeons, 2016 (US) | Surgical excision not required if radiologic pathologic concordant | Surgical excision | Surgical excision |
| Second International Consensus Conference on B3 lesions, 2018 (Europe) | (Category B3, lesion of uncertain malignant potential) Excision with VAB if visible on imaging; if findings are pathologic-radiologic concordant and no residual lesion then surveillance is appropriate | (Category B5a, malignant in situ) Surgical excision | (Category B5a, malignant in situ) Surgical excision |
| ESMO ² , 2019 (Europe) | Surgical excision not required | Surgical excision | Not mentioned |
| AGO ³ , 2019 (Germany) | Surgical excision not required if ALH/CLCIS involves ≤ 3 TDLUs in vacuum assisted biopsy and radiologic pathologic concordant | Open biopsy and preferably complete excision | Open biopsy and preferably complete excision |
| National Health System, 2018 (UK) | (Category B3, lesion of uncertain malignant potential) Surgical excision not required if diagnosed on 14G core or VAB and if radiologic-pathologic concordant | (Category B5a, malignant in situ) Surgical excision | Only referred as non-pleomorphic LCIS with necrosis or mass forming (Category 4, suspicious) Repeat sampling with 14g core or vacuum assisted biopsy |
| Cancer Australia, 2016 (Australia) | Surgical excision not required if radiologic pathologic concordant | Surgical excision | Surgical excision |

| CNB diagnosis Societies recommendations | Classic lobular neoplasia (ALH/Classic LCIS) | Pleomorphic LCIS | Florid LCIS |
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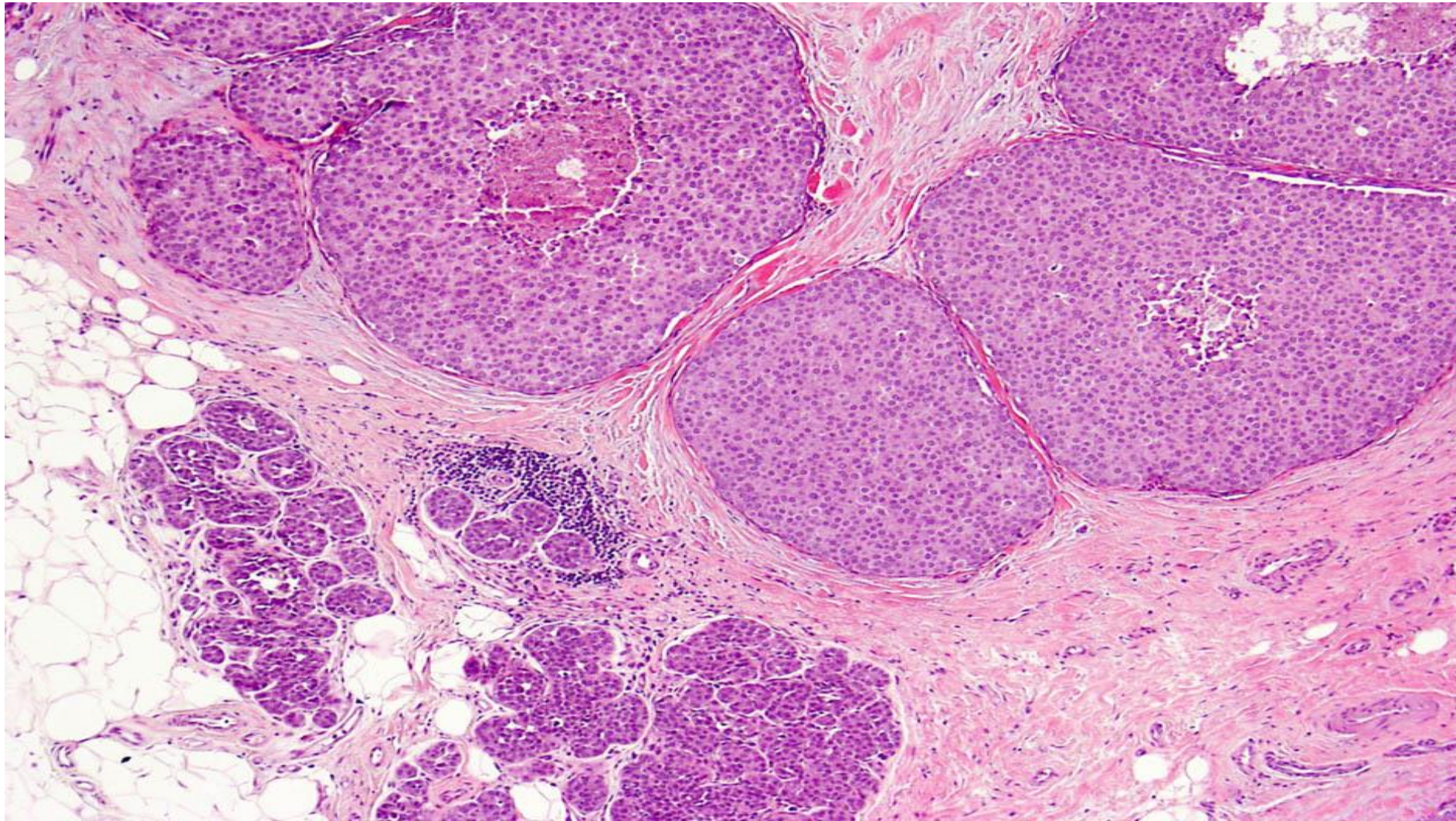
F/P-LCIS at/near margin: re-excise to clear margin

optimal margin clearance unknown (usually 2 mm clearance is suggested as for DCIS)



E-CADHERIN

Classic LCIS usually adjacent to F/P-LCIS



Classic LCIS → margin status is not reported



Regional guidelines on management of non-invasive lobular neoplasia in surgical excisions

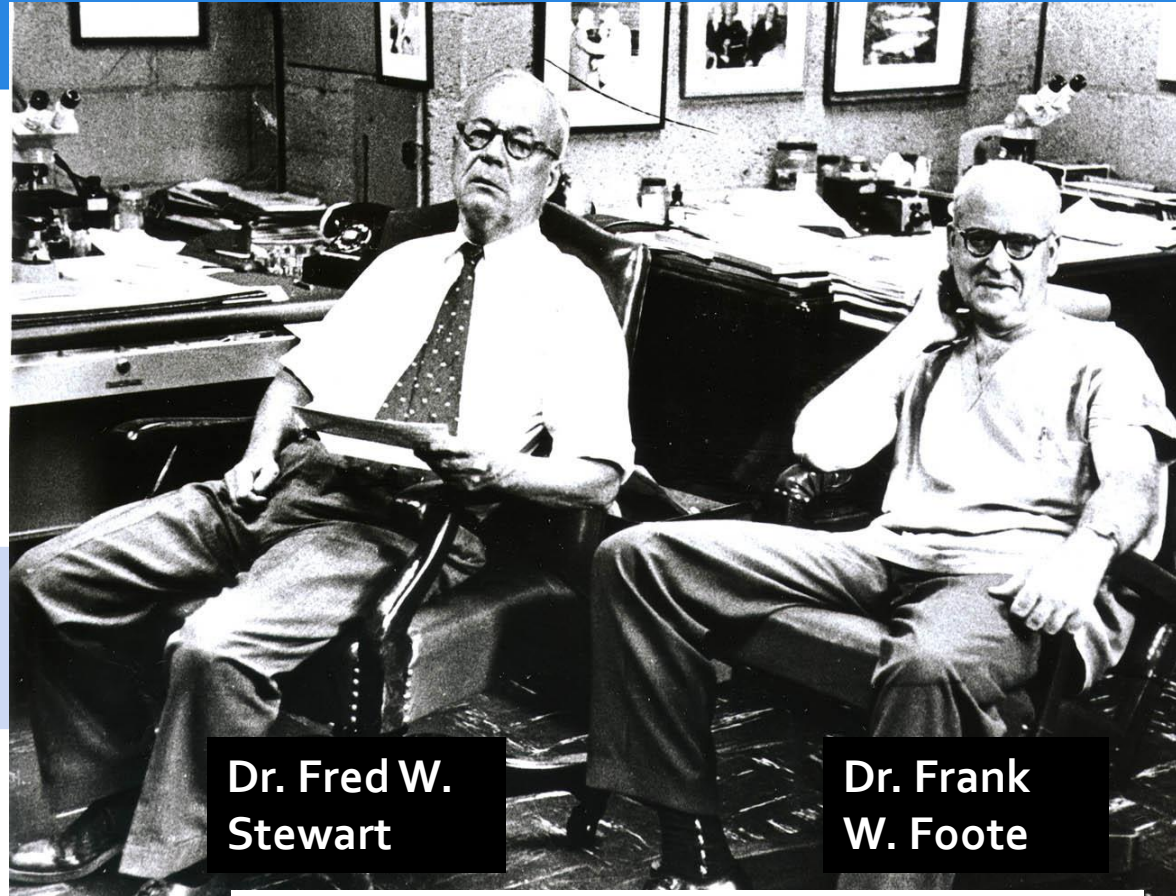
| | Classic lobular neoplasia (ALH/Classic LCIS) | Pleomorphic LCIS | Florid LCIS |
|---|---|---|---|
| NCCN ¹ , 2022 (US) | Size and margin status not reported | Negative margins should be considered | not specifically mentioned |
| American Society of Breast Surgeons, 2016 (US) | | Margin adequacy not mentioned | Margin adequacy not mentioned |
| ESMO ² , 2019 (Europe) | | Negative margins and radiation therapy should be considered | not specifically mentioned |
| AGO ³ , 2019 (Germany) | | Complete excision recommended | Complete excision recommended |
| NHS ⁴ /The Royal College of Pathologists, 2016, (UK) | | Extent of disease should be recorded Negative margins recommended | Margin adequacy not mentioned |
| Cancer Australia, 2016 (Australia) | | Margin status should be recorded Re-excision should be considered if positive margin | Margin status should be recorded Re-excision considered on a case-by-case basis after multidisciplinary discussion |

Classic LCIS

Precursor lesion

1941

- Morphologically similar to ILC
- Proximity to ILC



Dr. Fred W.
Stewart

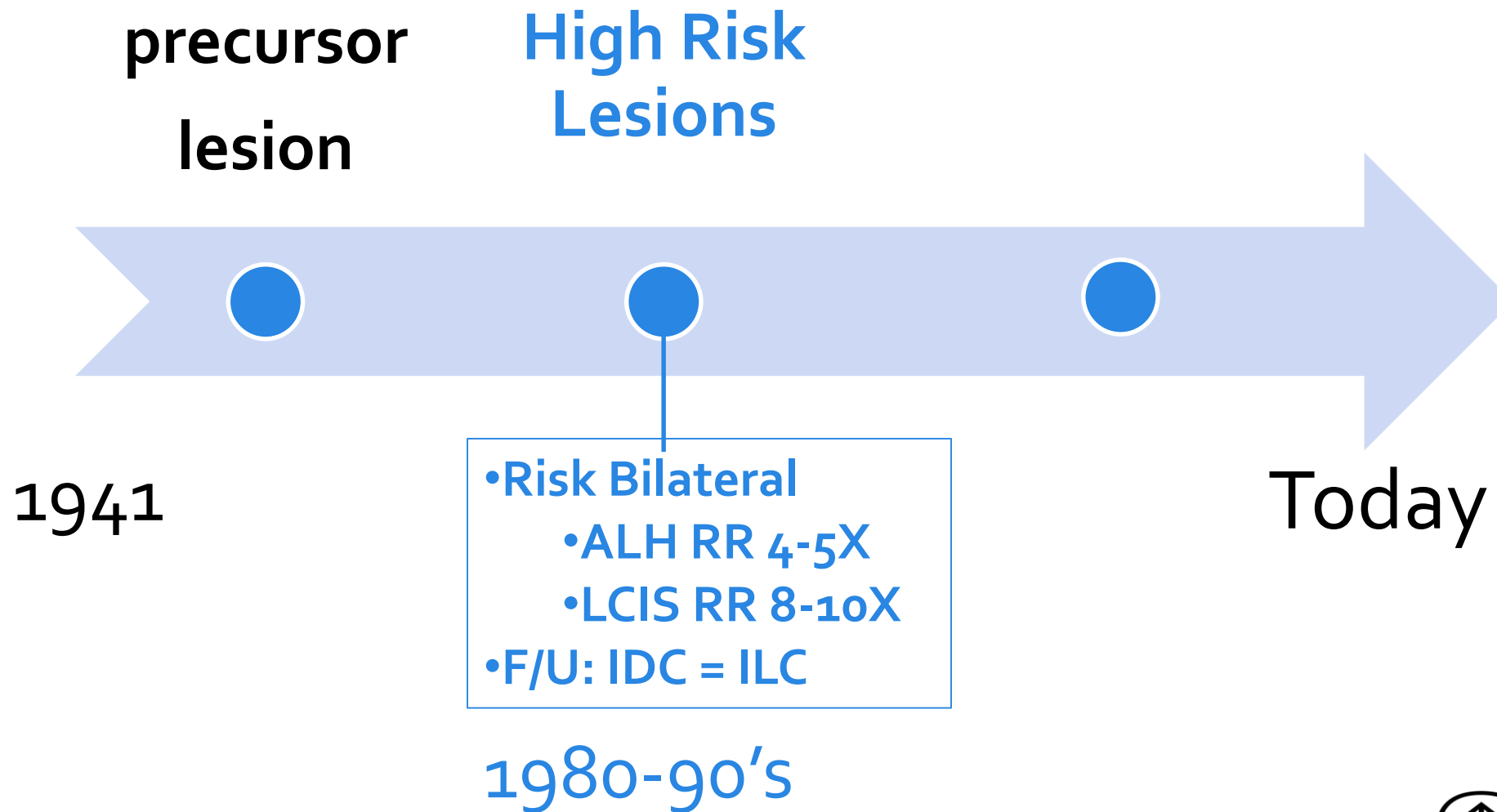
Dr. Frank
W. Foote

LOBULAR CARCINOMA IN SITU *
A RARE FORM OF MAMMARY CANCER
FRANK W. FOOTE, JR., M.D., and FRED W. STEWART, M.D.
(From the Pathological Laboratories of the Memorial Hospital, New York, N.Y.)

Am J. Pathol, 1941



Classic LCIS and ALH



Classic LCIS - long term follow-up studies

| Author Year | Population years | patients | Median age | F/U (years) | Carcinomas at F/U | | Carcinoma Laterality | | |
|-------------|----------------------------|----------|------------|-------------|-------------------------|--|---------------------------------------|---------------------------------------|------------|
| | | | | | Patients with Carcinoma | Type of carcinoma | Ipsi-lateral | Contra-lateral | Bi-lateral |
| Rosen 1978 | MSKCC 1940-1950 | 99 | 45 y | 24 | 29 (29%) | • IDC > ILC | Unclear | | |
| Page 1991 | Nashville Cohort 1950-1968 | 39 | 45 y | 19 | 9 (23%) | • 70% ILC • 2% Tubular • 10% IDC | 50% | 40% | 10% |
| King 2015 | MSKCC 1980-2009 | 1004 | 50 y | 6.75 | 150 (15%) | • 29% IDC • 35% DCIS • 27% ILC | 63% | 25% | 18% |
| Wong 2017 | SEER 1983-2014 | 19462 | 52 y | 8.1 | 1837 (9.4%) | • 42.4% IDC • 20.8% DCIS • 20% ILC | 55.2% 69% of ILCs 49.2% of IDCs | 44.5% 30% of ILCs 50.8% of IDCs | N/A |

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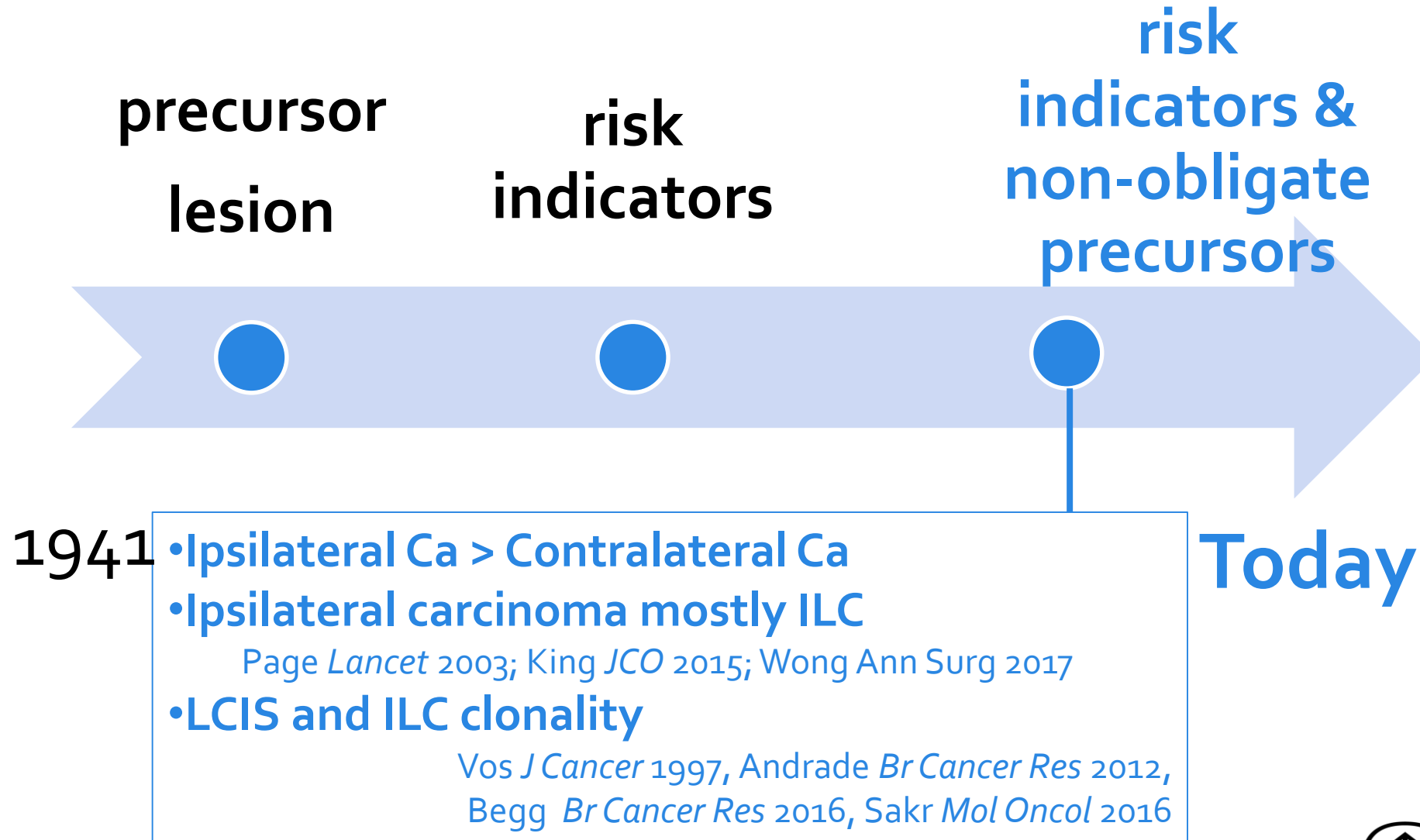
Classic LCIS - Long Term Follow-up

- 1004 women with classic LCIS only (diagnosis @MSKCC 1980-2009)
- Median age at Dx: 50 years (27-83)
- Median follow-up 81 months (6-368)
- 150/1004 (15%) women developed 168 BC
 - 63% ipsilateral, 25% contralateral, 12% bilateral
 - 56% invasive (IDC 29%, ILC 27%), DCIS 35%, other 9%
- **2% annual incidence of breast carcinoma**
- **Hormone chemoprevention significantly reduced the rate of subsequent breast carcinoma (p<0.001)**
 - **7% with hormone chemoprevention**
 - **21% without hormone chemoprevention**

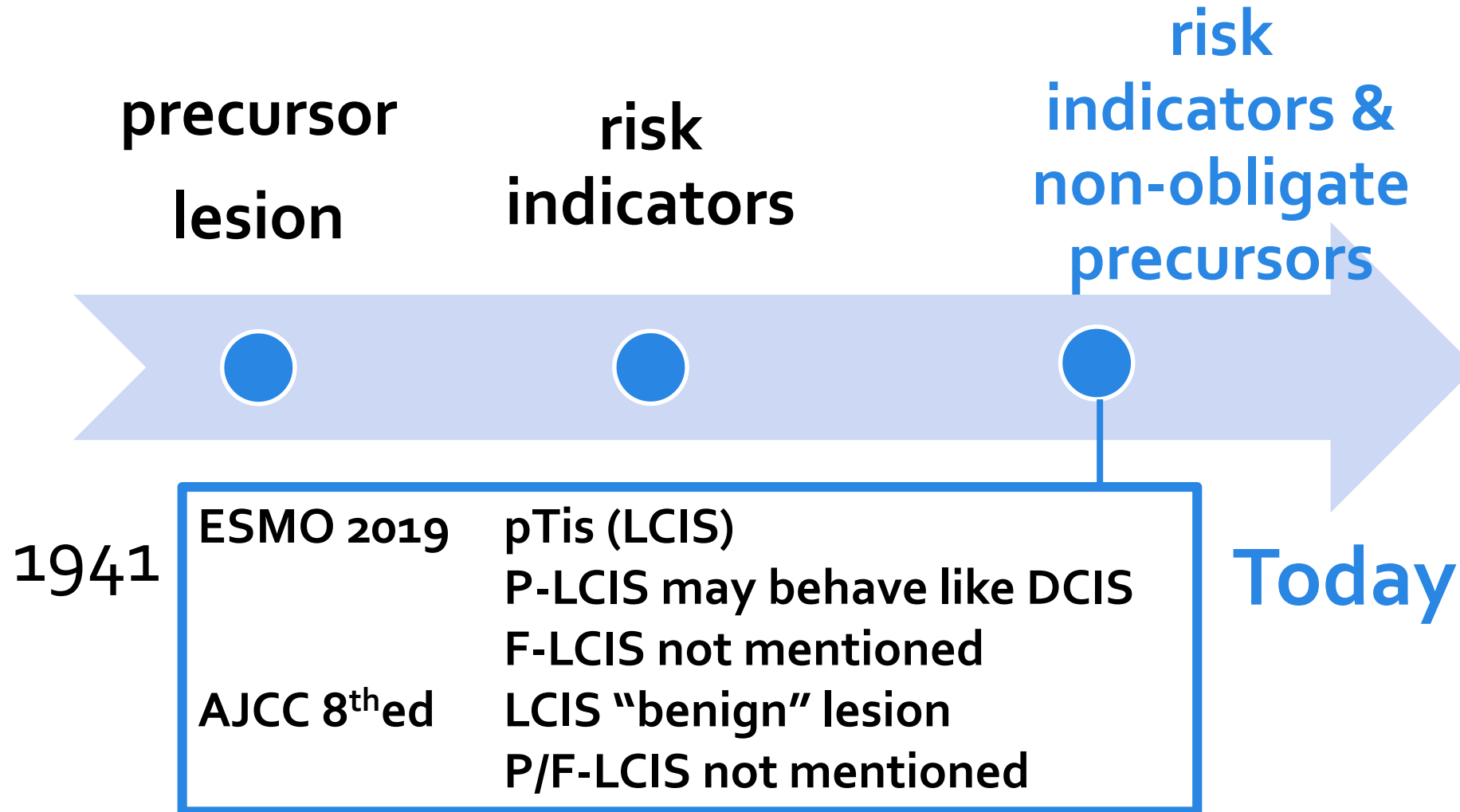
King T et al *J Clin Oncol* 2015



Classic LCIS and ALH



Staging – classic LCIS, P-LCIS (and F-LCIS)



P-LCIS (and F-LCIS) with no invasion: Limited Follow-up data

| Author year | Cases | F/U (m or y) (range) | Recurrence | | Pts with recurrence were treated with... at Dx of P/F-LCIS | |
|------------------|-------|------------------------|------------|----------------------------------|--|-----------------|
| | | | number | type | RadioTP | HormoneTP |
| Downs-Kelly 2011 | 26 | Mean 46 m (4-108) | 1 | 1 PLCIS | 0 | 1 (PLCIS) |
| Khoury 2014 | 31 | (7-91 m) | 6 | 3 ILC, 1 IDC, 2 PLCIS | 0 | 3 (2ILC, 1 IDC) |
| Flanagan 2015 | 7 | Mean 4.1 y | 0 | 0 | 0 | 0 |
| De Brot 2017 | 7 | Median 59 m (45-66) | 4 | 1 ILC, 1 microILC, 1 IDC, 1 DCIS | 0 | 1 (DCIS) |
| Savage 2018 | 12 | Median 3.4 y (1.3-9.2) | 0 | 0 | 0 | 0 |
| Desai 2018 | 11 | Median 47 m | 2 | 1 ILC, 1 PLCIS | 1 (ILC) | 1 (PLCIS) |
| Nakhlis 2019 | 25 | Median 58 m (1-224) | 1 | 1 DCIS | 0 | 0 |
| Kuba 2021 | 30 | Median 37.5 m | 3 | 2 P-ILC (1 pt DOD), 1 microILC | 1 (P-ILC) | 1 (P-ILC) |

P-LCIS (and F-LCIS) with no invasion: Limited Follow-up data

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| Kuba 2021 | 30 | Median 37.5 m | 3 | 2 P-ILC (1 pt DOD), 1 microILC | 1 (P-ILC) | 1 (P-ILC) |

149

17 (4 ILC, 2 microILC, 2 IDC, 3 PLCIS, 2 DCIS)



P-LCIS (and F-LCIS) with no invasion: Limited Follow-up data

| Author year | Cases | F/U (m or y) (range) | Recurrence | | Pts with recurrence were treated with... at Dx of P/F-LCIS | |
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149

17

2 ILC

3 ILC, 1 IDC, 2 PLCIS, 1 DCIS

Classic LCIS and ALH – Take home messages

- Many morphologic mimics and pitfalls – BEWARE!!!
- High risk lesions and *non-obligate morphologic precursors*
- Relative Risk of subsequent breast carcinoma
 - 4X ALH, 8X classic LCIS
 - Carcinoma at F/U
 - ipsilateral >>contralateral
 - Ipsilateral carcinoma: ILC more common
- Management
 - Margin status not reported
 - ALH and classic LCIS in ***rad-path concordant*** CBX
 - In USA: Excision may be spared
 - Elsewhere: follow local management guidelines

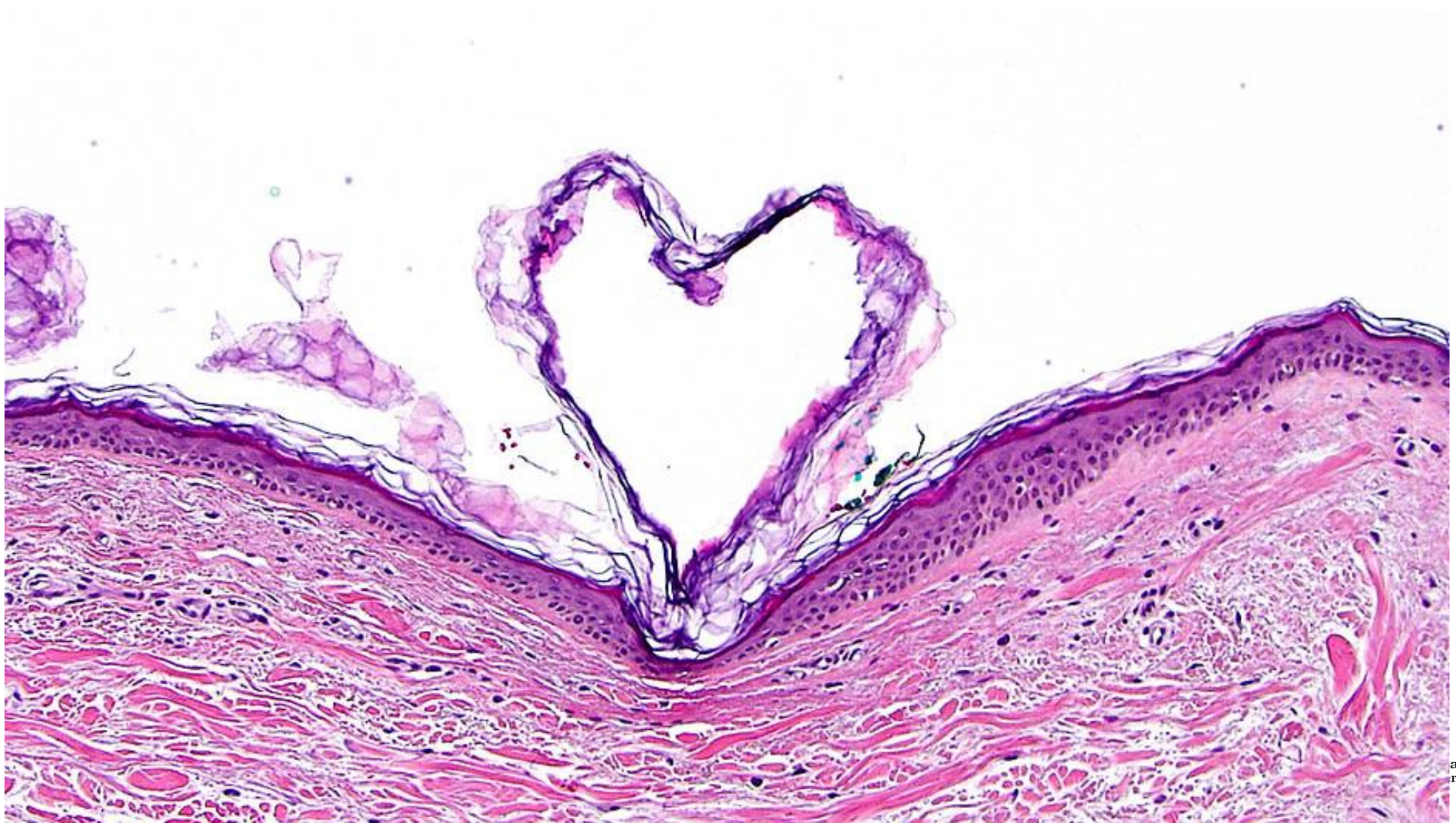


P-LCIS and F-LCIS – Take Home Messages

- Morphology - WHO 2019 criteria
 - Clinical and imaging presentation
 - Pleomorphic or indeterminate Ca²⁺
 - Mass with or without Ca²⁺
 - Immunohistochemical profile
 - Same as classic LCIS
 - Cytoplasmic p120 IHC if aberrant E-cadherin
 - *Molecular alterations: similar to classic LCIS, but a greater number*
 - (Micro)Invasion in 40-70% cases
 - Assess/ rule out (micro)invasion
 - Areas of inflammation +/- reactive stroma
 - Include “positive” IHC marker(s)
 - F-LCIS or P-LCIS in CNB → EXC
 - Regardless of rad-path concordance
- Limited F/U data
- F-LCIS or P-LCIS at ink → re-excision (if feasible)
 - *Very limited data on the benefits of HormoneTP and/or RadioTP*

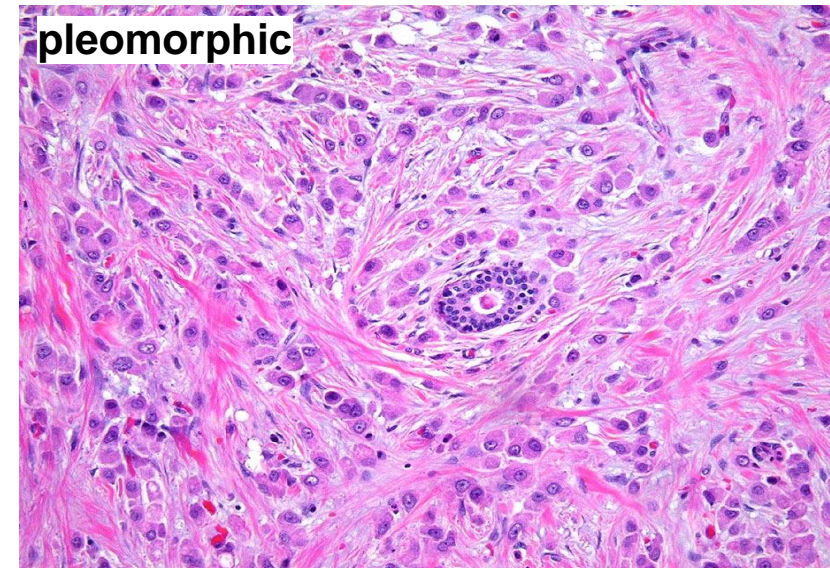
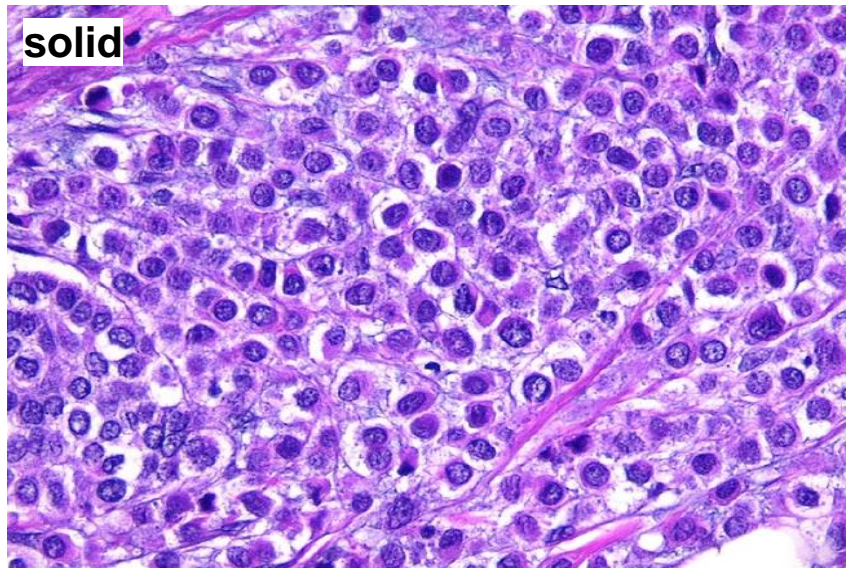
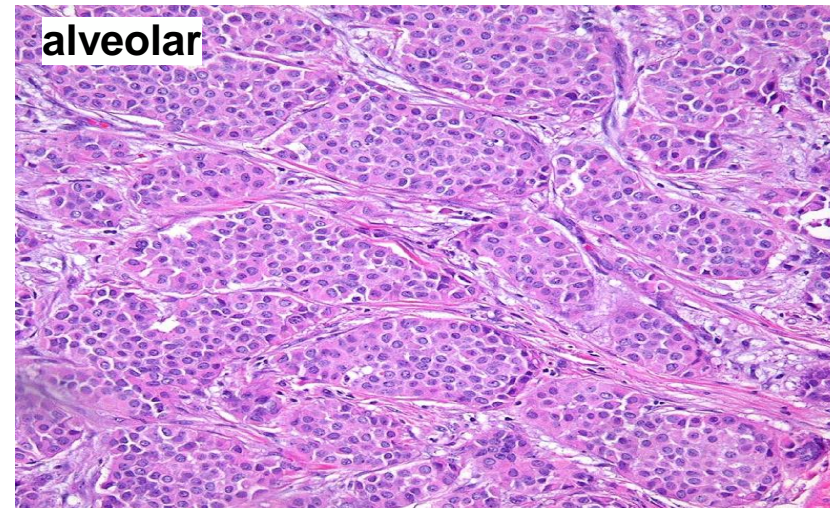
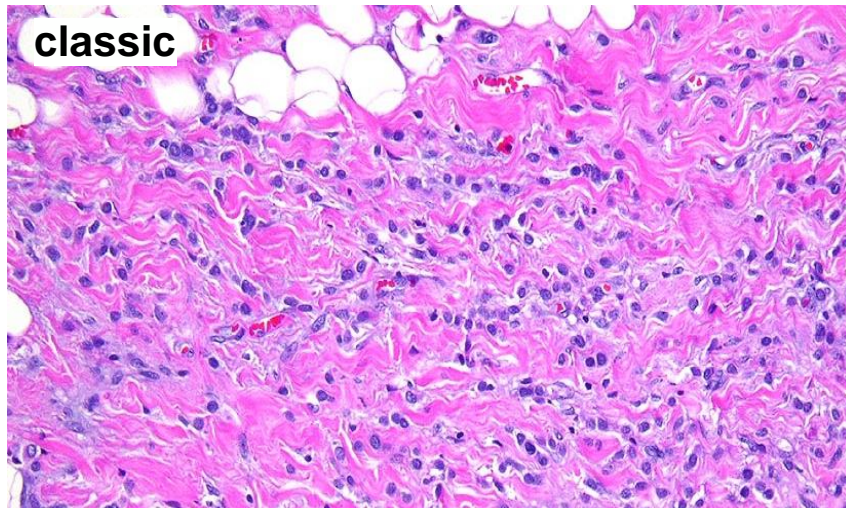


Thank you for your attention

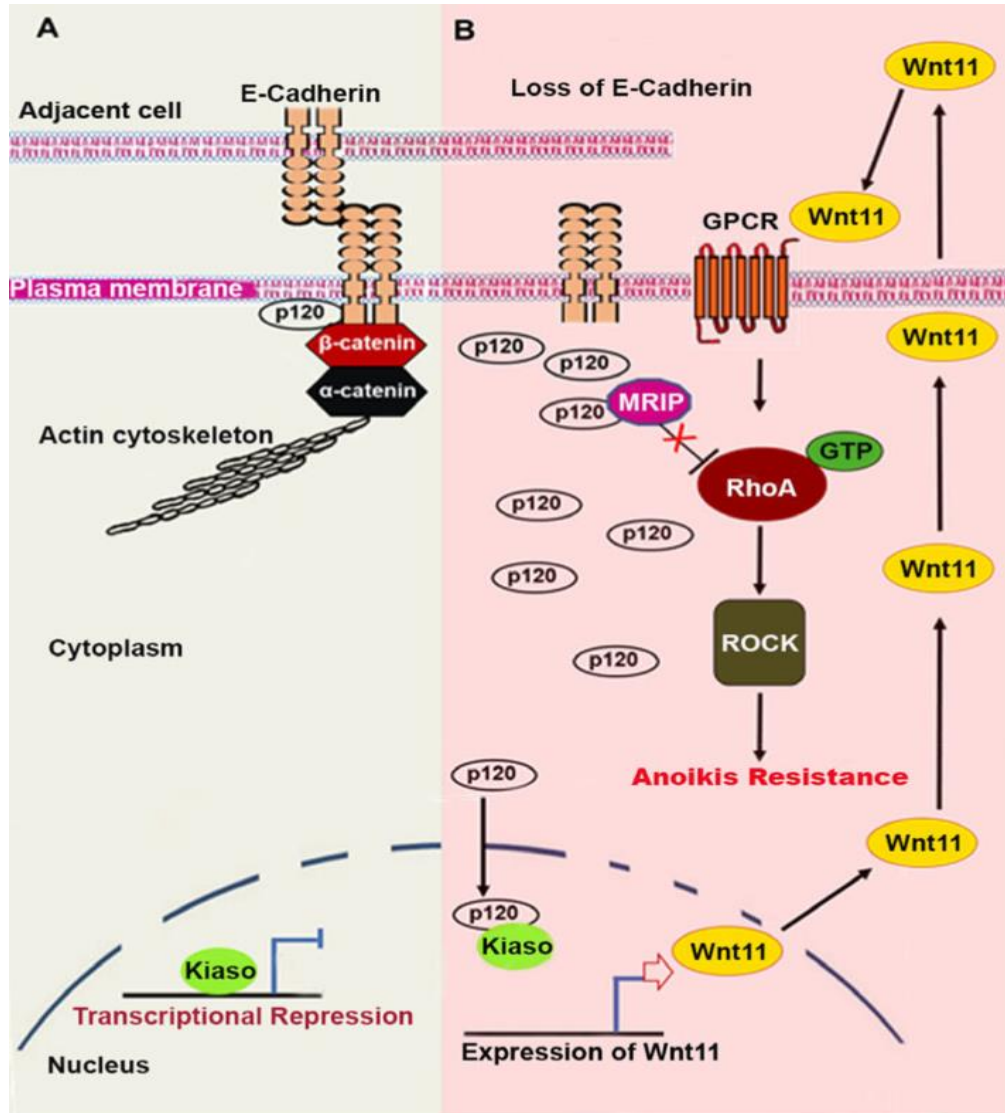




Pathology – ILC patterns



Pathology – E-cadherin

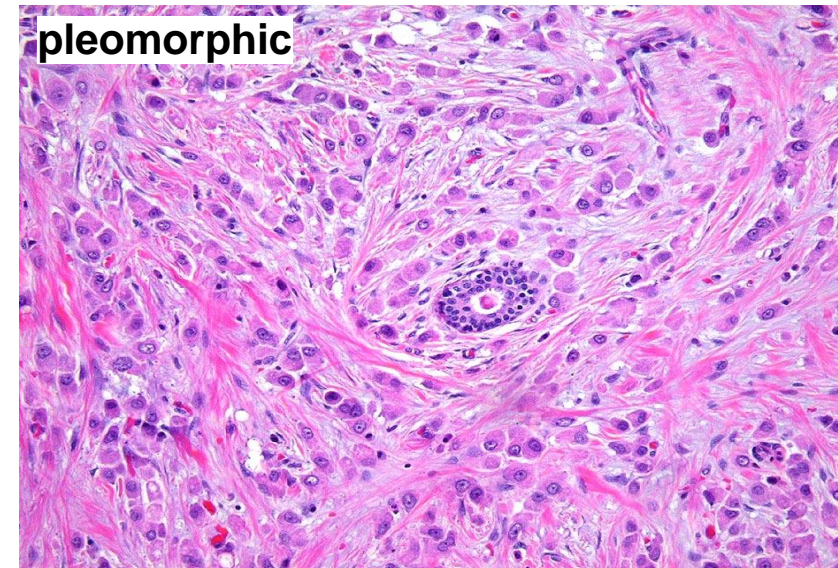
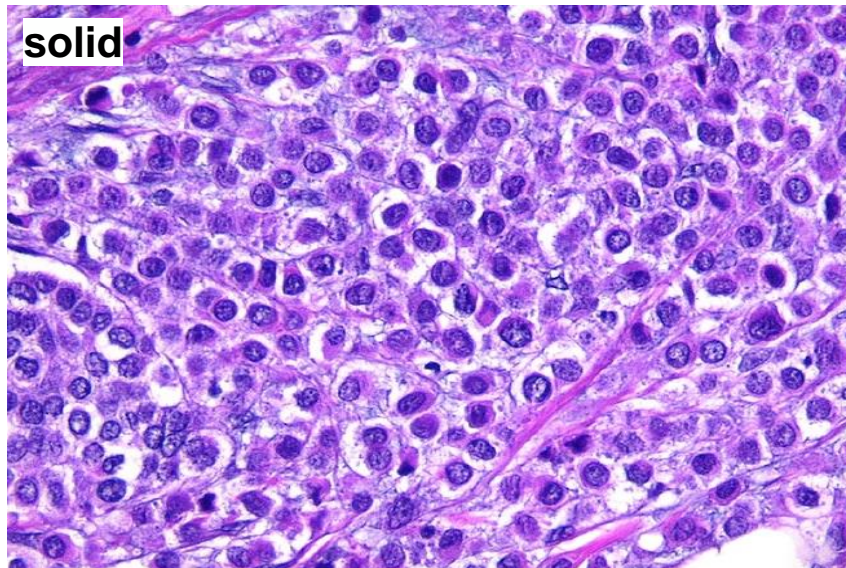
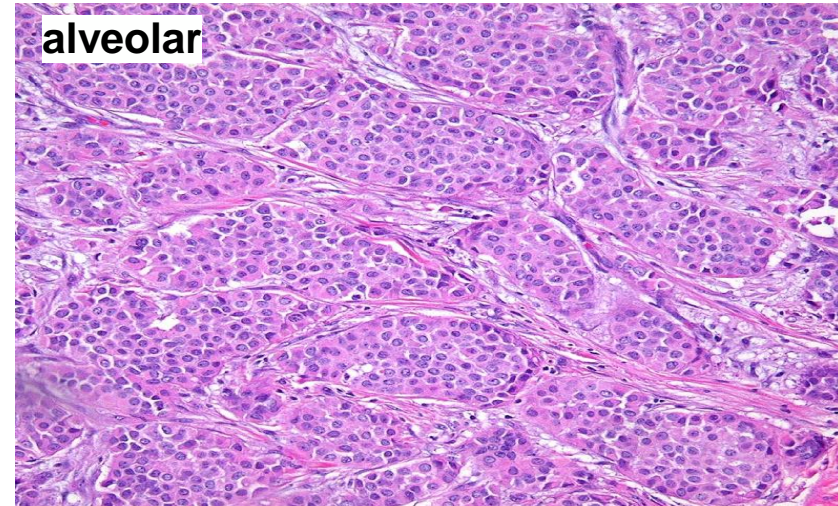
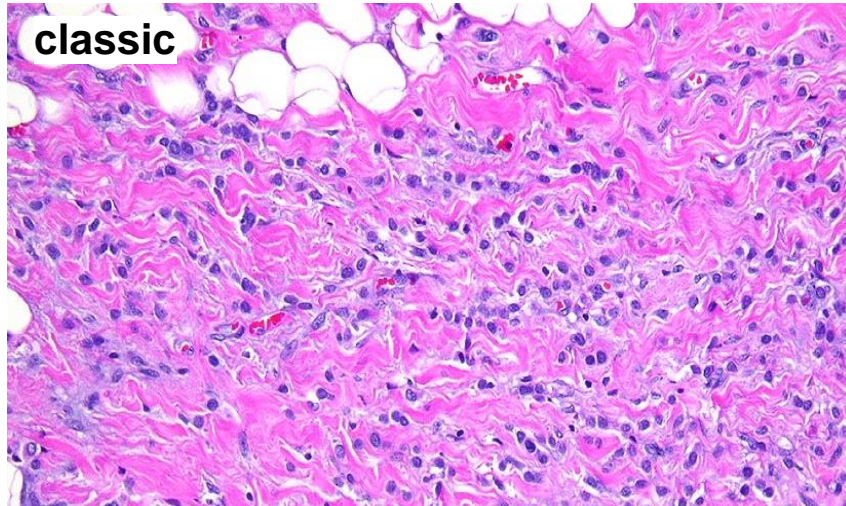


The E-cadherin gene, *CDH1*, is located on chromosome 16q22.1 and codes for a 120kDA transmembrane glycoprotein

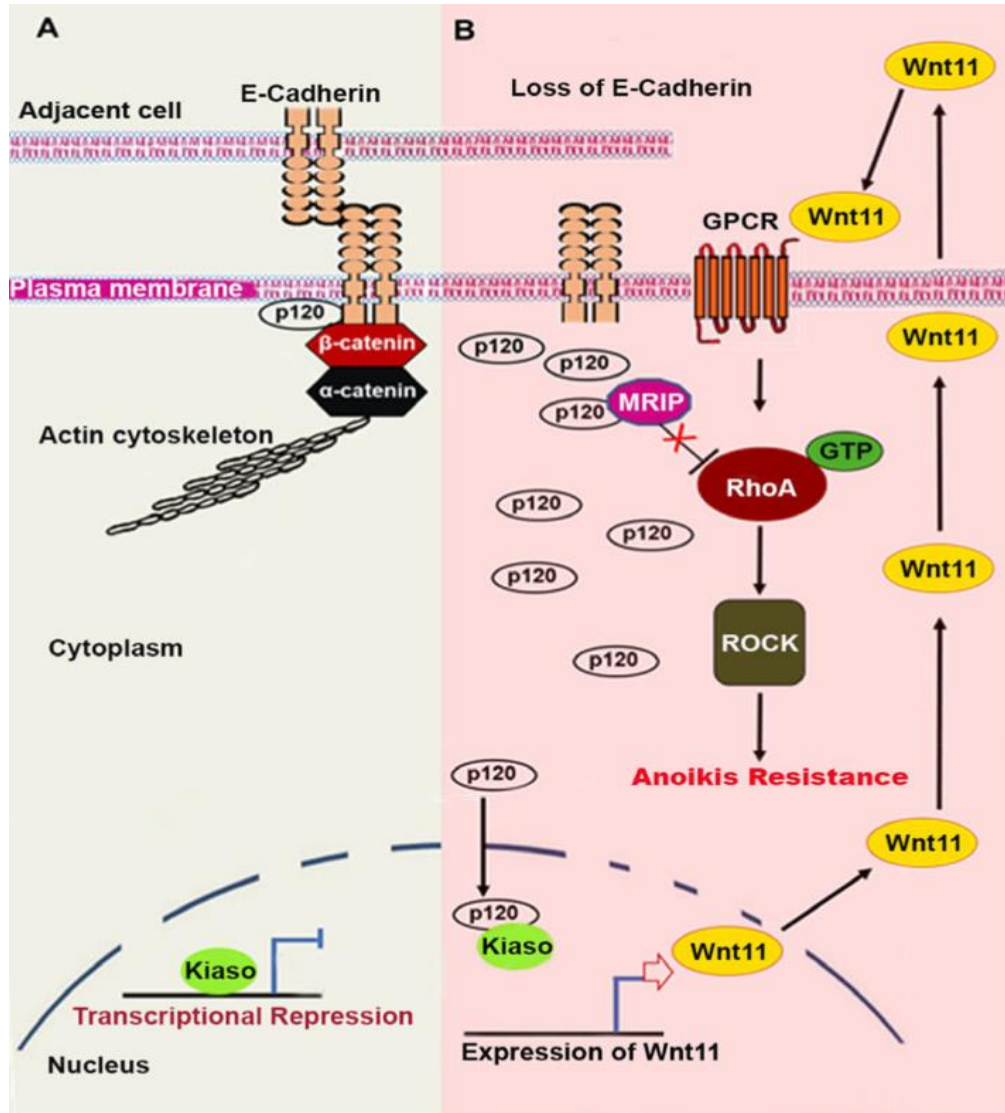
Loss of E-cadherin is characteristic of ILC and is predominantly attributed to *CDH1* mutation

Loss of E-cadherin increases cytoplasmic accumulation of p120 catenin

Pathology – ILC patterns



Pathology – E-cadherin



The E-cadherin gene, *CDH1*, is located on chromosome 16q22.1 and codes for a 120kDA transmembrane glycoprotein

Loss of E-cadherin is characteristic of ILC and is predominantly attributed to *CDH1* mutation

Loss of E-cadherin increases cytoplasmic accumulation of p120 catenin

CNBs with F-LCIS/or P-LCIS: upgrades @EXC

| Author, Year | CNB | | Carcinoma in Excision | | | Upgrade rate (%) |
|-----------------------|------------------|------------|-----------------------|----------------------|------------------------------|------------------|
| | Diagnosis | cases | DCIS | Invasive | all carcinomas/ all cases | |
| Chivukula, 2008 | PLCIS | 12 | 0 | 3 ILC | 3/12 | 25.0% |
| Carder, 2010 | PLCIS | 10 | 0 | 1 mIC; 2 ILC | 3/10 | 30.0% |
| Niell, 2012 | PLCIS | 4 | 1 | 2 ILC; 1 IDC | 4/4 | 100% |
| D'Alfonso, 2013 | FLCIS | 8 | 0 | 1 mIC; 1 ILC | 2/8 | 25.0% |
| Flanagan, 2015 | PLCIS | 17 | 3 | 5 ILC; 1 IC | 9/17 | 53.0% |
| Susnik, 2016 | PLCIS | 15 | 0 | 4 IC | 4/15 | 26.7% |
| Fasola, 2017 | PLCIS | 20 | 2 | 4 ILC | 6/20 | 30.0% |
| Guo, 2018 | PLCIS | 25 | 0 | 2 mIC; 13 ILC; 1 IDC | 16/25 | 64.0% |
| Shamir, 2018 | PLCIS | 8 | 0 | 3 ILC | 3/8 | 38.0% |
| | FLCIS | 6 | 1 | 1 ILC | 2/6 | 33.0% |
| Total Upgrades | PLCIS | 111 | 6 | 42 | 48/111 | 43.2% |
| | FLCIS | 14 | 1 | 3 | 4/14 | 28.6% |
| | PLCIS + FLCIS | 125 | 7 | 45 | 52/125 | 42.0% |

Rad-path concordant CNBs with F-LCIS/or P-LCIS: upgrades

@EXC

| Author, Year | CNB | | Carcinoma in Excision | | | Upgrade rate (%) |
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Rad-path concordant CNBs with F-LCIS/or P-LCIS: upgrades

| Author, Year | CNB | | @EXC | | | Upgrade rate (%) |
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| | <i>FLCIS</i> | 14 | 1 | 3 | 4/14 | 28.6% |
| Total Upgrades | PLCIS + <i>FLCIS</i> | 125 | 7 | 45 | 52/125 | 42.0% |

Classic LCIS/ ALH may mimic other lesions

Classic LCIS is a common mimic of Low Grade DCIS, solid

use E-cadherin/ p120

Classic LCIS/ ALH coexisting with other lesions → few possible scenarios various scenarios

UDH or acini (partial)

DDx: UDH, ADH, solid LG carcinoma in situ

collagenous spherulosis

DDx: low grade DCIS

adenosis

C

ALH or classic LCIS

| partial involvement acini | Involves UDH | With Collagenous spherulosis | In Sclerosing adenosis |
|---------------------------|----------------------|------------------------------|------------------------|
| May mimic ADH | May mimic ADH or Low | Low grade DCIS | Invasive carcinoma |



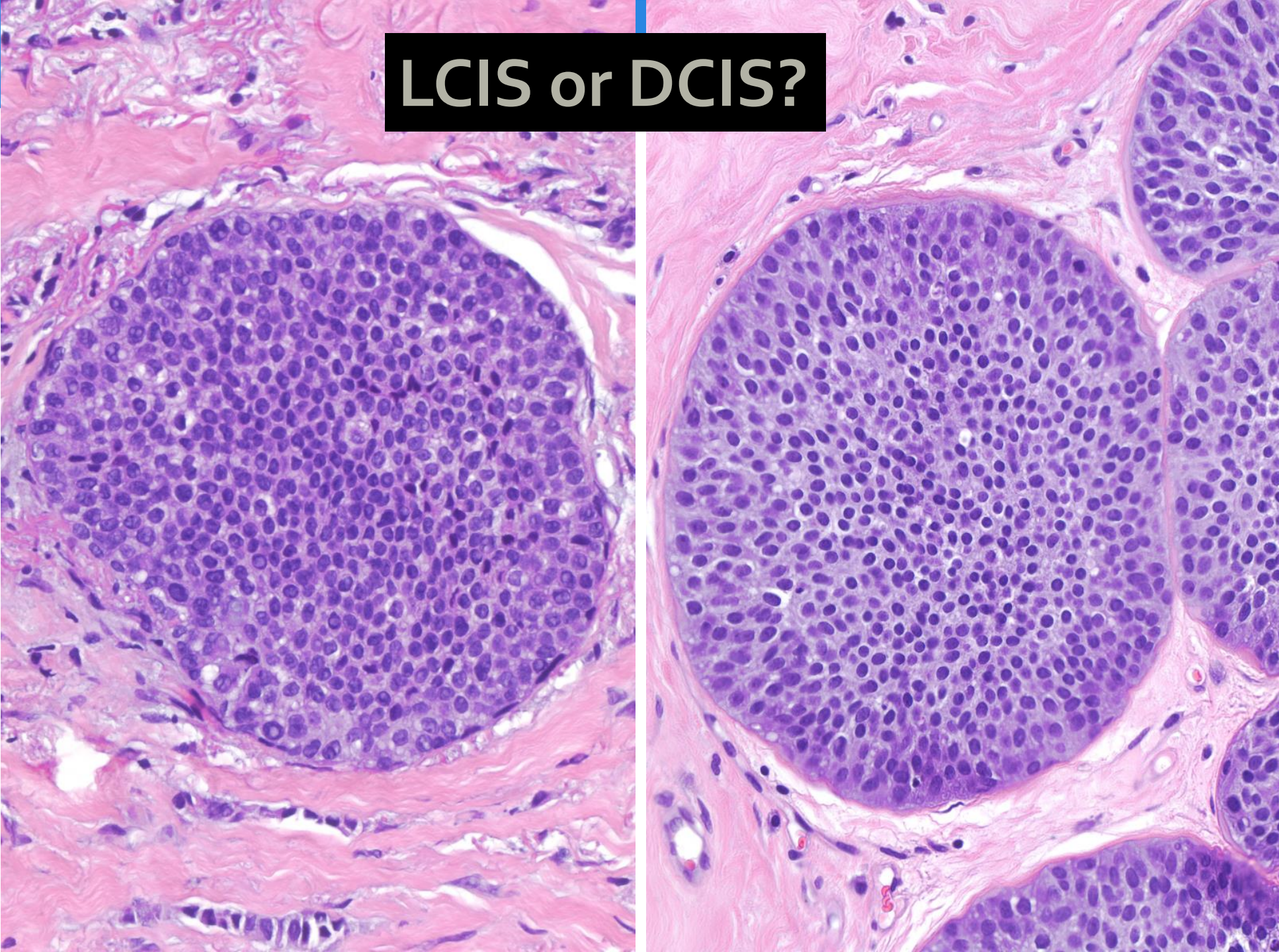
Classic LCIS/ ALH may mimic other lesions

**Classic LCIS can mimic
Solid Low Grade DCIS**
use E-cadherin/ p120

| | ALH or classic LCIS | | | |
|--------------|---------------------------------------|--|-------------------------|----------------------------|
| In ... | Normal acini (partial involvement) | UDH | Collagenous spherulosis | Sclerosing adenosis |
| May mimic... | ADH | UDH/ ADH/ Solid Low grade DCIS/ mammary carcinoma in situ | Low grade DCIS | Invasive lobular carcinoma |



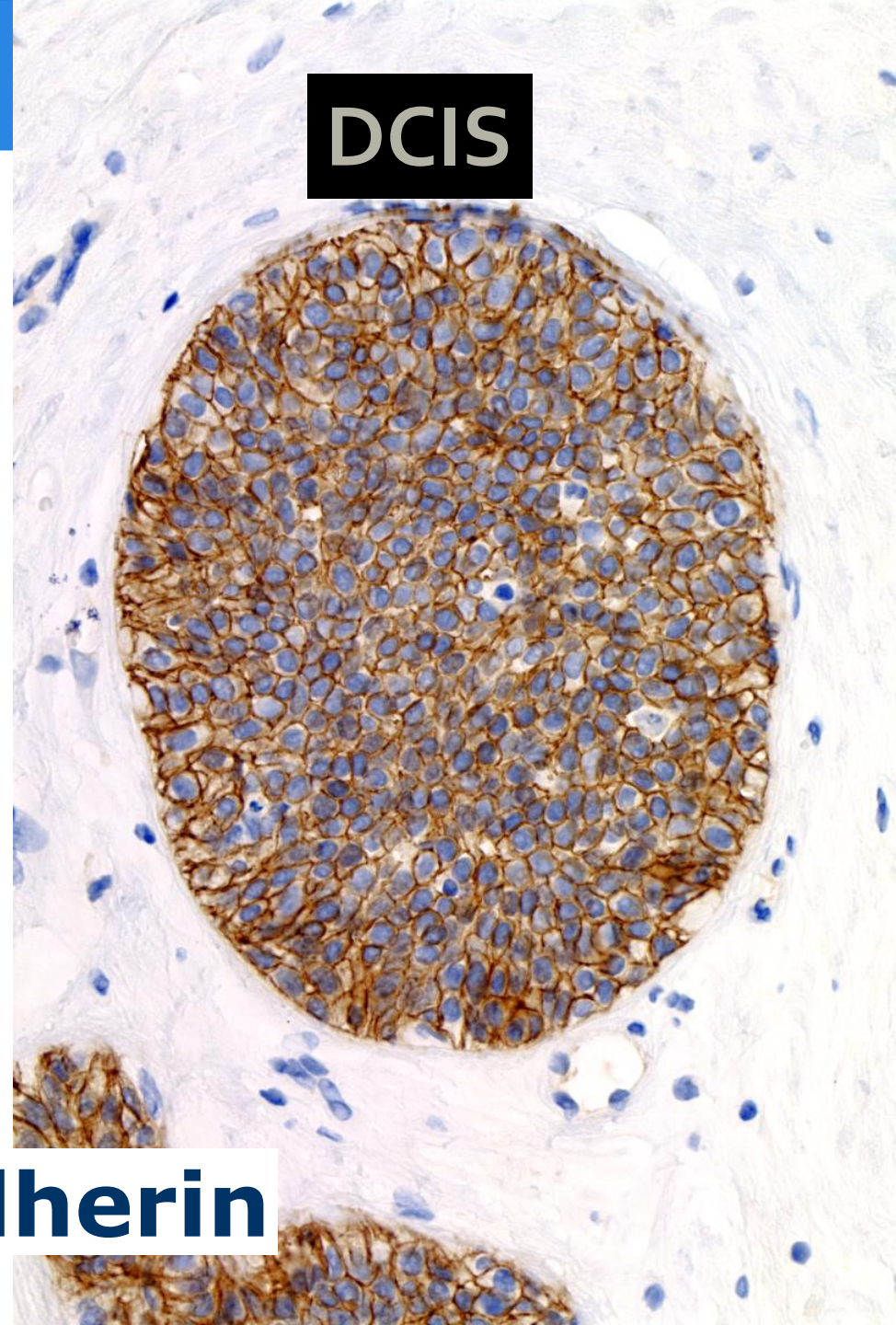
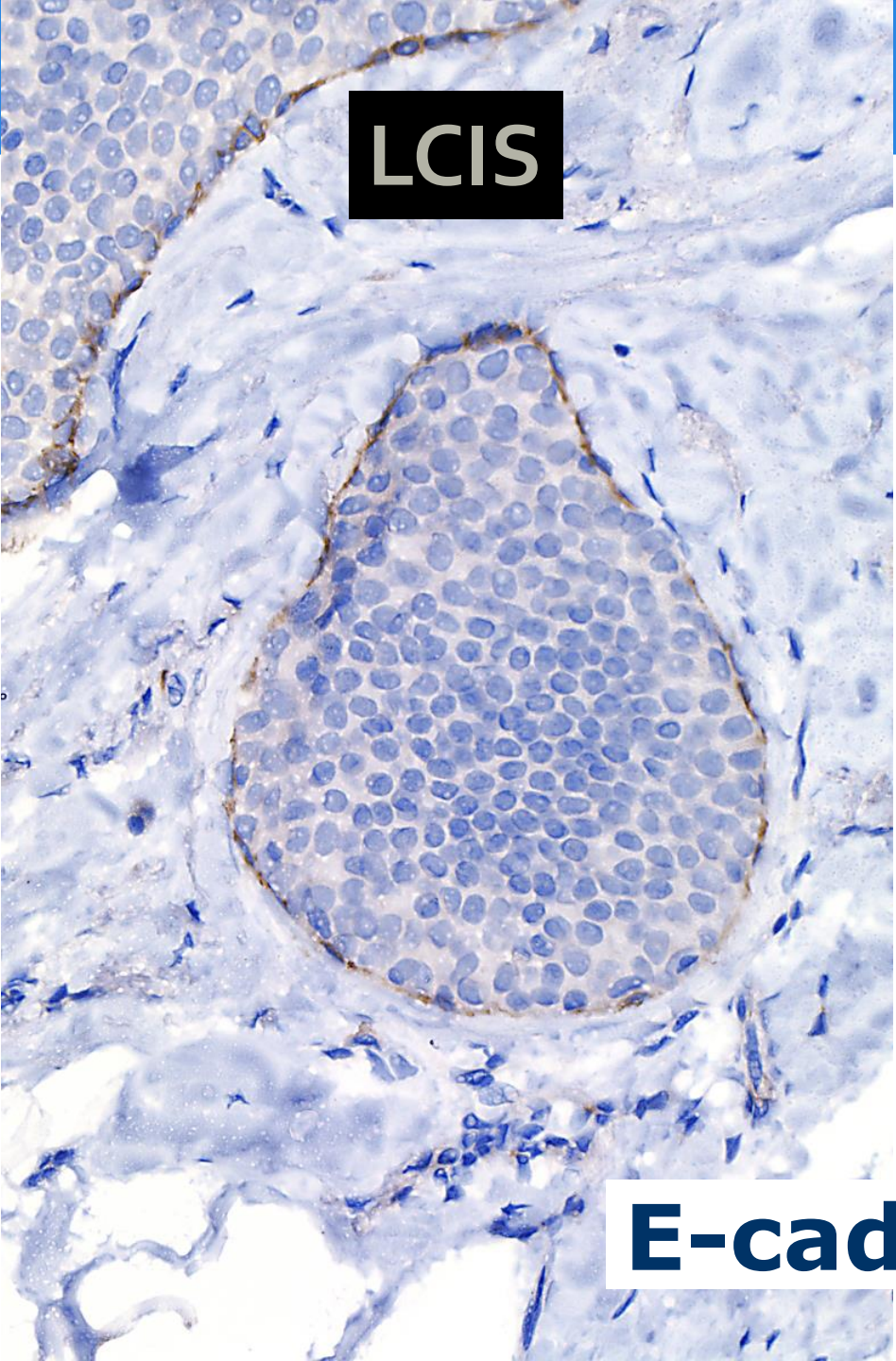
LCIS or DCIS?

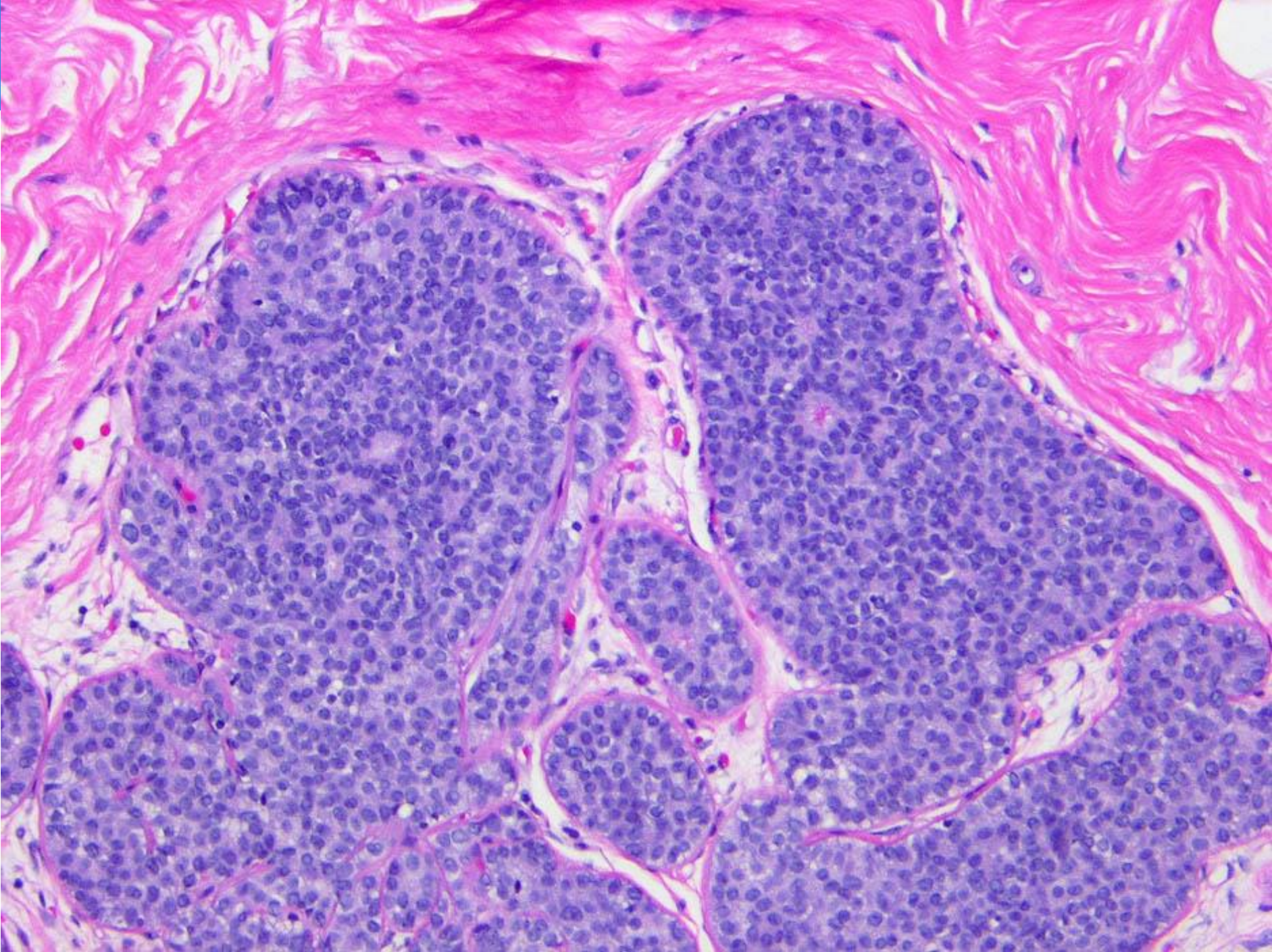


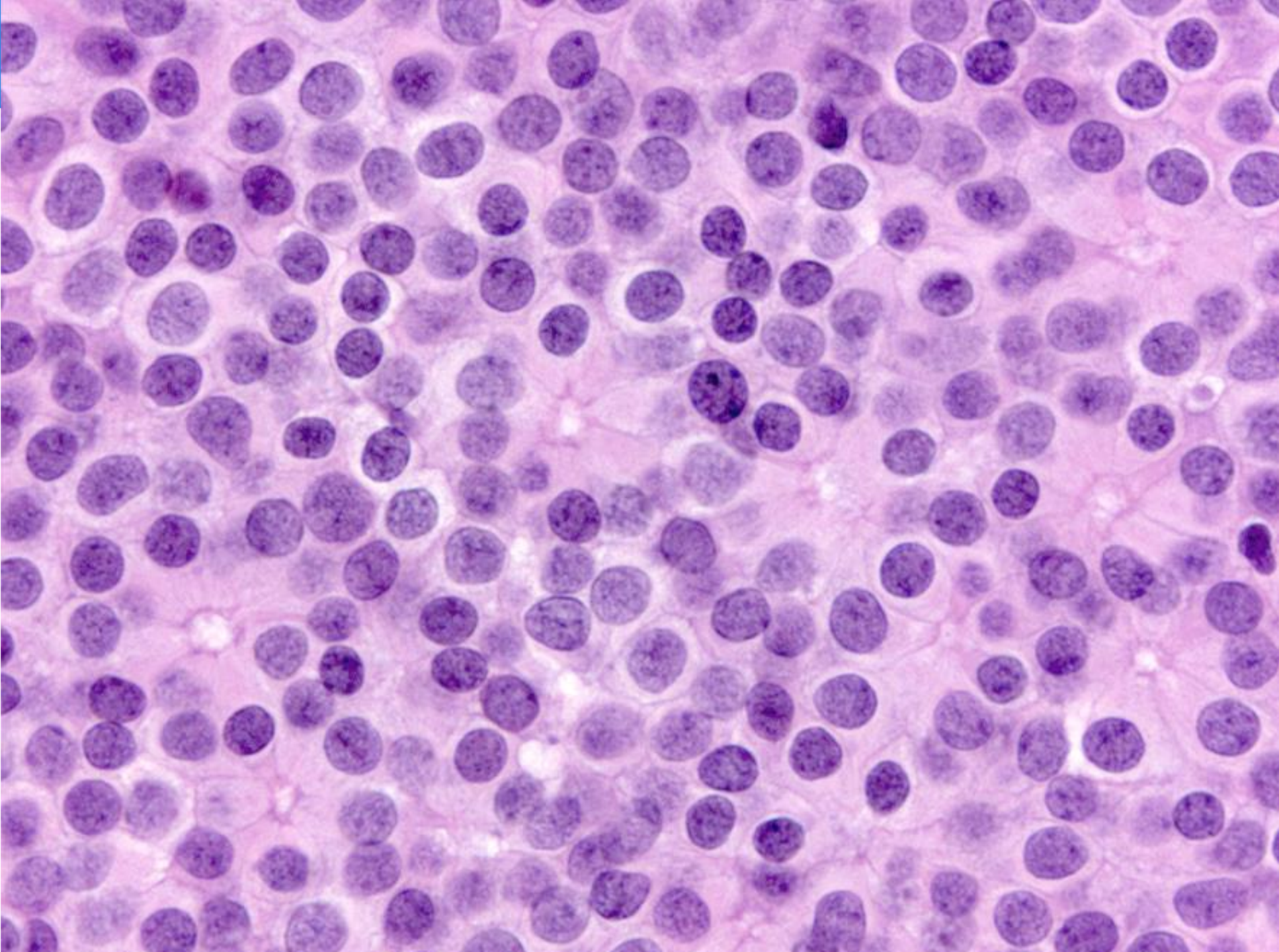
LCIS

DCIS

E-cadherin







Staging of LCIS

| | AJCC 7 th ed | AJCC 8 th ed |
|---|-------------------------|--|
| Classic LCIS (Florid LCIS) Pleomorphic LCIS | pTis (LCIS) | <ul style="list-style-type: none">• LCIS not classified as carcinoma in situ• Regarded as “benign” entity |

- P-LCIS (and F-LCIS) biology is not taken into account
- LCIS not recognized as non-obligate precursor of ILC

NCCN guidelines for Breast Cancer version 4.2022 – “Note: LCIS is a benign entity.”



American Joint Committee Cancer (AJCC) - Staging of LCIS

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| NCCN guidelines for Breast Cancer version 4.2022 – “Note: LCIS is a benign entity.” | | |

ESMO Staging recommendations for LCIS

| Diagnosis | Classification | Risk and management |
|---|---|--|
| Lobular neoplasia (formerly called LCIS) | Non-obligate precursor to invasive cancer | <ul style="list-style-type: none"> • Risk factor for subsequent invasive breast cancer (Relative Risk : 5.4-12) • Does NOT require surgical treatment • Radiotherapy not warranted for LCIS (except P-LCIS) |
| <i>Florid LCIS</i> | <i>Not mentioned</i> | <ul style="list-style-type: none"> • <i>Not mentioned</i> |
| Pleomorphic LCIS | "may behave similarly to DCIS..." | <ul style="list-style-type: none"> • "... and should be treated accordingly, after multidisciplinary discussion". • "... should be considered from a treatment perspective as high grade DCIS". (Radiotherapy recommended) |

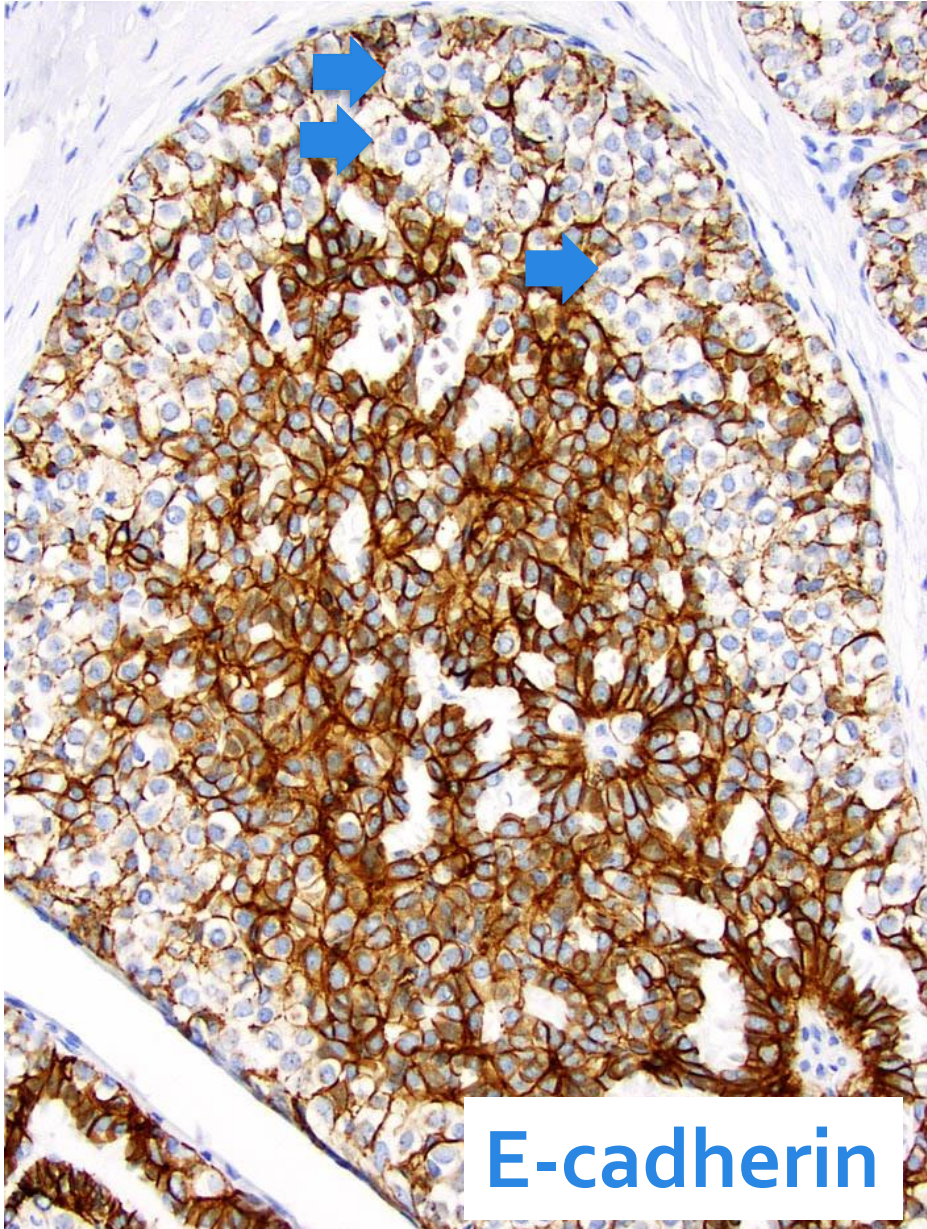
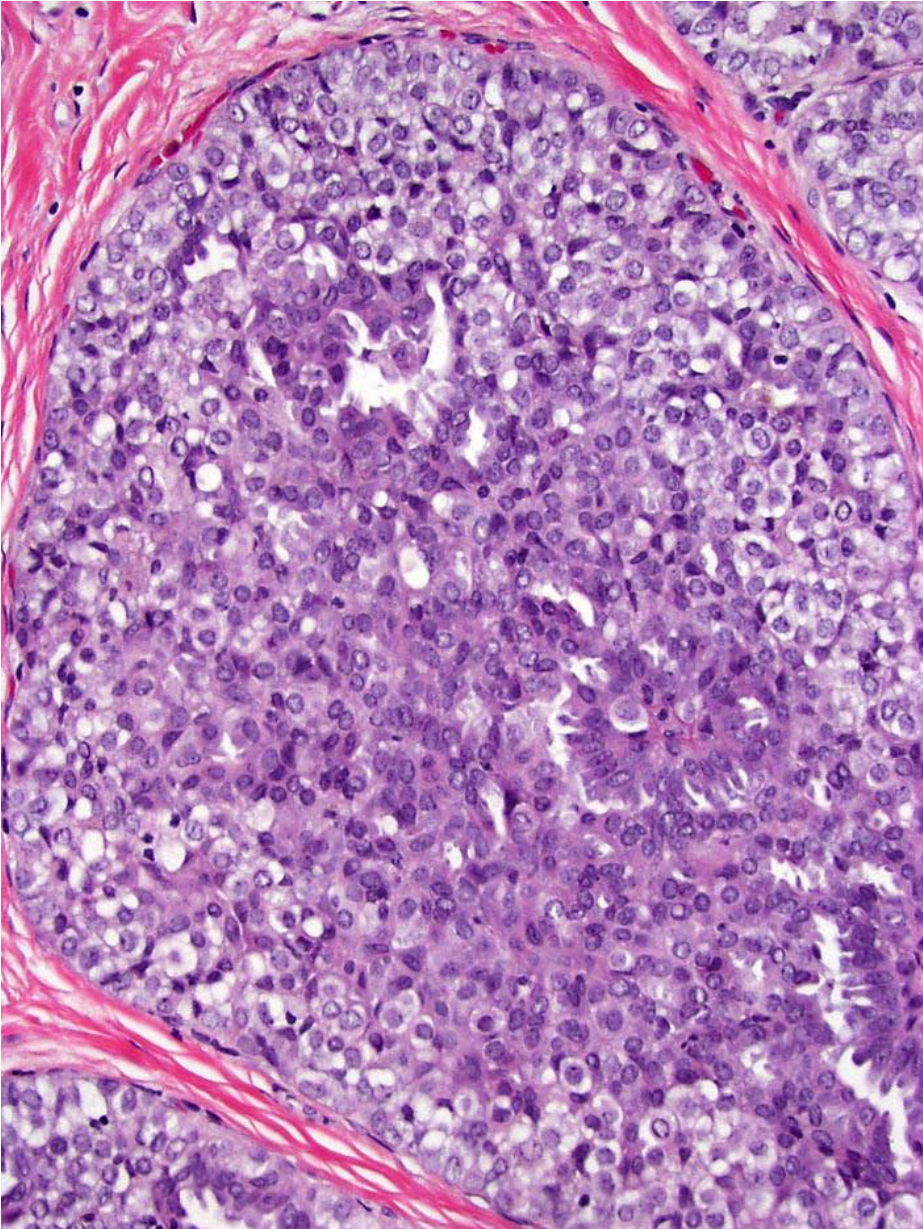
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ESMO Staging recommendations for LCIS

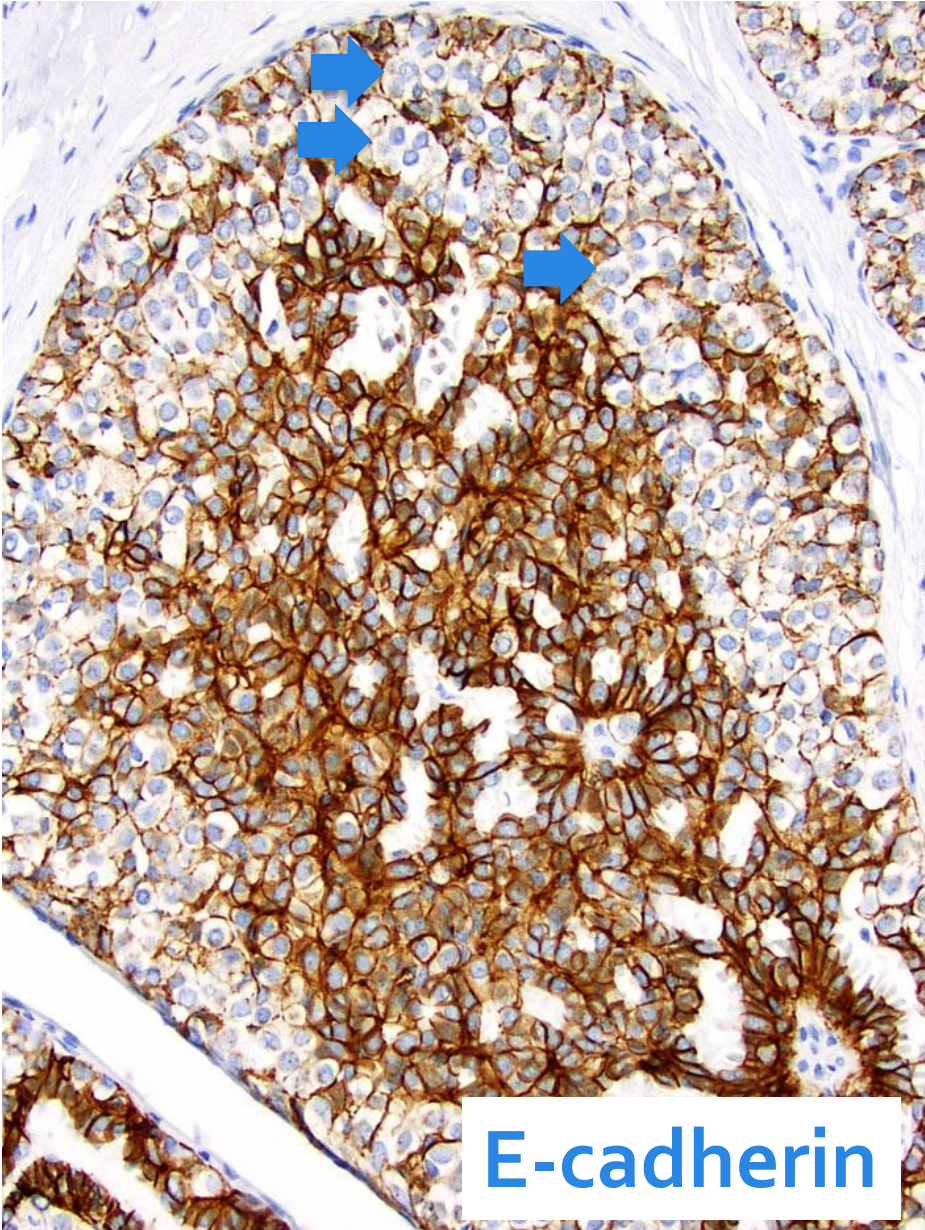
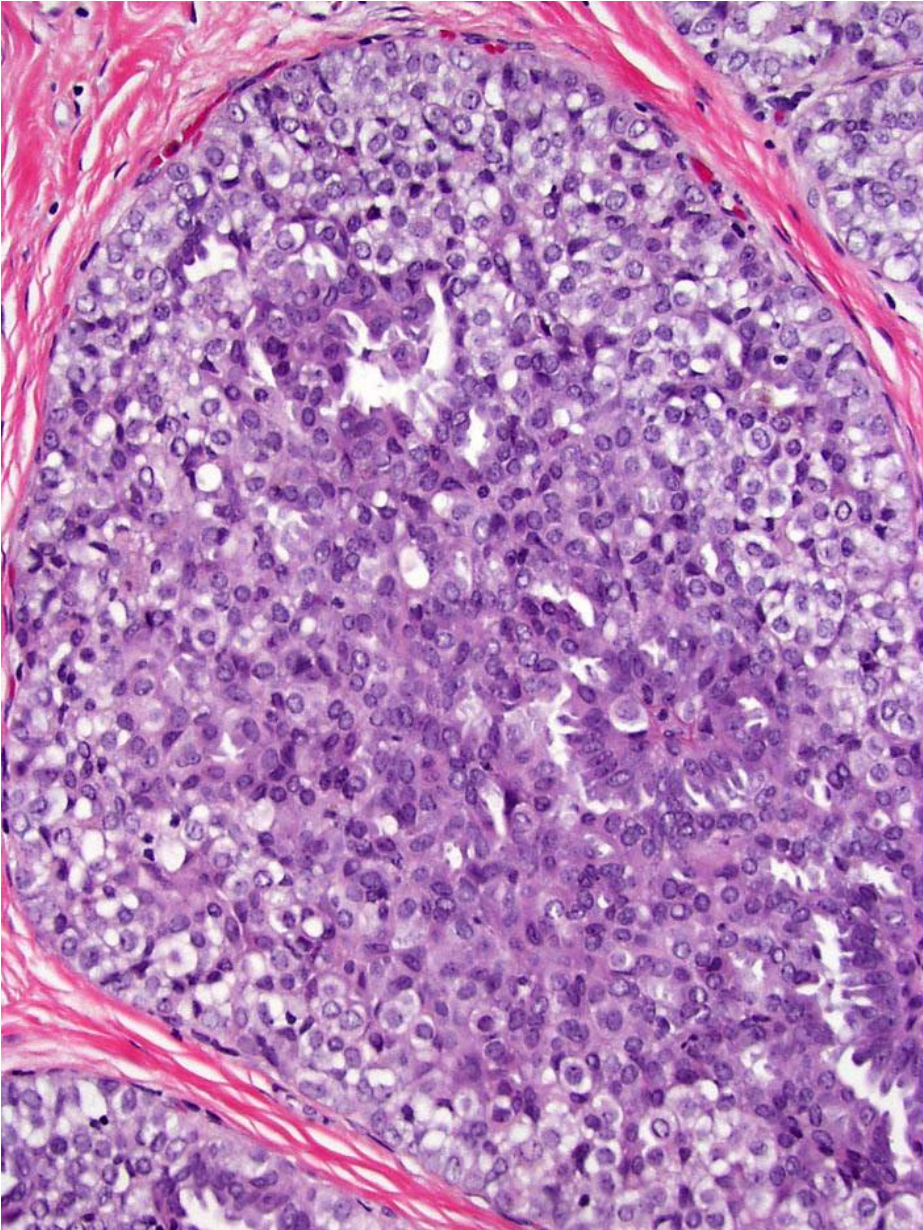
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Classic LN Involving Usual Ductal Hyperplasia



Classic LN Involving Usual Ductal Hyperplasia



Classic LCIS - long term follow-up studies

| Study | Cohort (years) | # | Median age | surgery | F/U (years) | Carcinomas at F/U | | Carcinoma Laterality | | |
|-----------------|---|-------|------------|--|-------------|-------------------------|--|---------------------------------------|---------------------------------------|-------|
| | | | | | | Patients with Carcinoma | Type of carcinoma | Ipsilateral | Contralateral | Bilat |
| Rosen 1978 | MSKCC 1940-1950 | 99 | 45 Y | | 24 | 29 (29%) | • IDC>ILC | Unclear | | |
| Page 1991 | Nashville Cohort 1950-1968 | 39 | 45 Y | | 19 | 9 (23%) | <ul style="list-style-type: none"> • 70% ILC • 2% Tubular • 10% IDC | 50% | 40% | 10% |
| King 2015 | MSKCC 1980-2009 | 1004 | 50 Y | | 6.75 | 150 (15%) | <ul style="list-style-type: none"> • 29% IDC • 35% DCIS • 27% ILC | 63% | 25% | 18% |
| Wong 2017 | SEER 1983-2014 | 19462 | 52 Y | | 8.1 | 1837 (9.4%) | <ul style="list-style-type: none"> • 42.4% IDC • 20.8% DCIS • 20% ILC | 55.2% 69% of ILCs 49.2% of IDCs | 44.5% 30% of ILCs 50.8% of IDCs | N/A |
| Van Maaren 2021 | Netherlands Cancer Registry (1989-2017) | 1890 | 51 Y | 505 None 904 BCS 193 Mastx 238 unkn | 8.5 | 318 (16.8%) | <ul style="list-style-type: none"> • 270 (14.2%) IBC • 48 (2.5%) DCIS | IBC in BCS pts 103 (64.8%) | IBCs in BCS pts 55 (34.6%) | NS |

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European perspective on the management of lobular lesions

VAB for classic LN: open excision for variant LCIS

Broad range of upgrade rates at EXC: 2% - 46%

Table 5 Summary of the recent literature on LN since 2015

| Author and year | Number of patients analyzed or type of publication if no patients have been analyzed (e.g., review or comment) | Findings | Conclusions |
|-----------------------------|--|---|--|
| Calhoun et al. 2016 [50] | n=76 on CNB Upgrade after 15 years follow-up | 10 cases (13%) with upgrade | The extent of LN in CNB may be an indicator of the likelihood of upgrade to carcinoma |
| Donaldson et al. 2018 [15] | n=393 on CNB with ADH/LN Upgrade rate and follow-up (87 months) | Upgrade in n=181 (46%) The 7-year cumulative breast cancer incidence was 9.9% | Multiple foci do not influence BC development Close clinical and radiologic follow-up for more than 5 years in this patient population |
| Fives et al. 2016 [51] | n=25 LN on CNB accompanying fibroadenomas | Upgrade in 1 case (5%) | Rare upgrade |
| King et al. 2015 [40] | n=1004 with /wo chemoprevention Median follow-up 81 months | 10-Year cumulative risk 7% With chemoprevention 21% (3.2% per year) with no chemoprevention | Chemoprevention reduced BC risk Volume of disease, (ratio of slides with LCIS to total number of slides) was associated with breast cancer development (p=0.008) |
| Mao et al. 2017 [52] | BC risk in LN -Hormone receptor status -Skin color | | LN was higher in HR positive and in black patients |
| Maxwell et al. 2016 [53] | n=392 pure LN 326 with OE | Upgrade to pleomorphic LN In 23/326 cases (7%) | Screen detected LN -In younger women -Unilateral -Non-pleomorphic |
| Nakhlis et al. 2016 [54] | n=77 on CNB | Upgrade in 2 of 77 cases (2%) | Routine excision is not indicated for patients with pure LN on CB and concordant imaging findings |
| Renshaw and Gould, 2016 [4] | n=69 CNB with LN Upgrade Follow-up | Upgrade in 17 of 69 cases (25.8%) | Immediate BC risk is higher for ADH than LN Long-term BC risk is higher for LN than ADH |
| Schmidt et al. 2018 [55] | n=178 on CNB 115 OE 54 Surveillance (55 months follow-up) | Upgrade in 13/115 cases (11%) 1/54 Cases developed BC after follow-up (2%) | Low-upgrade rate and low BC risk |
| Sen et al. 2016 [56] | n=447 (ALH and LCIS) | Upgrade ALH 2.4% Upgrade LCIS 8.4% | Excision is recommended for LCIS on CNB and for ALH surveillance at 6, 12, and 24 months |
| Susnik et al. 2016 [47] | n=302 of 370 Upgrade after OE | Upgrade In 3.5% (8/228) pure LN lesions In 26.7% in "LCIS variants" (4/15) in 28.3% in LN with ductal atypia (15/53) | LN with non-classic morphology or with associated ductal atypia requires surgical excision, this can be avoided in pure LN |
| Xie et al. 2017 [57] | Survival outcome in SEER database (n=208+5756 cases) Bilateral or partial mastectomy | OS after partial mastectomy without radiotherapy was not inferior to patients who underwent bilateral prophylactic mastectomy | Low breast cancer-specific mortality in patients with LCIS, therefore aggressive prophylactic surgery like bilateral prophylactic mastectomy should not be advocated for most patients with LCIS |

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Consensus recommendation of the panel

A lesion containing classical LN, which is visible on imaging should undergo excision with VAB. Thereafter surveillance is justified if there is no pathological–radiological discordance and no residual lesion.

In contrast, morphologic variants of LN (LIN 3, pleomorphic LCIS, and florid LCIS), which are reported as B5a lesions should undergo OE

B₃ lesions- consensus recommendations

| | Diagnosis made by CNB | Diagnosis made by VAB |
|-----|---|--|
| ADH | OE | OE. surveillance can be considered in a few special situations after discussion at the MDM |
| FEA | VAB to complete removal of the lesion visible in any imaging method | Surveillance is justified if the radiological lesion has been removed |
| LN | OE or VAB (remove US-visible lesion) | OE or high-risk surveillance if the radiological lesion has been removed |
| PL | Remove by VAB | |
| PT | OE. Free margins in borderline and malignant PTs | Follow-up in completely excised benign PTs surveillance is justified |
| RS | VAB or OE of visible lesion | Surveillance is justified if the radiological lesion has been removed |

VAB usually the lesion should not exceed 2.5 cm in diameter. For larger lesions, OE is preferred, LN only classical type. LN pleomorphic, LIN 3, LN extended, and LN with necrosis are defined as B5a lesions and should undergo OE, PL with atypia: Such a lesion should not be classified as papilloma, but rather as FEA or ADH according to the type of atypia found

OE = open excision

VAB = vacuum-assisted biopsy

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European multidisciplinary expert panel


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Table 9 Summary of the voting for each pure B3 lesion

| | A diagnosis of a visible (on imaging by mammography or ultrasound) lesion by means of spring-loaded core biopsy (14–18 g) has been made | | | What method of excision should be chosen | | | A lesion has been removed by means of VAB and the lesion on imaging seems to be removed | | | |
|-----|---|----------------------------------|-------------------|--|---------------------------------|-------------------|---|----------------------------------|---------------------------|-------------------|
| | The lesion should be removed | The lesion should not be removed | Undecided/abstain | VAB is acceptable | Open biopsy should be preferred | Undecided/abstain | An open re-excision should be performed | A repeat VAB should be performed | Wait and see is justified | Undecided/abstain |
| ADH | 35 (100%) | 0 | 0 | 8 (21.1%) | 28 (73.7%) | 2 (5.3%) | 20 (51.3%) | 0 | 18 (46.2%) | 1 (2.6%) |
| FEA | 43 (65.2%) | 14 (21.2%) | 9 (13.6%) | 51 (75%) | 15 (22.1%) | 2 (2.9%) | 2 (2.9%) | 0 | 67 (97.1%) | 0 |
| LN | 46 (68.7%) | 9 (13.4%) | 12 (17.9%) | 34 (50%) | 28 (41.2%) | 6 (8.8%) | 8 (11.6%) | 0 | 58 (84.1%) | 3 (4.3%) |
| PL | 39 (76.5%) | 9 (17.6%) | 3 (5.9%) | 37 (71.2%) | 12 (23.1%) | 3 (5.8%) | 0 | 0 | 52 (98.1%) | 1 (1.9%) |
| PT | 48 (98%) | 1 (2%) | 0 | 11 (22%) | 36 (72%) | 3 (6%) | 4 (7.8%) | 0 | 45 (88.2%) | 2 (3.9%) |
| RS | 28 (59.6%) | 15 (31.9%) | 4 (8.5%) | 37 (80.4%) | 7 (15.2%) | 2 (4.3%) | 2 (4.3%) | 0 | 42 (89.4%) | 3 (6.4%) |

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F-LCIS and/or P-LCIS at CNB: Excision warranted

F-LCIS

Not specifically mentioned in continental Europe and UK guidelines

Usually classified as

B₄ (suspicious of malignancy) (UK)

OR

B_{5a} (malignant in situ)

P-LCIS

- Classified as B_{5a} (malignant in situ) according to continental Europe and UK guidelines

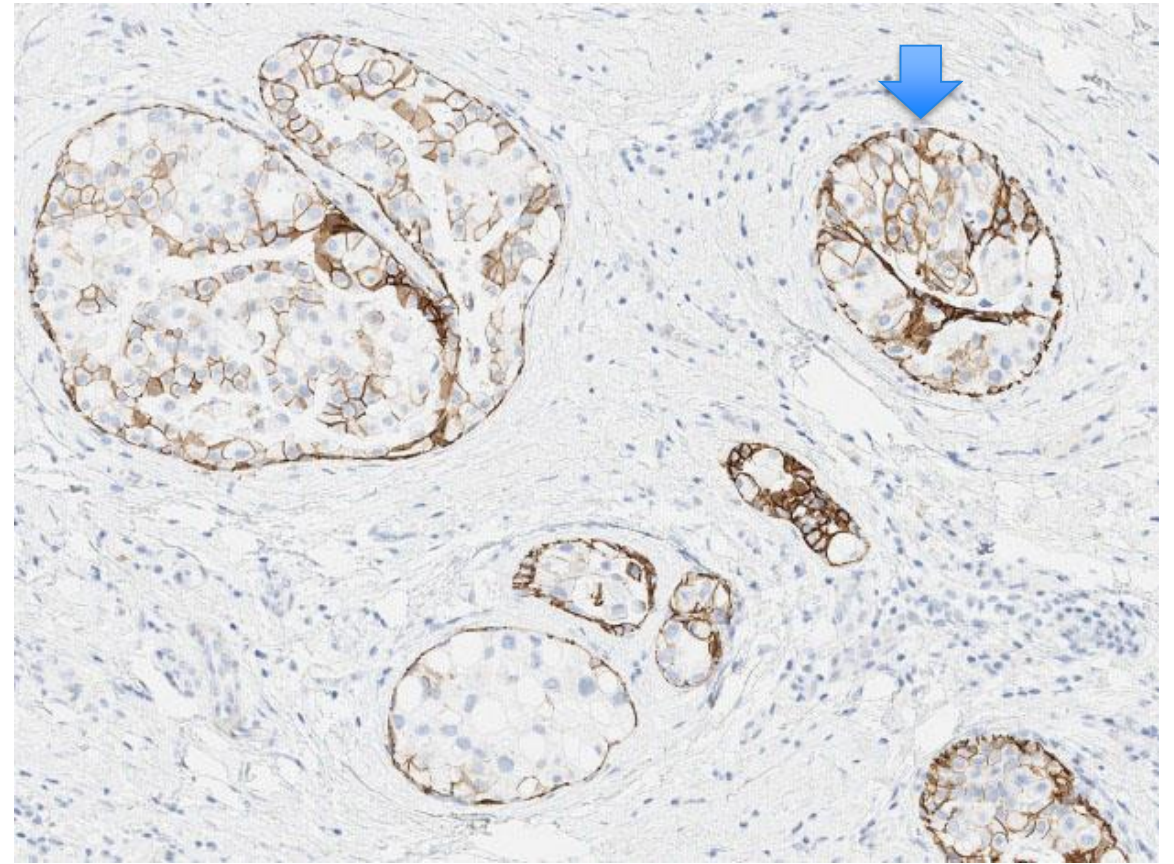
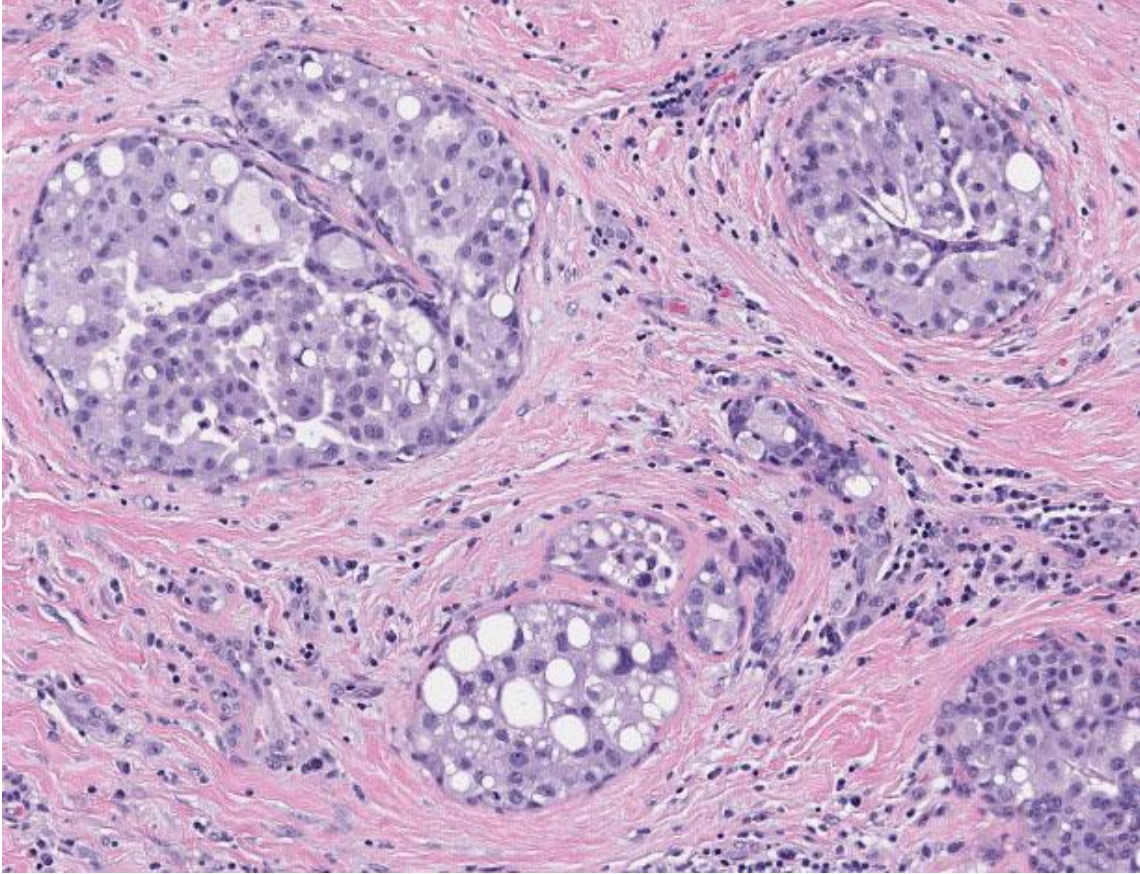
European guidelines for quality assurance in breast cancer screening and diagnosis Fourth Edition, 2006. https://screening.iarc.fr/doc/ND7306954ENC_002.pdf

Royal College of Pathologists. Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening. 2021 https://www.rcpath.org/uploads/assets/4b16f19c-f7bd-456c-b212f557f8_04of66/G150-Non-op-reporting-breast-cancer-screening.pdf



E-cadherin expression patterns in F-LCIS and P-LCIS

- Focal cohesive clusters with focal weak membrane stain



E-cadherin expression patterns in F-LCIS and P-LCIS

- Complete loss (most common)

