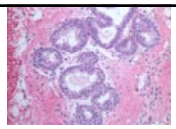
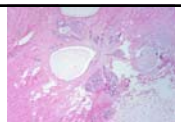

# High Risk Lesions on Breast Biopsies,

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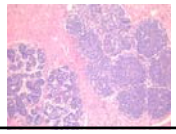
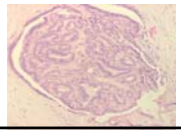
Hospital Pathology Associates
mara.rendi@allina.com

## Objectives

- Define the most common high risk lesions seen on core needle biopsy of the breast.
- Evaluate the various upgrade rates seen on surgical excision.
- Understand controversy still exists regarding management of many of these lesions.

## The High Risk Lesions…

- Columnar Cell Lesions/Flat Epithelial Atypia
- Atypical Ductal Hyperplasia
- Lobular In-Situ Neoplasia
- Radial Scars/Complex Sclerosing Lesions
- Papillomas with and without Atypia

## Why Risk Lesions?



Table 2
Long-term breast cancer risk associated with histologic findings

| Histologic Finding | Relative Risk | Absolute Risk |
|---|---|---|
| Normal (general population as reference) | 1 | 12% by 80 y of age |
| FEA | 1.5 (very limited data) | Unknown |
| Papillary lesions | ~2 | ~12%–15% at 20 y |
| Radial scar | ~2 | ~12%–15% at 20 y |
| ADH or ALH | ~4 | ~15%–20% at 20 y |
| LCIS | ~10 | ~1% per y;<br>~20%–25% at 20 y |

Degnim AC, King TA. Surgical management of high-risk breast lesions. Surg Clin North Am. 2013 Apr;93(2):329-40. doi: 10.1016/j.suc.2012.12.005. Epub 2013 Feb 8.

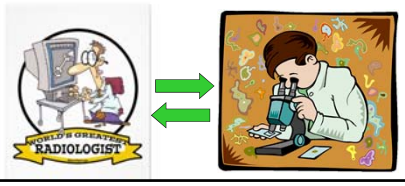
## What is an Upgrade?

- Defined as the rate at which a high risk lesion seen on core needle biopsy (CNB) is found to be associated with a "worse" diagnosis on a larger surgical excision.

"Worse" Diagnosis
Ductal Carcinoma In-Situ
Invasive Ductal Carcinoma
Invasive Lobular Carcinoma

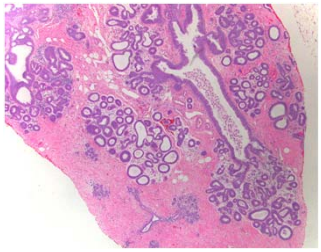
## Radiologic Pathologic Correlation is KEY

- Was the lesion adequately sampled?
- Is there an associated un-sampled mass?
- Is the lesion gone after biopsy?



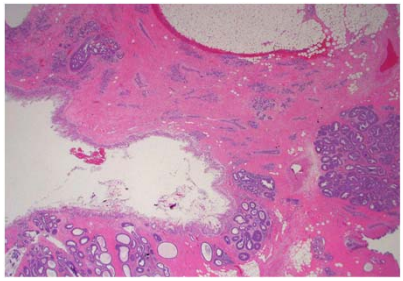
## Columnar Cell Lesions

- Columnar Cell Change
- Columnar Cell Hyperplasia
- Flat Epithelial Atypia



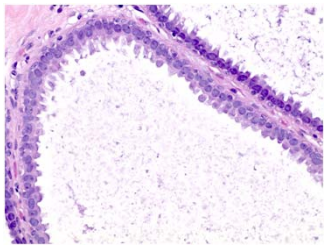
## Columnar Cell Lesions

- Seen more and more frequently with sensitive mammographic screening



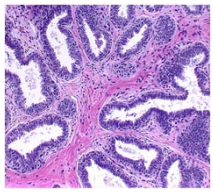
## Columnar Cell Change

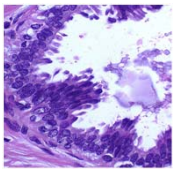
- Dilated acini lined by columnar cells arranged perpendicularly to the basement membrane
- Luminal secretions and calcifications
- Apical snouts



## Columnar Cell Hyperplasia

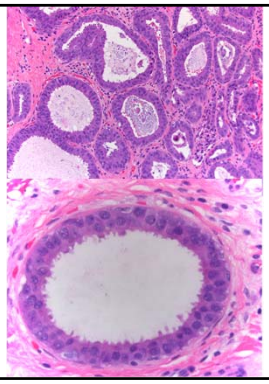
- Distended acini lined by cells arranged perpendicularly to the basement membrane with multilayer piling up of nuclei.
- Luminal secretions and calcifications
- Apical Snouts
- Irregular luminal contour





## Flat Epithelial Atypia

- Distended acini with MONOTONOUS cuboidal to columnar epithelium
- Luminal secretions and calcifications
- Apical snouts



## Management of Columnar Cell Lesions

- On CNB:
  - No excision for CCC and CCH (no atypia).
  - FEA management evolving
    - Imaging features of concern (distortion or mass)
    - Residual Calcifications
  - Careful evaluation for other lesions
  - If no other lesions radiographically, can leave alone
- Excision:
  - No further treatment if Columnar Cell Lesion with or without atypia
  - No margin reporting

Calhoun, Surg Pathol Clin. 2018 Mar;11(1):1-16.

## Subsequent Breast Cancer Risk?

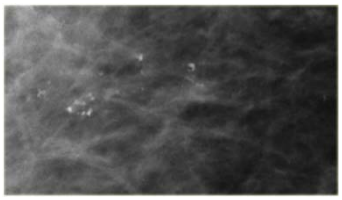
- Columnar Cell Lesions overall have little to no elevation in breast cancer risk beyond other proliferative lesions without atypia
- CCLs often associated with Atypical Hyperplasia
- Low grade invasive carcinomas, tubular carcinomas, lobular carcinomas often associated with CCLs

Said SM, Visscher DW, Nassar A, Frank RD, Vierkant RA, Frost MH, Ghosh K, Radisky DC, Hartmann LC, Degnim AC. Flat epithelial atypia and risk of breast cancer: A Mayo cohort study. Cancer. 2015 May 15;121(10)

Aroner SA, Collins LC, Schnitt SJ, Connolly JL, Colditz GA, Tamimi RM. Columnar cell lesions and subsequent breast cancer risk: a nested case-control study. Breast Cancer Res. 2010;12(4)

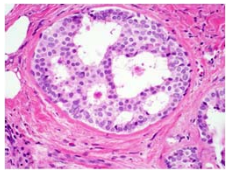
## Atypical Ductal Hyperplasia

- Often in CNB for calcifications
- Must be excised if found on CNB to exclude DCIS and Invasive carcinoma
- Unable to find a group that doesn't need excision- can't exclude a worse lesion



## Atypical Ductal Hyperplasia

- Neoplastic cells, round, monomorphic nuclei with architectural atypia
- Either incompletely involving the affected spaces
- Or if completely involved, there are fewer than 2 ducts involved or the area is less than or equal to 2 mm*



## *Marked Atypical Ductal Hyperplasia
## Atypical Ductal Proliferation, worrisome for DCIS

- 3 mm or less of lesion with low (to intermediate) grade nuclei
- Pathologists need to be CONSERVATIVE on the core!!!!
- "The single most problematic area of breast pathology"
- Radiation oncologists may still radiate any diagnosis of DCIS
  - Evolving…

## ADH…The Risk

- 3-5 fold increase in breast cancer risk across multiple studies
- A non-obligate breast cancer precursor
- Low grade invasive carcinomas, tubular carcinomas, lobular carcinomas often associated with ADH

Clinicopathologic Features of Breast Cancers that Develop in Women with Previous Benign Breast Disease Daniel W. Visscher et Cancer. 2016 Feb 1; 122(3): 378–385.

## Need Excision if on CNB?

- YES, in US
- Not so in Europe
- Paradoxically, trials begun for active surveillance of LG DCIS but not ADH

Upgrade rates to cancer for various lesions found on percutaneous breast biopsy

| Lesions on Core Biopsy | Upgrade Rate % | N | Article, Year |
|---|---|---|---|
| ADH | 13 | 5/40 | Burak et al,[18] 2000 |
| | 17 | 11/65 | Winchester et al,[7] 2003 |
| | 12 | 9/78 | Sohn et al,[20] 2007 |
| | 21 | 22/104 | Jackman et al,[5] 2002 |
| | 31 | 132/422 | Deshaies et al,[19] 2011 |

Upgrade Rate: 10-20%

May be select patients don't need excision…

Allison KH, Eby PR, Kohr J, DeMartini WB, Lehman CD. Atypical ductal hyperplasia on vacuum-assisted breast biopsy: suspicion for ductal carcinoma in situ can stratify patients at high risk for upgrade. Hum Pathol. 2011 Jan;42(1):41-50.

## ADH on Excision

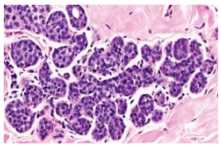
- If most significant lesion, no further management
- No inclusion of margin status
- Pathologists worry about this and get levels
- Clinical judgement if near a margin
  - May represent a larger lesion
  - May suggest re-excision in comment

## Classic Lobular In-Situ Neoplasia

- Atypical Lobular Hyperplasia (ALH) and Lobular In-Situ Carcinoma (LCIS)
- In-situ proliferation of atypical low grade cells lacking E-cadherin expression
- ALH and LCIS differ in extent of involvement

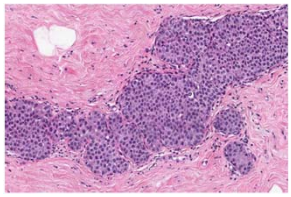
## Atypical Lobular Hyperplasia

- Spectrum with LCIS
- Similar genetic alterations
- Acini not expanded
- < 50% of Acini Involved of TLDU
- 4-5x increase risk of breast cancer



## LCIS

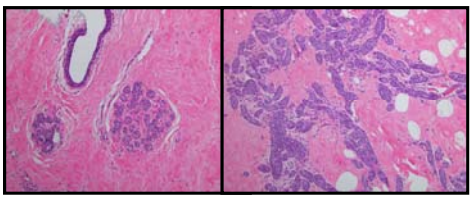
- Both a risk factor and non-obligate precursor
  - 9-10x risk general population
- Managed as a benign lesion
- Not staged at pTis in AJCC 8th edition
- Does not require complete removal or reporting of margins
- May use hormonal chemoprevention
- Observation after CNB may be reasonable if concordant



Atkins KA et al Radiology. 2013;269( 2): 340– 347.
Niell B AJR Am J Roentgenol. 2012;199( 4): 929– 935.
Hwang H Mod Pathol. 2008;21( 10): 1208– 1216. Rendi Ann Surg Oncol. 2012;19( 3): 914– 921.
Murray MP, Cancer. 2013;119( 5): 1073– 1079.
Cangiarella J Arch Pathol Lab Med. 2008;132( 6): 979– 983.

## Extent of ALH/LCIS Matters

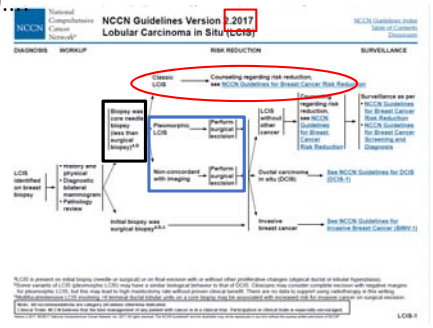
< 4 TDLUs involved by lobular neoplasia, upgrade rate = 0%



Focal Extensive

Rendi MH, Dintzis SM, Lehman CD, Calhoun KE, Allison KH. Lobular in-situ neoplasia on breast core needle biopsy: imaging indication and pathologic extent can identify which patients require excisional biopsy. Ann Surg Oncol. 2012

## 2020…

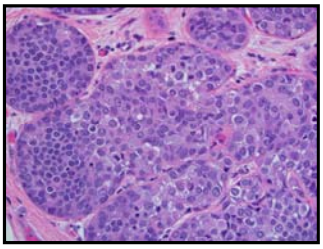



May follow ALH/LCIS if imaging is concordant and not pleomorphic

## Pleomorphic Lobular Caricnoma In-Situ (PLCIS)

- Distinct form of LCIS
- 45% of cases of PLCIS are associated with invasive carcinoma
- Should **always** be excised if seen on CNB

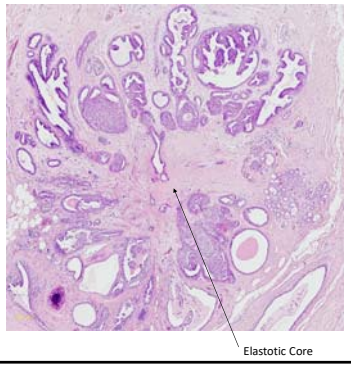
## Pleomorphic LCIS



## Radial Scar/Complex Sclerosing Lesion

- Benign glands entrapped and distorted by fibrous or fibroelastotic stroma.
- Terms often used interchangeably.

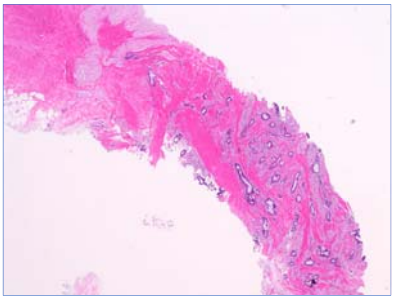
## Radial Scar/CSL




## Significance of Radial Scar on CNB?

- Multiple studies upgrade rates 0-43%
- No evidence that they are pre-malignant (don't evolve into CA)
- But can be associated with atypia
- Do co-exist with with cancers at a higher frequency than chance
  - Cancers typically exist at the periphery of scar
- No increased future risk if radial scar alone

## Radial Scar/Complex Sclerosing Lesion with Carcinoma



## What to do with Radial Scar on CNB?

- Controversial, no clear consensus
- When cancer found on excision, often the needle biopsy missed the cancer by 6mm or less
- More tissue at core relative to radiologic size of lesion is better
- "No magic core biopsy volume that will ensure absence of upgrade"

**Radial Scars of the Breast Encountered at Core Biopsy: Review of Histologic, Imaging, and Management Considerations**

Michael A. Cohen[1] and Mary S. Newell[1]

## Radial Scar: Need for excision if on CNB?

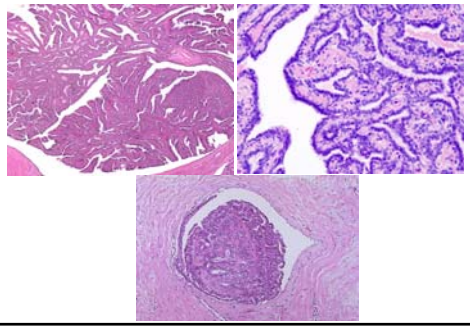
- Depends….
  - If incidental or of very small size, probably not
  - If presents as architectural distortion without an associated mass and no atypia, probably not
  - If large (>1.0 cm) or presents as mass, maybe yes
  - If any epithelial atypia present, yes

Upgrade Rate: < 5%
Upgrade Rate: 8-43%

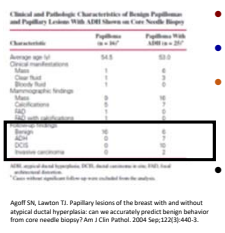
## Intraductal Papilloma

- Epithelial proliferation often involving large central duct with arborizing fibrovascular cores.
- Papillary fronds are lined by at least two epithelial cell layers but can have more extensive proliferation.
- Can be peripheral involving TDLU.
- The concern is there is associated atypical epithelium (ADH or DCIS)

## Intraductal Papilloma



## Need for Excision if Intraductal Papilloma without Atypia on CNB



Agoff SN, Lawton TJ. Papillary lesions of the breast with and without atypical ductal hyperplasia: can we accurately predict benign behavior from core needle biopsy? Am J Clin Pathol. 2004 Sep;122(3):440-3.

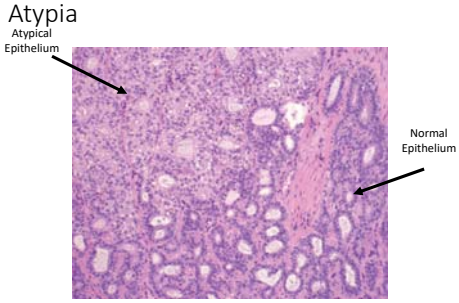
- Evolving area, varies between institutions
- Size and symptomatic
- Risk factors: > 1cm, > 50 yo, > 3 cm from nipple, mammographic lesion with calcifications
- Need careful rad/path concordance

Nakhlis et al 2015

## Papilloma Comment

- "Please ensure the mass lesion seen on radiologic studies was adequately sampled"

Intraductal Papilloma with Atypia




## Any Papilloma with Atypia (or Atypical Papillary Lesion) MUST BE EXCISED

Dx: Atypical papillary lesion, favor encysted papillary carcinoma
Atypical papillary lesion, favor papillary DCIS
Atypical papillary lesion, cannot exclude invasive carcinoma, NOS

**Trends in frequency and outcome of high-risk breast lesions at core needle biopsy in women recalled at biennial screening mammography, a multiinstitutional study**

Jacky D. Luiten[1,2], Bram Korte[3], Adri C. Voogd[4,5], Willem Vreuls[6], Ernest J.T. Luiten[7], Luc J. Strobbe[8], Matthieu J.C.M. Rutten[9], Menno L. Plaisier[10], Paul N. Lohle[11], Marianne J.H. Hooijen[12], Vivianne C.G. Tjan-Heijnen[2,13] and Lucien E.M. Duijm[14,15]

Int. J. Cancer: 00, 00–00 (2019) © 2019 The Authors. *International Journal of Cancer* p

- Reviewed management and outcome of high-risk breast lesions in a large screened population over 6 years
- Recall rate and number of patients undergoing CNB remained stable
- Number of patients with high risk lesion on CNB TRIPLED
- Rate of excision tripled over this time
- Proportion of surgical excisions with DCIS or Invasive Carcinoma did NOT increase
- Increase in surgical excisions with benign outcomes

More High Risk Lesions Diagnosed on CNB, more excisions per population screened, no change in percentage of malignant diagnosis on excision

Why this increase in High Risk Lesions?

Most High Risk Lesions were associated with masses or calcifications
- While total masses and calcs recalled went down

Saw an increase in asymmetries

?Radiologists getting more specific ?

? Increased pathologist awareness of FEA/ADH ?

Most upgrades from high risk lesion were to LOW GRADE DCIS, or LOW GRADE INVASIVE CARCINOMA

Table 5. Type and grading of malignancy in women with high-risk lesions at core needle biopsy

| | Ductal carcinoma *in situ* | | | Invasive cancer[1] | | |
|---|---|---|---|---|---|---|
| Histology at percutaneous biopsy, *n* | Low | Intermediate | High | I | II | III |
| Papillary lesion | 10 | 3 | 1 | 2 | 1 | 2 |
| Columnar cell lesion, flat epithelial atypia | 1 | | | | | |
| Atypical ductal hyperplasia | 10 | 8 | | 2 | 2 | |
| Radial scar, complex sclerosing lesion | | | | 1 | | |
| Combination of high-risk lesions | 3 | | | | | |
| Other | | | | 1 | | 2 |
| Total | 24 | 11 | 1 | 6 | 3 | 4 |

[1]Bloom and Richardson.

49 upgrades (36 to DCIS, 13 to Invasive Carcinoma)

71% of High Risk Lesion on CNB is Benign at Excision

14% of High Risk Lesion on CNB is LG DCIS at Excision

If we start watching LG DCIS, then 85% of high risk lesions may not need excision at all

What does this tell us?

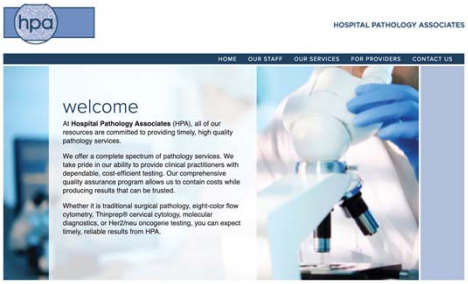
- We may be diagnosing (and subsequently excising) more high risk breast lesions
- The upgrade rate remains relatively stable for high risk lesions
- More excisions = unnecessary surgery and more difficulty in future screenings

Lots more studies forthcoming to better inform us what lesion and in which patient actually needs excision

One of the first studies to evaluate trends of detection of high risk lesions

High Risk Breast Lesions…

- Management guidelines not yet completely defined for several high risk lesions
- Individualized care with ***multidisciplinary input*** is essential in these cases
  - Radiologic/pathologic concordance must occur
  - Surgery, medical oncology, radiology, and pathology must all talk to one another
  - If you are unsure of what your pathologist saw, CALL.

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