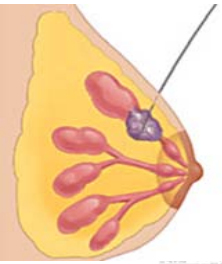


PANEL DISCUSSION

XXI ANNUAL IAP-ID CME 7TH OCTOBER 2018

MUMBAI

INTRAOPERATIVE EVALUATION OF BREAST LESIONS: WISH I KNEW THEN ,WHAT I KNOW NOW !

ANITA S. BHADURI -MODERATOR

PANELISTS:

DR R.F.CHINOY

DR SANJAY SHARMA

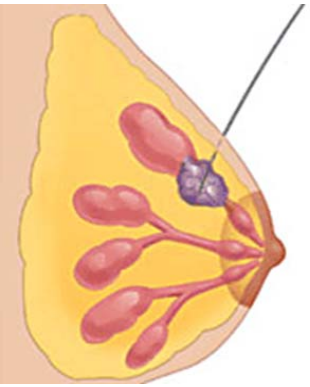
DR RUCHIKA GOEL

DR MEHBOOB BASADE

DR SHILPA LAD

INTRAOPERATIVE EVALUATION OF BREAST LESIONS : WISH I KNEW THEN , WHAT I KNOW NOW !

`` TAKEAWAY PEARLS OF WIS

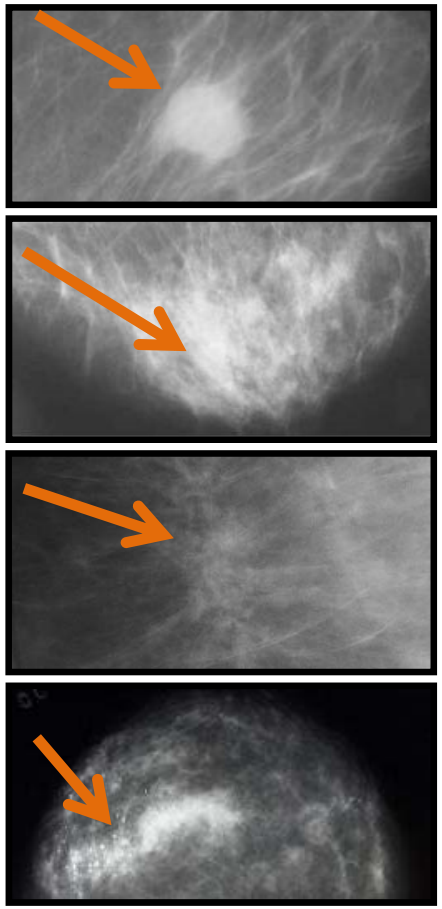


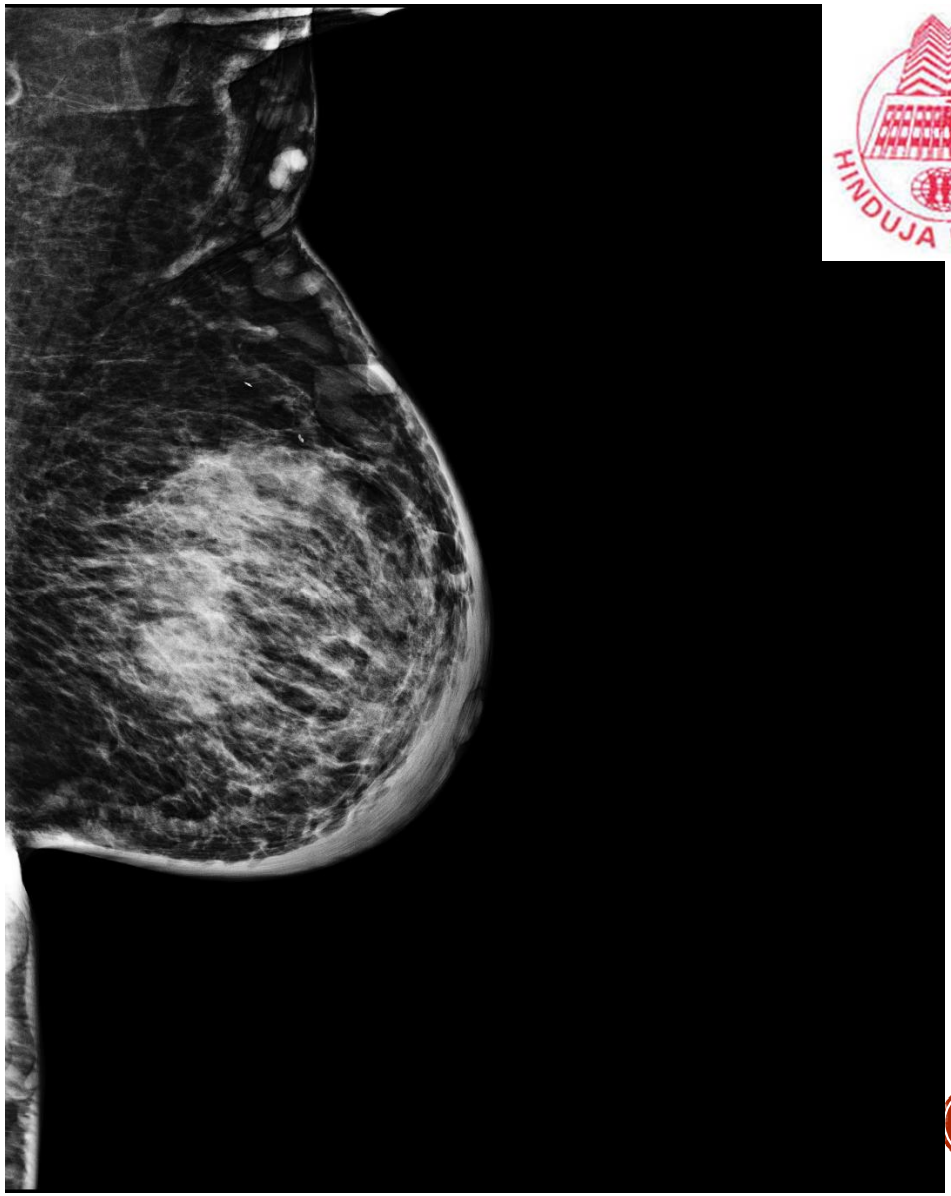
CASE 1
CLINICAL HISTORY

52 year-old-lady, 5 years post- renal transplant ,with a swelling in the left breast noticed recently. Had swelling in right breast too.

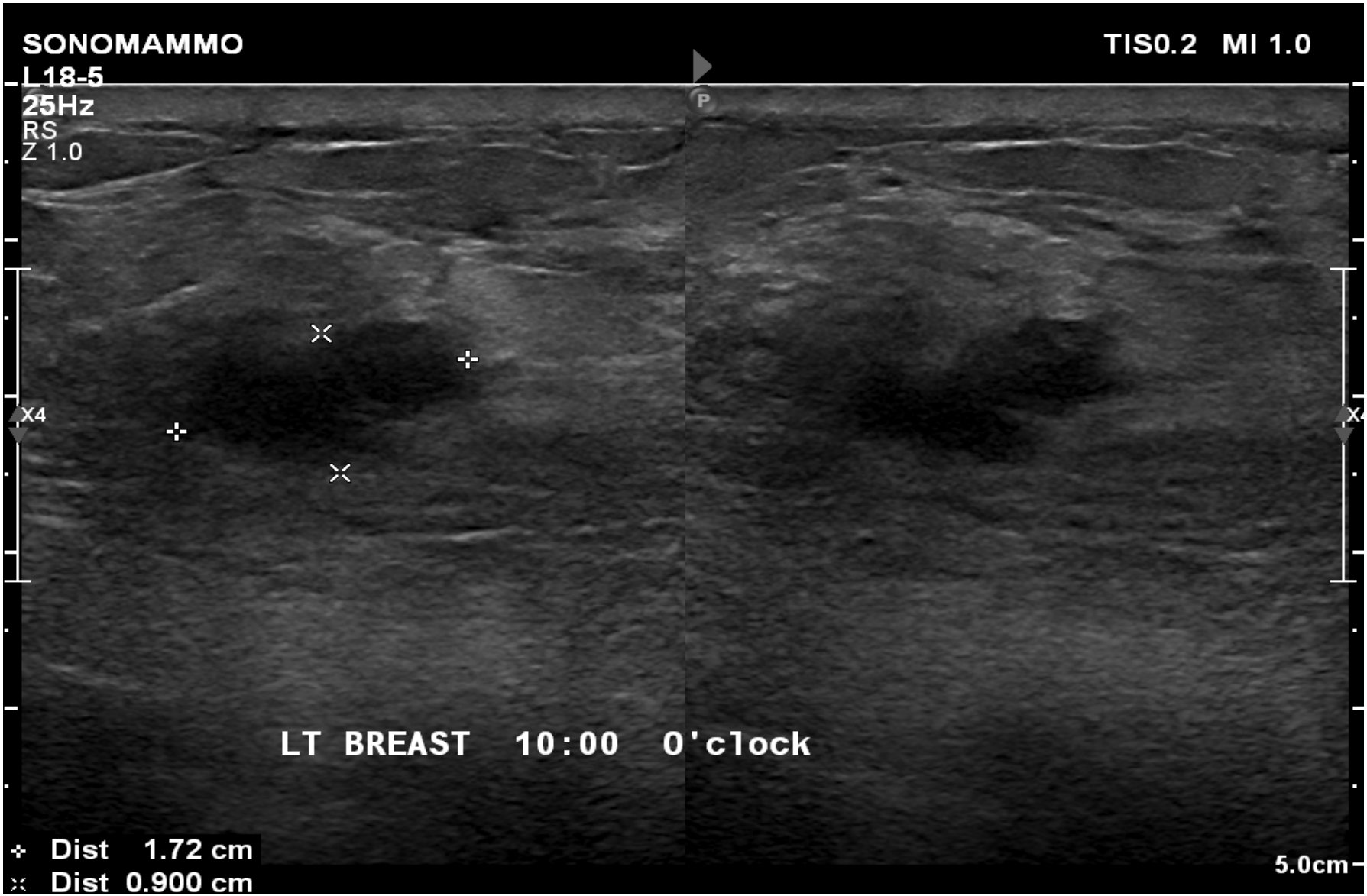
Types of mammographic abnormality

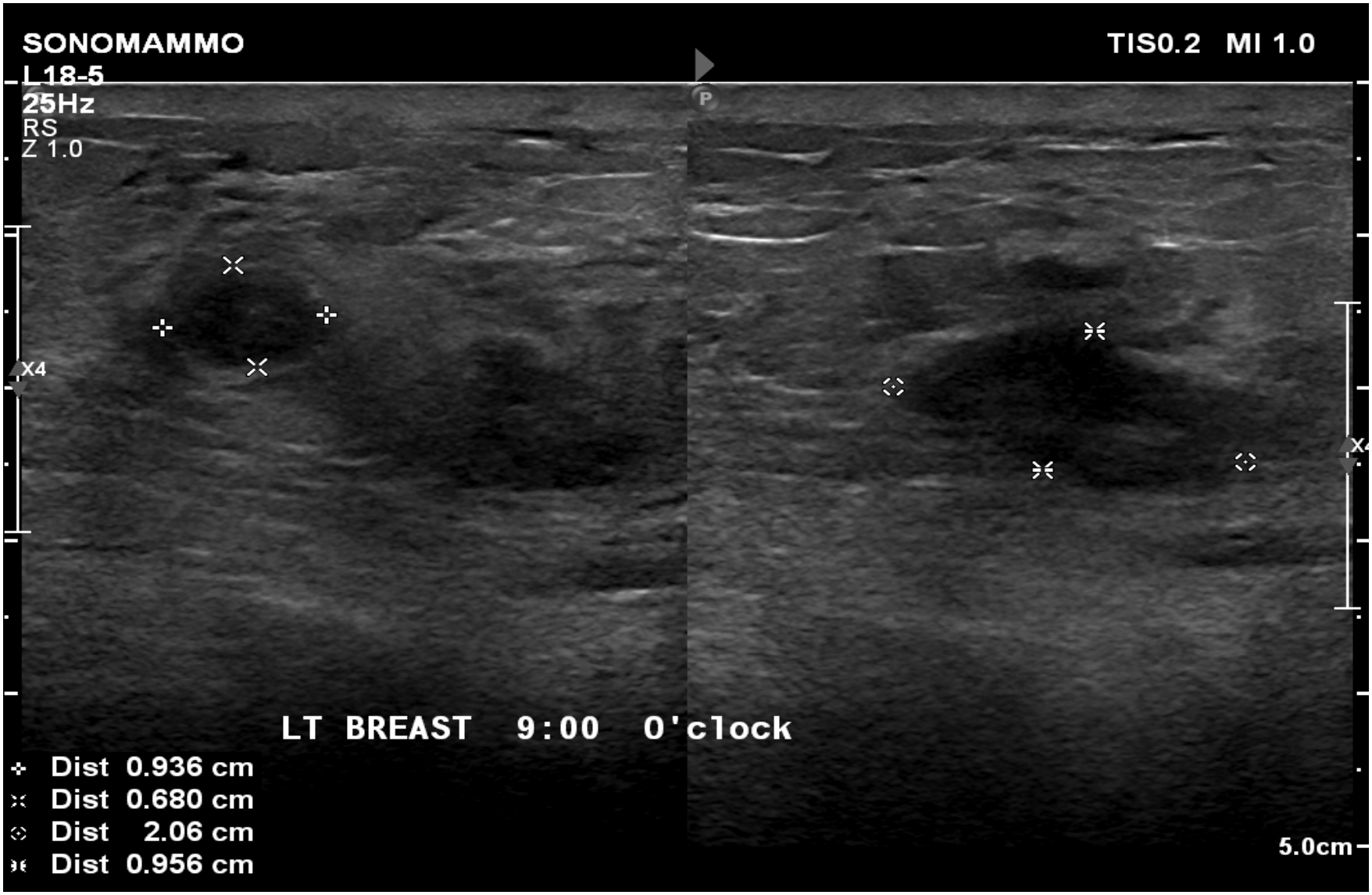
- Mass (rounded/stellate)
- Asymmetric density (ASD)
- Radial lesion
- Microcalcifications





HINDUJA HOSPITAL


SONOMAMMO
L18-5
25Hz
RS
Z 1.0
TIS0.2 MI 1.0
X4
LT BREAST 10:00 0'clock
Dist 1.72 cm
Dist 0.900 cm
5.0cm


SONOMAMMO
L18-5
25Hz
RS
Z 1.0
TIS0.2 MI 1.0
X4
LT BREAST 9:00 0'clock
Dist 0.936 cm
Dist 0.680 cm
Dist 2.06 cm
Dist 0.956 cm
5.0cm

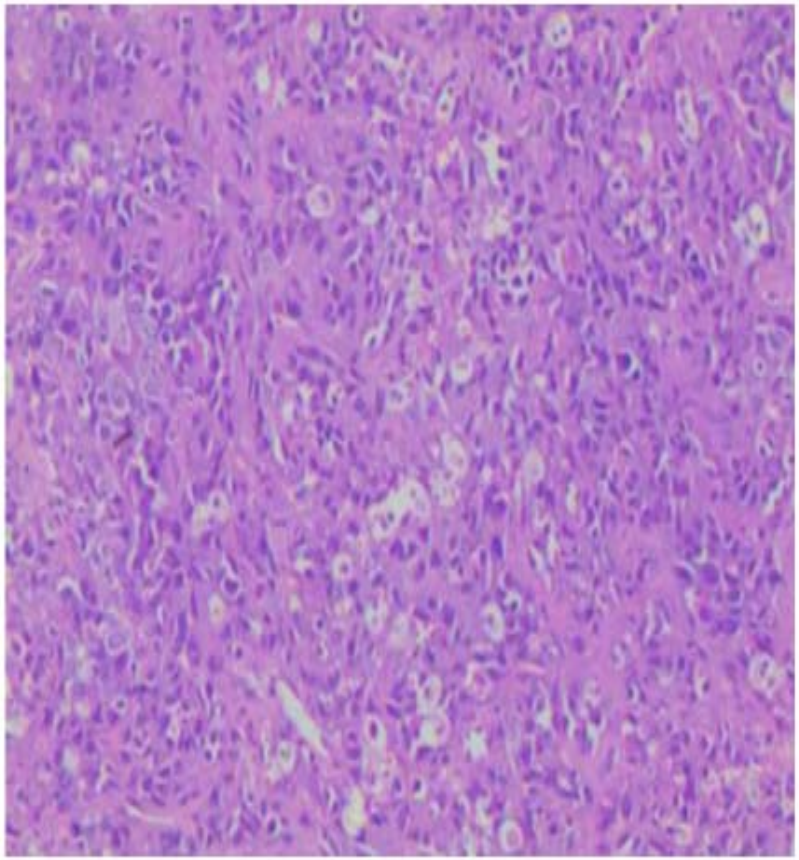
DIAGNOSIS ?? ISSUES AT HAND

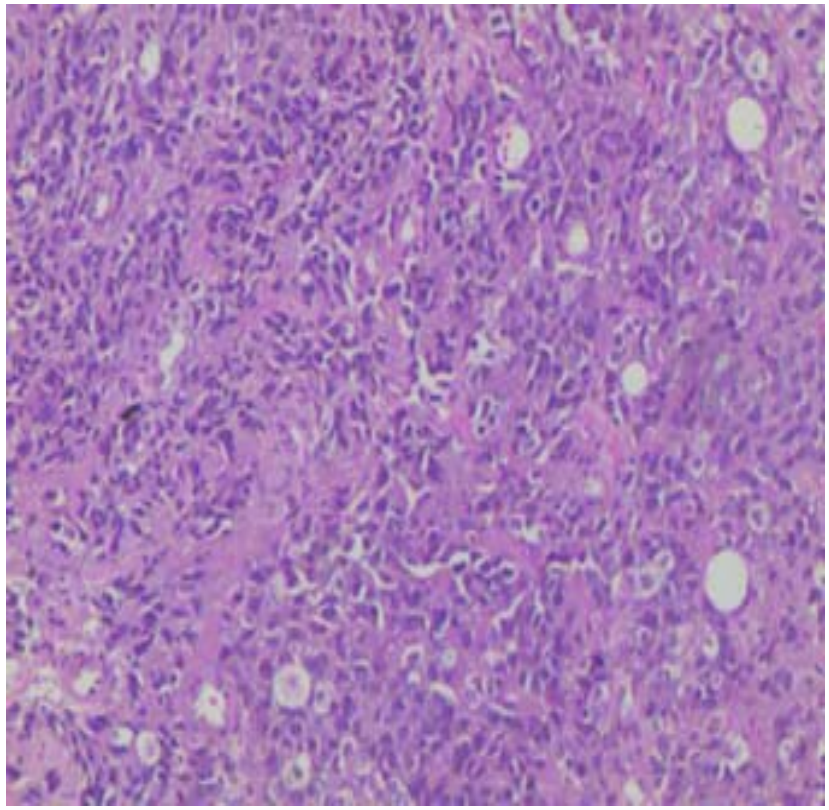
- Q1] WHAT IS THE RADIOLOGICAL OPINION ? BIRADS ?
- Q2]DO YOU WANT UPFRONT SURGERY OR CORE BIOPSY ? NACT?
- Q3]FROZEN SECTION REQUIRED?
- Q4] SLN OR ALND?
- Q5] BCS in invasive low grade T2N1 tumors, indications & contraindications

SONOMAMMO FINDINGS

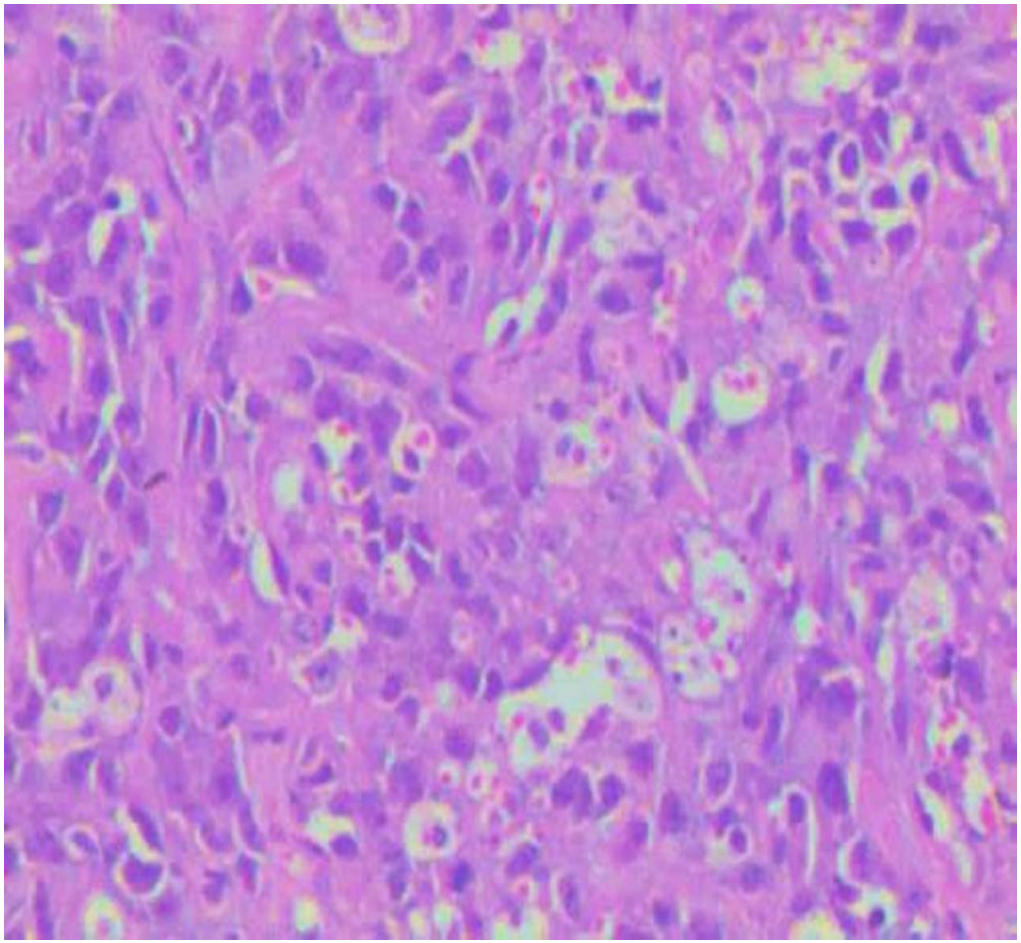
- MMG: Fibroadenoma-like lesion on right and a suspicious lesion between 9 and 10 o`clock on left.

- MMG guided core biopsy done on both lesions followed by excision



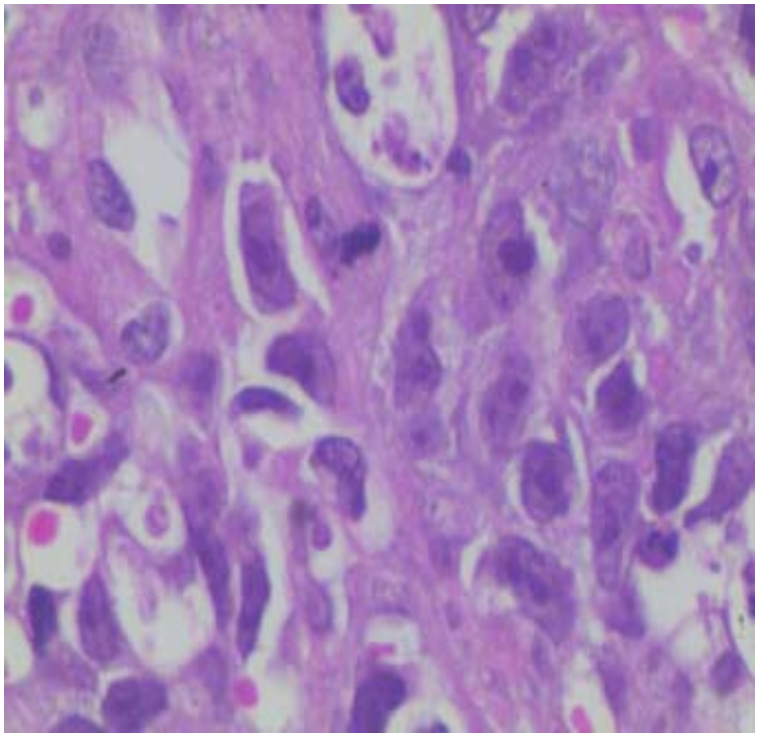


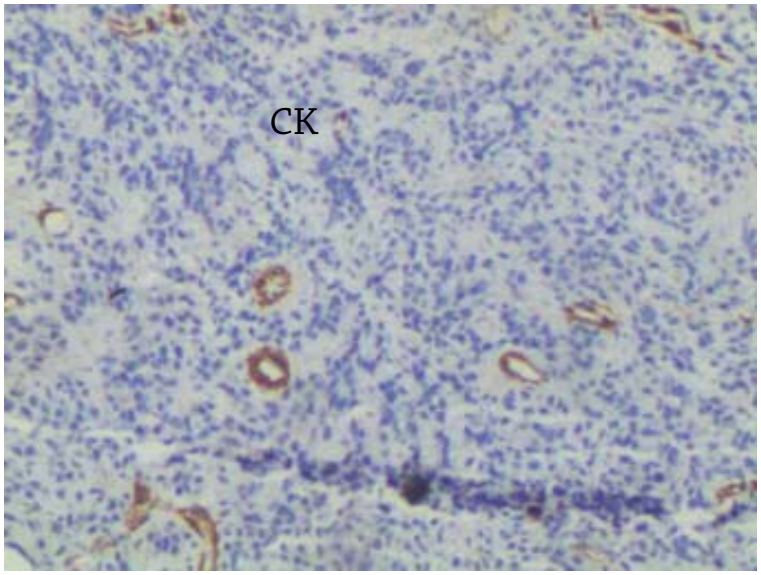
HINDUJA HOSPITAL

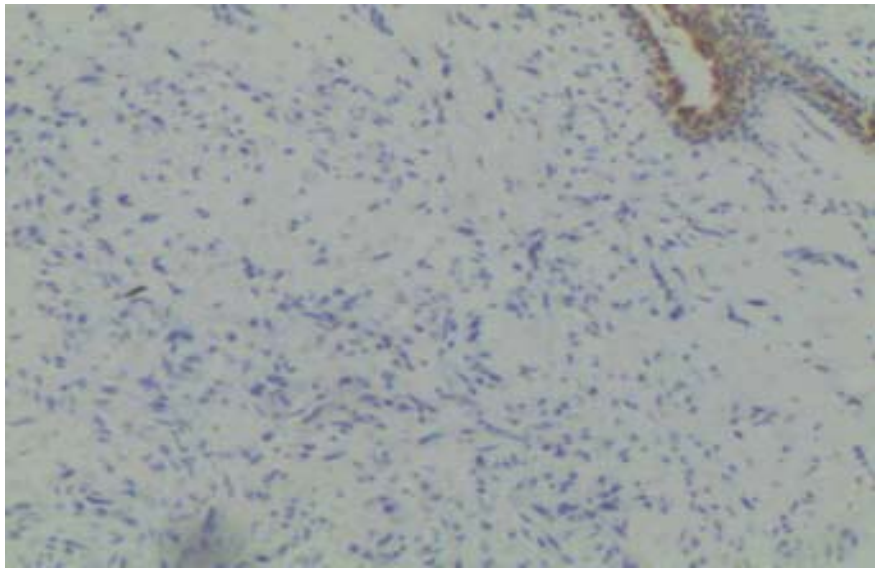


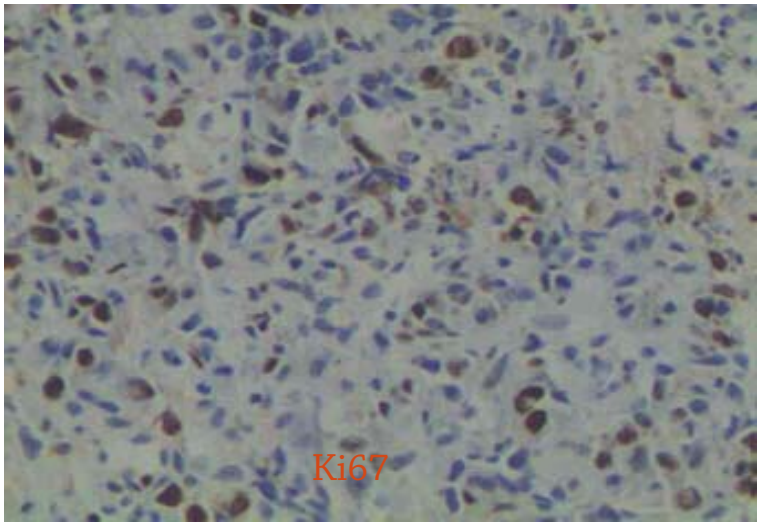
DIAGNOSIS?

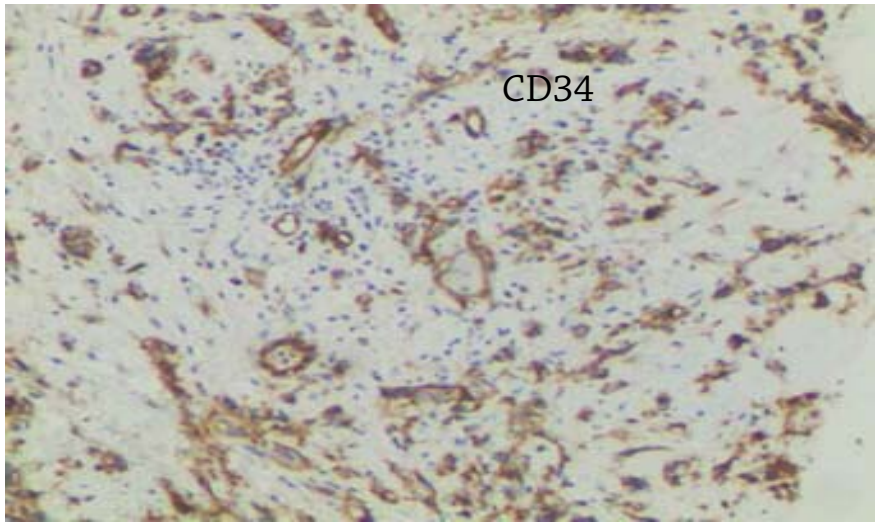
IHC ??

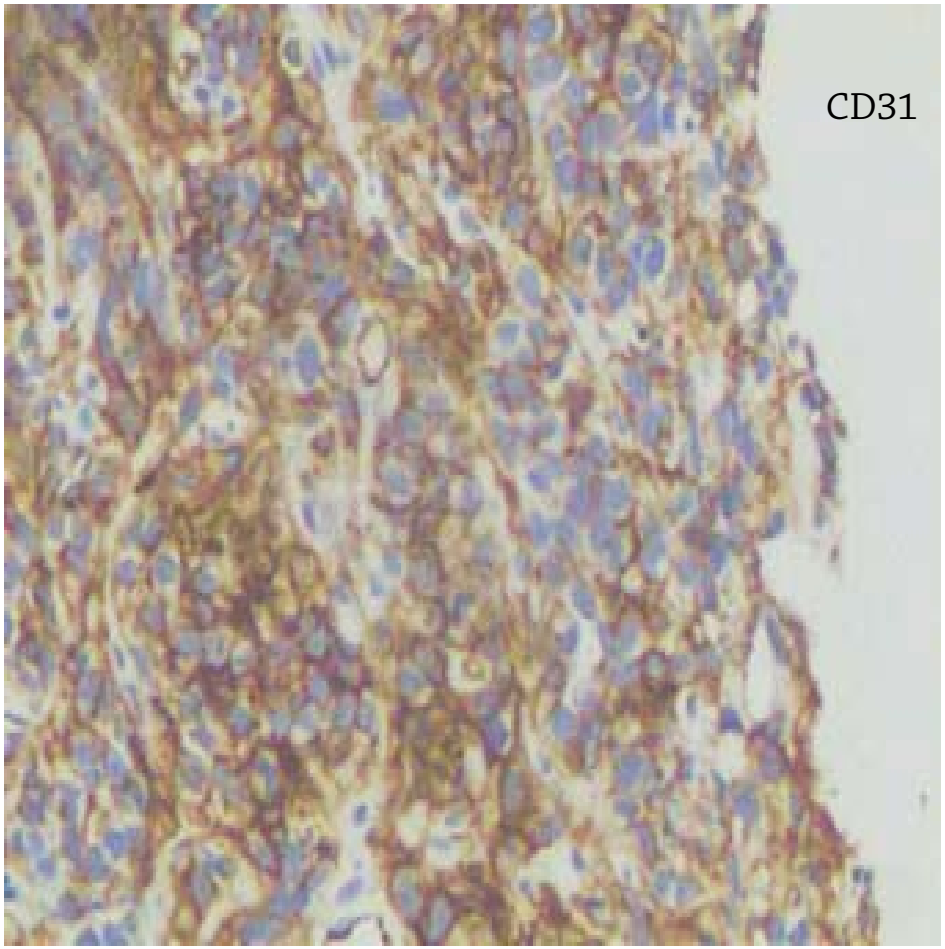


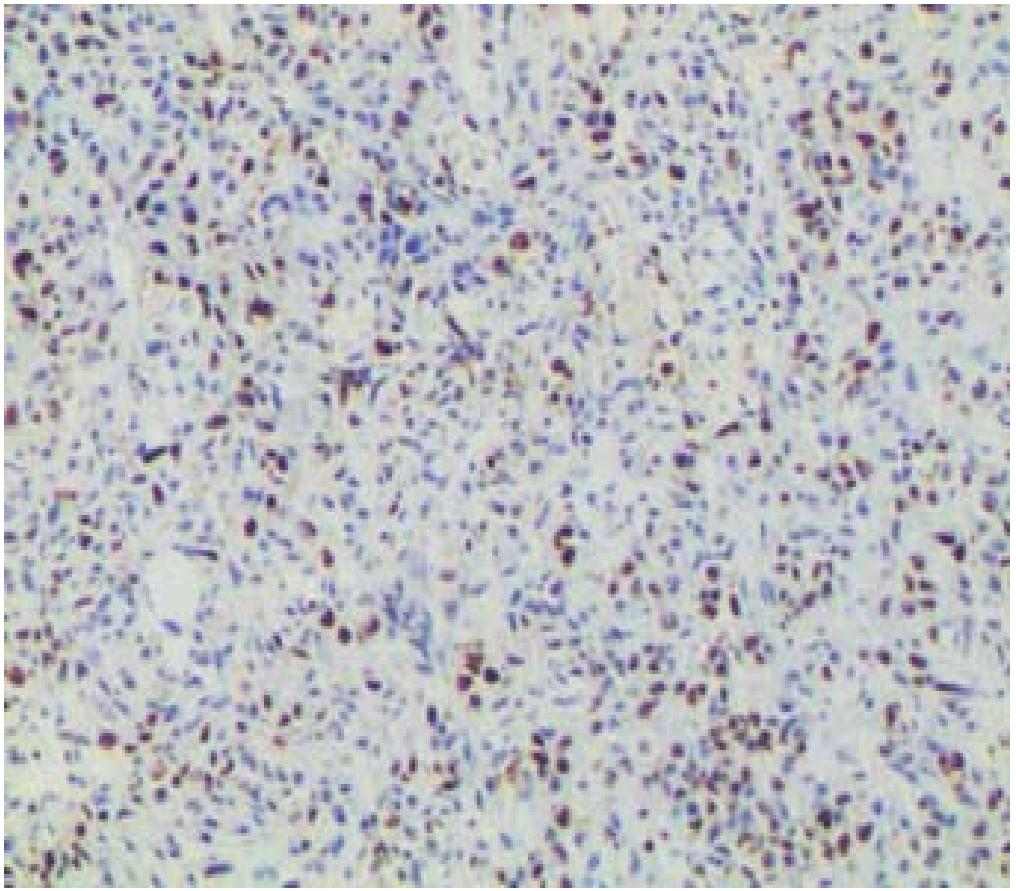

CK



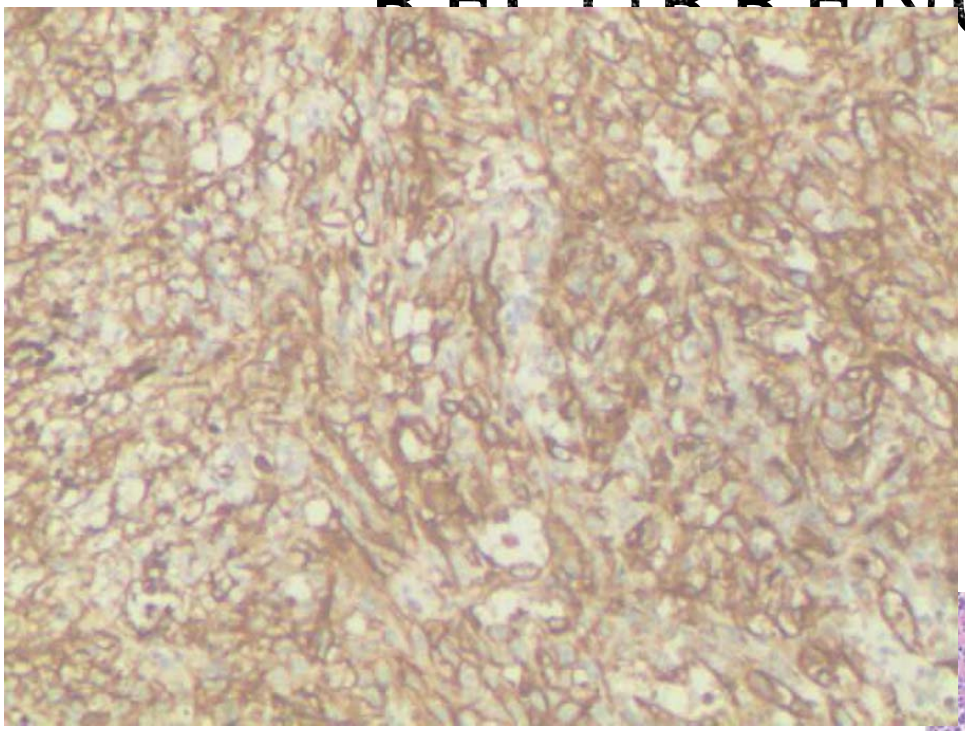

Ki67

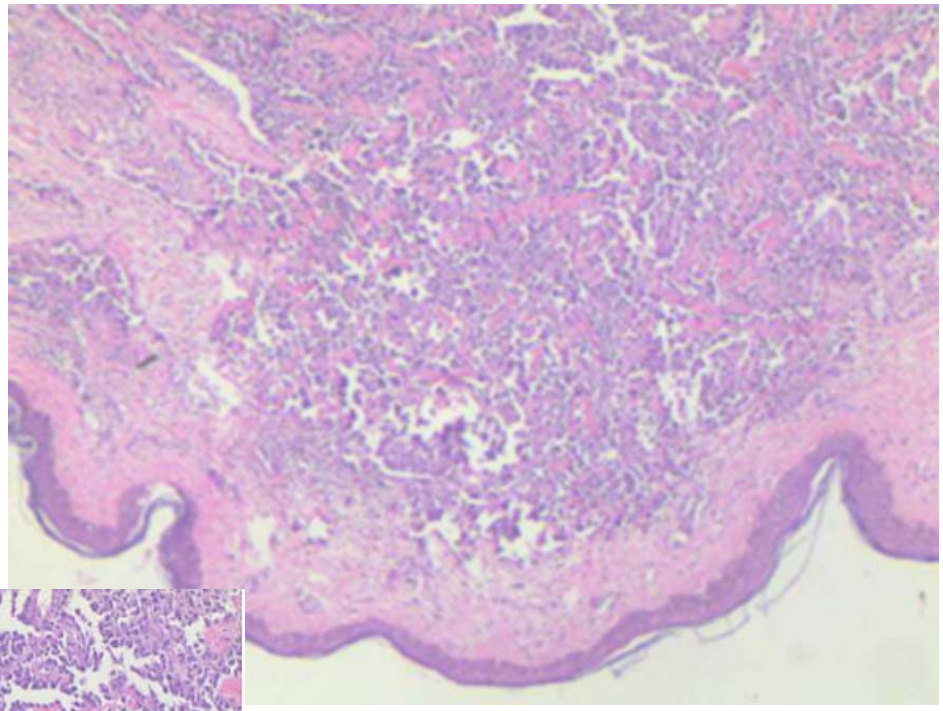

CD34

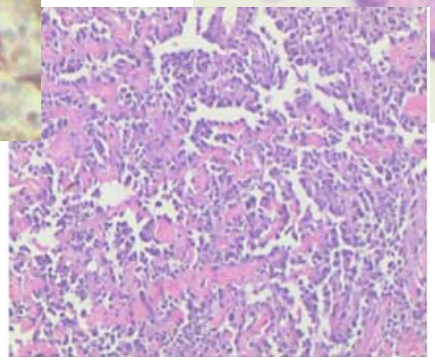

CD31



DEVELOPED A CHEST WALL RECURRENCE







ANGIOSARCOMA

- VASCULAR LESIONS OF BREAST
- IMPORTANT GUIDELINES
- Always at least consider Angiosarcoma
- Needle biopsies may be misleading and appear more worrisome
- Try to obtain decent clinical history
- location / depth / prior treatment
- Architecture / growth pattern may be more helpful than endothelial morphology
- Knowledge of lesional depth / location is critical
- Among truly intra-parenchymal lesions, Angiosarcoma is more common than haemangioma
- Low grade mammary angiosarcoma is often deceptively bland – pay attention to the growth pattern !
- Beware cellular (areas of) angiolipoma on needle biopsy !

- Special importance of nipple and areola exam?
- Margin evaluation in BCS intraop
- Intraop RT for breast cancer[IORT]
- Male breast cancer management.any different?

ISSUES AT HAND

IORT for breast cancer

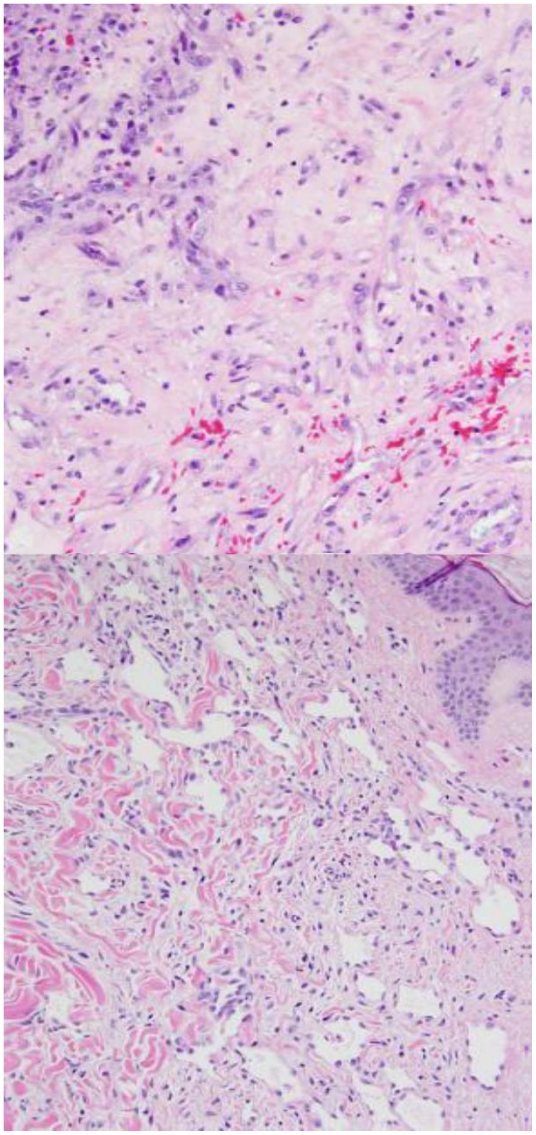
Nipple reconstruction

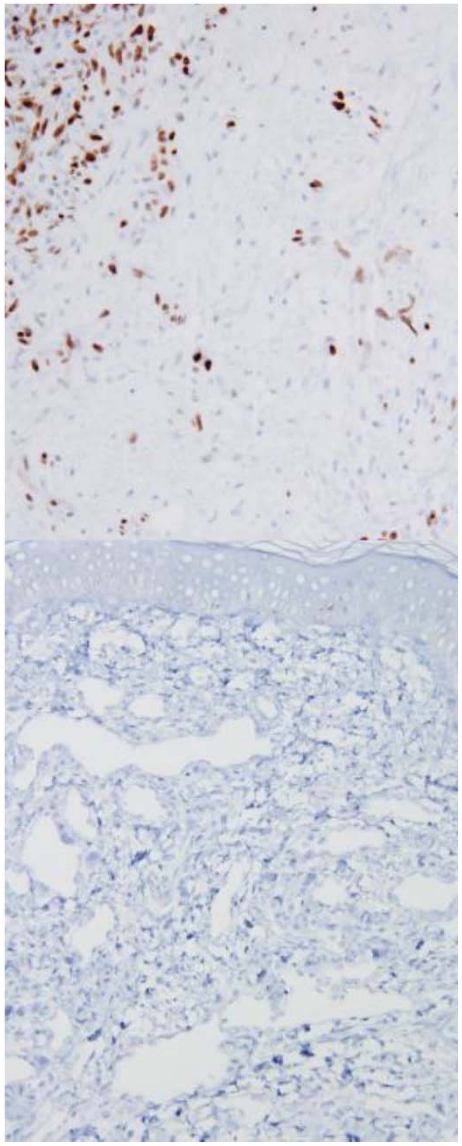
3D nipple tattoo

Fat grafting

Is management any different for male breast cancers

When not to FISH for HER2?





IHC FOR MYC HELPS DD

POST-RADIATION ANGIOSARCOMA

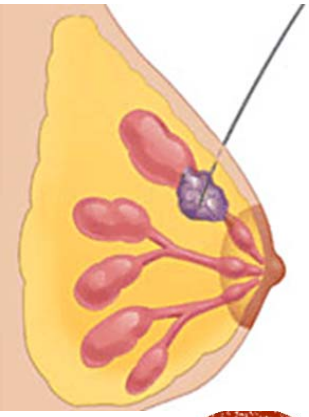
VS

ATYPICAL POST-RADIATION

VASCULAR PROLIFERATION - Morphologic (and likely biologic) continuum}

PATHOLOGY PEARLS: ANGIOSARCOMA, BRE

- 5 year survival 30-50%
- Commonest true sarcoma in the breast, **DO NOT** diagnose on frozen section
- Rule out Carcinoma and PT first by IHC for pan CK,p63,CK14,ER,PR,Her2
- Usually seen after breast conservation in next 10 years following irradiation
- Spectrum from APRVP to Angiosarcoma, Is an aggressive FIELD CHANGE DISEASE.
- IHC for MYC for d/d of Angiosarcoma(+) from APRVC(-)



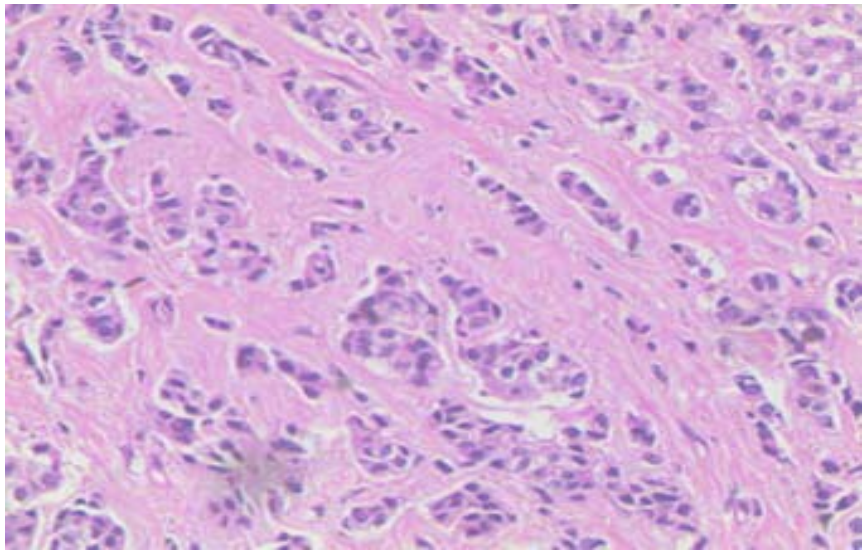
CASE 2

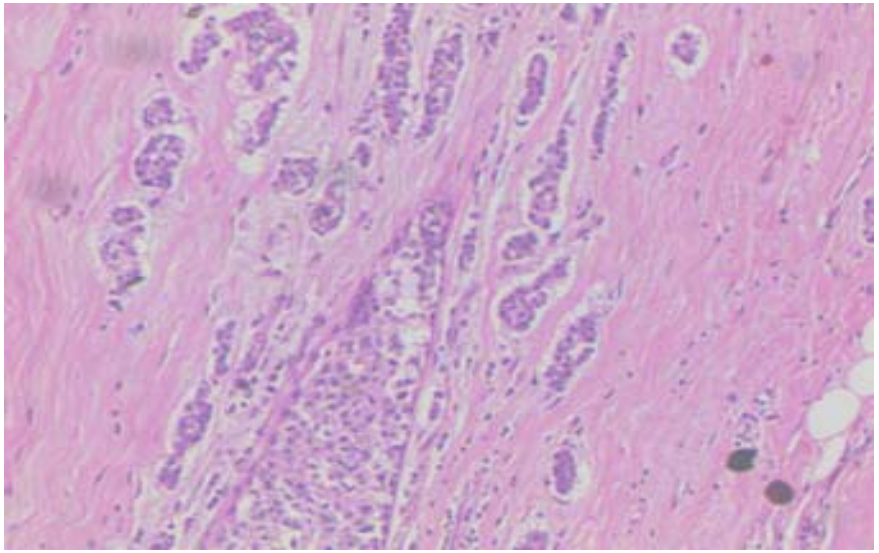
CLINICAL HISTORY

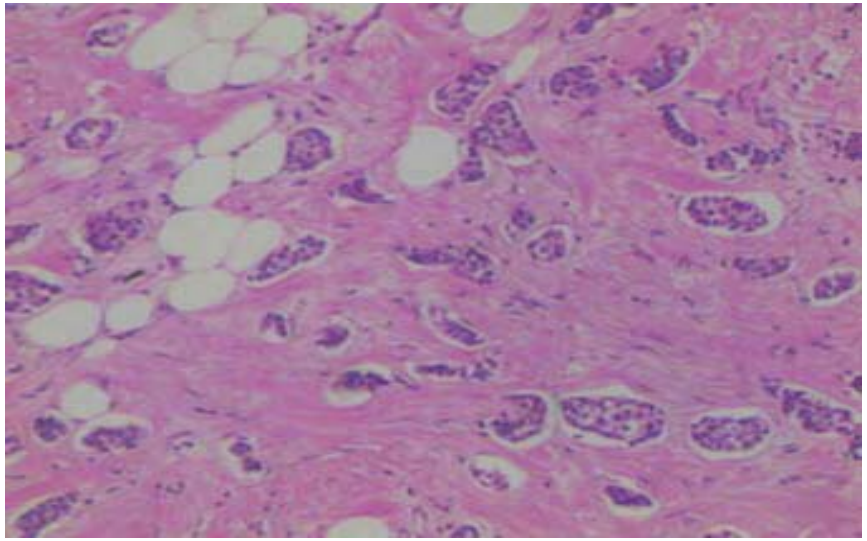
•Post NACT multisite T1 lesions in left breast in 66/F

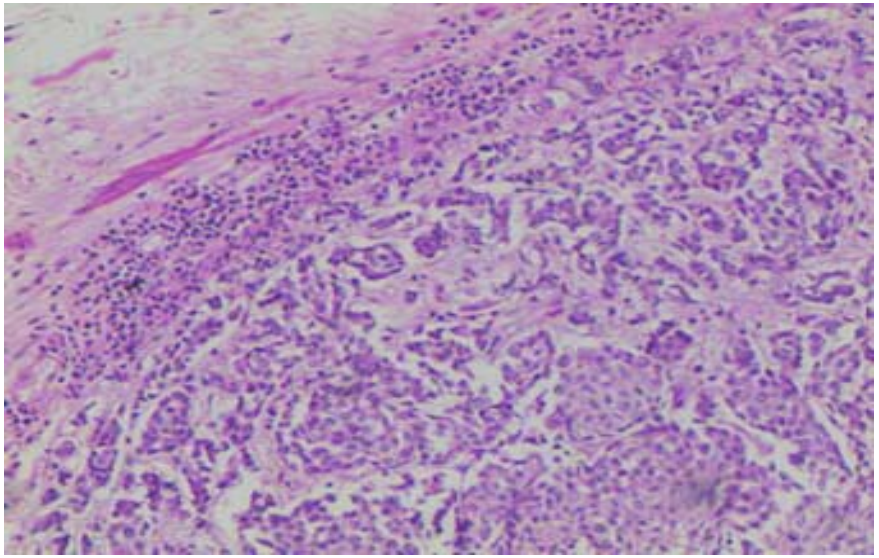
1.8cm at 2 o`clock,0.5cm at 8 o`clock, 0.7 cm at 3 o`clock,1.5cm at 4 o`clock and 1.7cm at 5 o`clock

Core bx : IDC,grade 2,ER/PR +,Her 2 neg and Ki 67 high









T SIZE IS CRITICAL IN T1 &T2 TUMORS,MULTICENTRIC TUMORS, POST NACT
CURRENTLY ADDED CAVEATS TO T SIZE ARE CELLULARITY AND T SIZE ON THE SLIDE

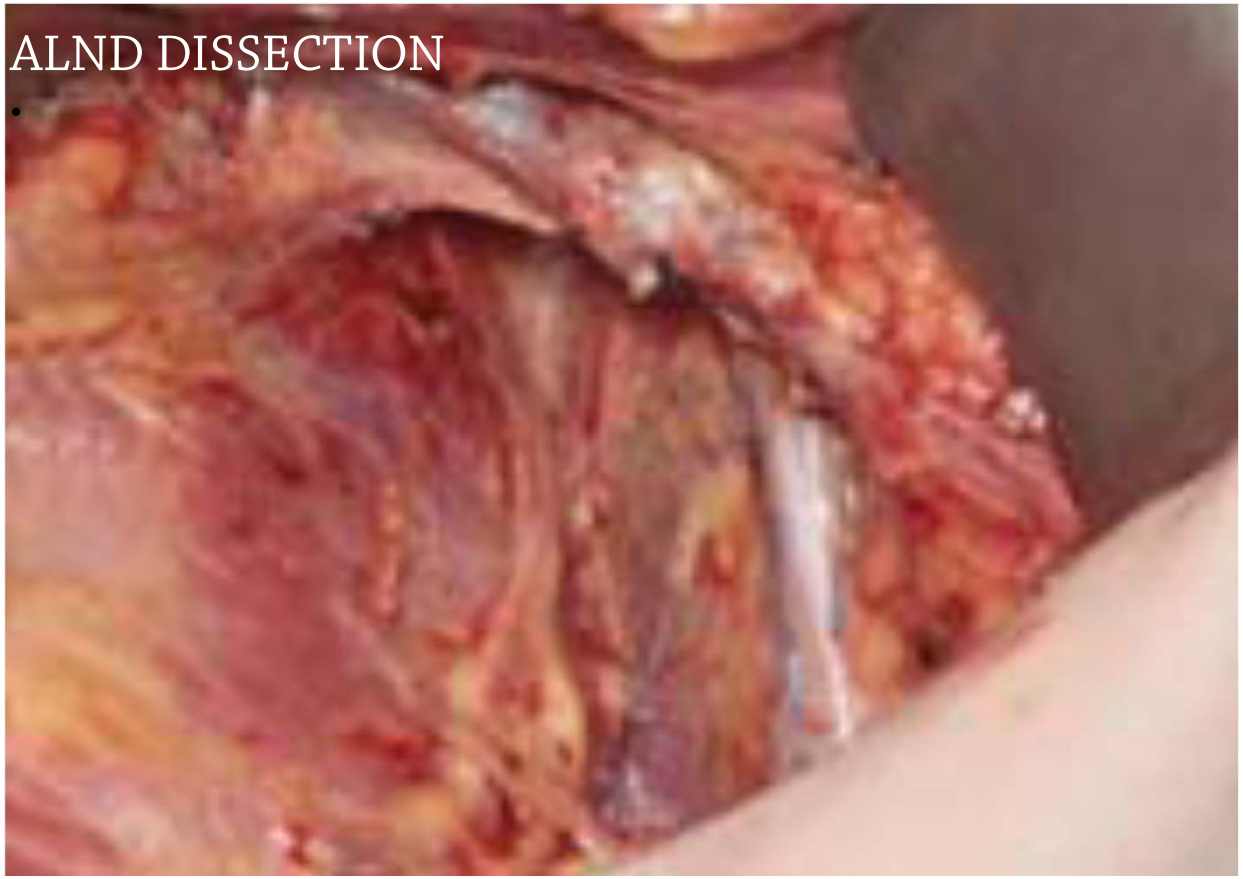
DEFINITION OF pCR post NACT ?

When to reassess biomarkers?

ISSUES AT HAND

- How do you measure the T size?
- SLND Post NACT?
- Pathologic complete remission ?
- Margins evaluation intraop?
- Emboli at the margin?
- Biomarkers? Reassess post NACT?

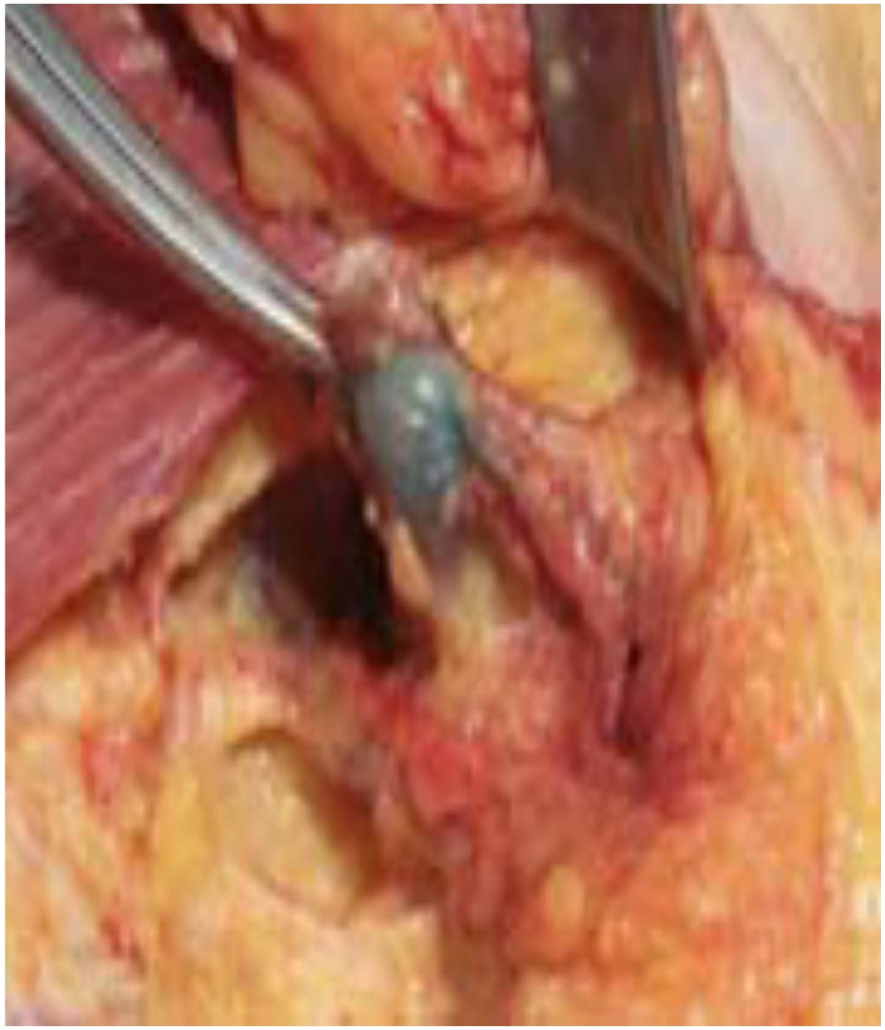
ALND DISSECTION



ALND

15-25 LN's removed

- Lymphedema ~25%
- 70-75% of pts with breast cancer are node negative



INDICATIONS

- T1 and T2 tumors
- Multicentric tumors
- Prior excisional biopsy
- Prior breast augmentation
- Larger tumors
- After neoadjuvant chemotherapy

SLN SURGERY

- Less invasive
- Lower morbidity rate
- Accuracy rate ↑
- False negative rate ↓

AT SURGERY

DAY OF SURGERY

Surgeon requests an intraoperative evaluation of the node [SLN]

Five blue SLNs were removed - all negative on frozen section

- ACOSOG Z0011, IBCSG 23–01, and AMAROS trials have shown that early-stage breast cancer patients who have limited metastatic involvement of the SLNs do not benefit from completion axillary dissections.
- It is not necessary for pathologists to search for all small metastases to predict non-SLN involvement, regional recurrence, or death due to disease.
- Processing should be designed with the goal of detecting **macrometastases**[>2mm]
- Multiple levels, routine immunohistochemistry, and molecular testing are not recommended
- "These results support the clinical practice of omitting axillary dissection when disease burden in the sentinel nodes is moderate,"[*International Breast Cancer Study Group (IBCSG) 2301trial]Lancet Oncol. Published online September 5, September 5, 2018..*

ISSUES AT HAND

SLND vs ALND

Handling

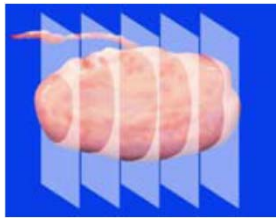
H&E vs IHC

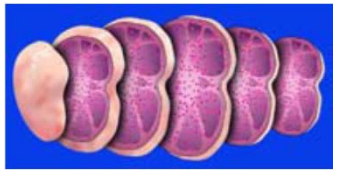
Types of involvement

Biomarkers

Cold ischemia time

HANDLING THE SENTINEL NO

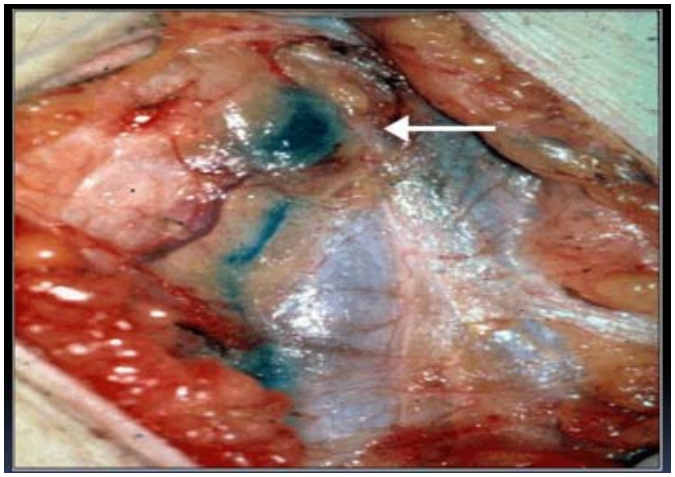


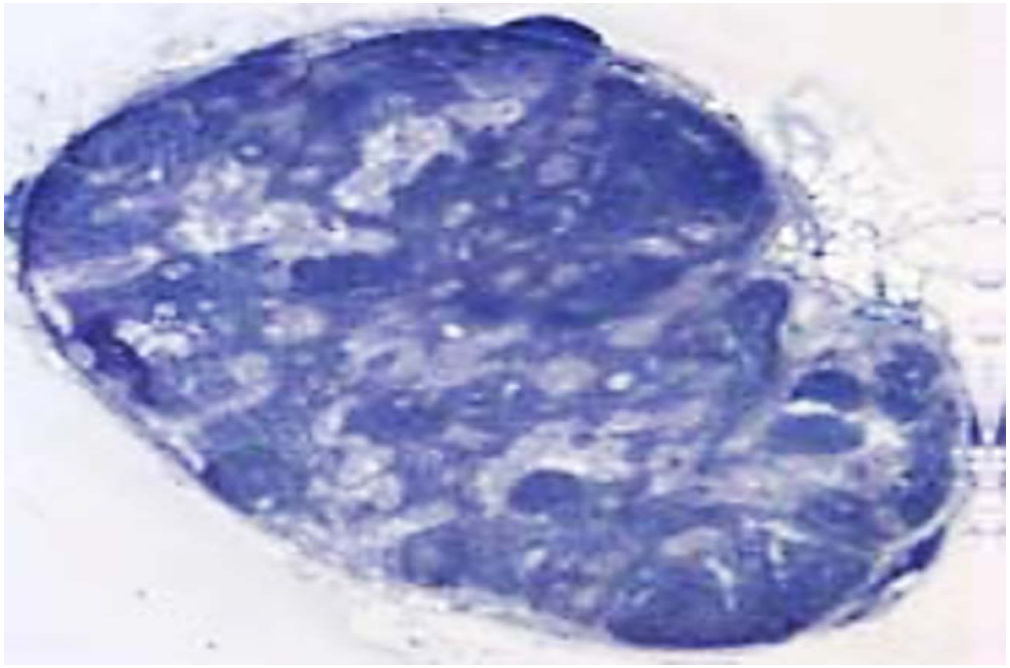


Imprint cytology
"touch prep"

- Frozen section

- GeneSearch™ BLN assay





FROZEN SECTION SN

FALSE NEGATIVE RATE

- Cytology "touch" imprint

36% (range 0 – 71%)

- Frozen section

H&E 25% (range 14 - 28%)

IHC

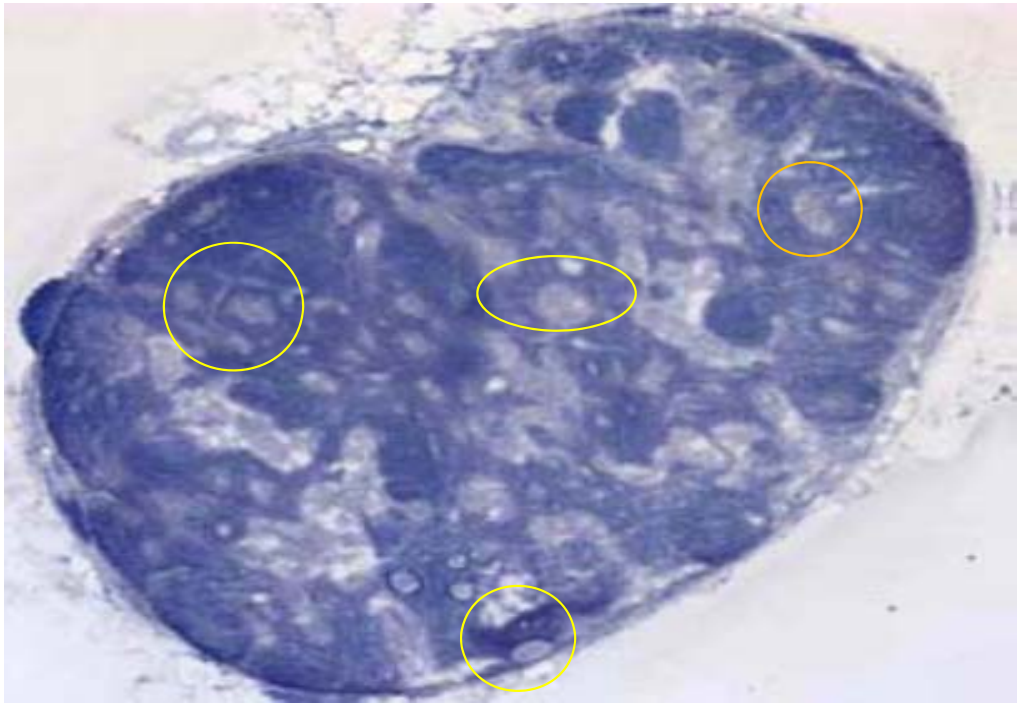
CK 37% (range 28 – 52%)

- Frozen serial sections

Two studies, both reported 0%

- WHAT DO YOU DO WITH MULTIPLE TUMOR DEPOSITS IN THE SENTINEL LYMPH NODE?

E.G.
0.3 mm
0.6 mm
0.6 mm
1.0 mm



AJCC STAGING

AJCC pN1mi

ITCs

Micromets and mets

SUMMARY

• Evaluation of the SLN should be based on clinical evidence and standardized

• Entire SLN submitted for examination

• When metastasis detected, the largest contiguous dimension should be used for
nodal staging classification

CAP RECOMMENDATIONS

- SLN sectioned (2mm) and entirely submitted
- One H&E from each lymph node block
- Routine keratin IHC NOT recommended
- Intra-operative assessment

Gross examination with imprint cytology, if needed.

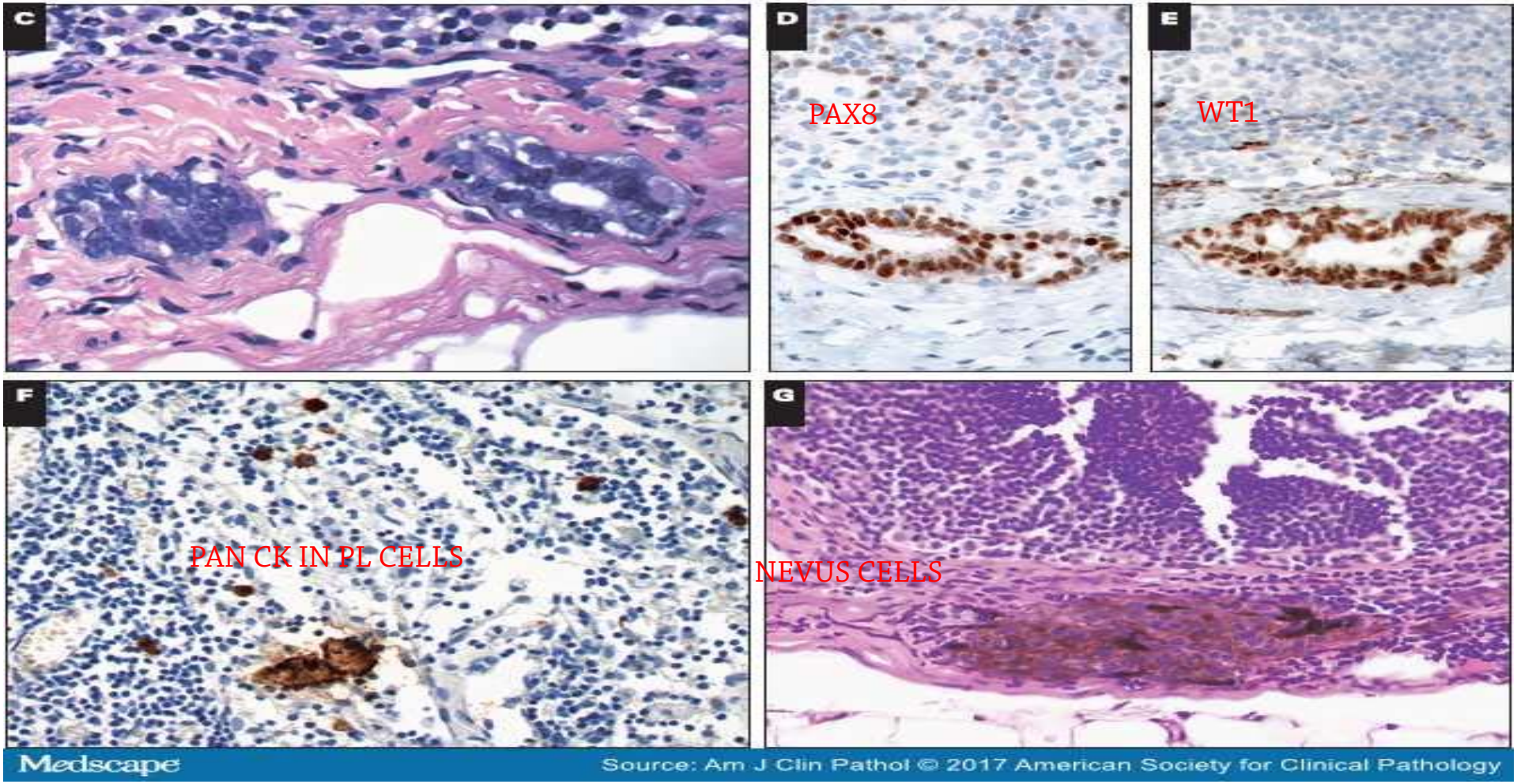
Arch Pathol Lab Med. 2009;133:1515–2009;133:1515–1538.

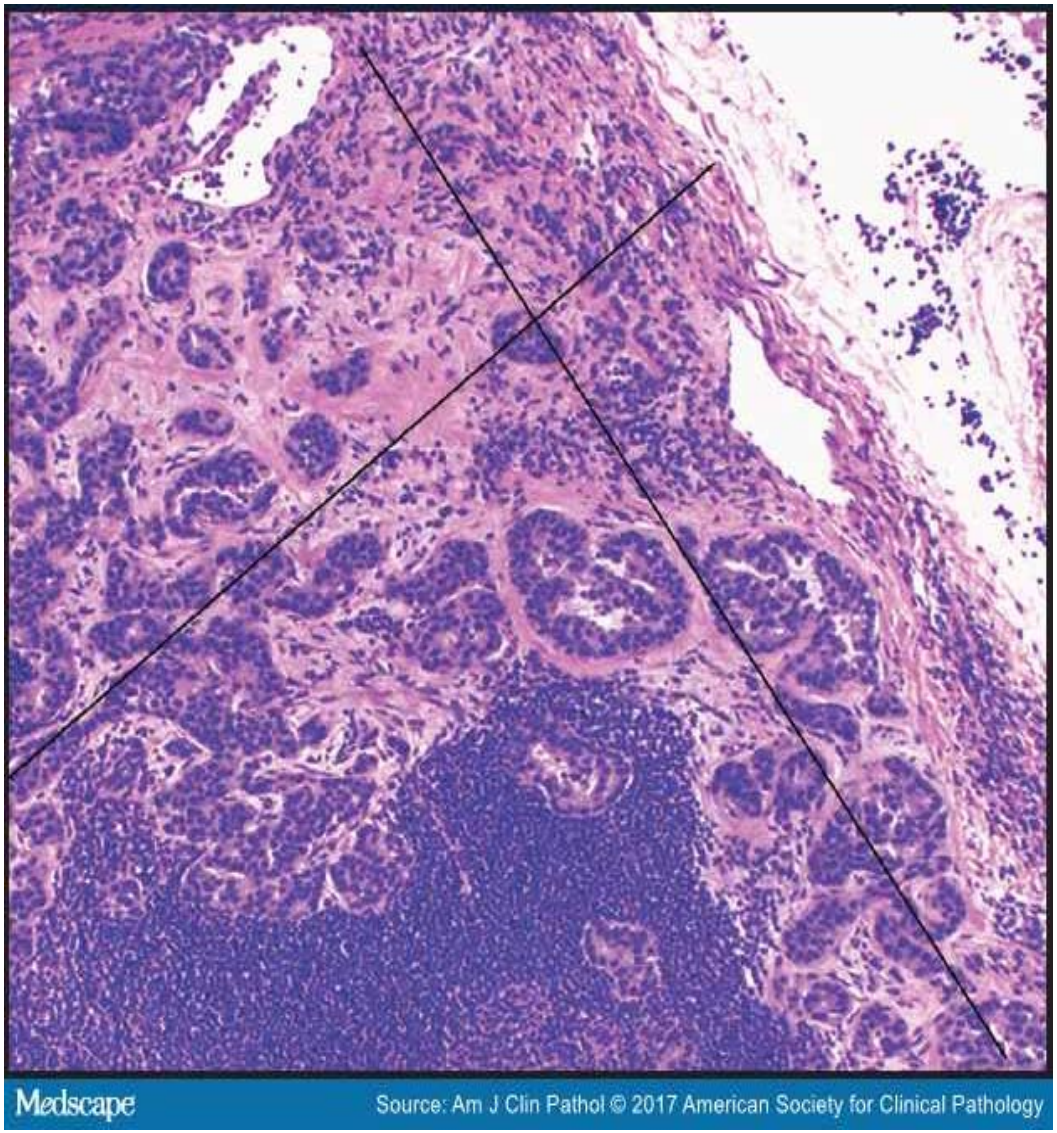
ADASP RECOMMENDATIONS

- Frozen section/imprint cytology appropriate
- More than 1 section, ? number
- Use of CK-IHC unclear
- If metastases are identified by CK-IHC ONLY, state in pathology report.

Mod Pathol. 2001;14:629–632.

PITFALLS IN DIAGNOSIS OF SLN METS AT FROZEN





The recent ACOSOG Z1071 trial[JAMA. 2013;310:1455–1461.] investigated the false-negative rate of SLNB following neoadjuvant chemotherapy.
As micrometastases and isolated tumor cells found after neoadjuvant therapy are predictors of worse survival, specimens with these findings should not be designated as having a pathologic complete response.
[*Standardization of pathologic evaluation and reporting of postneoadjuvant specimens in specimens in clinical trials of breast cancer: cancer: recommendations from an international working group.* ***Mod Pathol. Pathol. 2015;28:1185–1201]***

PATHOLOGY PEARLS:

All organizations agree that the goal is to detect all macrometastases (>2 mm). They recommend that the SLNs should be sliced no thicker than 2 mm and submitted entirely and that one H&E level is sufficient.The size of the largest metastatic deposit and the presence of extranodal extension should be reported.

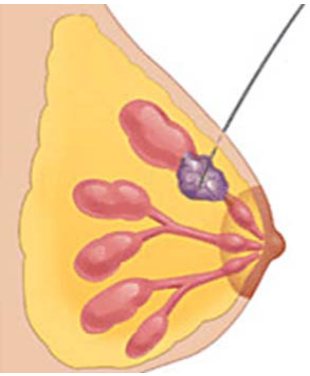
Lyman GH, Giuliano AE, Somerfield MR, et al; American Society of Clinical Clinical Oncology. American Society of Clinical Oncology guideline recommendations recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin cancer. J Clin Oncol. 2005;23:7703–7720.

HINDUJA HOSPITAL

LATEST RECOMMENDATIONS FOR ALND

July 12, 2018 in JAMA Oncology.

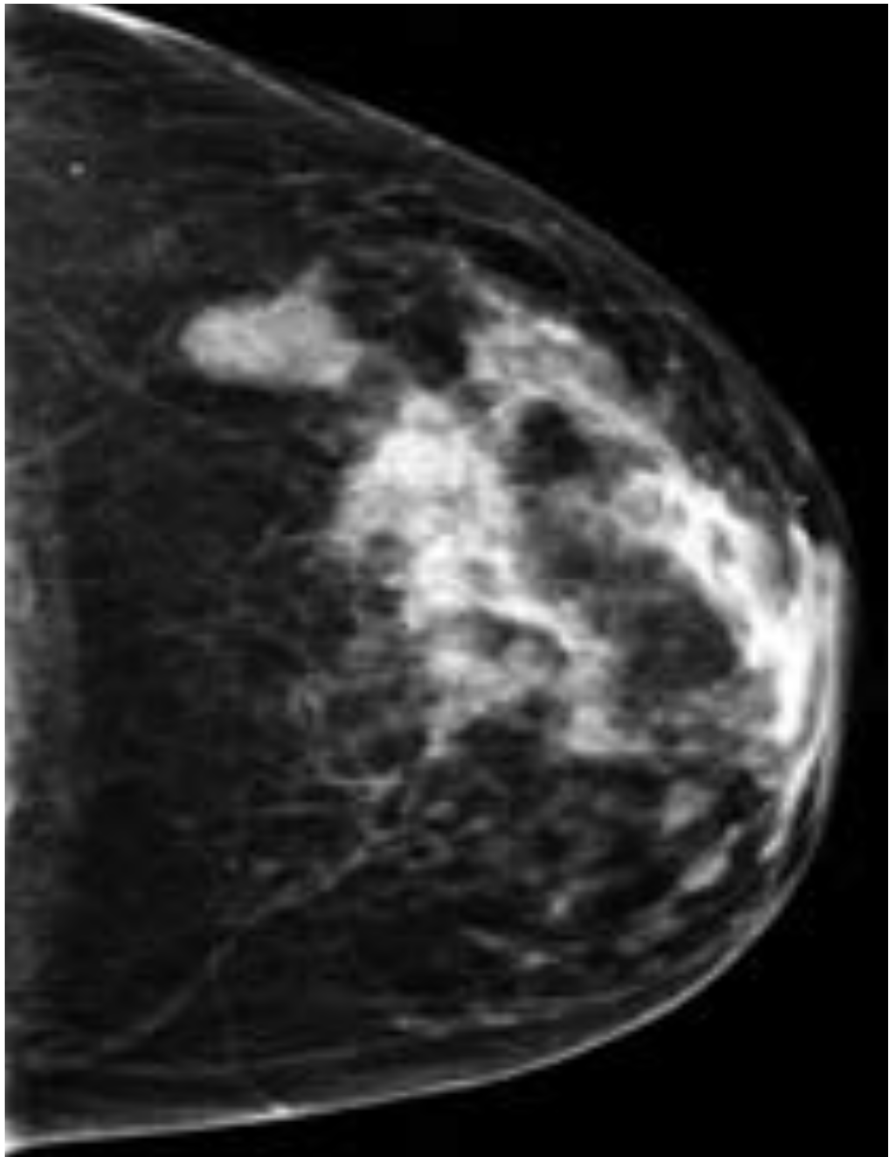
- A survey of 376 surgeons in the United States who treated 5080 patients with stage I/II between 2013 and 2015 were invited for the study.
- It has found wide variation in their views on the omission of axillary lymph node in patients with early breast cancer, even though clinical guidelines now recommend certain patients.
- The surgeons who perform the most surgeries were the most willing to omit of ALND; the fewest surgeries were the least likely to omit it. These results suggest that in many patients are undergoing ALND unnecessarily and thus, in essence,are being overtreated, Sloan Kettering Cancer Center, New York City].
- They recommend that "women with clinically node negative cancer undergoing breast treatment with whole breast irradiation who are advised that ALND is routine for the sentinel node (SN) metastases should seek a second opinion."
- In addition, patients should "reserve consent for ALND until final surgical pathologic are available to ensure a complete discussion of the alternatives to ALND when SN present,"



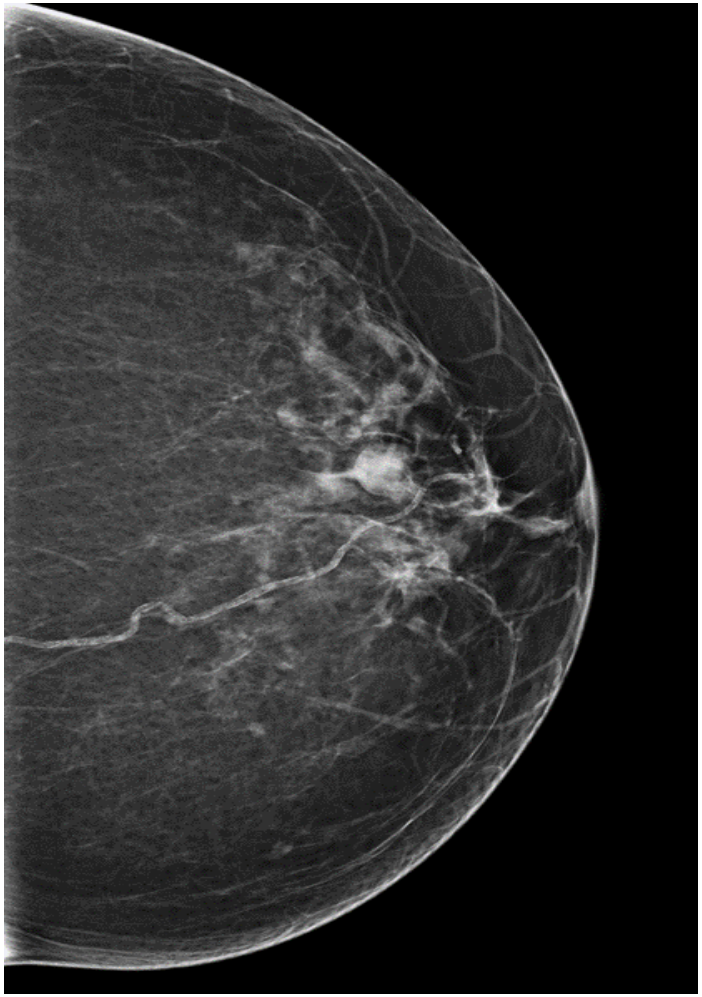
CASE 3

CLINICAL HISTORY

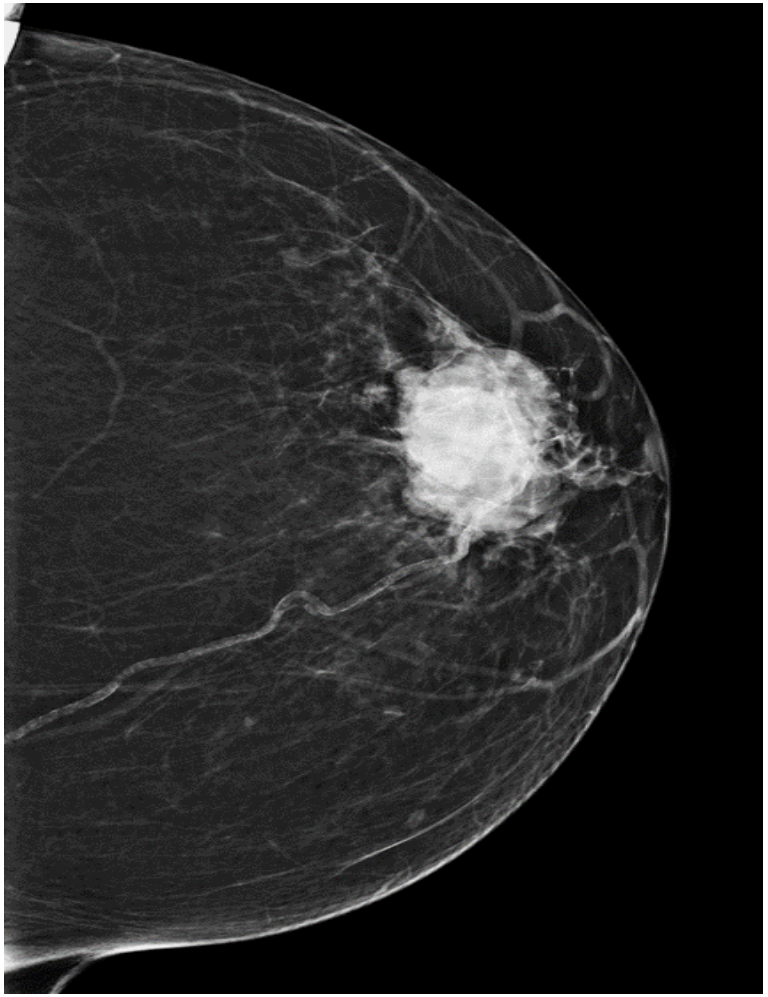
- 55 year old female with a treated carc in right breast
- New nodularity in left breast,RETROAREOLAR
- Ultrasound core needle biopsy

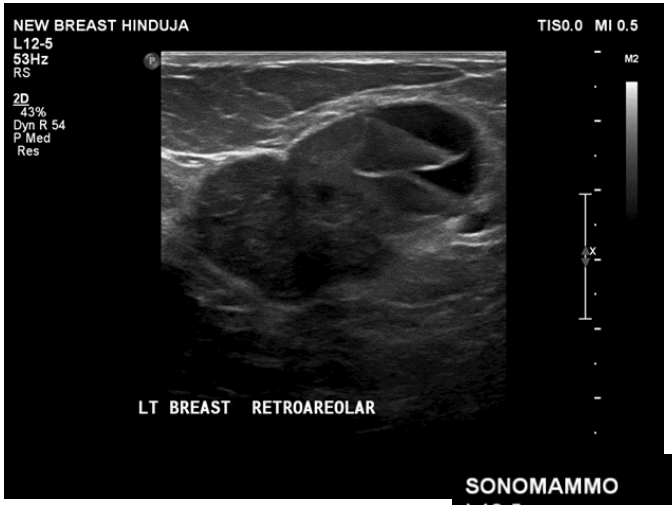


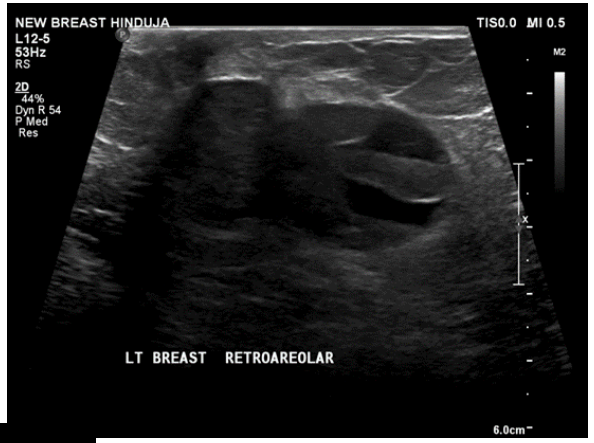

LEFT TRANS 1:00 6CM

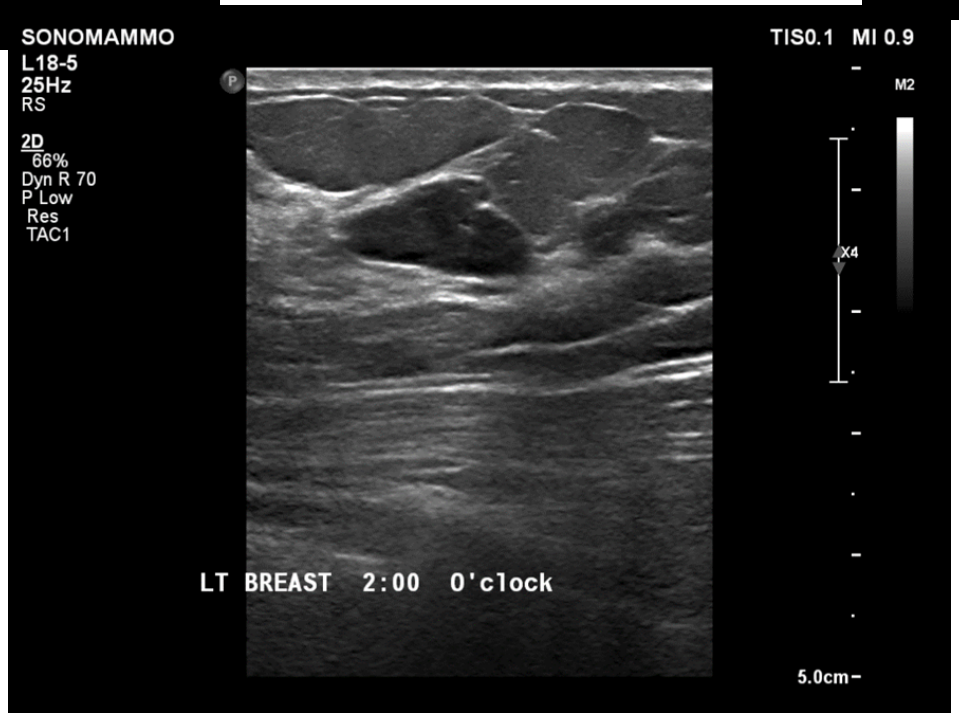


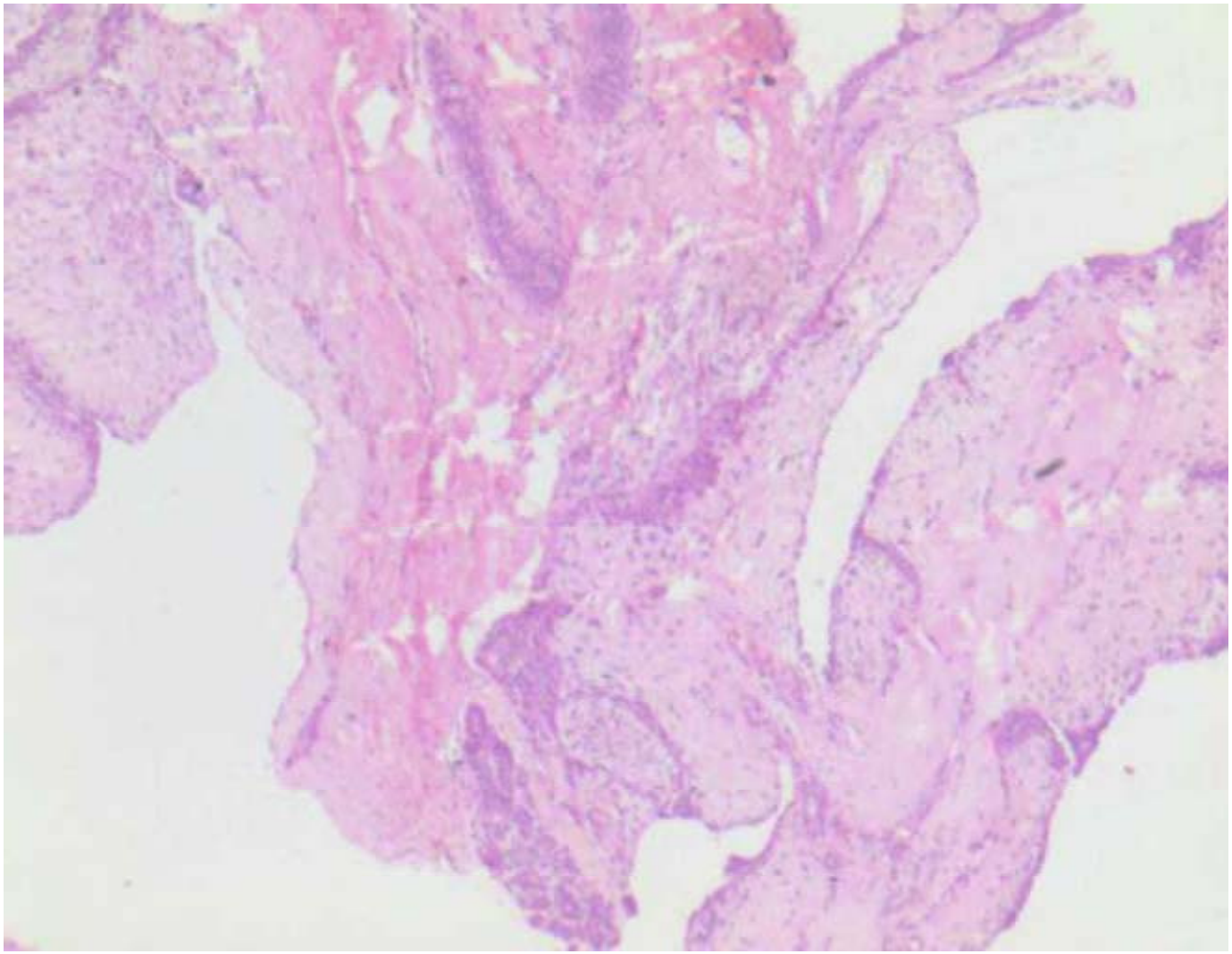
OVER TIME,INCREASE IN SIZE

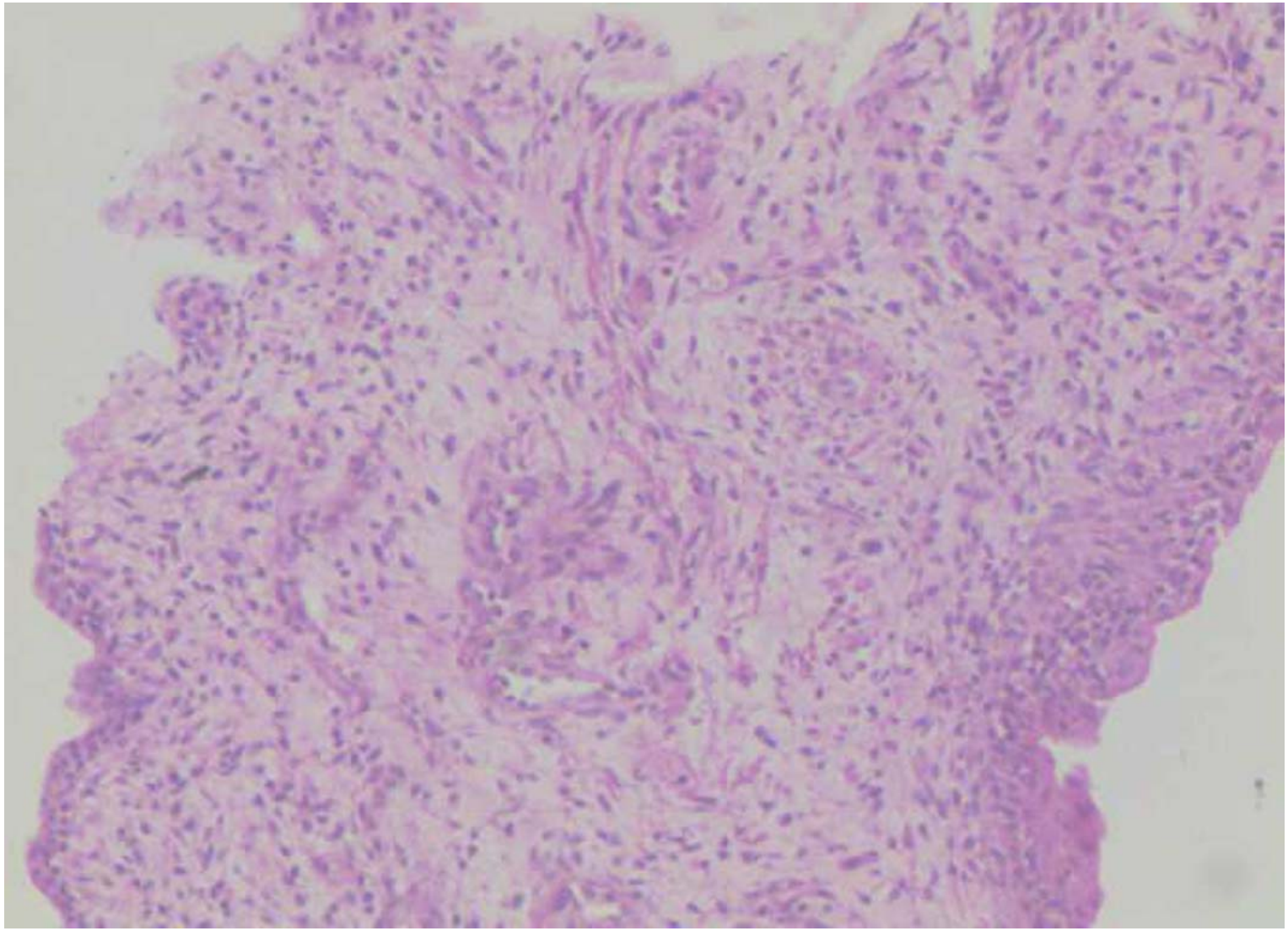



NEW BREAST HINDUJA
L12-5
53Hz
RS
2D
43%
Dyn R 54
P Med
Res
TIS0.0 MI 0.5
M2
LT BREAST RETROAREOLAR

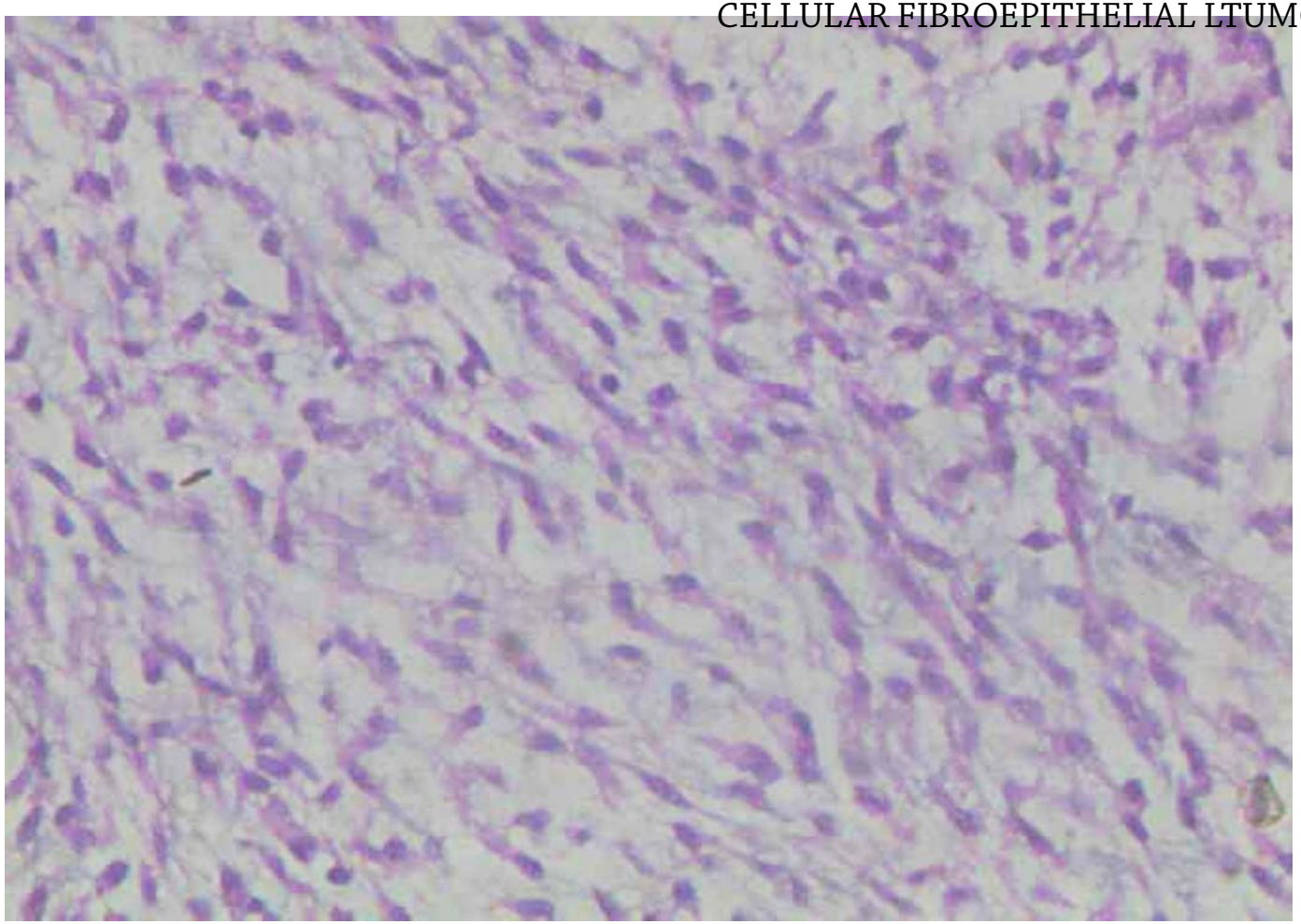

NEW BREAST HINDUJA
L12-5
53Hz
RS
2D
44%
Dyn R 54
P Med
Res
TIS0.0 MI 0.5
M2
LT BREAST RETROAREOLAR
6.0cm


SONOMAMMO
L18-5
25Hz
RS
2D
66%
Dyn R 70
P Low
Res
TAC1
TIS0.1 MI 0.9
M2
LT BREAST 2:00 O'clock
5.0cm

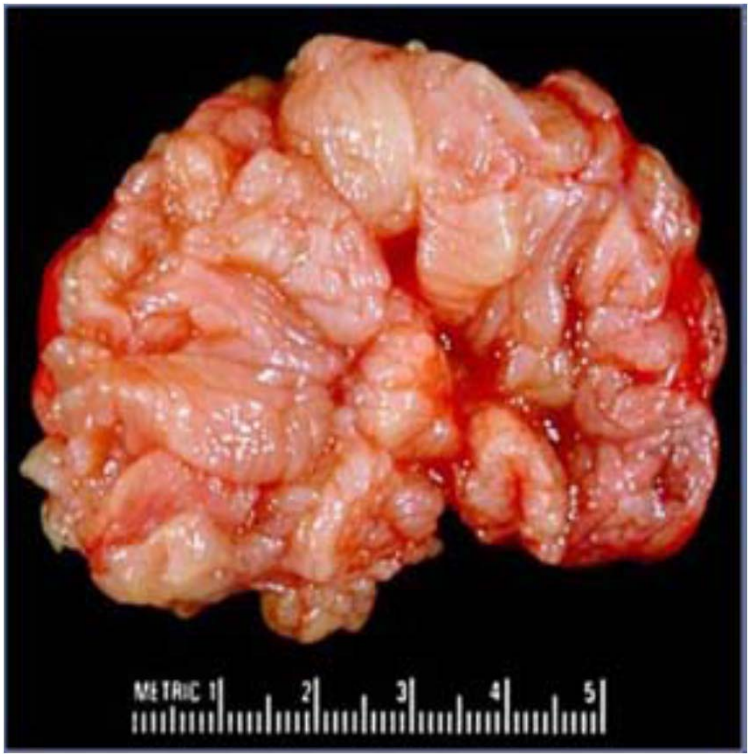




CELLULAR FIBROEPITHELIAL LTUMOR,PT LIKELY



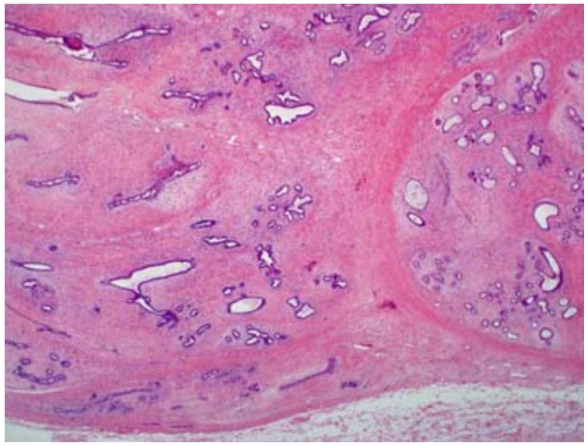
THE LESION IS EXCISED……Frozen Section?????

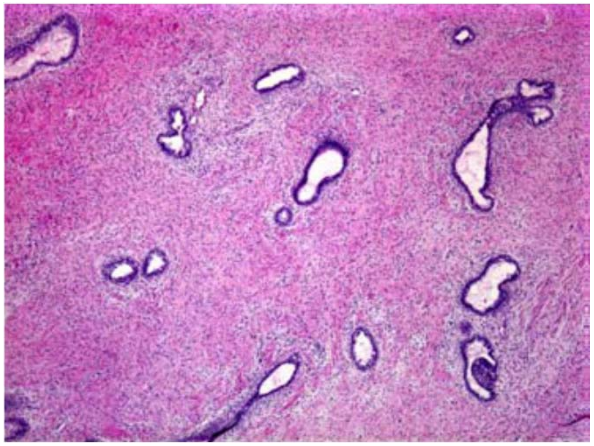


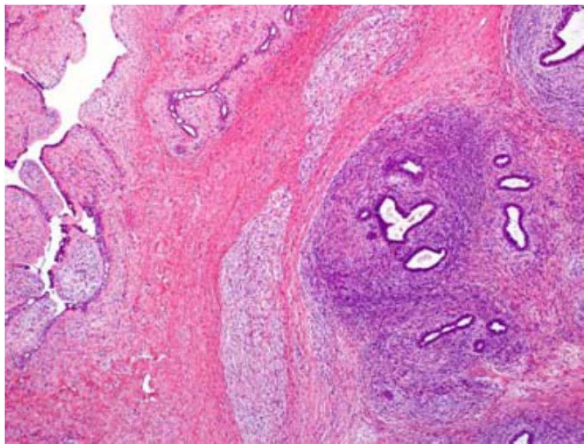
WHAT HISTOLOGIC FEATURES HELP DETERMINE THE LIKELIHOOD OF PHYLLODES TUMOR ON EXCISION?

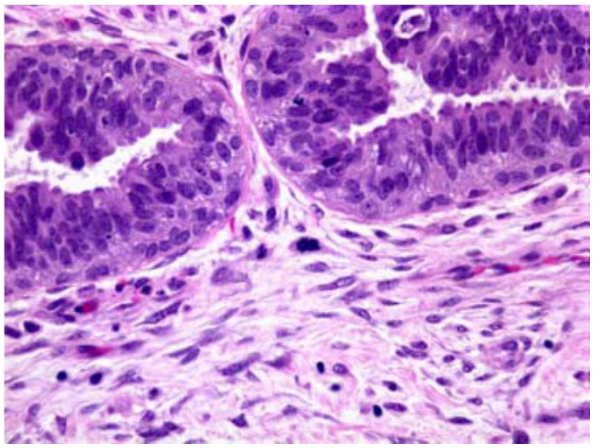
Lee et al. (Histopathology 51:336, 2007)
74 excisions; 38 FA and 36 PT

Four features found in cnbx more common in PT
1. Stromal cellularity > than typical FA in at least 50% of the cnbx
2. Stromal overgrowth (10X field)
3. Fragmentation
4. Adipose tissue within stroma





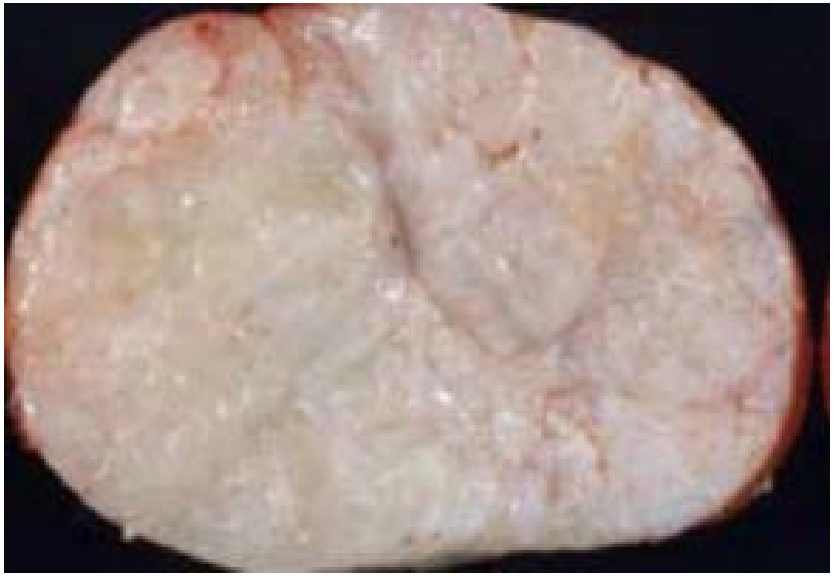


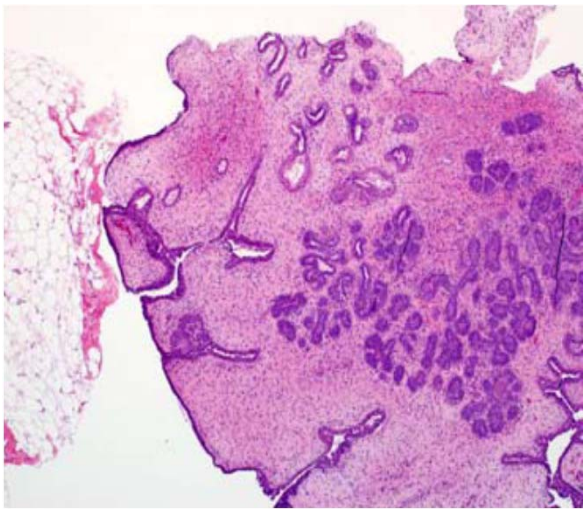


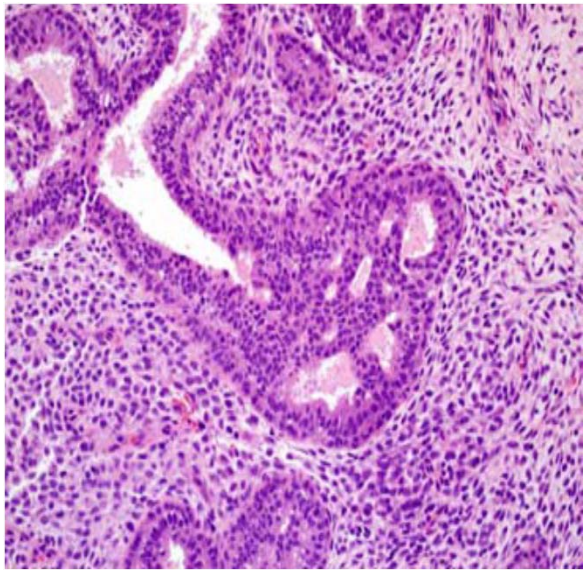
On excision :

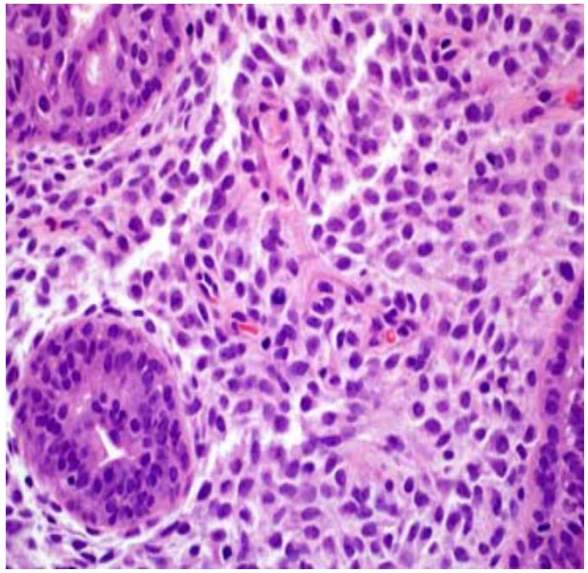
- Mild to moderate stromal cellularity without significant atypia
- No stromal overgrowth
- Stromal mitotic activity (2/10 HPFs)
- Tumor interface circumscribed

WHAT TO DO WITH A FIBROADENOMA WITH SLIGHT INCREASE IN STROMAL CELLULARITY AND PROMINENT INTRACANALICULAR GROWTH?





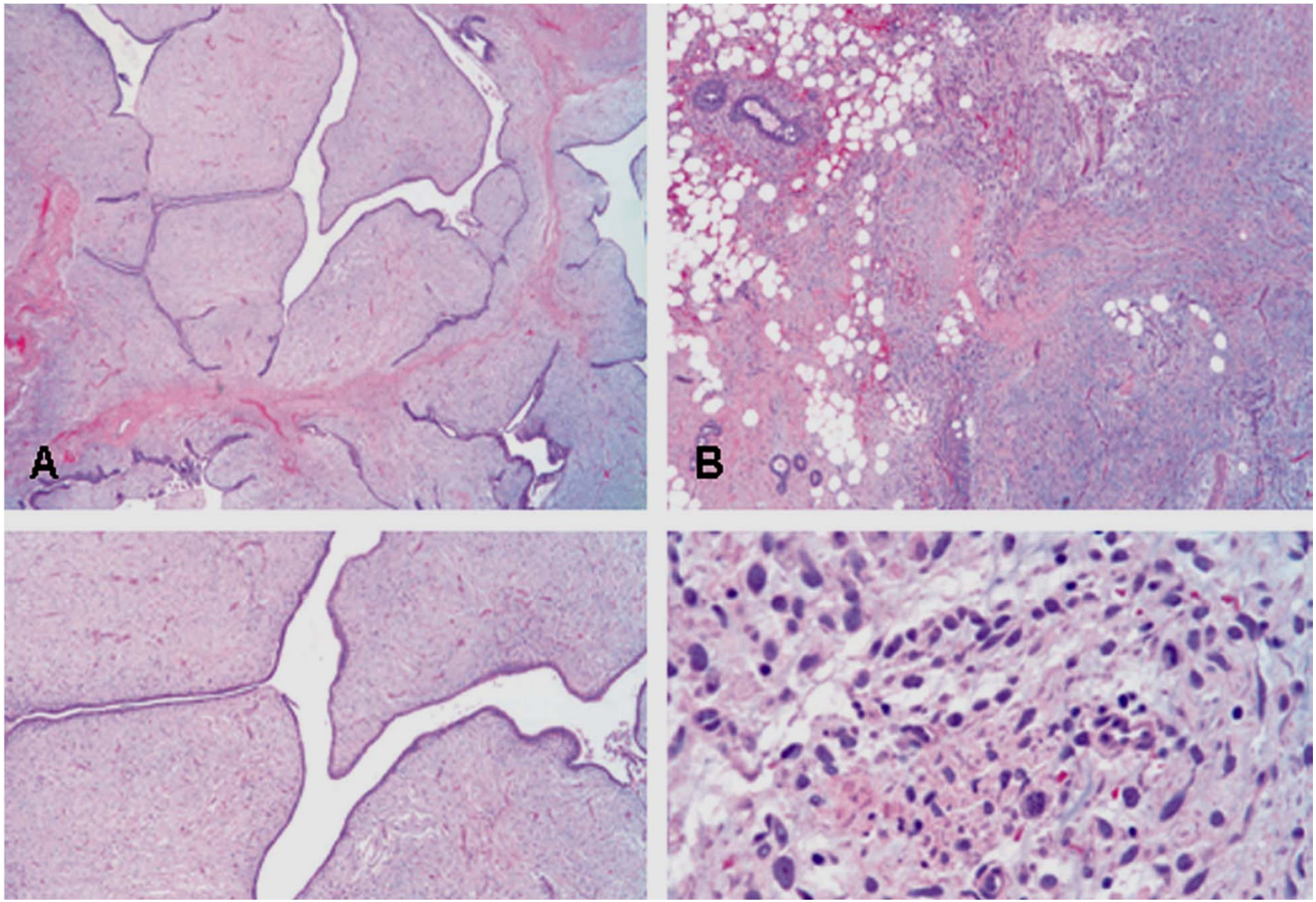




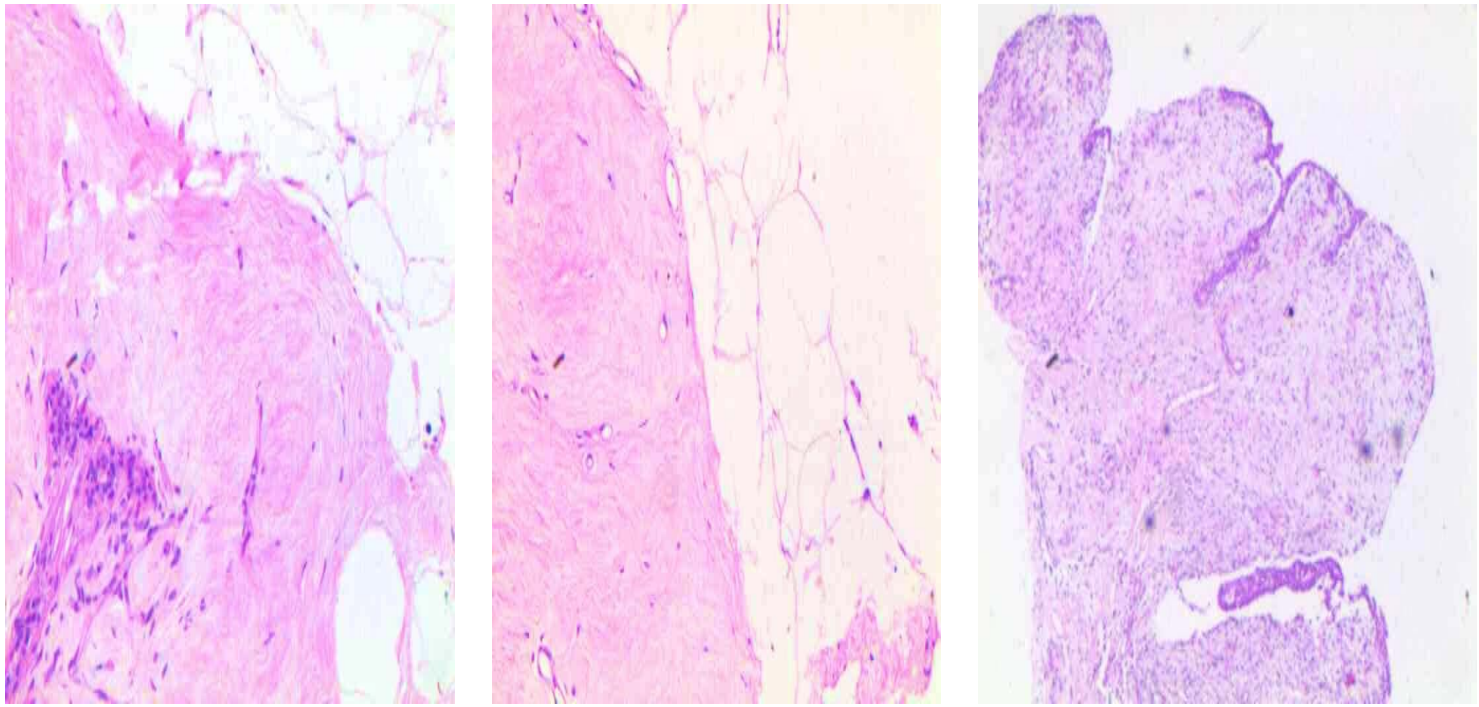
RECOMMENDATIONS

- Markedly ↑ stroma ,excise as PT
- Moderately ↑ stroma, >2/10 HPFs, and high proliferation indices excise as PT
- Moderately ↑ stroma, no mitotic activity, low proliferation indices excise as FA
- Minimal stromal cellularity, no mitoses, low proliferation MAYBE excise as FA

Jacobs et al. AJCP 124:342, 2005


A
B

Tumor borders

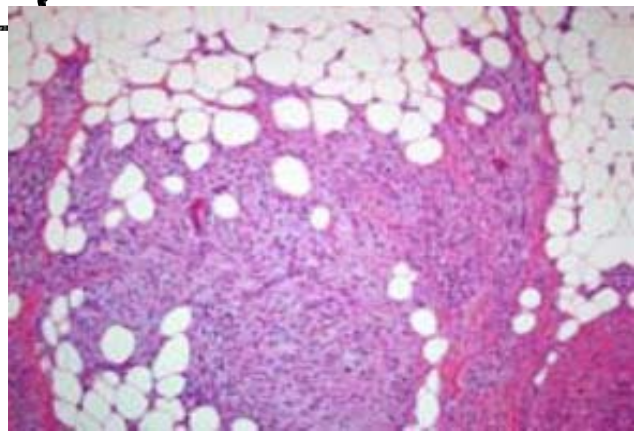


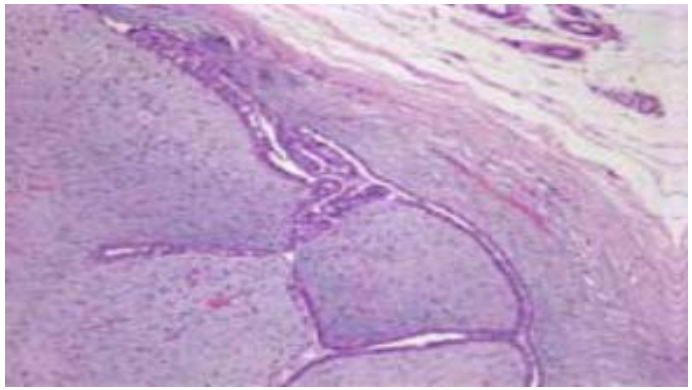
Fragmentation leaf-like intracanalicular growth

WHEN DOES INTRACANALICULAR GROWTH BECOME LEAF- LIKE AND PT ENTER AS DIFFERENTIAL?

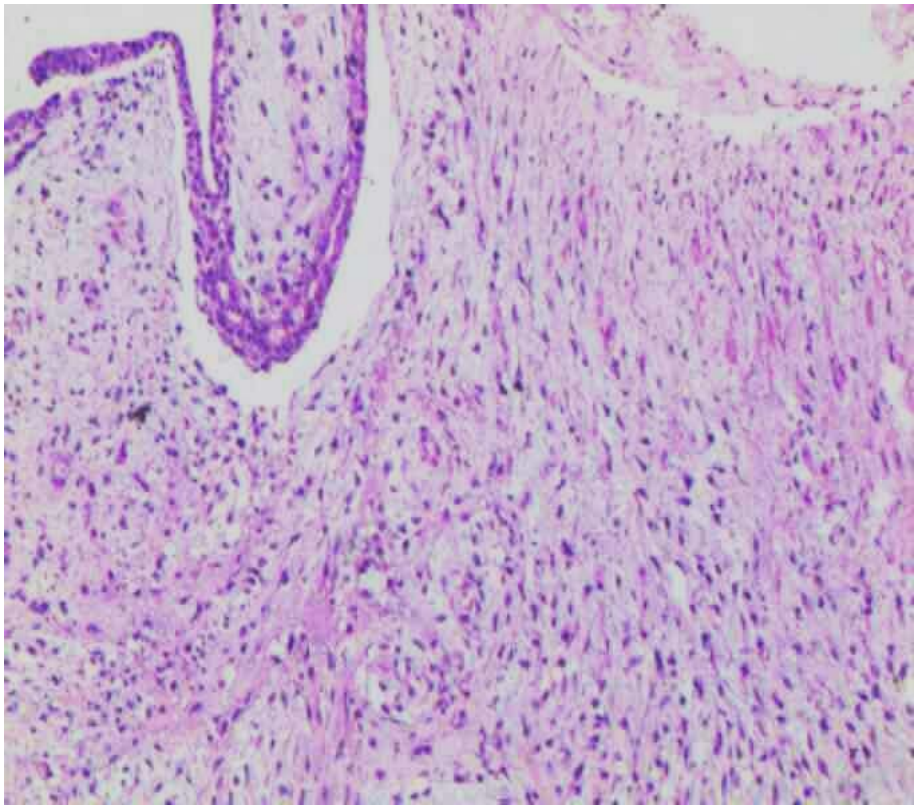
STROMAL OVERGROWTH

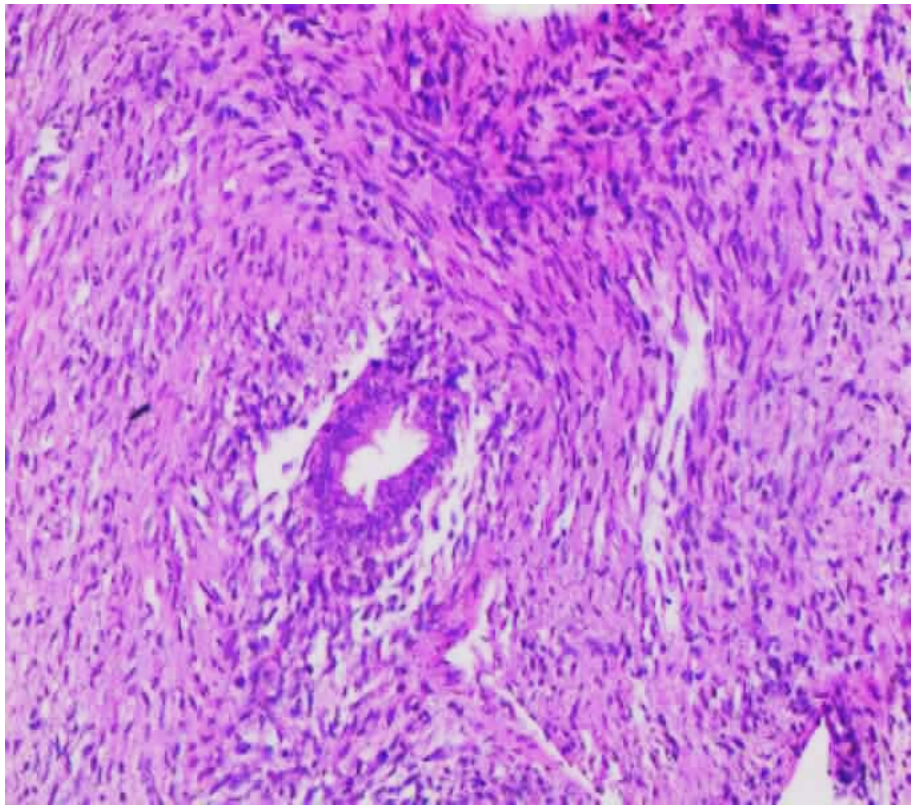
- **Classically defined as 40x field of 'pure' stroma without epithelial elements**
- **Some authors have used 10x field**
- **Feature most frequently associated with aggressive/metastatic behavior in numerous studies**



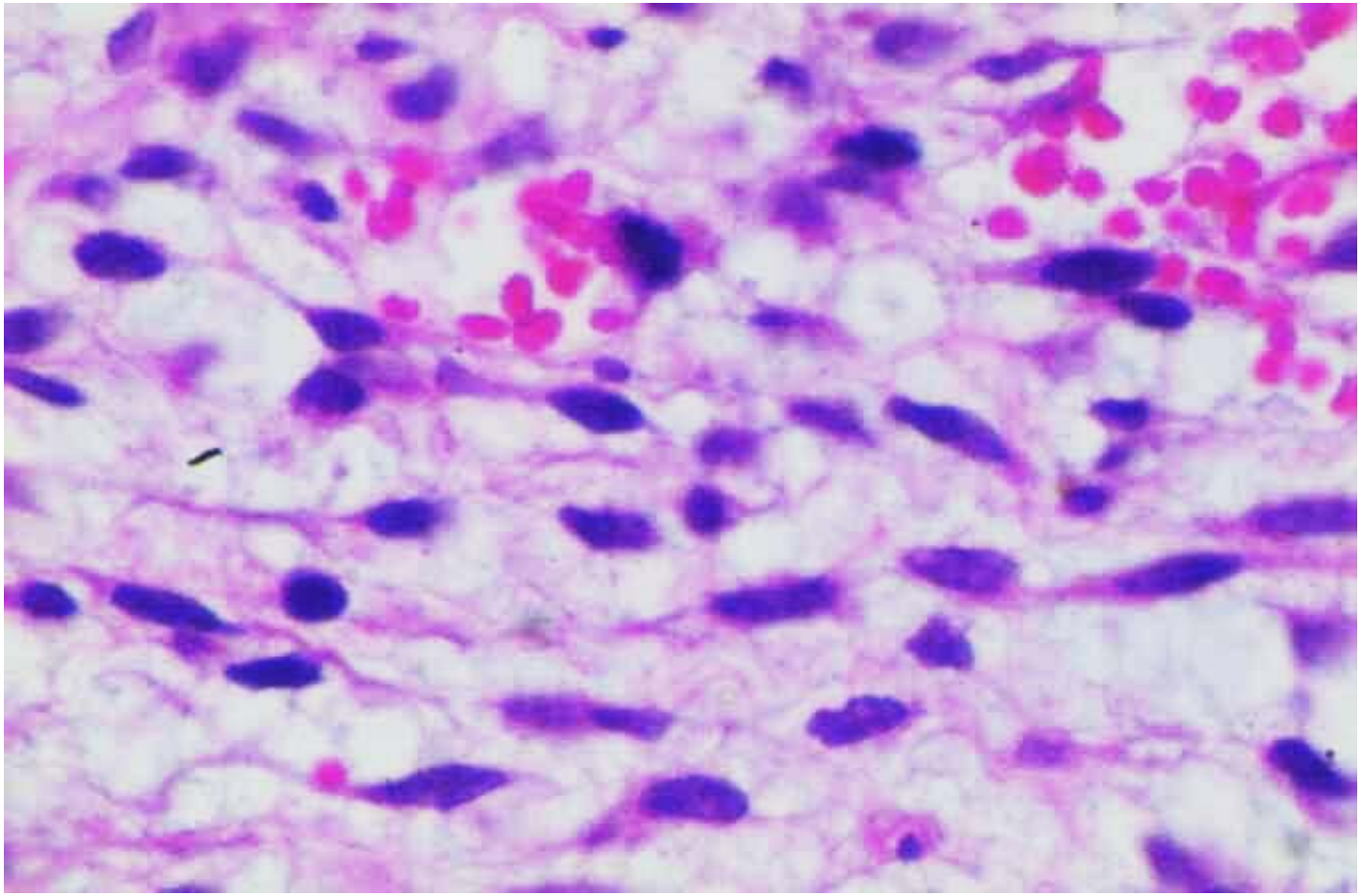


Stromal overgrowth

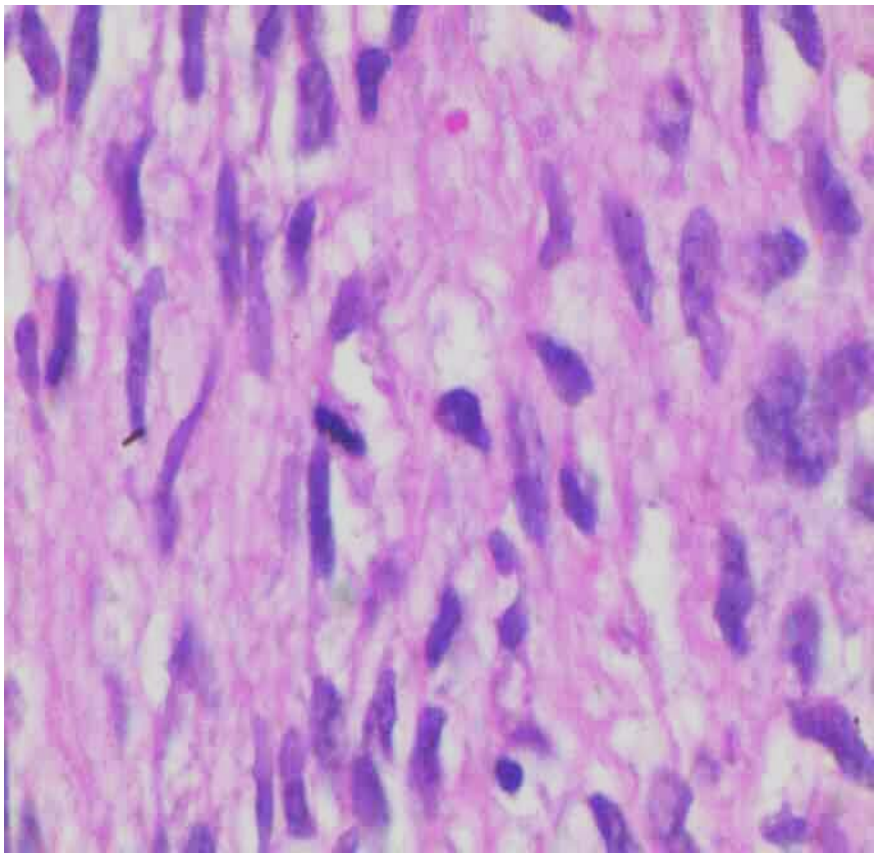


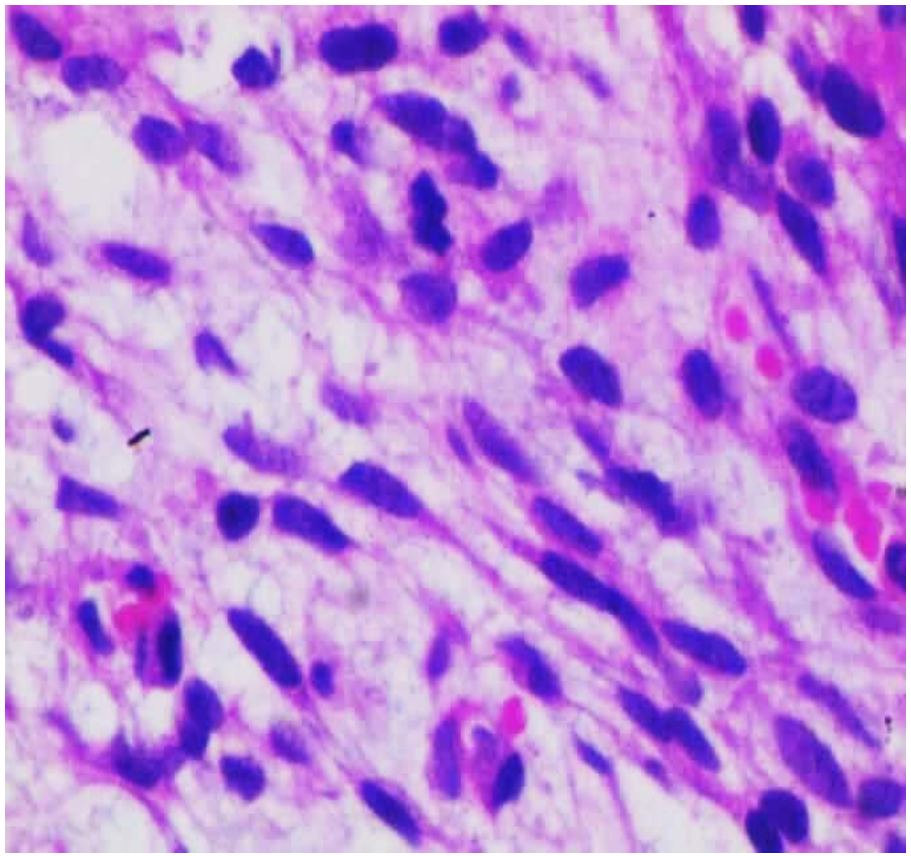


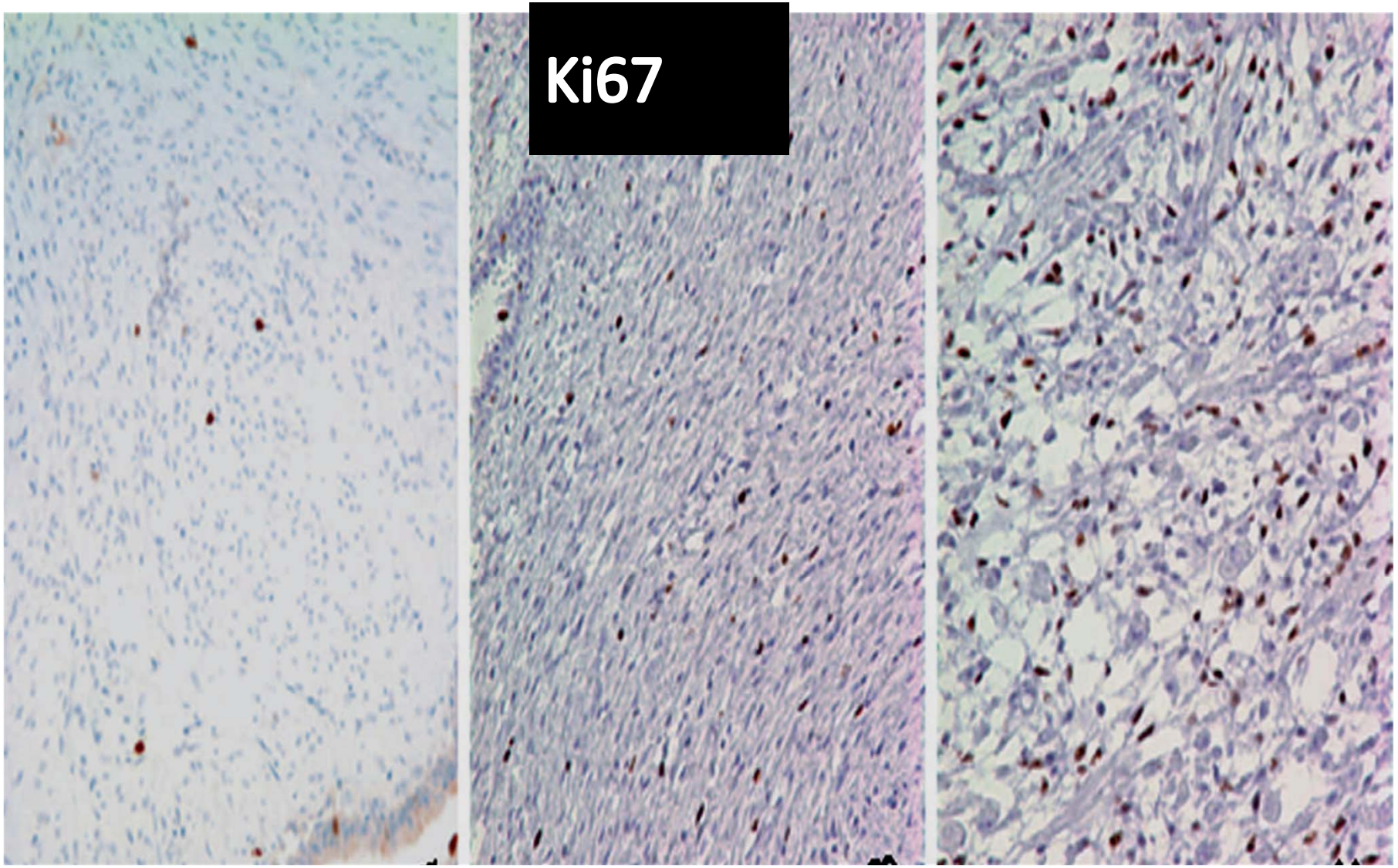
Stromal cellularity



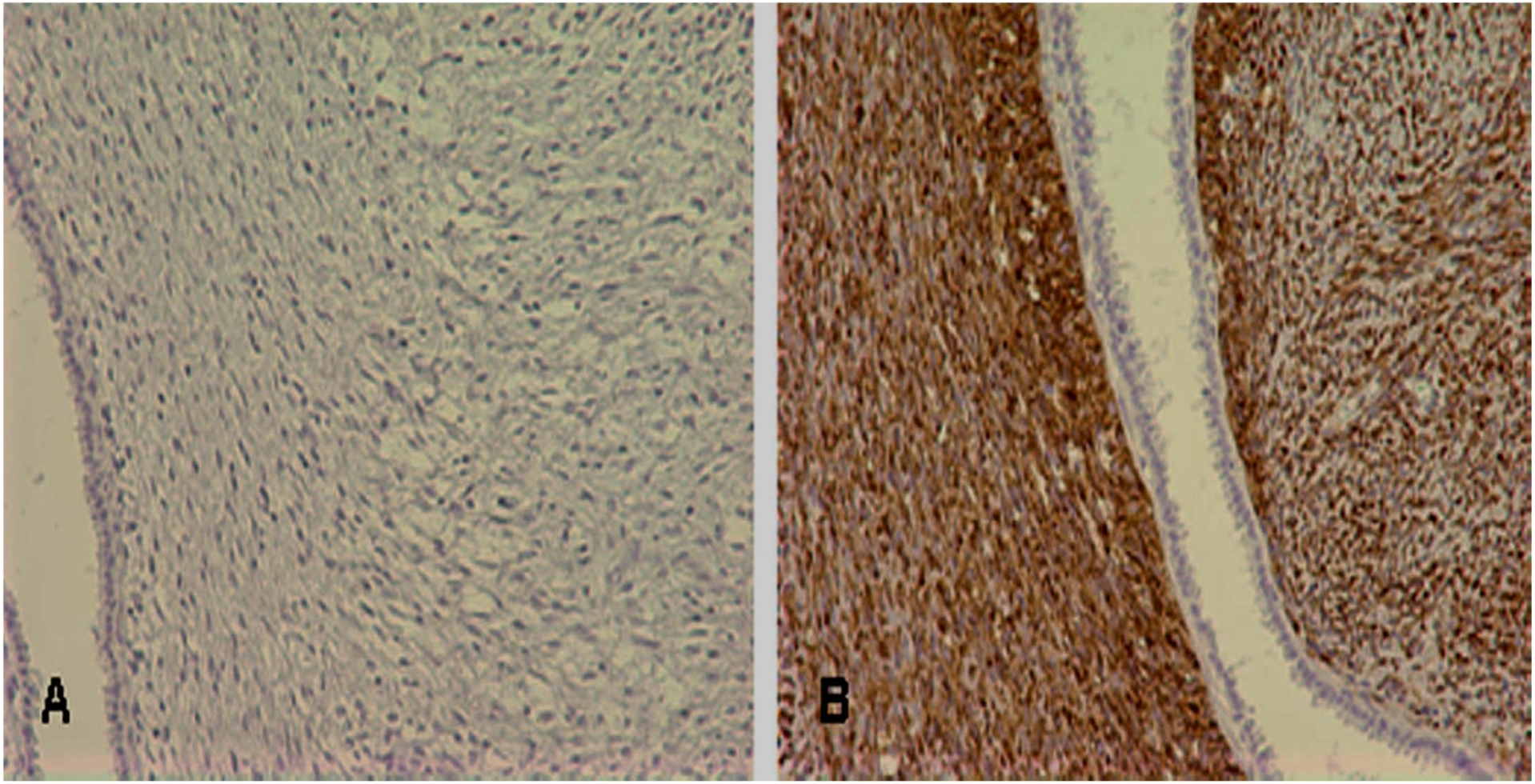
Stromal atypia & mitoses






Ki67

IMP3 IHC in borderline and malignant PT



PATHOLOGY PEARLS

Excision with negative margins should be achieved for recurrent, borderline and malignant Phyllodes tumors.
Although the literature often refers to a margin width of at least 10 mm ,robust evidence to support this approach is lacking.
Therefore an **ideal margin width** remains to be determined, and may need to be considered in relation to factors such as tumor size and cosmesis.

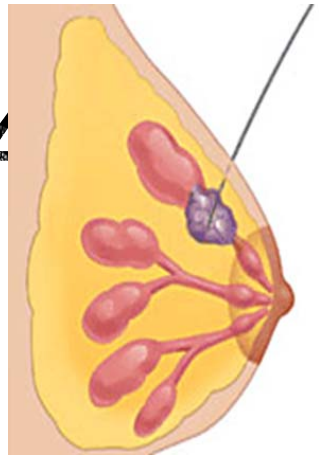
PATHOLOGY PEARLS

From a diagnostic and management perspective, it is important to accurately recognize malignant Phyllodes tumors, which should be surgically eradicated and effectively treated at diagnosis, as these tumors have a well-established but relatively infrequent risk of metastasis and death..

The role of adjuvant RT in borderline and malignant Phyllodes tumors remains to be defined.

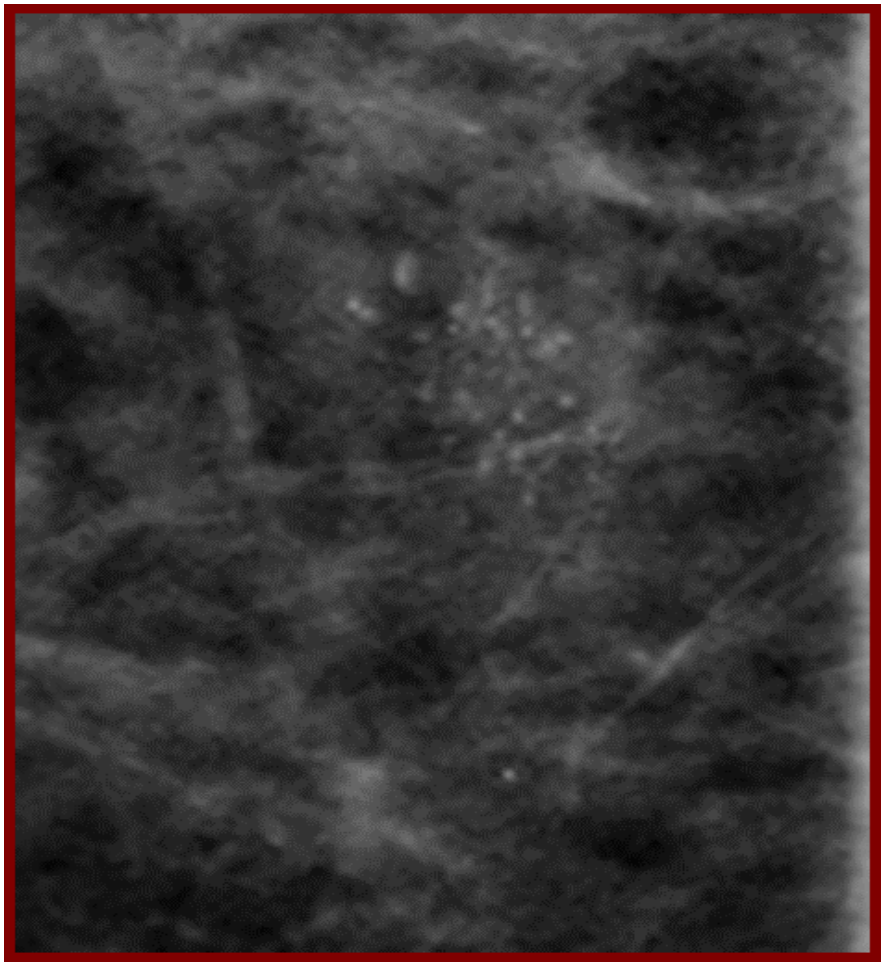
Routine axillary dissection is not recommended.

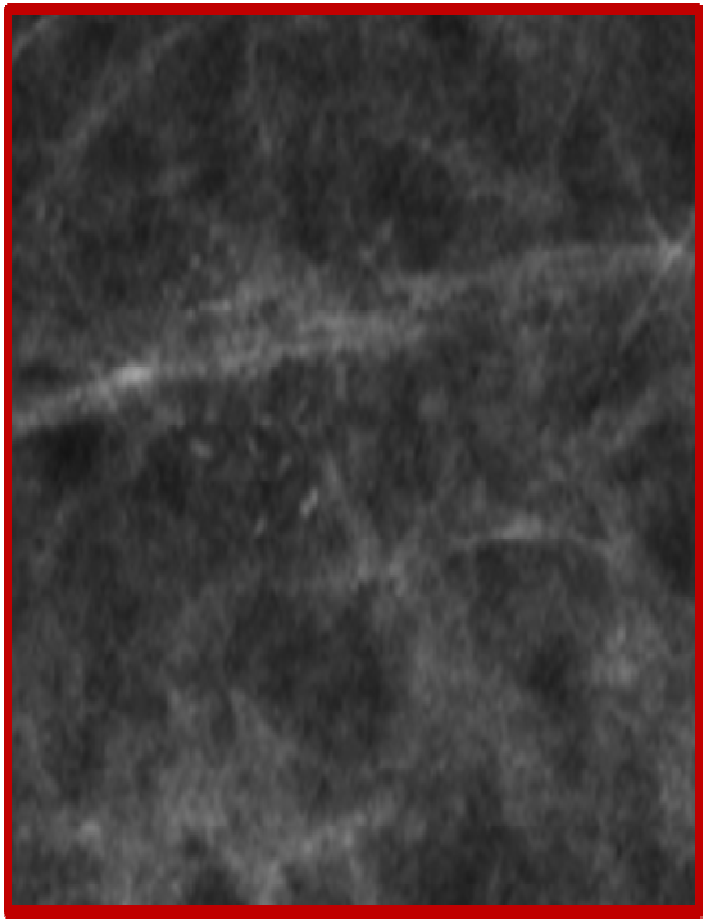
CASE 4

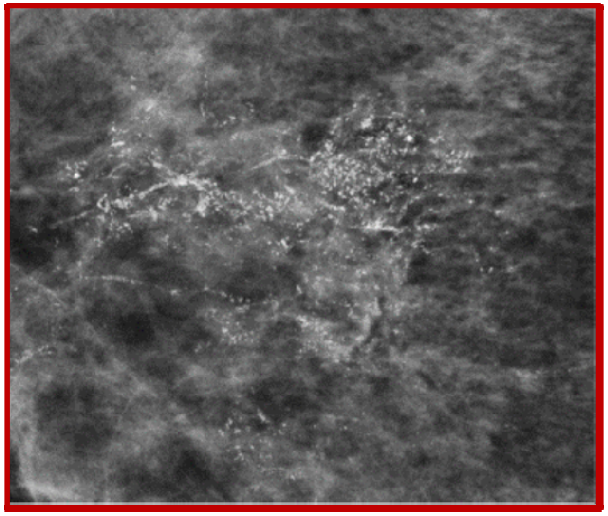


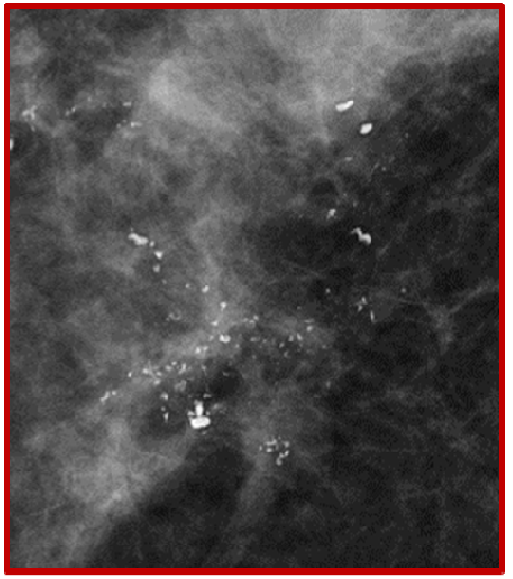
CLINICAL HISTORY

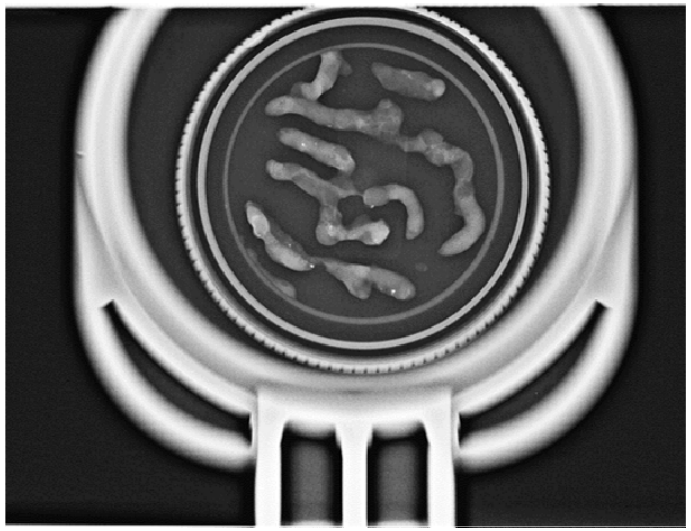
- 42- year -old female
- Small cluster of low suspicious calcifications seen on screening mammogram
- Stereotactic core needle biopsy

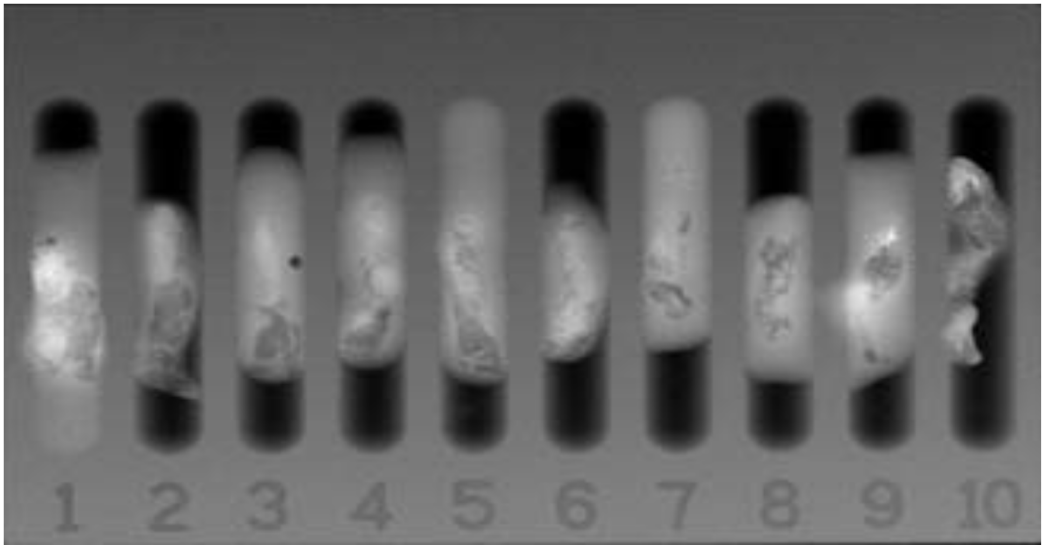


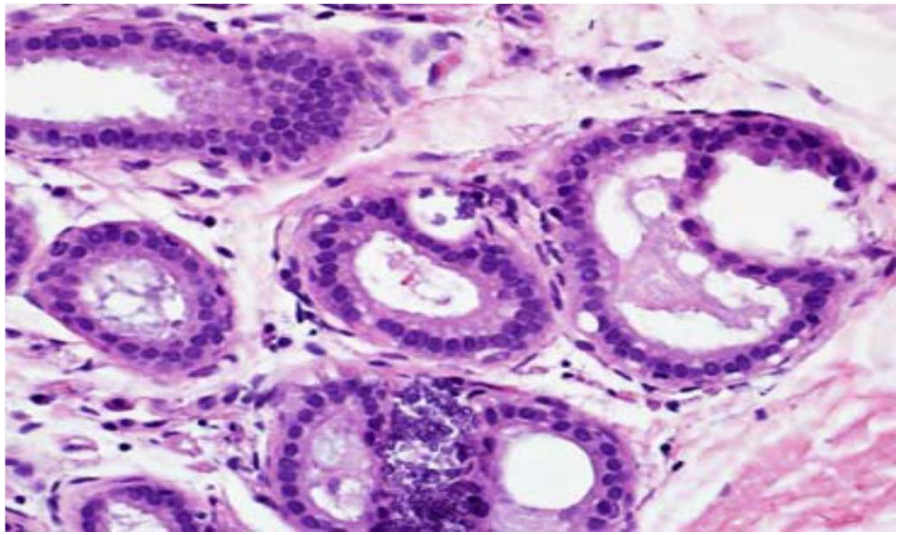


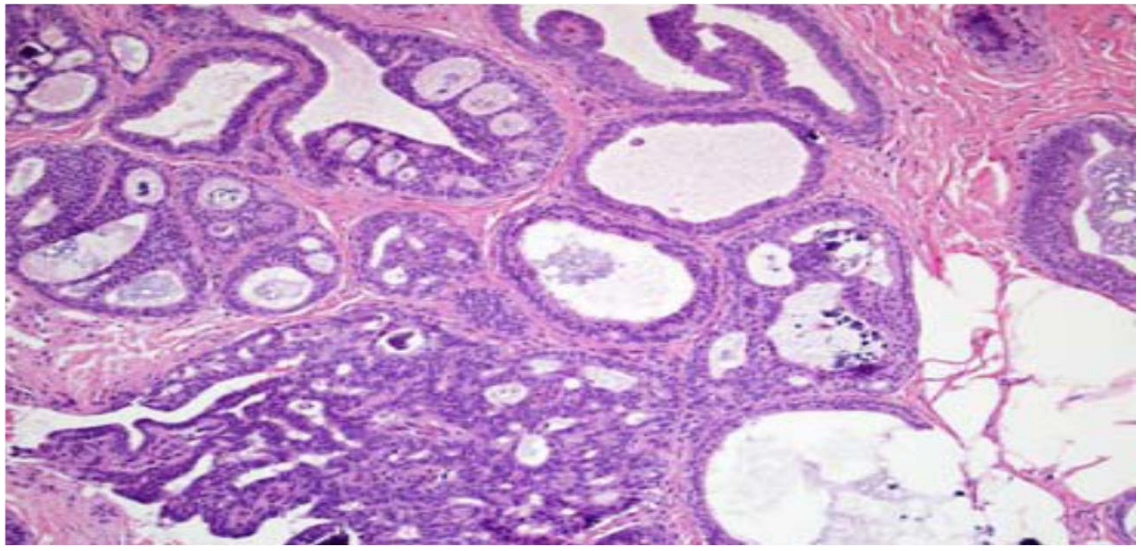


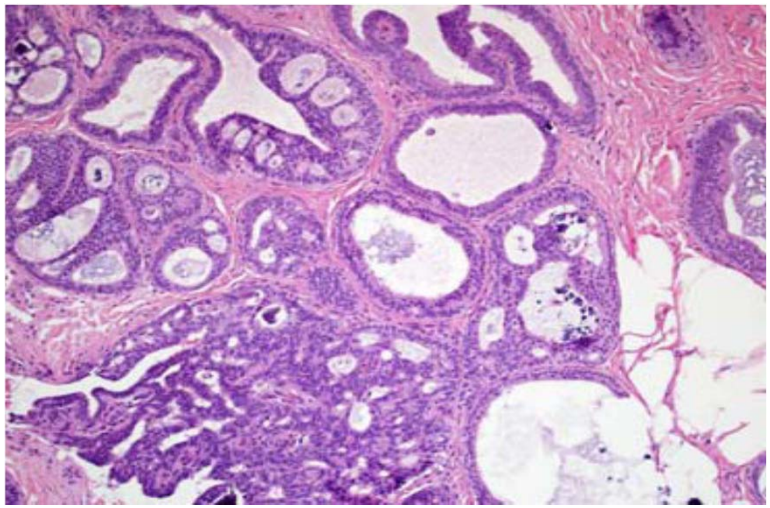


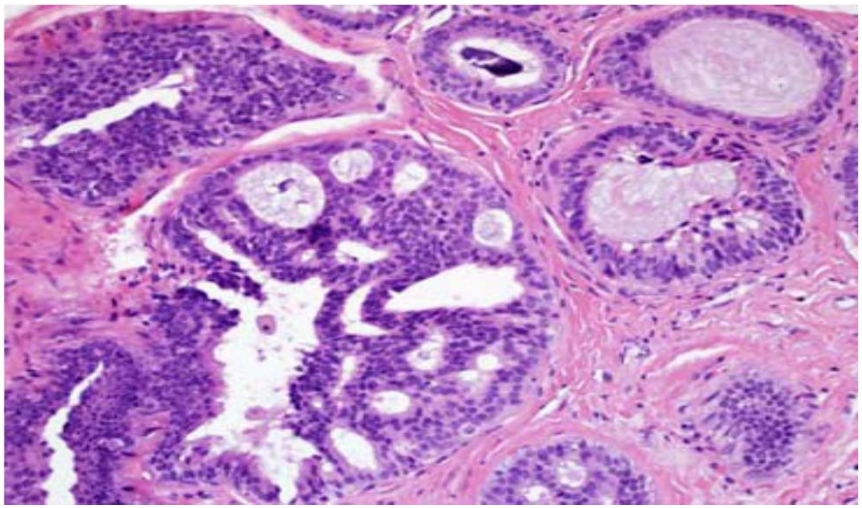


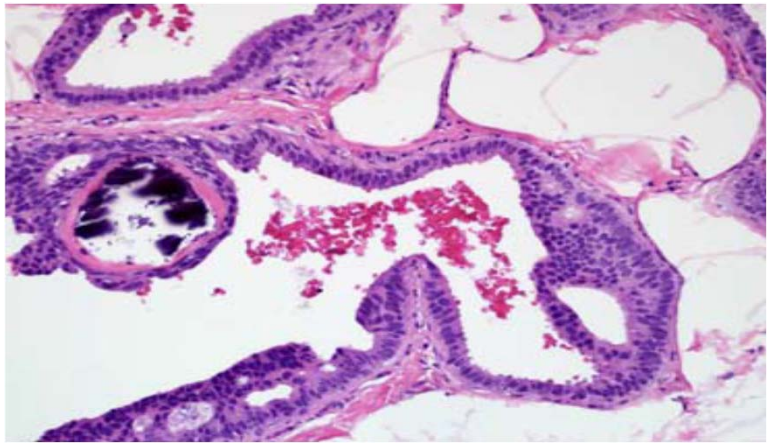

1 2 3 4 5 6 7 8 9 10









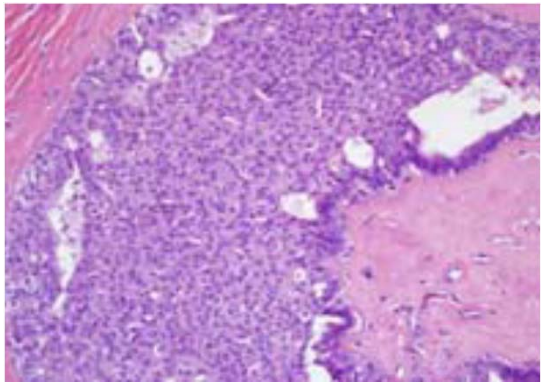


HOW DO WE MAKE THE DIAGNOSIS OF ATYPIA????

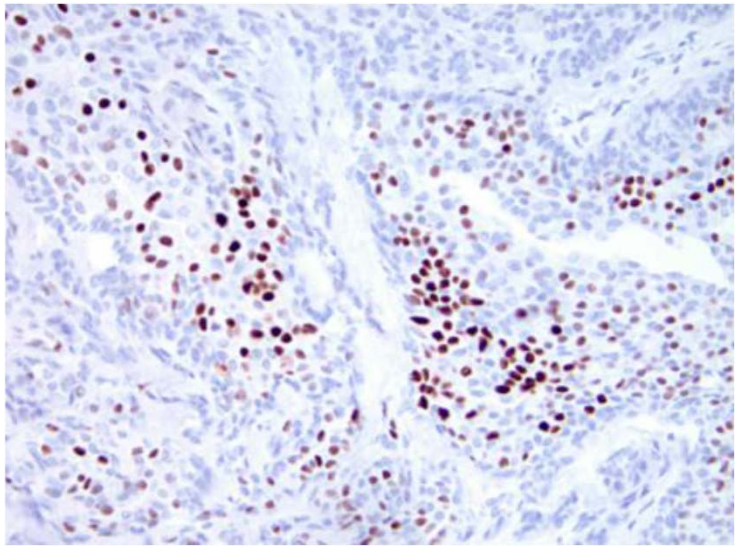
PREANALYTIC VARIABLES

- Especially important for biomarkers – warm and cold ischemia time
- Fixative used
- Weekend issues?
- IHC4,CK5/6,AR,HER2 FISH/CISH
- EXCLUSION criteria for IHC
- Gene testing,BRCA1 testing,Multigene assays

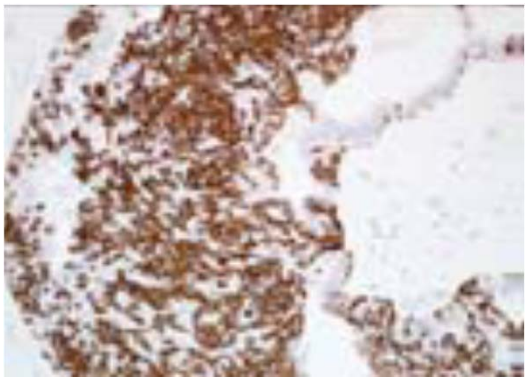
IS IT IMPORTANT TO DIFFERENTIATE BETWEEN UDH - ADH – DCIS?

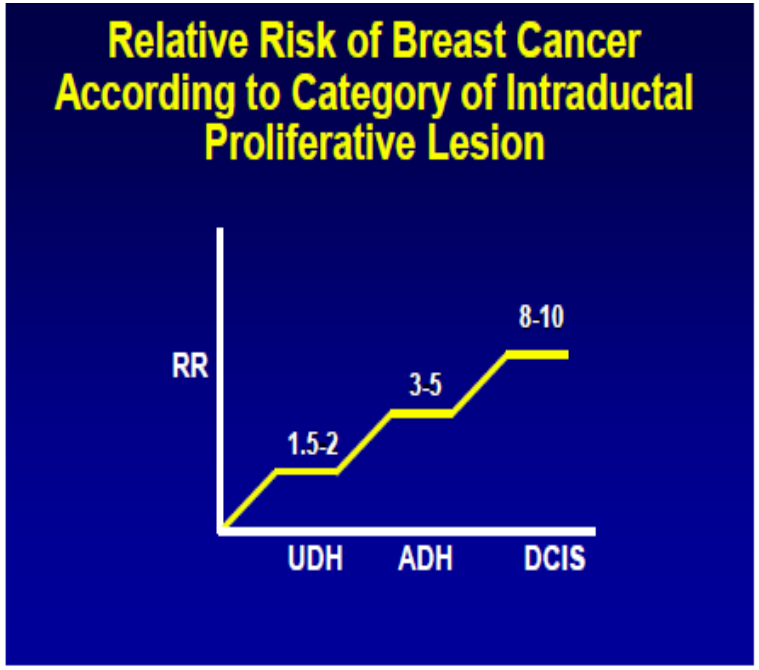


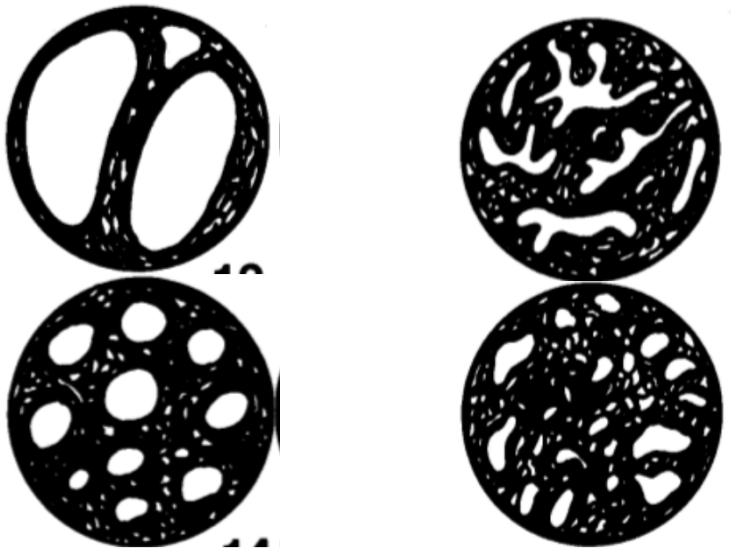
DO IMMUNOHISTOCHEMICAL MARKERS IMPROVE DIAGNOSTIC ACCURACY?



CK5/6







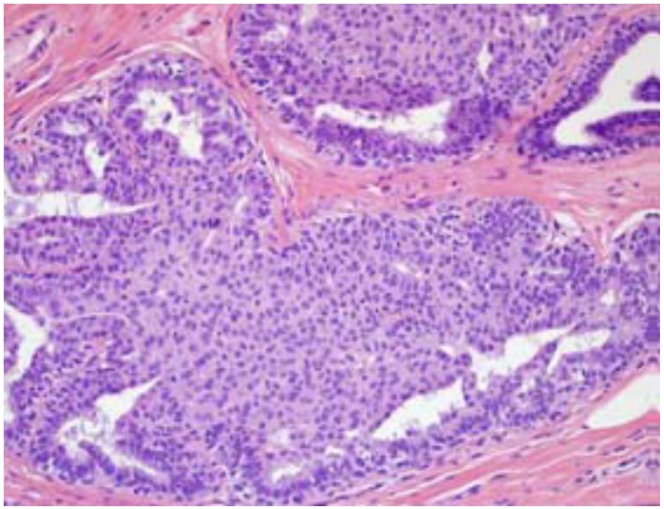
Page and Anderson, 1987

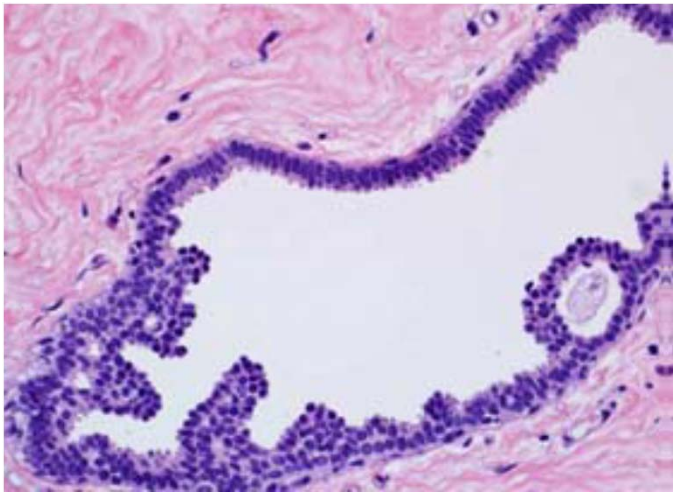
Original Investigation

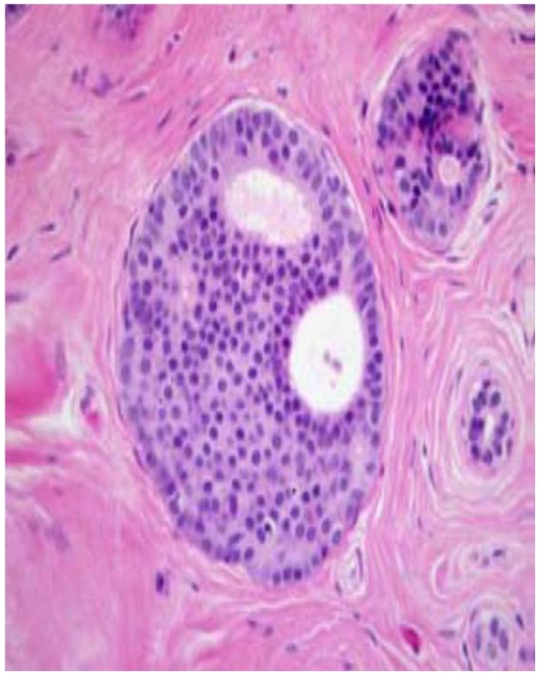
Diagnostic Concordance Among Pathologists Interpreting Breast Biopsy Specimens

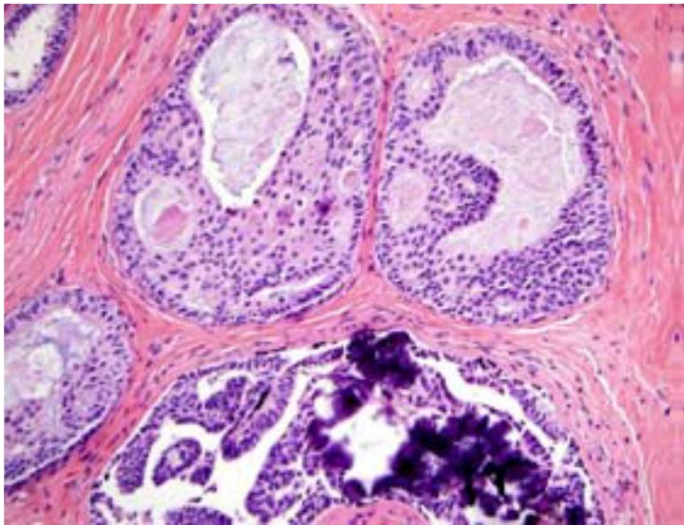
Joann G. Elmore, MD, MPH; Gary M. Longton, MS; Patricia A. Carney, PhD; Berta M. Geller, EdD; Tracy Onega, PhD; Anna N. A. Tosteson, ScD; Heidi D. Nelson, MD, MPH; Margaret S. Pepe, PhD; Kimberly H. Allison, MD; Stuart J. Schnitt, MD; Frances P. O'Malley, MB; Donald L. Weaver, MD

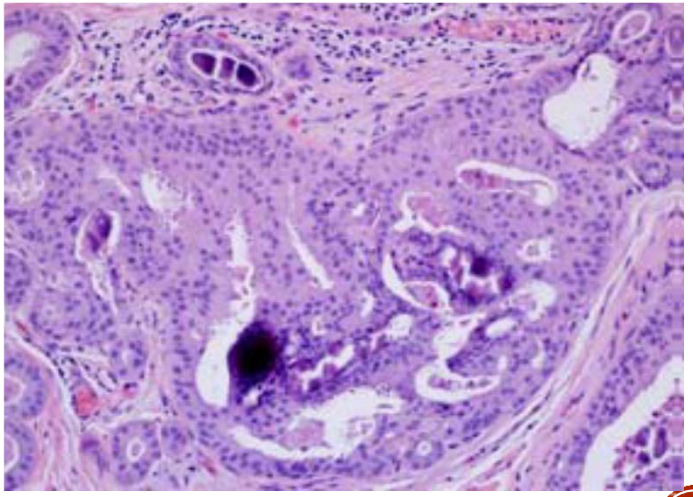
ADH vs DCIS

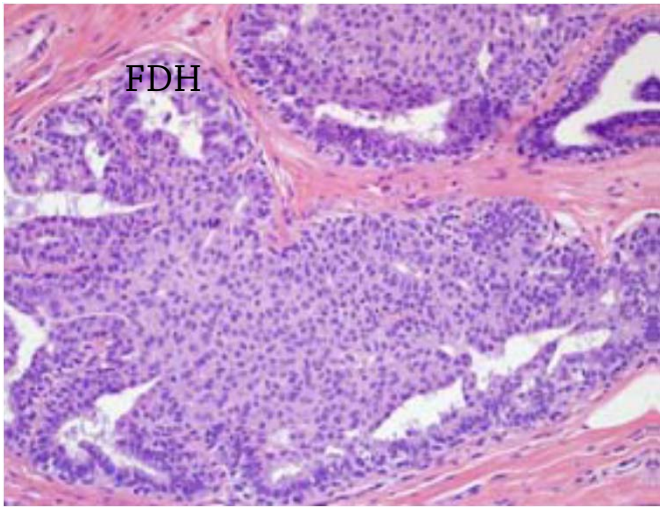


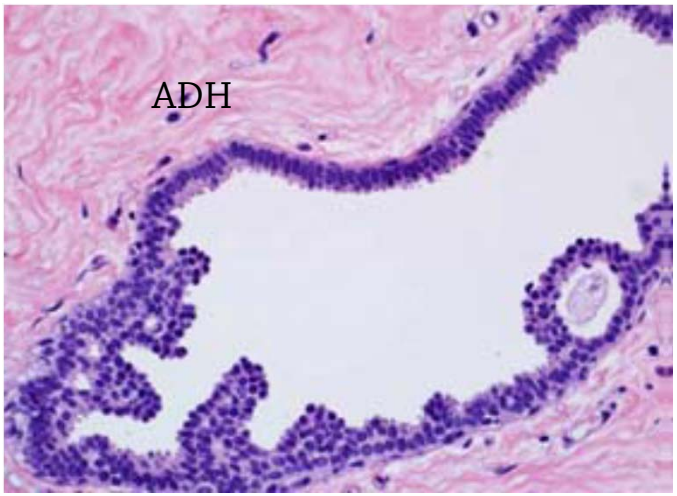


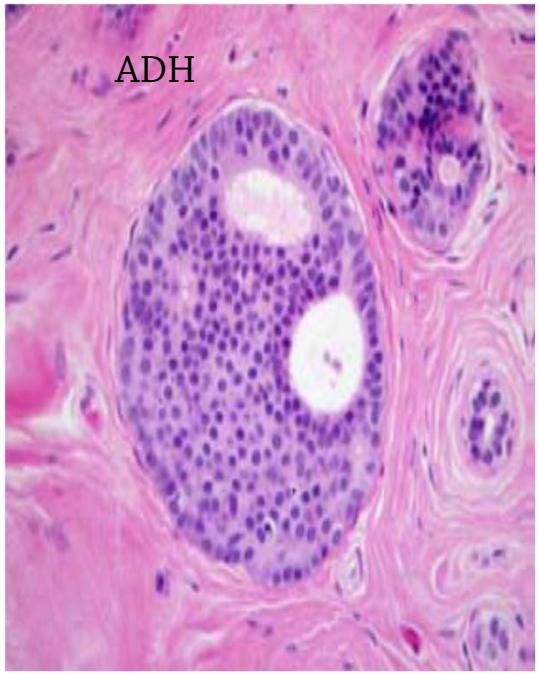


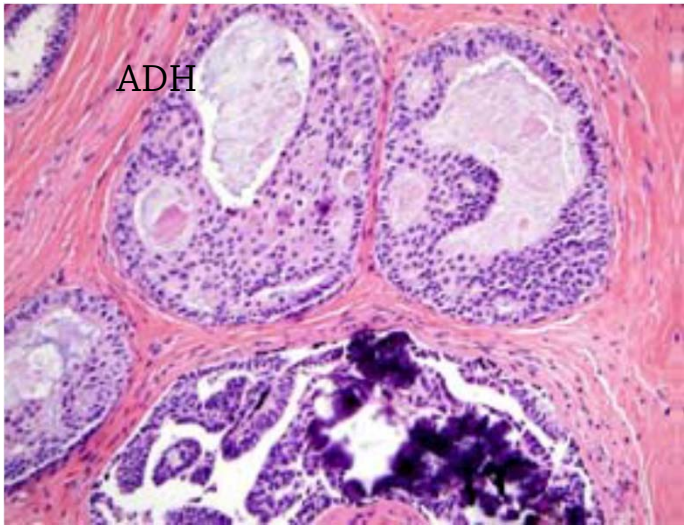


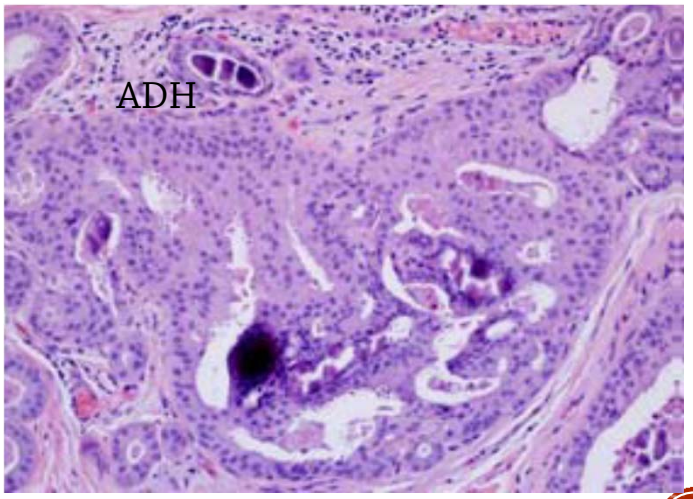



FDH


ADH


ADH


ADH


ADH

ADH VS LG-DCIS

Why Bother to Make This Distinction?

ADH

↓

Marker

↓

- Observation
- Chemoprevention
- (Bilateral mastectomy)

LG-DCIS

↓

Precursor

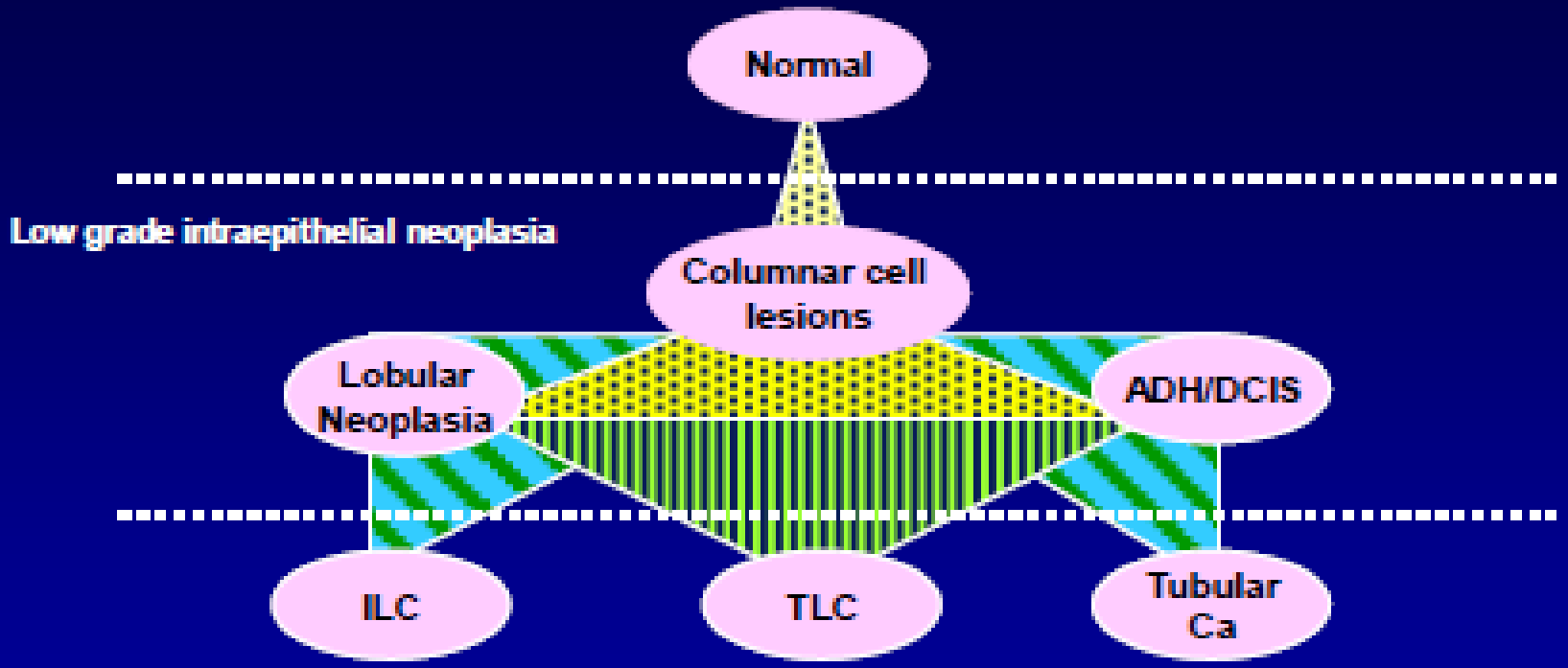
↓

Complete local eradication

Extent Criteria to Distinguish ADH from Low Grade DCIS

- Lesions that show partial involvement of spaces by cells similar to those of LG-DCIS are given the diagnosis of ADH

Low Grade Breast Neoplasia Family



Adapted from Ellis, Mod Pathol 2010

PATHOLOGY PEARLS :ADH VS LG-DCIS

WHAT TO DO?????

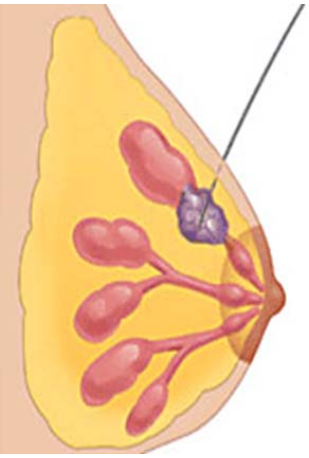
DOES ADH NEED TO BE EXCISED?

- Excise if found on core needle biopsy
- Do not report margins on excision

TAMOXIFEN?

• In 1998, FDA approved TAMOXIFEN for breast cancer risk reduction for 5 years

- Most beneficial for younger, premenopausal women and women who had a hysterectomy



THANK YOU

- “Cancer makes a woman out of you. After survival that you become a warrior is not so much about the body , but rather it is about the triumph of the human spirit”

- Danita Vance