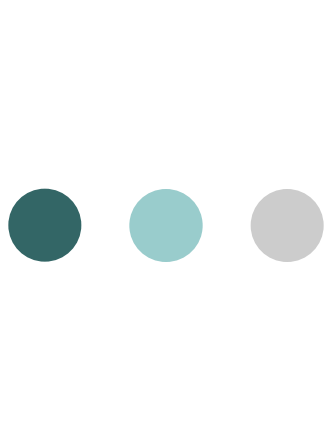
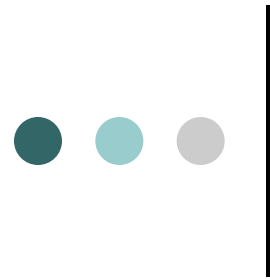




Breast Pathology

Elena Provenzano



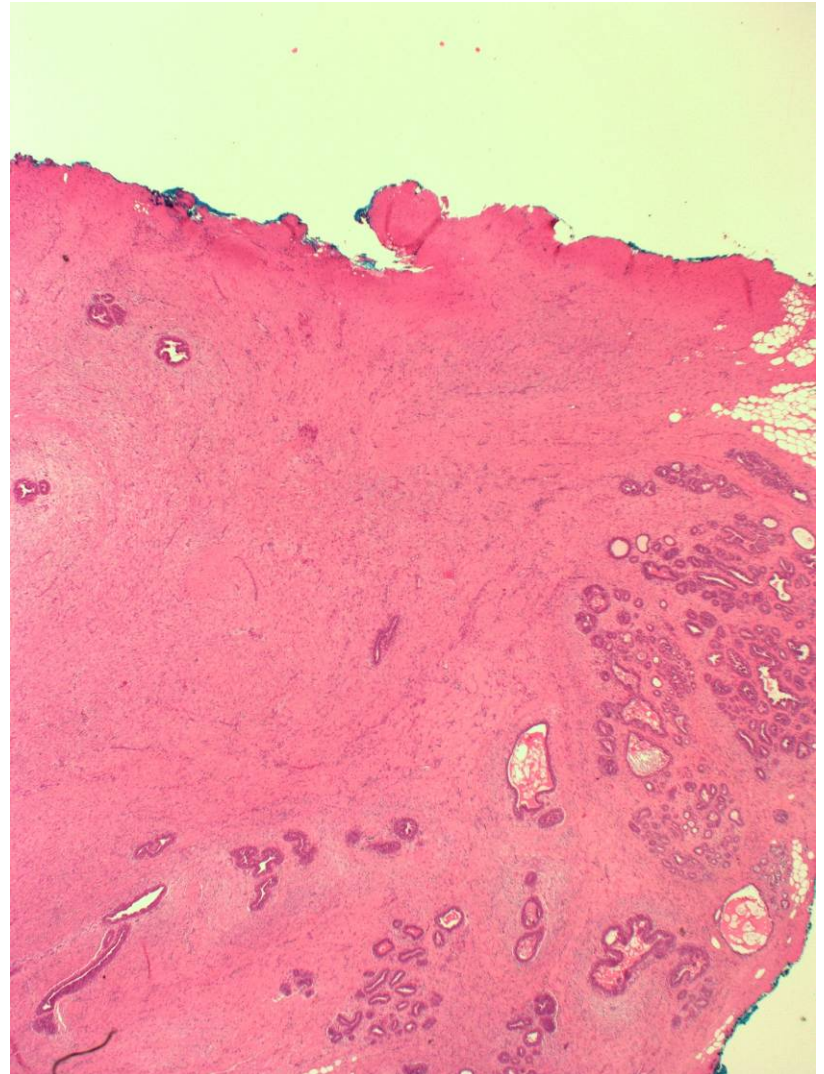
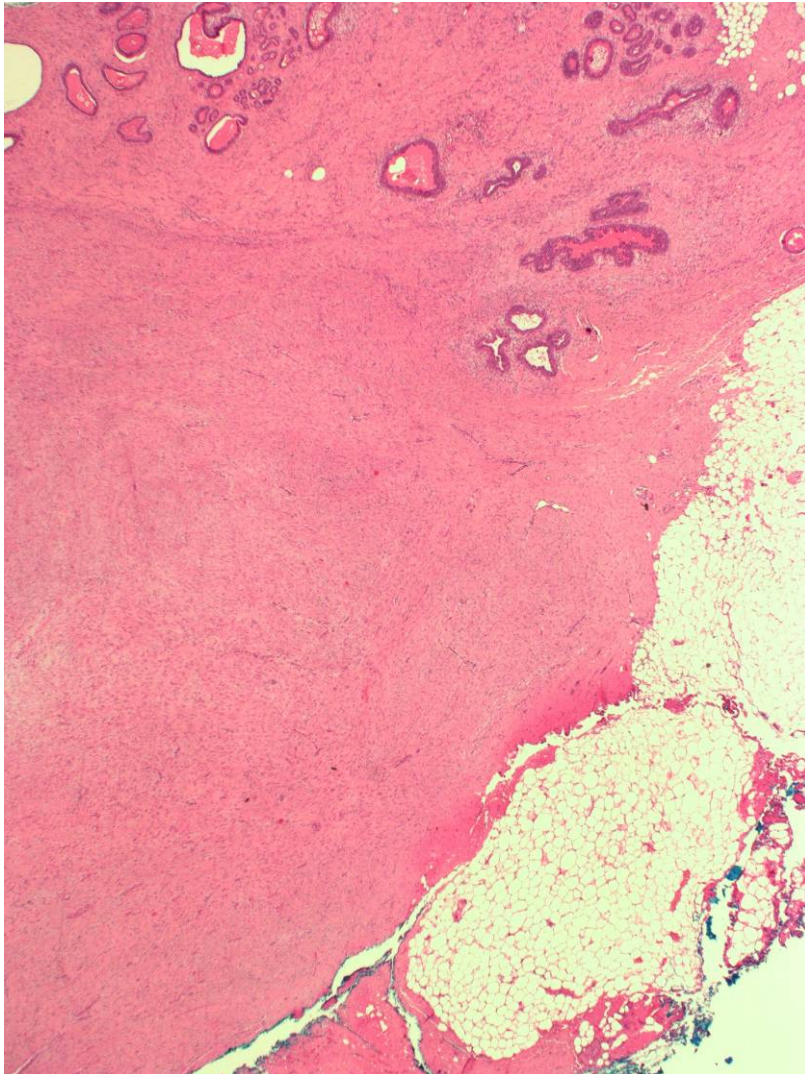
Case 1:

46 yo female.

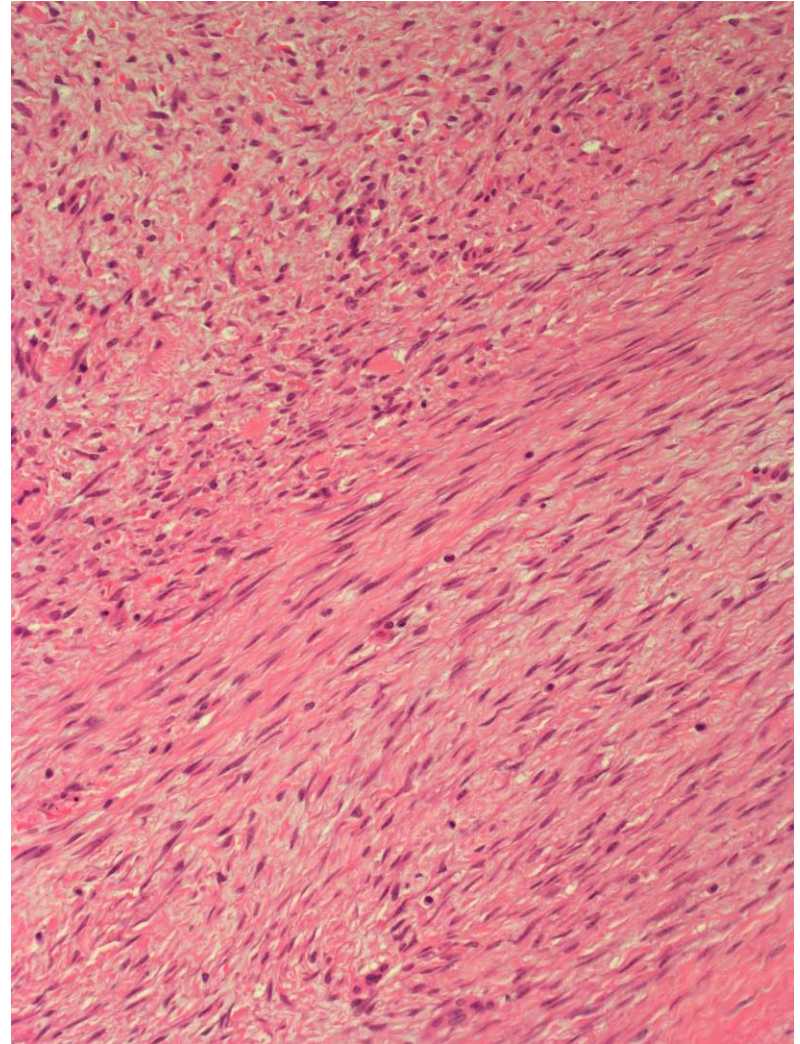
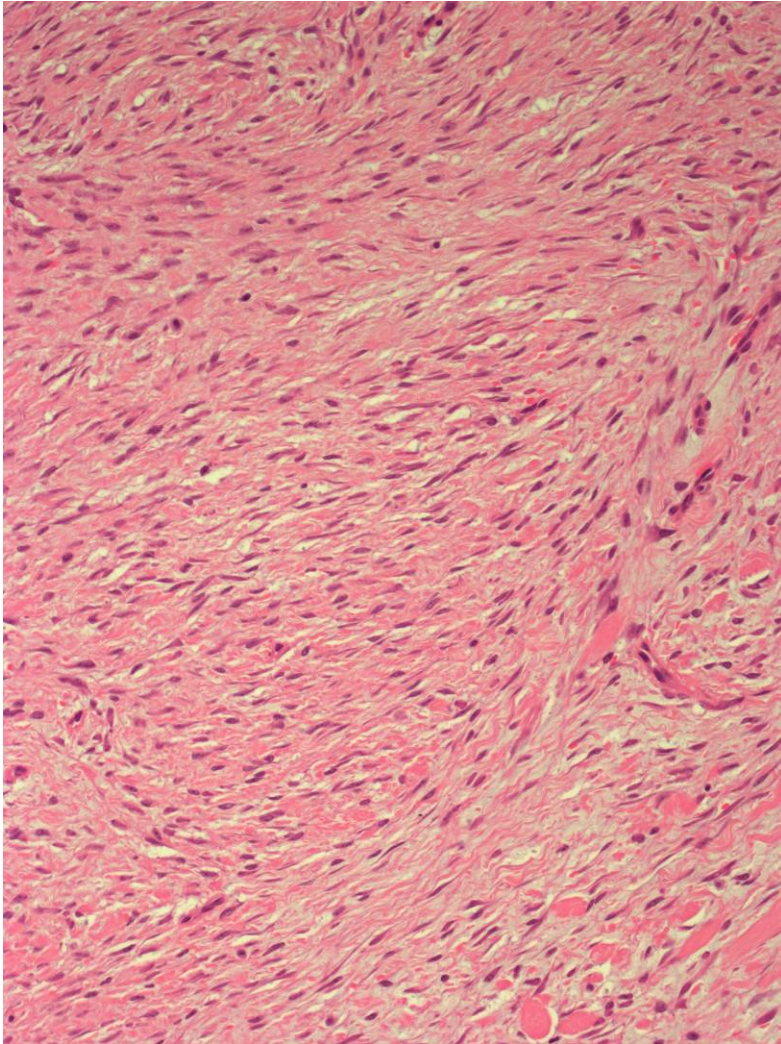
**Hx Familial Adenomatous
Polypsis.**

Lump R breast.

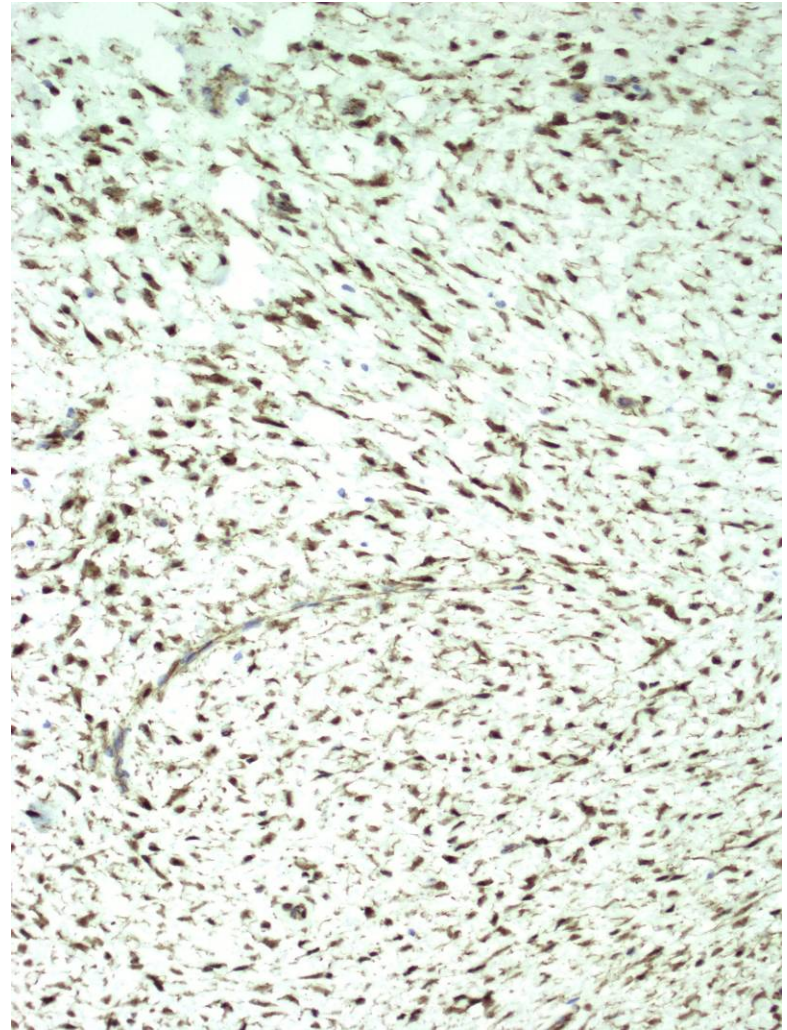
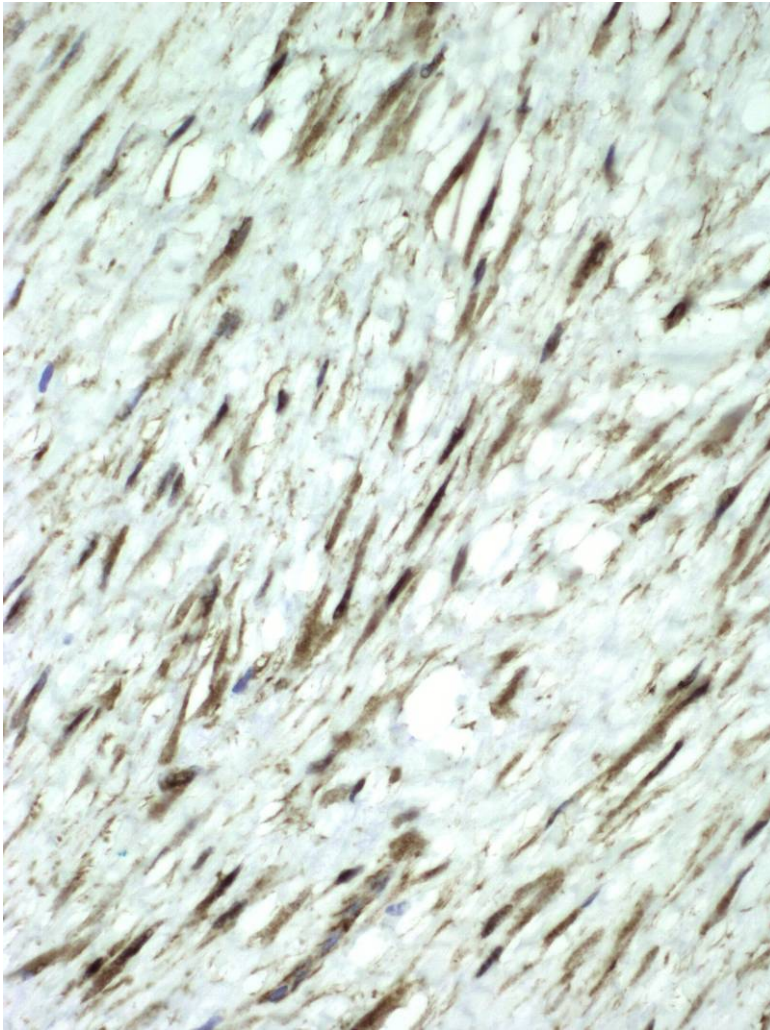
Case 1:



Case 1:

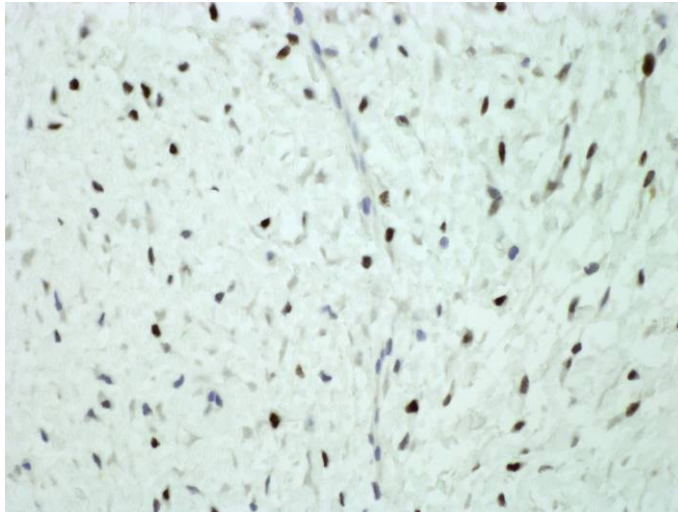


Case 1: B catenin

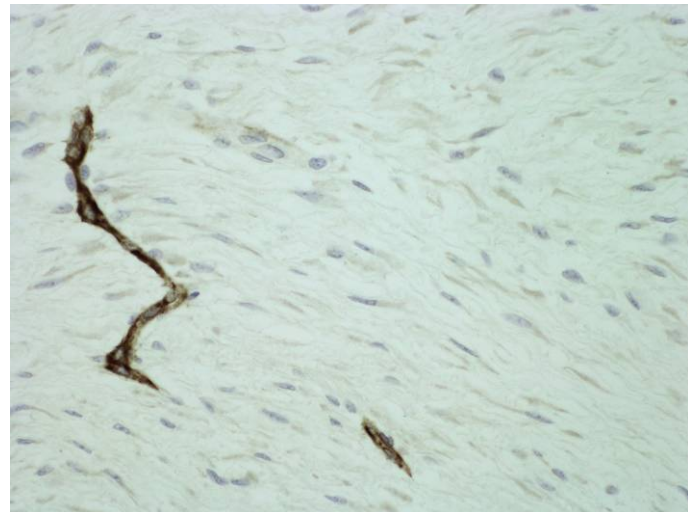


Case 1:

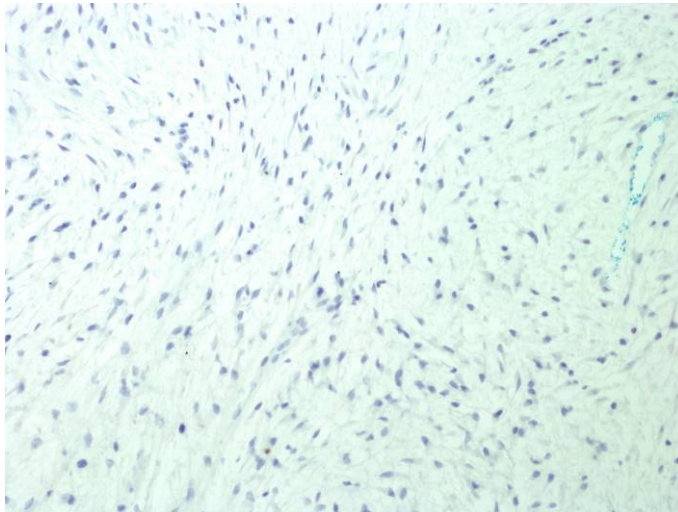
ER



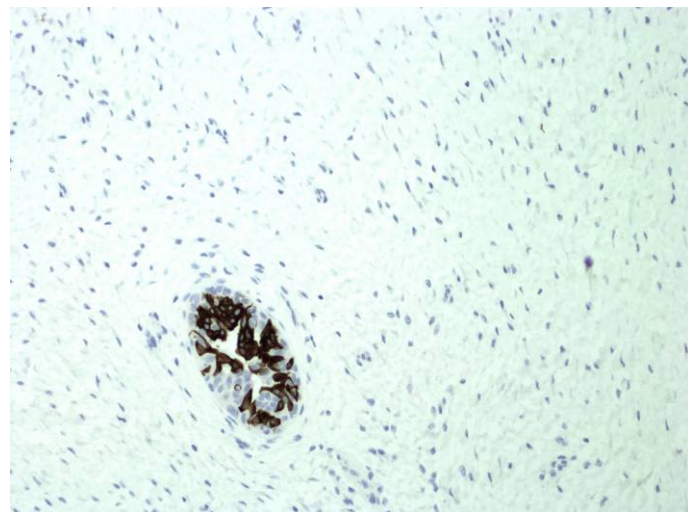
CD34

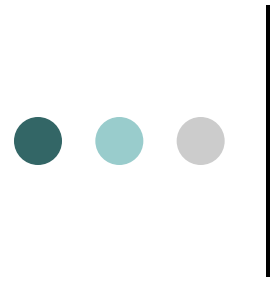


CK MNF



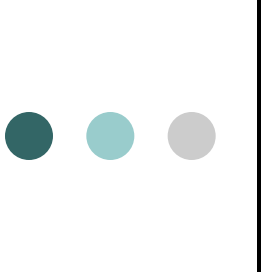
CK 5/6





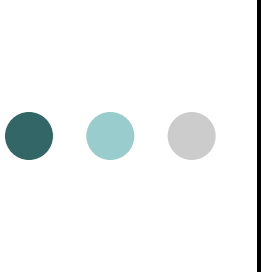
Case 1:

Fibromatosis



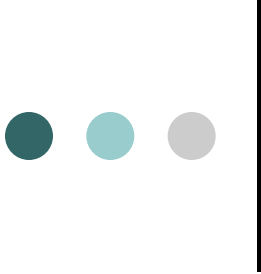
Fibromatosis

- Long intersecting fascicles of bland spindled cells
- Infiltrative edge invades around pre existing structures
- Nuclear β -catenin expression in 80% (but may also be seen in PT, spindle cell ca)
- Can be ER positive
- Negative for CD34, cytokeratins



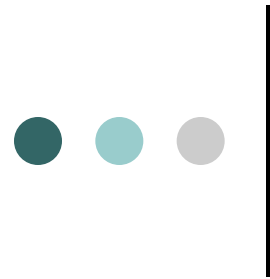
Fibromatosis

- DDx
- Scar – look for foamy macrophages, haemosiderin, fat necrosis
- Spindle cell ca – cytological atypia, epithelioid foci, DCIS, CK positivity
- Myofibroblastoma – CD 34 positive



Fibromatosis

- Locally infiltrative benign neoplasm
- Local recurrence in 20-30%
- Reports of spontaneous regression
- Association with previous trauma including surgery, implants
- Can be seen in patients with FAP but majority in breast sporadic
- Activating mutations in β -catenin gene in 45%
- APC gene mutation or 5q loss in 33%

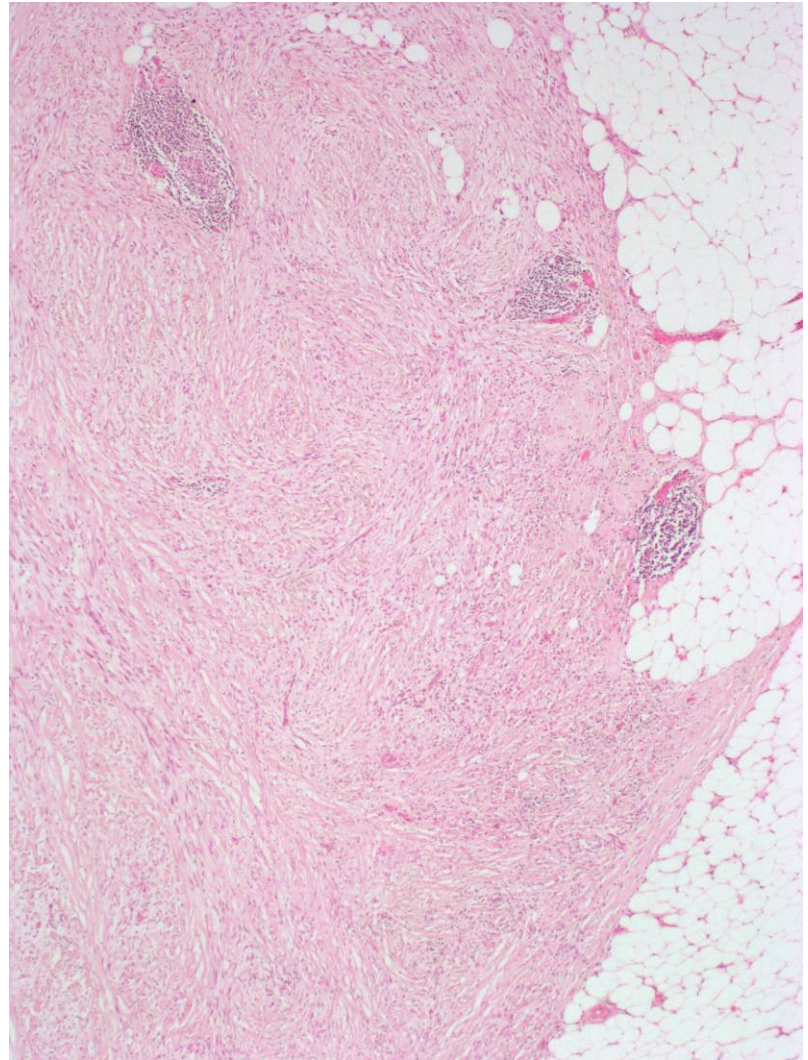
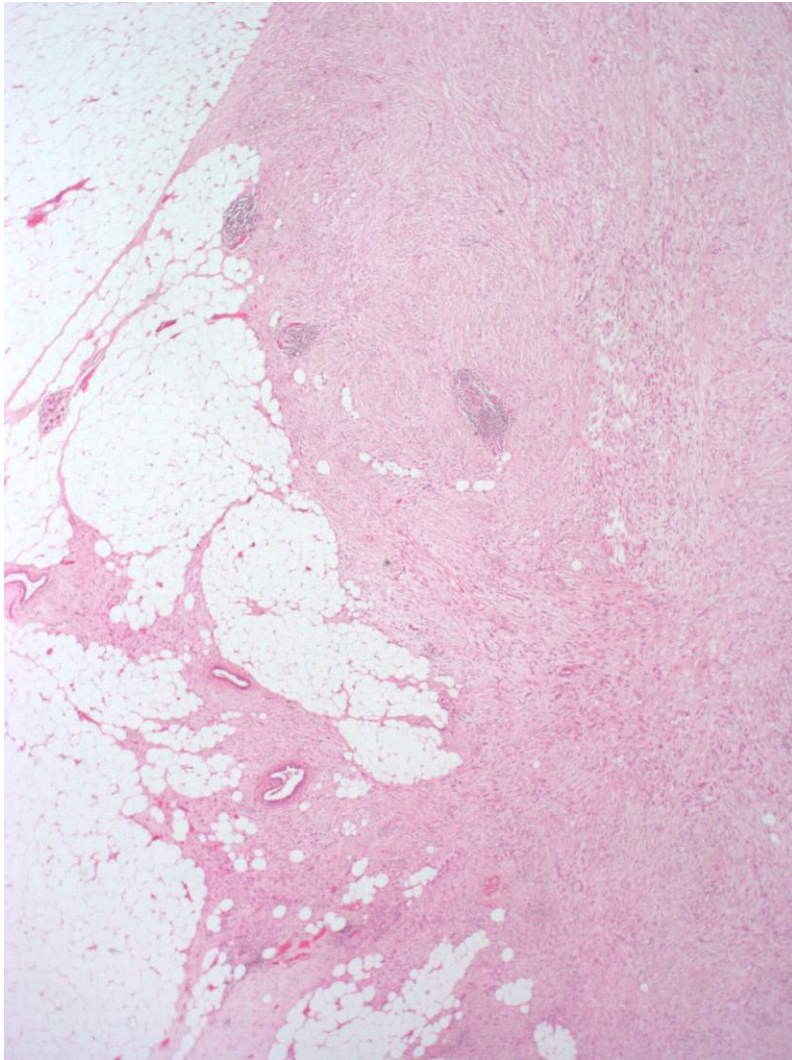


Case 2:

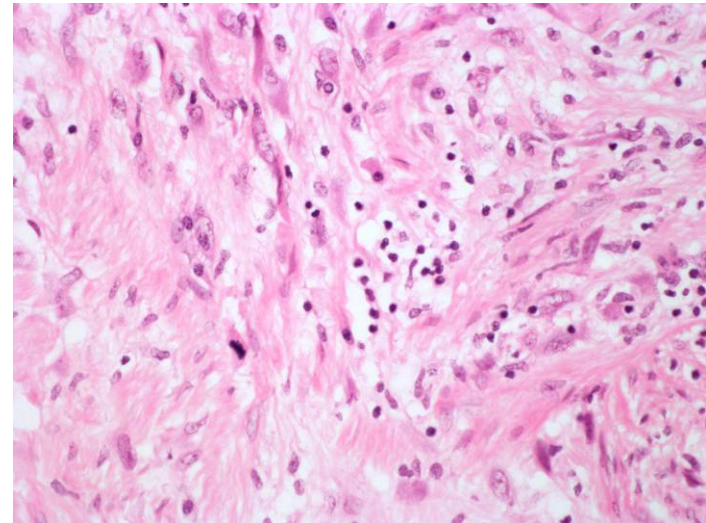
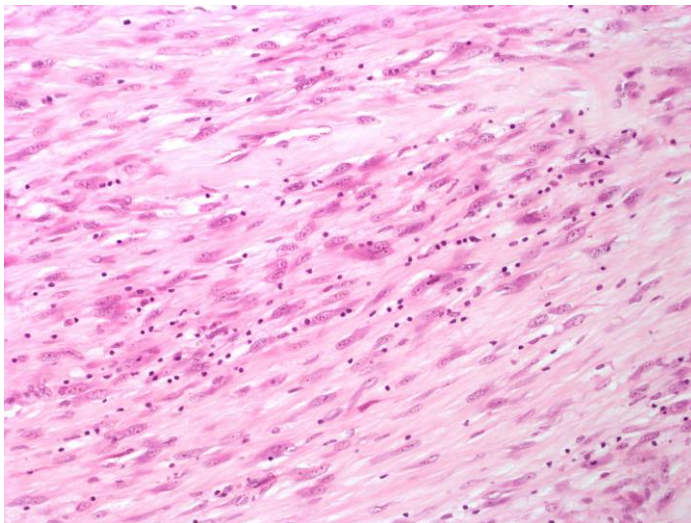
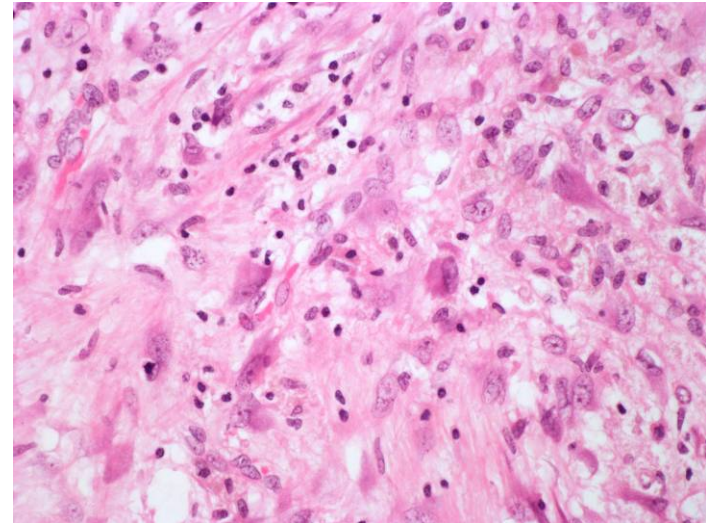
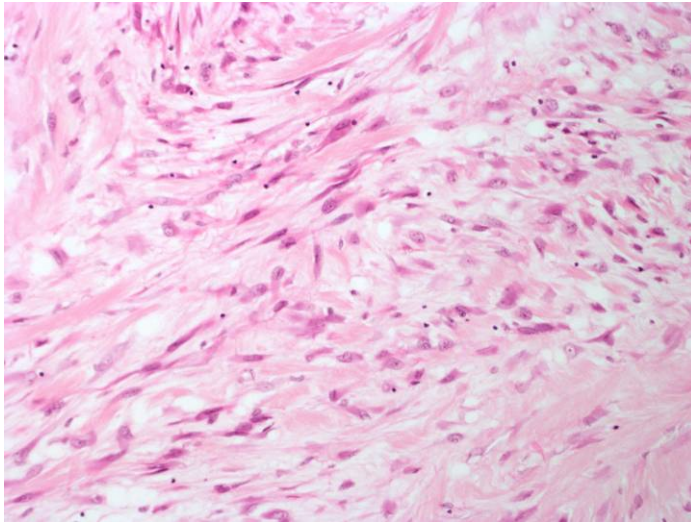
75 yo female.

Central L breast lump.

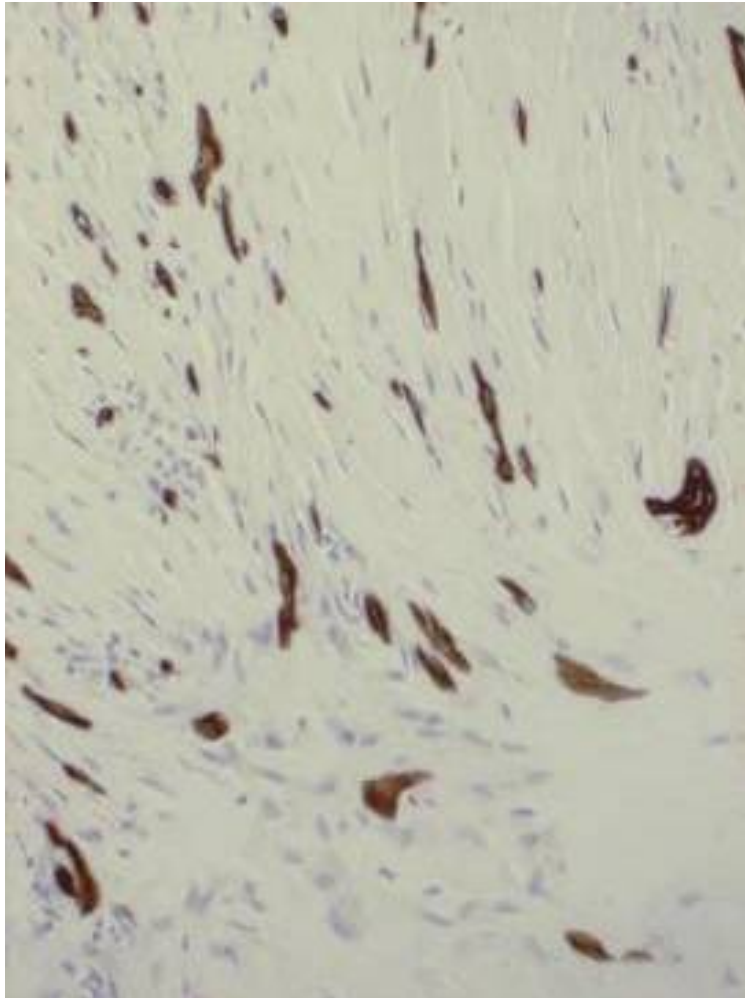
Case 2:



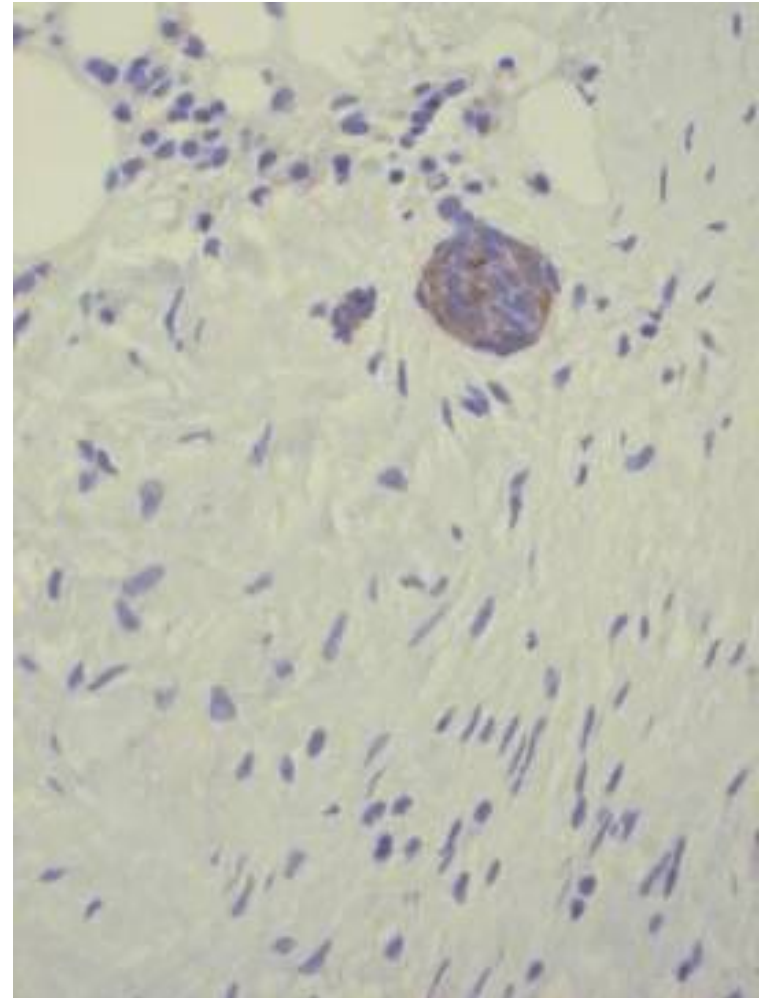
Case 2:



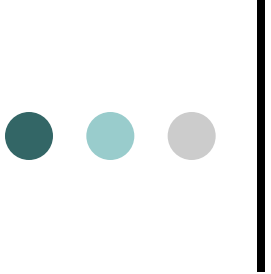
Case 2:



CK MNF 116

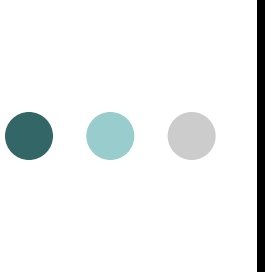


CK AE1/ AE3



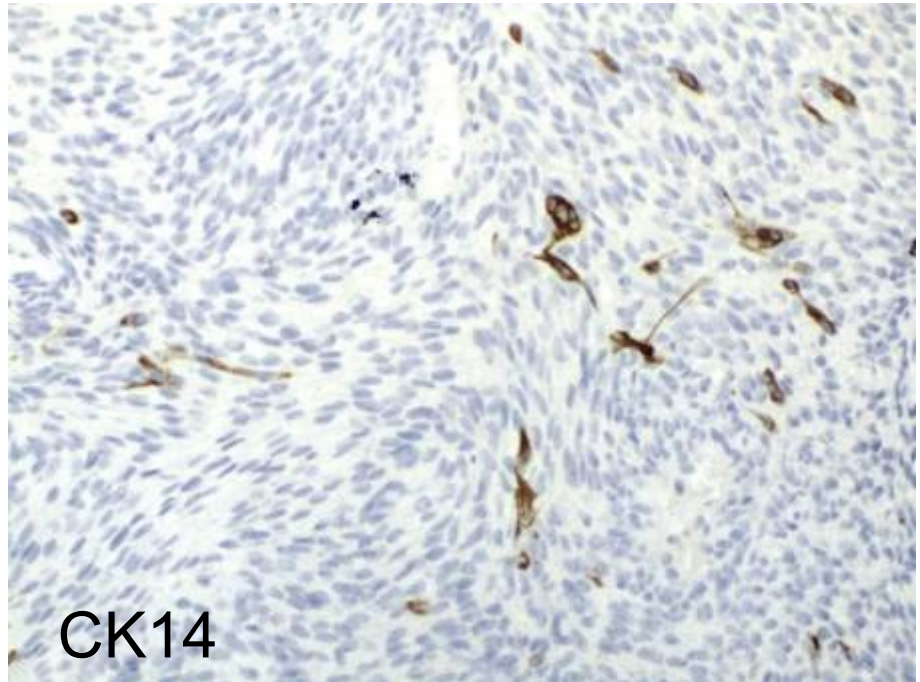
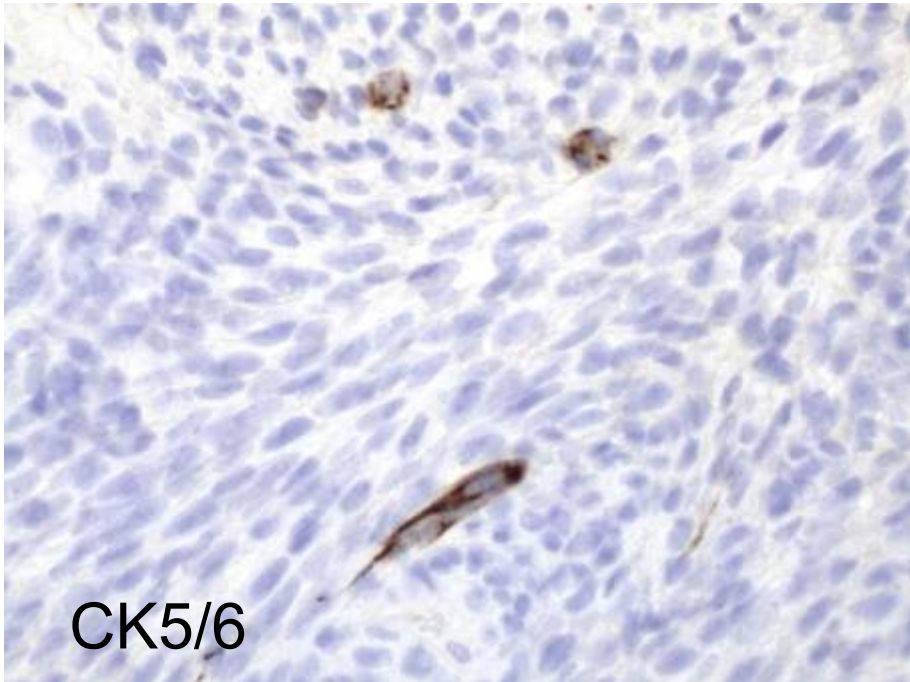
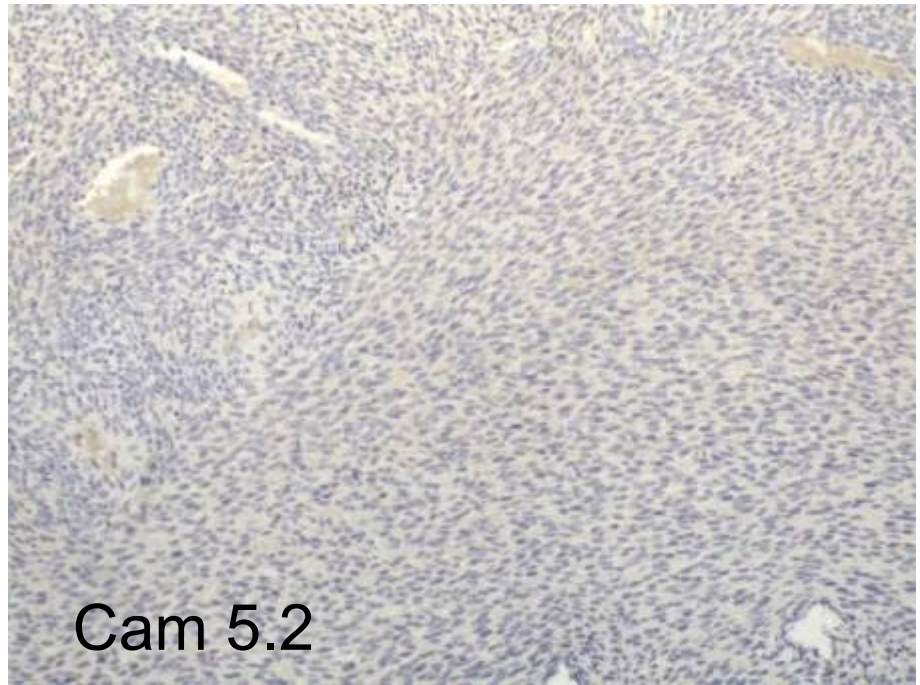
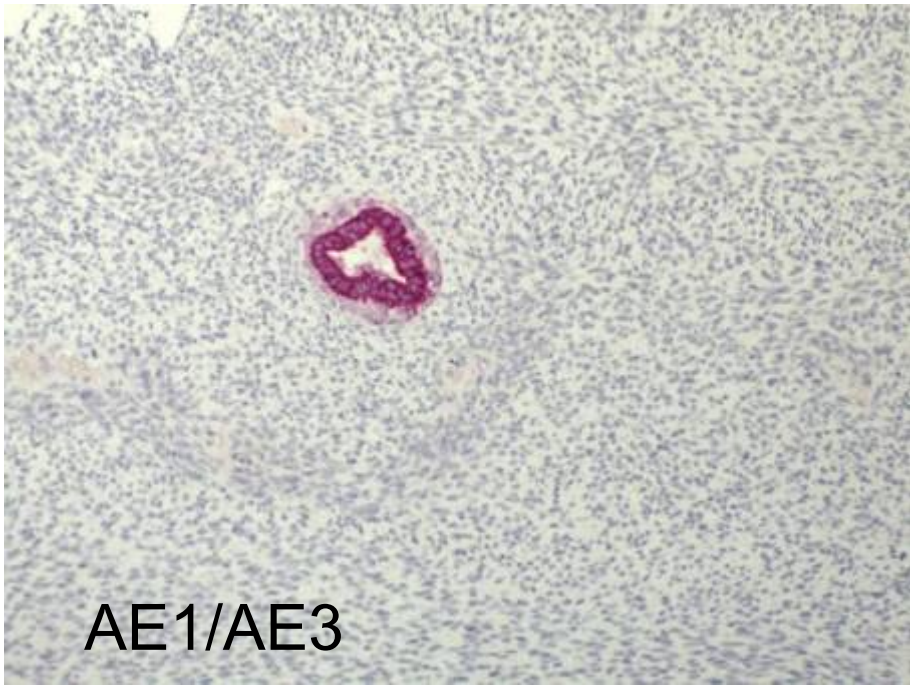
Case 2:

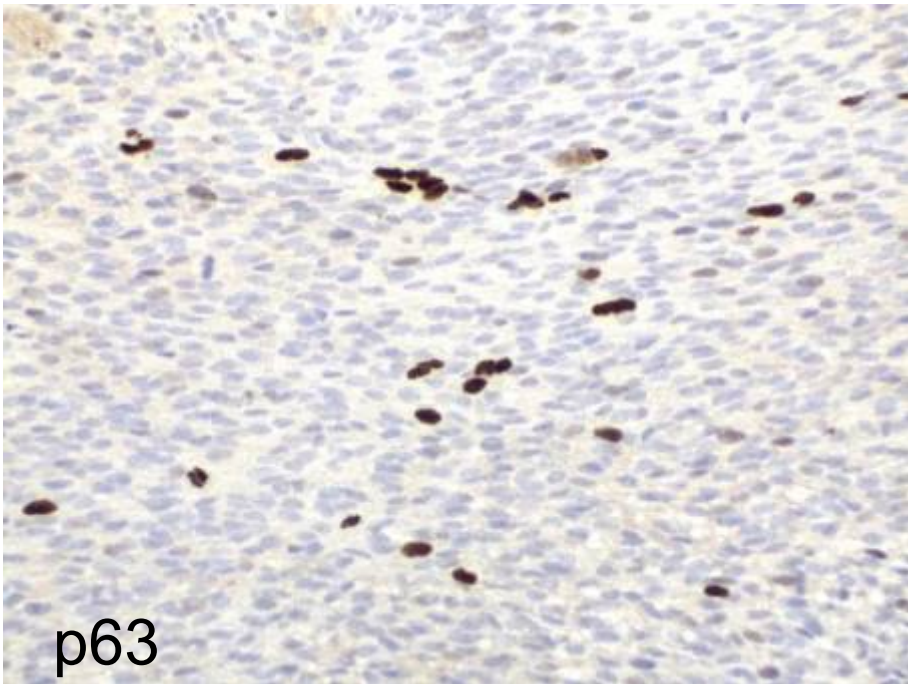
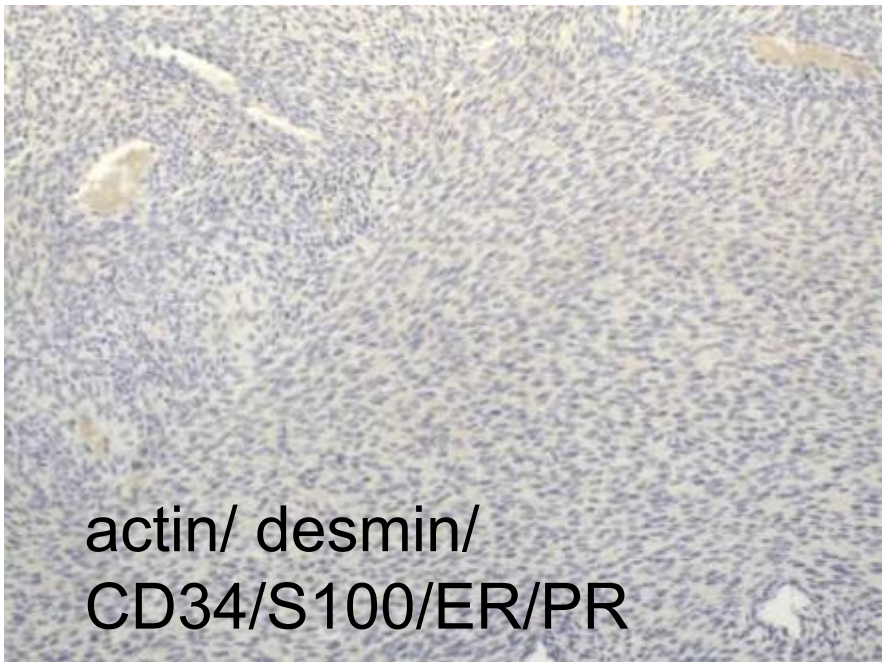
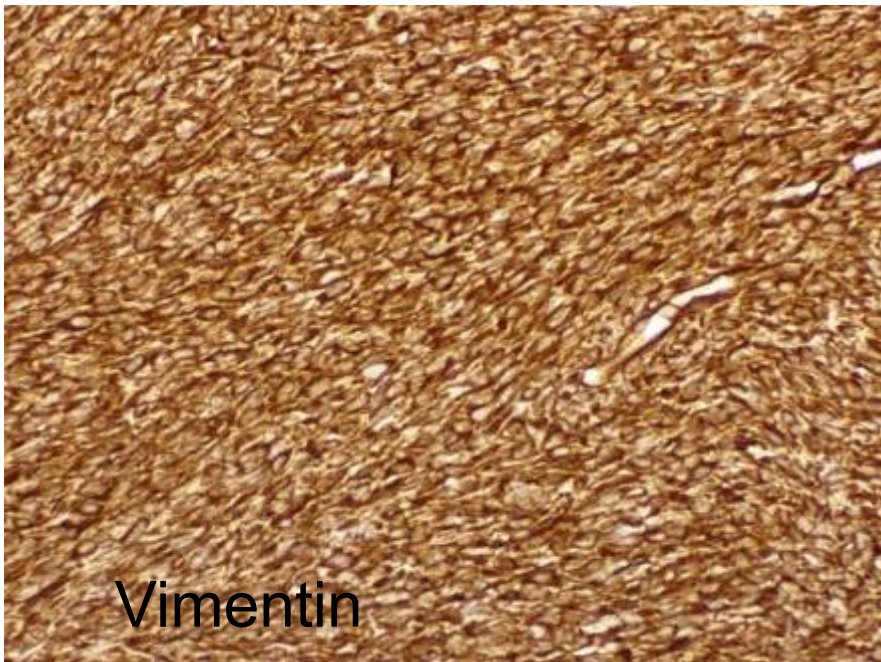
Metaplastic Carcinoma Fibromatosis-like

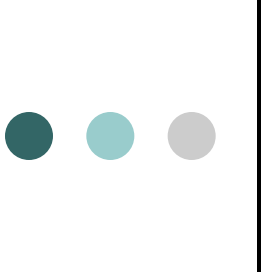


Metaplastic carcinoma

- Low grade adenosquamous
 - Fibromatosis-like
 - Spindle cell carcinomas
 - Matrix producing carcinomas
 - Squamous cell carcinomas
-
- ‘All spindle cell lesions of the breast are metaplastic carcinoma until proven otherwise’
 - Sarah Pinder







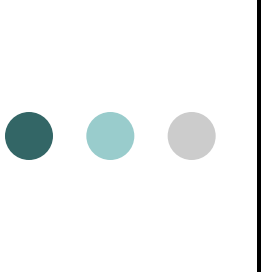
Metaplastic carcinoma

- Cam5.2 – 21% -52%
- AE1/AE3 – 79% -85%
- EMA – 33% positive
- Broad spectrum CK – 96% positive, 74% in >50% cells
- CK8/18 – 82-100%
- CK5 – 39%; CK14 – 33%
- CK7 – 17%
- CD34 – 0%
- **NEED TO USE A PANEL OF CYTOKERATINS INCLUDING BROAD SPECTRUM AND BASAL CYTOKERATINS**
- **STAINING CAN BE VERY FOCAL**

Metaplastic carcinoma

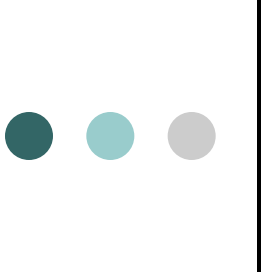
	CK	p63	Nuclear B-catenin	CD34
Phyllodes tumour	- (rare focal)	- (rare focal)	+	+/-
Metaplastic carcinoma	+ (often focal)	+/-	-/+	-
Fibromatosis	-	-	+	-

- Focal CK positivity seen in PT – MNF116 12%, CK7 28%, CK14 and Cam5.2 2%, AE1/3 8% . Associated with malignant subtype.
- Focal CK and p63 positivity identified in malignant PT (21% and 57% respectively);
- CD34 – 57% malignant PT positive, no staining in sarcomatoid carcinoma



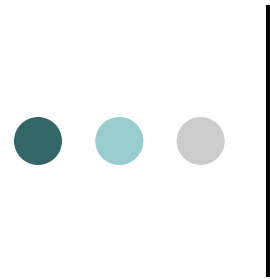
Metaplastic carcinoma

- Clues – associated NST carcinoma or DCIS
nuclear atypia or mitoses
associated chronic inflammation
- ER/ PgR/ HER2 negative



Metaplastic carcinoma

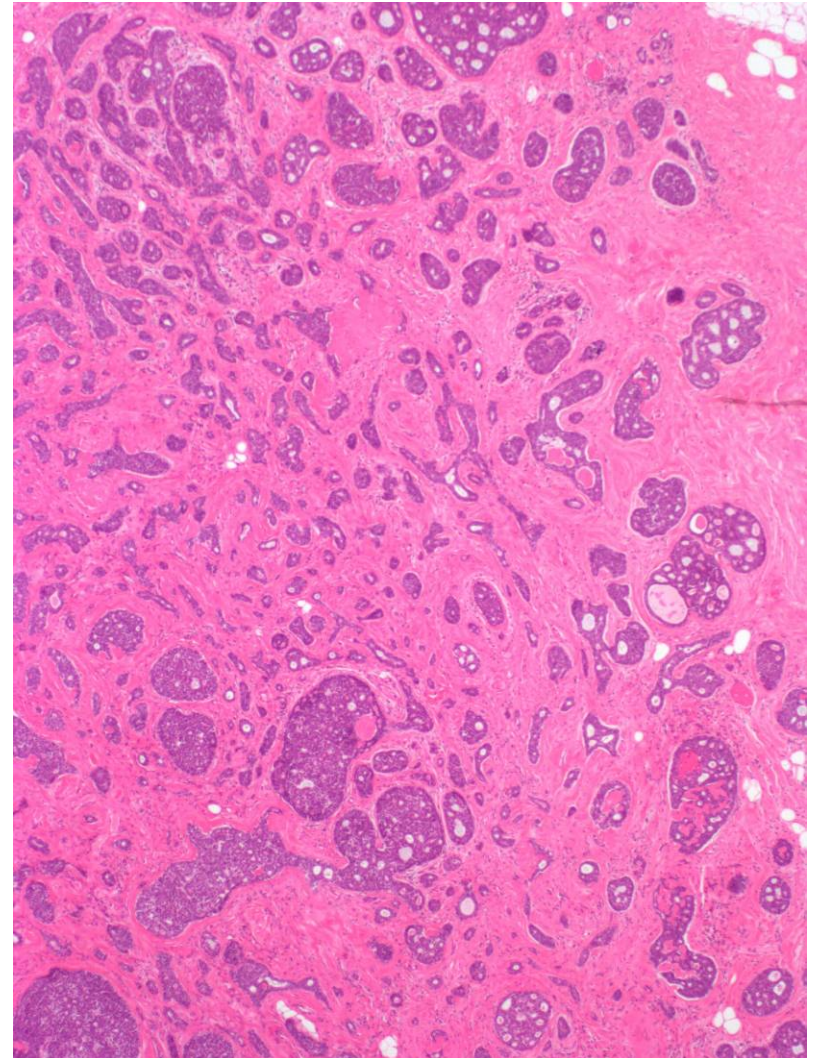
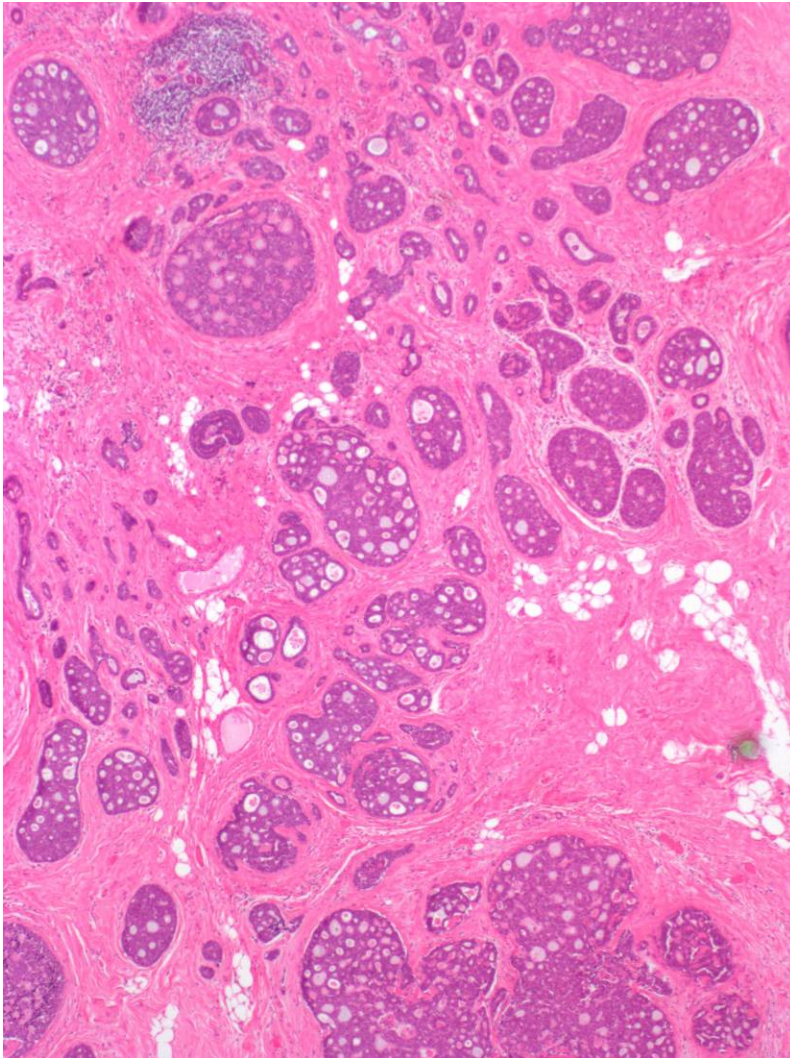
- Behaviour intermediate between carcinoma and sarcoma
- Intermediate risk of axillary LN metastases – may relate to proportion of carcinomatous component
- Tendency to visceral metastases particularly lung
- Poor response to neoadjuvant chemotherapy
- Increased risk of local recurrence even with mastectomy – complete excision with good margins and RT important
- Poor survival: Median DFS 7 months (2-109/12)
- Median OS 18 months (4-109)



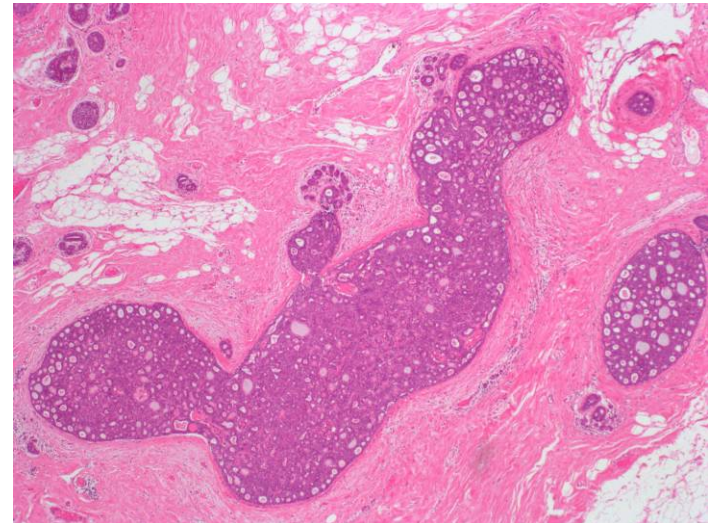
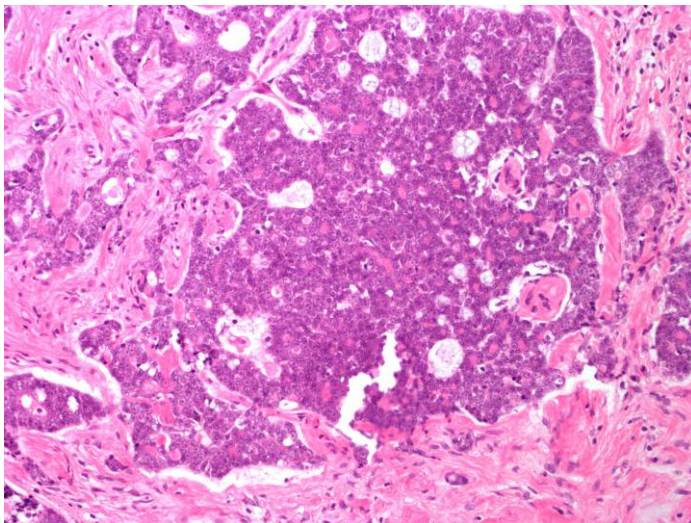
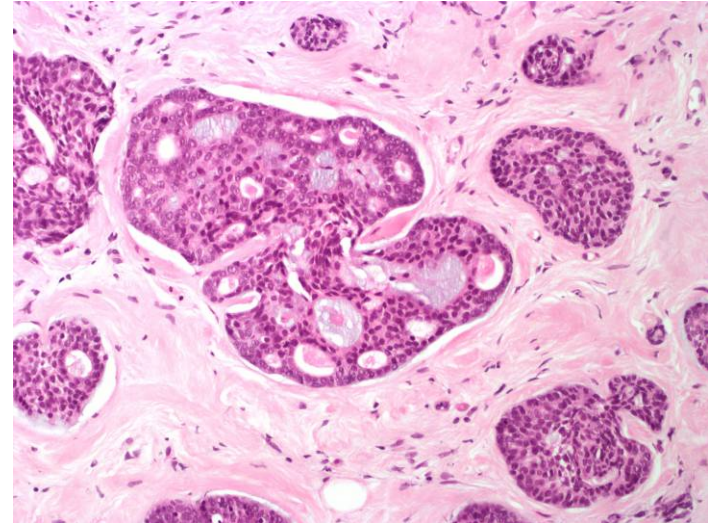
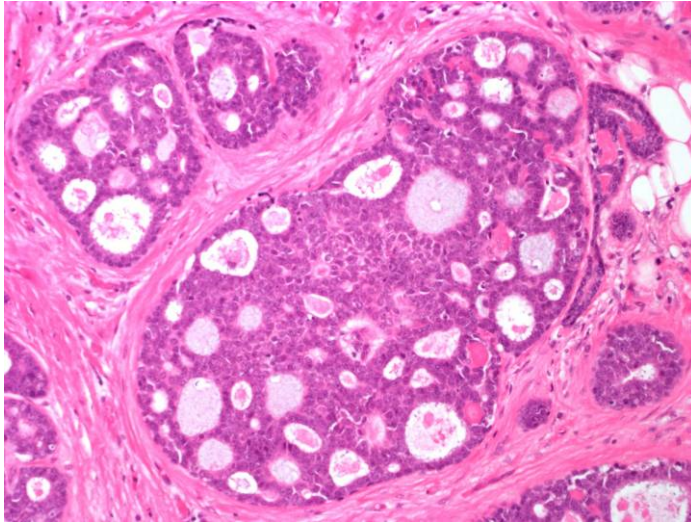
Case 3:

63 yo female.
L breast lump.

Case 3:

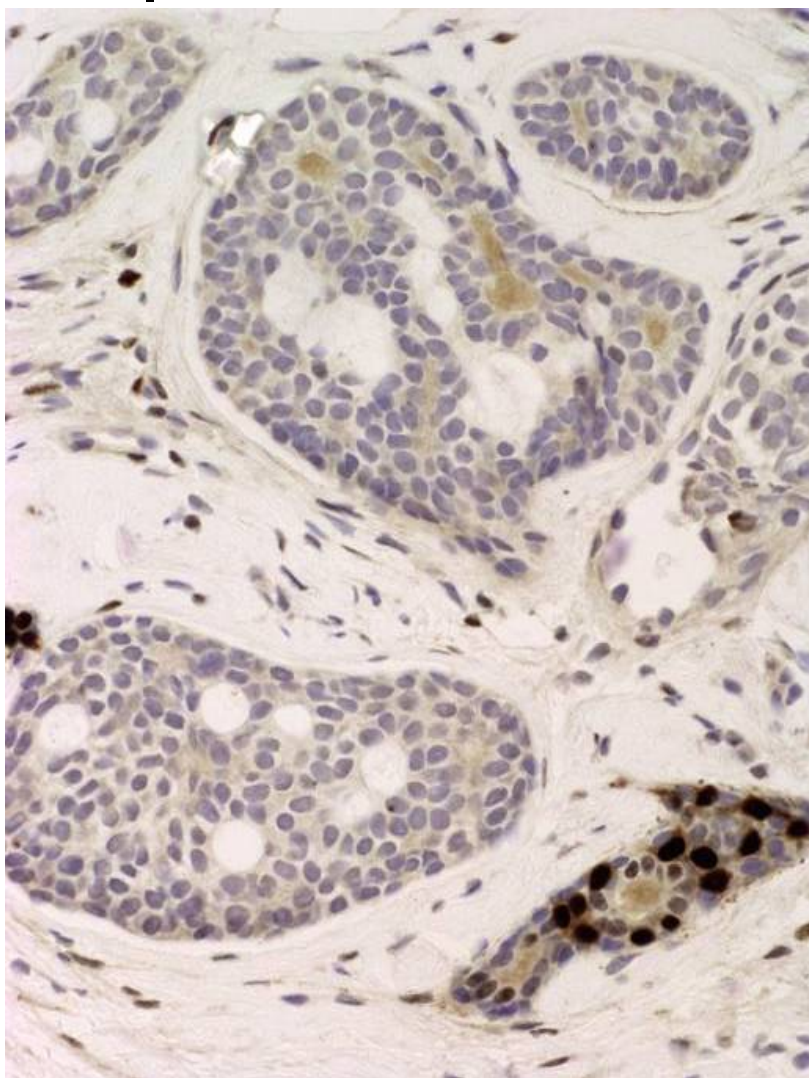


Case 3:

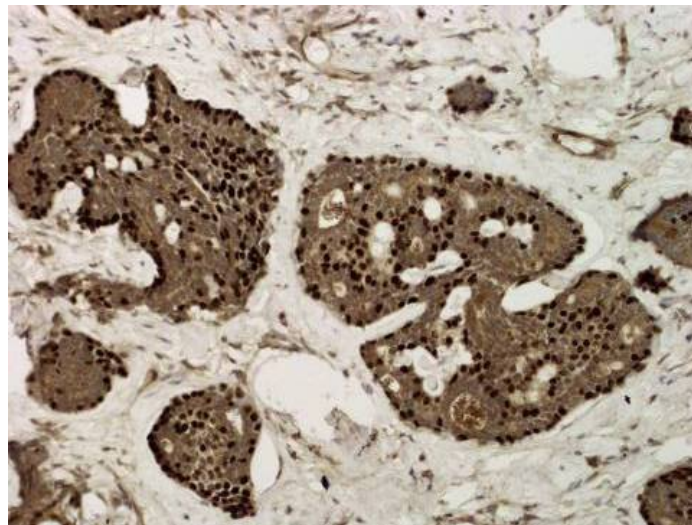


Case 3:

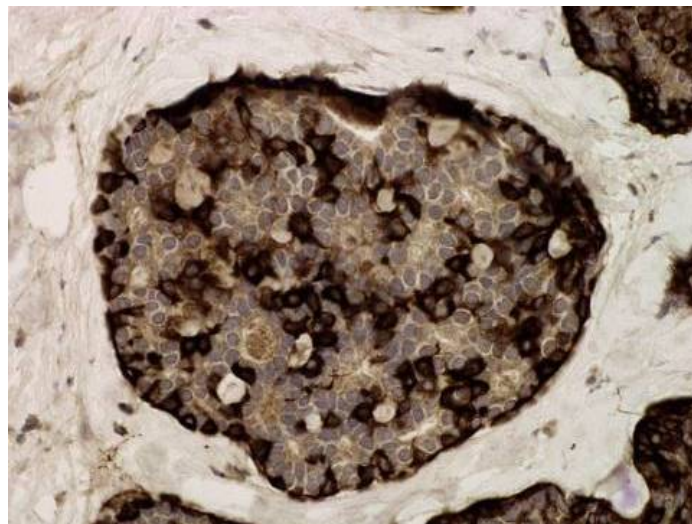
ER

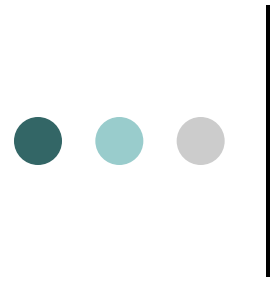


p63



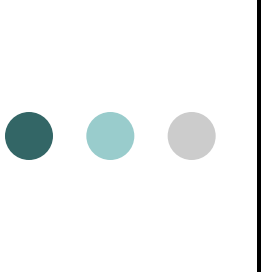
SMMHC





Case 3:

Adenoid Cystic Carcinoma

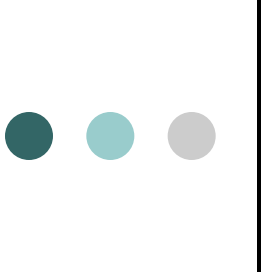


Adenoid cystic carcinoma

Low grade lesion with cribriform architecture

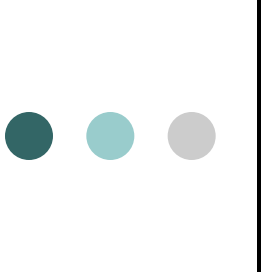
DDx:

- Low grade DCIS
 - Cribriform carcinoma
 - Adenoid cystic carcinoma
-
- ER negative = Adenoid cystic carcinoma



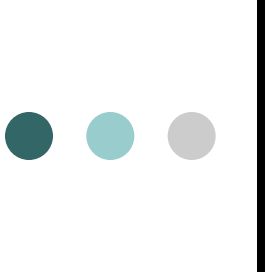
Adenoid cystic carcinoma

- Salivary gland tumour also found in breast
- <1% of breast cancers
- Two cell populations;
- basal/ myoepithelial cells – CK5/6, CK14, p63
- luminal/ epithelial cells – CK7, CK8/18, CD117
- Triple negative with expression of basal markers
- BUT older age group
- Commonly grade 1 or 2
- Low incidence nodal involvement – up to 5%
- Excellent prognosis with 88-98% 5 year survival



Adenoid cystic carcinoma

- Distinct genetic profile to other basal breast cancers
- Less genetic instability, fewer copy number aberrations, intact BRCA1 pathway
- Characteristic translocation t(6:9) with formation of MYB NFIB fusion gene



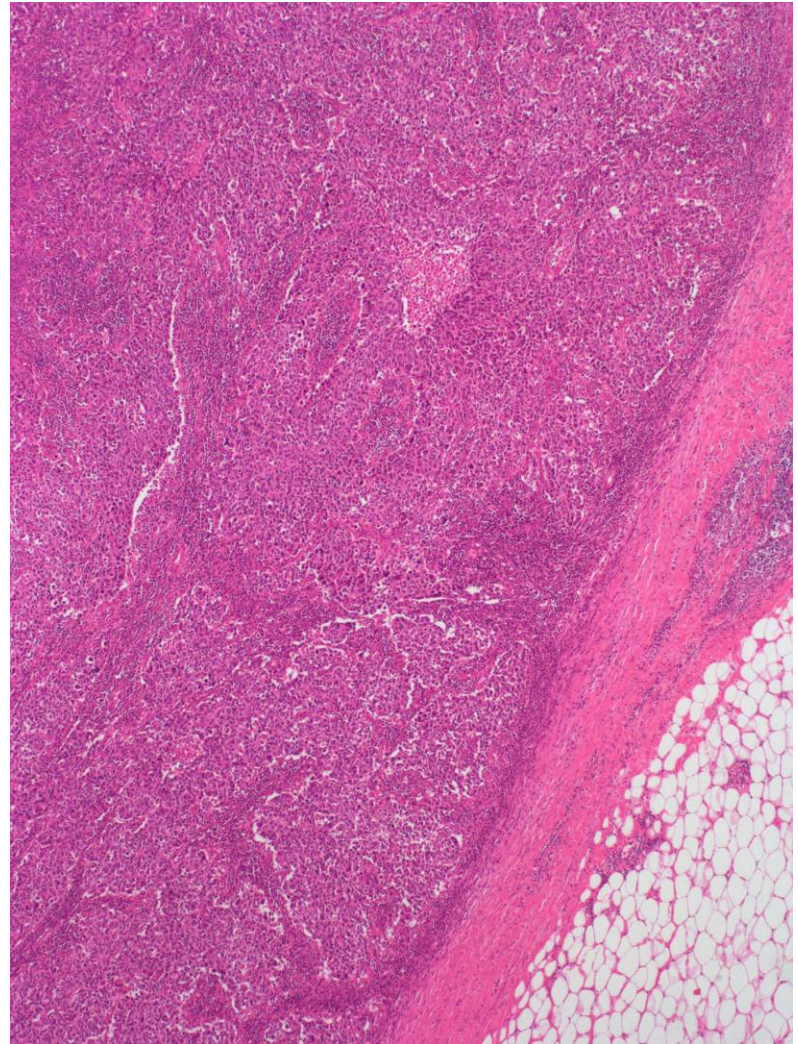
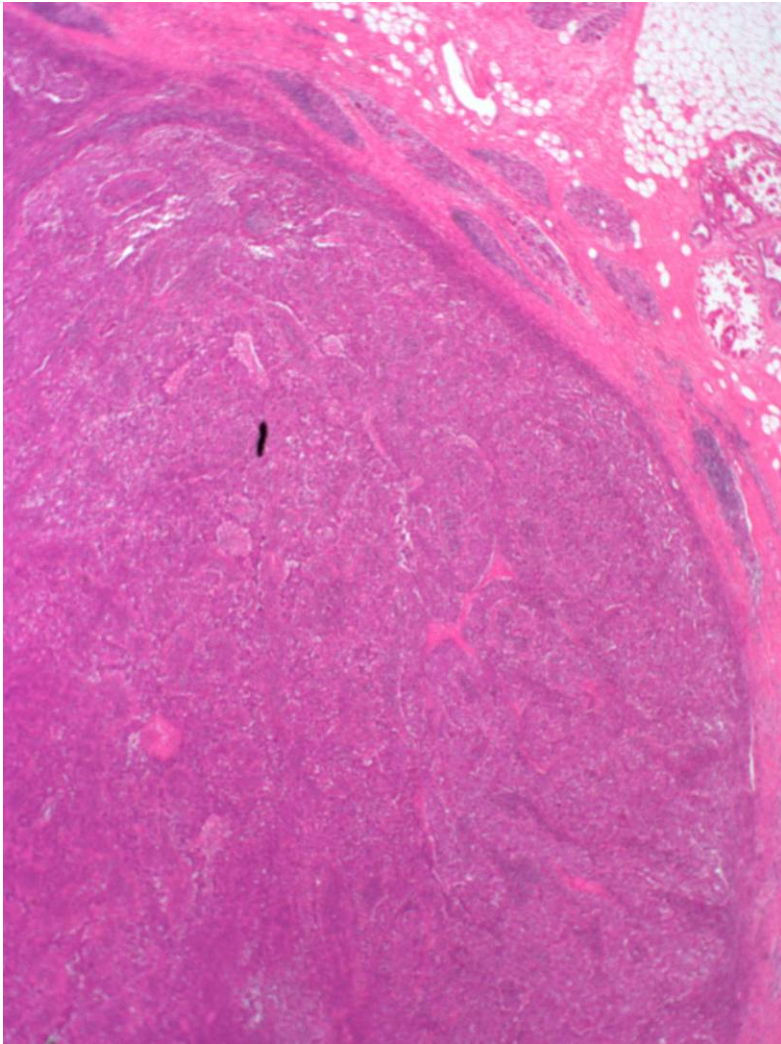
Case 4:

35 yo female.

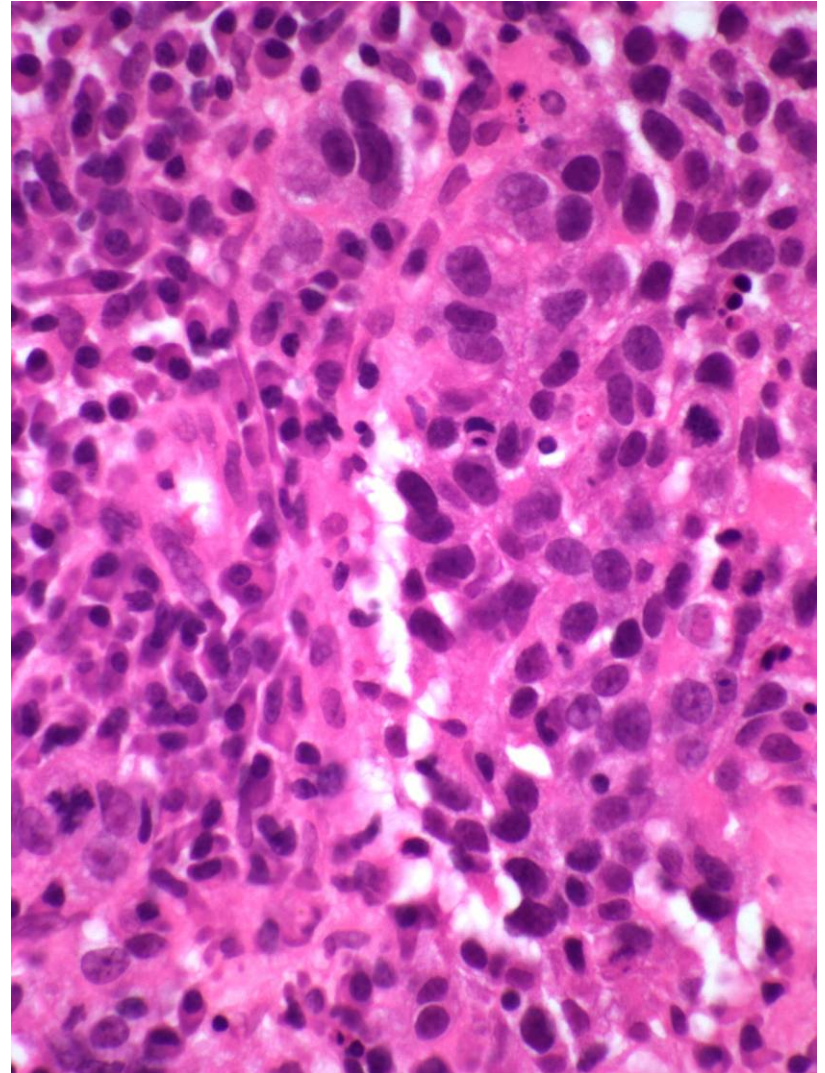
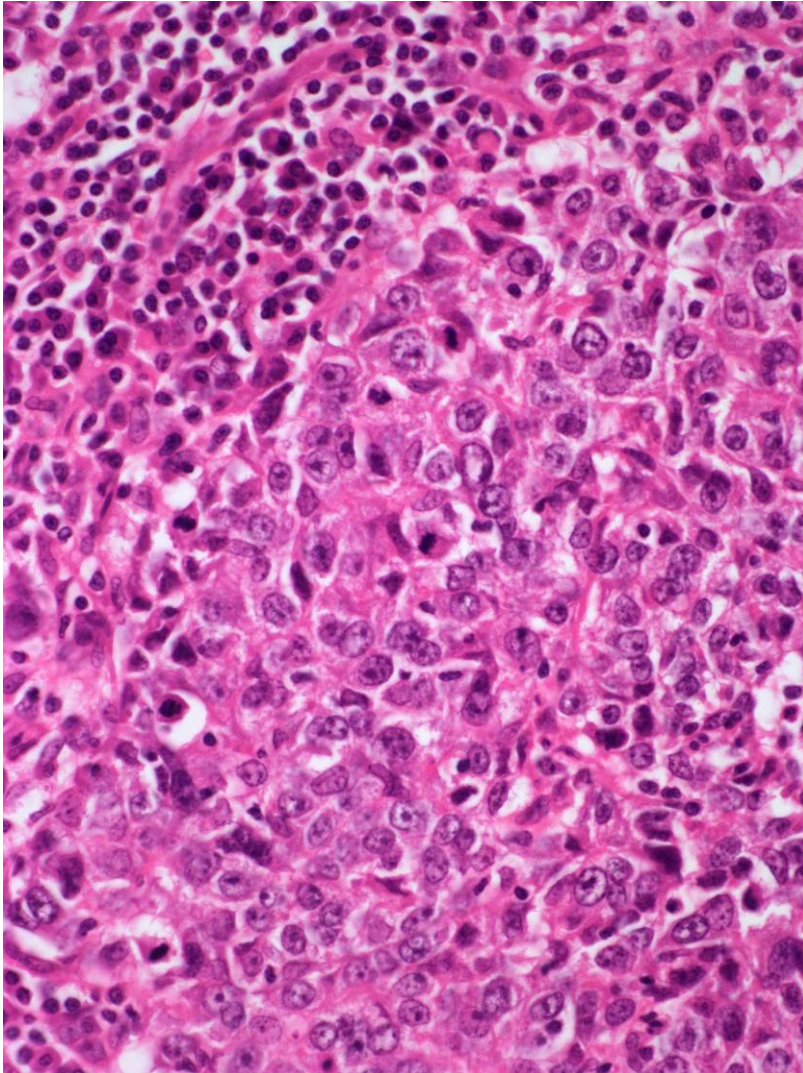
L breast lump.

M3U3 ? fibroadenoma

Case 4:

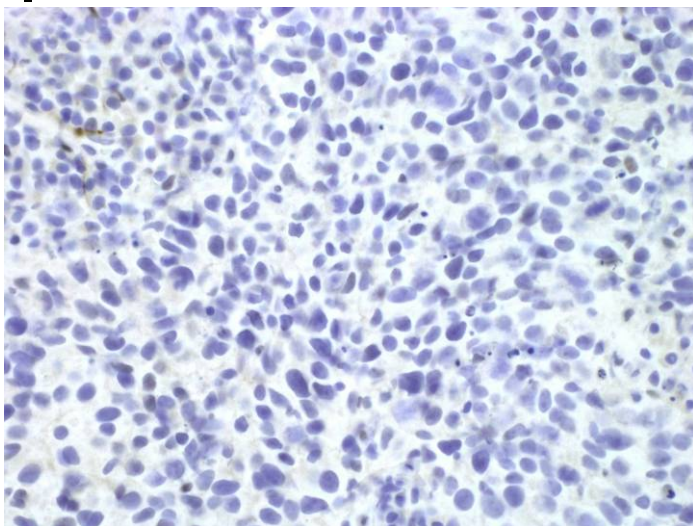


Case 4:

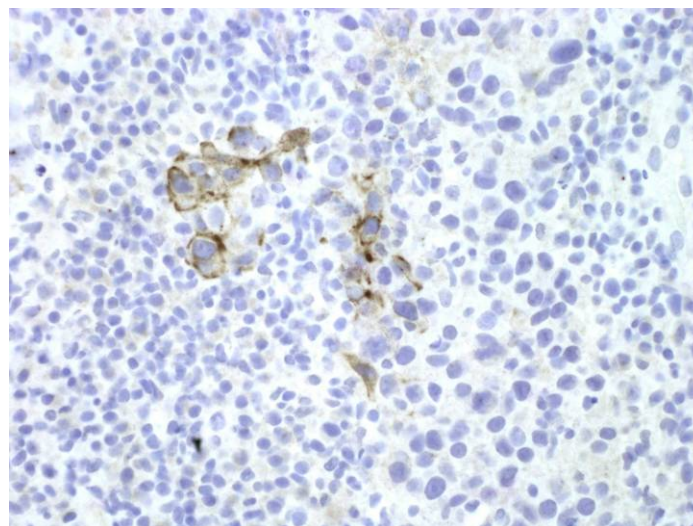


Case 4:

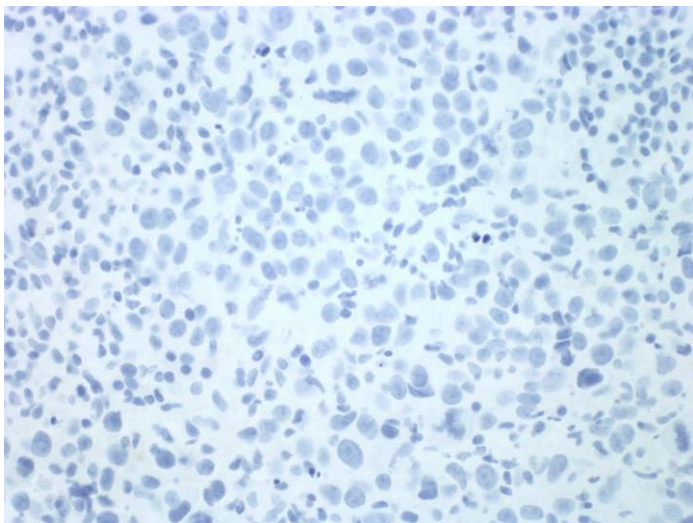
ER



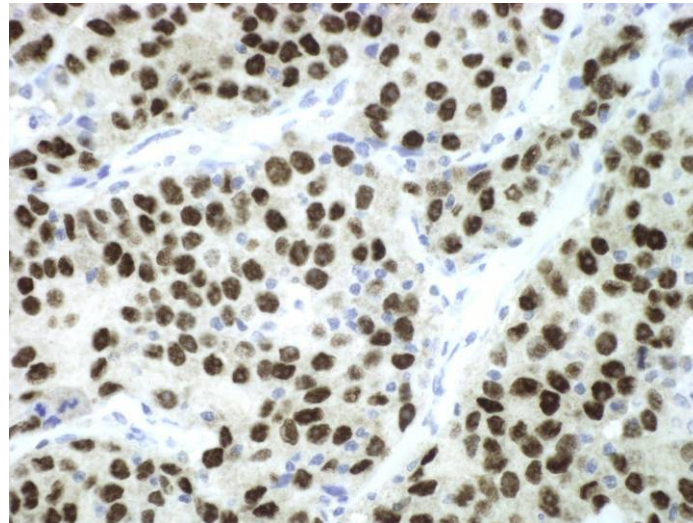
CK5/6

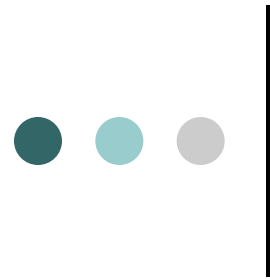


HER2



Gata 3



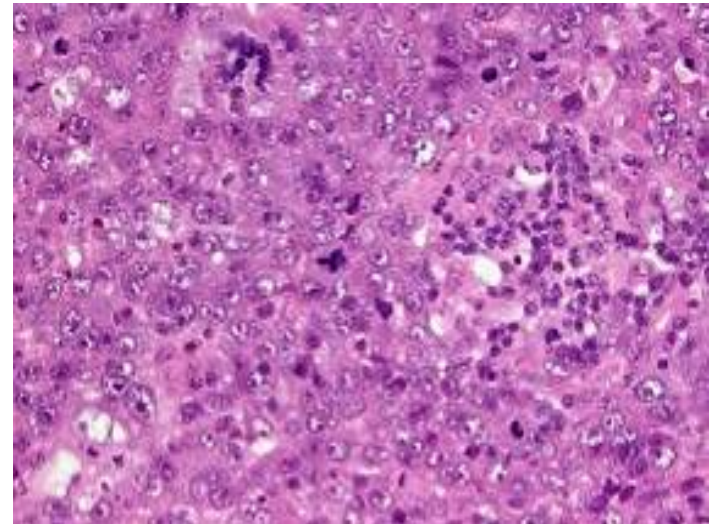
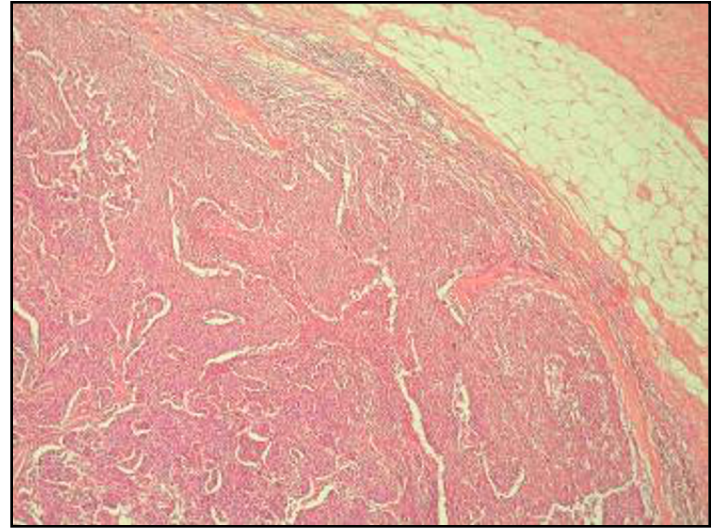


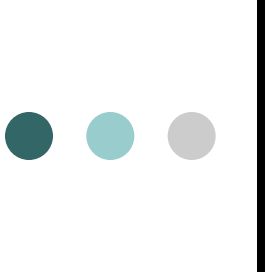
Case 4:

Carcinoma with Medullary Features

Carcinoma with medullary features

- Circumscribed tumour with pushing rather than infiltrating margin
- Interconnecting sheets of large, bizarre and pleomorphic carcinoma cells forming a syncytial network
- Prominent lymphocytic inflammatory cell infiltrate
- Usually ER/ HER2 negative
- Association with BRCA1 mutations



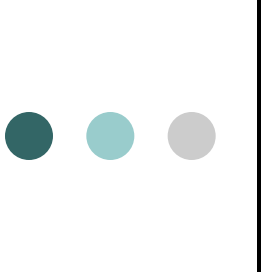


Basal Breast Cancers

- 'Triple negative' – ER, PgR and HER2 negative
- Express basal cytokeratins – CK 5/6, CK14
- Express EGFR
- Distinct morphology – high grade, central acellular zones, necrosis, high mitotic count
- Associated with BRCA1 mutations in young women
- Associated with worse prognosis and distant metastasis, particularly visceral metastases

● ● ● | Basal breast cancers

- Heterogeneous group of tumours
- Grade 3 NST
- Medullary-like
- Metaplastic carcinomas
 - sarcomatoid
 - squamous
 - fibromatosis – like**
 - low grade adenosquamous**
- **Adenoid cystic carcinoma**
- **SUBSET WITH A GOOD PROGNOSIS**

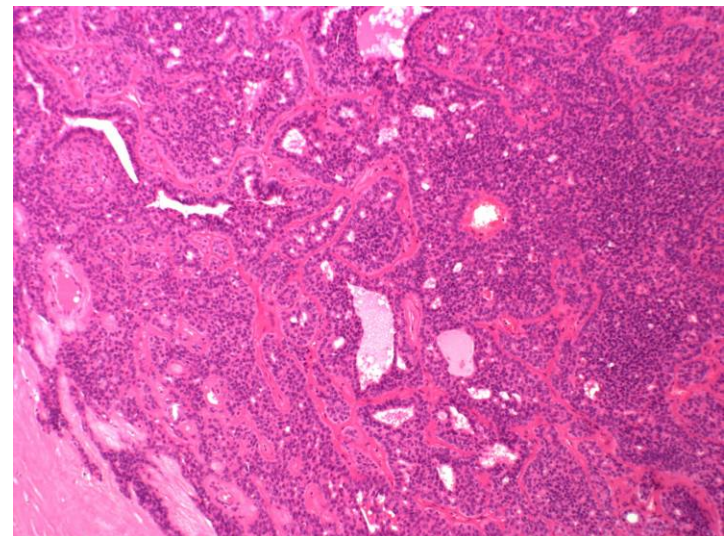
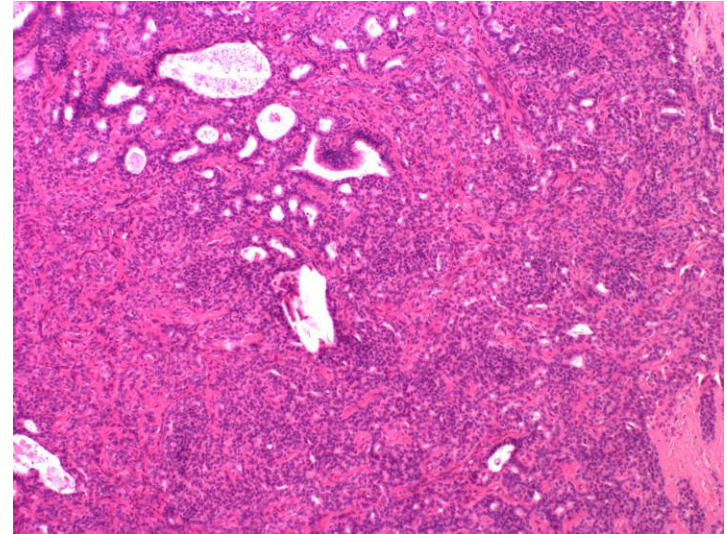
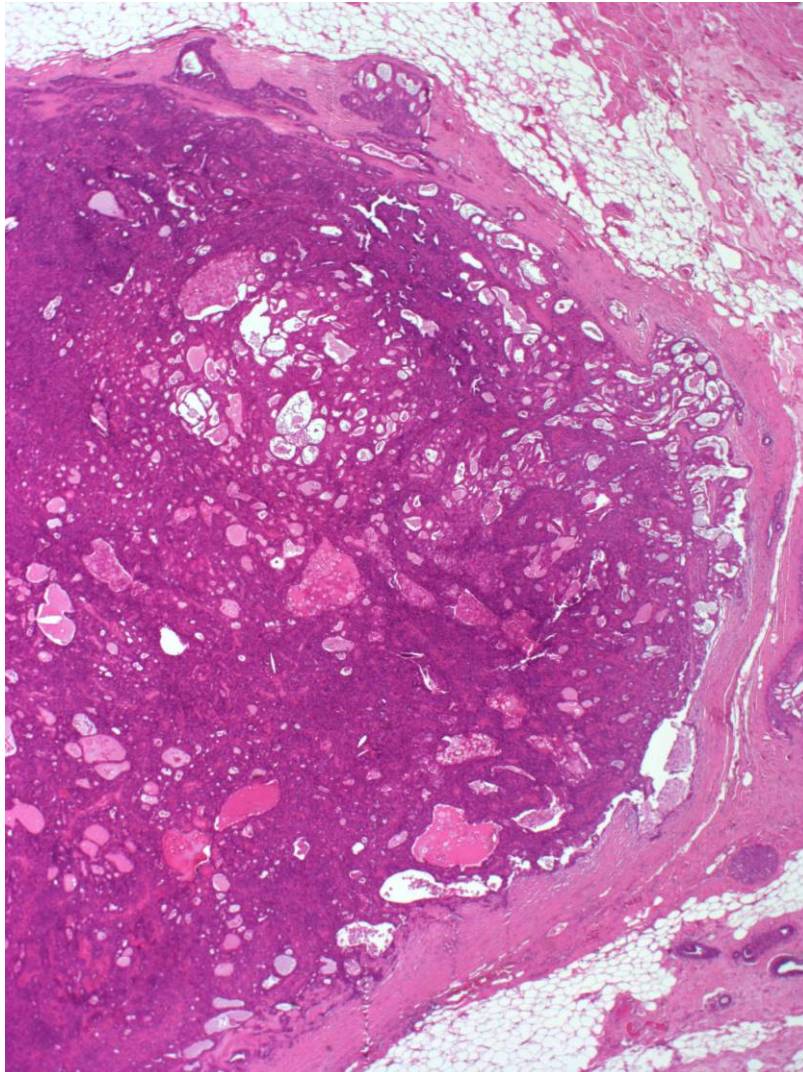


Case 5:

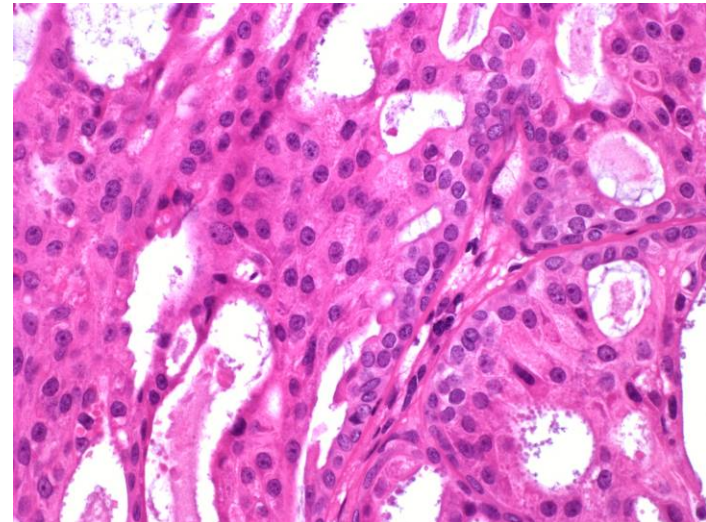
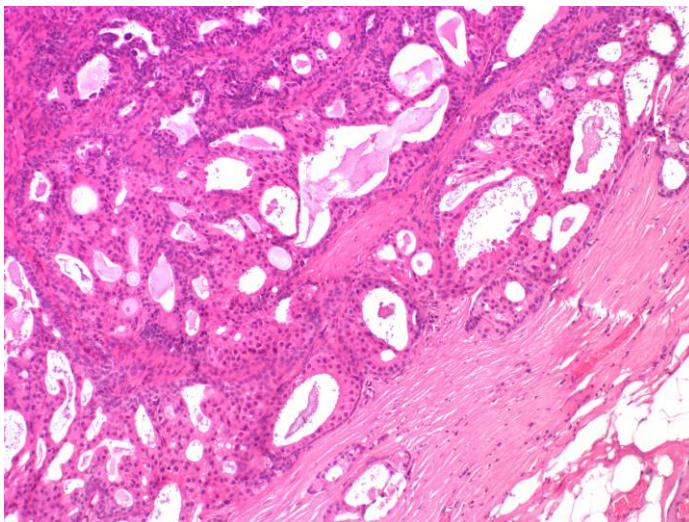
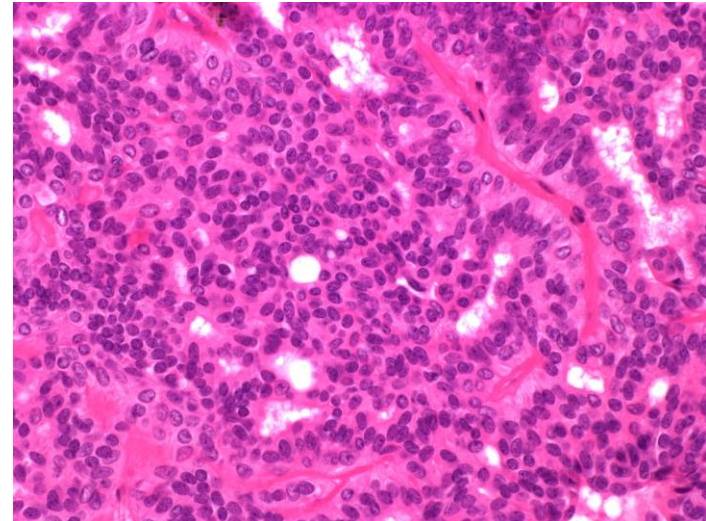
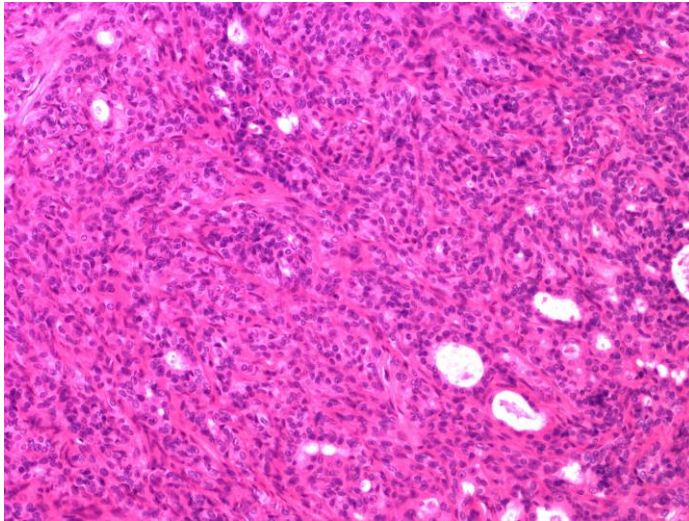
81 yo female.

**R breast mass
discovered on CT.**

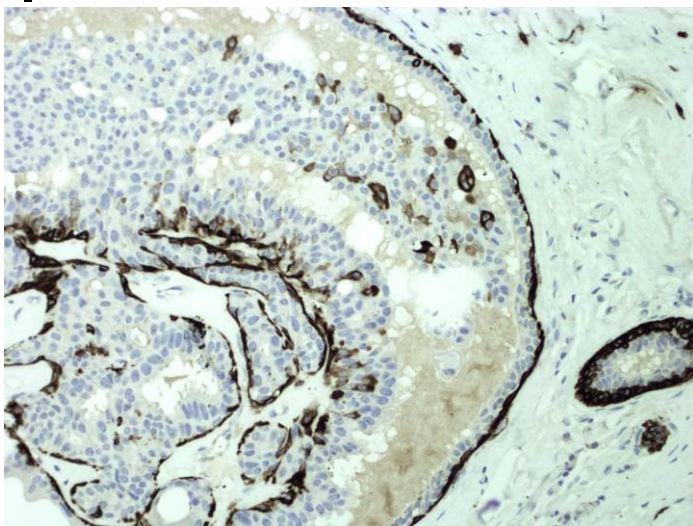
Case 5:



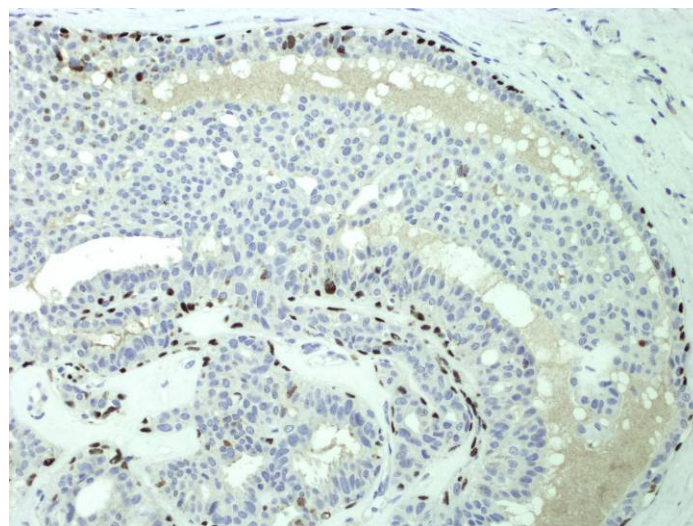
Case 5:



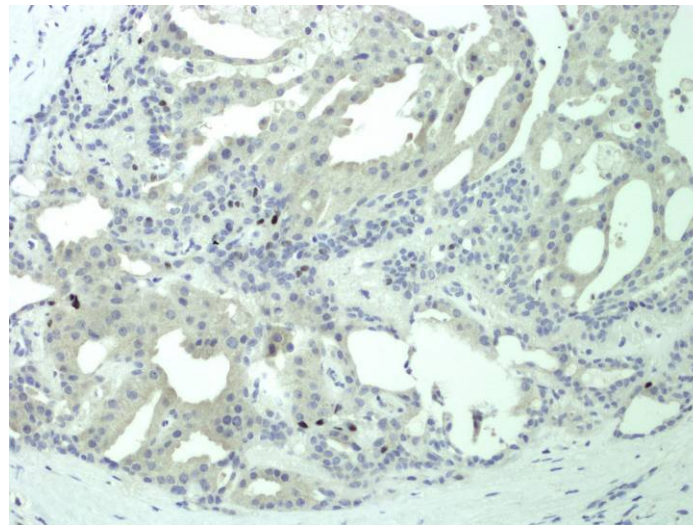
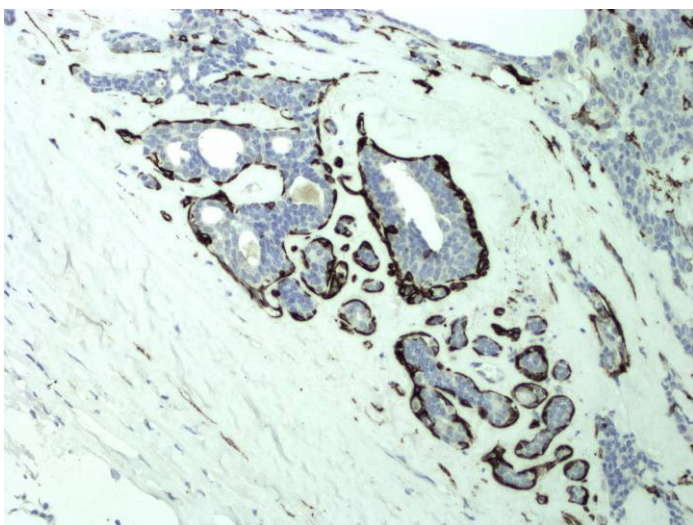
Case 5:



SMMHC

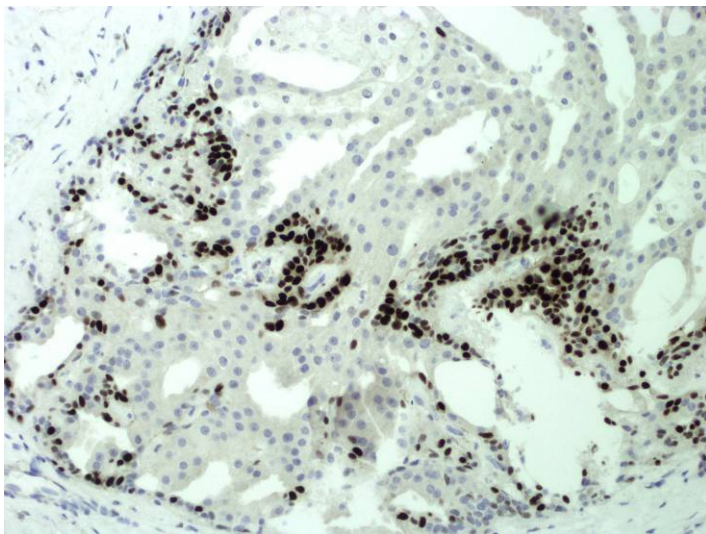
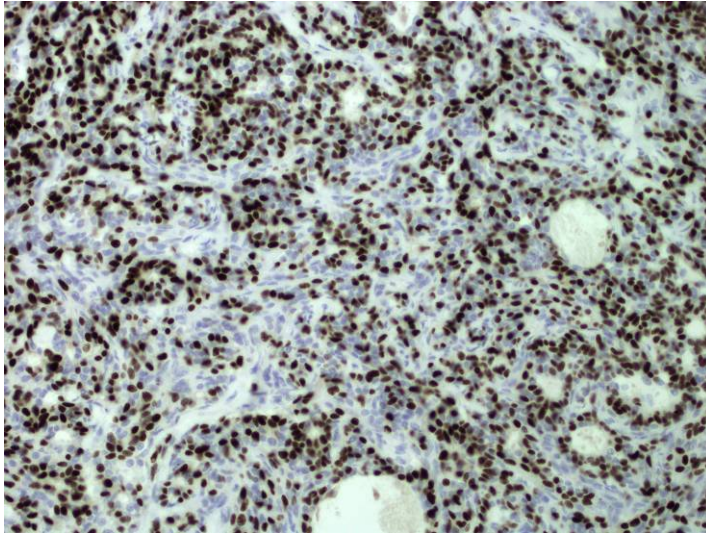


p63

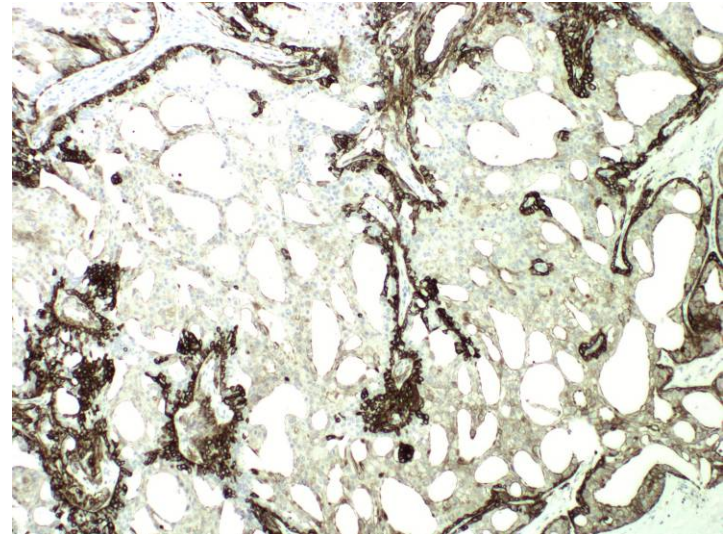
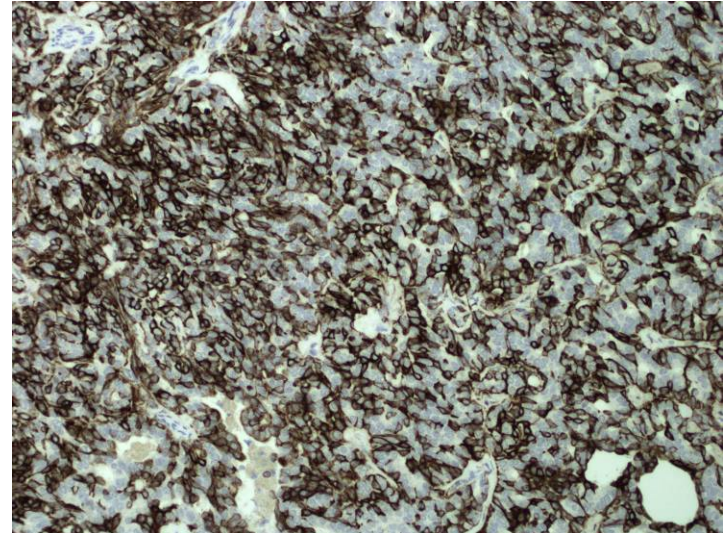


Case 5:

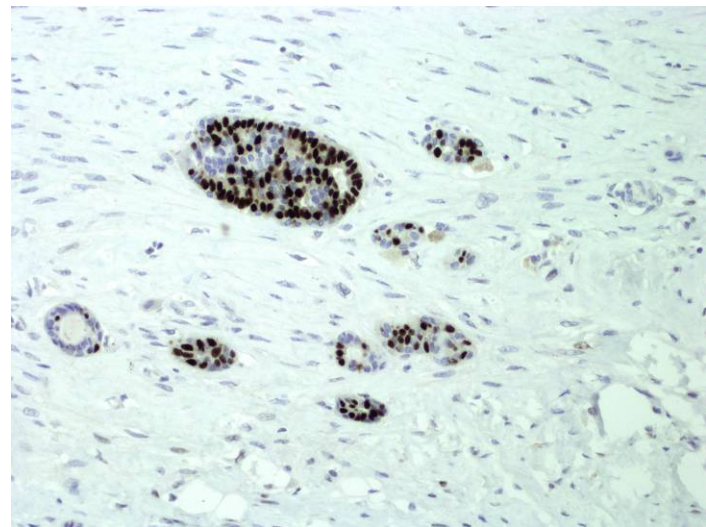
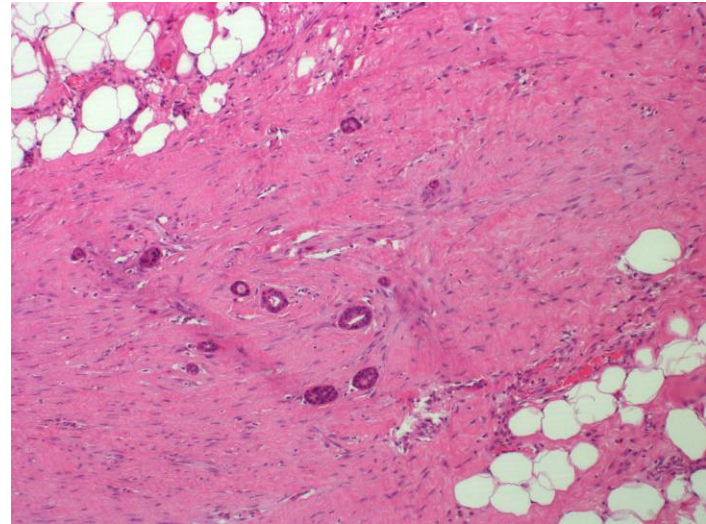
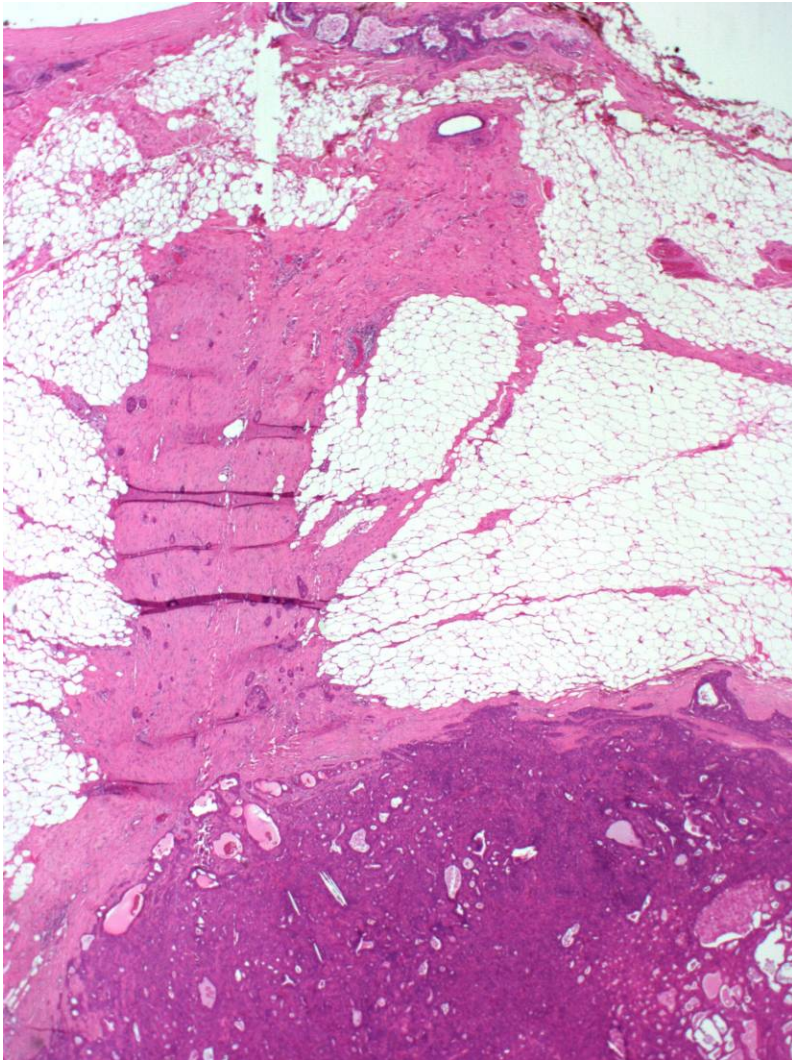
ER

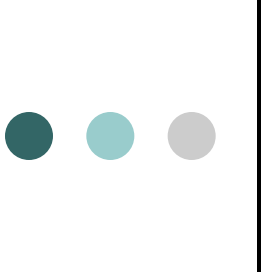


CK5/6



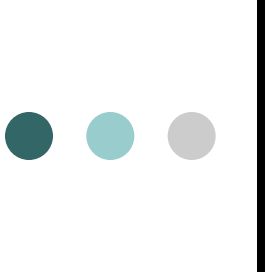
Case 5:





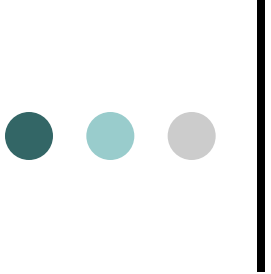
Case 5:

**Papilloma with florid
usual type hyperplasia**



Latest WHO Classification

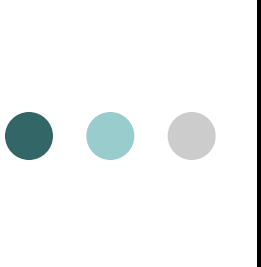
- Intraductal papilloma
- Intraductal papilloma with atypia/ DCIS
- Intraductal papillary carcinoma /
Papillary DCIS
- Encapsulated papillary carcinoma
- Solid papillary carcinoma
- Invasive papillary carcinoma



Papillary lesions

Classification dependent upon

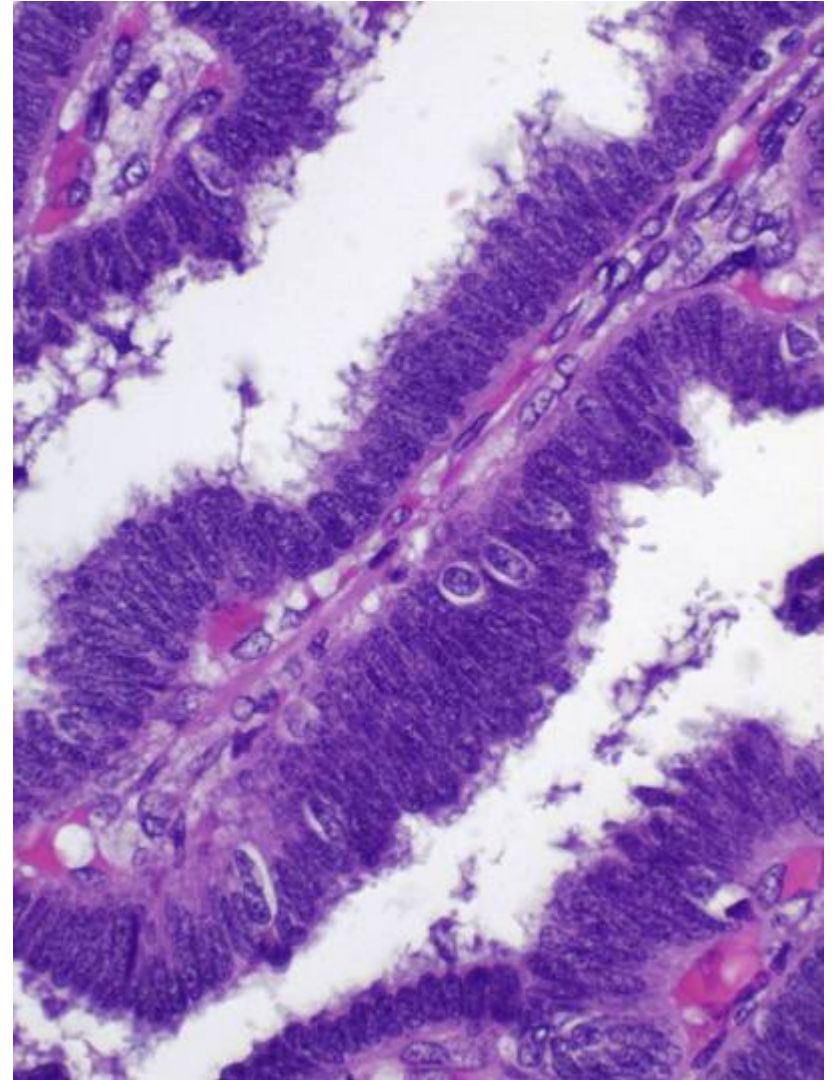
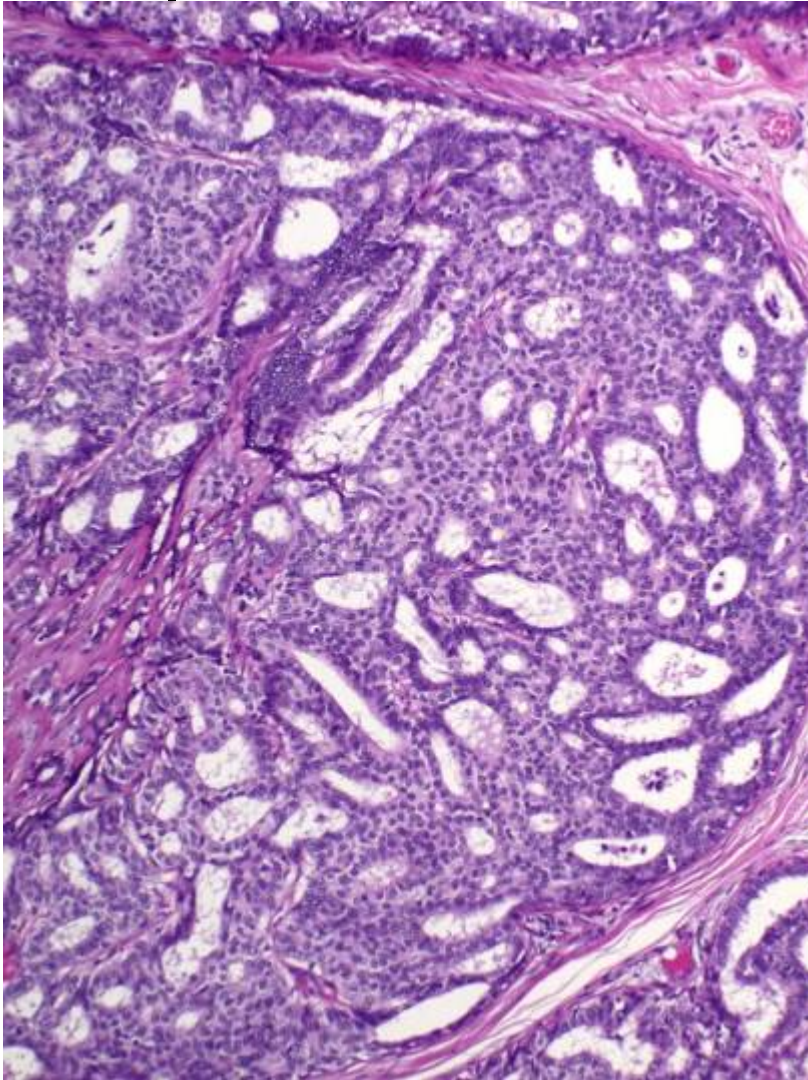
- presence of cytological and architectural atypia
- presence of an internal and/ or external myoepithelial layer

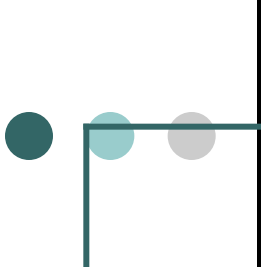


Histopathological characteristics

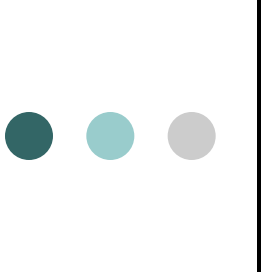
	Intraductal Papilloma	Papilloma with ADH/ DCIS	Papillary DCIS	Encapsulated Papillary Carcinoma	Solid Papillary Carcinoma
Architecture	Broad, blunt fronds	Broad, blunt fronds	Slender fronds, sometimes branching	Slender fronds, sometimes branching	Solid with inconspicuous delicate fibro vascular septa
Epithelial Component	Heterogeneous +/- haphazard orientation: luminal cells, myoepithelial cells, usual hyperplasia, apocrine metaplasia	Focal areas with architecture and cytology of DCIS, usually low grade (monotonous cell pop'n, solid or cribriform spaces) Background heterogeneous	Entire lesion composed of cells with architecture and cytology of DCIS; usually low/ intermediate grade	Entire lesion composed of cells with architecture and cytology of DCIS; usually low/ intermediate	Entire lesion composed of cells with low grade cytology Spindle cell component Neuroendocrine diff'n common May show mucin production
Adjacent ducts	Usual hyperplasia	DCIS	DCIS	DCIS	DCIS

Atypical features





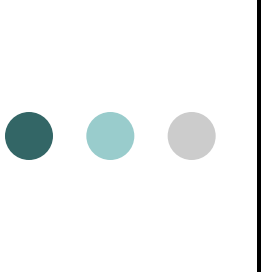
	MEC in Papillae	MEC at Periphery
Papilloma	Present	Present
Papilloma with atypia/DCIS	Present – may be absent/ reduced in atypical areas	Present
Papillary DCIS	Absent	Present
Encapsulated Papillary Ca	Absent	Absent
Solid Papillary Ca	Absent	Present/ Absent
Invasive Papillary Ca	Absent	Absent



IHC in diagnosis of papillary lesions

Two main settings

- Myoepithelial markers – p63, SMMHC, calponin
- ER and basal CKs – for epithelial proliferations to distinguish usual hyperplasia from ADH/ DCIS



IHC – ER and basal CK's

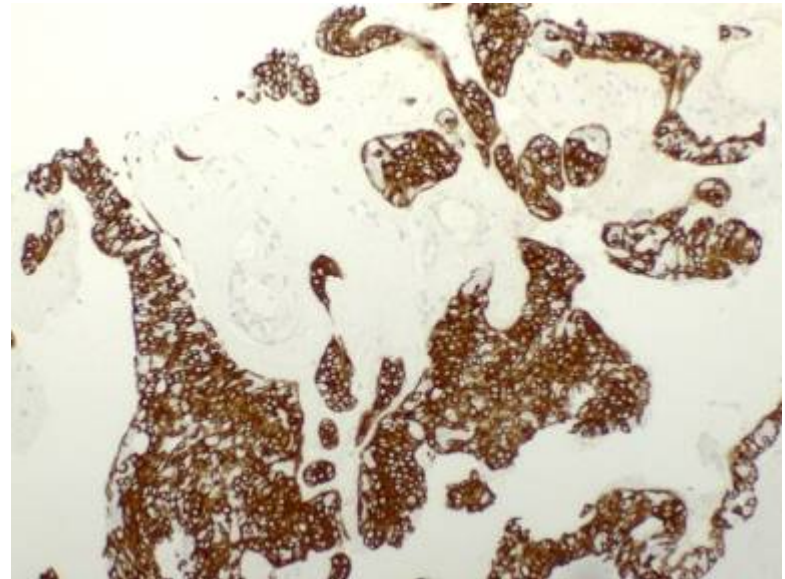
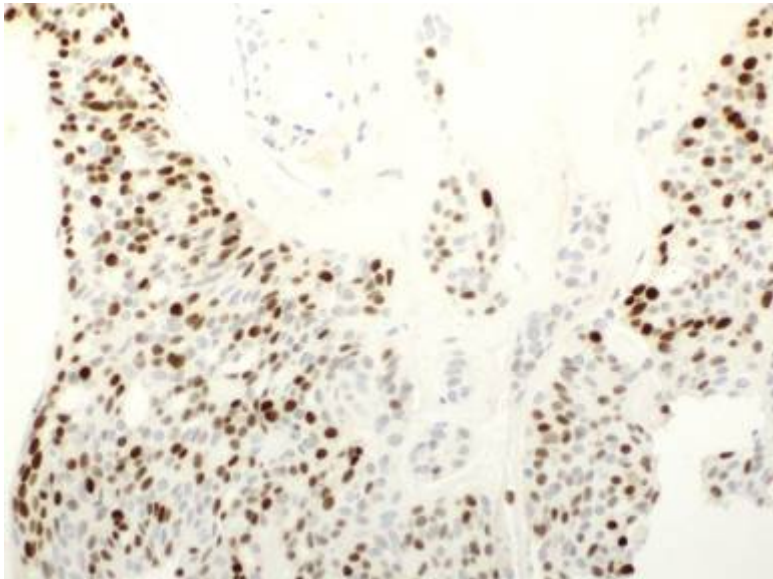
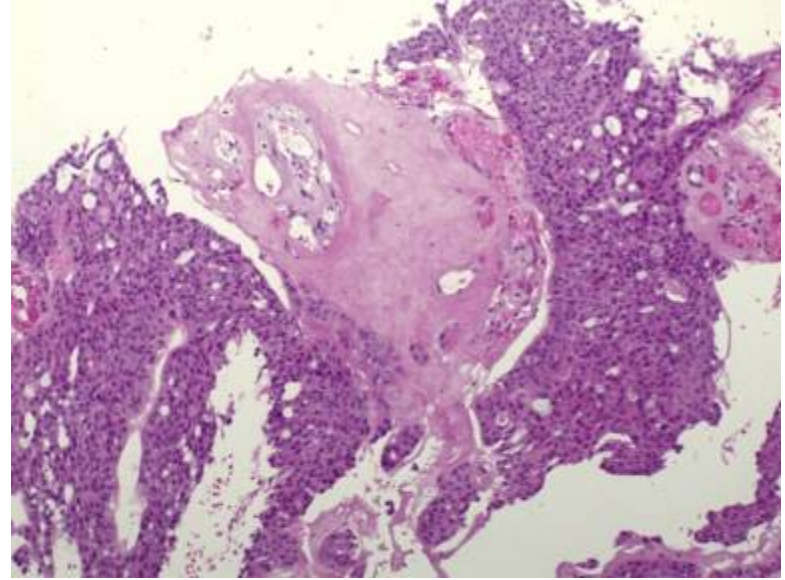
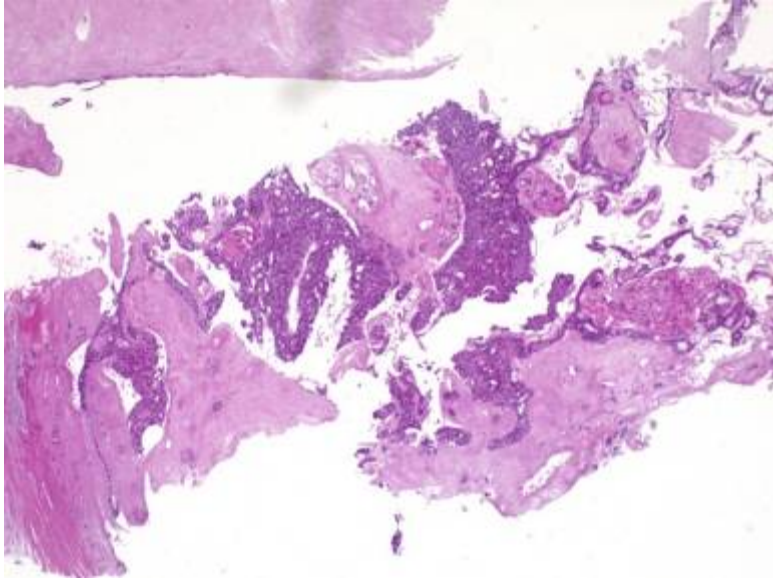
- UDH is a polyclonal proliferation with a mosaic pattern of staining for ER and CK5/ CK14*
- ADH/ DCIS is a monoclonal proliferation with uniform strong staining for ER and negative staining for CK5/ CK14**

* Apocrine proliferations are ER negative

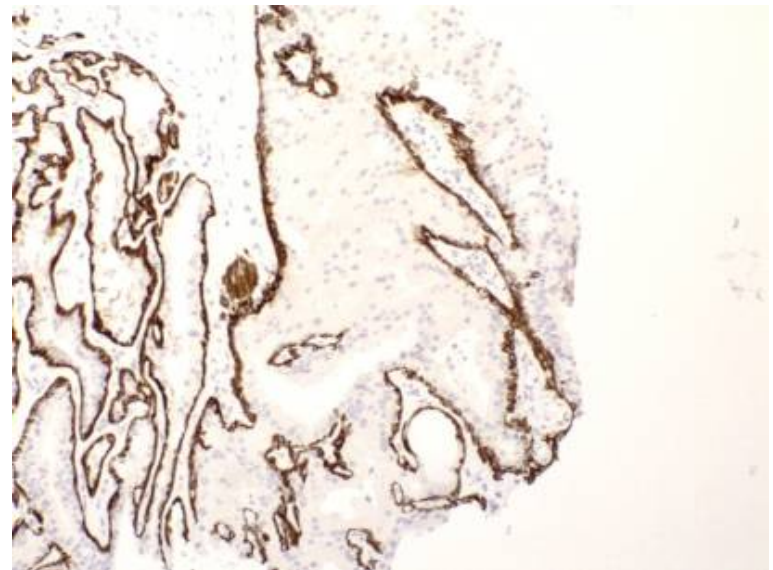
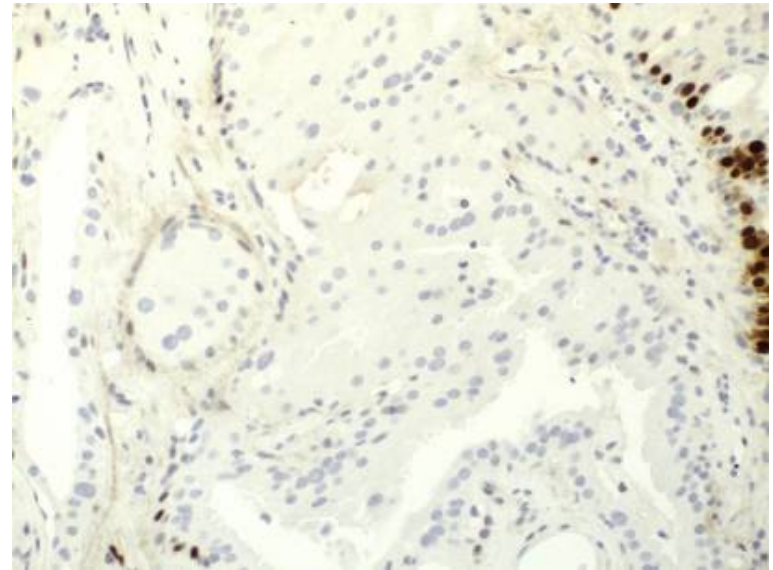
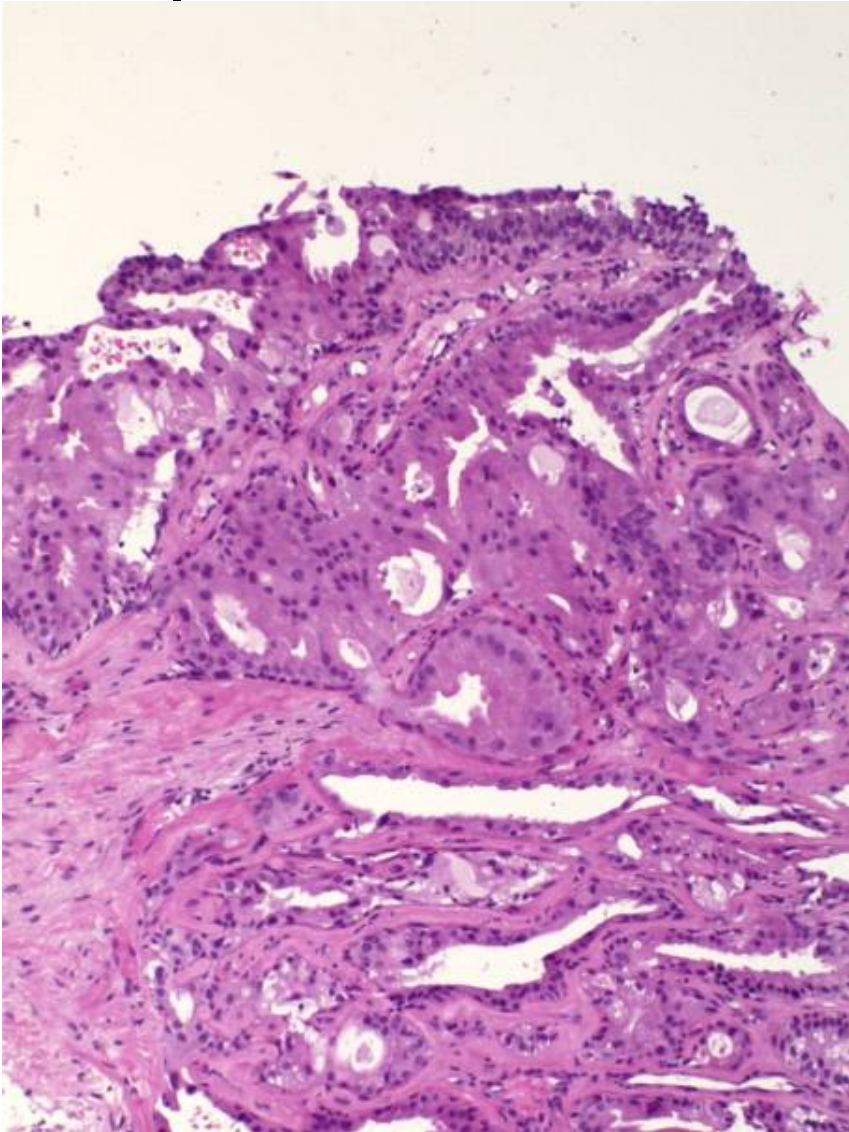
** Basal DCIS is very rare in papillary lesions, but is ER negative and CK5/ CK14 positive with severe nuclear atypia

** This refers to epithelial cell staining, in papillomas with ADH/ DCIS myoepithelial cells will stain positively for basal CK's but appear as rare basally situated cells. With the mosaic pattern in UDH, 50-80% cells positive

IHC – Papilloma with UDH



IHC – Apocrine metaplasia



Papilloma with atypia/ DCIS

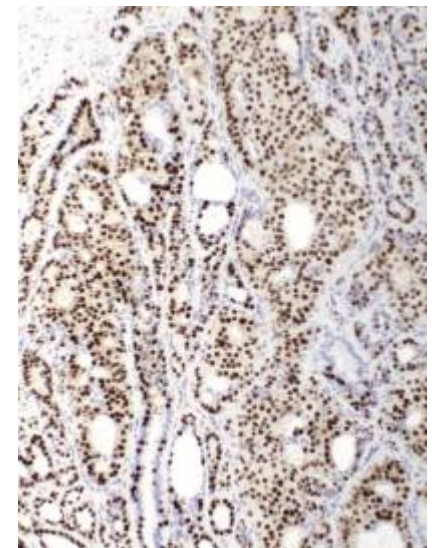
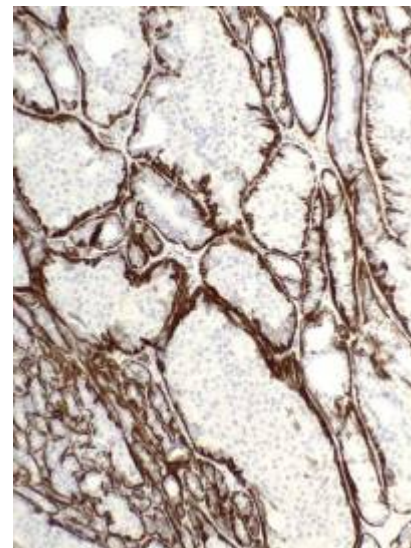
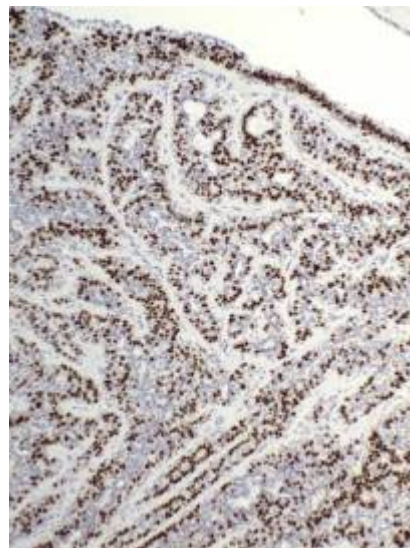
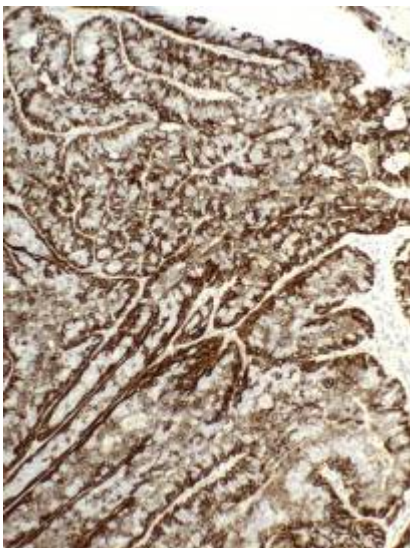
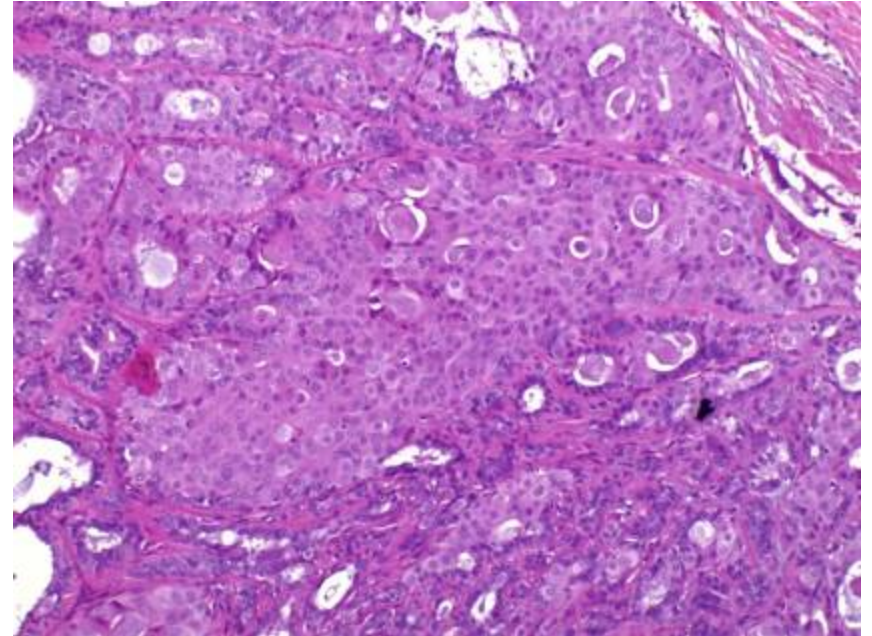
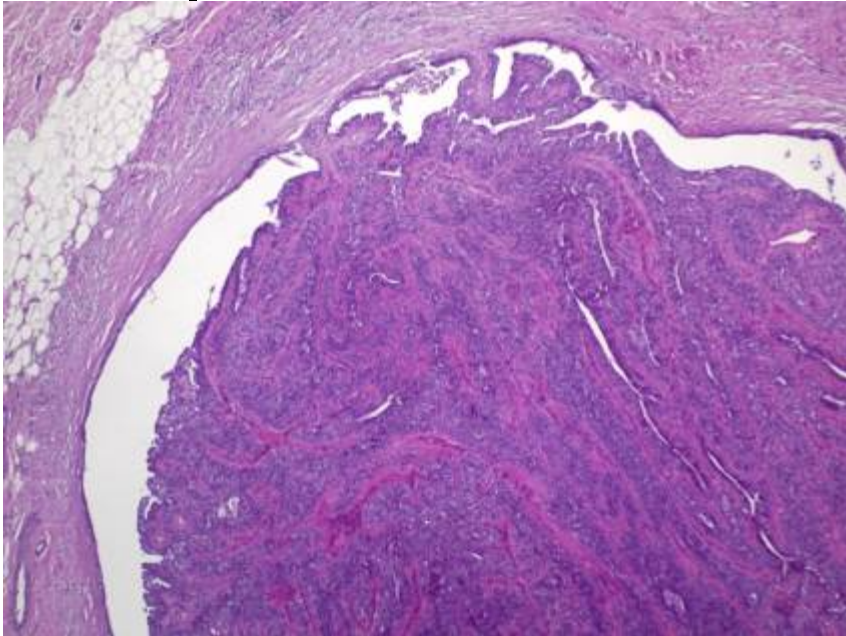
- Background benign papilloma with focal atypia/ DCIS
- DCIS usually low or intermediate grade with solid or cribriform architecture
- Myoepithelium may be reduced or absent in areas of atypia
- ?? Definition

Page >3mm = DCIS – used in WHO

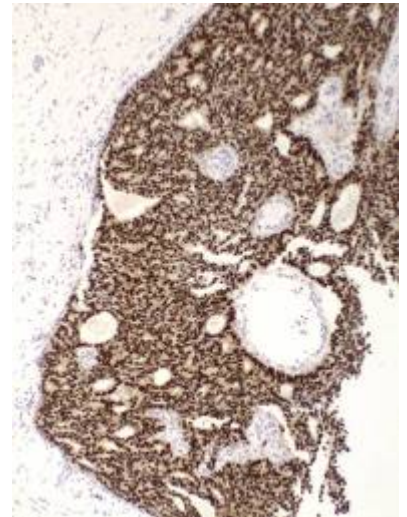
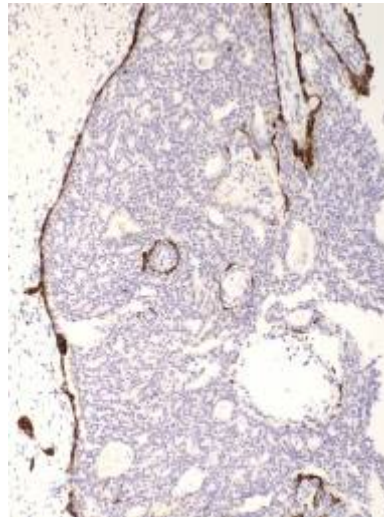
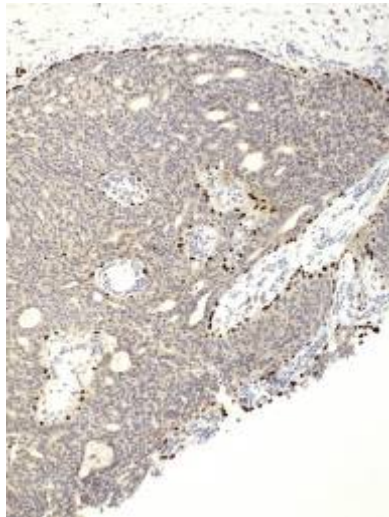
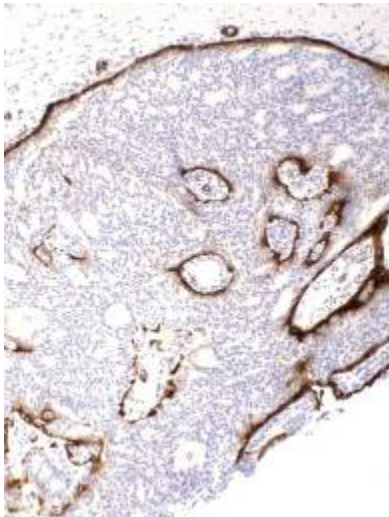
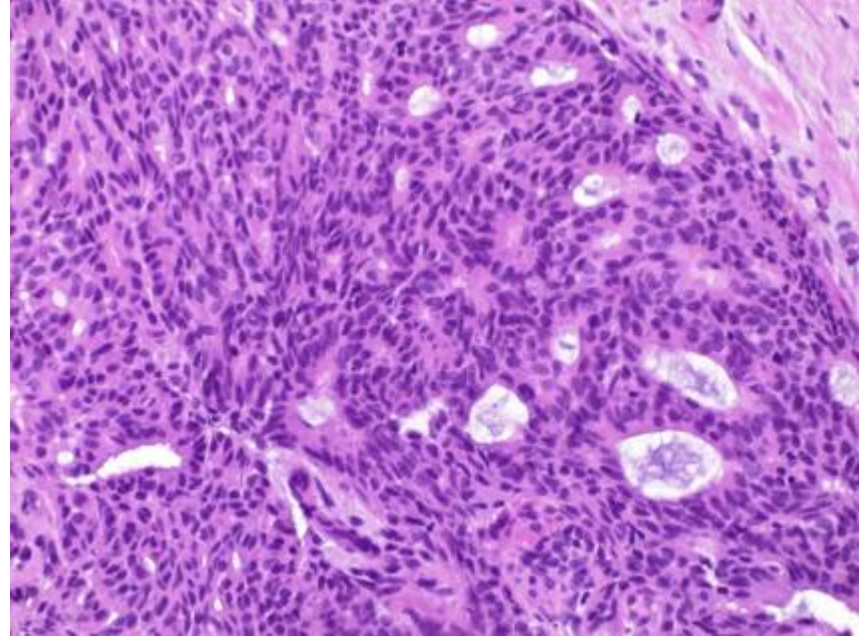
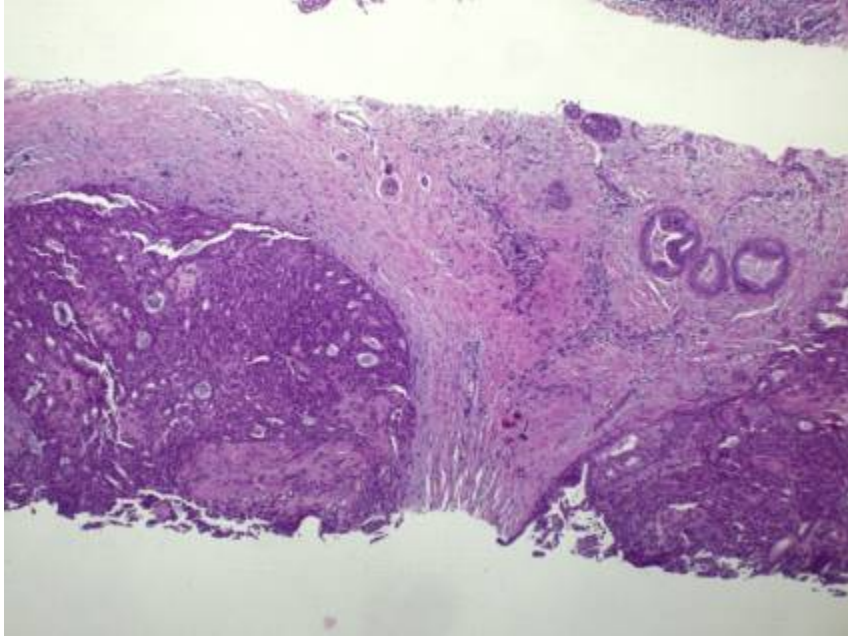
Tavassoli <33% = atypia, 30-90% = DCIS

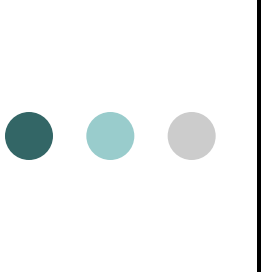
Schnitt – architectural features of DCIS = DCIS regardless of extent

IHC – Papilloma with atypia



IHC – Papilloma with DCIS

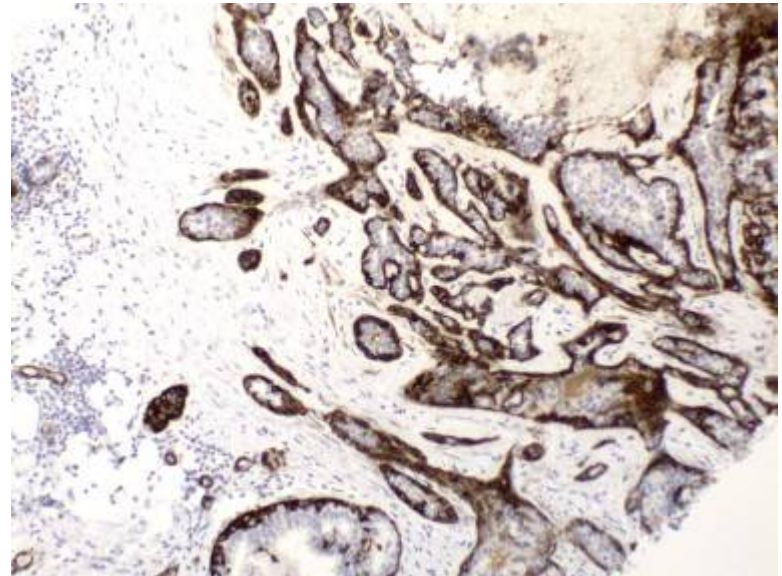
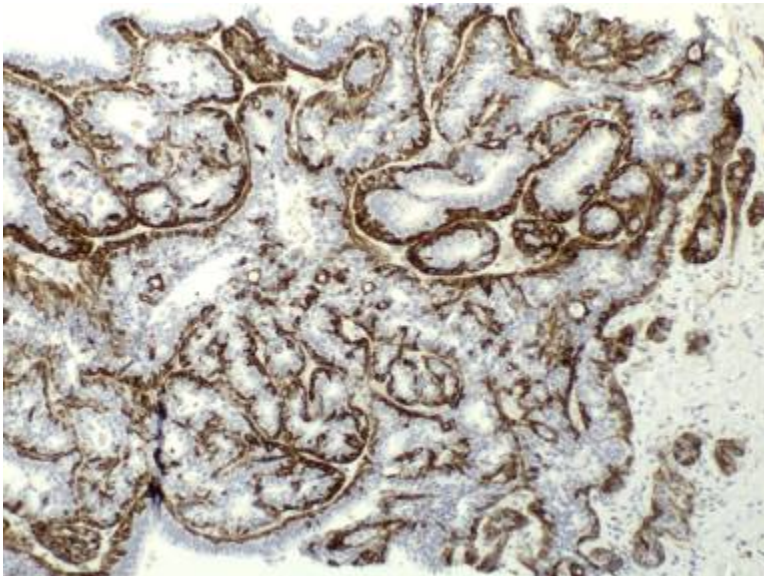
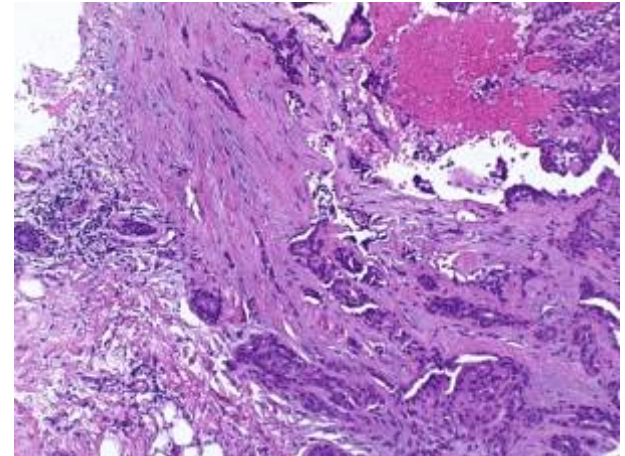
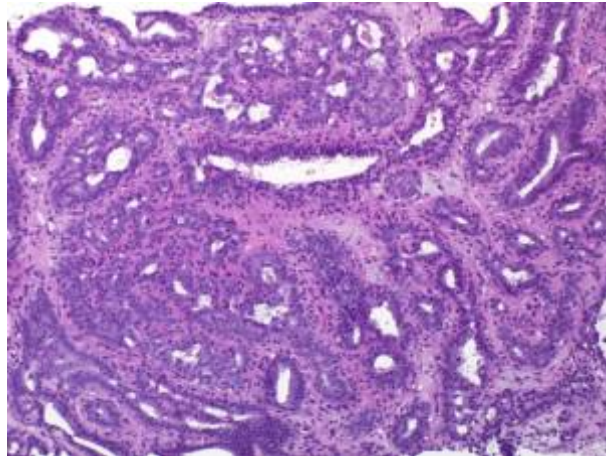
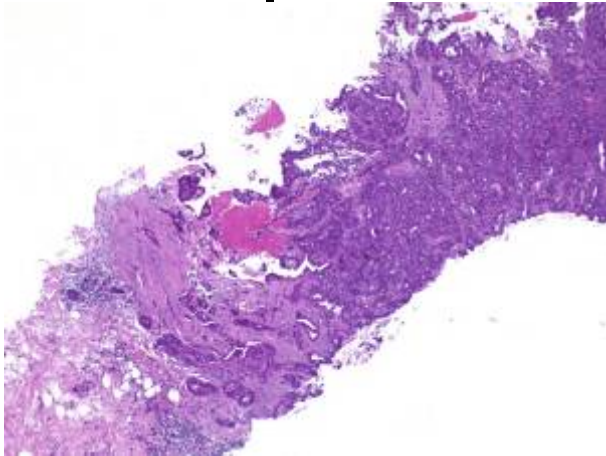


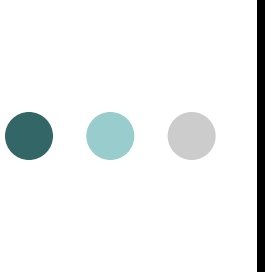


IHC – myoepithelial markers

- p63 – high sensitivity 99-100%
low stromal cross reactivity (90% specificity)
- Calponin – 93% sensitivity
cross reactivity with myofibroblasts (79% specificity)
- SMA – 88% sensitivity
high cross reactivity with myofibroblasts (65% specificity)
- SMMHC – high sensitivity, but some cross reactivity with myofibroblasts and vascular smooth muscle

IHC – myoepithelial markers





Case 6:

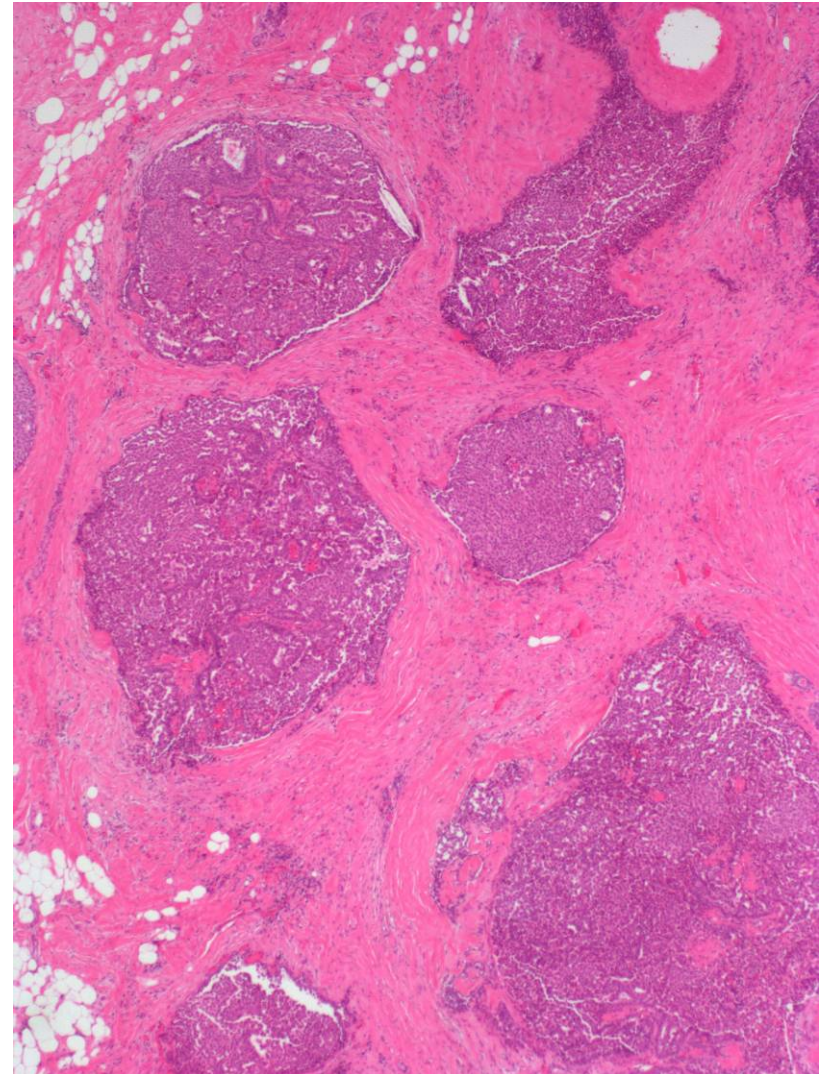
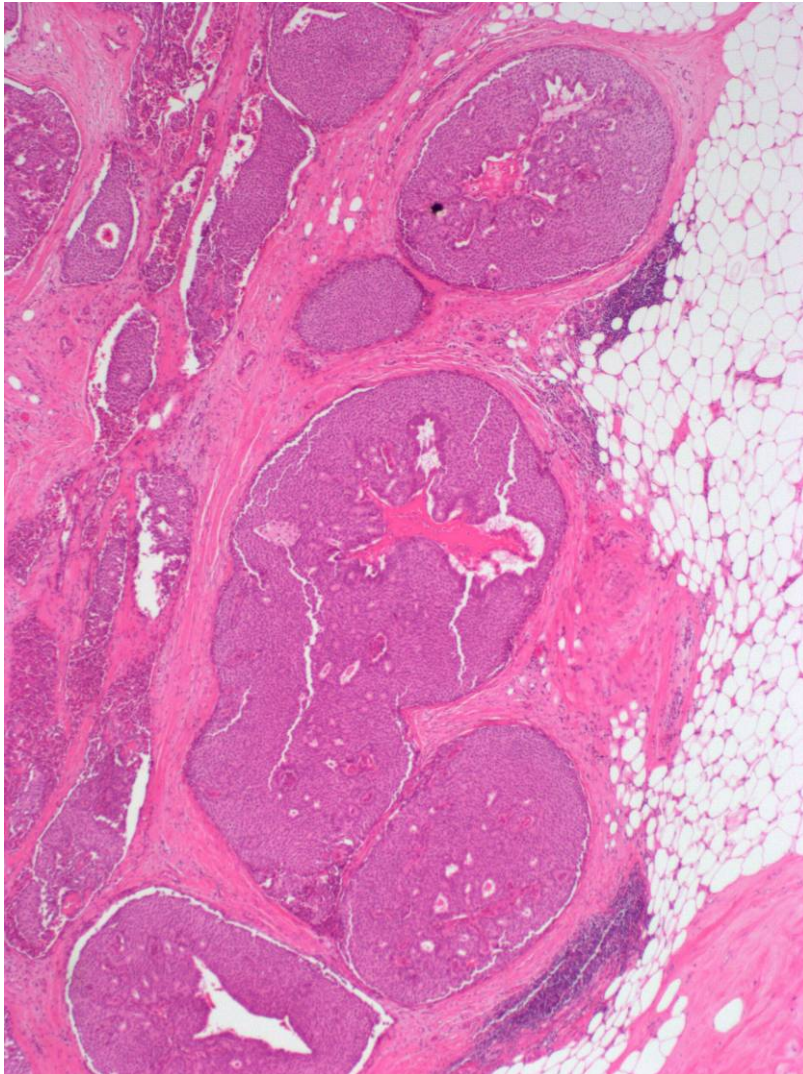
77 yo female.

L breast lump.

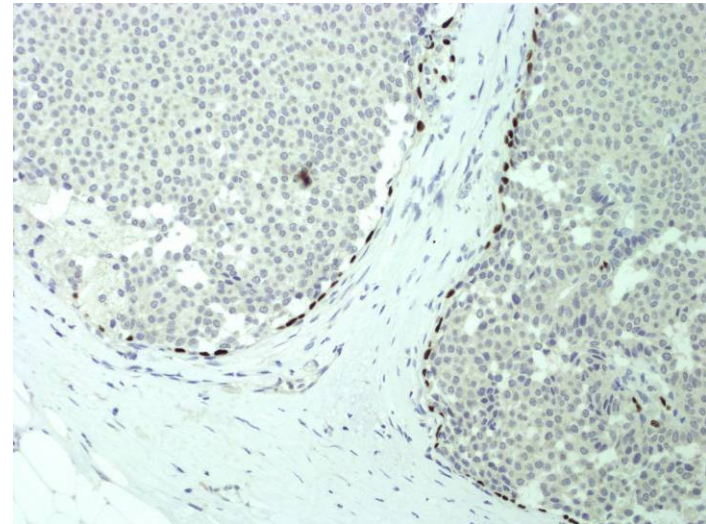
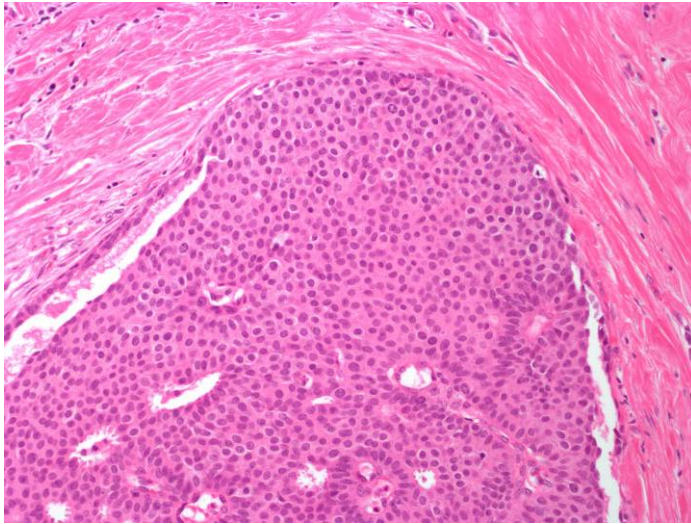
MMG normal.

Indeterminate lesion on US.

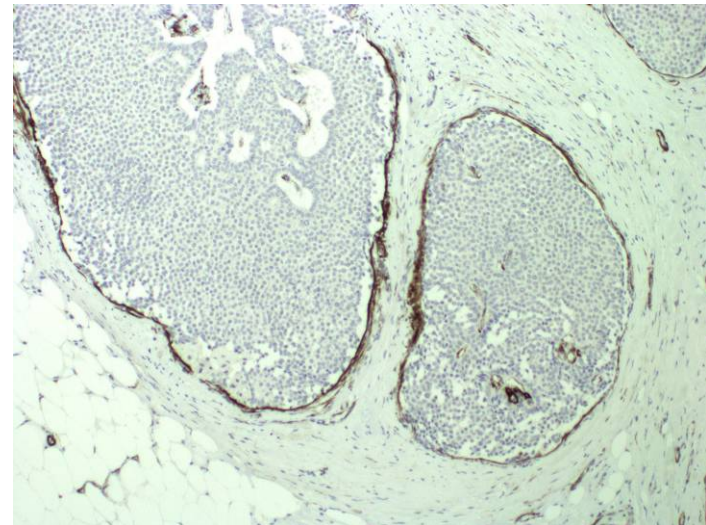
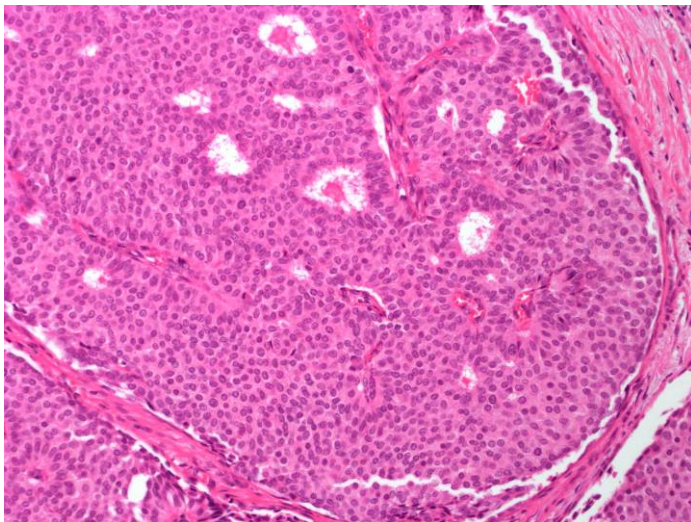
Case 6:



Case 6:

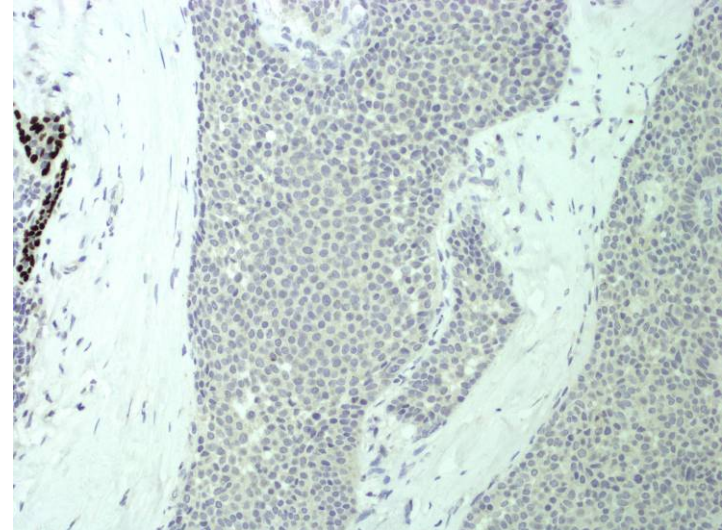
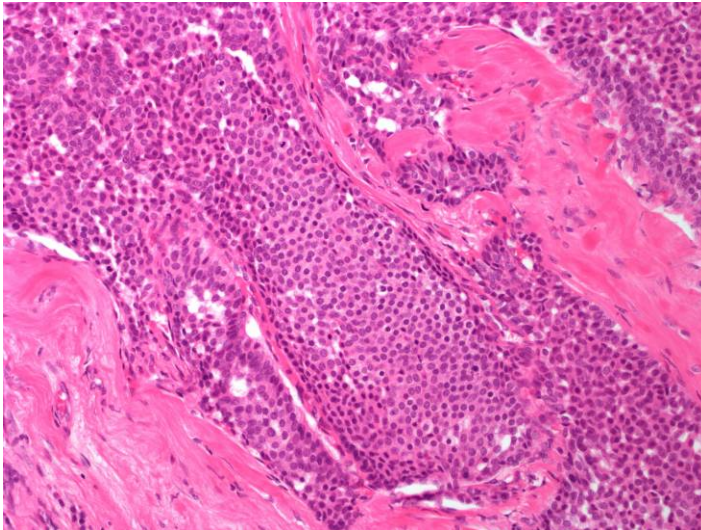


p63

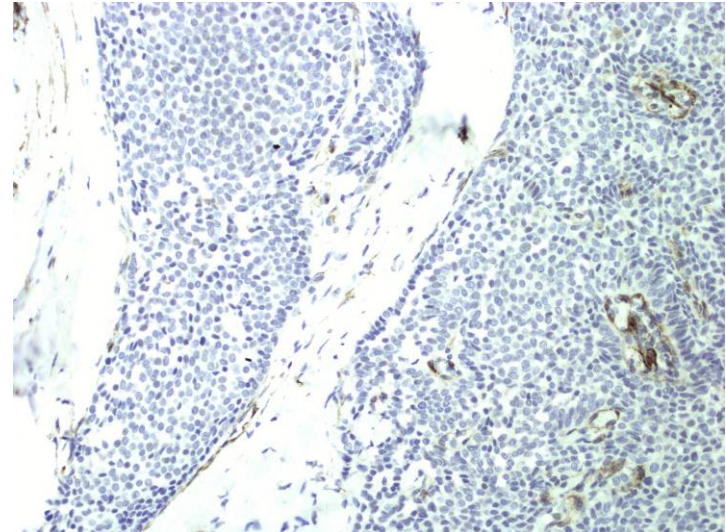
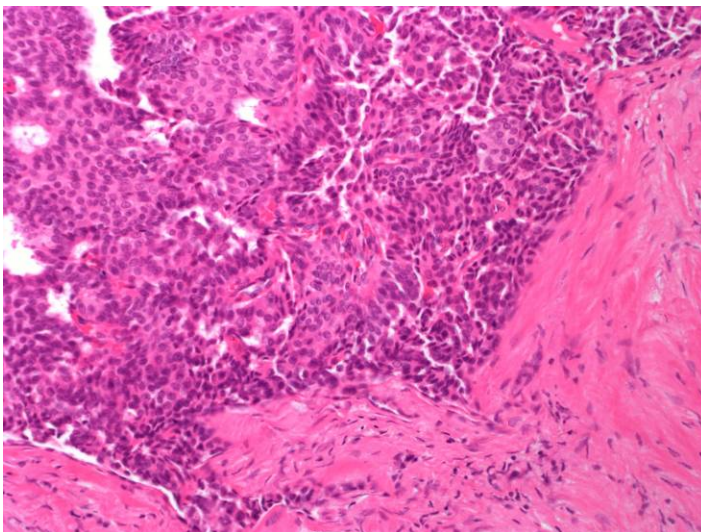


SMA

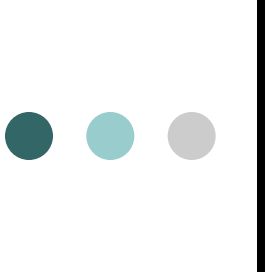
Case 6:



p63

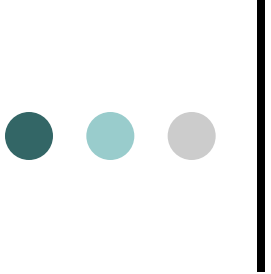


SMA



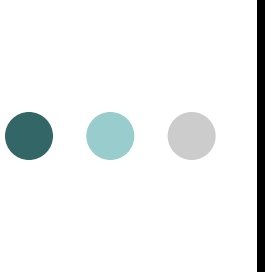
Case 6:

**Solid papillary
carcinoma – mixed
in situ and invasive**



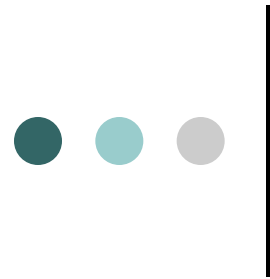
Solid Papillary Carcinoma

- Previous edition subtype of EPC – now separate entity
- Expansive cellular nodules with delicate fibrovascular cores that are inconspicuous at low power
- Neuroendocrine differentiation, spindle cell morphology and mucin production are common
- Myoepithelial cells may be present or absent surrounding the nodule



Solid Papillary Carcinoma

- Presence of outer myoepithelial cell layer, or rounded nodular masses without an infiltrative pattern are regarded as DCIS
- Rare variants with irregularly shaped islands arranged in a jigsaw pattern in a desmoplastic stroma, without a MEC layer on IHC = invasive solid papillary carcinoma



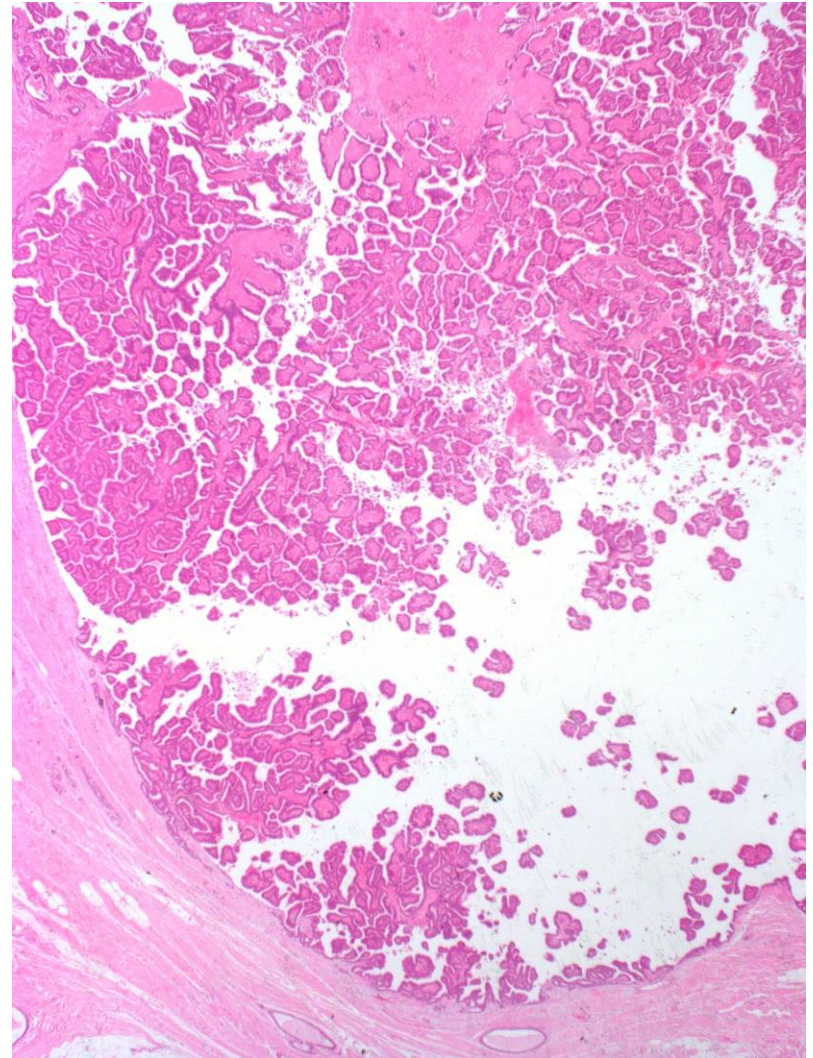
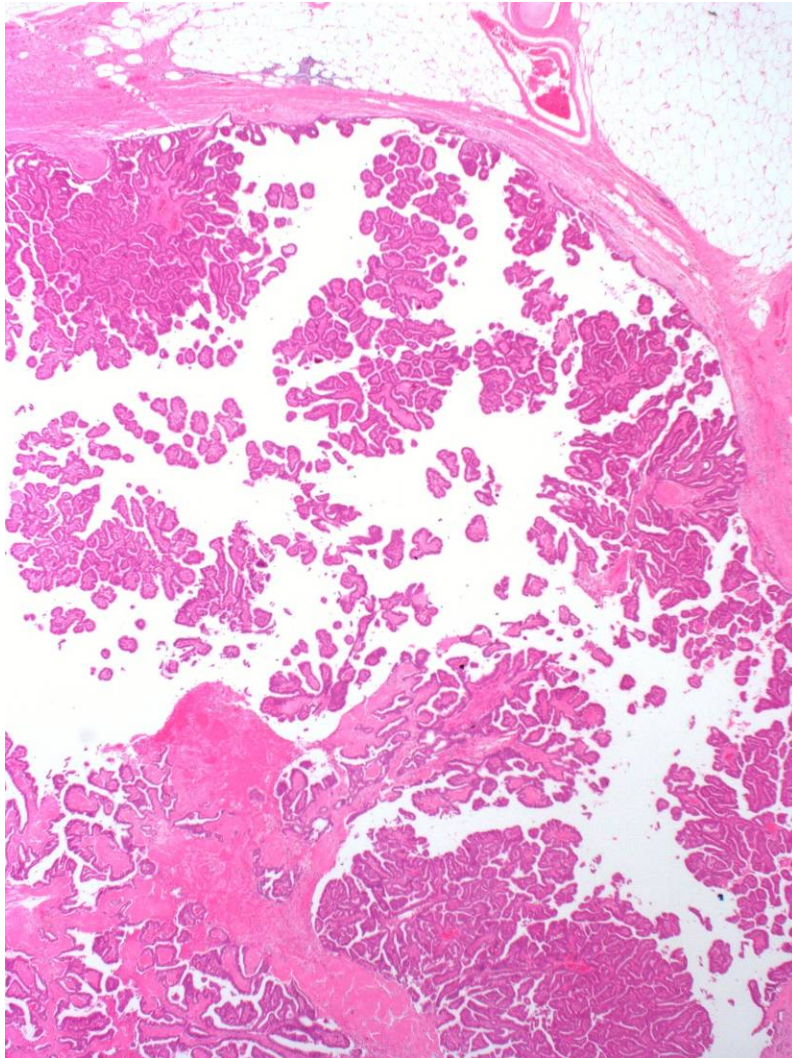
Case 7:

74 yo female.

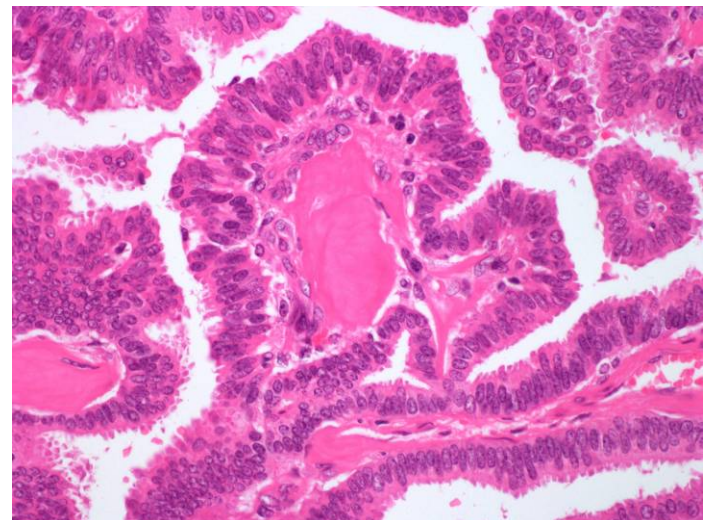
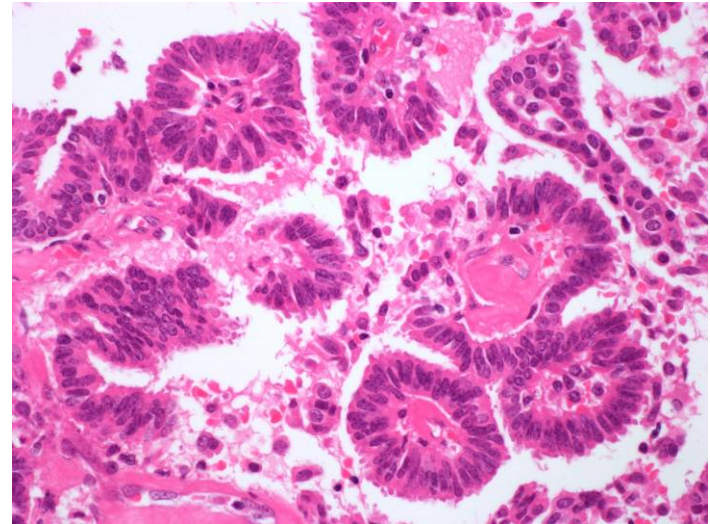
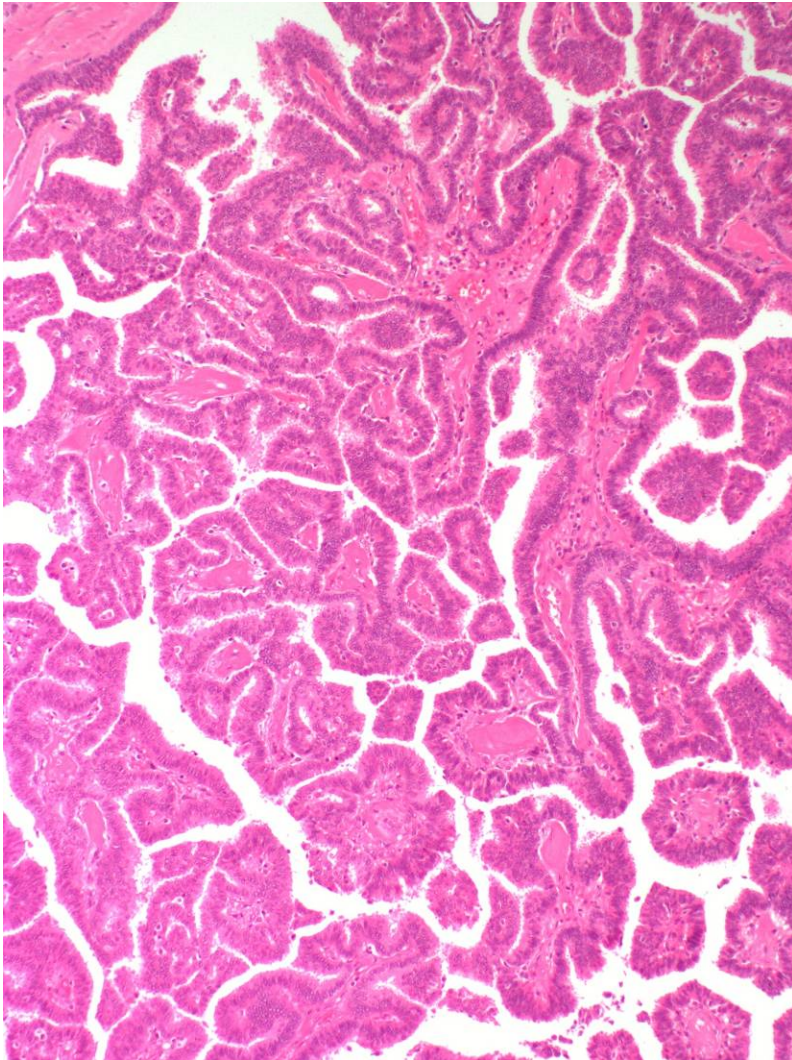
L breast lump.

? malignant.

Case 7:

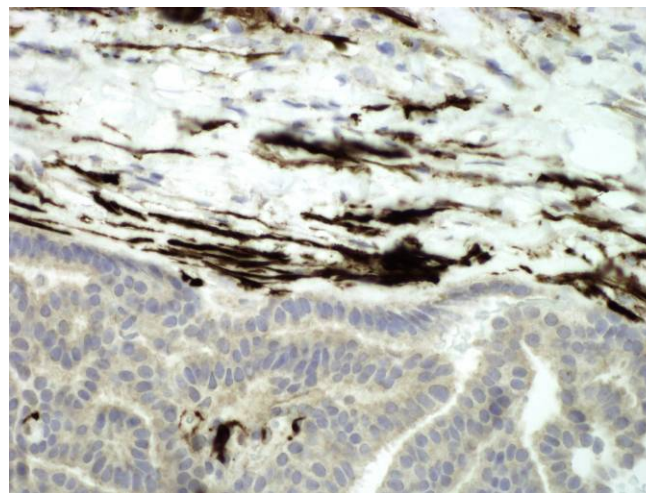
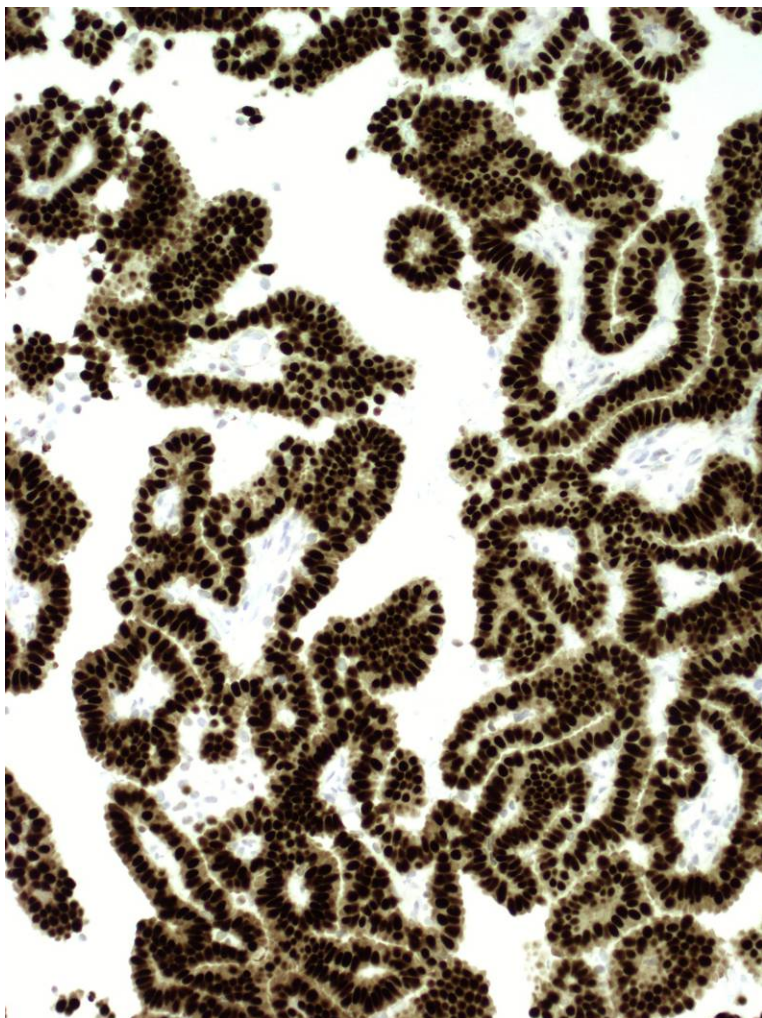


Case 7:

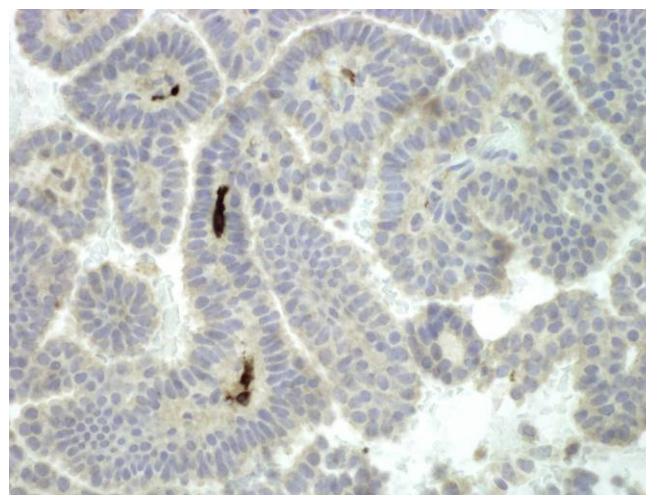


Case 7:

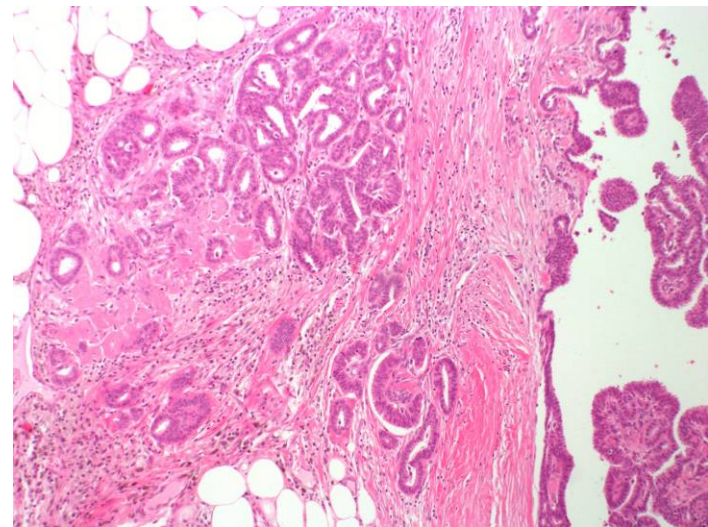
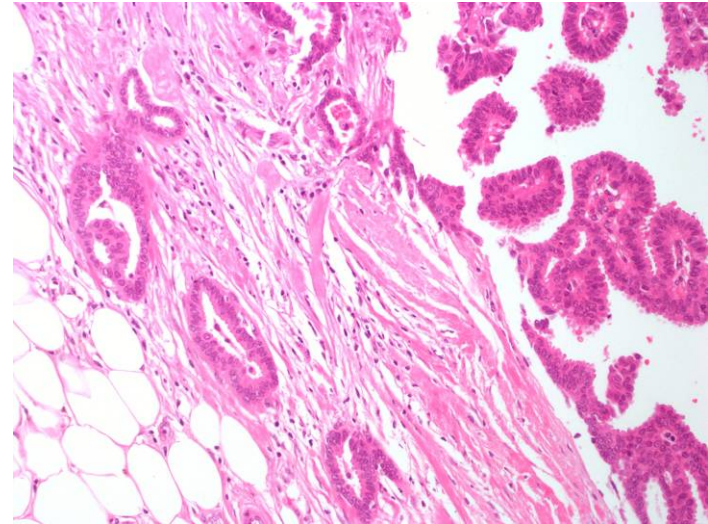
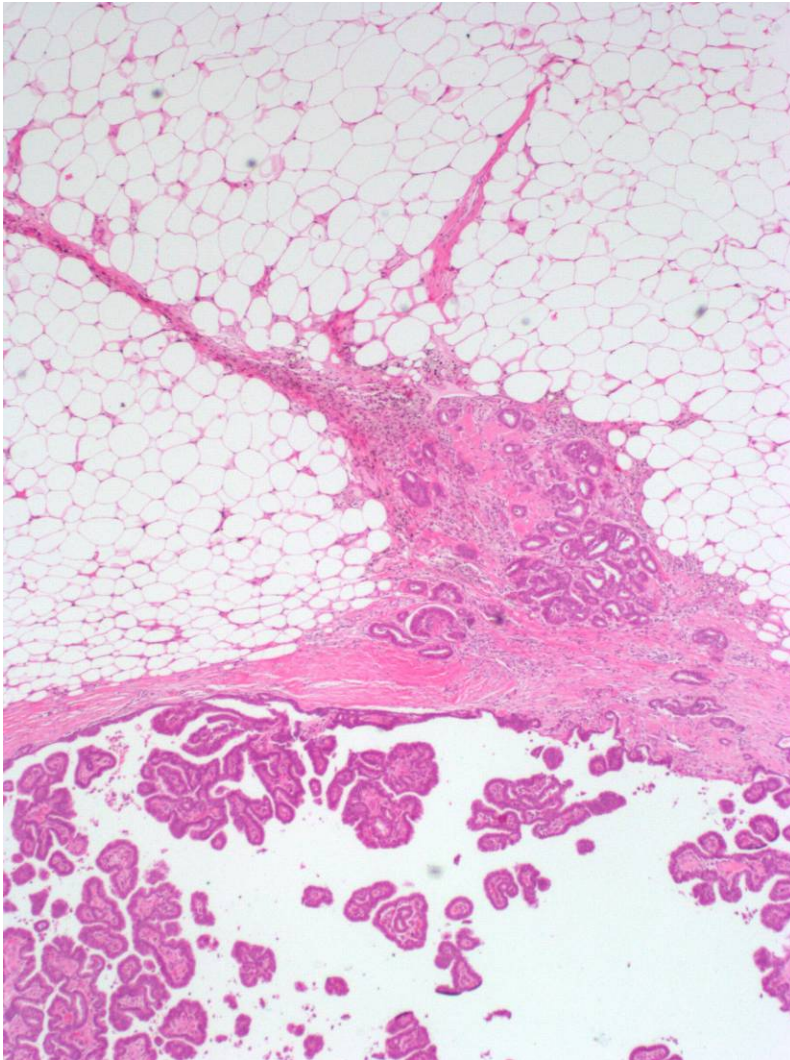
ER

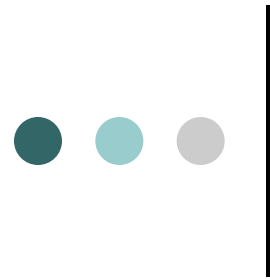


SMMHC



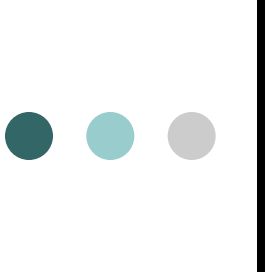
Case 7:





Case 7:

**Encapsulated
papillary
carcinoma**

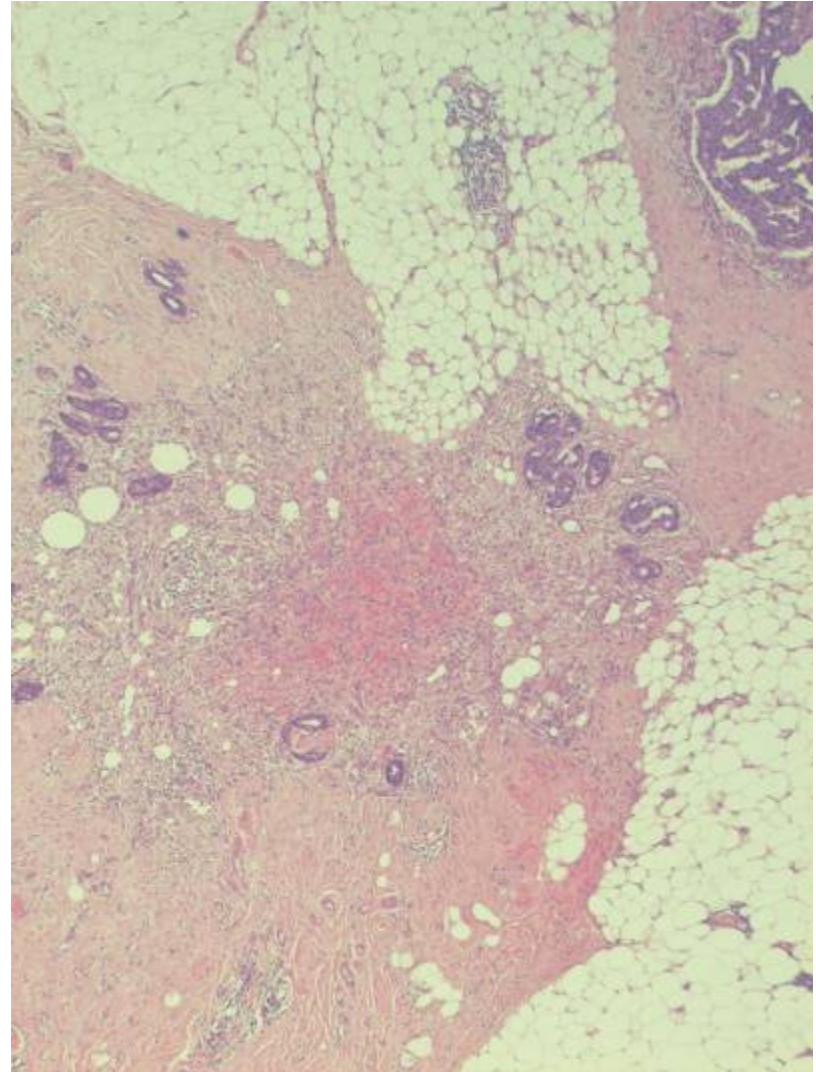


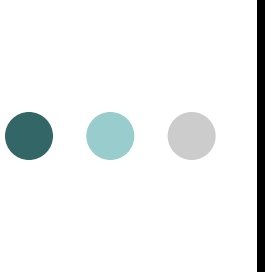
Encapsulated Papillary Ca

- Variant of papillary carcinoma characterised by fine fibrovascular cores covered by neoplastic cells of low to intermediate grade, surrounded by a thick fibrous capsule
- Lacks a myoepithelial layer
- Low incidence of lymph node metastasis (1-3%)
- Local recurrence rare (7%)
- Rare cases showing skeletal muscle invasion – only if previous surgery
- Favourable prognosis with adequate local excision alone
- WHO – stage as Tis unless frank invasive component
- Associated invasive carcinoma usually NST; present in 13-32% of cases
- For invasion requires infiltration beyond fibrous capsule
- Measure invasive component only

Epithelial displacement

- Common finding in resection specimens following CB
- Nests of epithelial cells lying within the biopsy tract – fibrosis, fat necrosis, haemosiderin laden macrophages
- In case of papillary carcinoma cells will be atypical
- Myoepithelial stains unhelpful
- Should not be called invasion





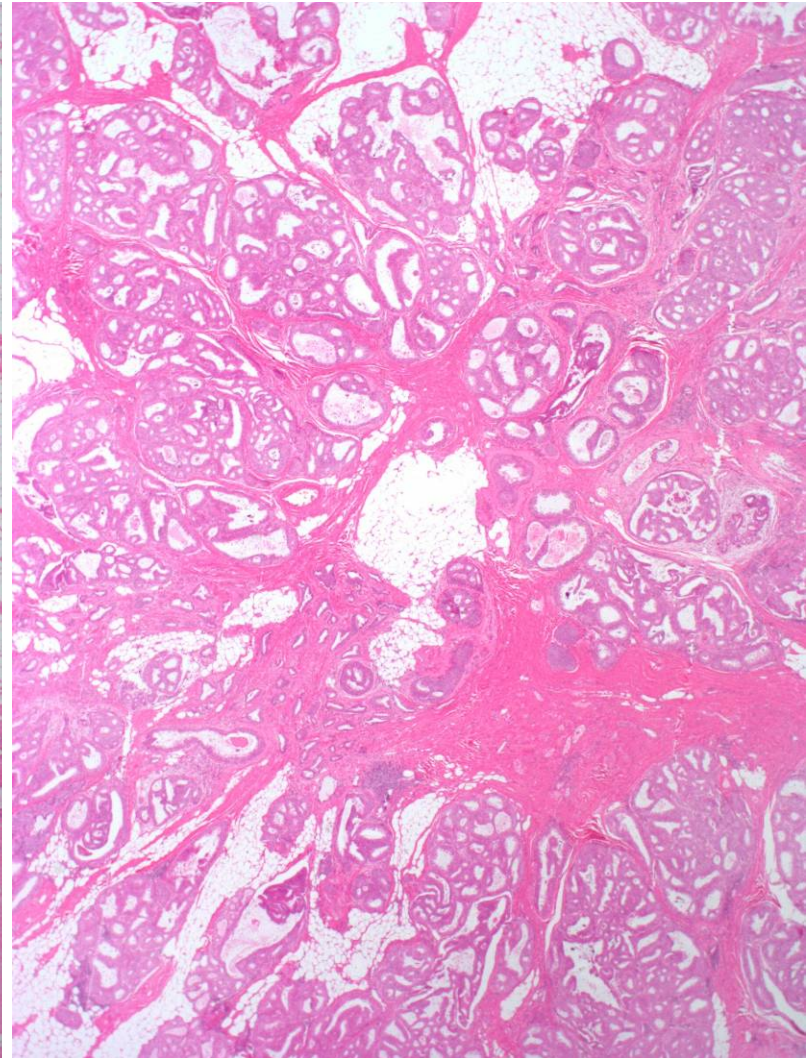
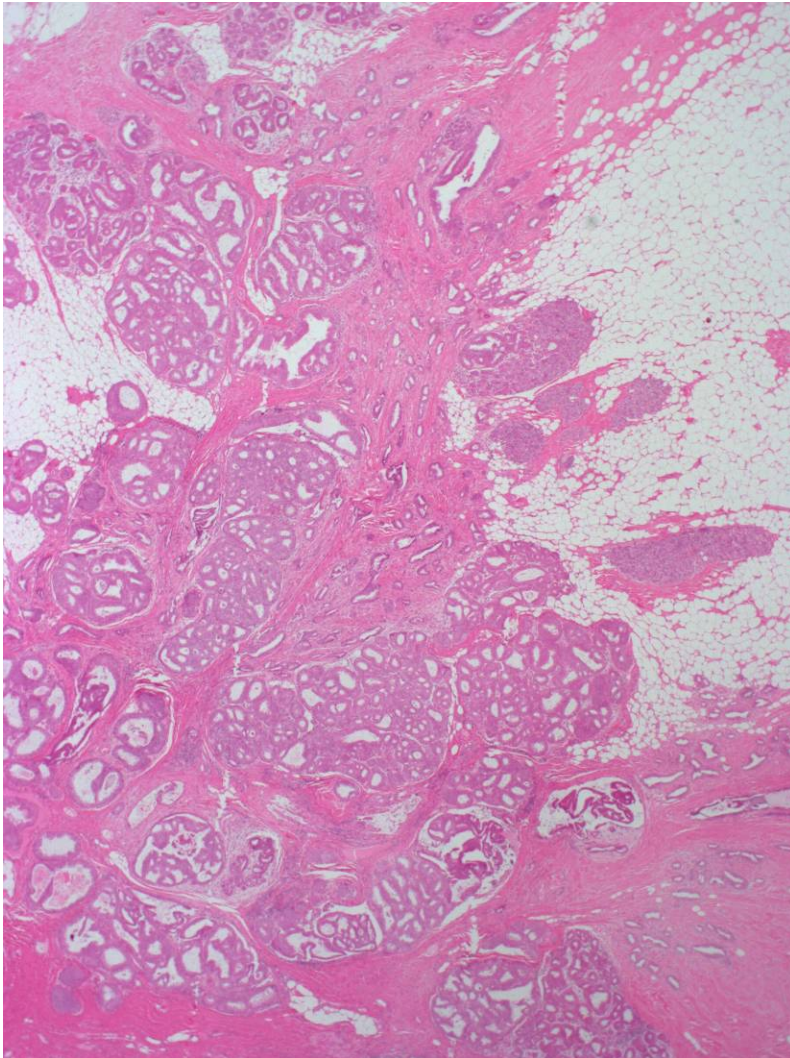
Case 8:

46 yo female.

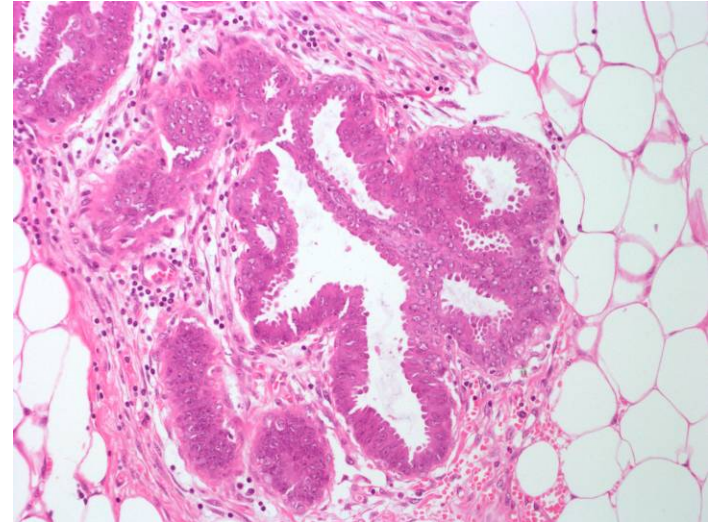
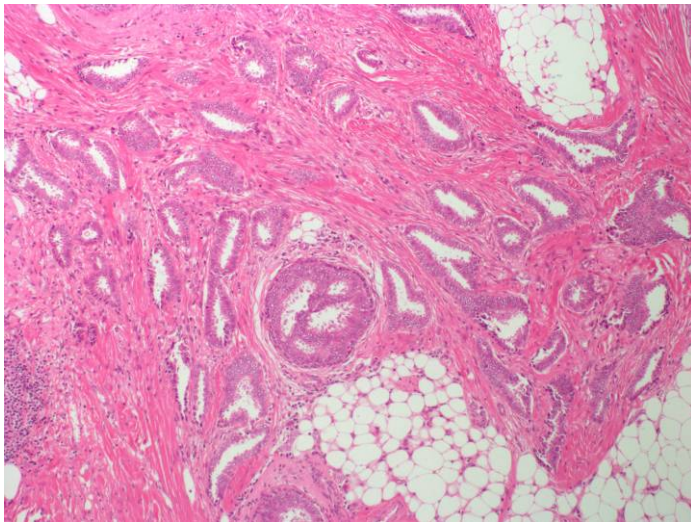
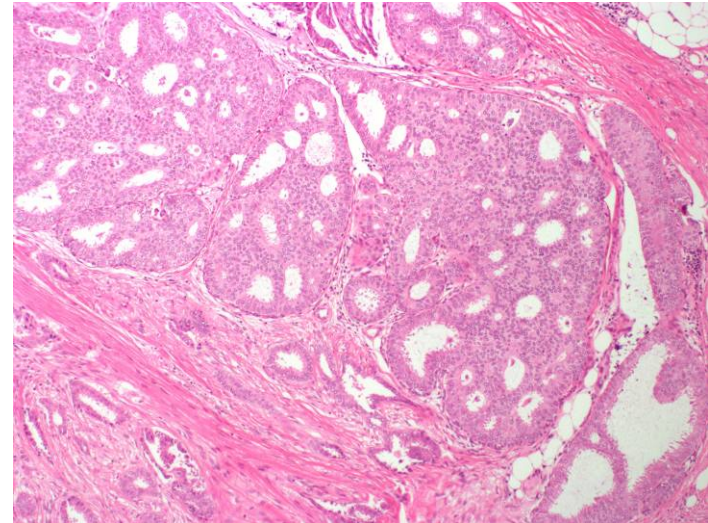
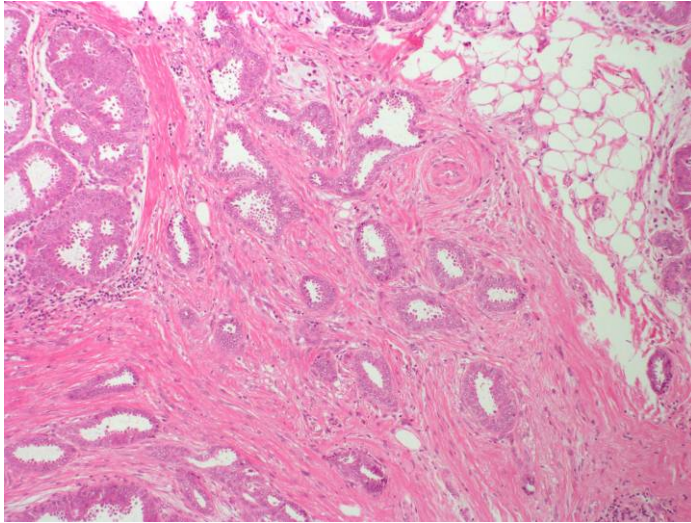
Private screening MMG.

Distortion RUOQ.

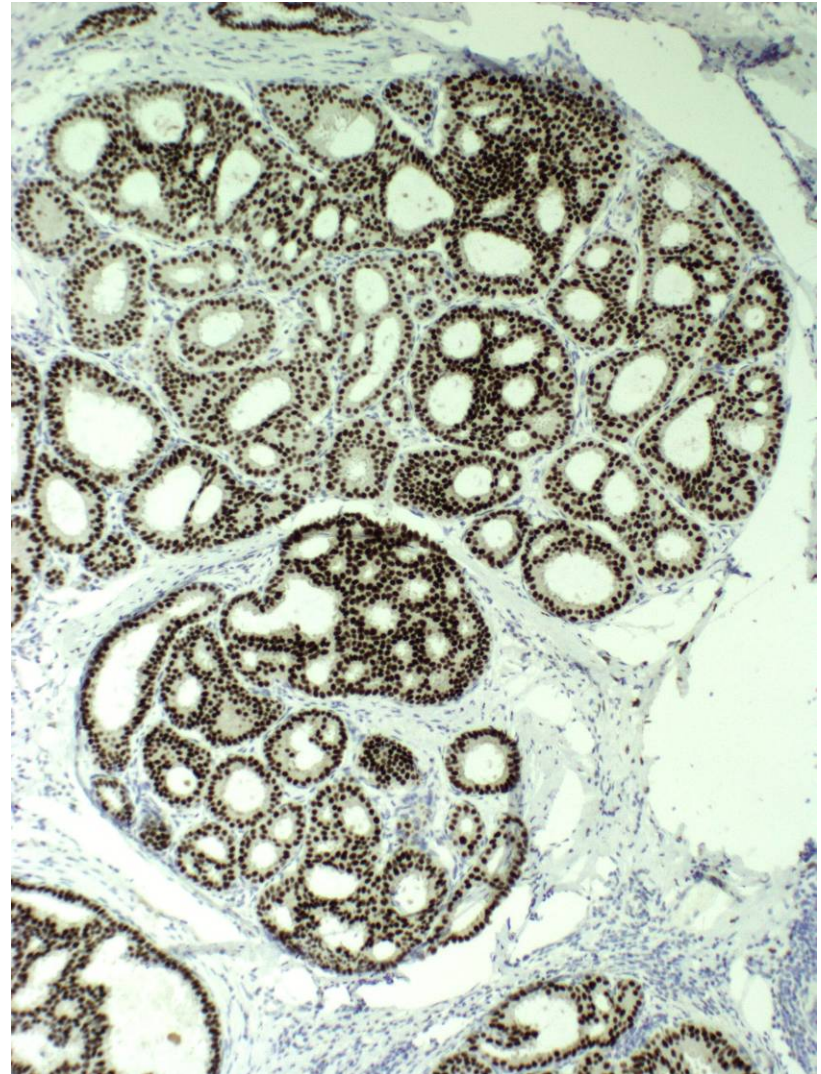
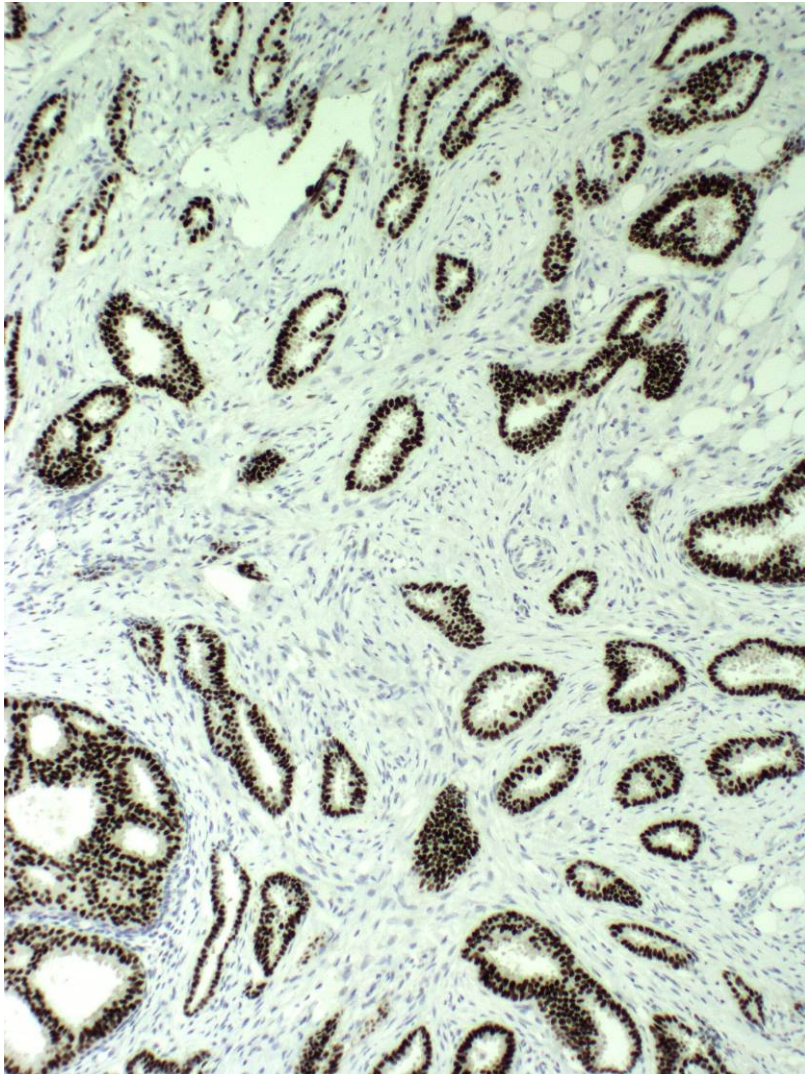
Case 8:



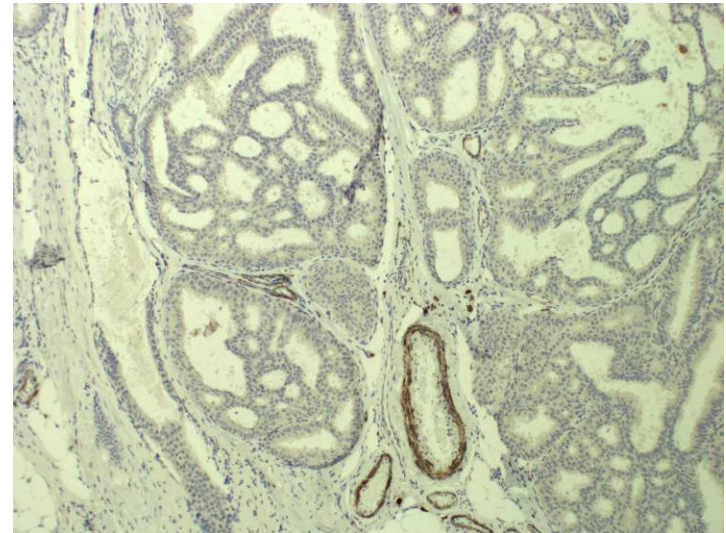
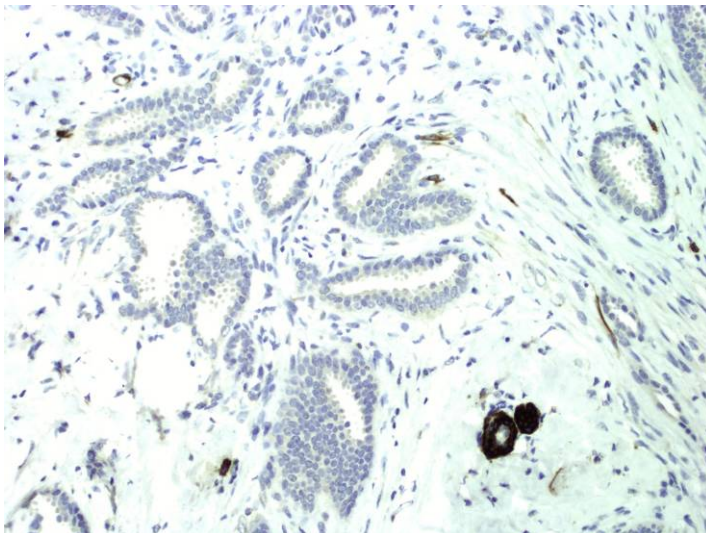
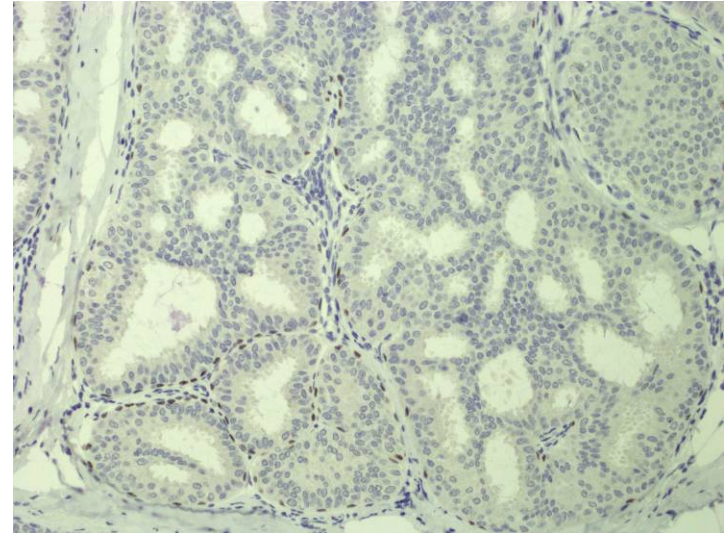
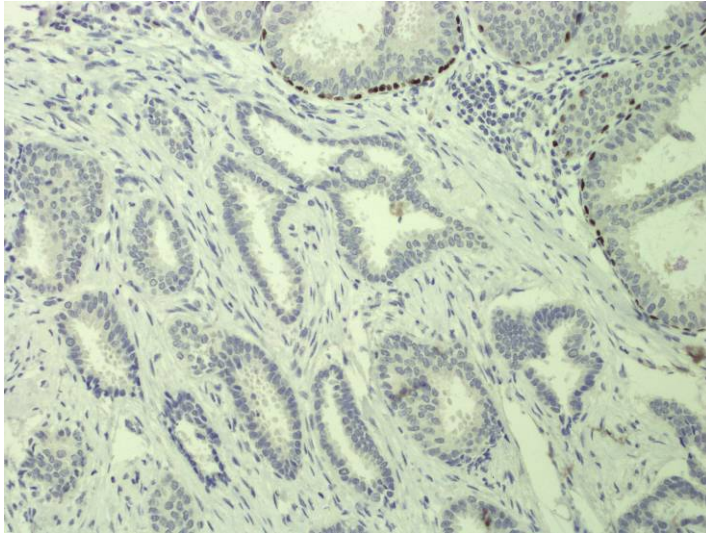
Case 8:

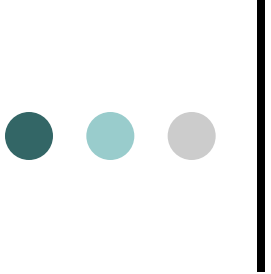


Case 8: ER



Case 8: p63 and SMMHC



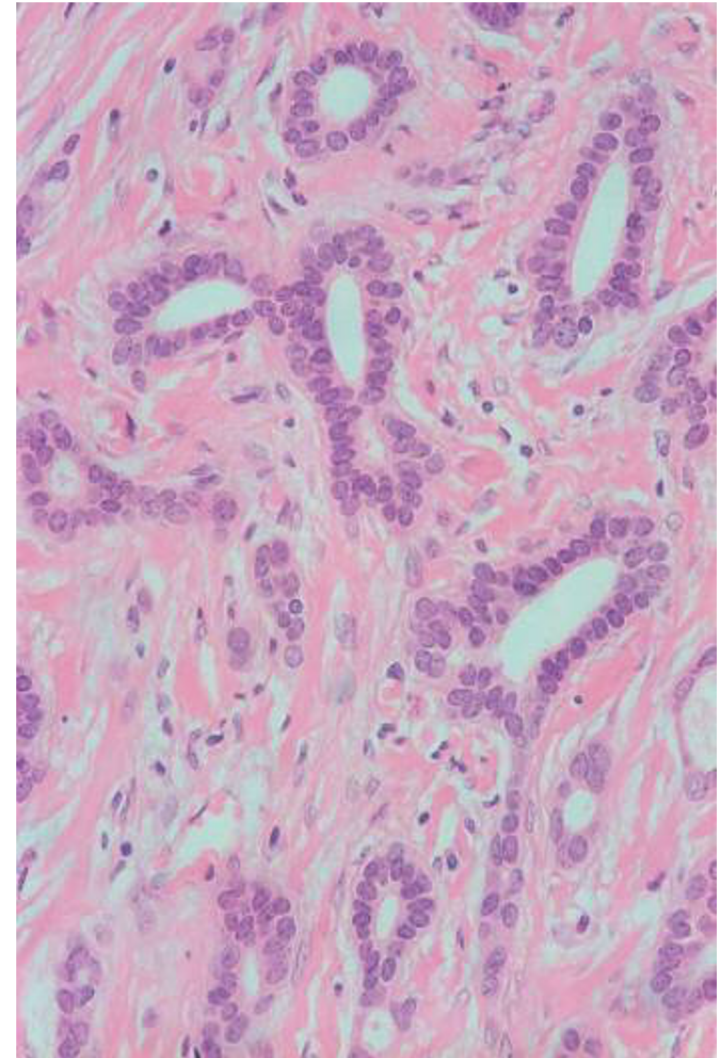


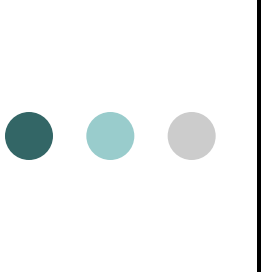
Case 8:

**Invasive tubular
and cribriform
carcinoma with
low grade DCIS**

Tubular Carcinoma

- Composed of small, oval or rounded tubules lined by a single layer of epithelium – no myoepithelial layer
- Tumour cells are small and uniform with minimal nuclear atypia; cytoplasmic apical snouts may be present
- Connective tissue stroma is usually desmoplastic
- ER positive and HER2 negative
- Excellent prognosis





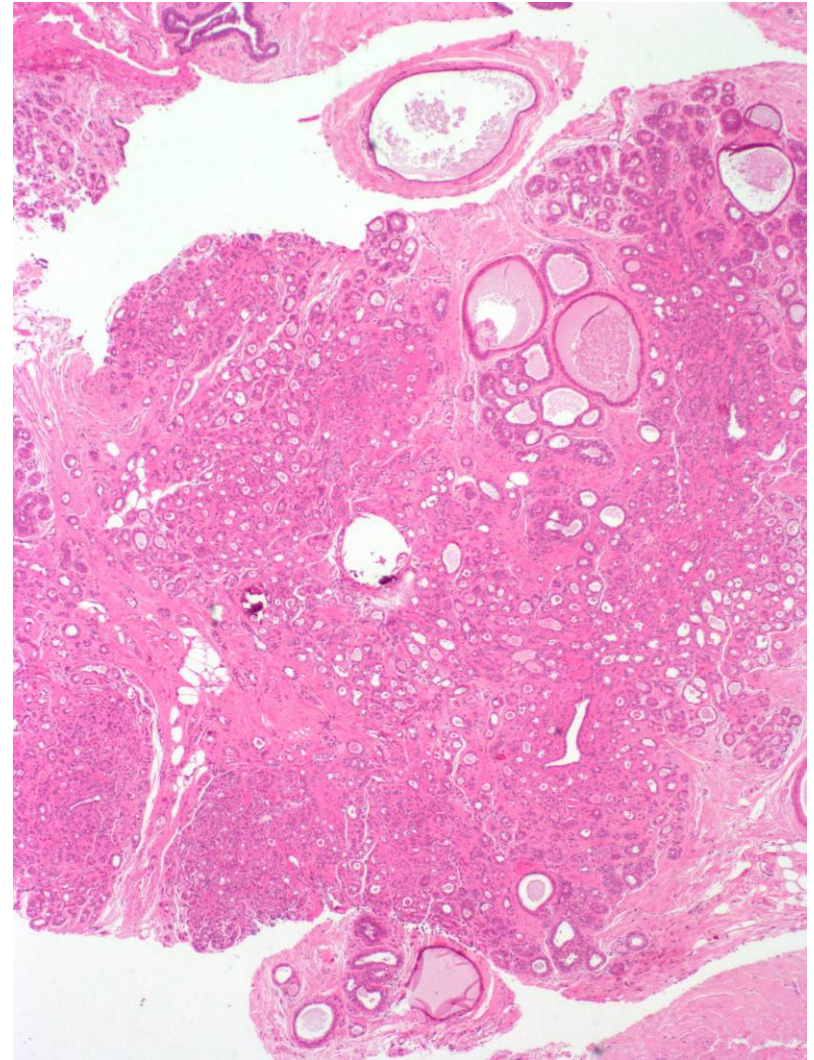
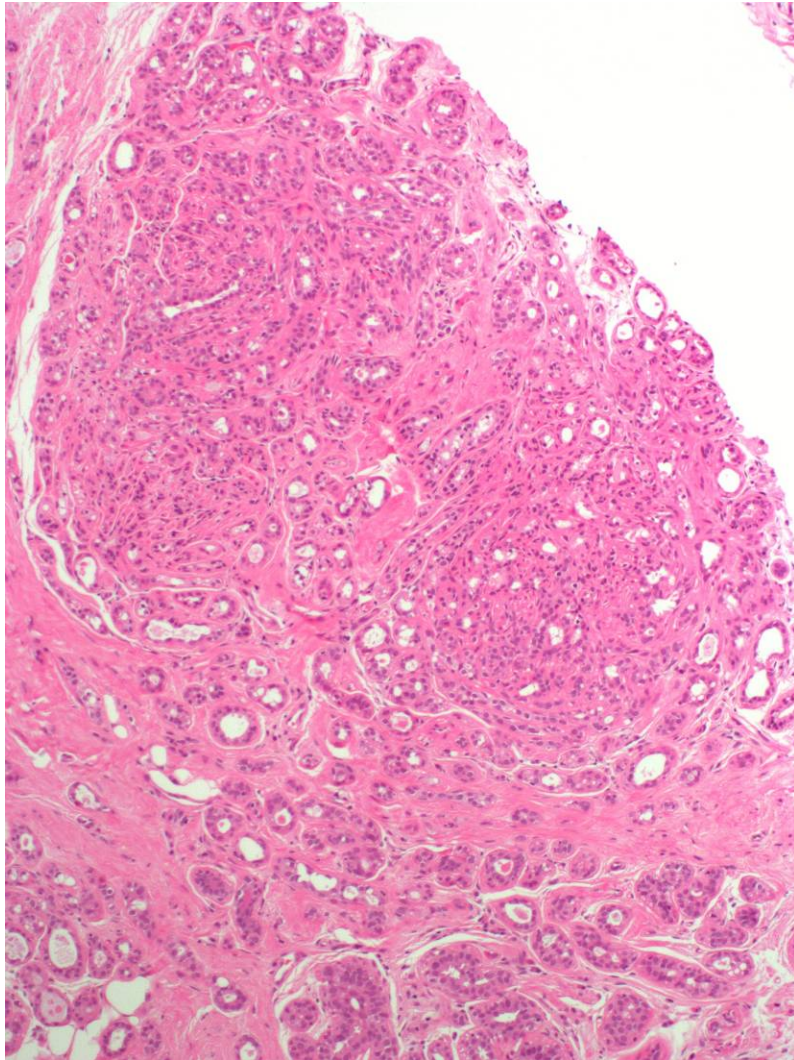
Case 9:

56 yo female.

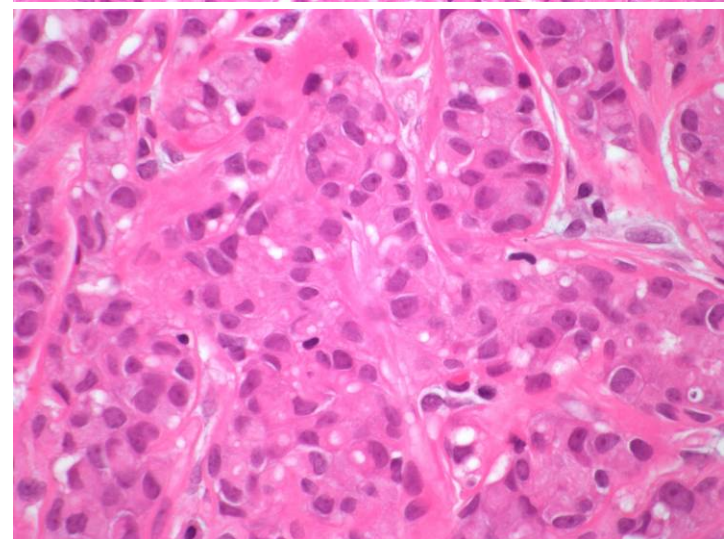
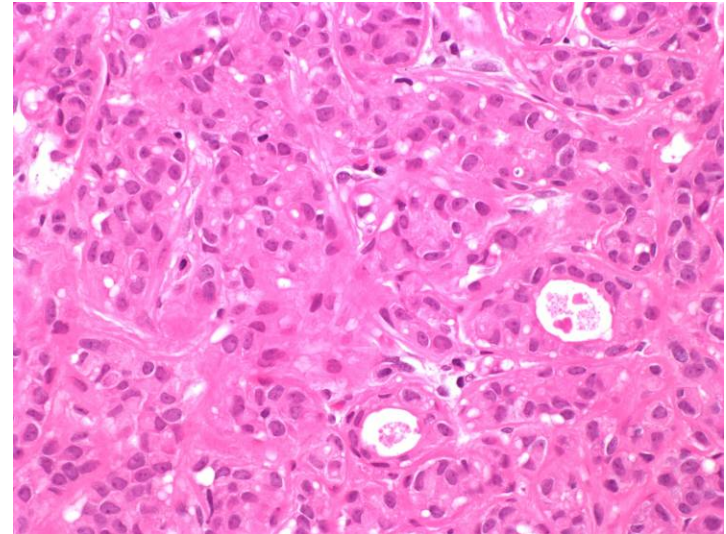
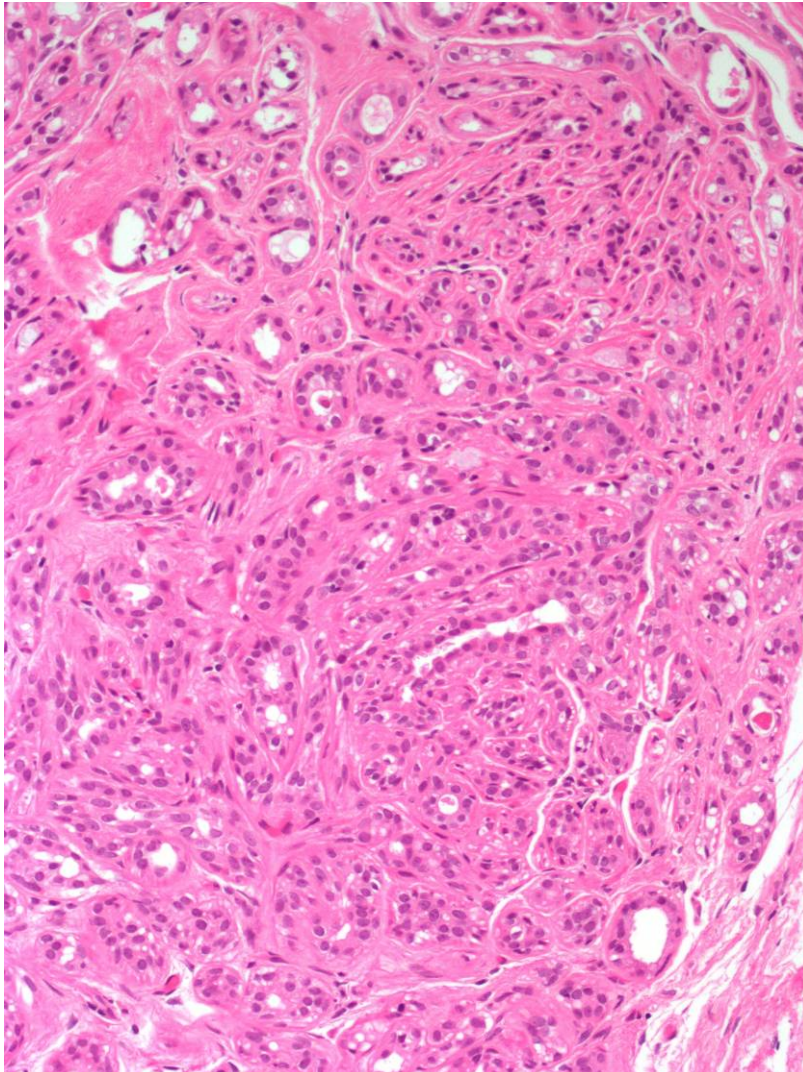
Known Ca R breast.

Ca++ LUOQ on MMG M3.

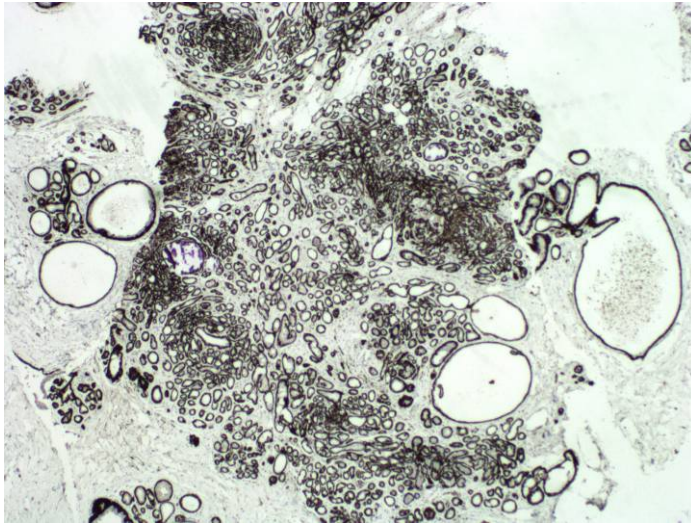
Case 9



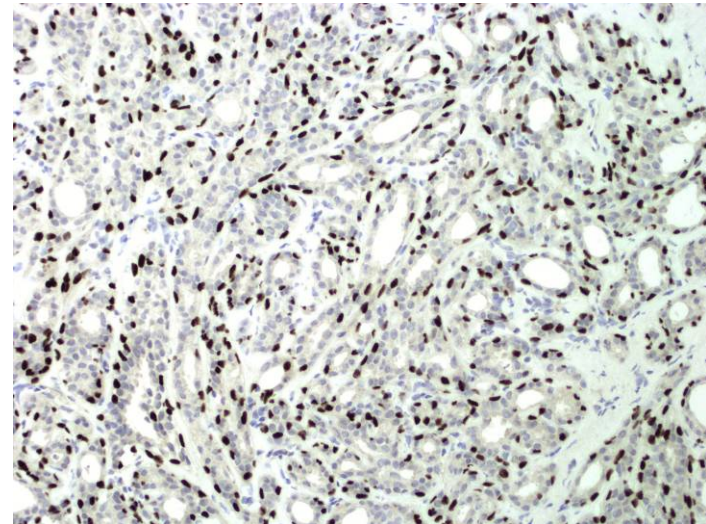
Case 9



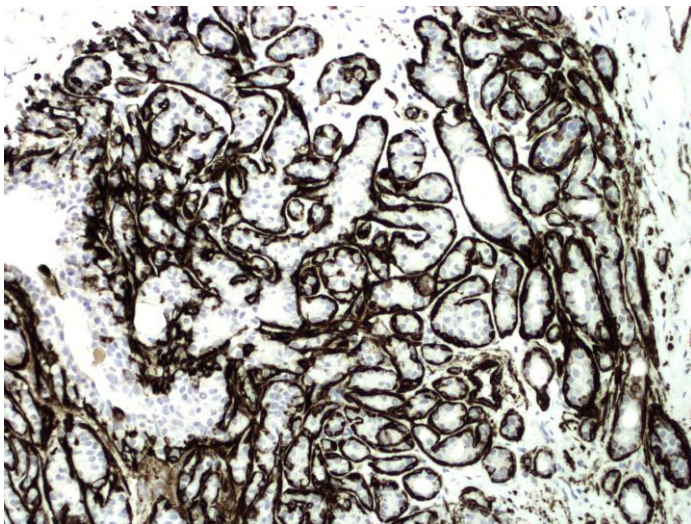
Case 9



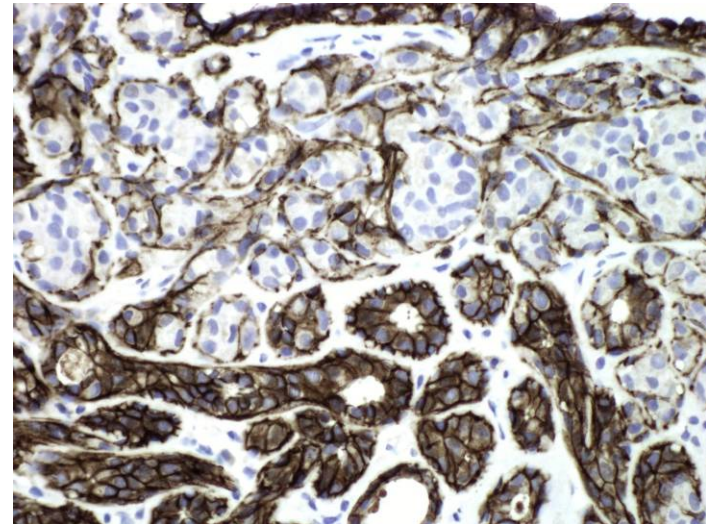
SMMHC

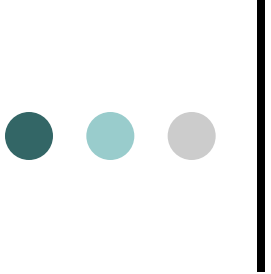


p63



Ecad

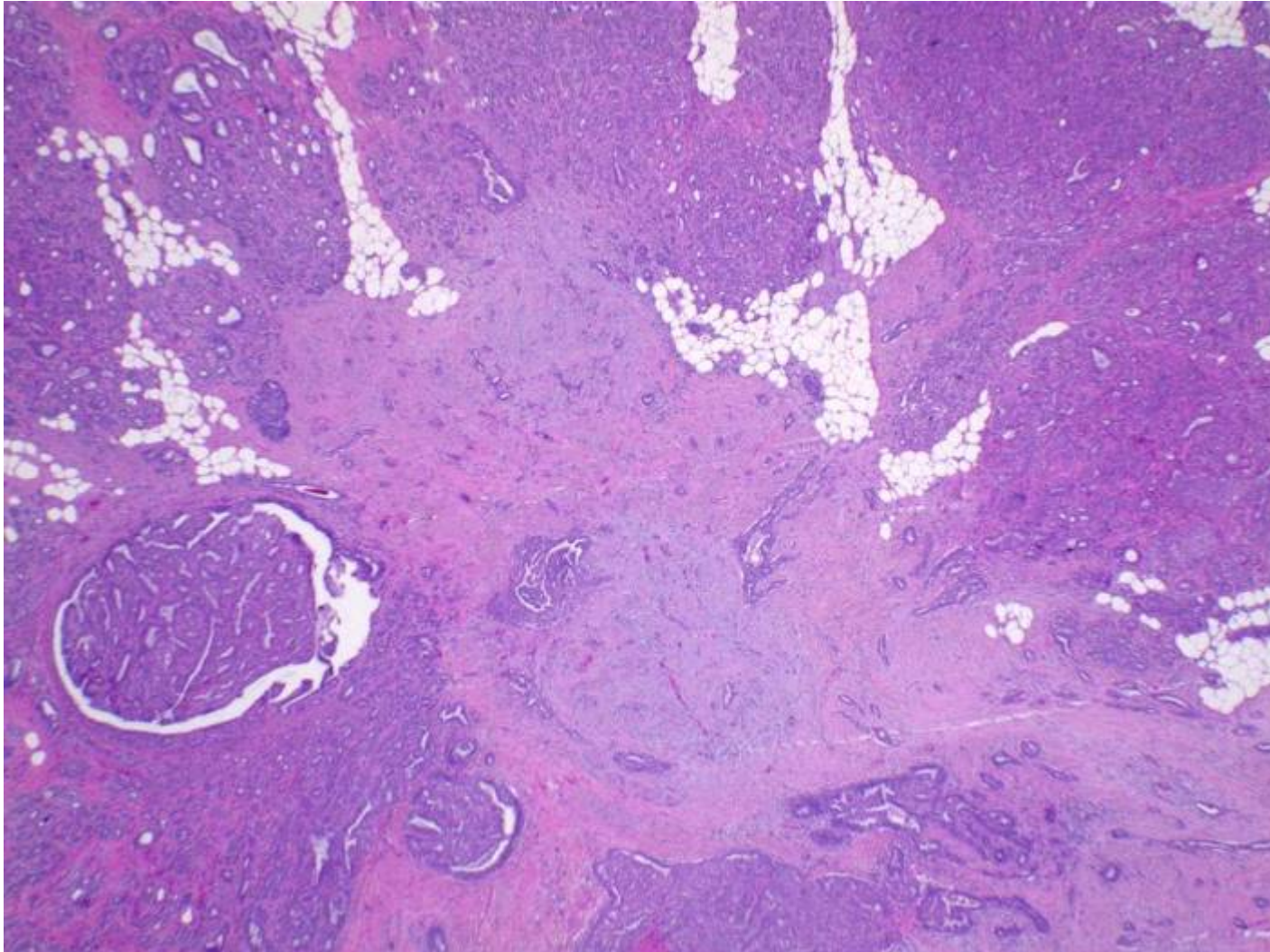




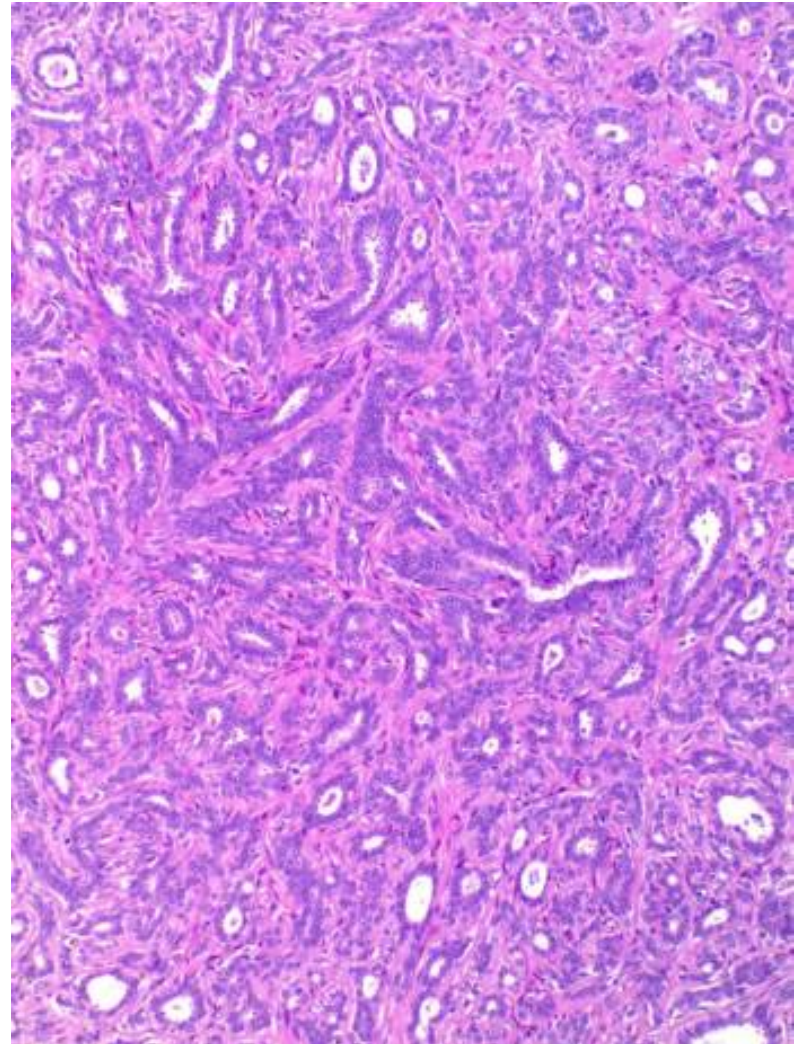
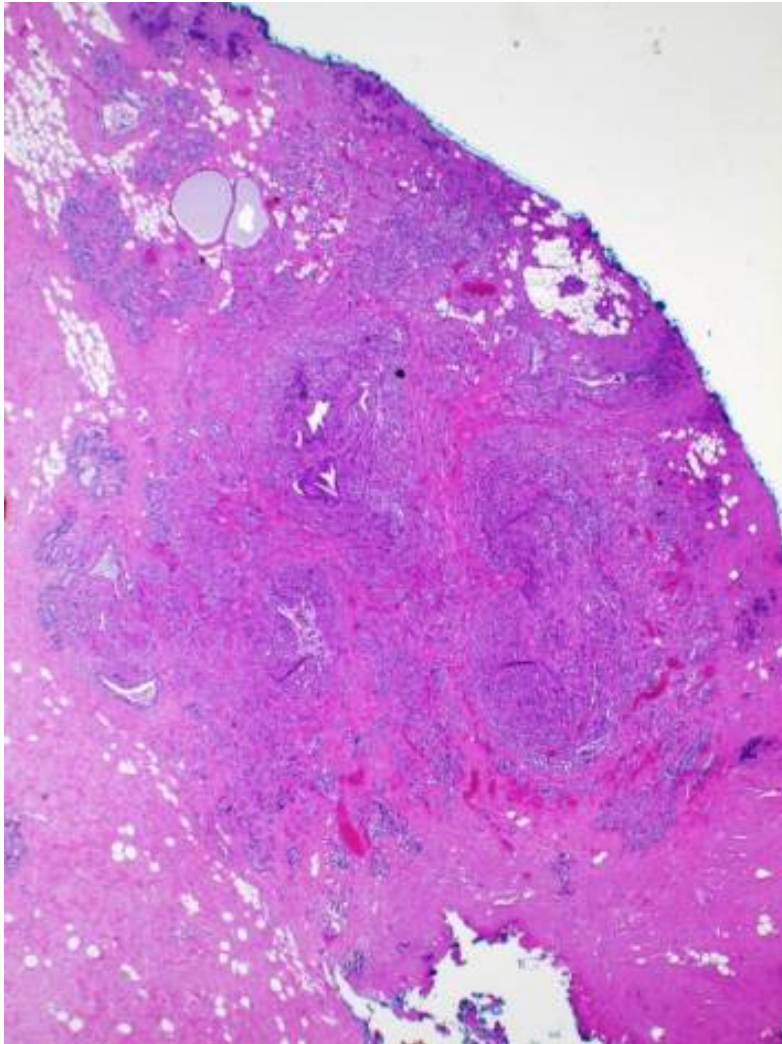
Case 9:

**Complex Sclerosing
Lesion with focal
LCIS**

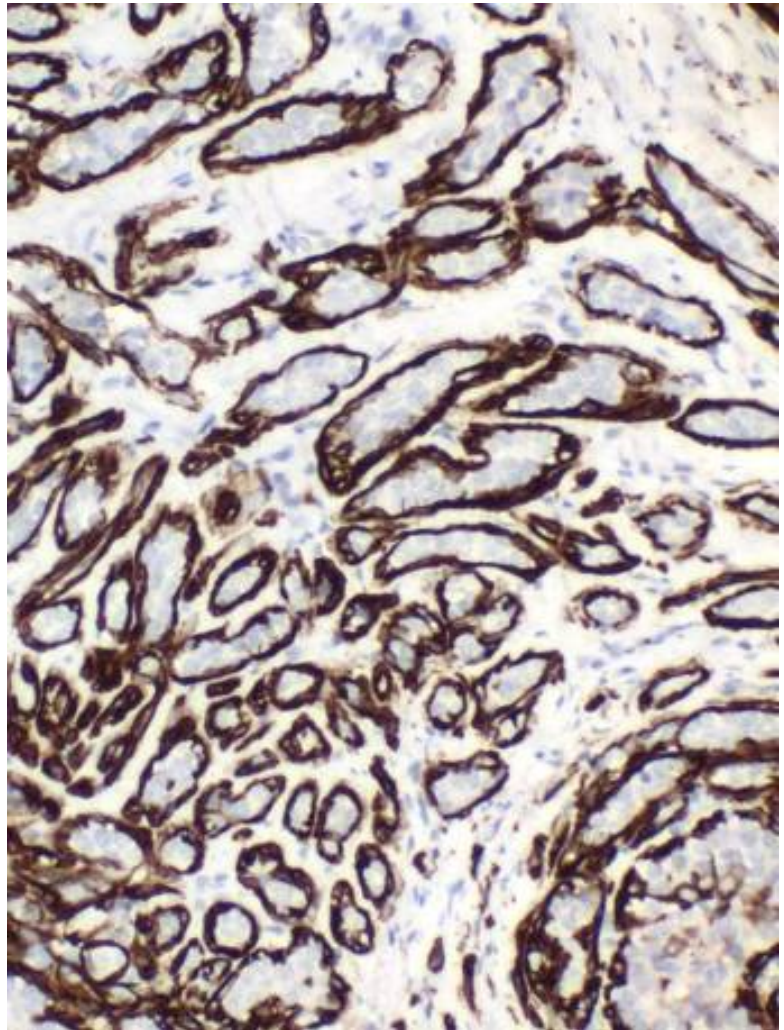
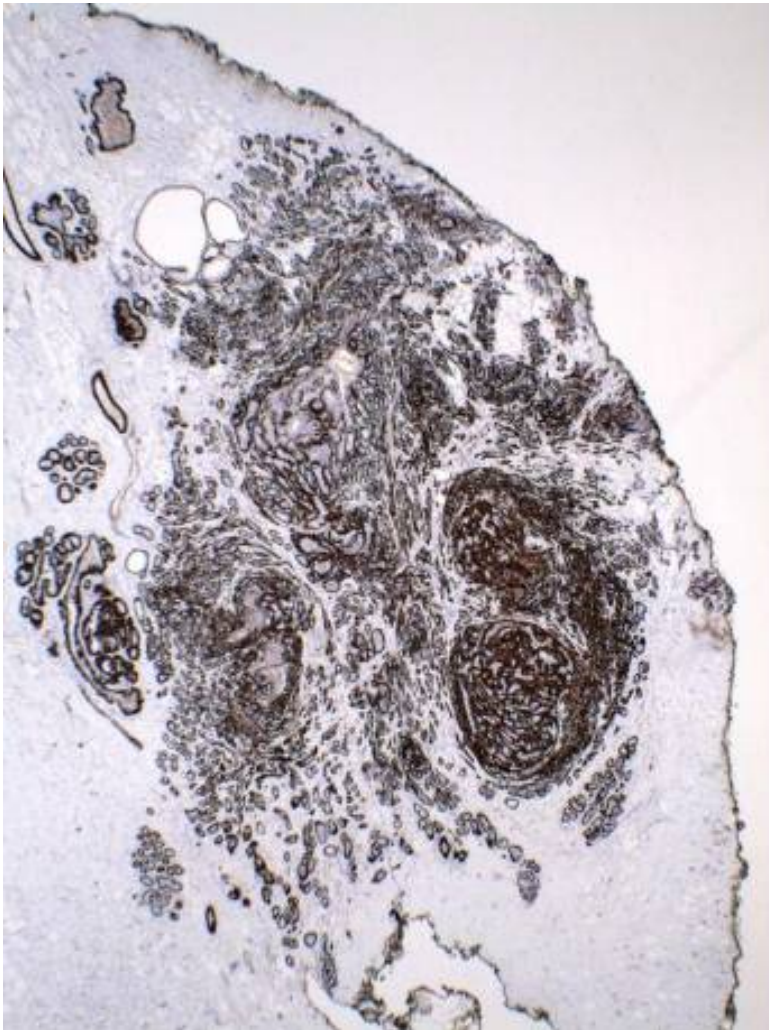
Radial scar/ CSL

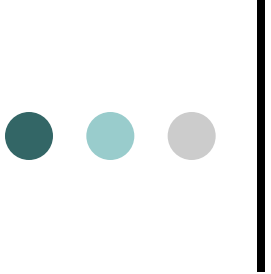


Sclerosing adenosis



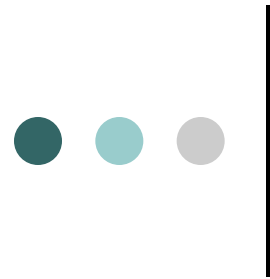
Sclerosing adenosis - SMMHC





Radial Scar/ CSL

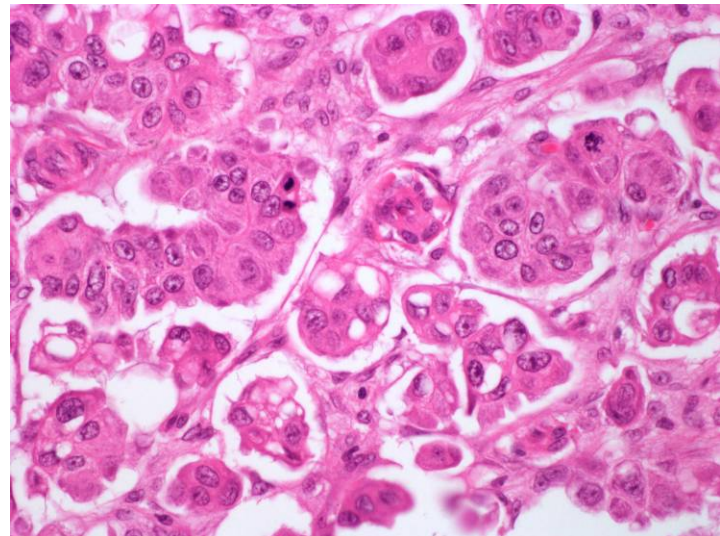
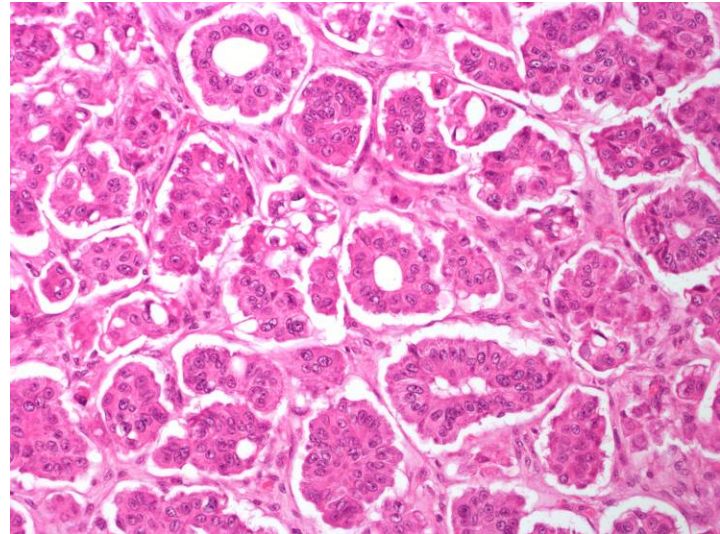
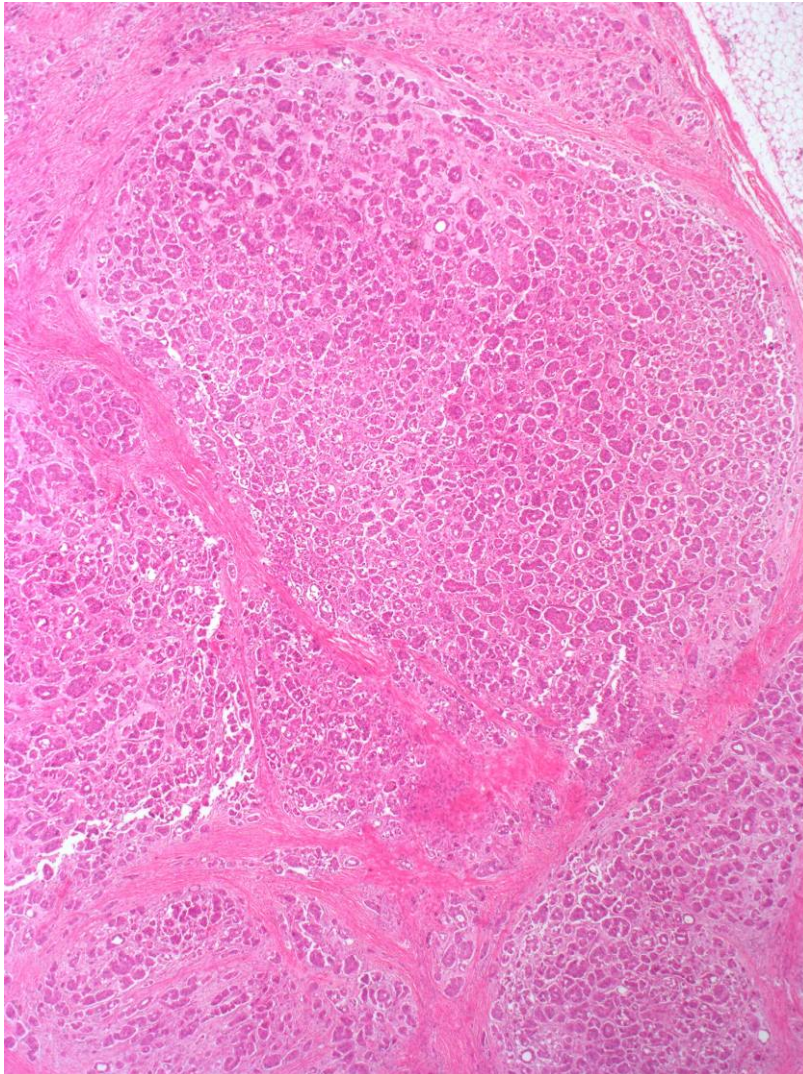
- B3 lesion
- Risk of associated malignancy is related to the presence of cytological atypia
 - Atypia present – 28-44% upgraded
 - No atypia – 4-6%
- Malignancy is usually in the form of low grade DCIS or low grade invasive carcinoma, particularly tubular carcinomas



Case 10:

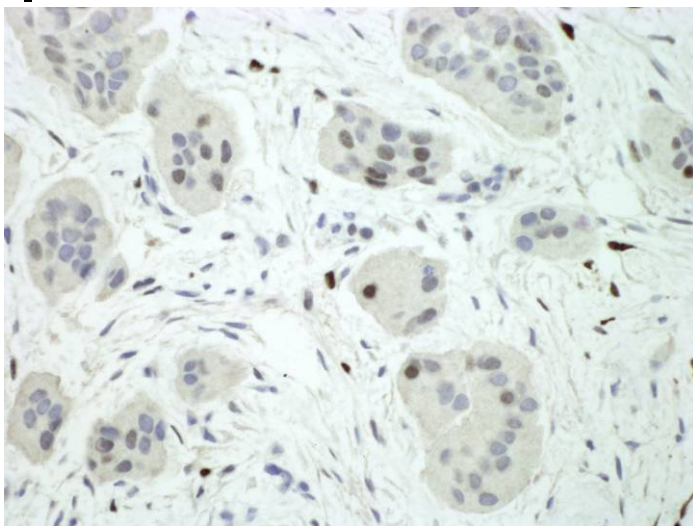
83 yo female.
L breast lump.

Case 10

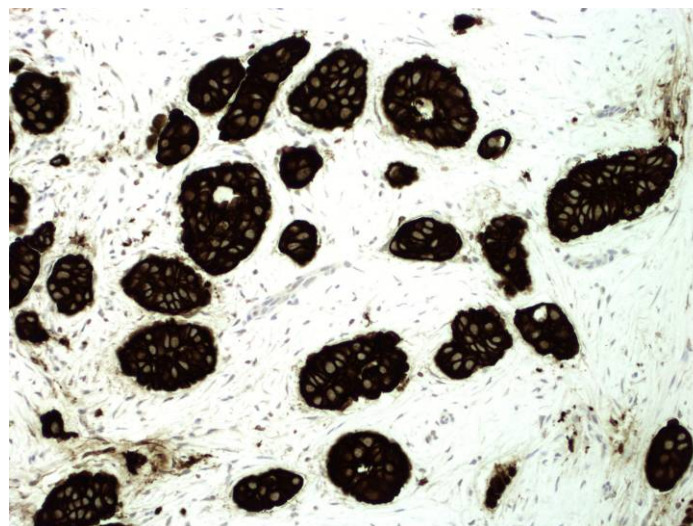


Case 10

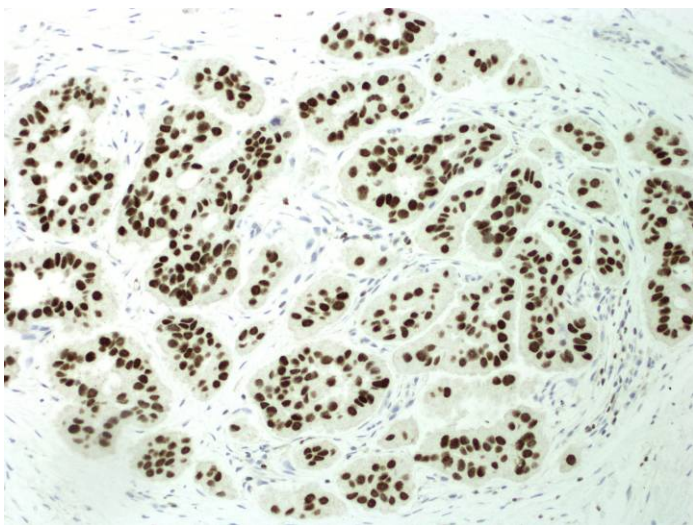
ER



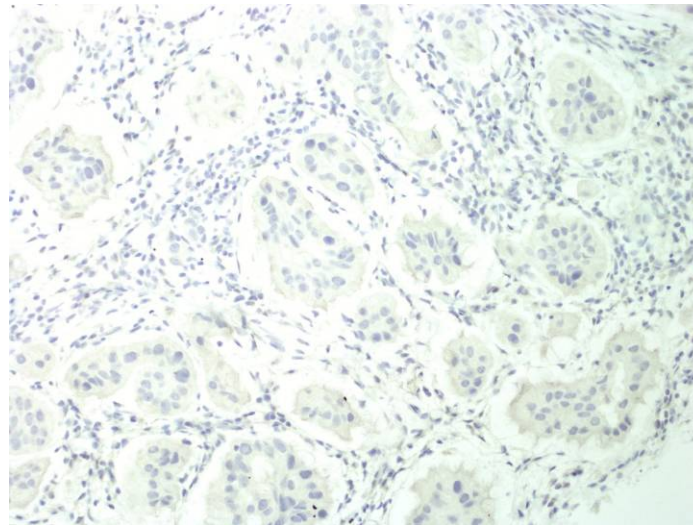
CK7

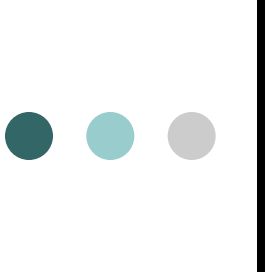


GATA3



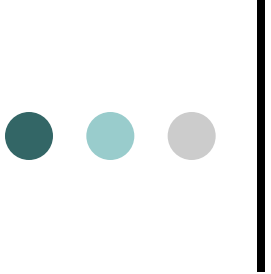
CK20





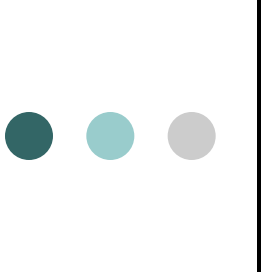
Case 10:

**Invasive
micropapillary
carcinoma**



Invasive Micropapillary Ca

- Reverse polarity with ‘inside-out’ tubules
- 1-2% of invasive breast cancers
- Majority ER positive
- 10-30% HER2 positive – may show incomplete pattern strong staining
- LVI and LN involvement common, however stage matched prognosis similar to NST

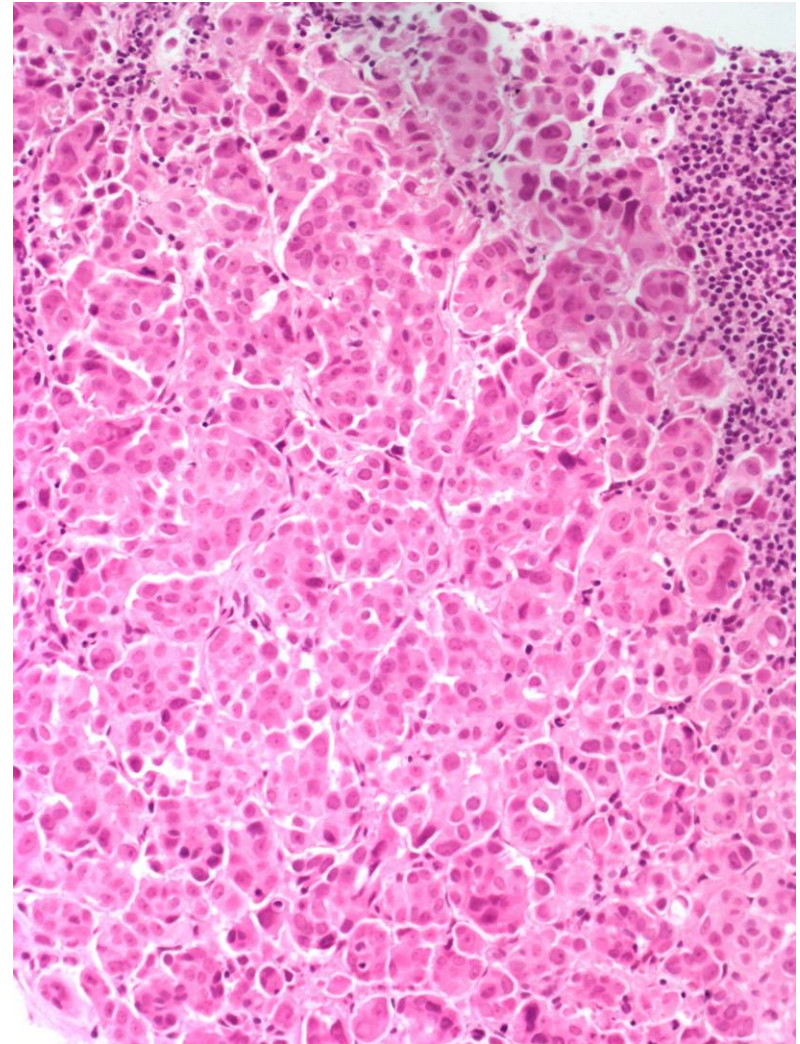
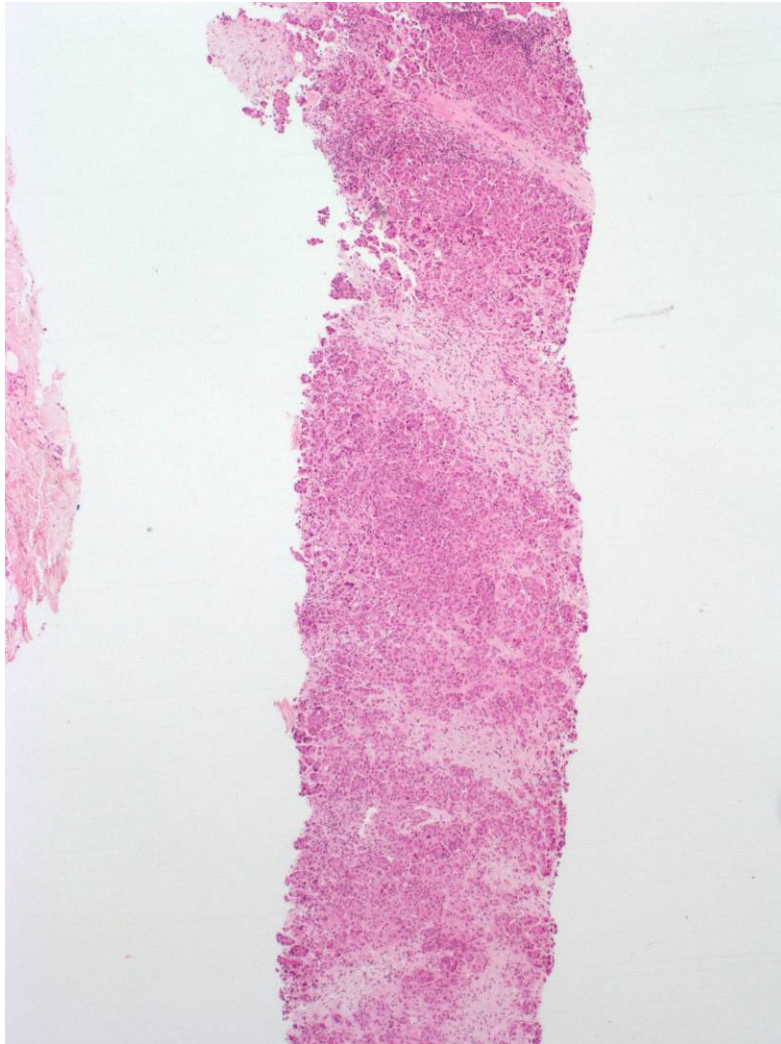


Case 11:

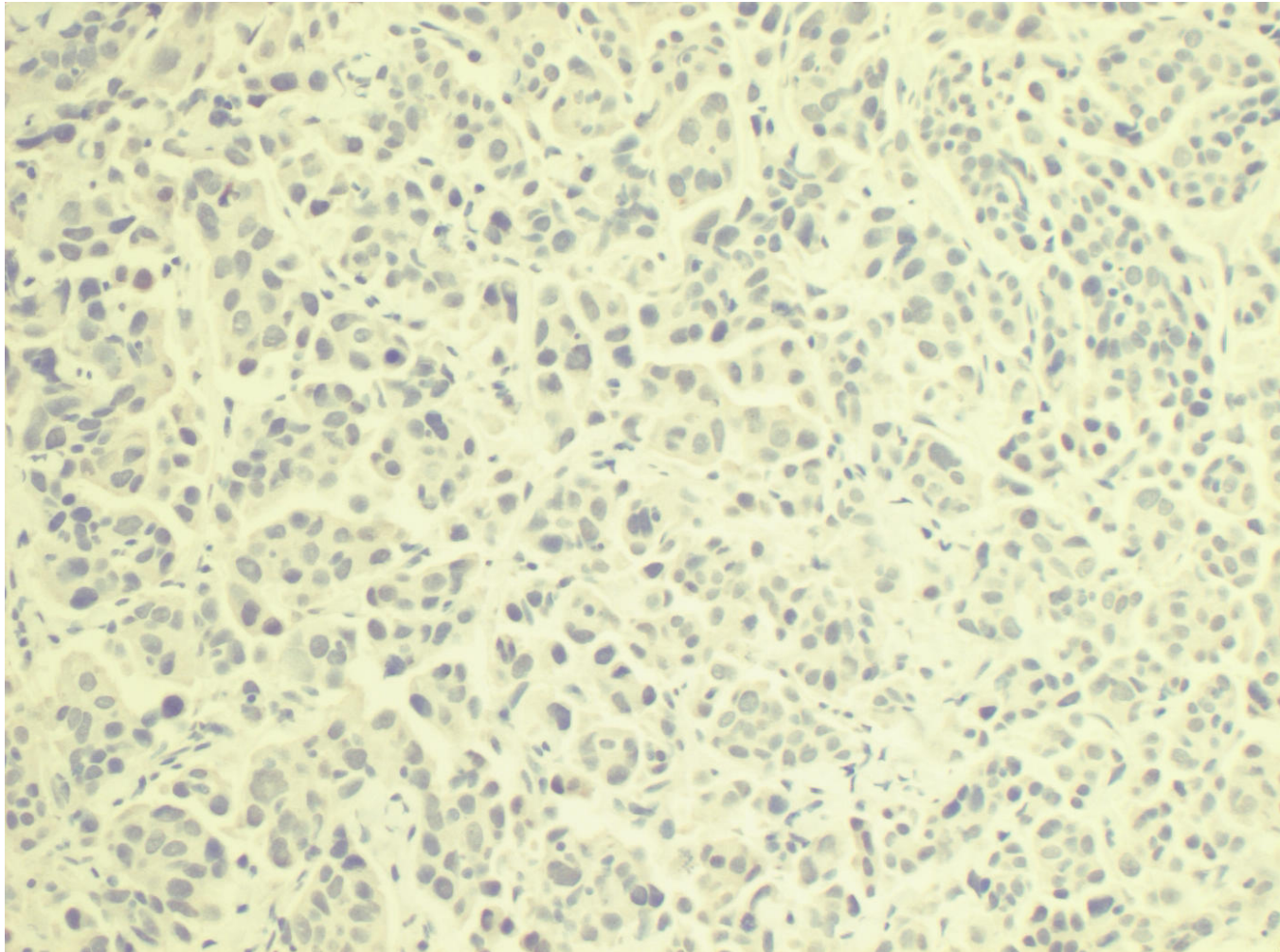
50 yo female.

**Suspicious lump L
breast and palpable
axillary lymph node.**

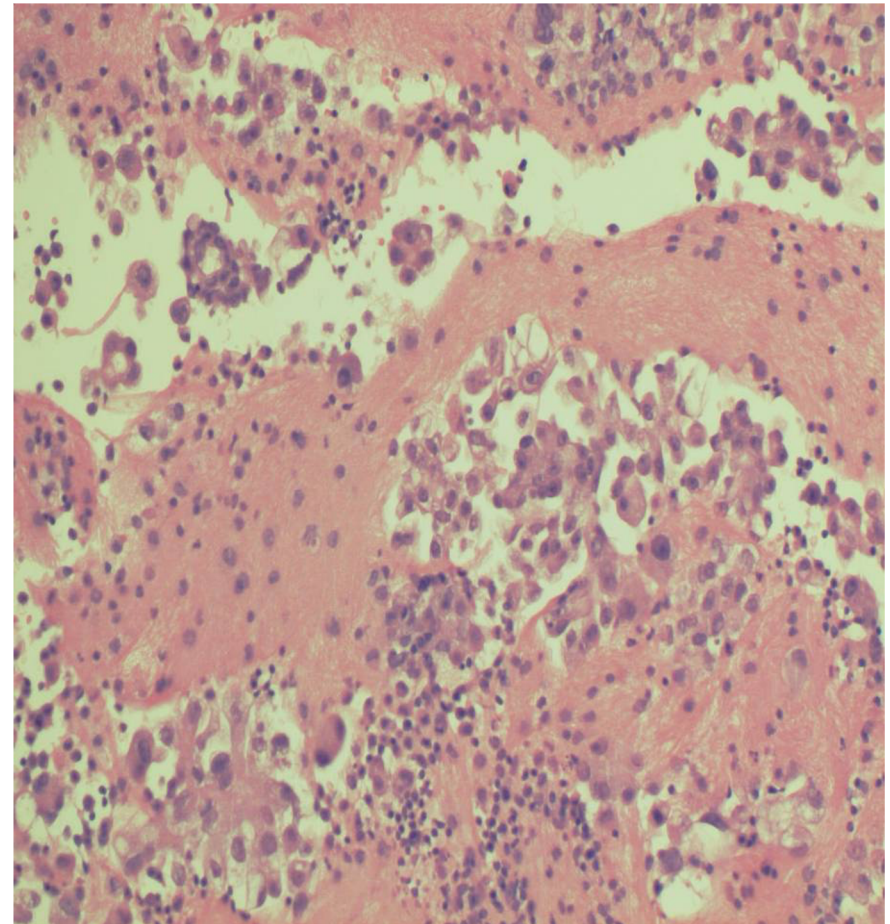
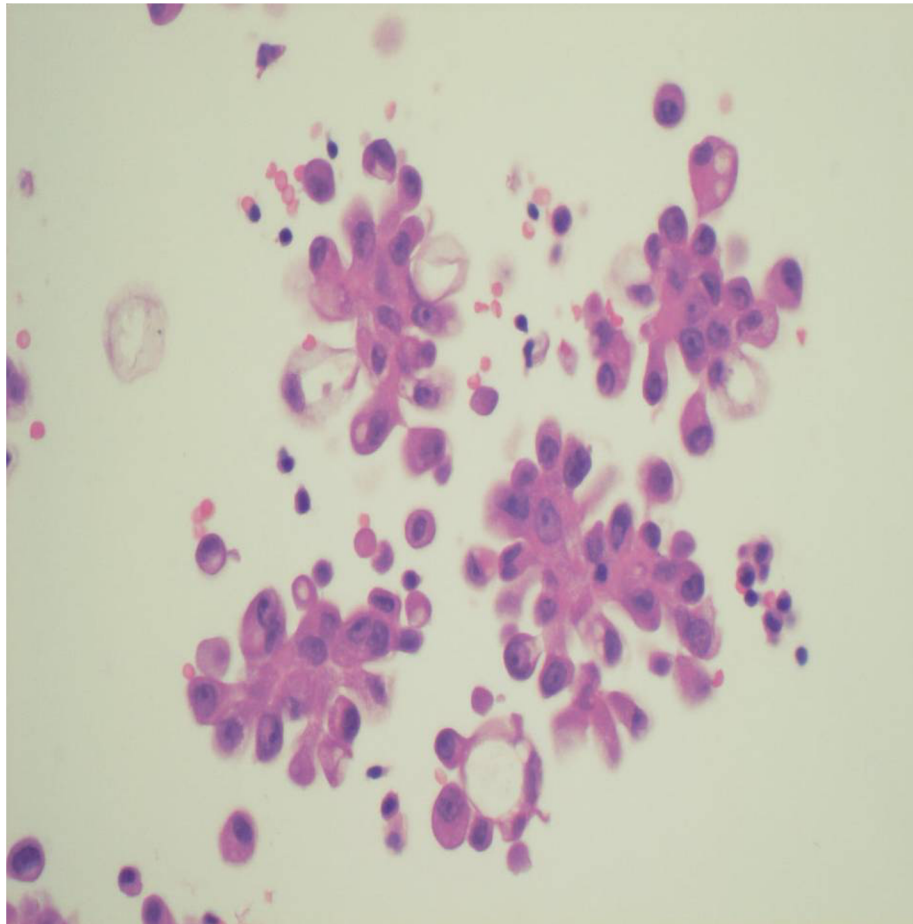
Case 11



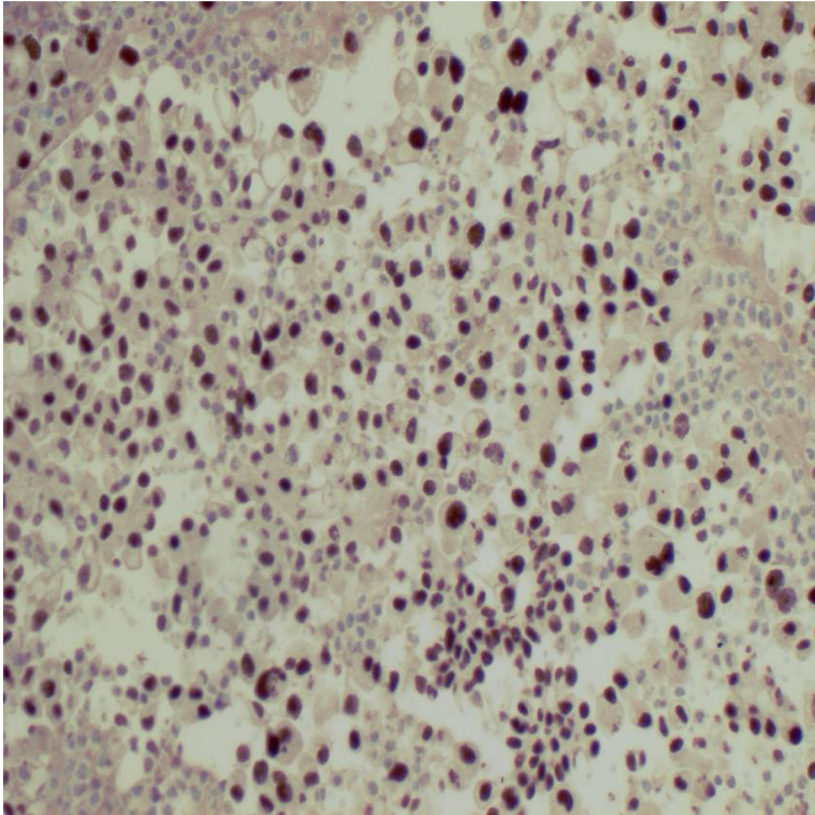
Case 11: ER



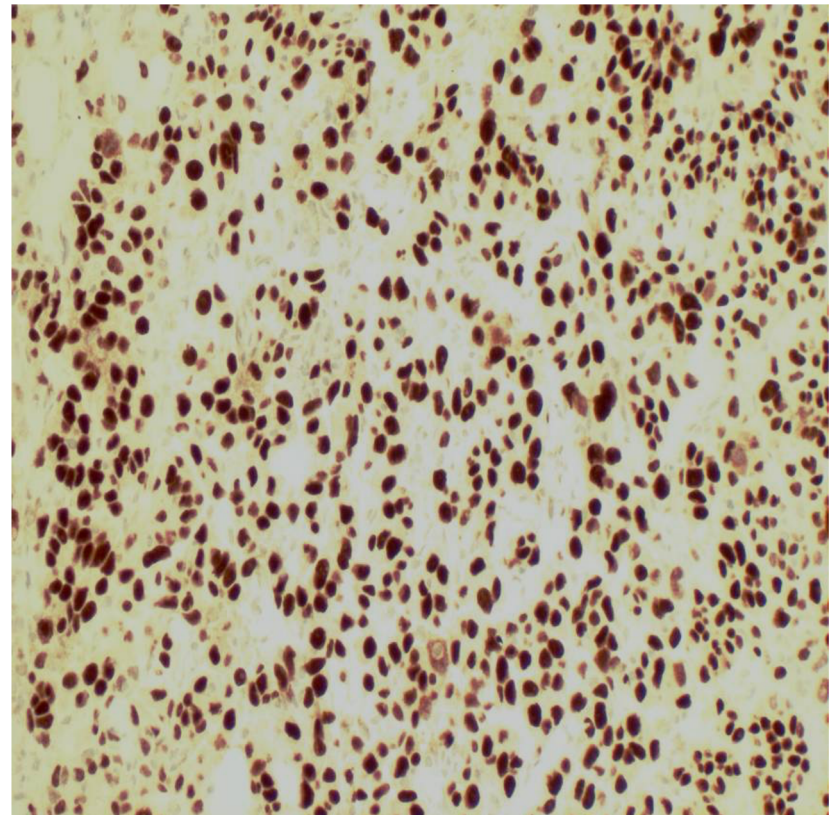
● ● ● | BUT.....pleural aspirate



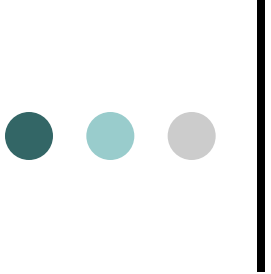
WT1



Pleural aspirate

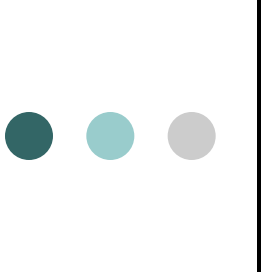


Breast biopsy



Case 11:

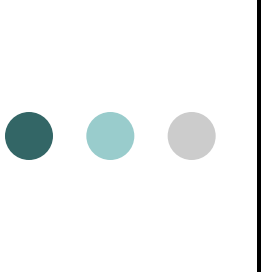
Metastatic Serous Papillary Carcinoma



Metastasis to Breast

- 0.2-1.3% of breast masses
- Presenting symptom in 30%
- Clinical history
 - 88% previous history of malignancy
 - 30% 1st site of met with no other disease
 - 10% previous met, isolated breast disease
 - 54% disseminated disease
- Examination findings
 - 77% mass, 85% unilateral, 53% solitary
 - 15% skin/ subcutaneous nodules
 - 2% inflammatory
 - 1% diffuse parenchymal involvement
- Median survival 10 months
- Improved survival with surgery – 15 vs 8 months

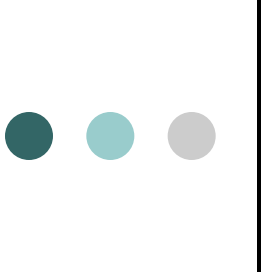
Williams et al. Cancer 2007;110:731-7



Metastasis to Breast

- Histological findings:
 - appearance not typical of breast primary, DCIS, elastosis and Ca++ all favour breast origin
- rarely clues such as pigment
- Patterns:
 - discrete mass
 - growth around ducts/ lobules (esp lymphomas)
 - lymphangitis
 - diffuse infiltration

Lee et al. J Clin Pathol 2007;60:1333-41



Metastasis to Breast

- Commonest sites:
 - melanoma
 - haematological malignancies
 - lung
 - ovary (serous papillary ca)
 - prostate, gastric, renal cell ca
 - carcinoid tumours

Lee et al. J Clin Pathol 2007;60:1333-41

| Metastasis to Breast – IHC

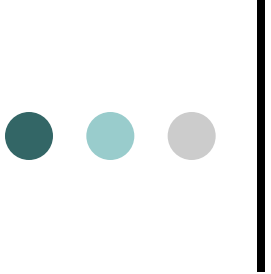


Breast		CK7 +, CK20 – EMA 100% GCDFP 70% (23-45%)
Serous Papillary Ca Ovary	WT1 95% Ca125 90% Mesothelin >90%	<10%, weak, focal 10-20% 3-15%, weak
Lung	TTF1 – small cell, adenoca	small cell can be pos, primary breast rare
Prostate	PSA PSAP CK7 & CK20 negative	15% positive 0% positive
Gastric	ER negative CDX2 20-70% CK20 50% positive	Lobular ER positive
Renal Cell Carcinoma	CD10 Renal cell ca marker 90%	5% positive 15% positive
Carcinoid/ Neuroendocrine	ER negative CDX2/ CK20 – GI origin TTF1 – lung/thyroid	ER positive



Breast Markers

Marker	Sensitivity	Specificity	Other Tumours	Comment
ER	85-90% primary, 50% mets		Gynae tract, thyroid, skin adenexal	Strong positive staining, weak may be non-sp
GCDFP- 15	10-70% (TNBC 10- 20%)	98-100%	Apocrine glands Rare ovarian and lung primaries	Apocrine differentiation Often focal
GATA3	>90% (TNBC 40- 70%)	70-93%	Urothelial ca Skin, salivary gland, kidney, SqCC	Nuclear Typically diffuse
Mamma globin	50-70% (TNBC 7- 23%)	90-100%	Salivary, skin adnexal, 5- 10% ovary/ endometrial	



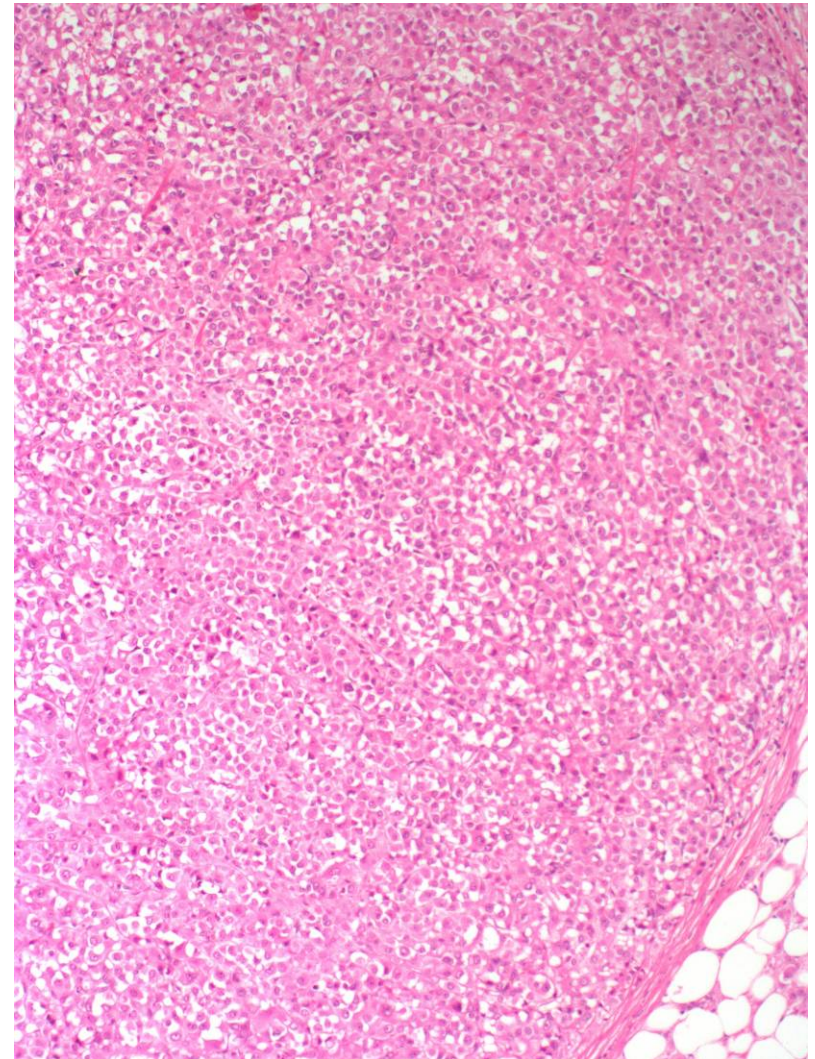
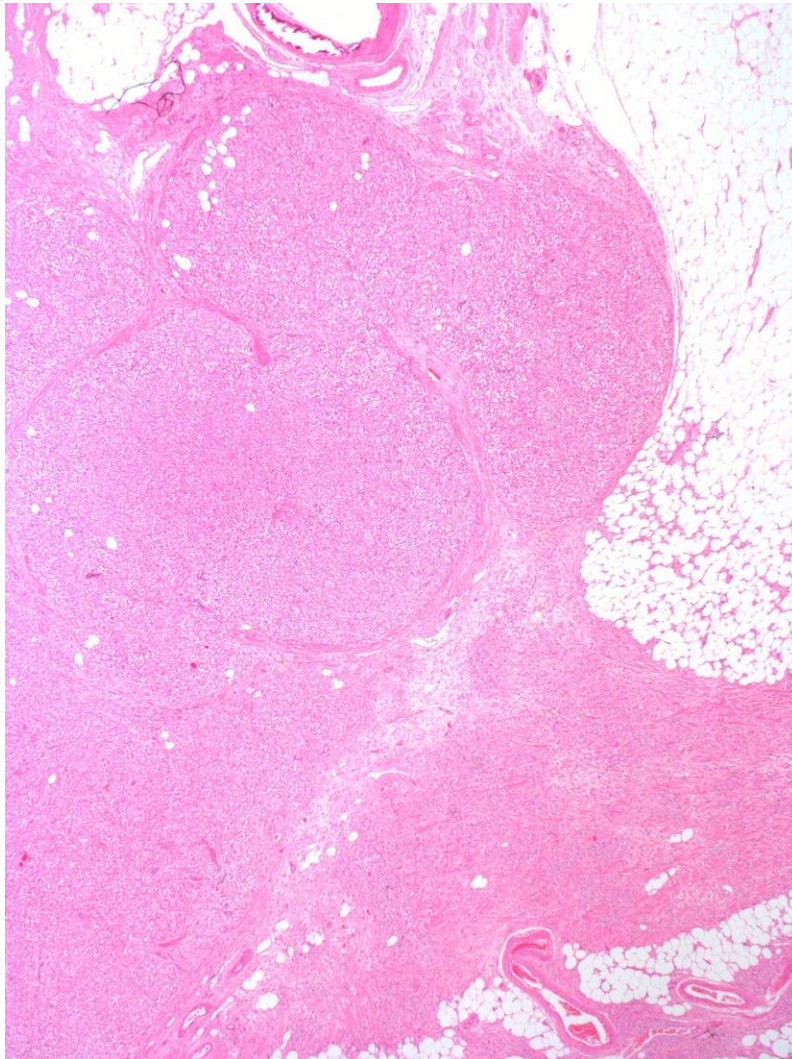
Case 12:

78 yo female.

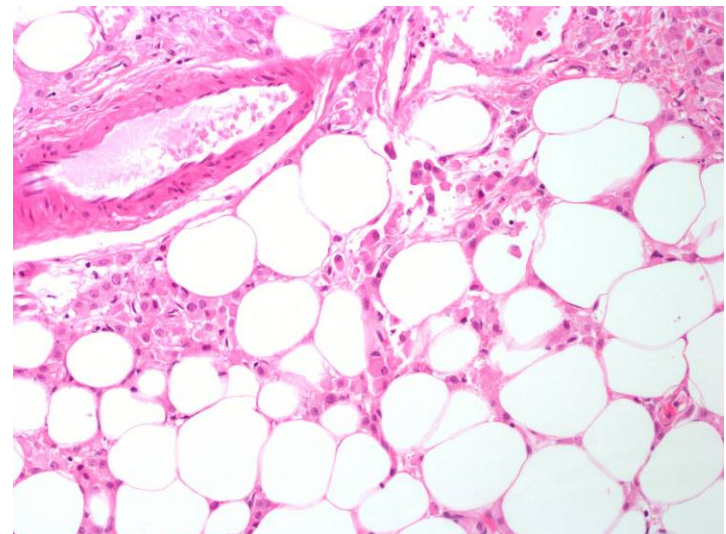
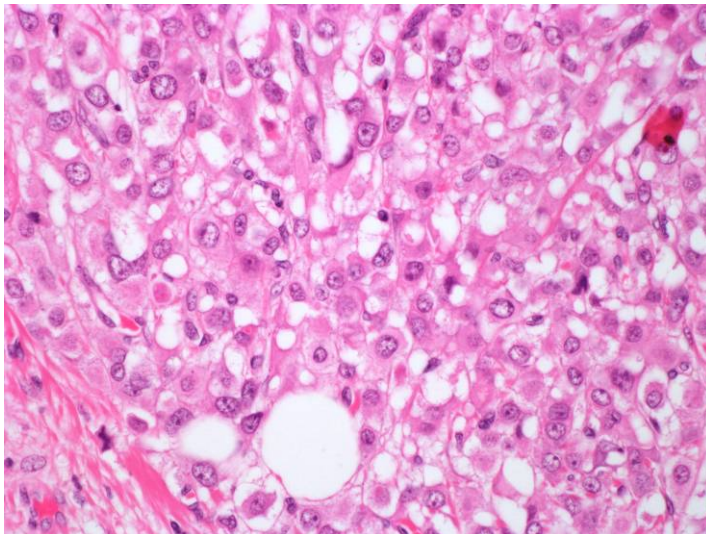
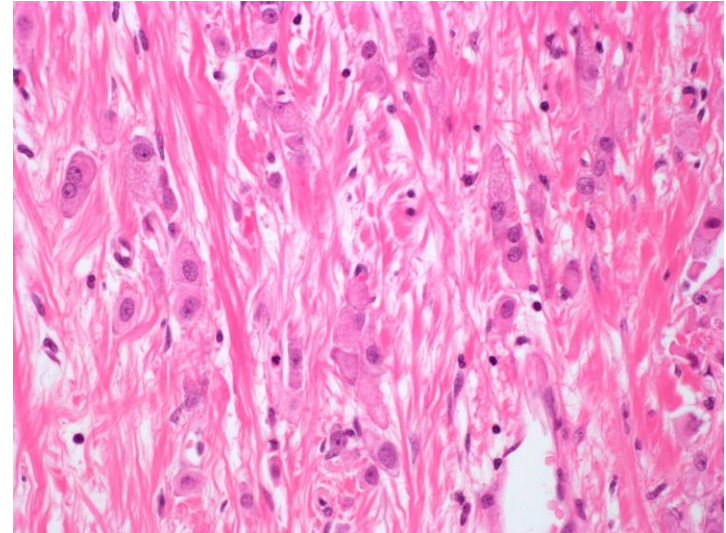
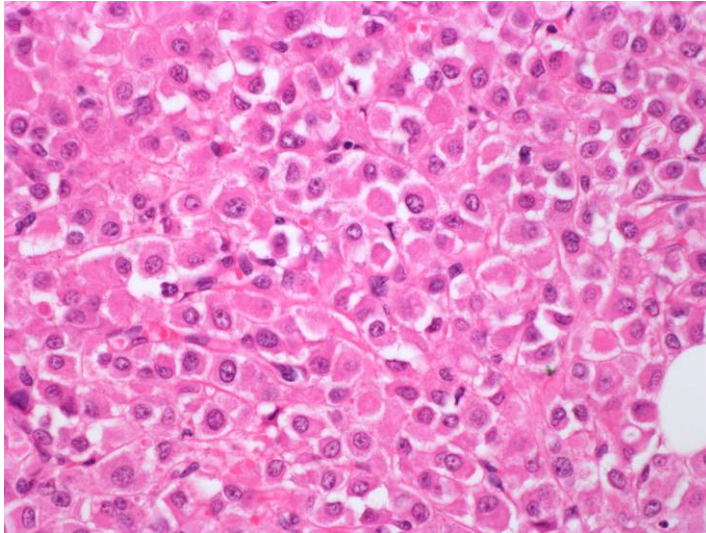
R breast lump.

M5U5.

Case 12

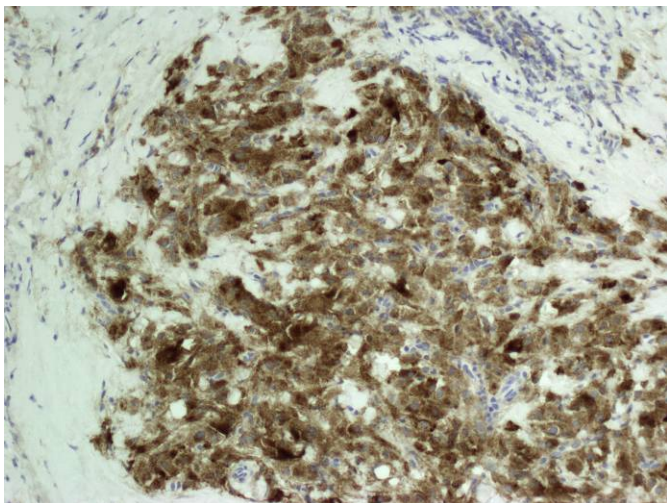


Case 12

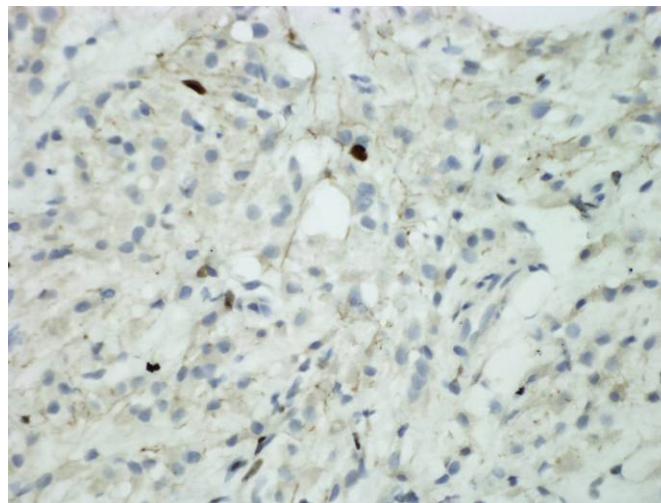


Case 12

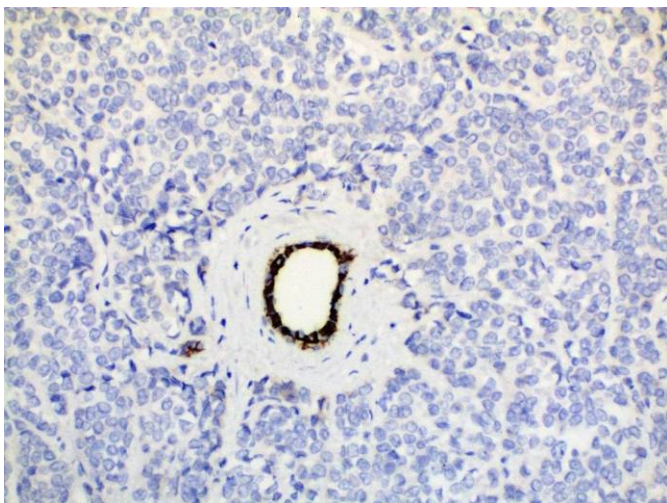
GCDFP
15



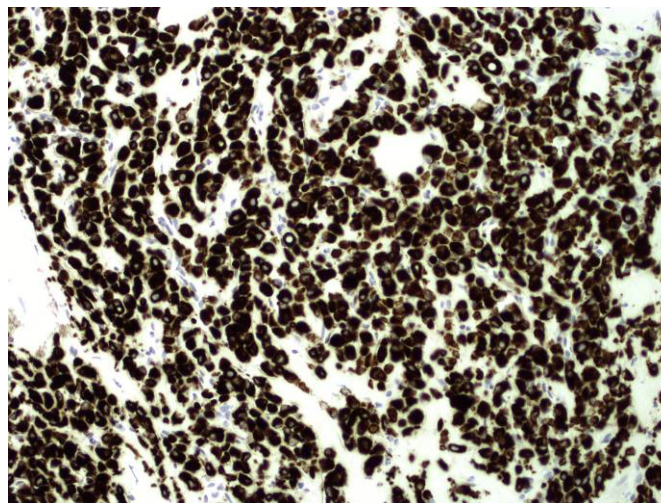
ER

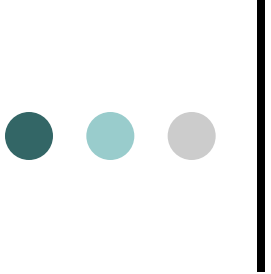


Ecad



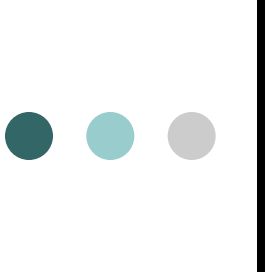
CK MNF





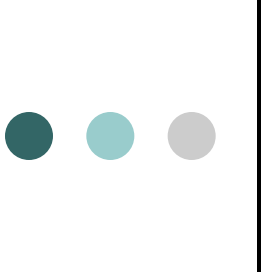
Case 12:

**Invasive lobular
carcinoma –
pleomorphic variant**



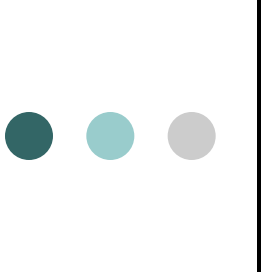
Pleomorphic Lobular Ca

- Growth pattern of lobular carcinoma but marked nuclear pleomorphism
- May have apocrine or histiocytoid morphology
- Majority GCDFP15 positive
- 75% ER positive (cf 96% classical ILC)
- 15- 40% HER2 positive
- Worse survival compared with classical ILC



IHC - Ecadherin

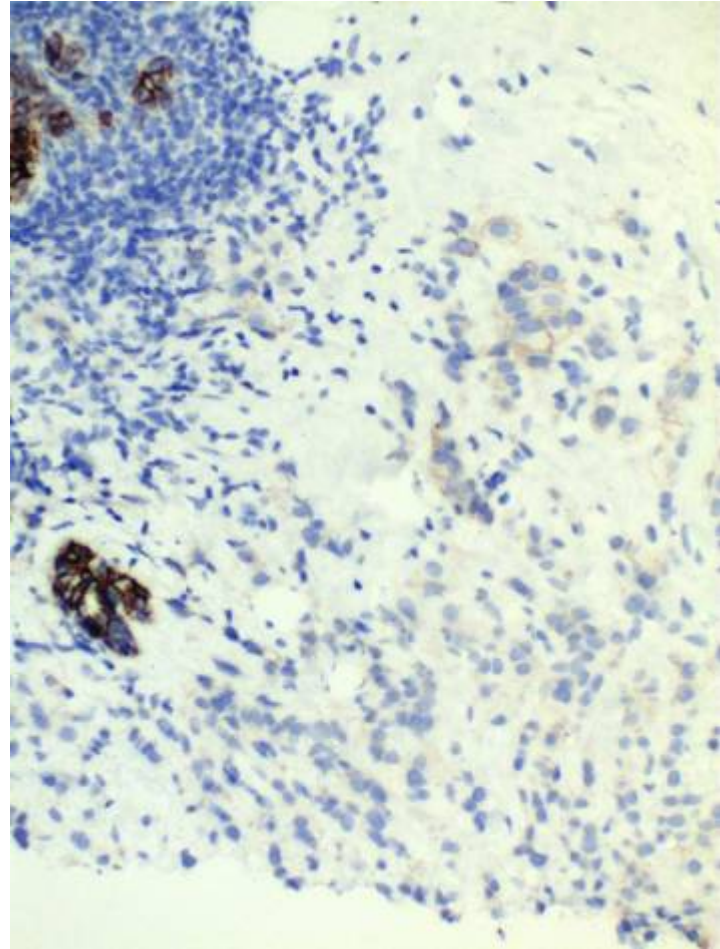
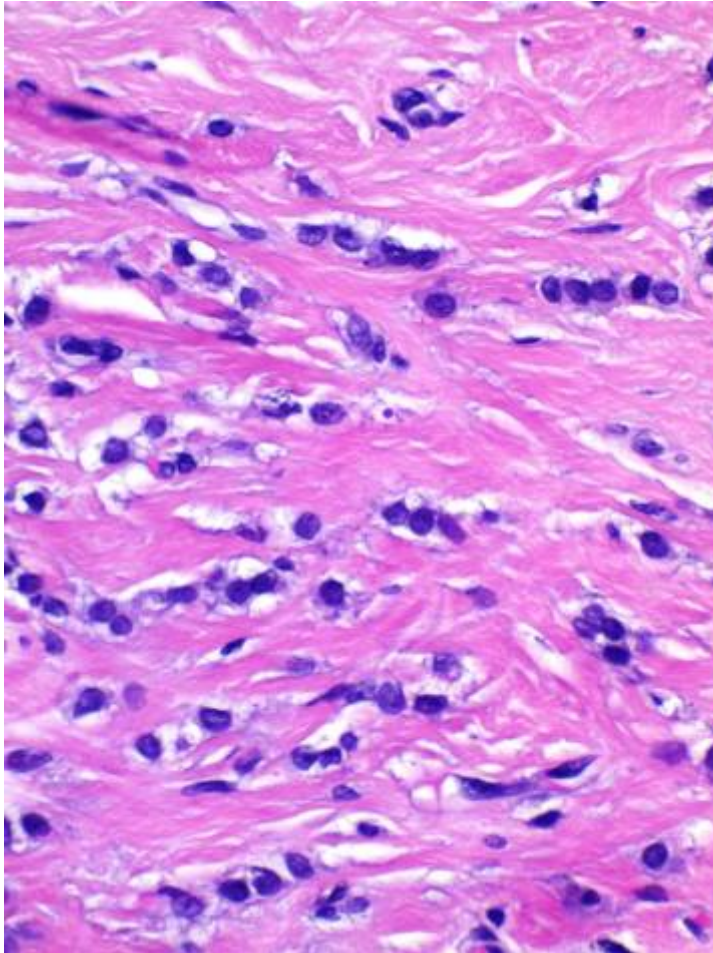
- Ecadherin is a membrane bound protein involved in cell adhesion and forms part of the cadherin-catenin complex
- Loss of expression of Ecadherin is a feature of lobular carcinoma (LCIS and Invasive Lobular Carcinoma)
- BUT expression of Ecadherin is preserved in around 12% of ILC
- AND 25-50% of Invasive Ca NST (ductal) show reduced or absent expression of Ecadherin, especially high grade basal-like cancers
- Tumours are primarily classified as lobular or NST/ ductal on the basis of their morphology NOT Ecadherin staining
- Ecadherin IHC is most useful in CIS and for invasive cancers with a single file growth pattern where you are not sure if it is NST or lobular



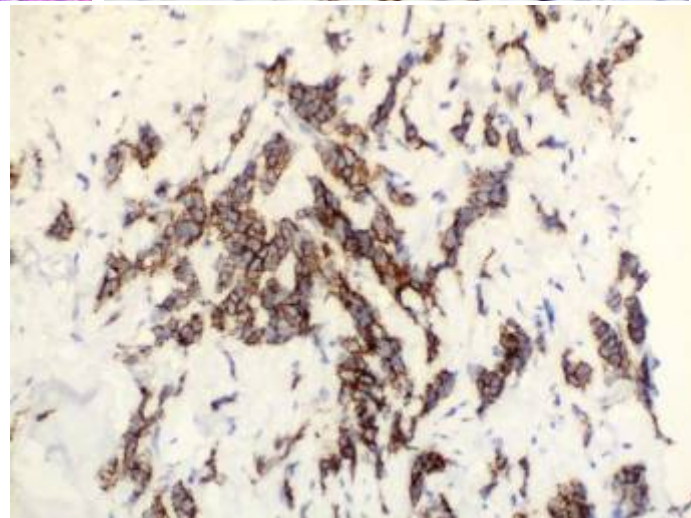
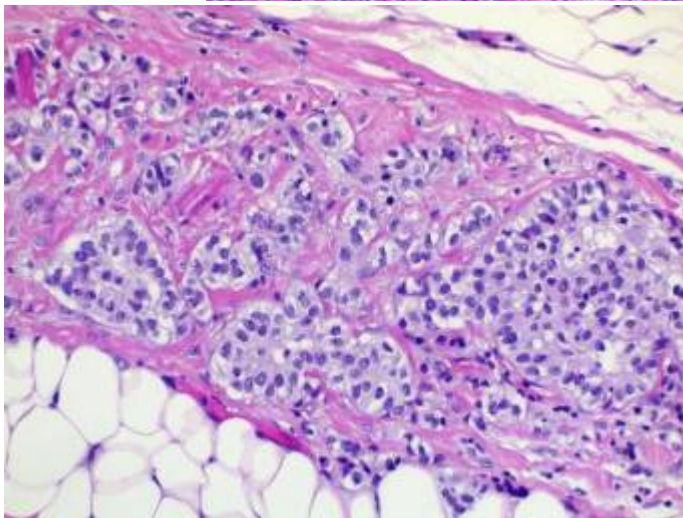
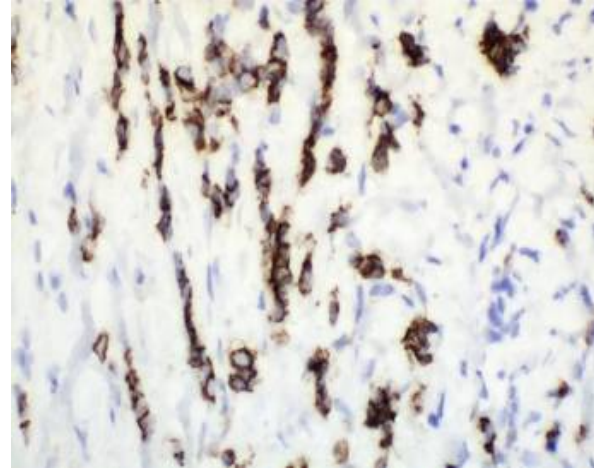
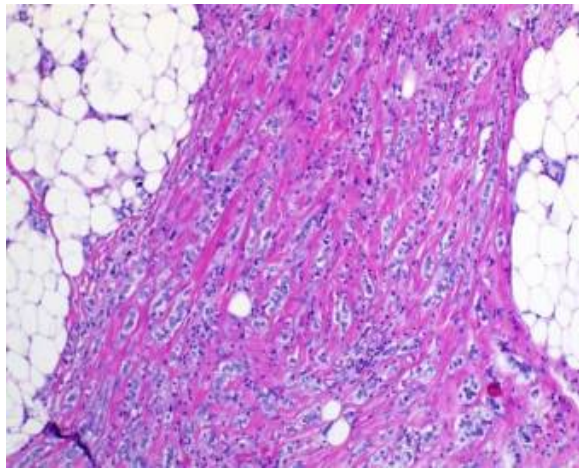
IHC - Ecadherin

- Can get aberrant patterns of Ecadherin staining
- Partial fragmented membrane staining
- Cytoplasmic staining with perinuclear dot-like pattern
- Remember residual myoepithelial cells or ductal cells will be positive

Invasive lobular carcinoma

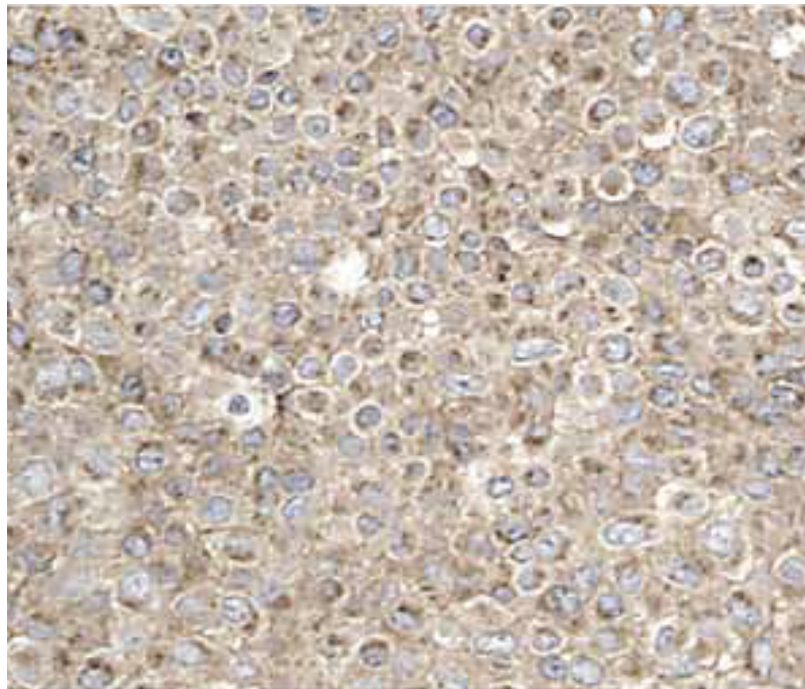


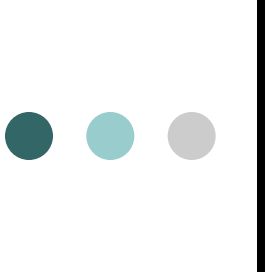
● ● ● NST “with lobular features”



IHC – p120 catenin

- p120 catenin
- Cytoplasmic localisation in lobular lesions
- Membrane localisation in ductal/ NST lesions





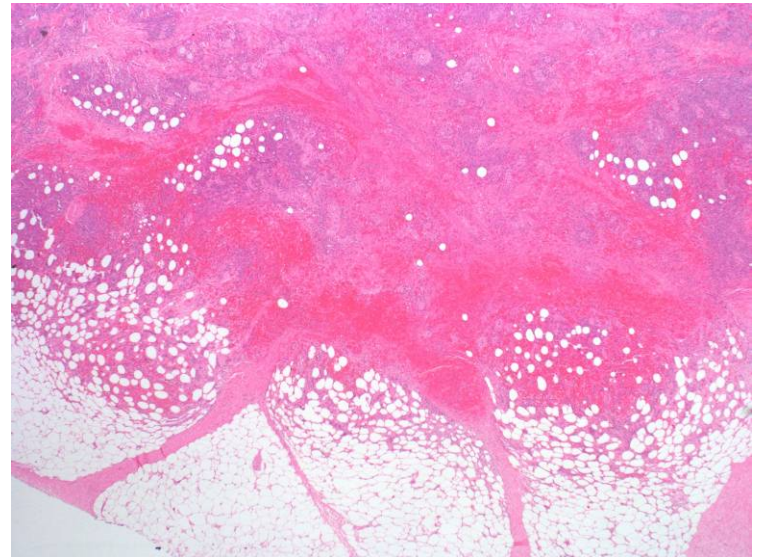
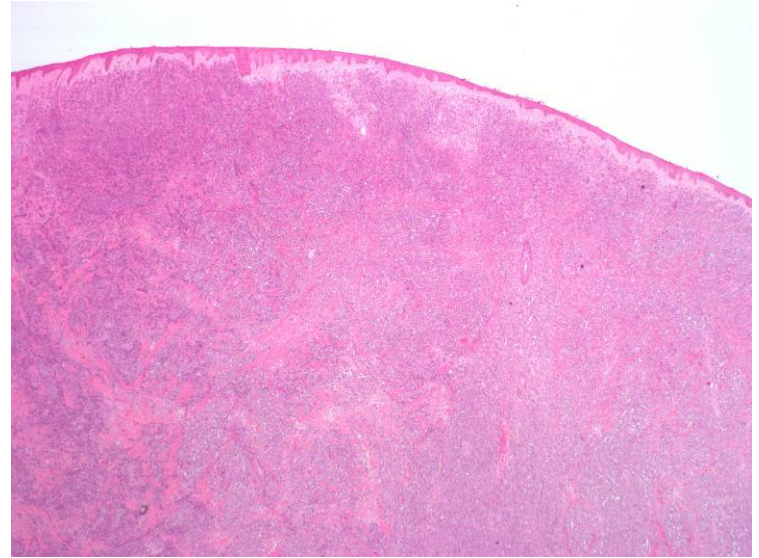
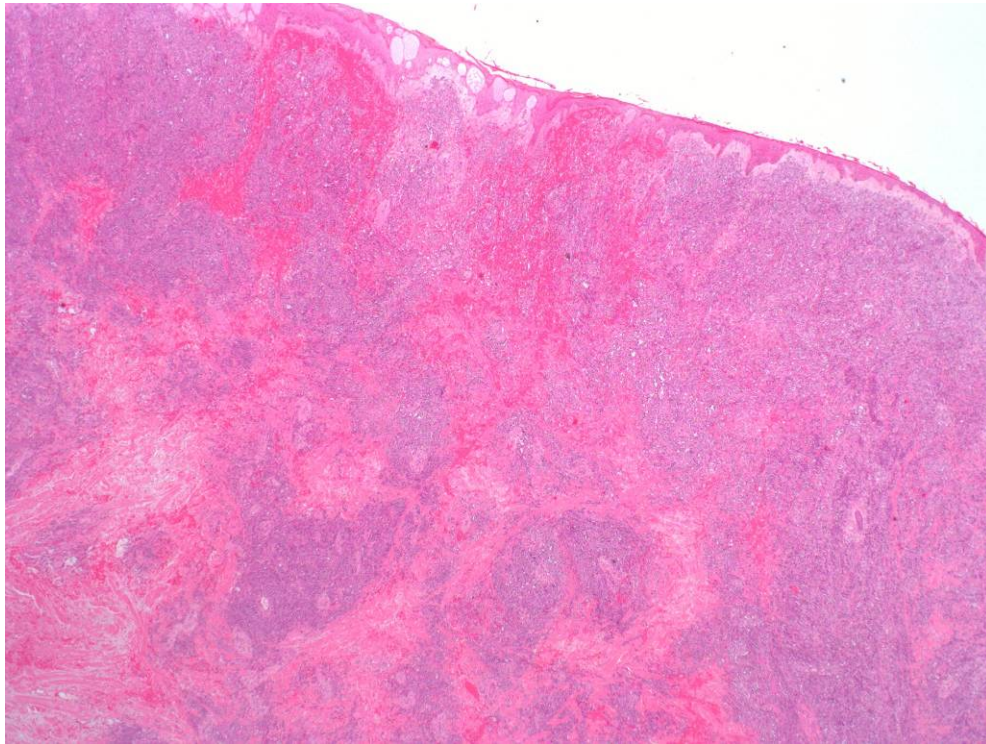
Case 13:

55 yo female.

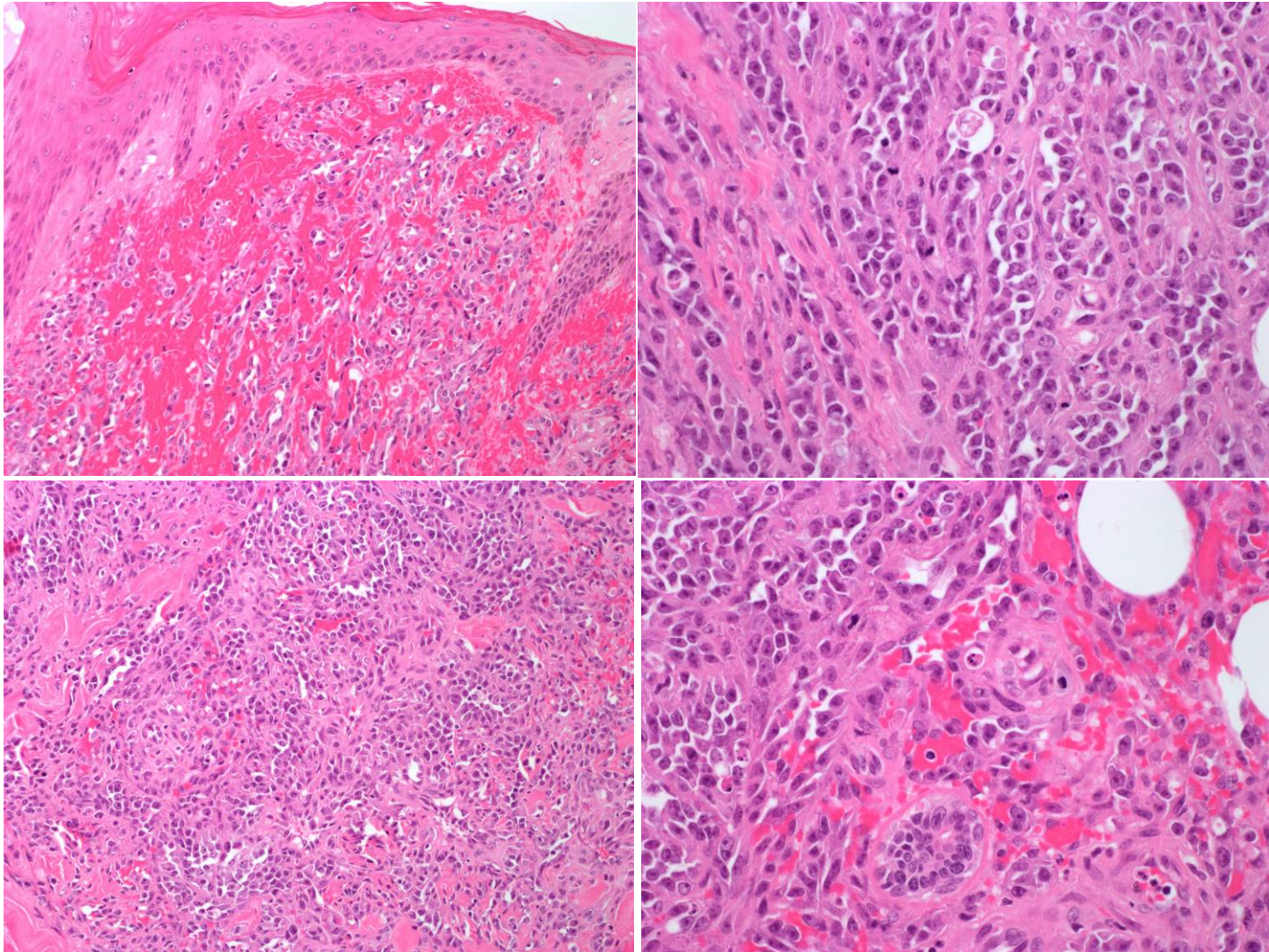
**WLE and Axillary
clearance 2010.**

**Now unresolving bruise
L breast.**

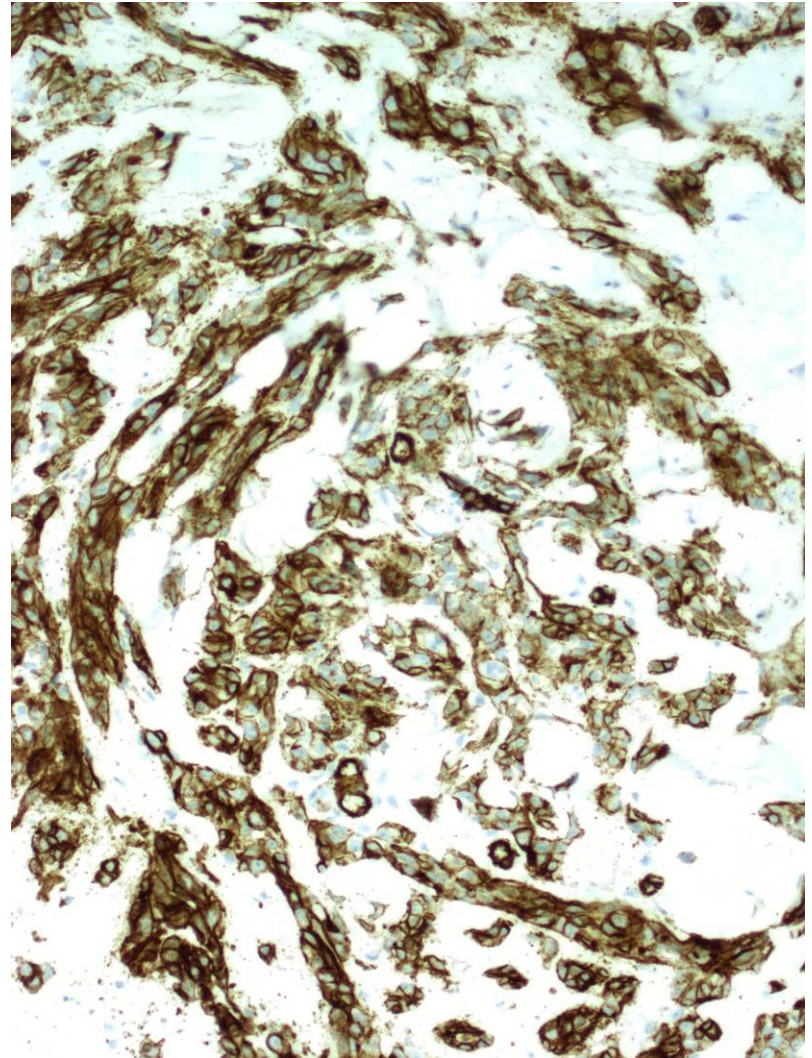
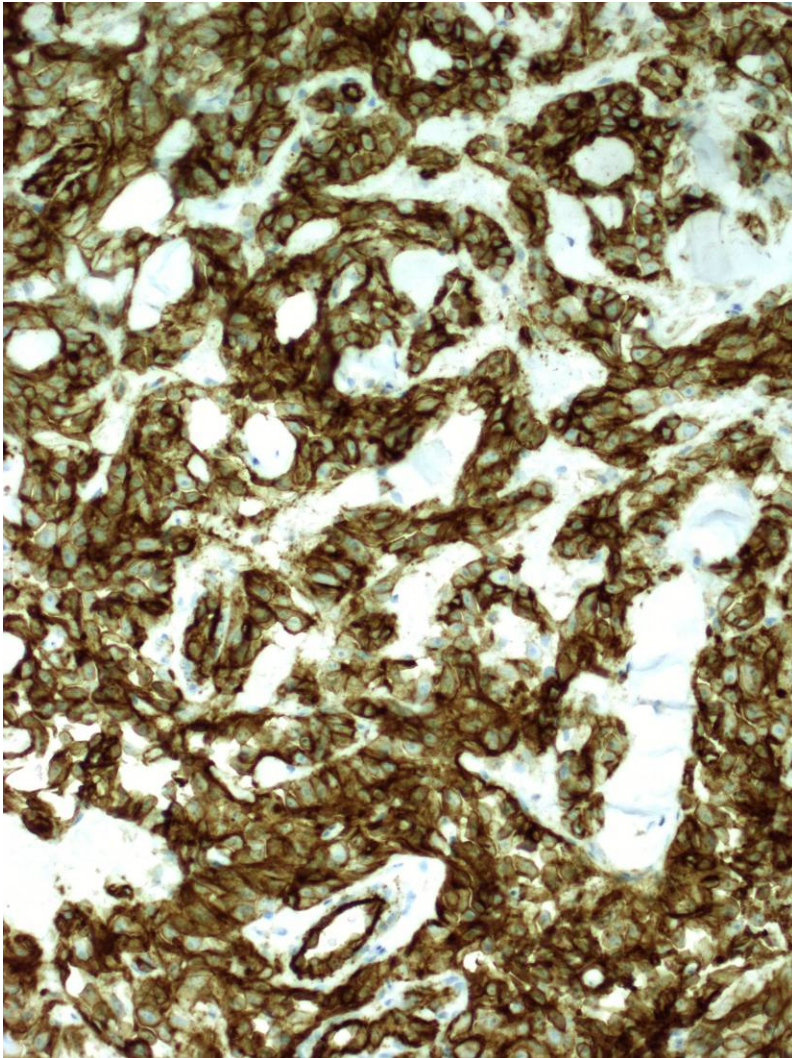
Case 13

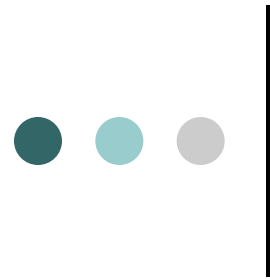


Case 13



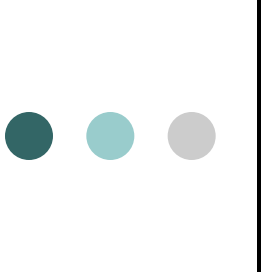
Case 13: CD34 and CD31





Case 13:

Post Radiation Angiosarcoma

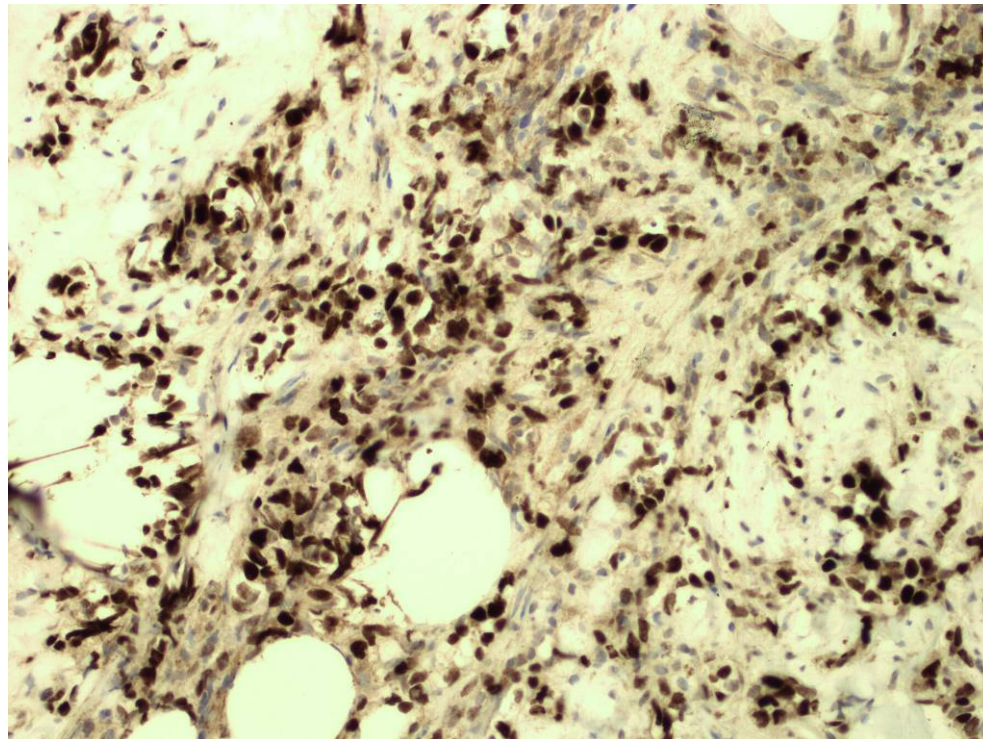


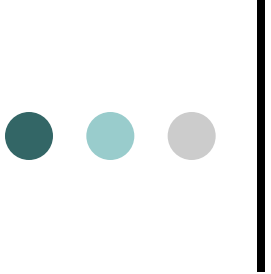
Post Radiation Angiosarcoma

- **Originates in dermis, cf primary AS which arises within breast parenchyma**
- **Vascular proliferation with atypia; nuclear enlargement and hyperchromasia, necrosis and mitoses in high grade lesions**
- **Atypia may be minimal at periphery – Ddx AVL**
- **AS poorly circumscribed, infiltrates subcutis**
- **CD31 and CD34 positive**
- **Epithelioid variant can be CK positive – panel of markers**
- **Association with amplification of the MYC gene (55% of cases)**
- **Results in MYC protein overexpression – IHC can be useful in differential diagnosis from AVL**

Post Radiation Angiosarcoma

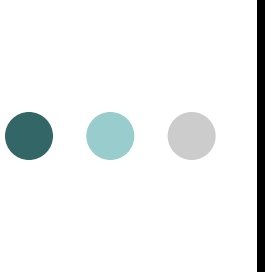
- Association with amplification of the MYC gene (55% of cases)
- Results in MYC protein overexpression – IHC can be useful in differential diagnosis from AVL





Post Radiation Angiosarcoma

- **Two contexts:**
 - **Chest wall post radiotherapy**
 - **Upper limb following chronic lymphoedema post mastectomy**
- **Rare: 1.27/1000 patients**
- **Latency 6-204 months; maximum risk at 5-10 yrs**
- **Locally aggressive – tendency to multiple local recurrences before development of metastases**
- **Therapy – surgical excision with clear margins**
- **Role for chemotherapy**



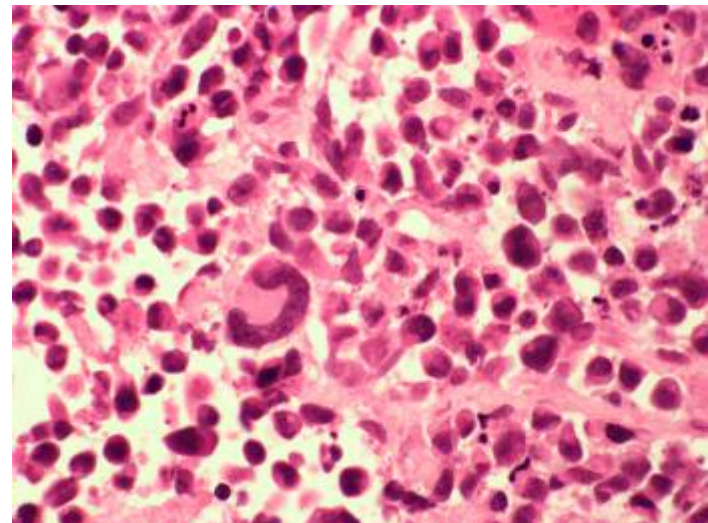
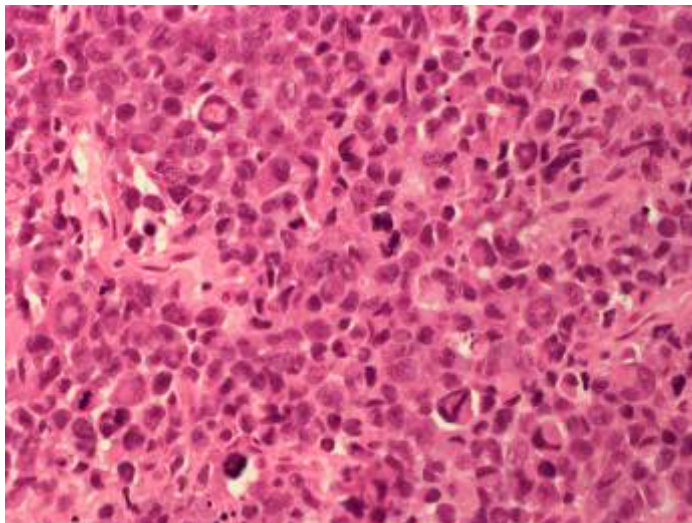
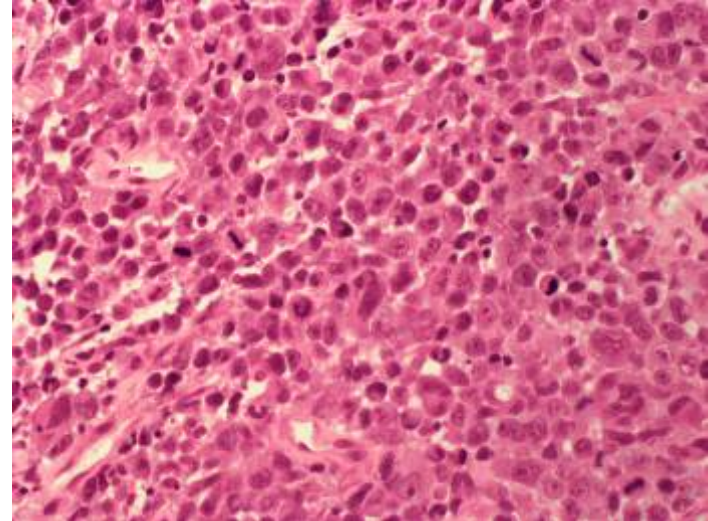
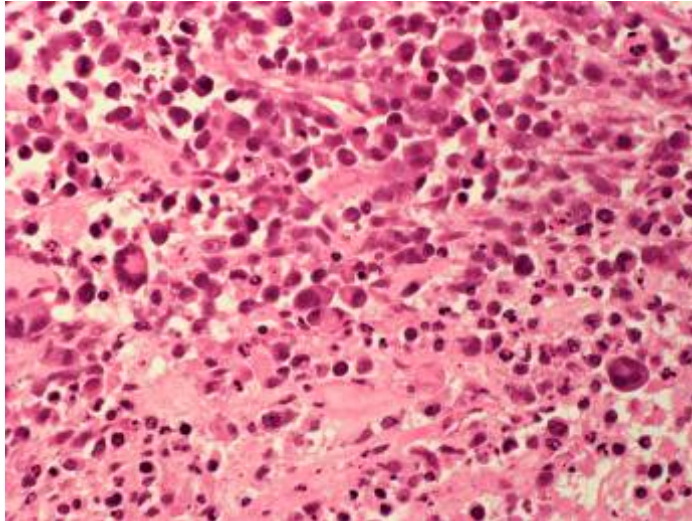
Case 14:

50 yo female.

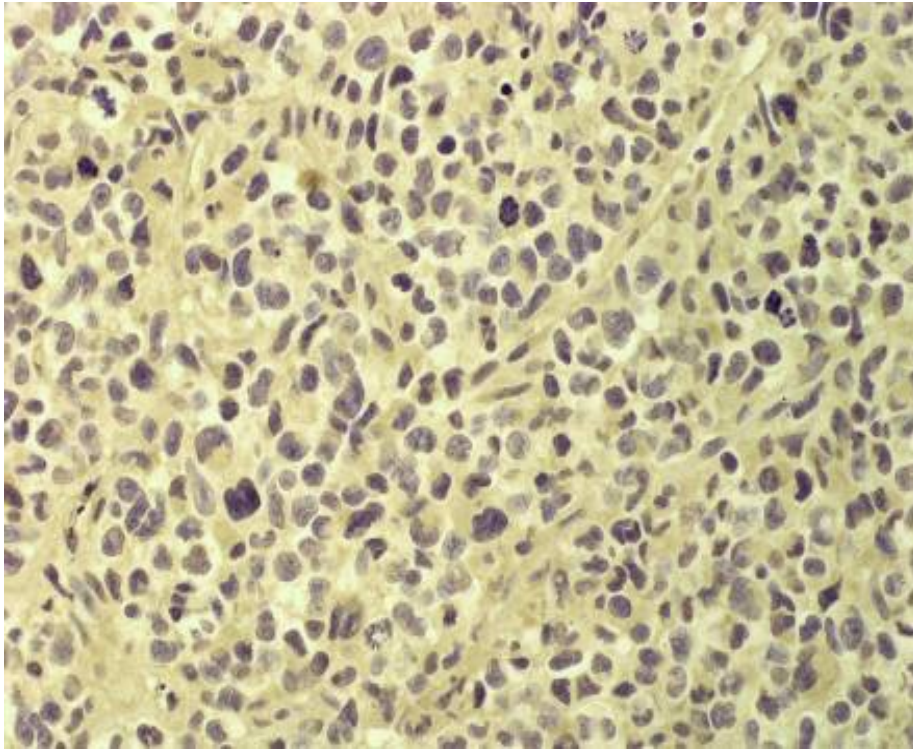
Breast implants.

New lump R breast.

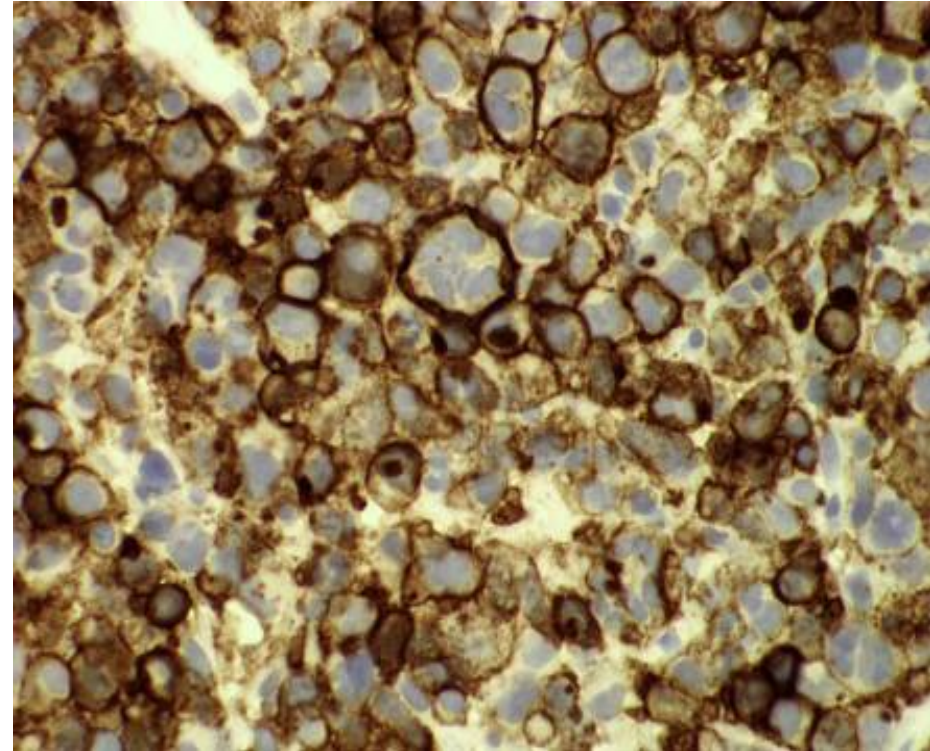
Case 14



Case 14



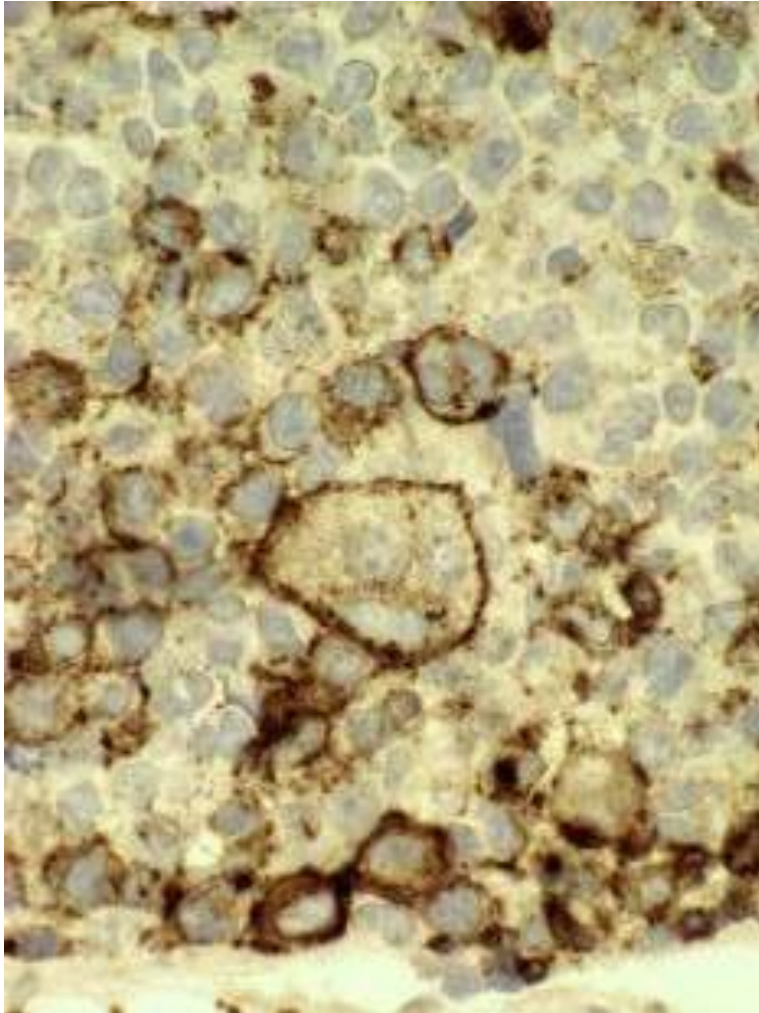
CK MNF



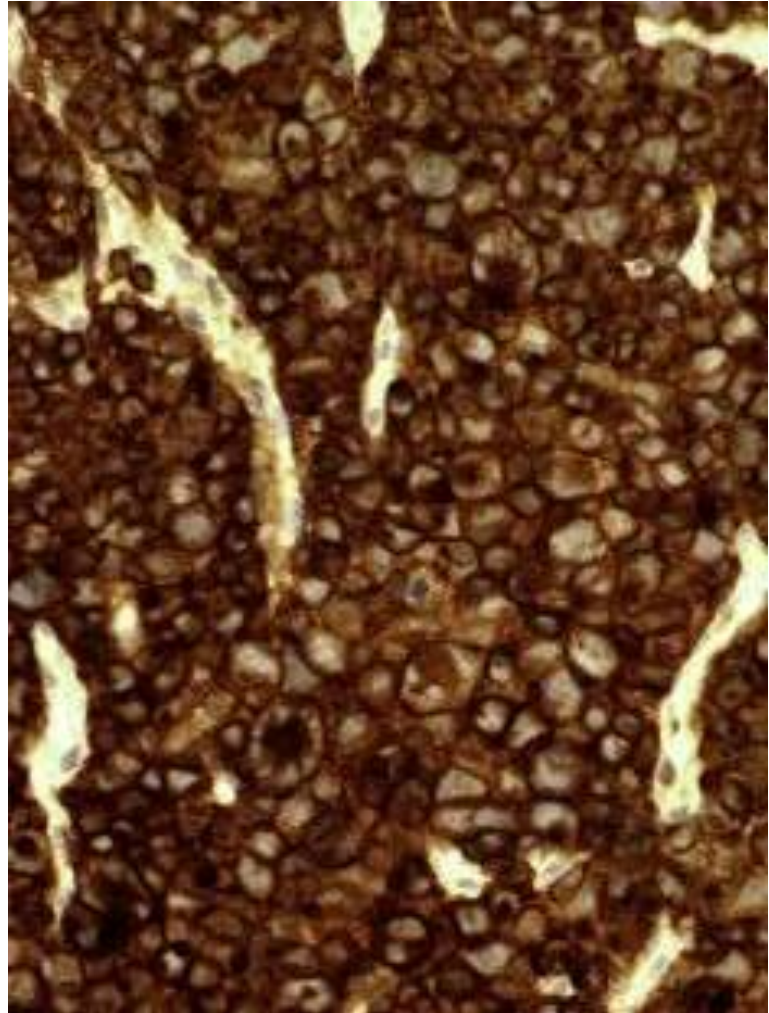
CD 45

Case 14

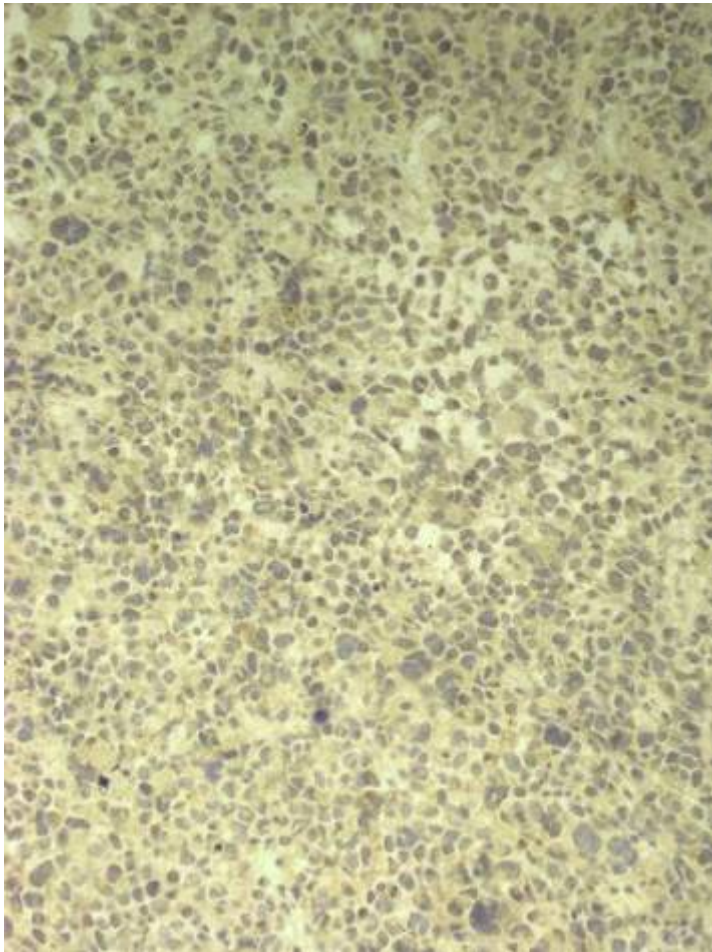
CD2



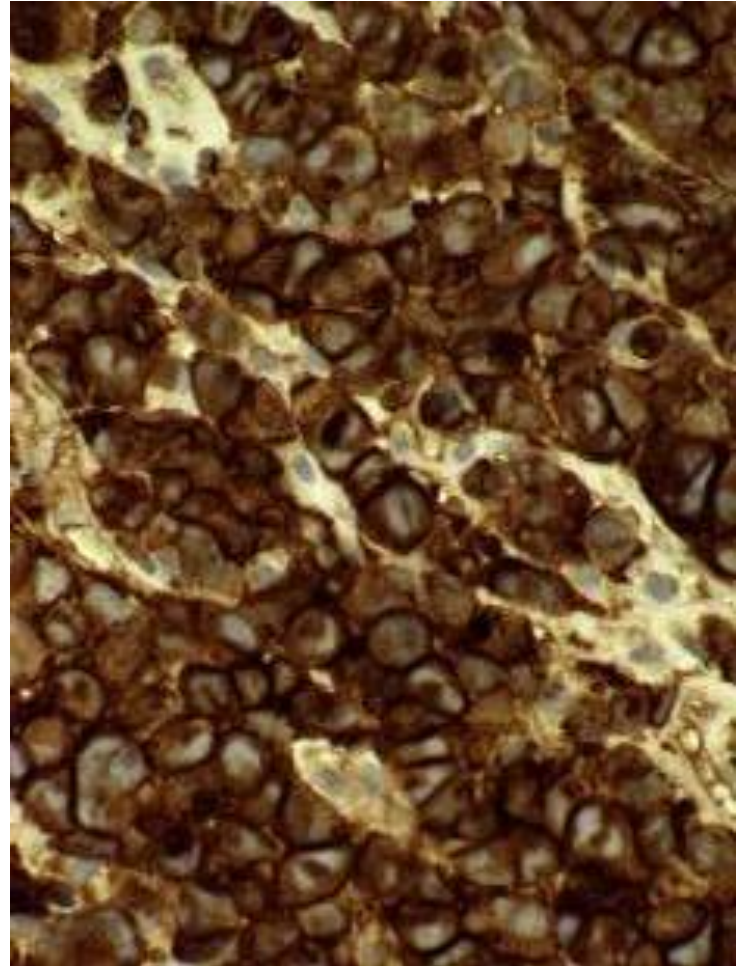
CD4



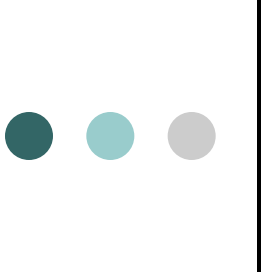
Case 14



ALK

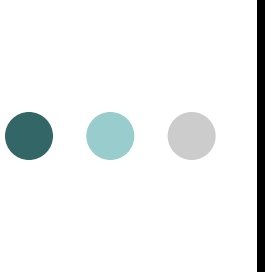


CD 30



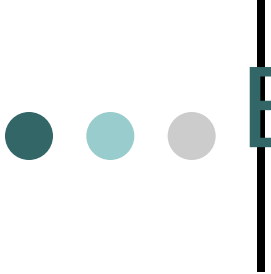
Case 14:

**Breast Implant
Associated Anaplastic
Large Cell Lymphoma
(BIA-ALCL)**



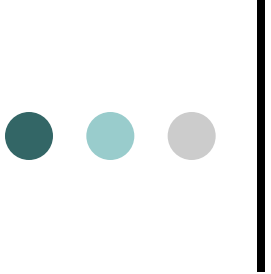
BIA-ALCL

- CD30 positive, ALK negative
- Variable expression of T cell markers; CD4 (80-84%), CD43 (80-88%), CD3 (30-46%), CD2 (30%)
- CD45 positive in 36%
- Negative for CD5, CD7, CD8 and CD15
- Up to 70% positive for EMA
- Majority of tested cases show monoclonal T-cell receptor gene rearrangements



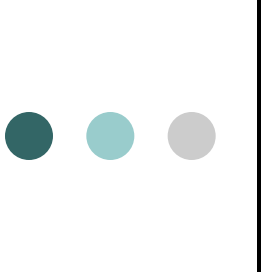
BIA-ALCL

- Primary ALCL of the breast – 3/100 million/ year
- 18.2 times risk with implants but still incredibly rare – 1/500,00 women with implants
- BIA-ALCL arises within the implant capsule not the breast parenchyma
Commonest presentation: late onset seroma causing breast swelling
- Excellent prognosis – recommended management is removal of and **and** observe
- Patients who prcapsuleimplantesent with a mass / extension beyond the capsule may require more aggressive treatment with chemotherapy and / or radiotherapy



Breast Lymphoma

- Primary lymphoma of the breast 0.04-0.5% of breast tumours
- Conversely, 1-2% of extranodal lymphomas arise in the breast
- Commonest is diffuse large B cell lymphoma
- Next commonest are low grade B cell lymphomas; MALT and follicular lymphomas
- Rare – Burkitt lymphoma, ALCL, peripheral T cell lymphomas



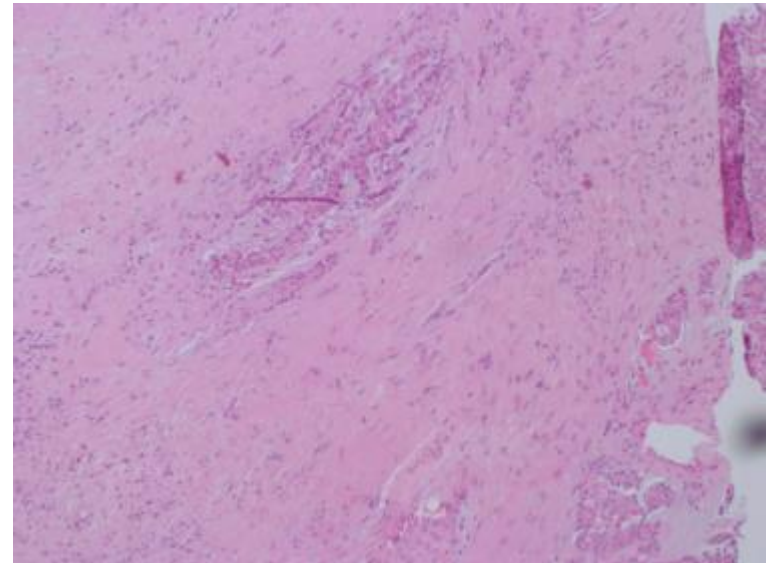
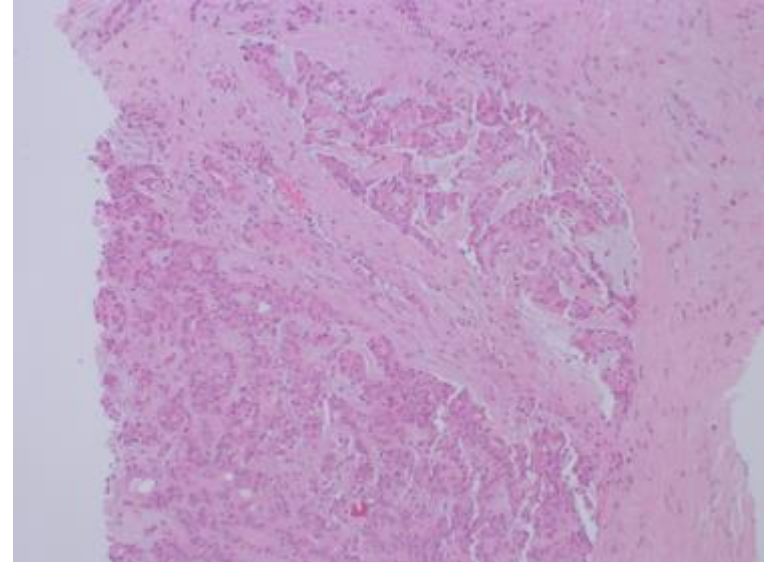
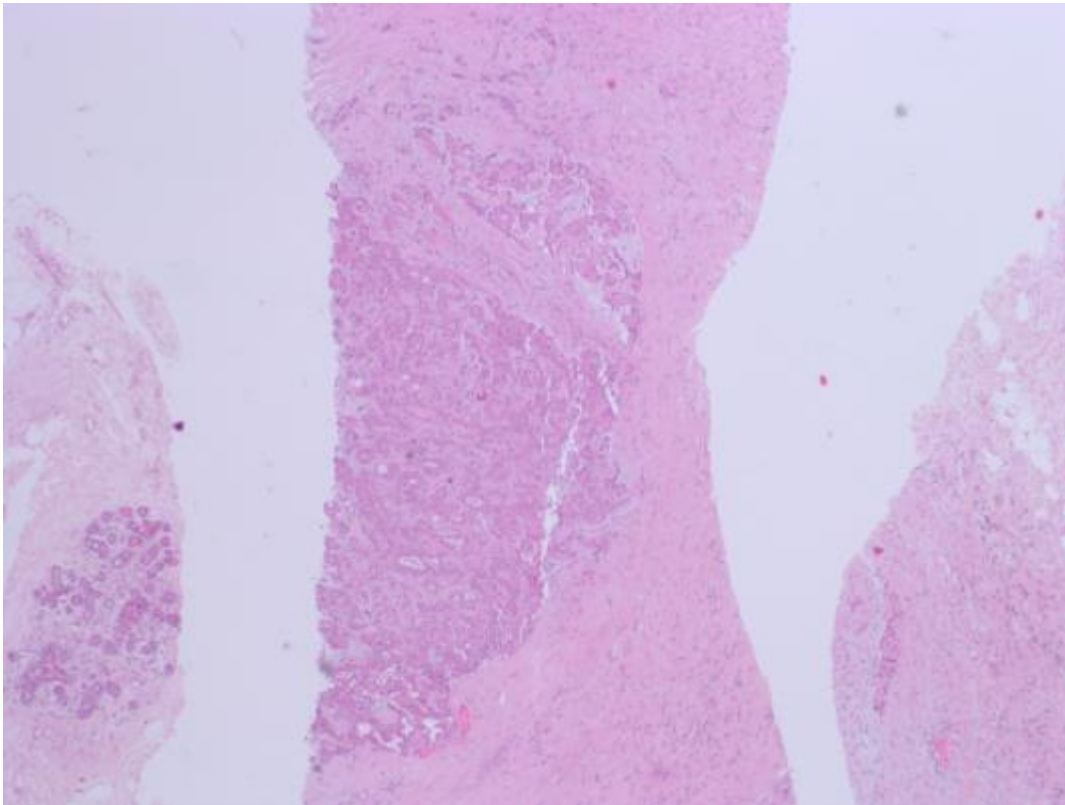
Case 17

Clinical history:

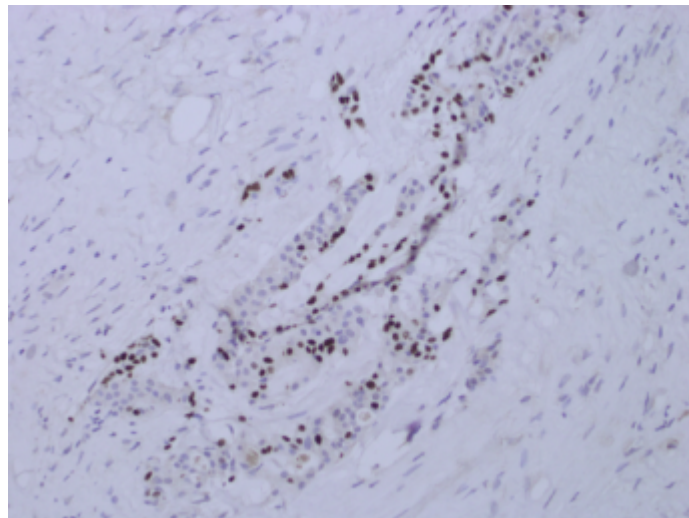
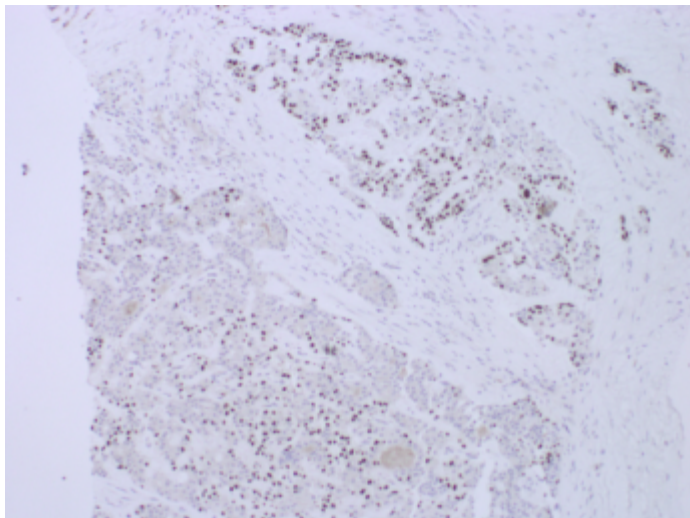
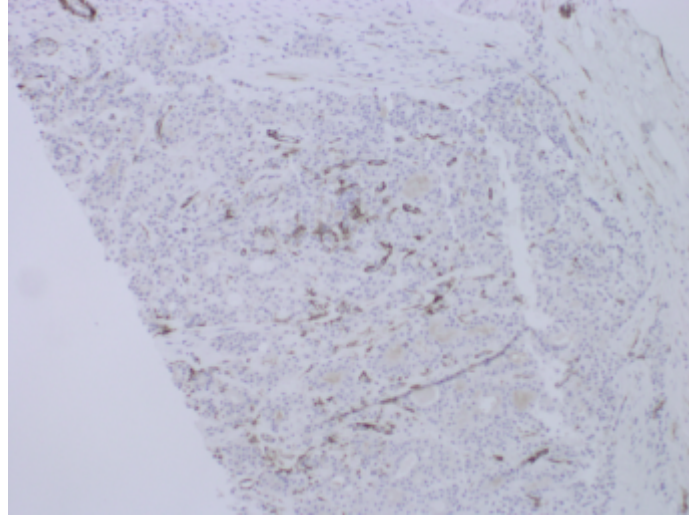
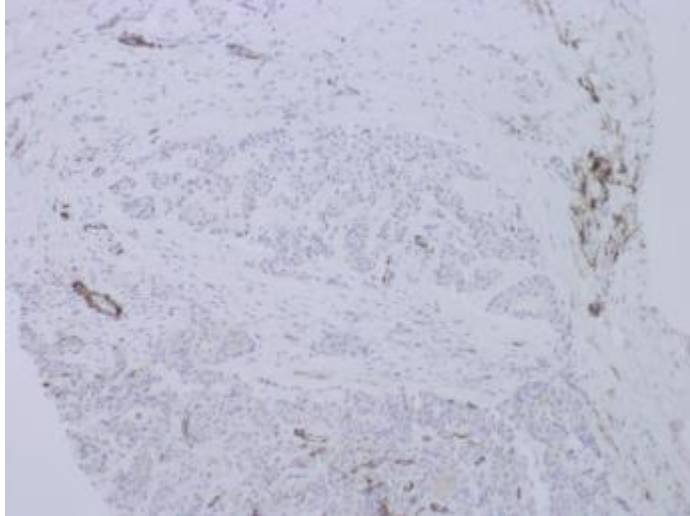
43 year old female

**Diagnostic excision
following B4 core biopsy**

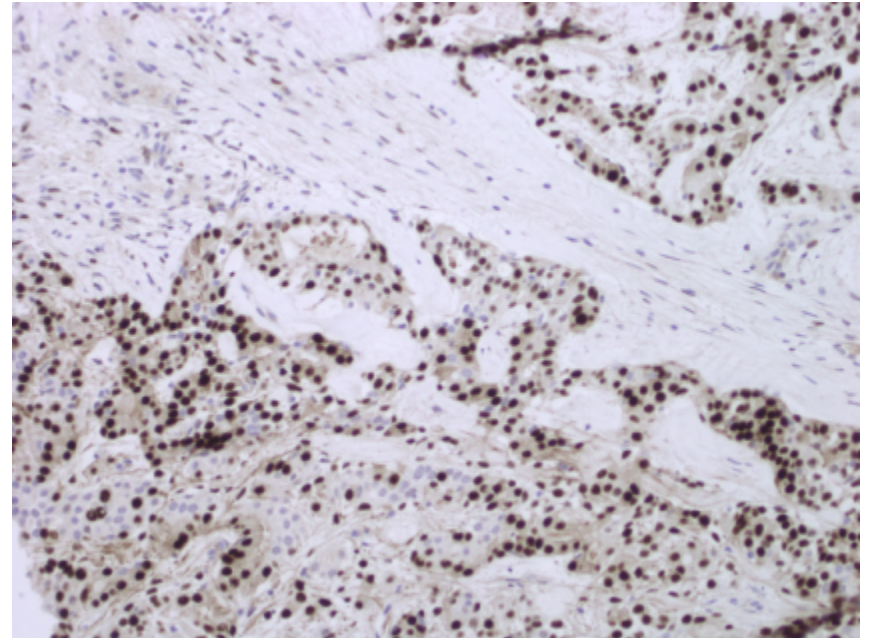
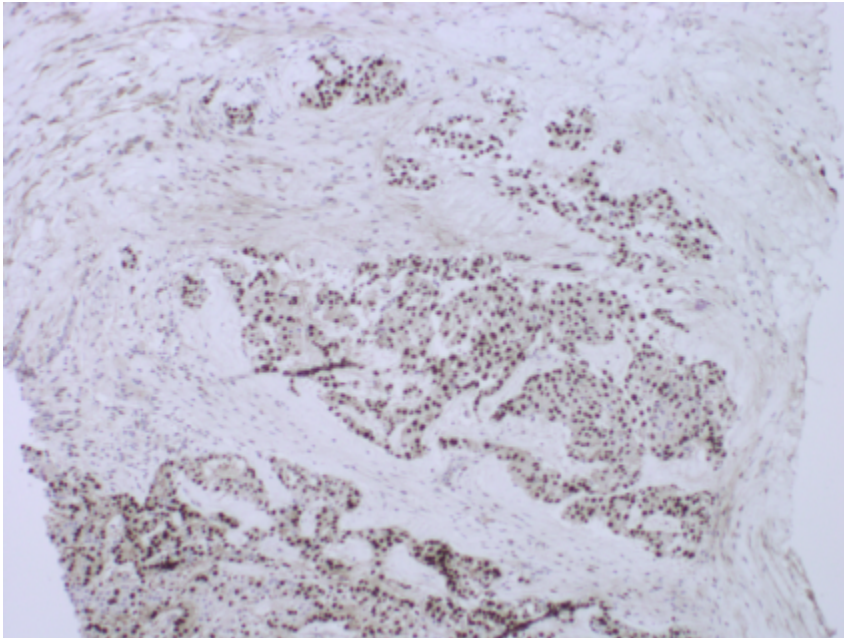
Core biopsy



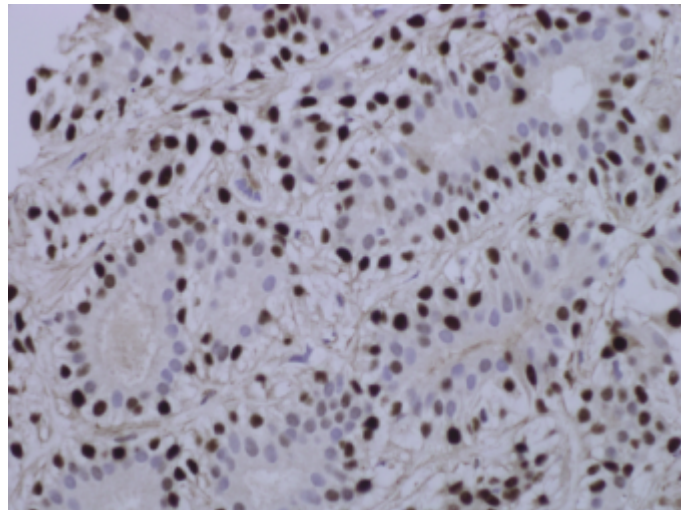
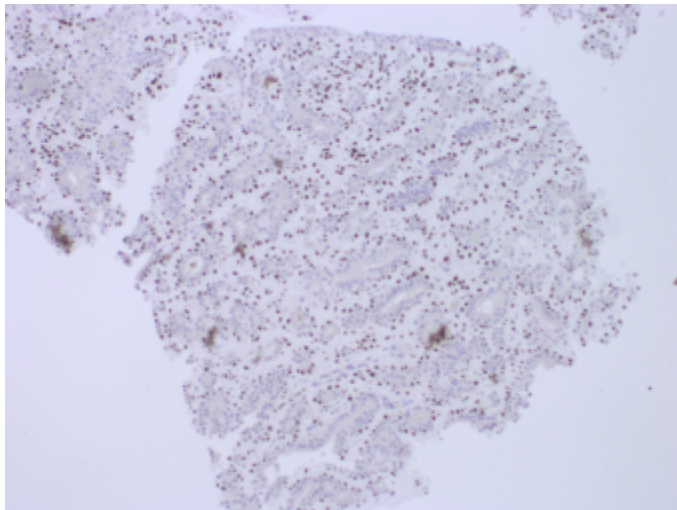
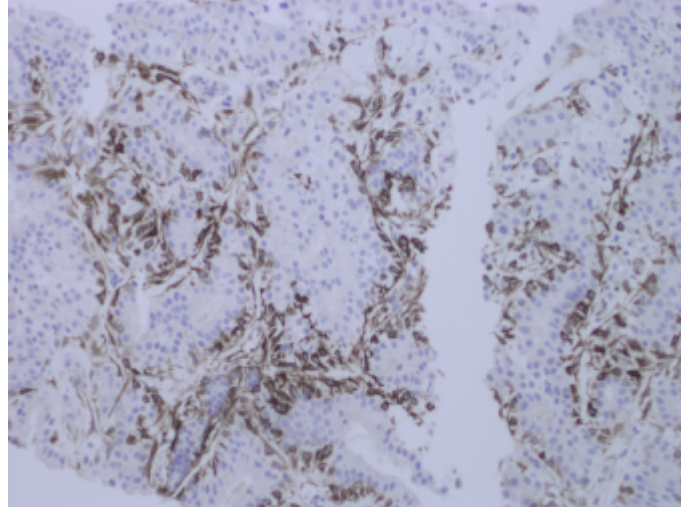
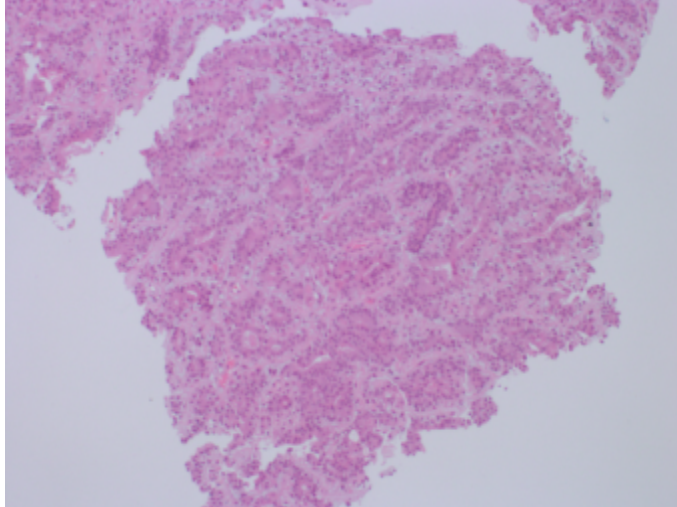
Core biopsy

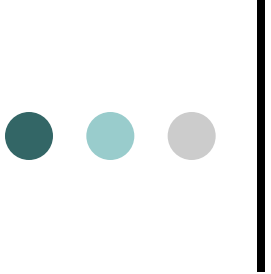


Core biopsy



Core biopsy

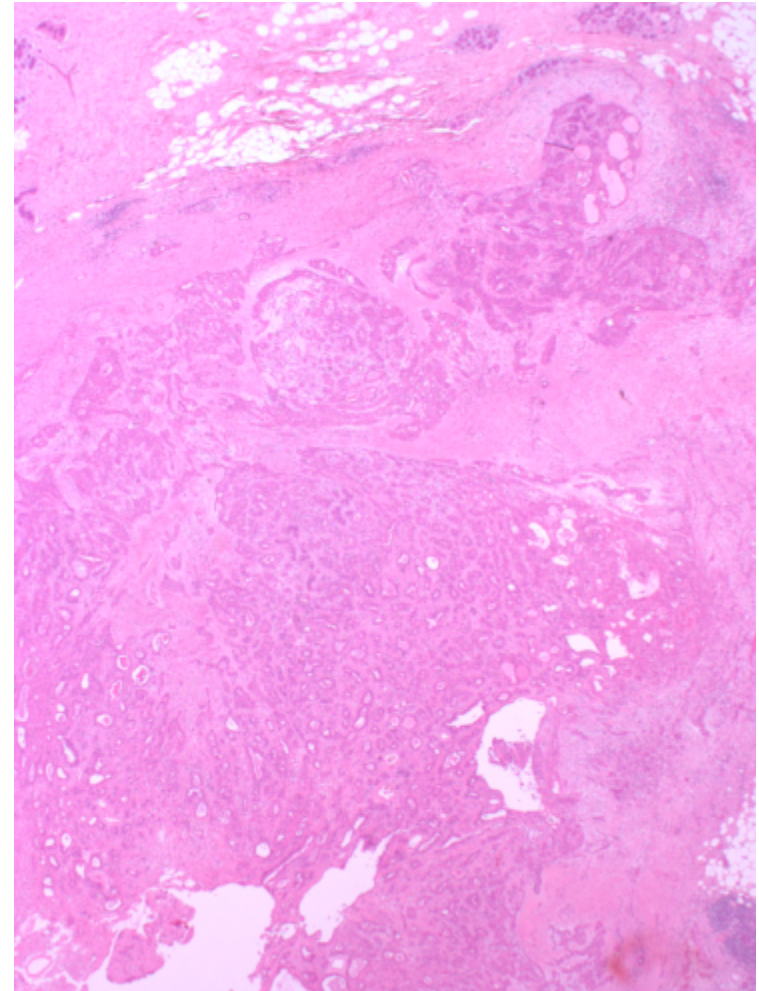
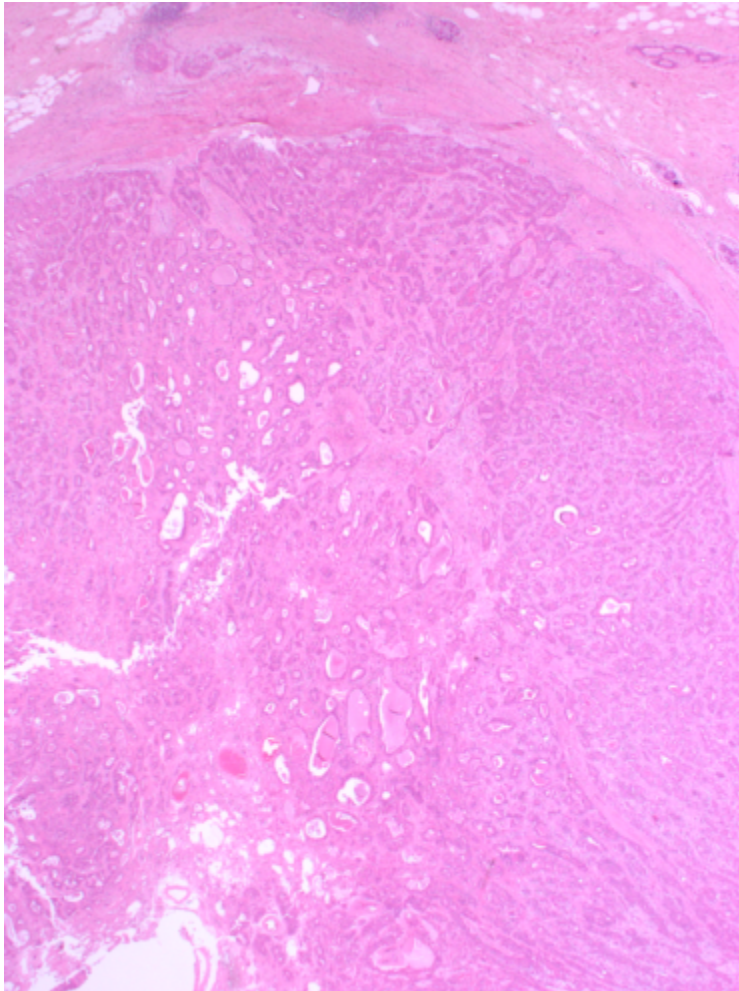




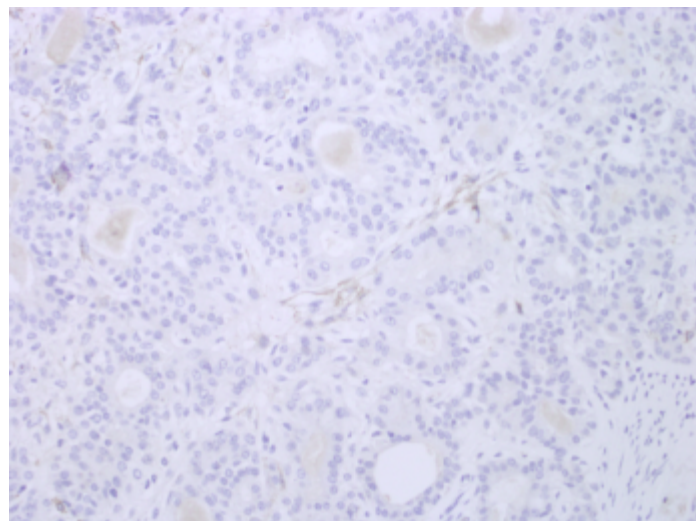
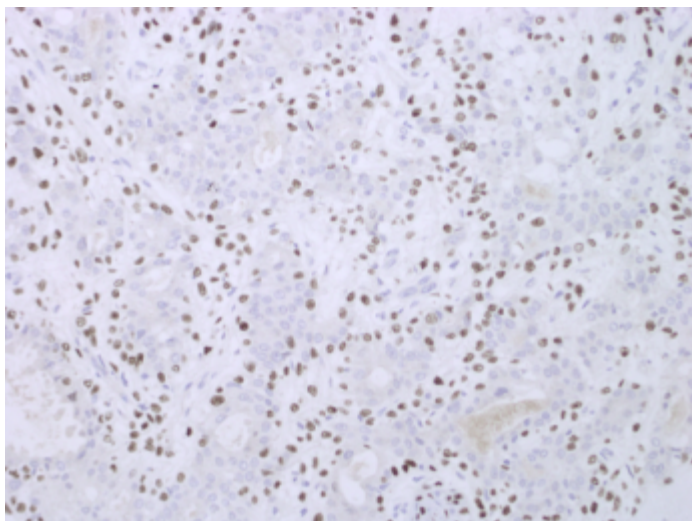
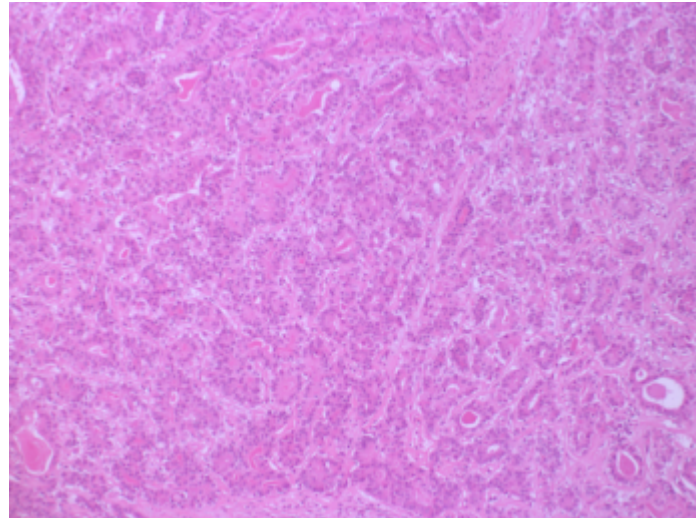
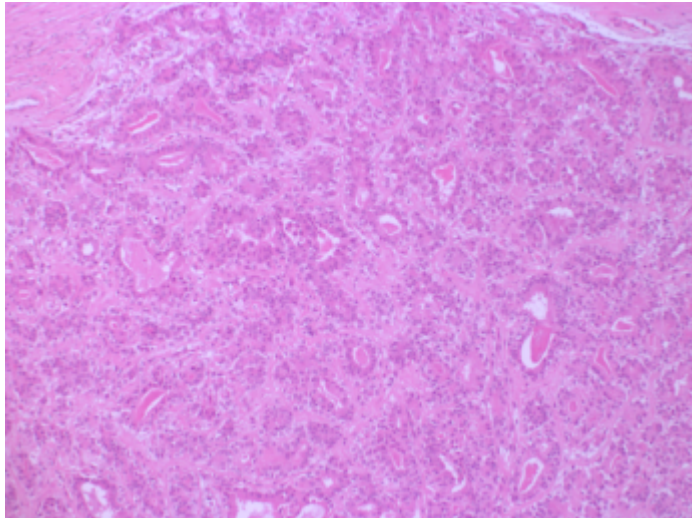
Core biopsy

- Biphasic lesion with epithelial and myoepithelial components
- Mild cytological atypia
- Heterogeneous staining for ER
- Foci at periphery ? Stromal invasion
- B4

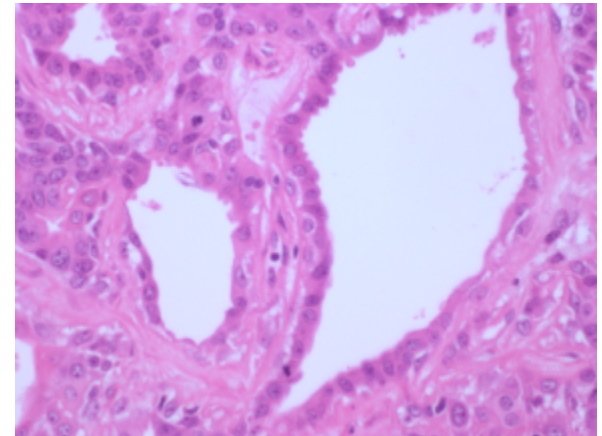
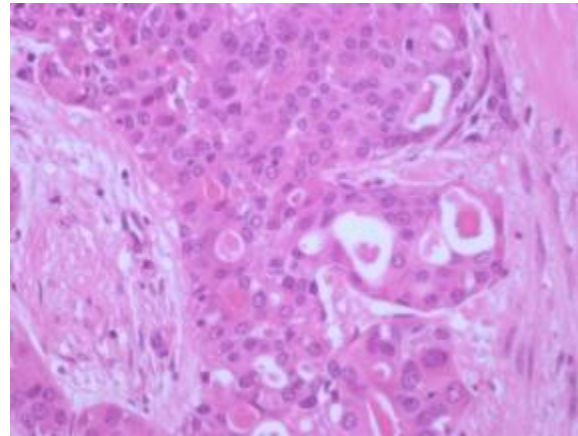
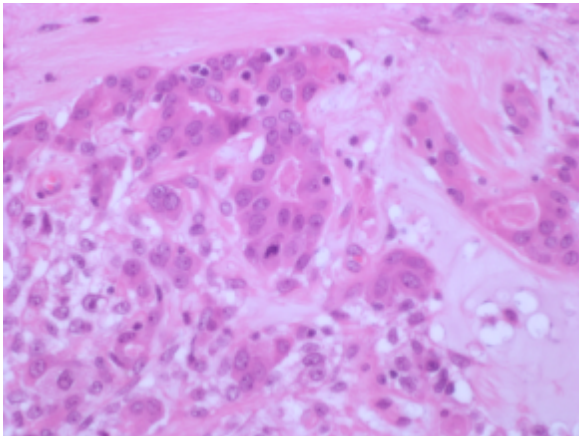
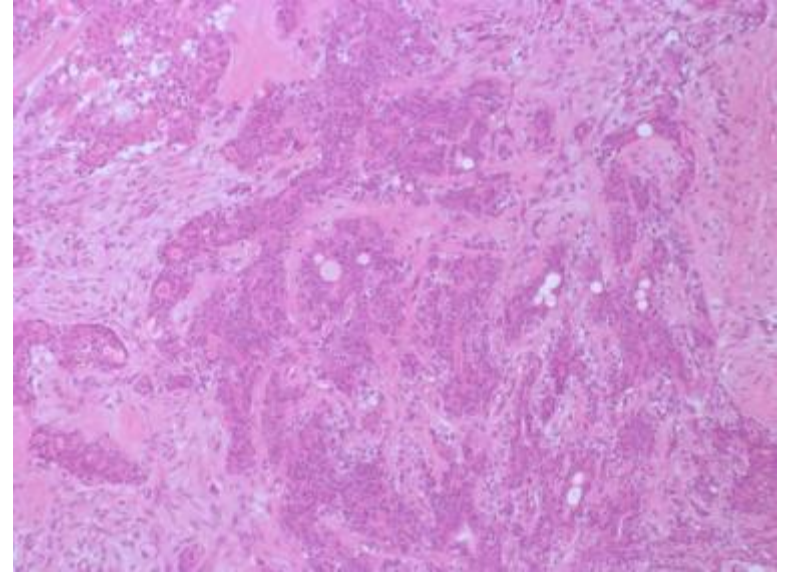
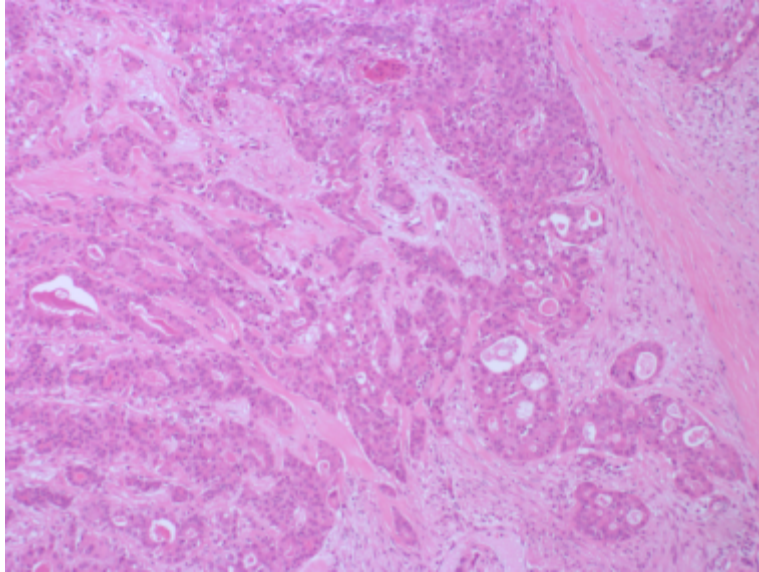
WLE specimen



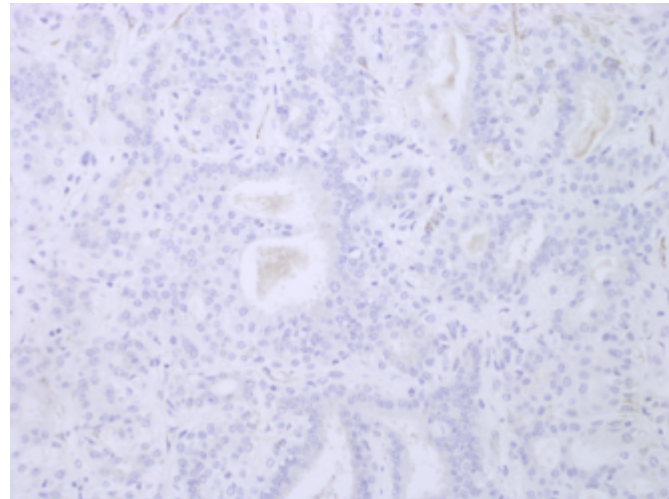
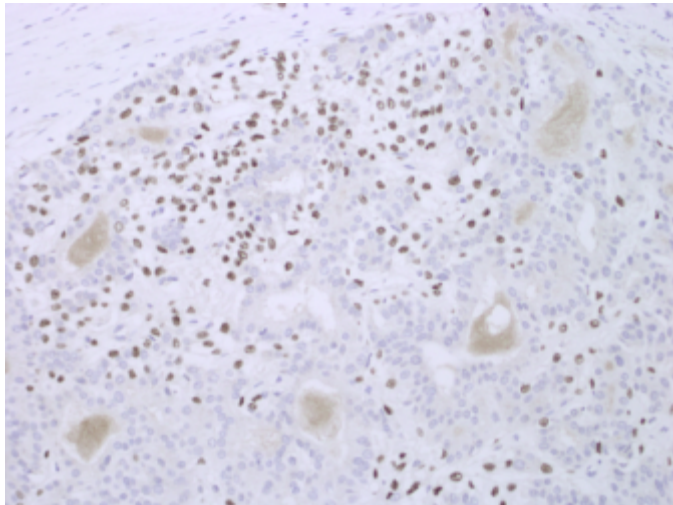
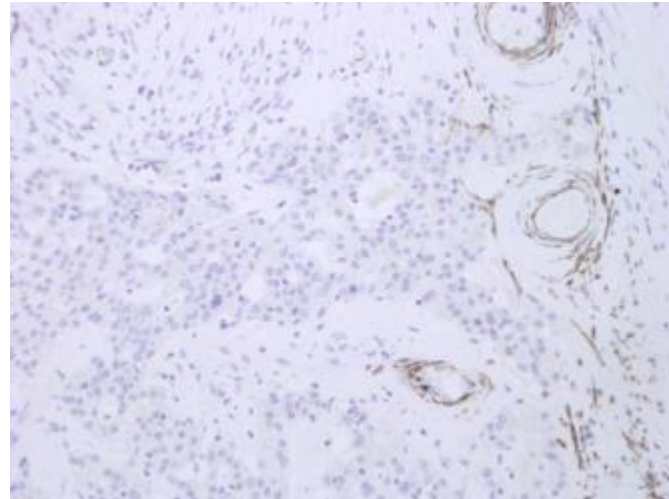
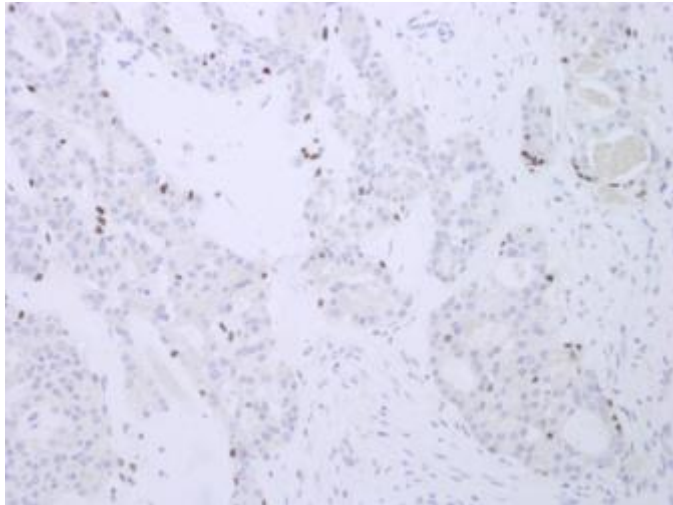
WLE specimen



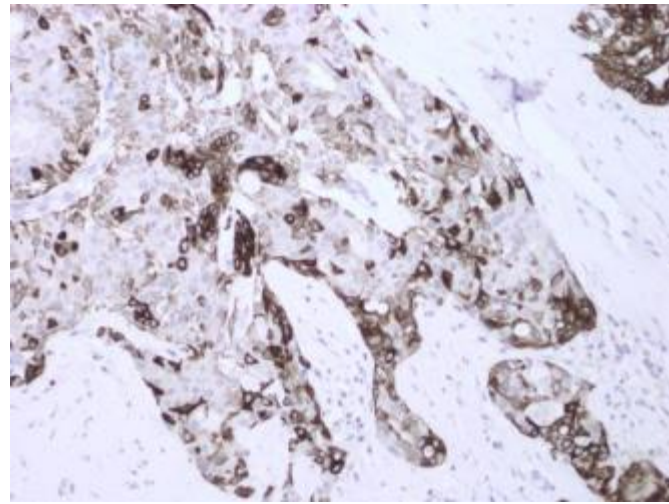
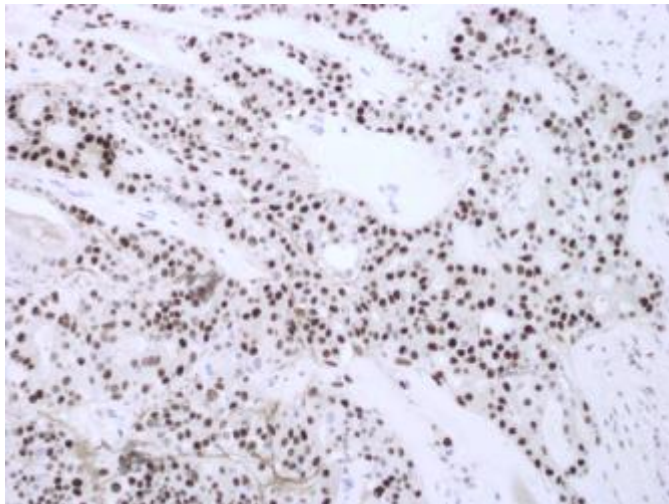
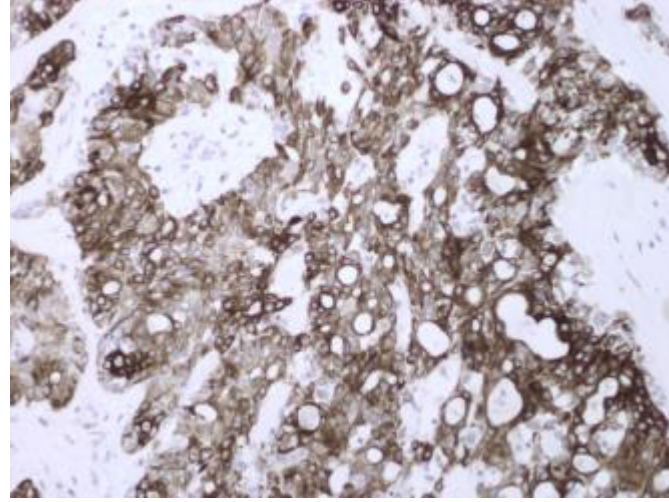
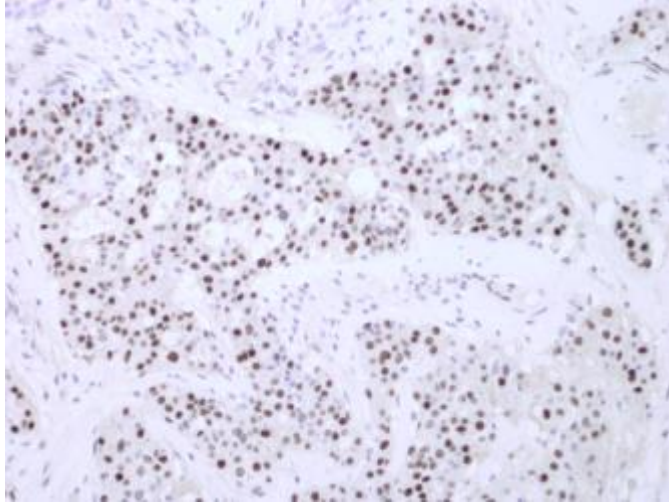
WLE specimen

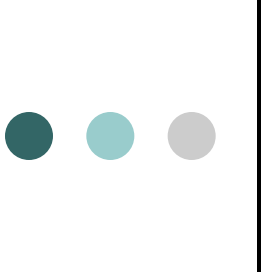


WLE specimen



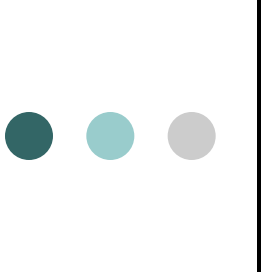
WLE specimen





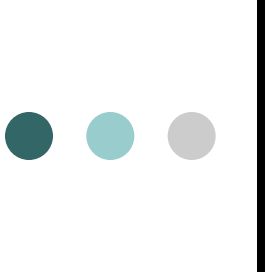
Final Diagnosis:

- **Adenomyoepithelioma with atypia**
- **Areas at periphery ? Invasion
=> Emed for 2nd opinion**
- **P63 positivity throughout**
- **Lack of high grade atypia or other features of frank malignancy**
- **Final diagnosis = atypical**



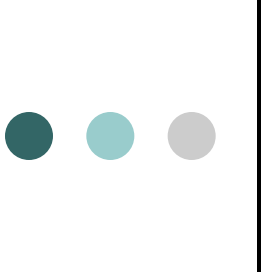
Adenomyoepithelioma

- Biphasic tumour composed of a proliferation of myoepithelial cells around small epithelial spaces
- Resembles epithelial-myoepithelial carcinoma of the salivary gland
- Majority of patients post menopausal but can occur at any age; rare cases described in men
- Presents as a solitary mass lesion; may be history of rapid growth in a longstanding mass with malignant transformation
- Mammography – circumscribed mass with lobulated outline similar in appearance to a fibroadenoma
- U/S – solid or combined solid and cystic mass
- 1-8 cm in size; mean 2.5 cm



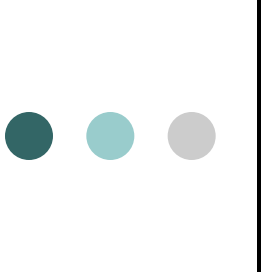
Adenomyoepithelioma

- Circumscribed lesion with multilobulated architecture on low power, may have central sclerosis
- Lobulated, papillary, tubular or mixed patterns
- Papillary lesions with myoepithelial hyperplasia best regarded as papillomas
- Myoepithelial component predominates and may be spindled or epithelioid; latter often has clear cell appearance. Myoid and plasmacytoid variants also described.
- Epithelial component can show squamous, apocrine or sebaceous metaplasia
- Epithelial elements may be difficult to detect on light microscopy, particularly in spindle cell variant - IHC
- Lacks cytological atypia, mitoses rare (<3/10 HPF)



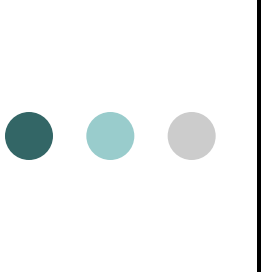
Adenomyoepithelioma

- Dual cell population demonstrated by IHC
- Epithelial component – positive for CK7, CK8/18, EMA and ER
- Myoepithelial component – positive for p63, SMMHC, calponin, actin, CK5/6, CK14. May stain with S100. Negative for desmin.



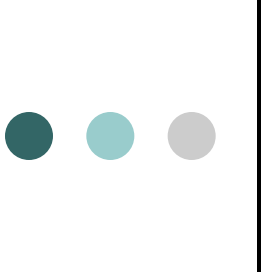
Adenomyoepithelioma

- Differential diagnosis includes papilloma, tubular adenoma, sclerosing adenosis, fibroadenoma
- Distinguishing feature is degree of presence of myoepithelial hyperplasia throughout the lesion
- Papillary lesions without nests, nodules or increased proportion of MEC classed as papillomas
- Ductal adenoma – central location with surrounding fibrous capsule (no fibrous



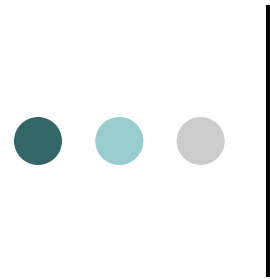
Malignant Adenomyoepithelioma

- Atypical adenomyoepithelioma – nuclear pleomorphism, increased mitoses (>4-5/10 HPF)
- Malignant adenomyoepithelioma – requires presence of associated benign AME for diagnosis
- Malignant transformation can occur in epithelial component, myoepithelial component, or both
- Malignant features: nuclear pleomorphism, increased mitoses, necrosis, overgrowth of myoepithelial component, infiltrative growth pattern



Malignant adenomyoepithelioma

- Two patterns:
- Typical adenomyoepithelioma that merges with an adjacent infiltrating carcinoma
- Epithelial – invasive carcinoma NST, spindle cell or squamous metaplastic carcinoma, undifferentiated carcinoma
- Associated carcinoma often triple negative
- Myoepithelial carcinoma
- Epithelial-myoepithelial carcinoma – similar to poorly differentiated salivary gland counterpart
- Lesion with the low power appearance of adenomyoepithelioma but on close examination has marked cytological atypia and mitotic activity

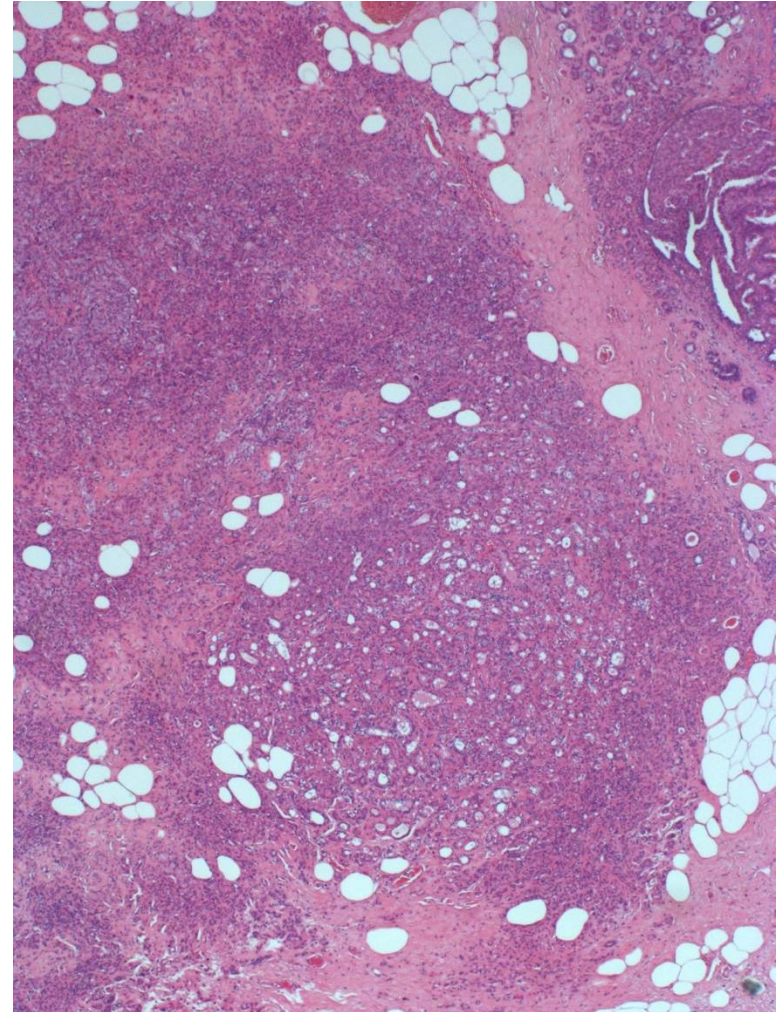
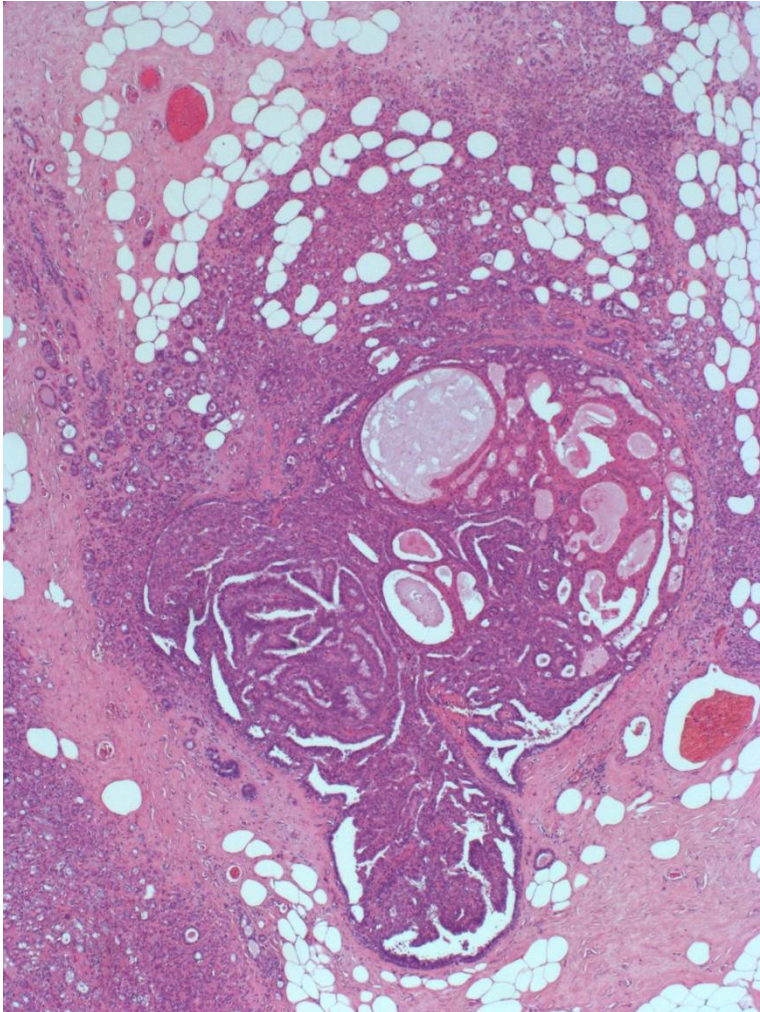


Case 20:

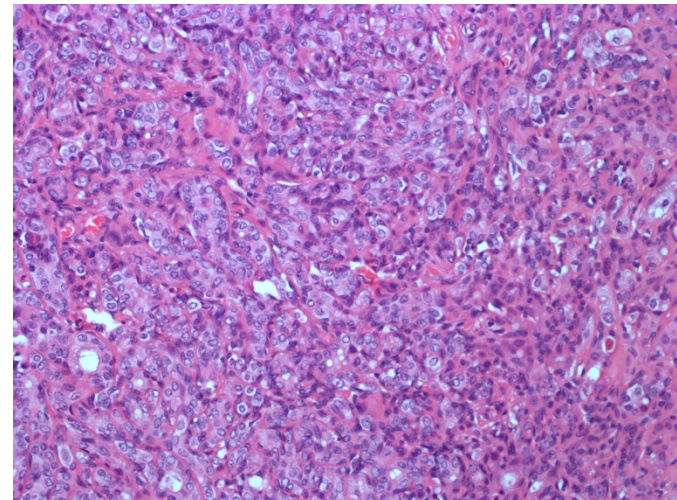
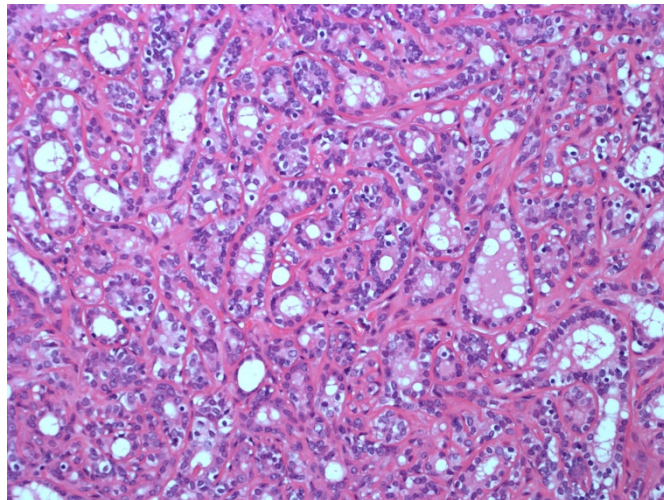
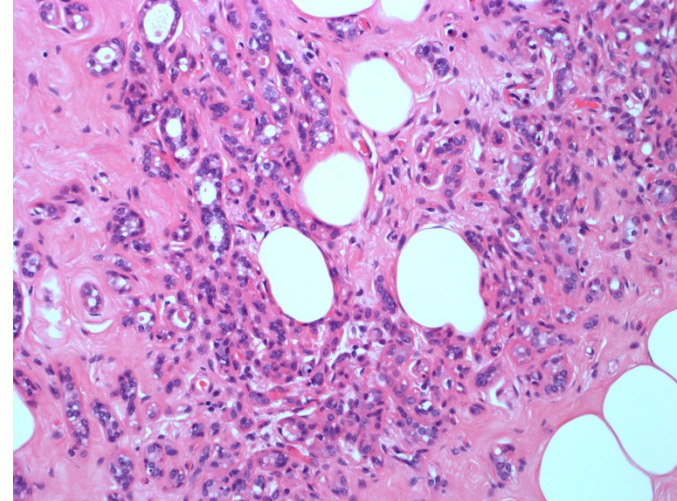
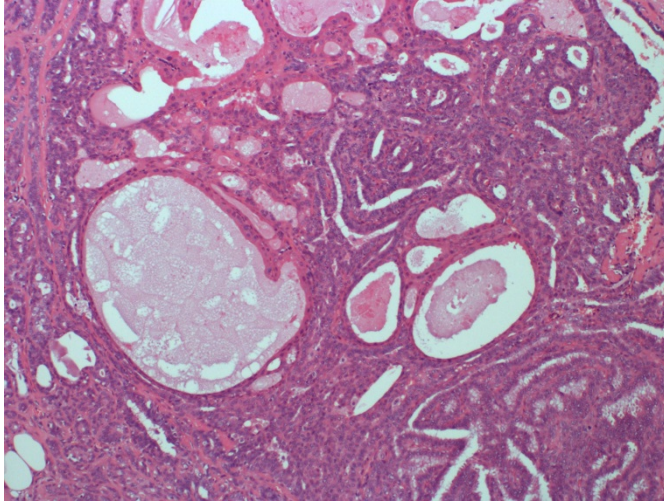
57 yo female.

WLE for high grade DCIS

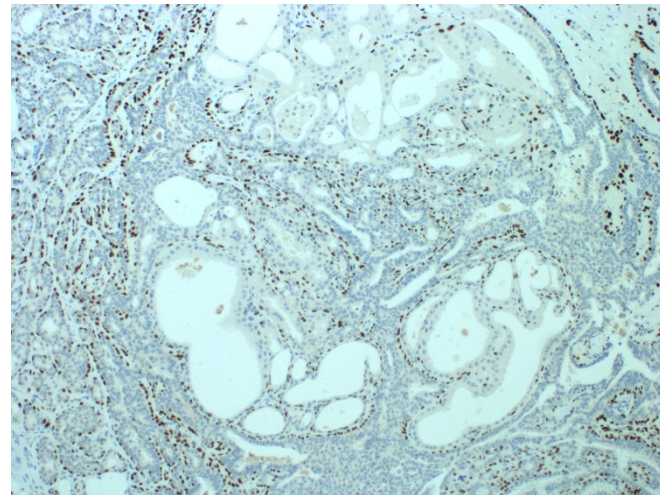
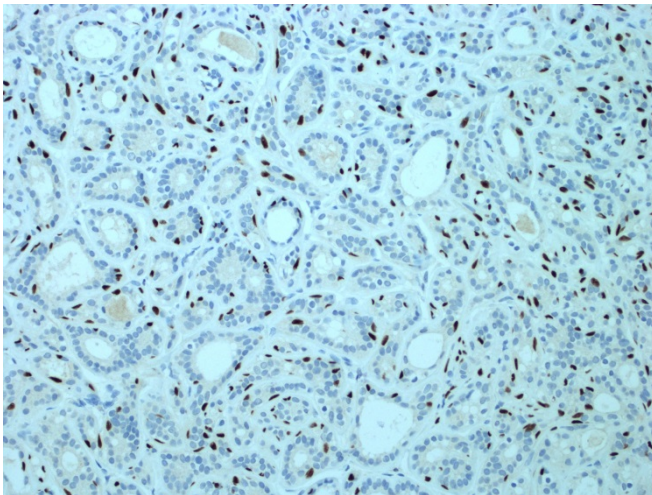
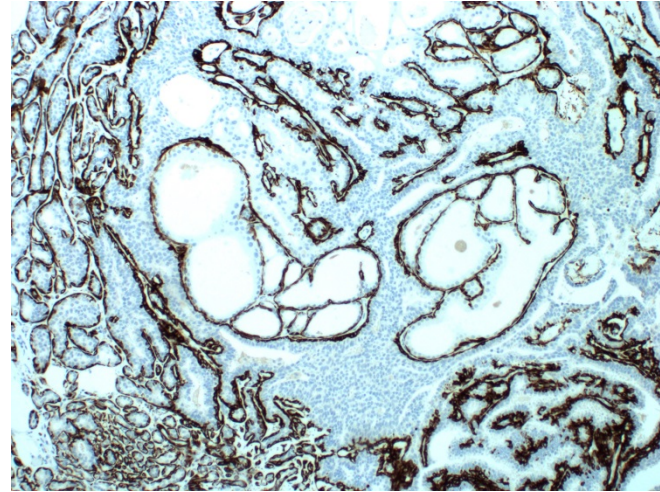
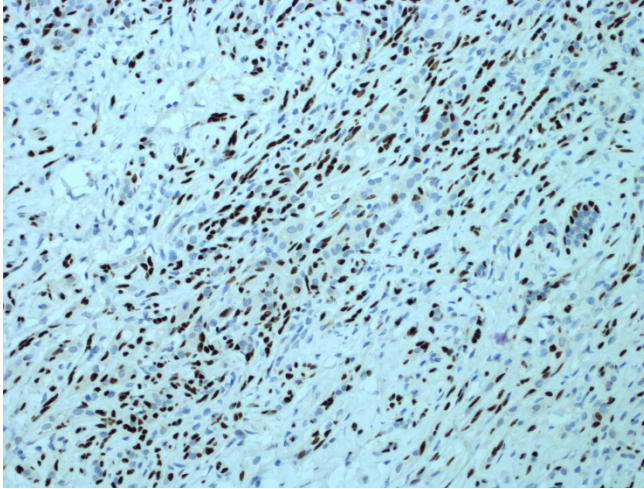
Case 20:



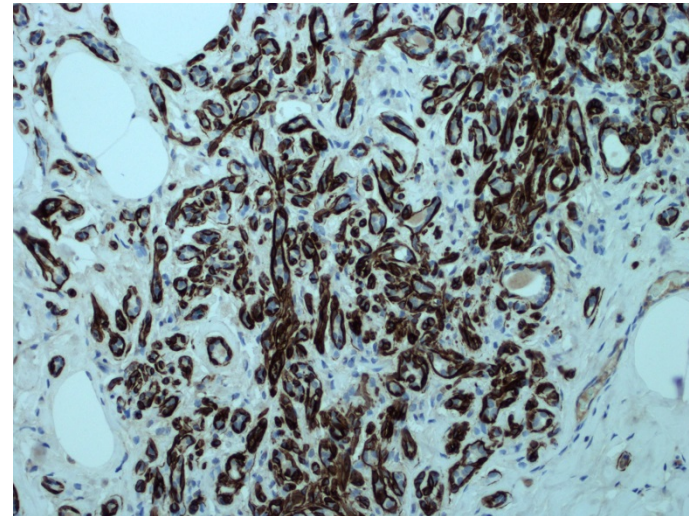
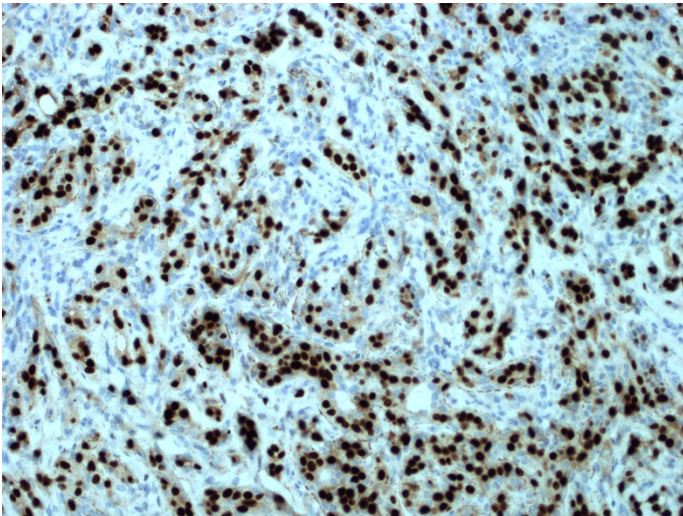
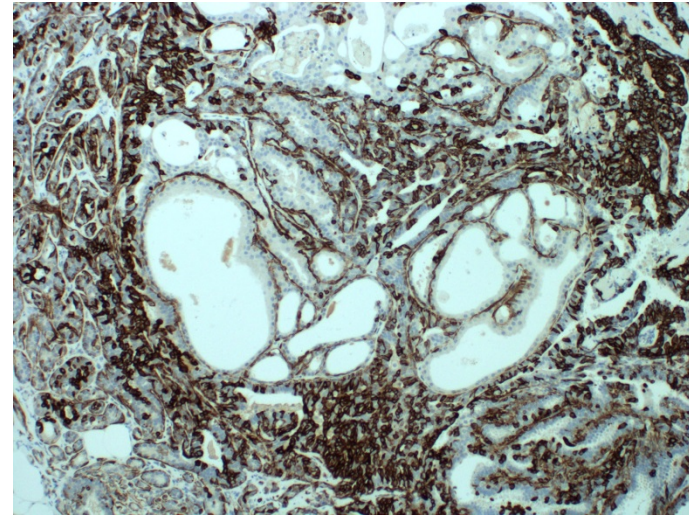
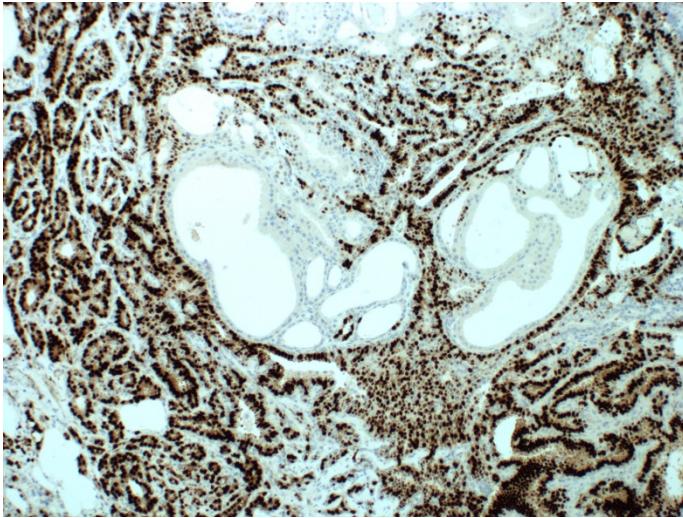
Case 20:

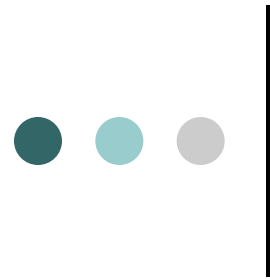


Case 20: IHC



Case 20: IHC



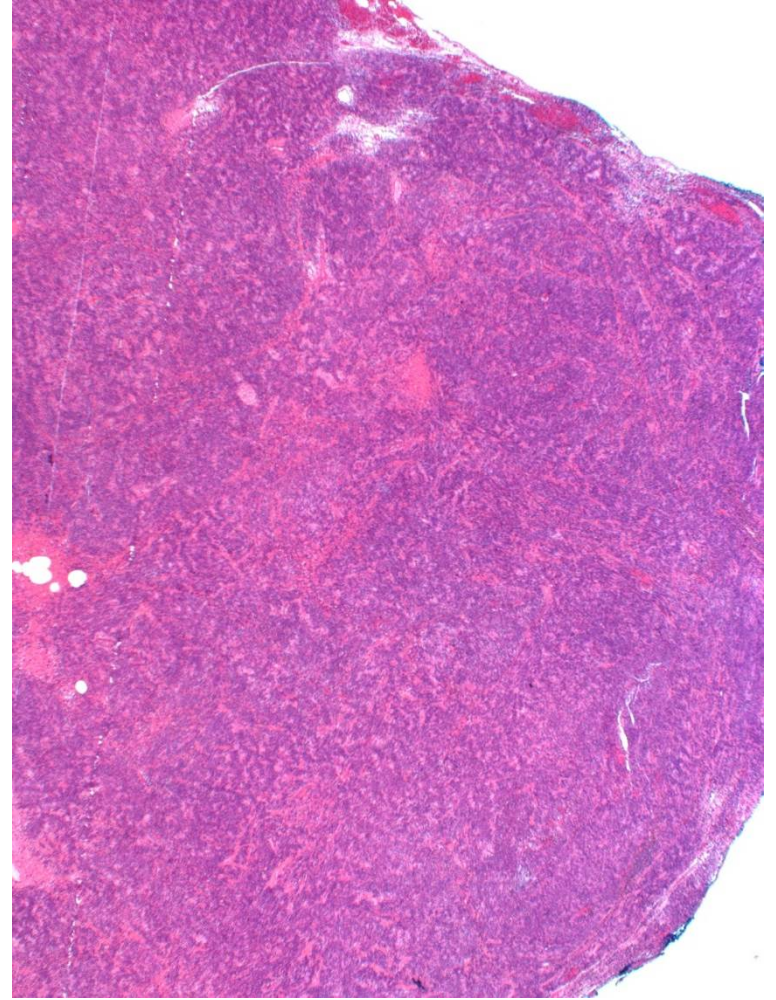
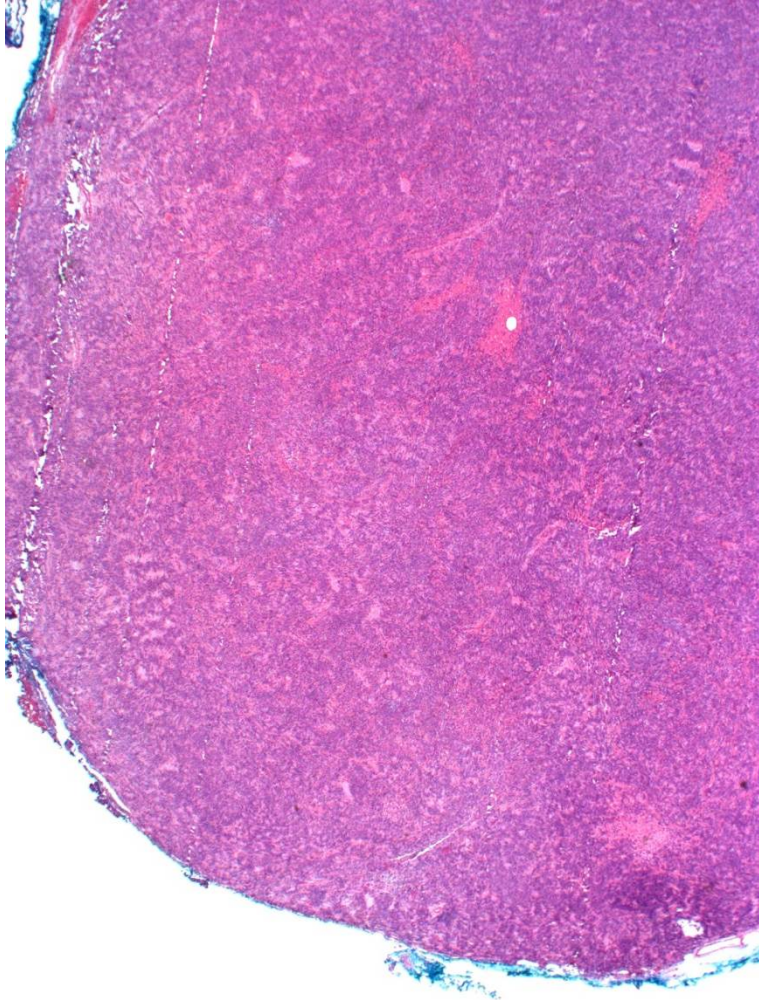


Case 21:

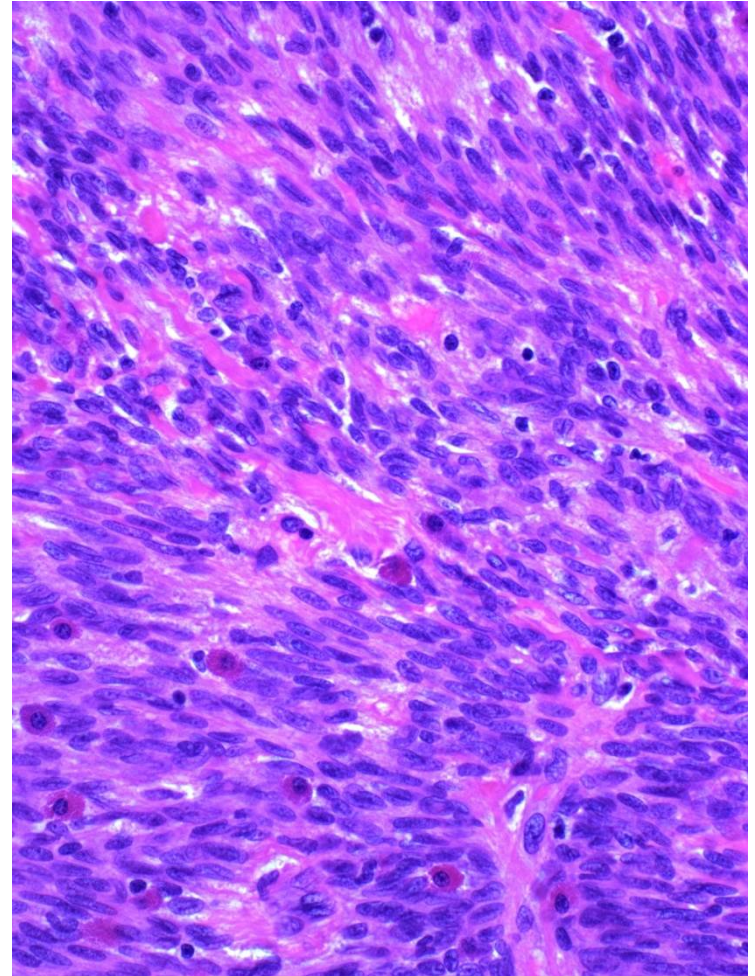
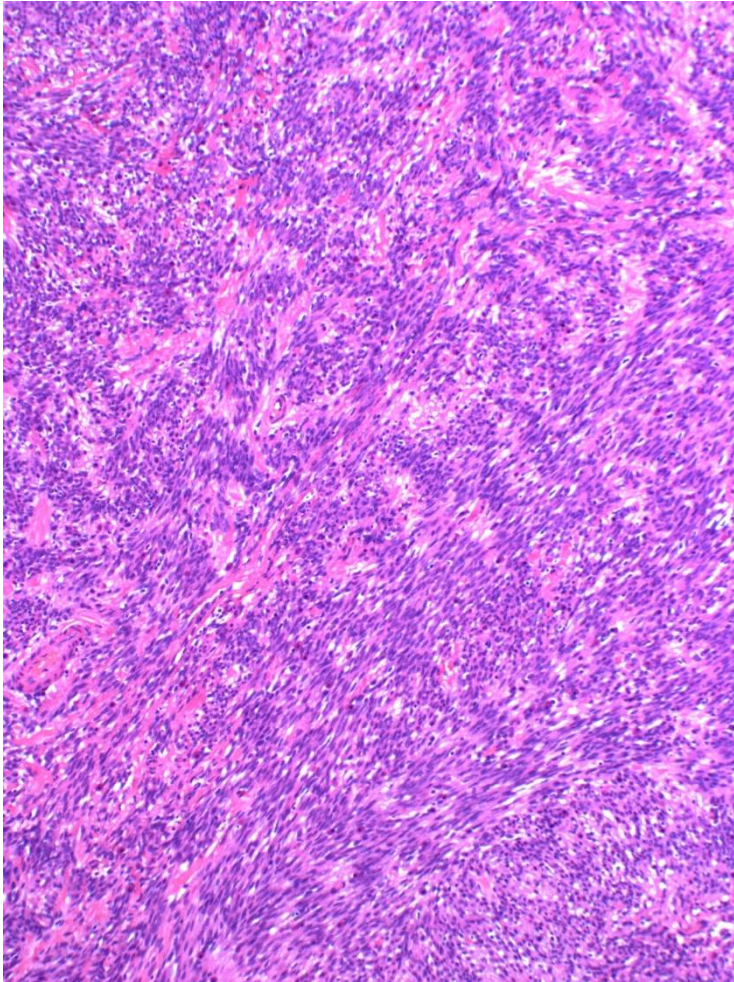
79 yo male.

Left 'breast' excision.

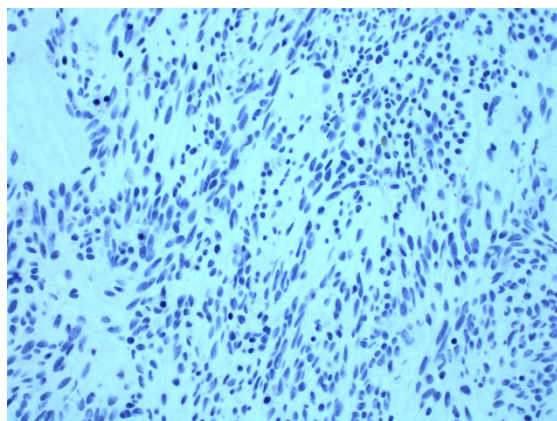
Case 21:



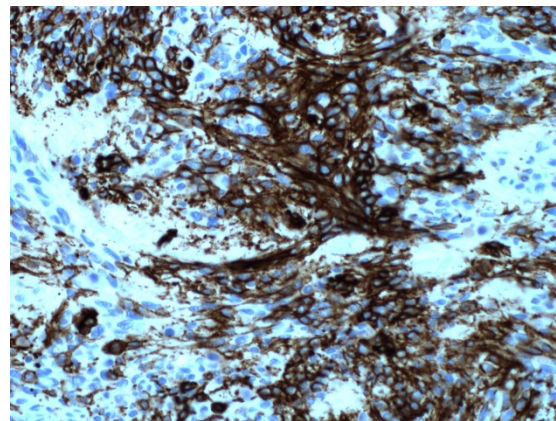
Case 21:



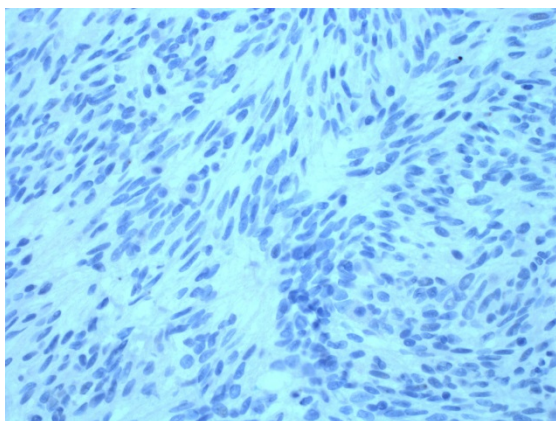
Case 21:



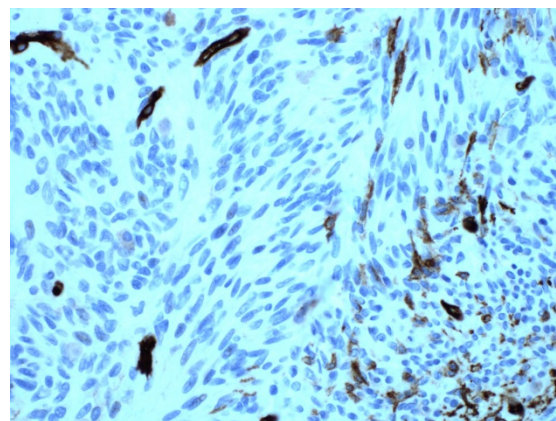
CK MNF 116



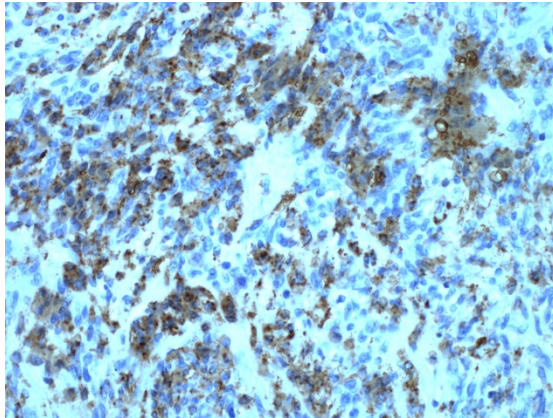
CD 34



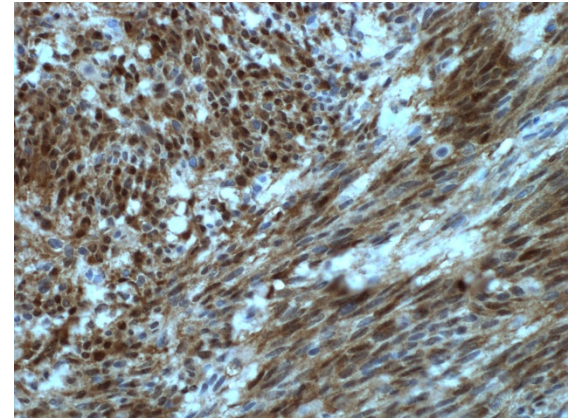
S-100



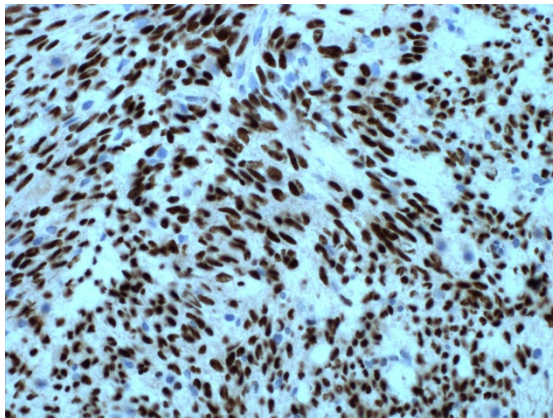
Case 21:



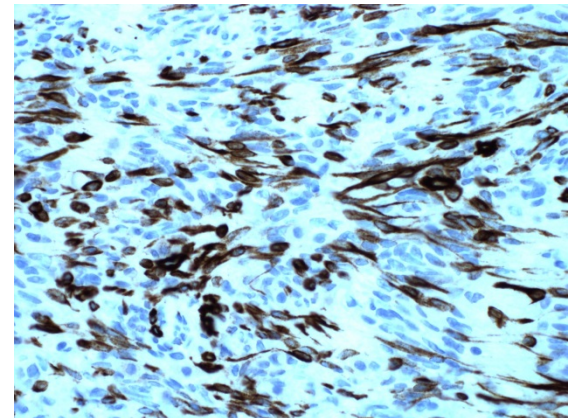
Actin



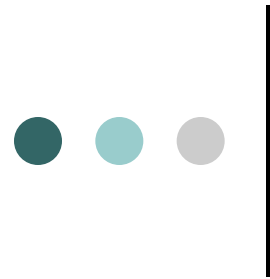
Stat 6



ER

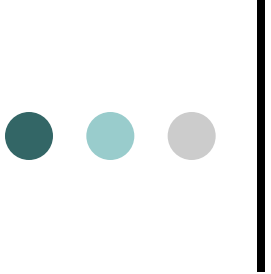


desmin



Case 21:

Myofibroblastoma



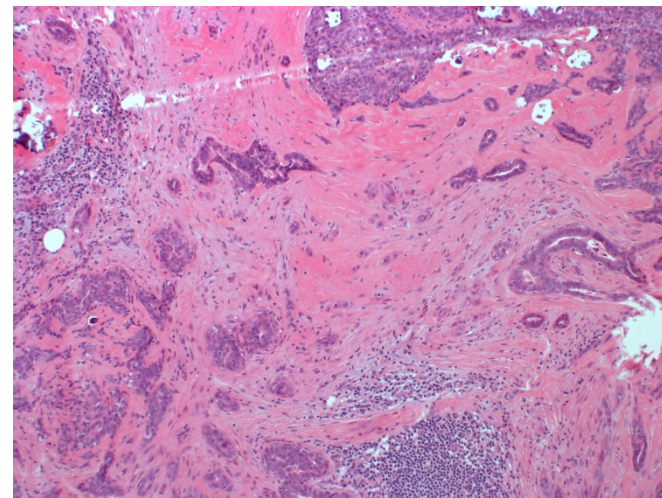
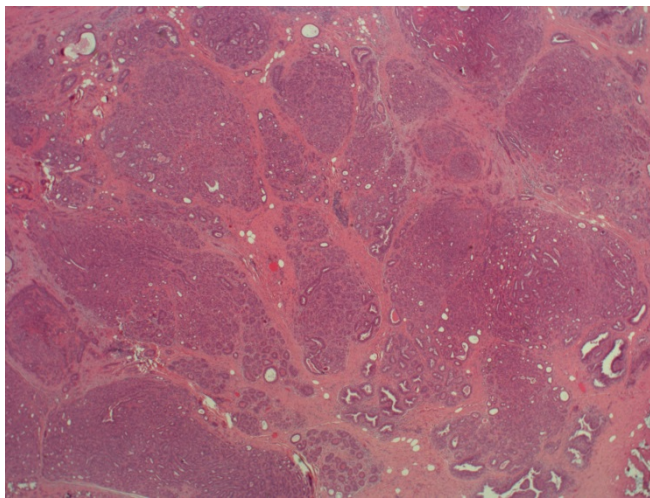
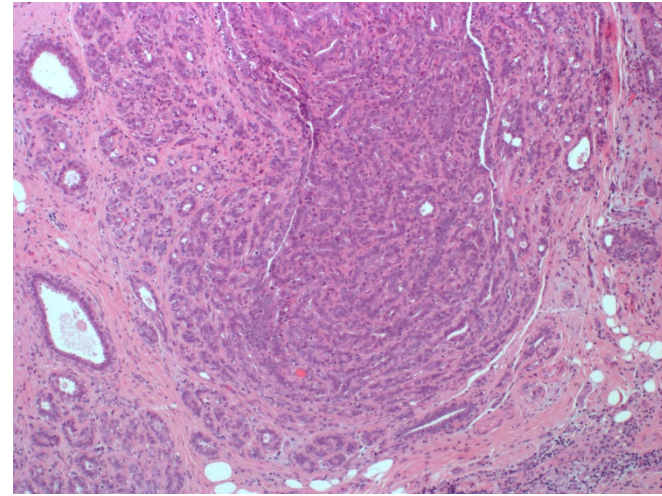
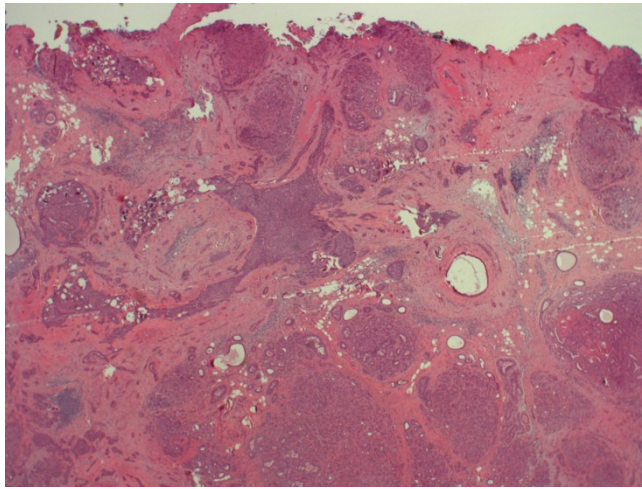
Case 22:

24 yo female.

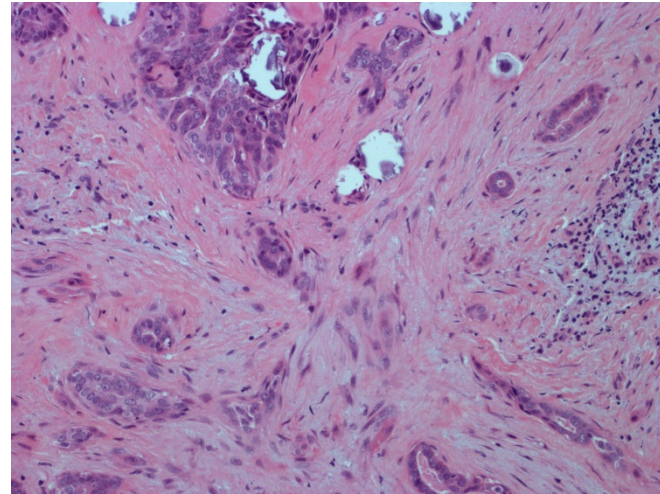
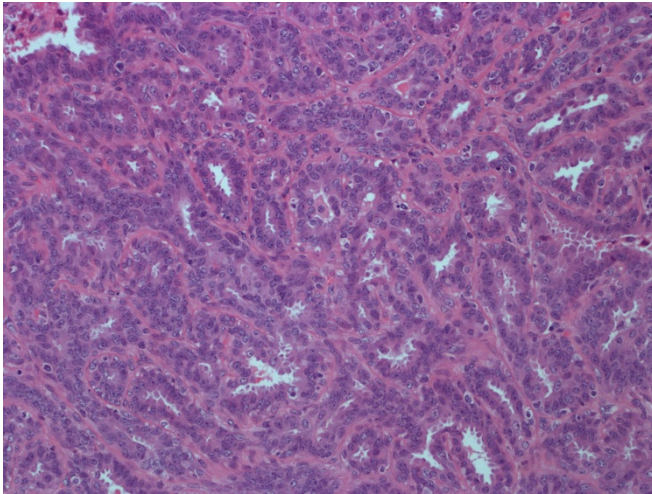
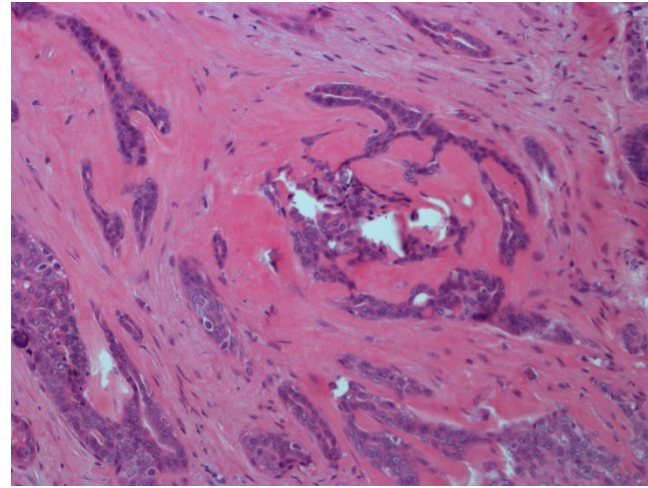
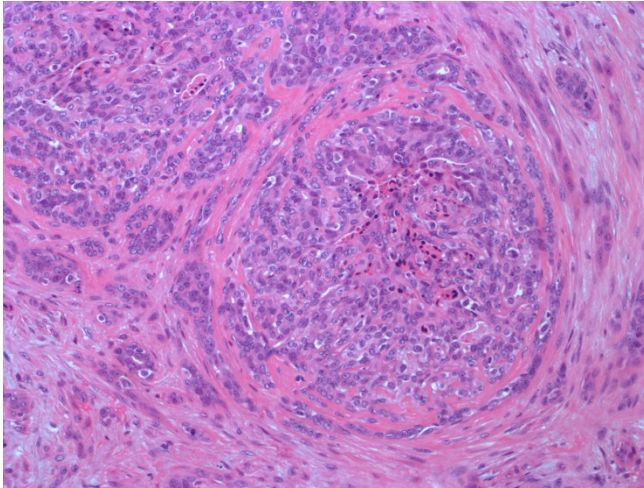
Excision biopsy B3

lesion R breast

Case 22:

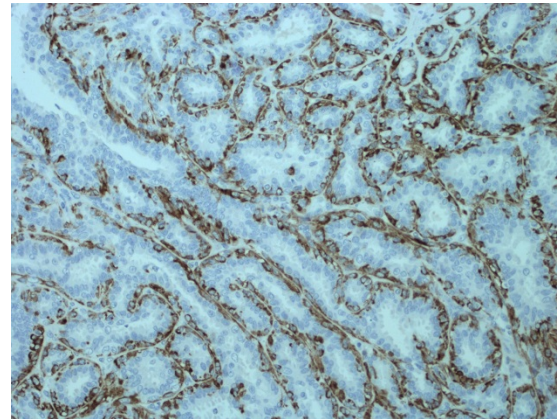
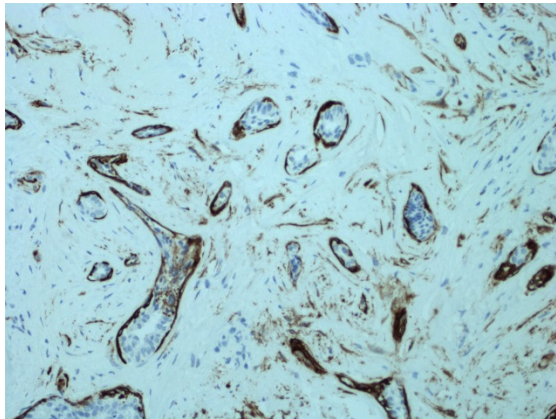
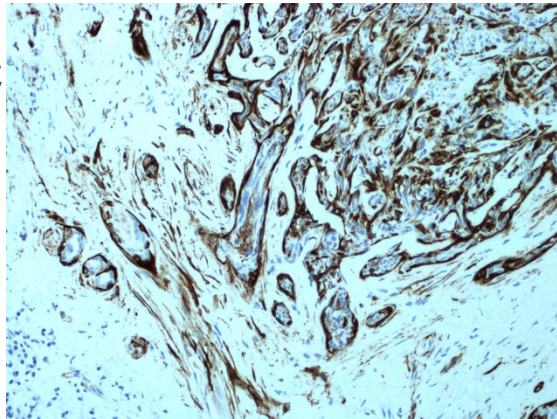


Case 22:

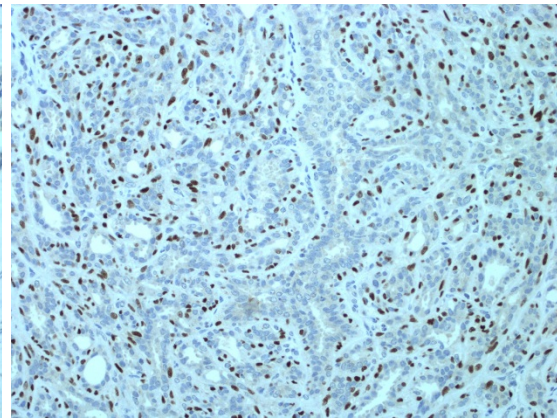
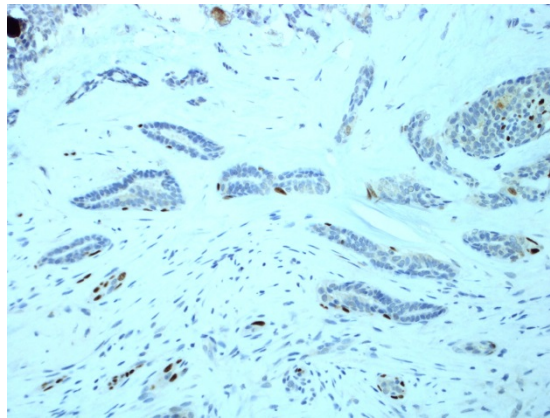
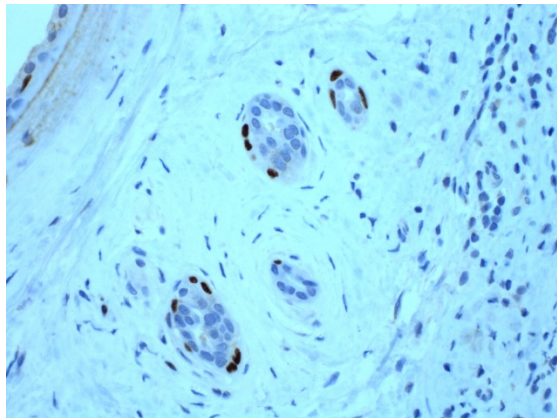


Case 22:

SMMHC

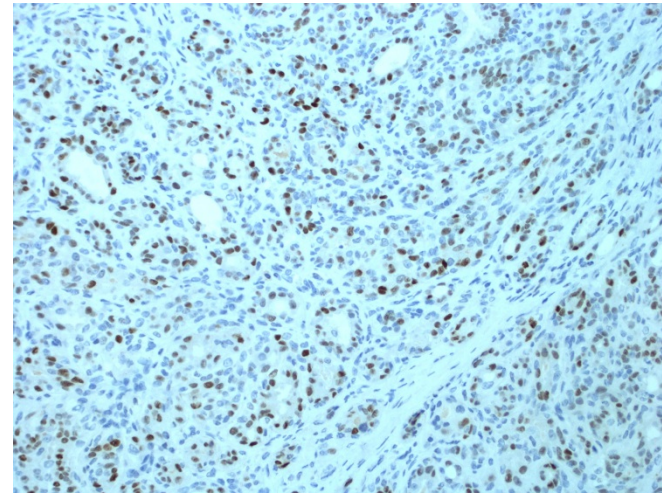
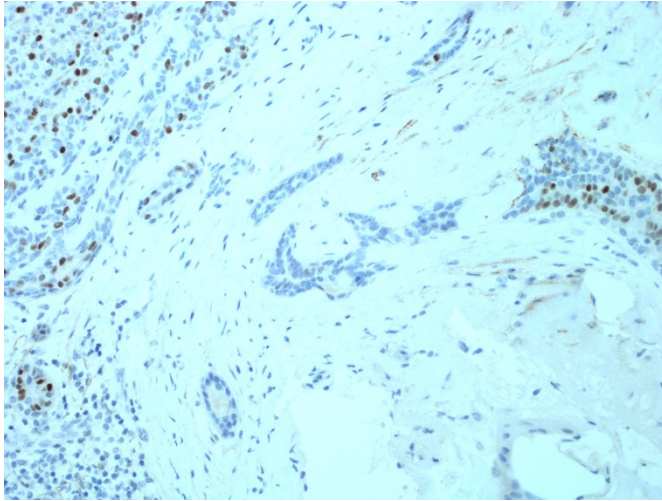


p63

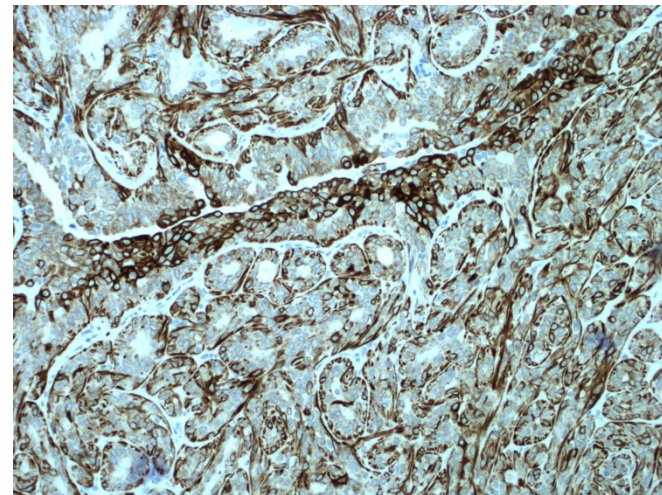
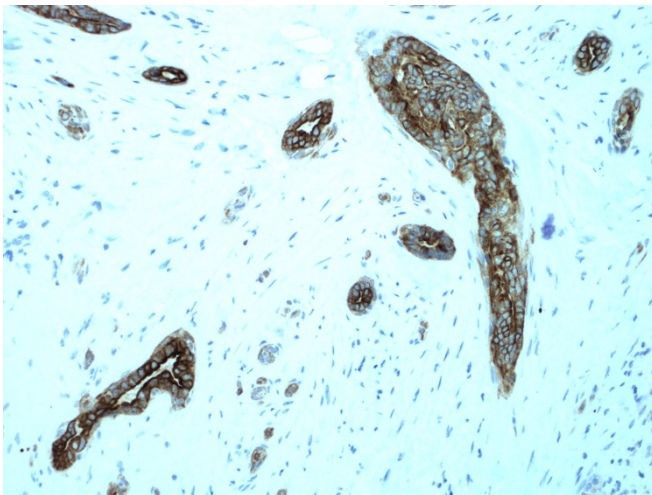


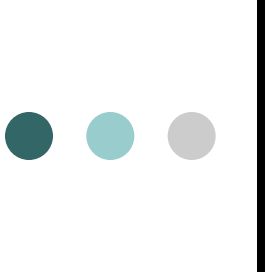
Case 22:

ER



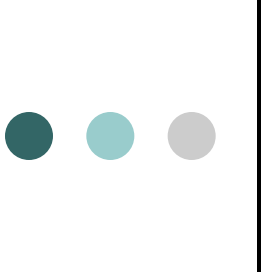
CK 5/6





Case 22:

**Complex
sclerosing lesion
with usual
hyperplasia**

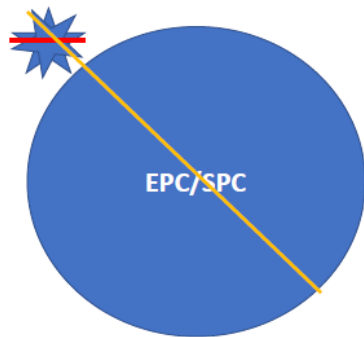


Case 23

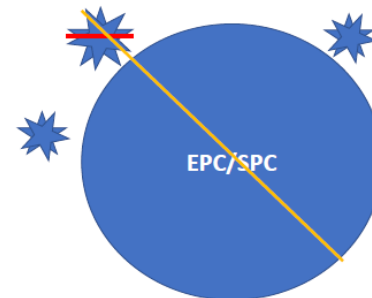
**Encapsulated papillary
carcinoma with
associated invasive ca
NST**

Case 23

Invasive size
Whole tumour size

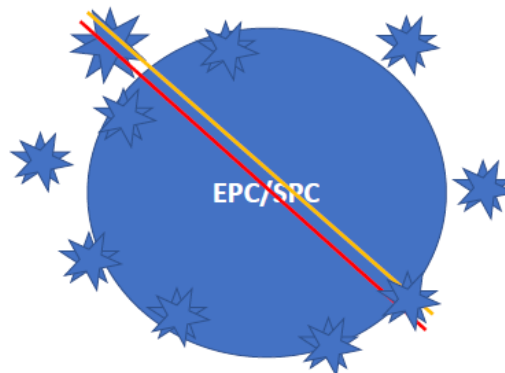


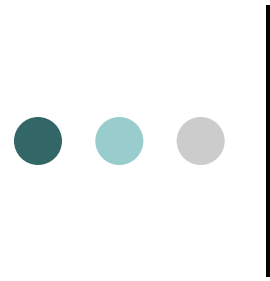
Invasive size
Whole tumour size



Multifocal

Invasive size
Whole tumour size



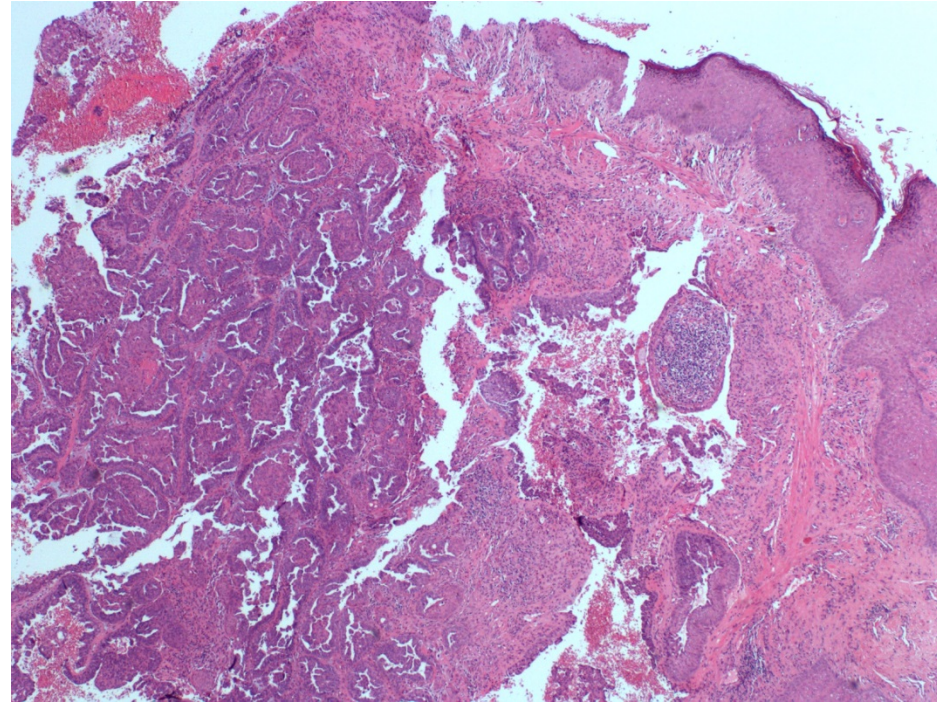
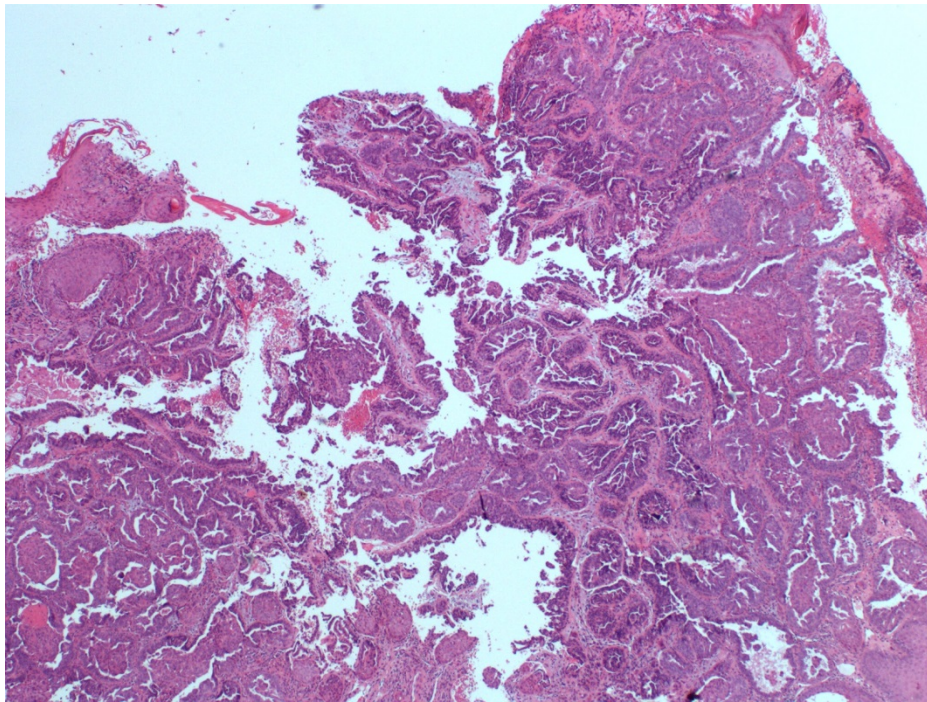


Case 24:

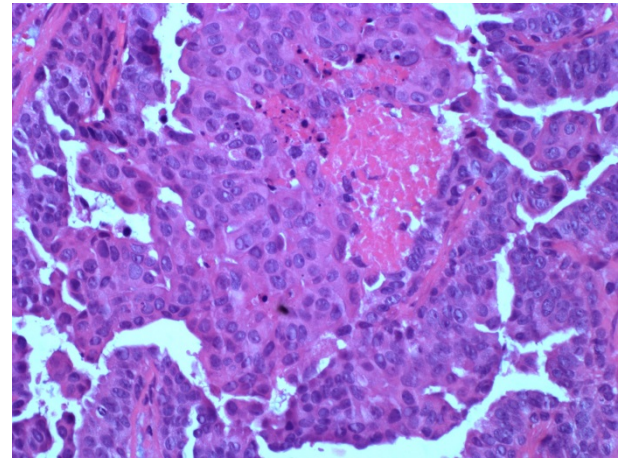
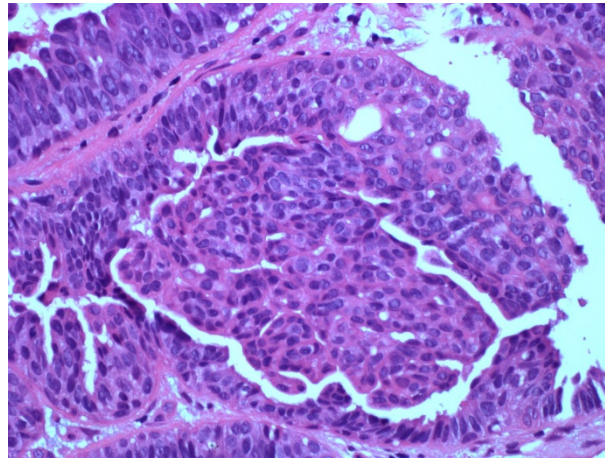
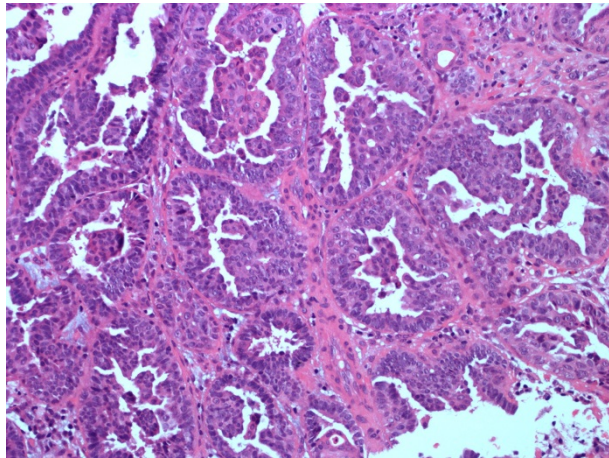
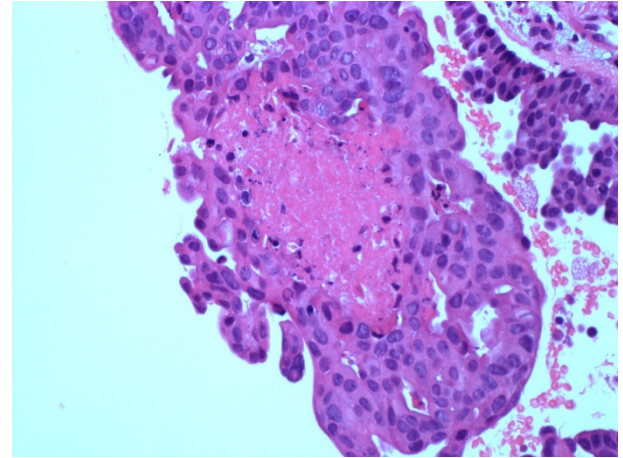
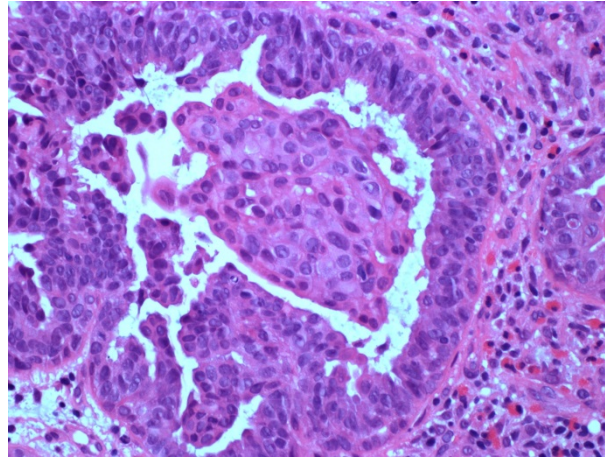
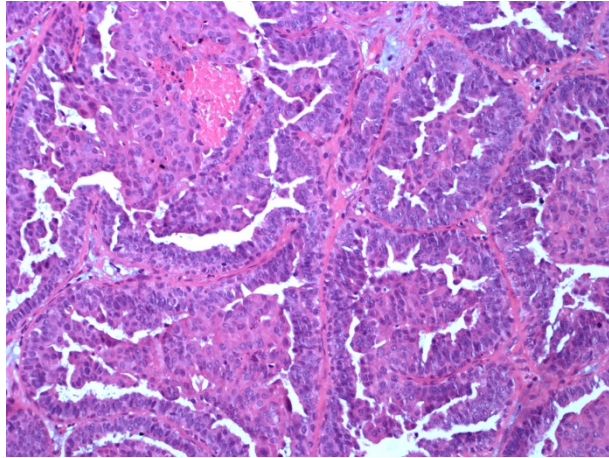
46 yo female.

Ulcerating lesion left nipple.

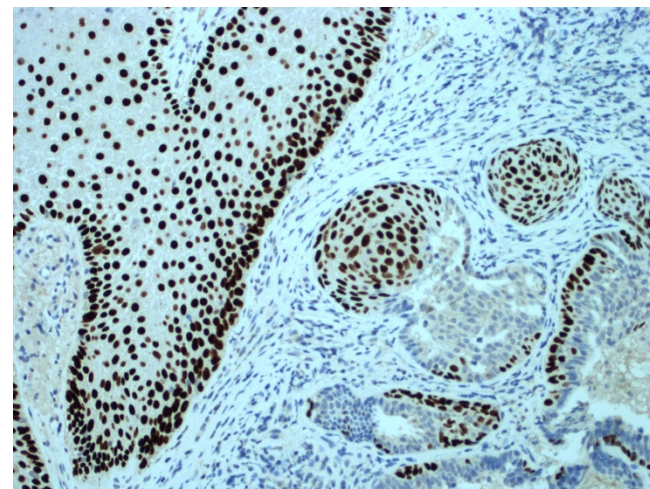
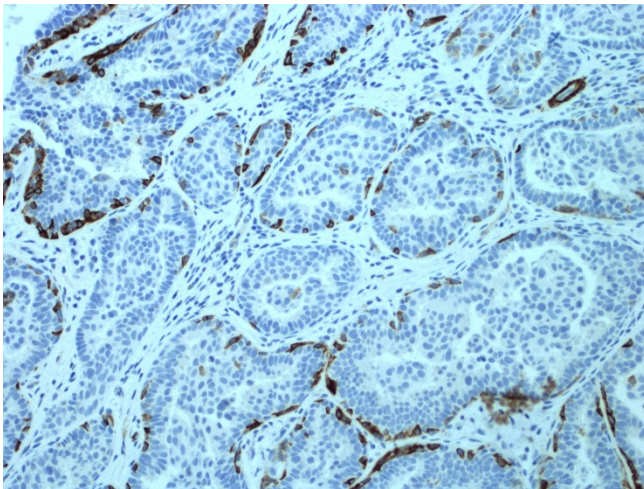
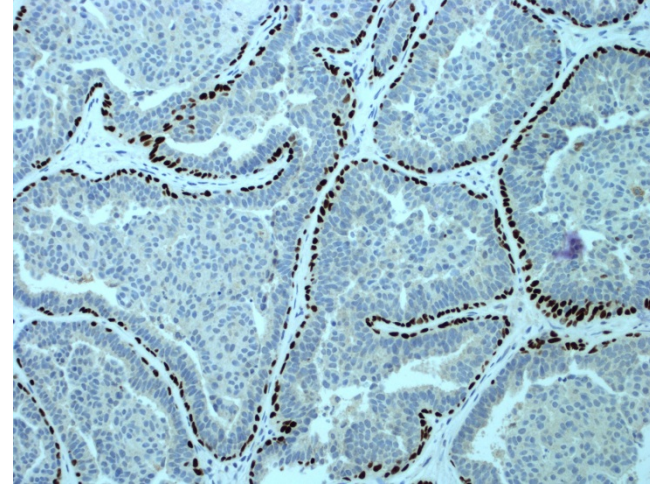
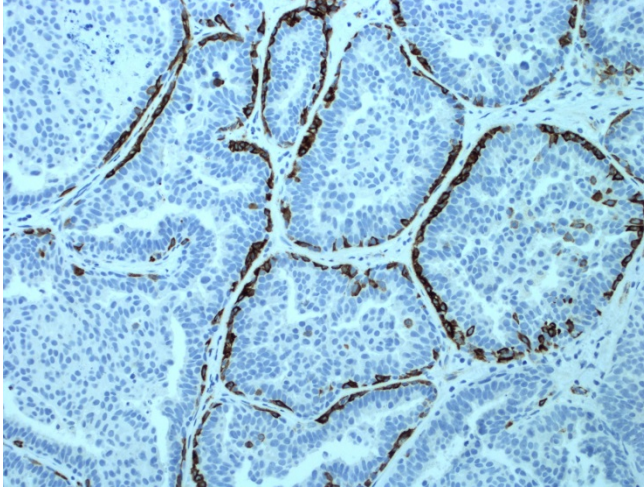
Case 24:



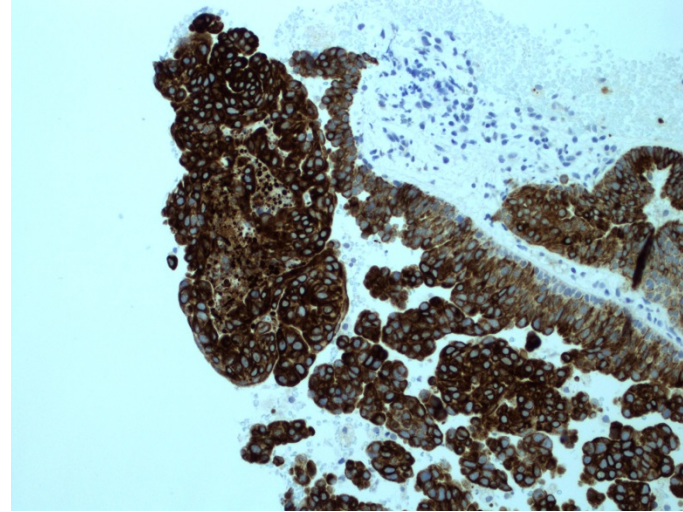
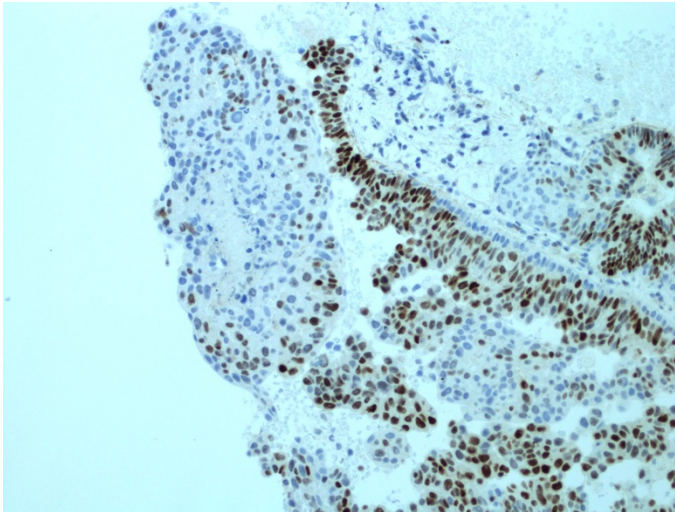
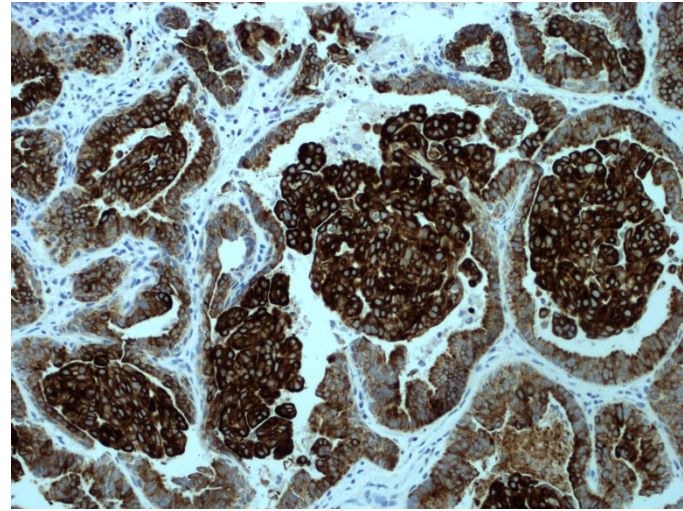
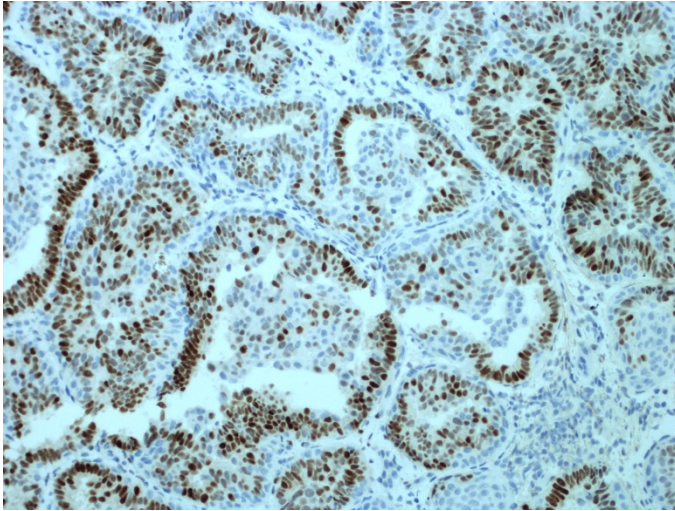
Case 24:

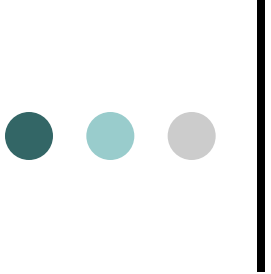


Case 24: IHC



Case 24: IHC

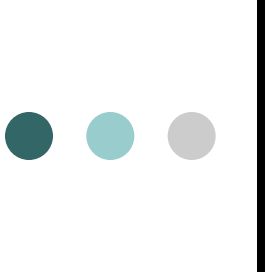




Case 24

Diagnosis:

Nipple adenoma with florid
usual type hyperplasia

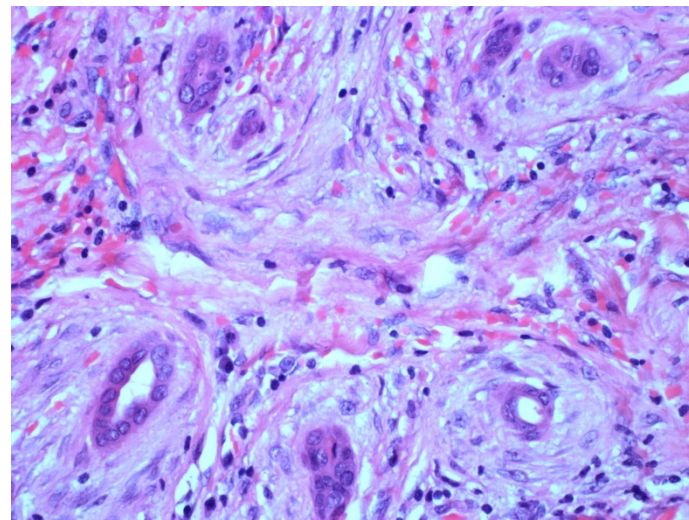
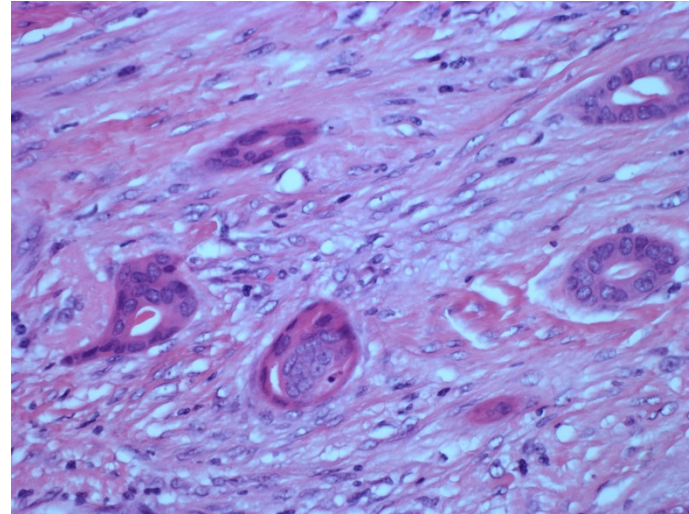
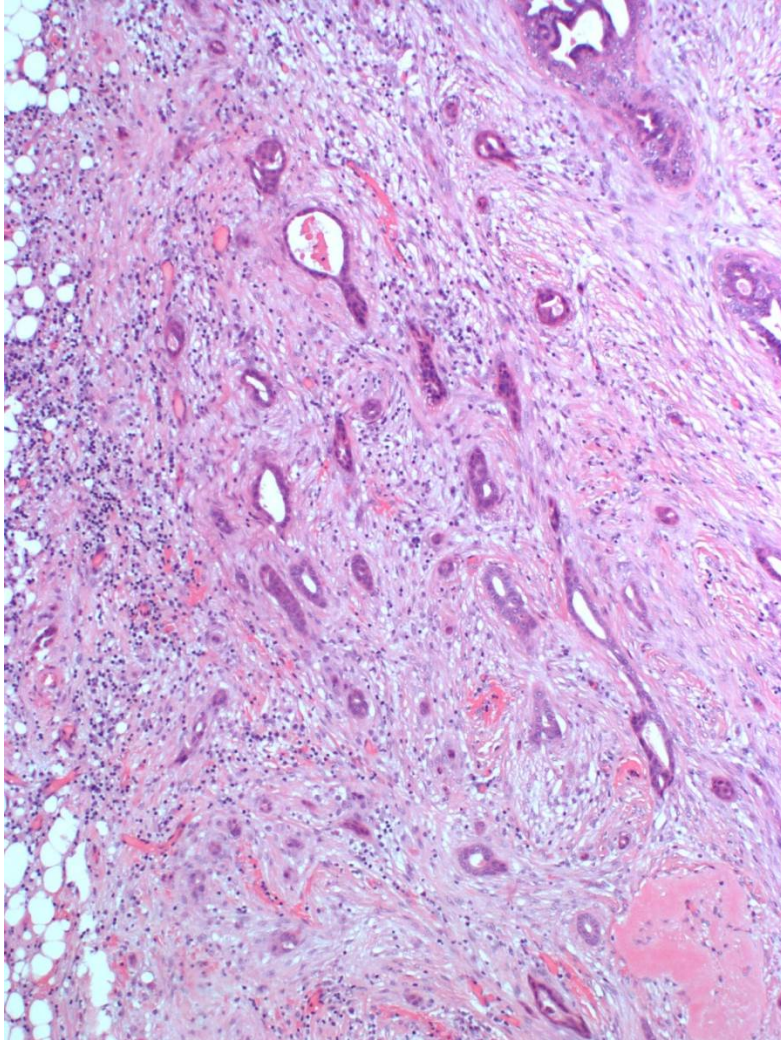


Case 25:

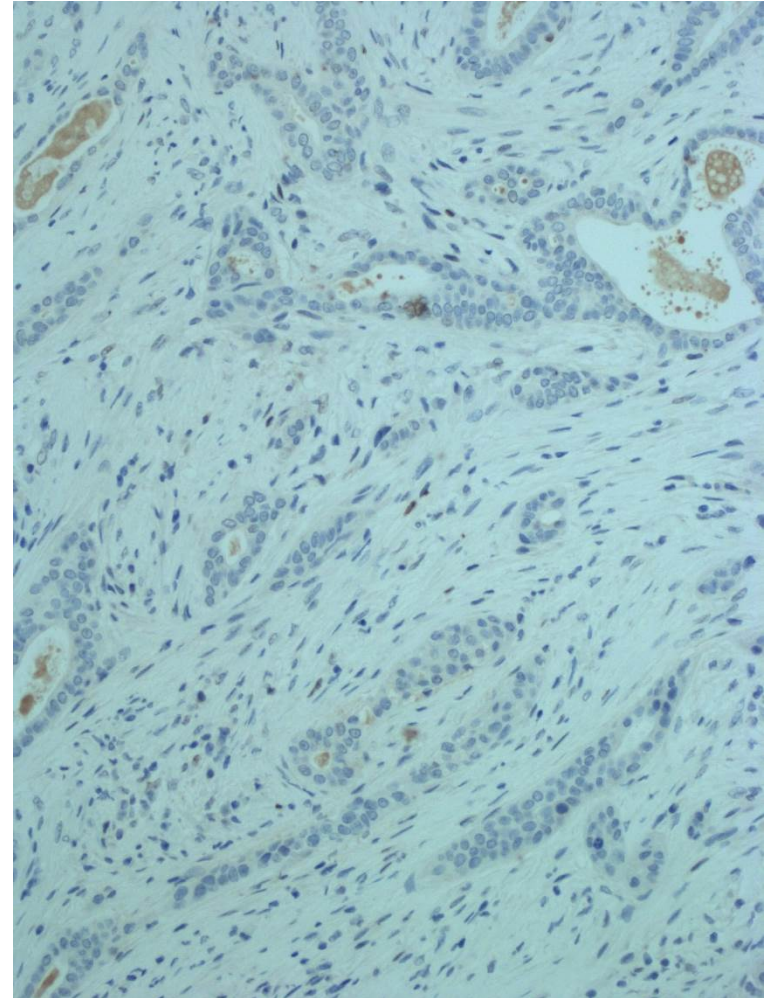
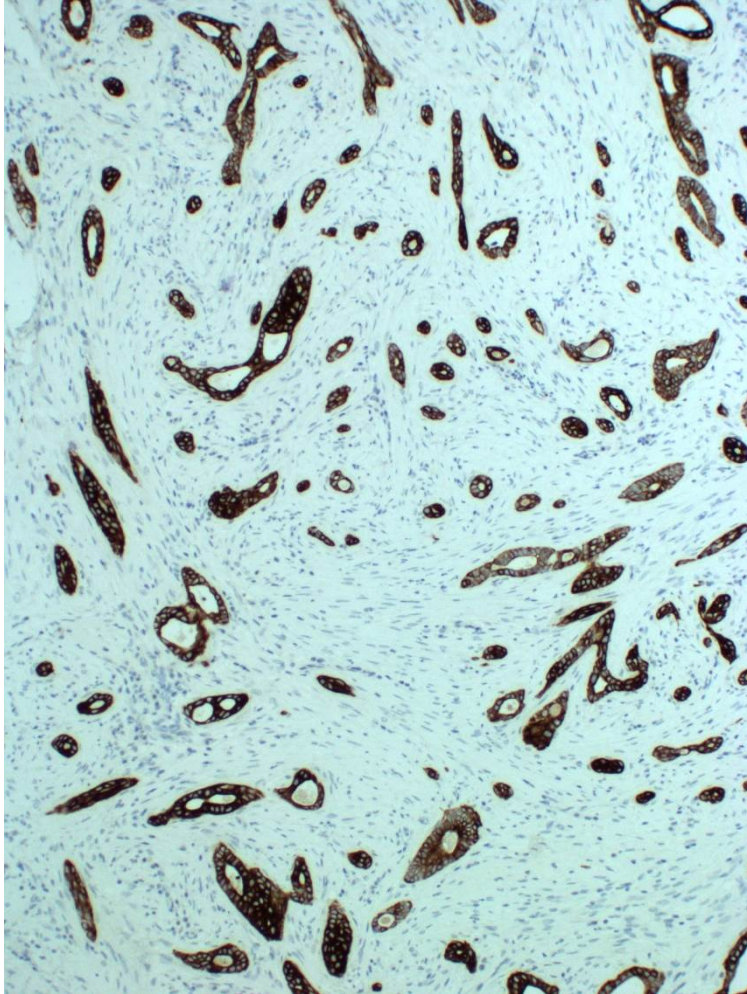
60 yo female.

Right mastectomy.

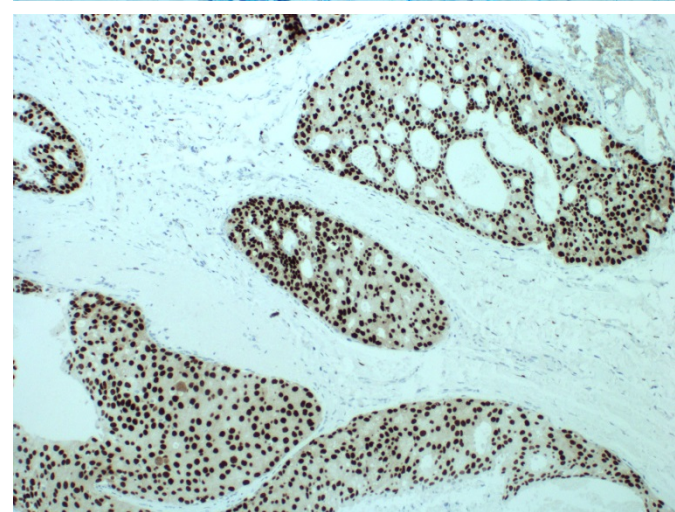
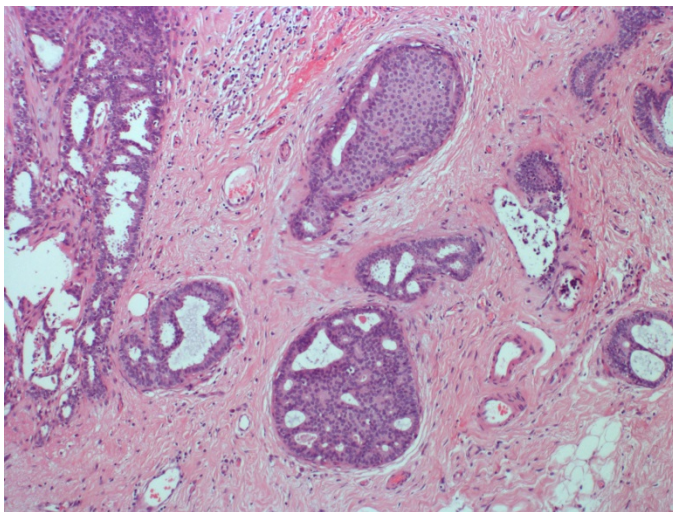
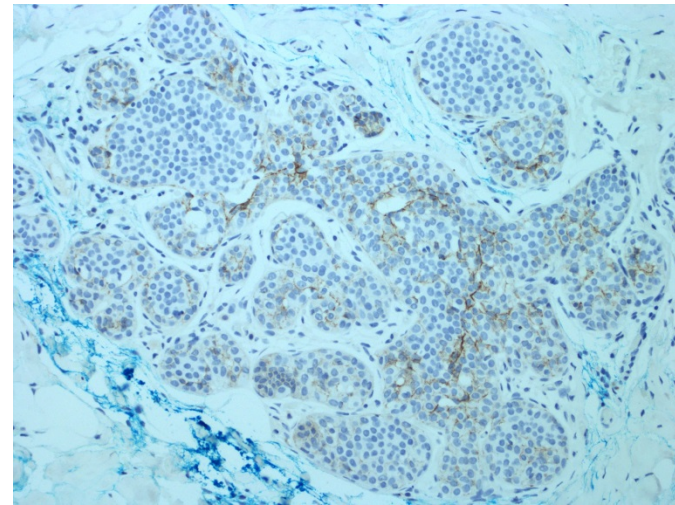
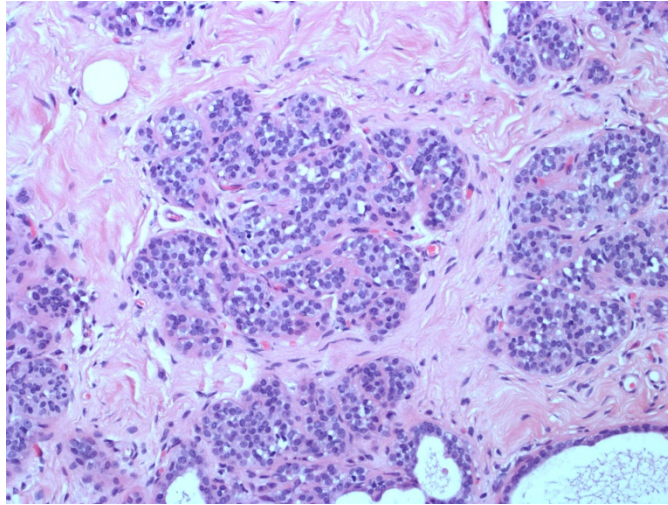
Case 25:

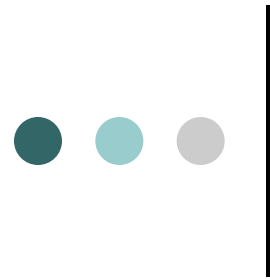


Case 25:



Case 25:





Case 25:

Diagnosis:

**Low grade adenosquamous
ca with DCIS and LCIS**