"Patologia neoplastica borderline della mammella"

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B3 Lesion of uncertain malignant potential

This category mainly consists of lesions which **may provide benign histology on CB**, but either are known to
•show **heterogeneity** or
•to have an **increased risk (albeit low) of associated malignancy.**

Nonmalignant lesions in breast core needle biopsies: to excise or not to excise?

JacobsT, Connolly J, Schnitt,SJ
Am J Surg Pathol *26(9): 1095–1110, 2002*

- columnar cell lesions
- atypical ductal hyperplasia
- lobular neoplasia (atypical lobular hyperplasia and lobular carcinoma in situ)

- papillary lesions
- radial scars

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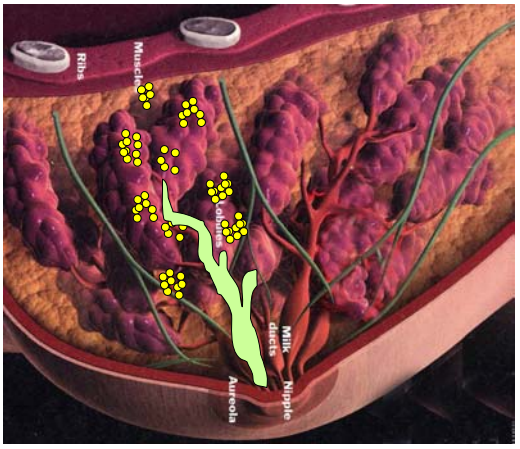
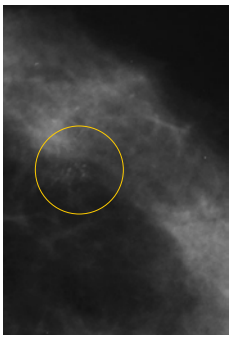
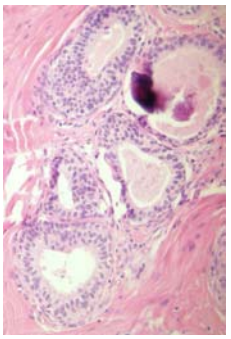
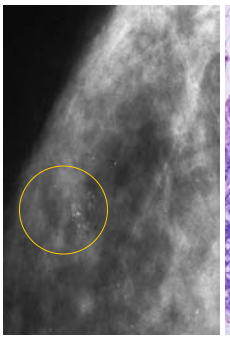
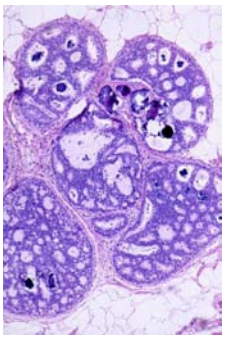
sedi di origine

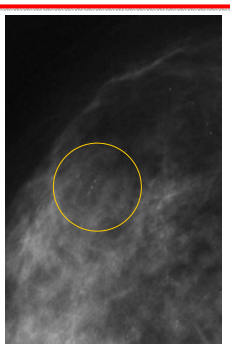


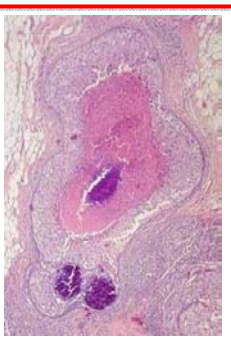


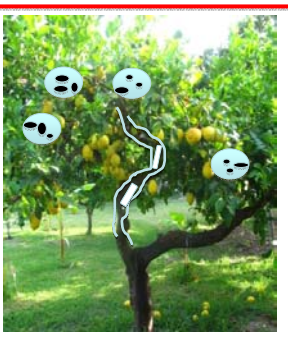


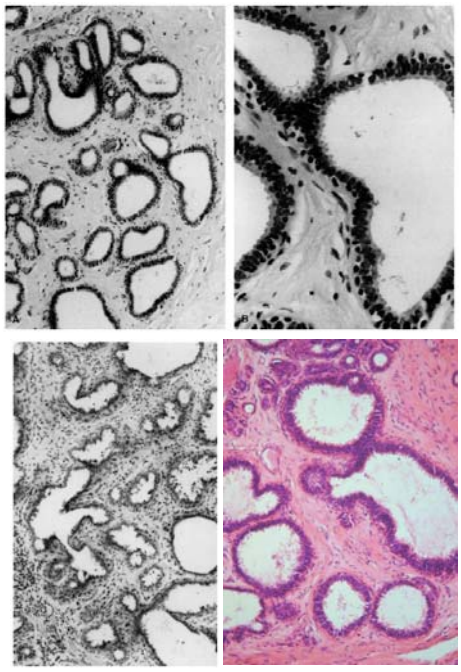












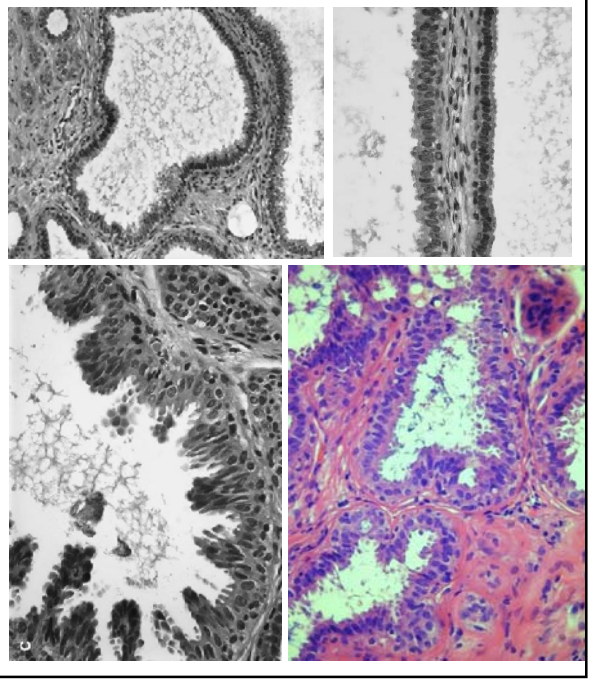
Am J Surg Pathol. 1998 Dec;22(12):1521-7.

Columnar alteration of lobules.
This lesion is characterized by an enlarged lobule with slightly dilated acini (A).
The acini are lined by a single layer of columnar epithelial cells with elongated nuclei (B).
Apical snout

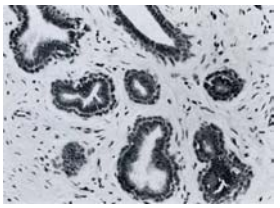
Advances in Anatomic Pathology 10: 113–124 (2003)

Columnar cell change

Columnar cell hyperplasia

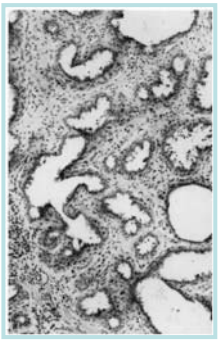


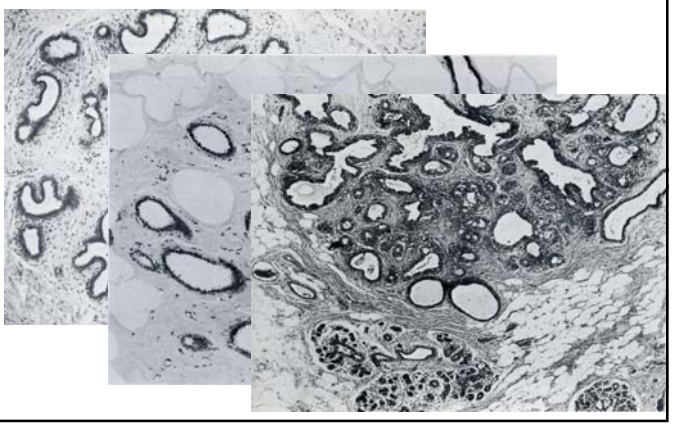
Bonser, Dossett and Jull. 1961
Columnar metaplasia

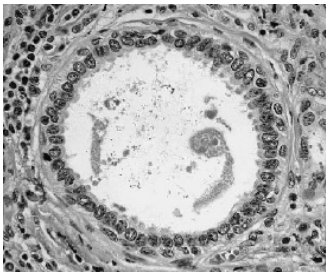


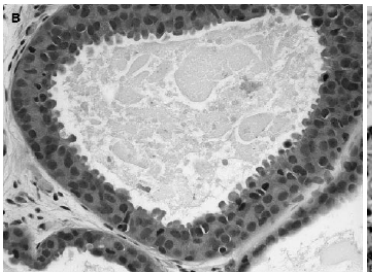
Azzopardi 1979. Blunt duct adenosis

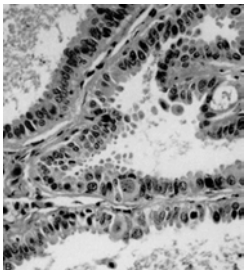
- BDA with response of the specific stroma (organoid)
- Non-organoid BDA
- Microcystic BDA



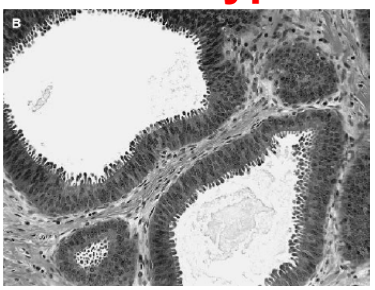


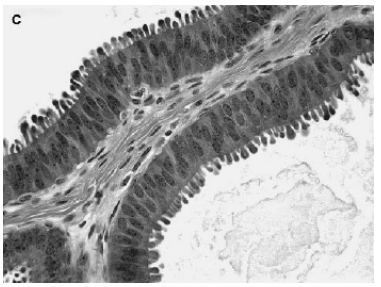






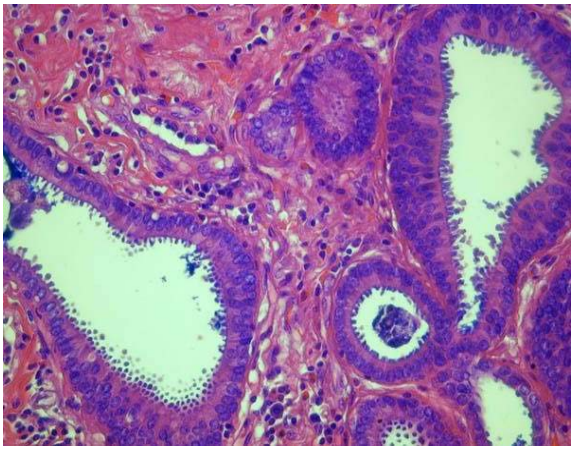
Columnar cell lesion with atypia/flat epitheliel atypia/FEA

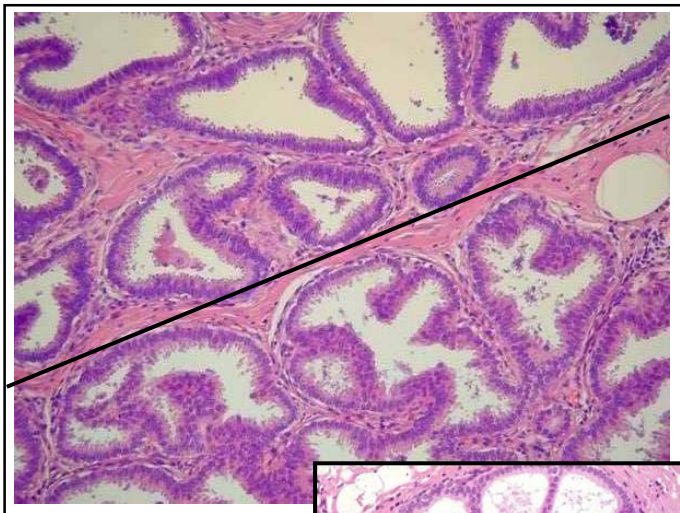




Advances in Anatomic Pathology
Vol. 10, No. 3, pp. 113–124 (2003)

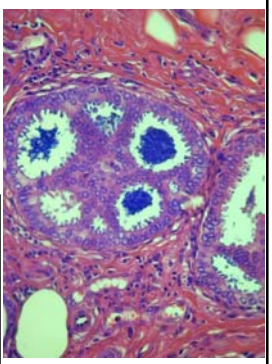
Flat epithelial atypia

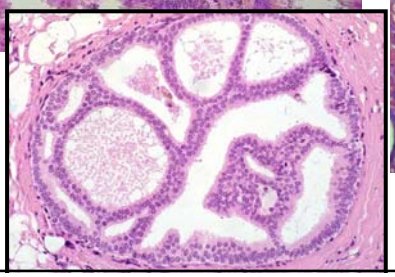




FEA/DIN1A

ADH/DIN1B



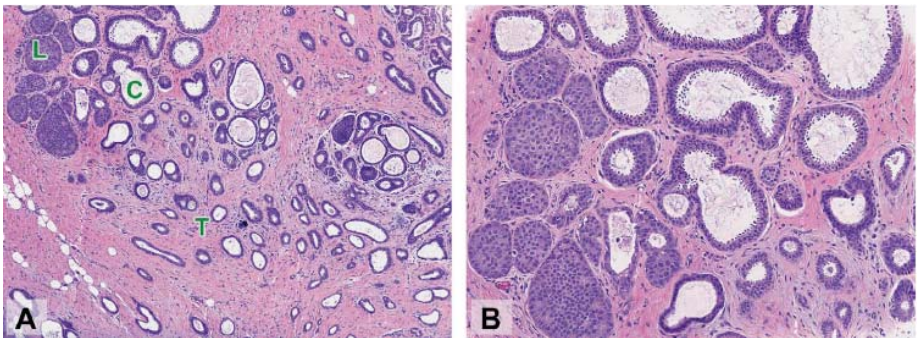


DCIS/DIN1C

The "Rosen Triad":
Tubular Carcinoma, Lobular Carcinoma In Situ, and Columnar Cell Lesions

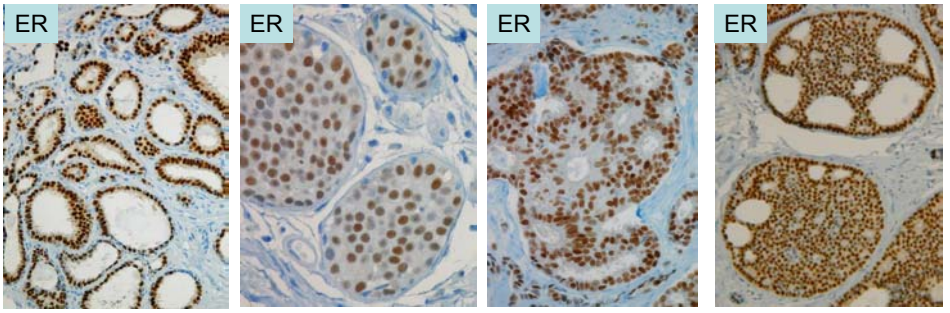
Suzanne M. Brandt, MD, Gloria Q. Young, MD, and Syed A. Hoda, MD

Adv Anat Pathol. 2008 May;15(3):140-6



IMMUNOPHENOTYPE

1. High ER expresion
2. HER2 negative
3. Low proliferation

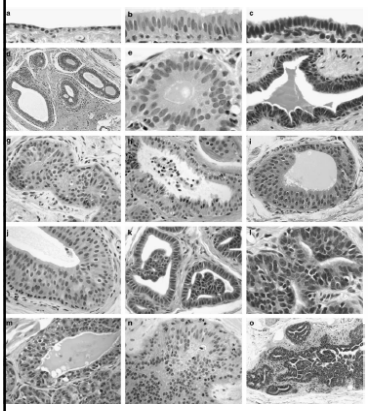


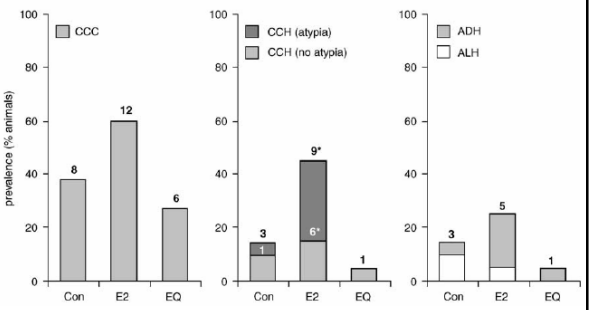
FEA/DIN1a **CLIS/LIN** **ADH/DIN1b** **DCIS/DIN1c**

Estrogen effects on epithelial proliferation and benign proliferative lesions in the postmenopausal primate mammary gland

Charles E Wood, Joy M Hester, Susan E Appt, Kim R Geisinger and J Mark Cline

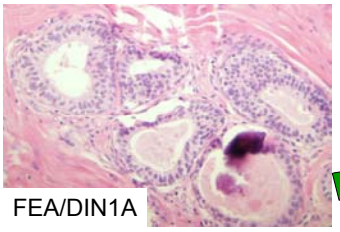
Laboratory Investigation (2008) 88, 938–948



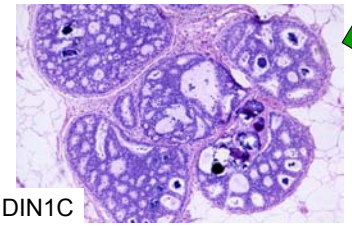


J Clin Oncol 27:5138-5143. 2009

Estrogen-progestagen menopausal hormone therapy (EP-MHT) and breast cancer risk varies according to the delay between menopause onset and treatment initiation. **When initiated close to menopause, even short durations of use are associated with an increased breast cancer risk.**



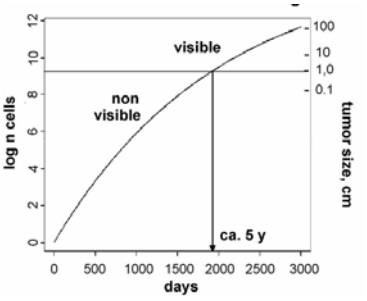
FEA/DIN1A



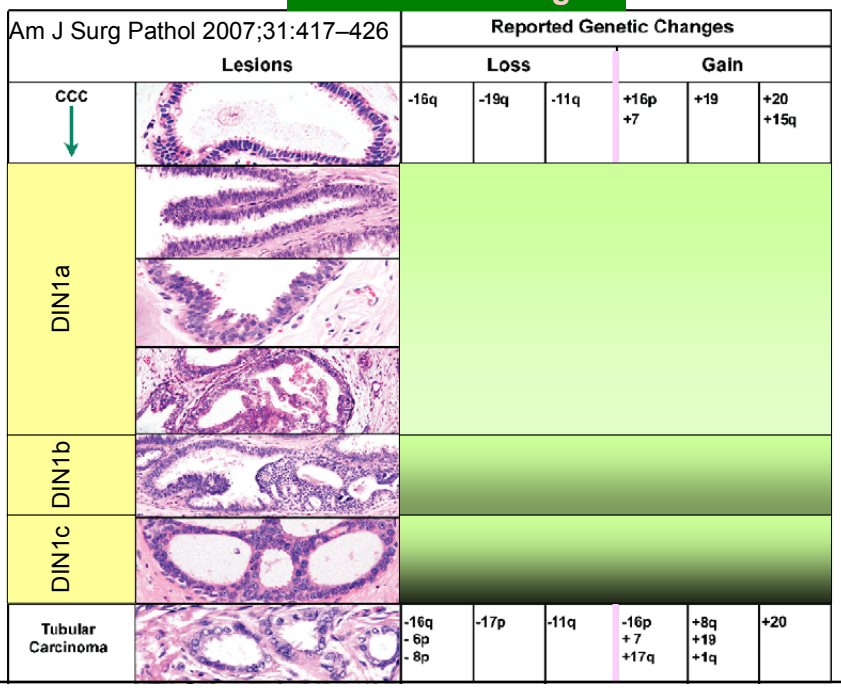
DIN1C

Maturitas 65 (2010) 183–189

HRT is more likely to be a tumor promoter than a de novo-inducer of breast cancers



Continuum biologico



Hormonal therapy for menopause and breast-cancer risk by histological type: a cohort study and meta-analysis.

Lancet Oncol. 2006 Nov;7(11):910-8

1.031.224 postmenopausal women recruited in 1996-2001

14 102 breast cancers

RR in current users compared with never users of hormone therapy

INVASIVE CARCINOMA		
lobular	2.25	(95% CI 2.00-2.52)
mixed ductal-lobular	2.13	(95% CI 1.68-2.70)
tubular cancers	2.66	(95% CI 2.16-3.28)
ductal	1.63	(95% CI 1.55-1.72)
mucinous cancers	1.58	(95% CI 1.08-2.31)
medullary cancer was not increased	0.74	(95% CI 0.43-1.28)
IN SITU CARCINOMA		
lobular carcinoma in situ	2.82	(95% CI 1.72-4.63)
Ductal carcinoma in situ	1.56	(95% CI 1.38-1.75)

($p<0.0001$)

Columnar cell lesions associated with breast calcifications on vacuum-assisted core biopsies: clinical, radiographic, and histological correlations

Rebecca Senetta[1], Pier Paolo Campanino[2], Giovanna Mariscotti[2], Sara Garberoglio[2], Lorenzo Daniele[1], Francesca Pennecchi[3], Luigia Macrì[1], Martino Bosco[1], Giovanni Gandini[2] and Anna Sapino[1]

Modern Pathology (2009) 1–8

HRT in 209 women of screening program

Yes	14 (18)
No	65 (82)

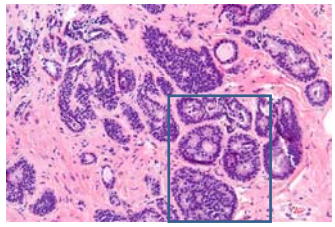
	CCLs	
	Atypical° (7cases)	*Benign* (7 cases)
HRT time exposure (range)	Median 5 years	Median 2 years

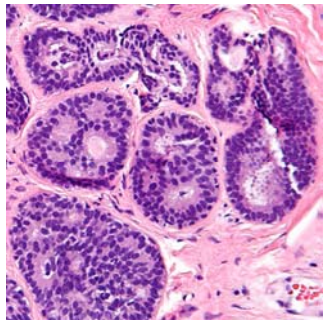
Women should be advised of the possible hormone dependency of CCLs.

ADH

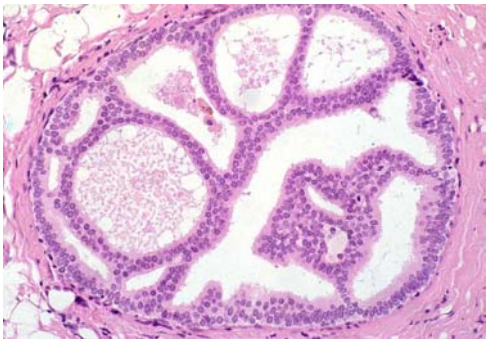
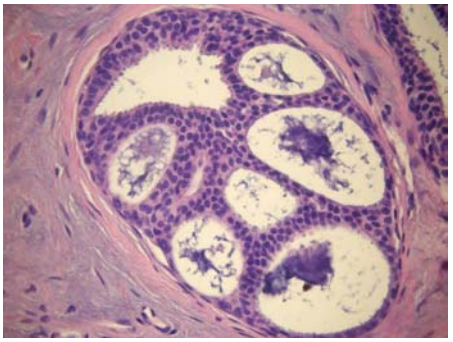
- Page's view that the cellular changes of DCIS are present but occupy less than 2 separate duct spaces is widely accepted
- Others use a 2 mm cut-off; a lesion less than 2 mm in maximum dimension being classified as ADH and a larger area as DCIS (Tavassoli 1992).
- Others mention the involvement of a single TDLU.

These criteria recognise essentially the same lesions. In essence, ADH is usually small and focal, measuring less than 2 to 3 mm. Larger foci are accepted if associated with a radial scar/complex sclerosing lesion or a papilloma.



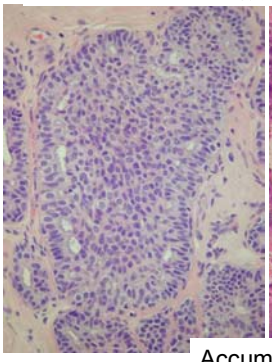
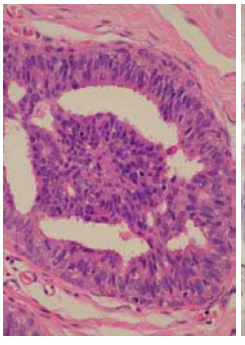
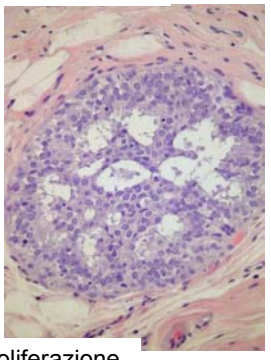


European Guidelines for quality assurance in breast cancer screening and diagnosis
Fourth edition- Supplement 2012

- ADH is formed from a **uniform** population of **small** or **medium-sized round, cuboidal or polygonal hyperchromatic** cells, which are **regularly arranged**.
- The nuclei are **evenly distributed** and may form a **rosette-like pattern**. Single small nucleoli only are present. **Mitoses**, particularly abnormal forms, **are infrequently seen**.
- **Geometric spaces** are noted and, in the **cribriform type**, the cells are arranged at right angles to the bridges formed. **Micropapillary** ADH is also recognised and a **solid pattern** may very rarely be seen.
- **Small foci of necrosis** may rarely be identified in ADH and do not indicate that the process should be classified as DCIS

http://www.breastpathology.info/Benign%20proliferative%20disease.html

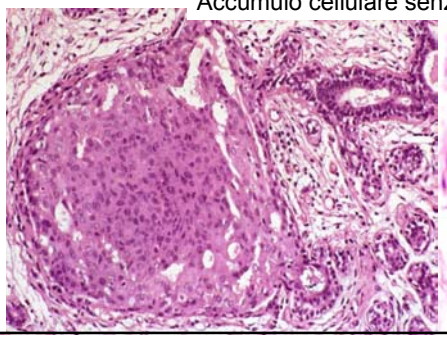
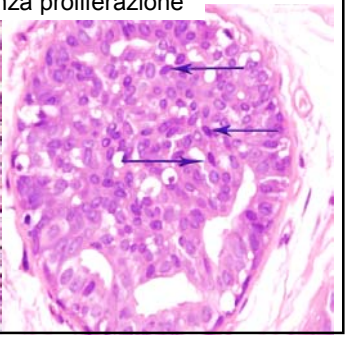
Accumulo cellulare senza proliferazione

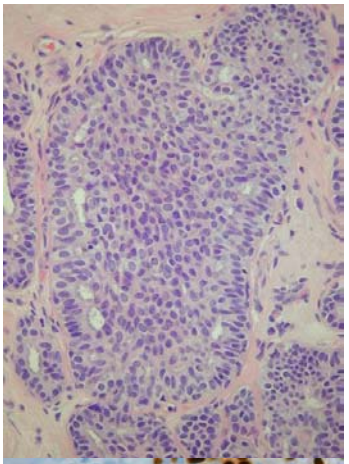
•Aspetto a corrente

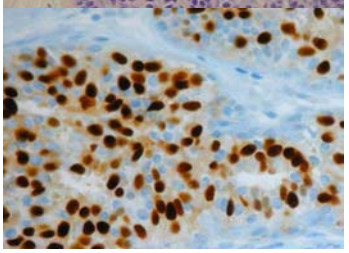
•Fenestrature periferiche

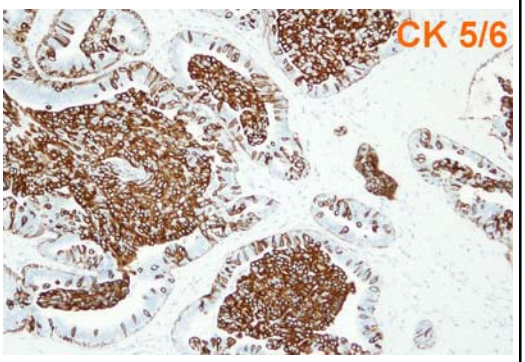
•Variabilità nucleare

•No mitosi





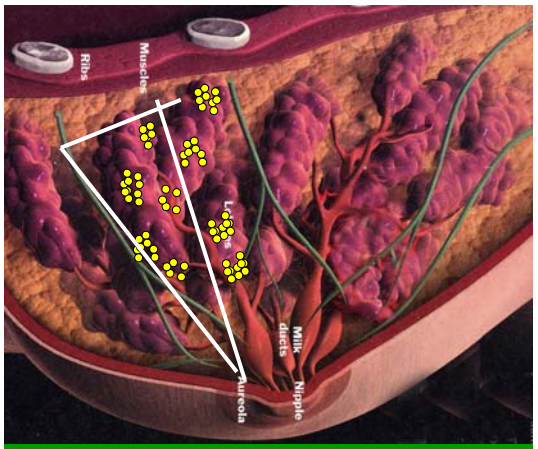


Hum Pathol. 2006;37:787-93.

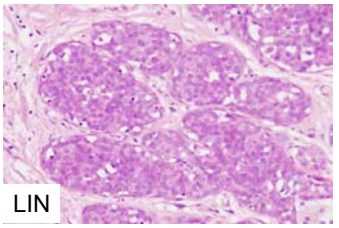
	UEH	ADH/low-grade DCIS
Architecture		
a. Fenestrations	Peripheral and irregular	Central and 'punched out
b. Streaming pattern	Present	Absent
c. Nuclei	Prominent overlapping	Minimal overlapping
Cellular features		
a. Cellular variation	Present	Monomorphic
b. Cell margins	Indistinct	Distinct
c. Nuclear variation	Present	Minimal
. Immunoprofile		
a. Cytokeratins	Mixed luminal and basal type (CK7, CK19, CK5/6, CK14)	Luminal type only (CK7, CK18, CK19)
b. Oestrogen receptor	Heterogeneous pattern	Homogeneous expression

ADH is a clonal process,
uniform phenotype and immunophenotype

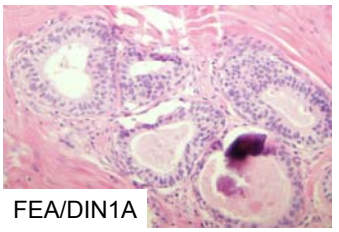
LIN1/2	CLIS
DIN1A	FEA
DIN1B	ADH
DIN1C	DCIS low grade



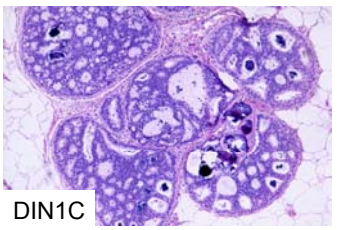
RESECTION MARGIN



LIN

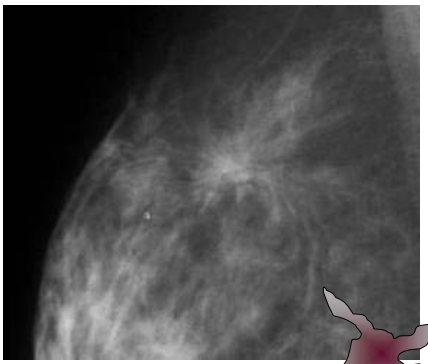


FEA/DIN1A

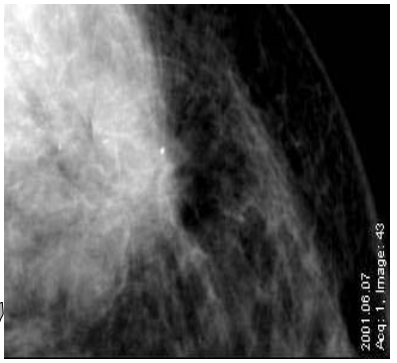


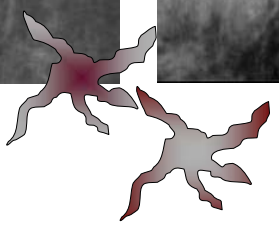
DIN1C

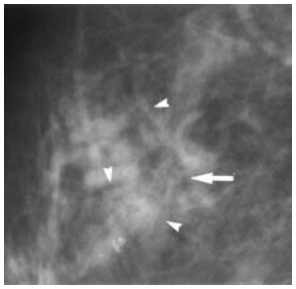
Lesione stellata



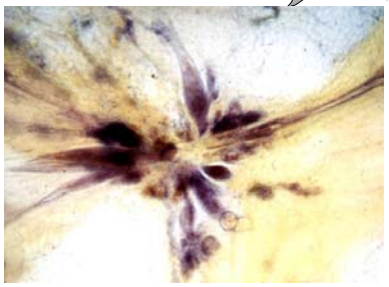
Distorsione architetturale

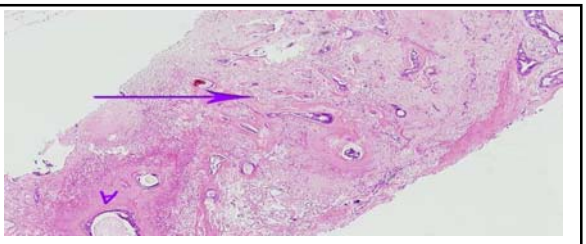


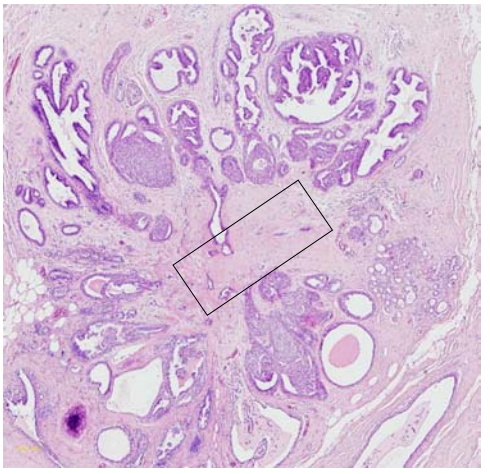


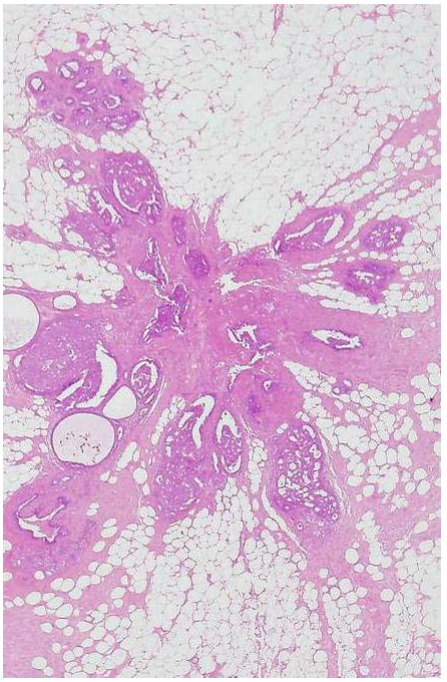


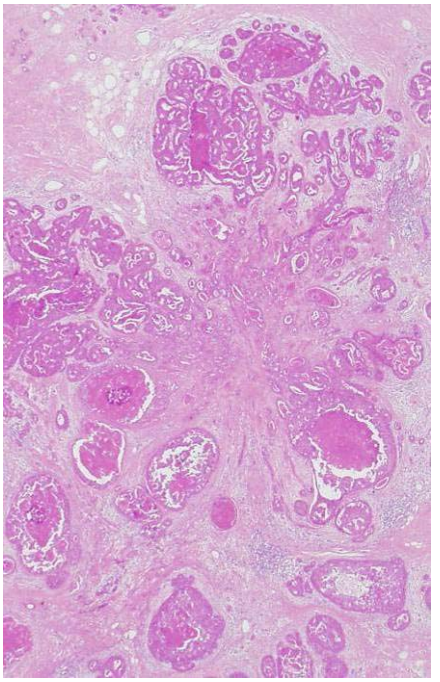
BLACK STAR









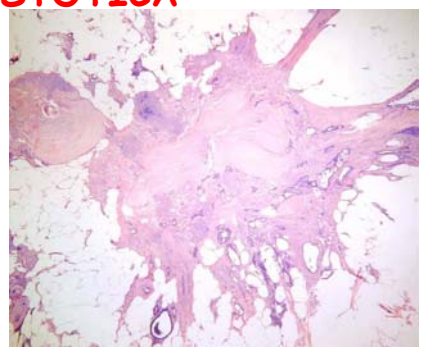


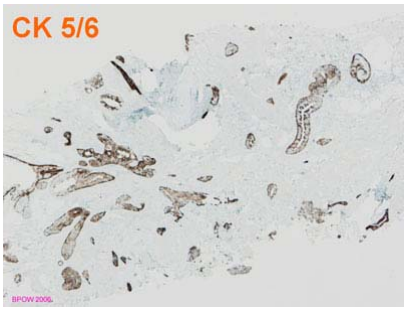
CICATRICE SCLERO-ELASTOTICA

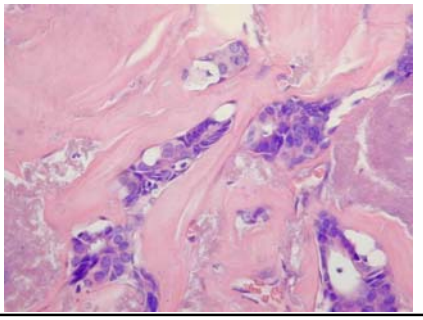
1- deposito di connettivo FIBRO-ELASTICO "cicatrice"

2- rari dotti con epitelio e mioepitelio inglobati

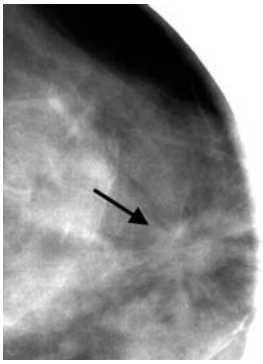
3- iperplasia o carcinoma in situ intorno alla cicatrice



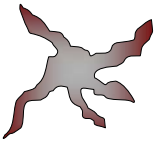


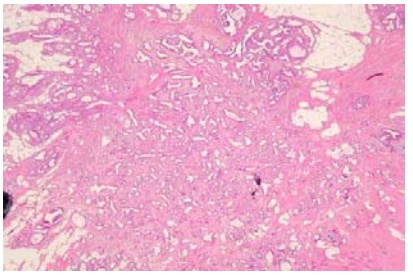


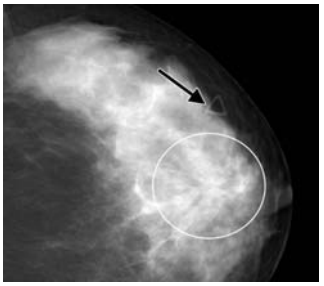
CARCINOMA TUBULARE

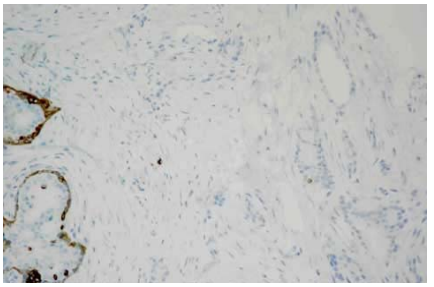


WHITE STAR

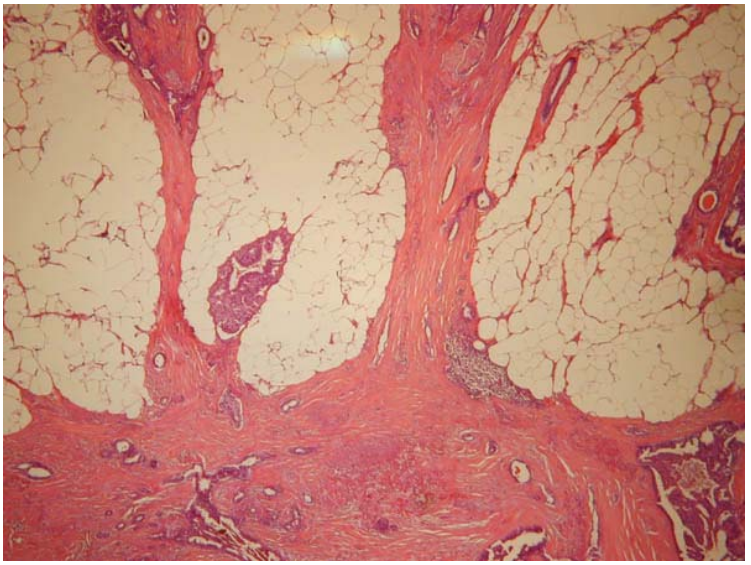


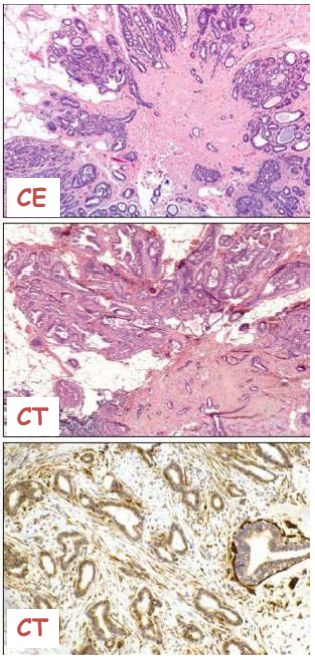


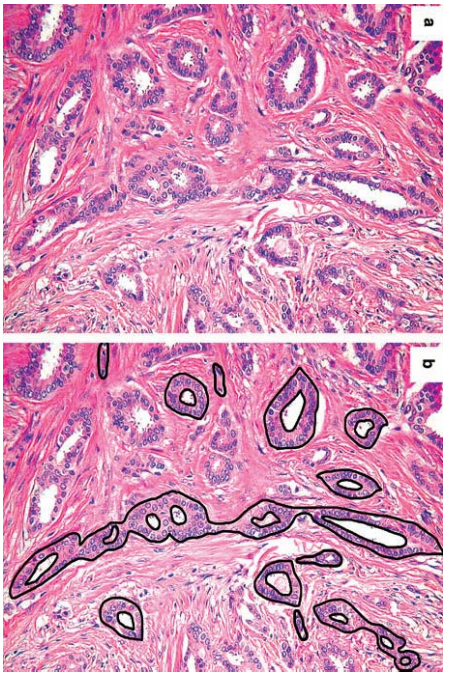




CK5/6

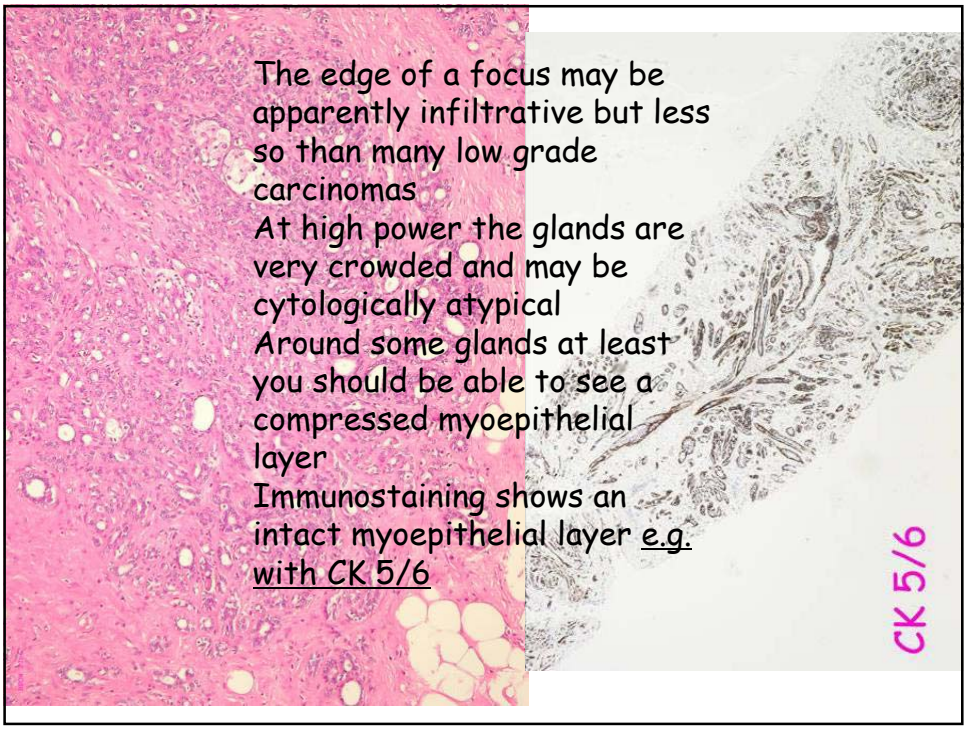



CE
CT
CT

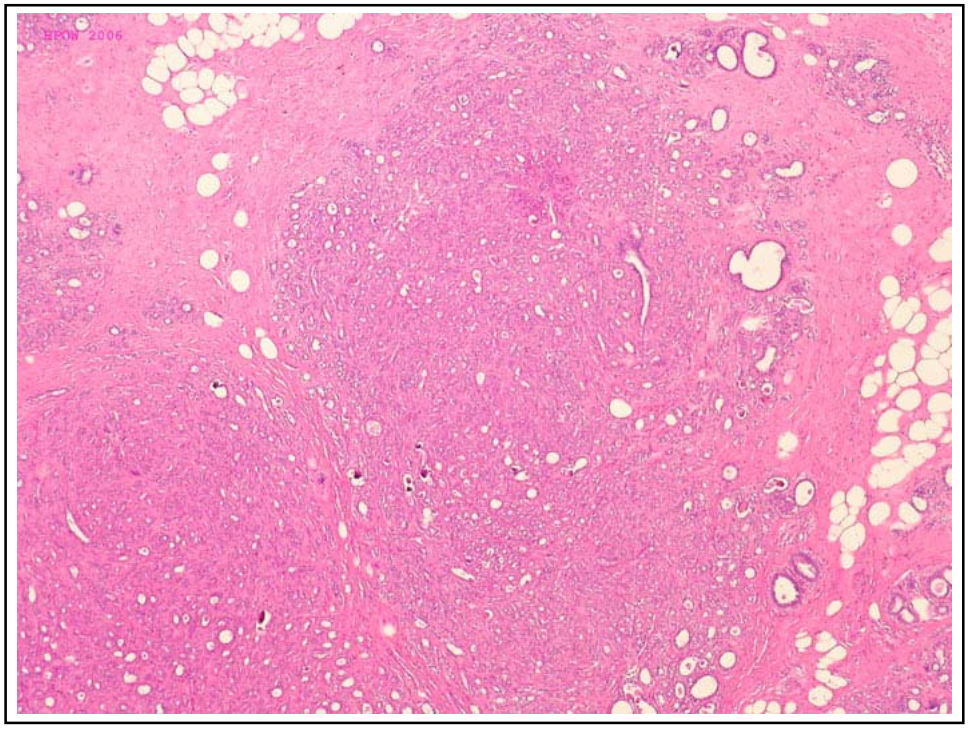

a
b

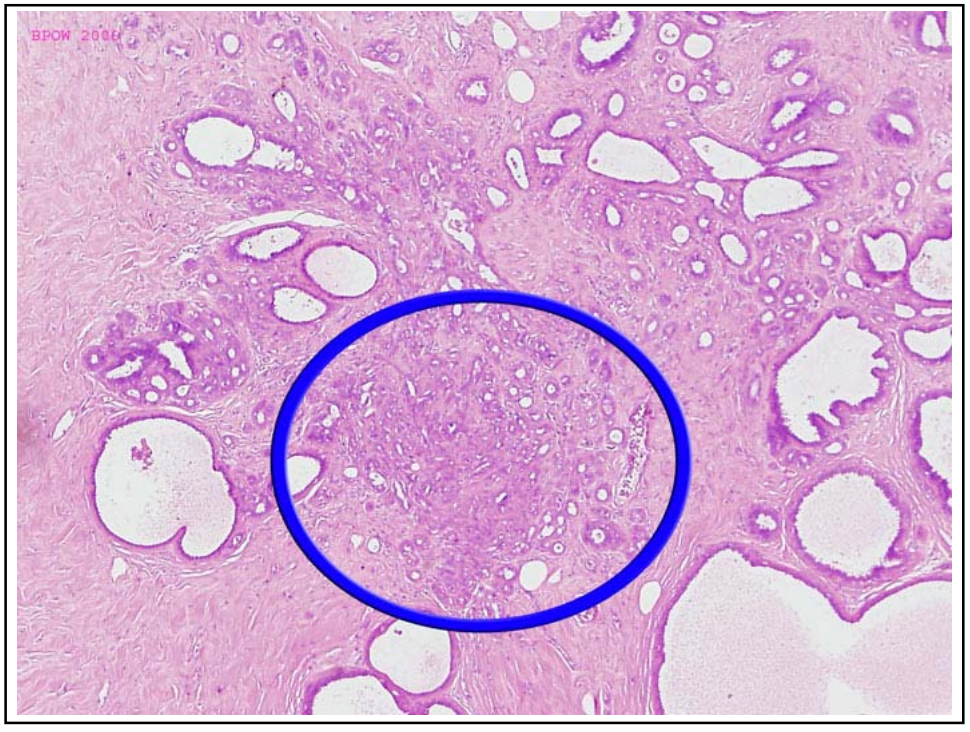
ADENOSI SCLEROSANTE

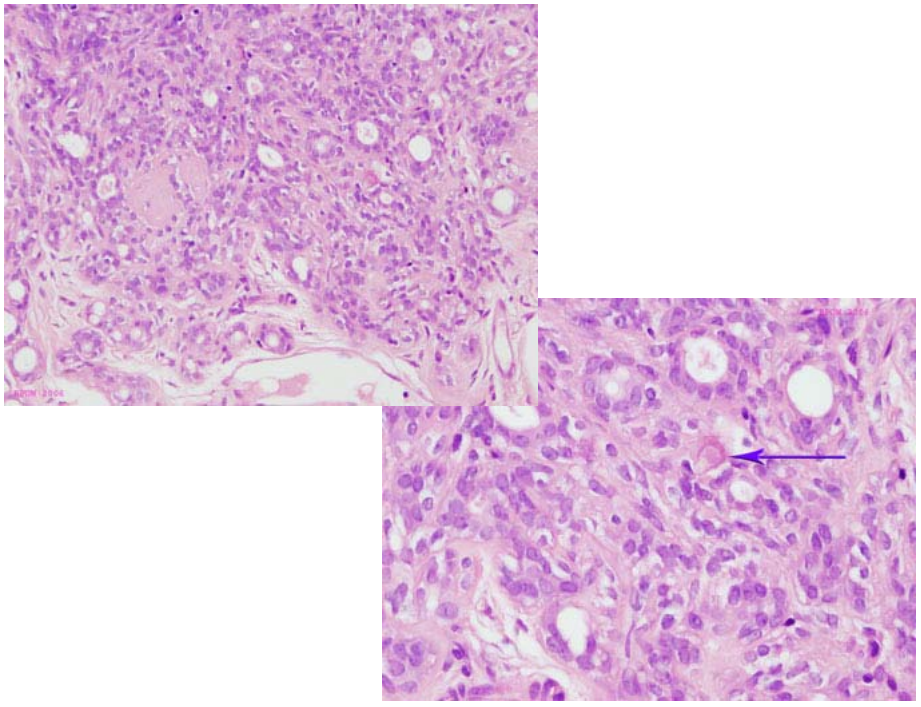
Usually incidental but may be a mass lesion
Often associated calcs - picked up on screening
May be confused with cancers histologically
Low power view critical to make correct diagnosis.....



The edge of a focus may be apparently infiltrative but less so than many low grade carcinomas
At high power the glands are very crowded and may be cytologically atypical
Around some glands at least you should be able to see a compressed myoepithelial layer
Immunostaining shows an intact myoepithelial layer e.g. with CK 5/6

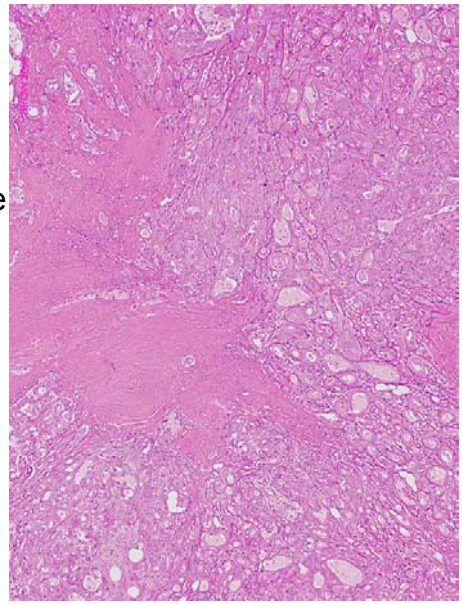

BPOW 2006

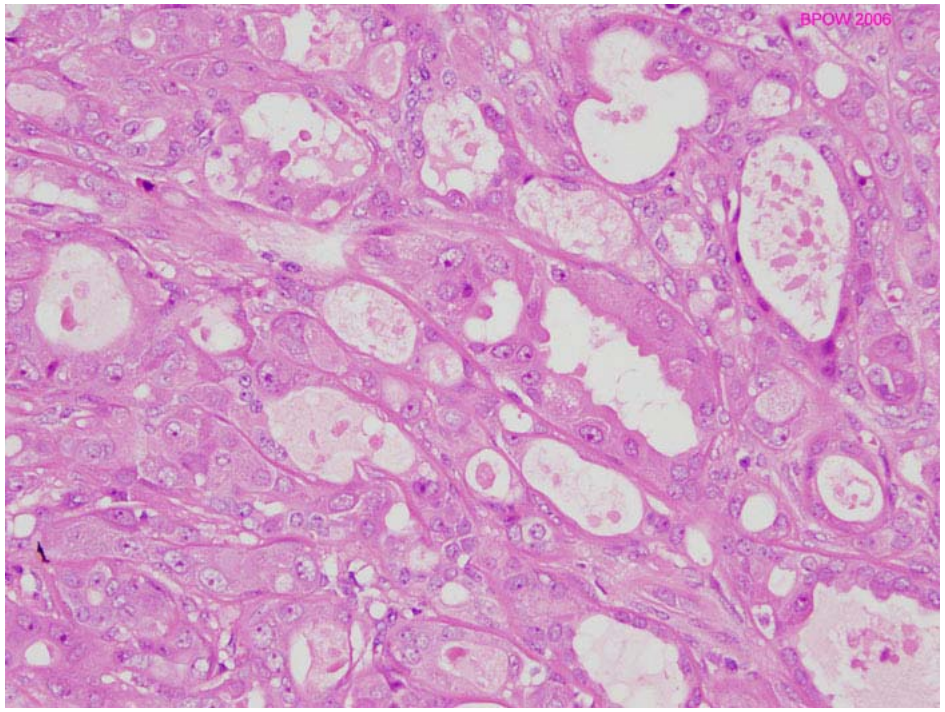

BPOW 2006



Atypical* apocrine *sclerosing lesion

Sclerosing adenosis lesion with superimposed apocrine metaplasia
Atypia may be moderately severe - distinction from apocrine DCIS (with lobular cancerisation) may be difficult
Immunostaining will demonstrate an intact myoepithelial layer and basement membrane
Follow up of patients showed no greater cancer risk than other atypical lesions

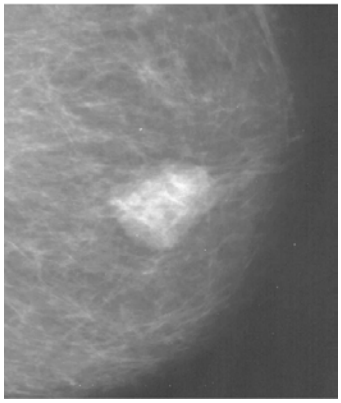




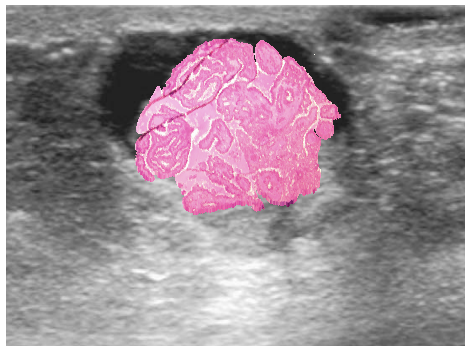
Radiological appearances of papillary breast lesions

Clinical Radiology (2008) 63, 1265e1273

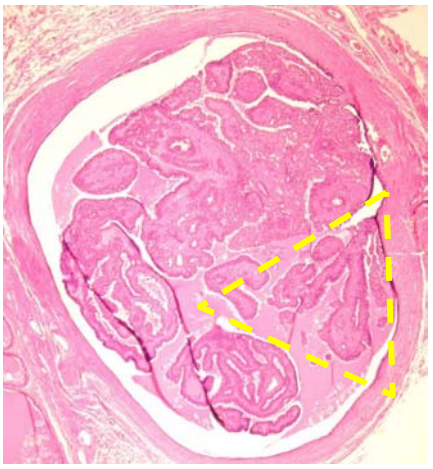
M.J. Brookes*, A.G. Bourke

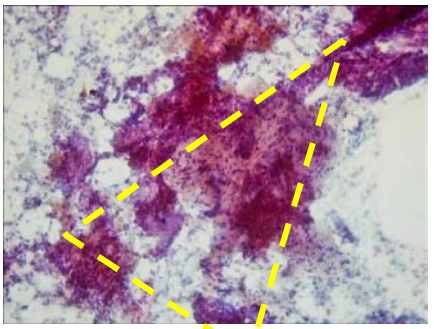


well-defined margins and a surrounding lucent "halo'



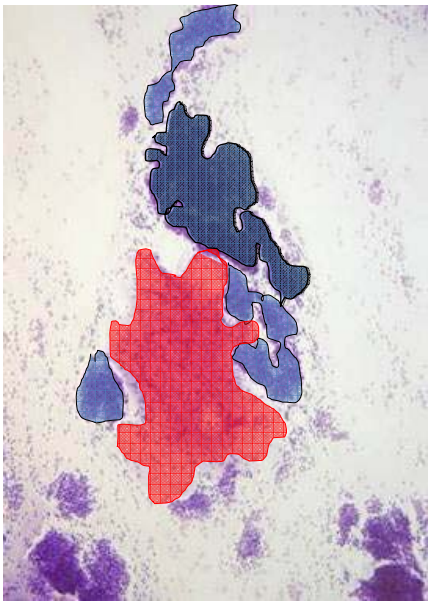
well-defined, ovoid mass, predominantly solid appearance, but with a cystic component marked posterior acoustic enhancement

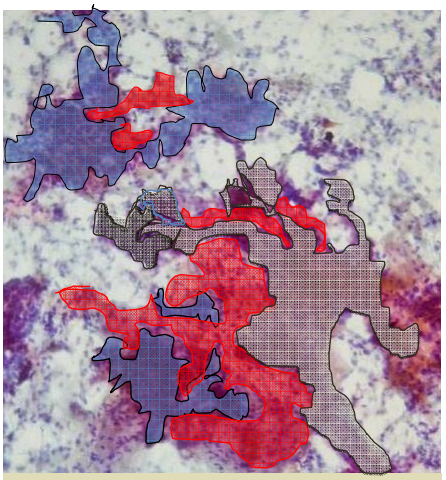




Background: debris +; histiocytes +; blood +;

Cellularity: +++ (poor if sclerotic);
Large 3D sheets: ++





Large 3D sheets , origami like folding

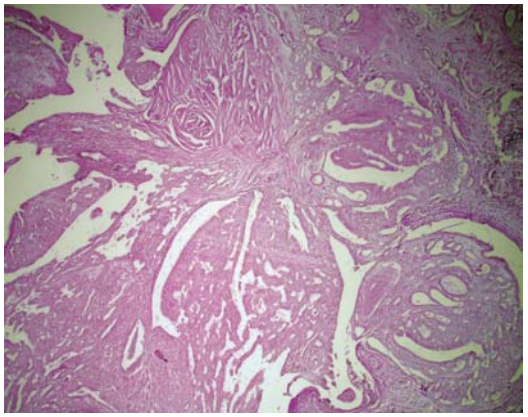
Fibrovascular cores: ++;

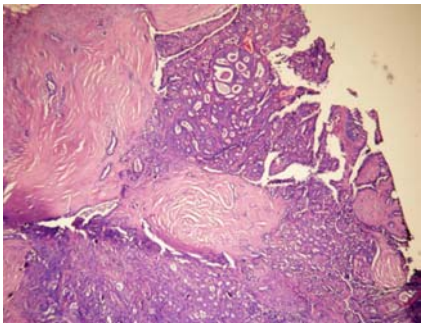
Cell clusters: ++
Single cells: ++; Myoepithelial cells: +
Histiocytes:++

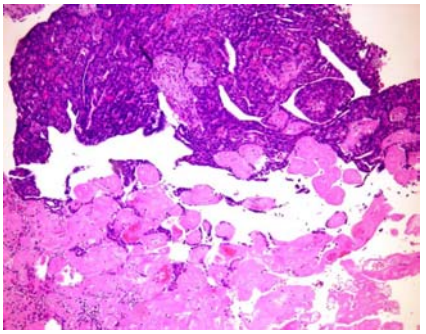
fibroadenoma

papillary lesion

Lesione sclerosante complessa



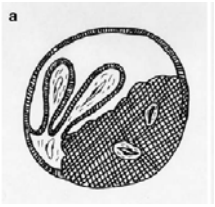


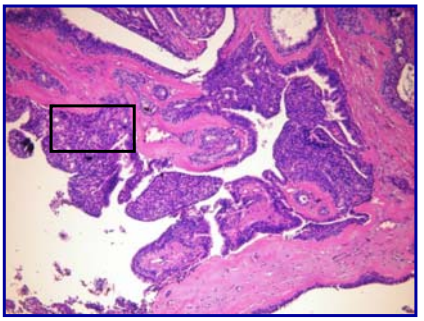


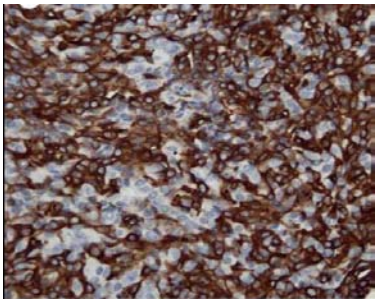
Virchows Arch (2003) 443:60

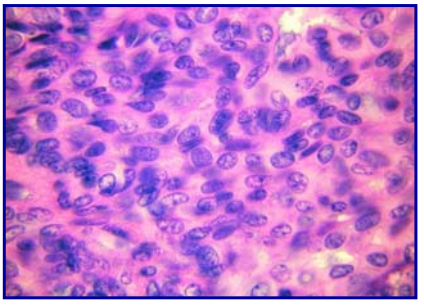
•Aree Solide

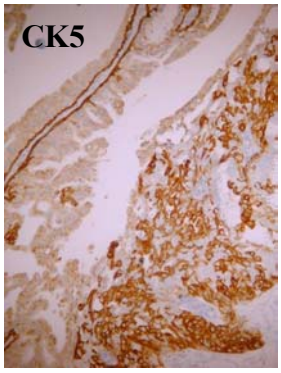
(iperplasia duttal atipica)

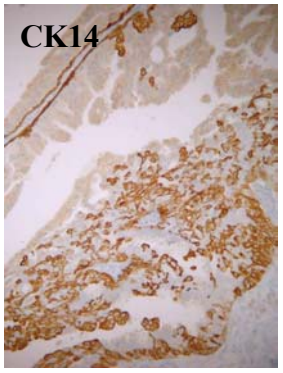


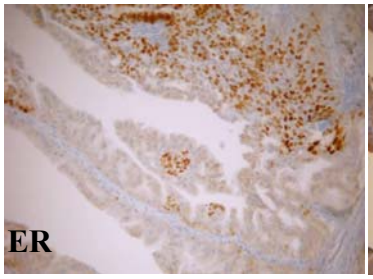


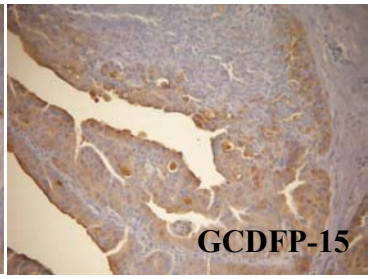






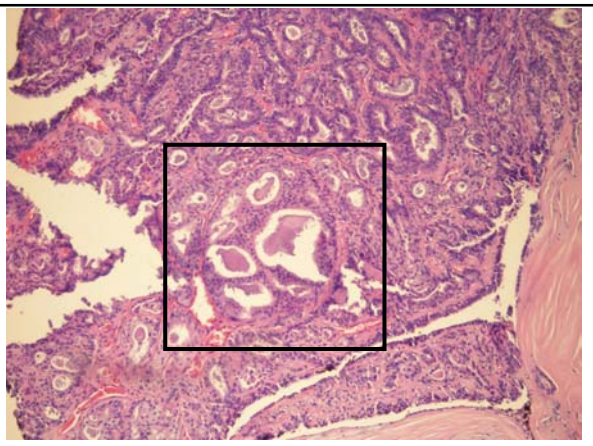


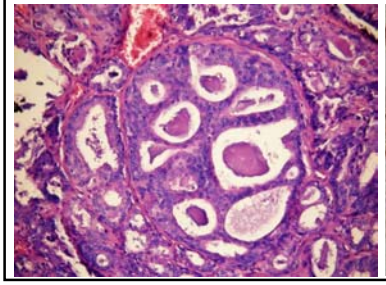


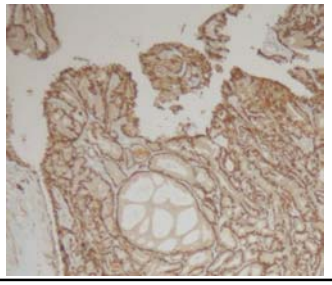


Papilloma atipico

Virchows Arch. 2007;450:539

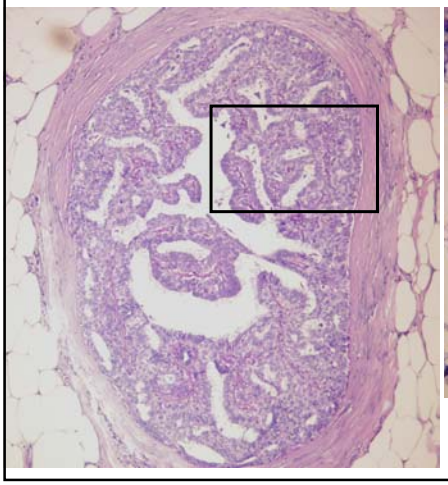


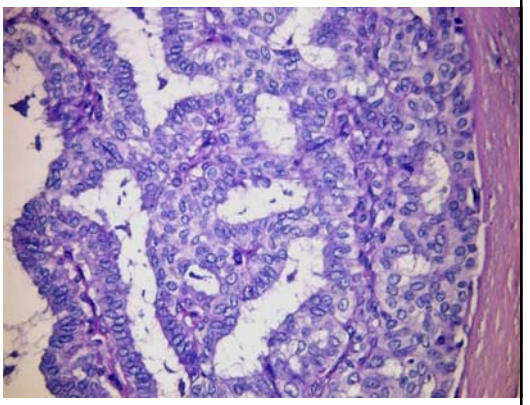


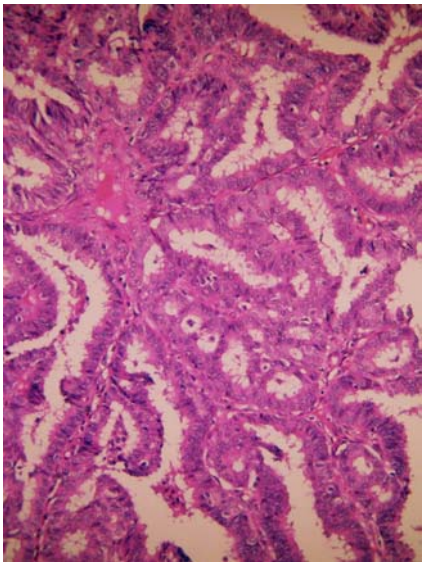


Cribriform pattern (iperplasia duttale atipica)

Carcinoma Papillare in situ







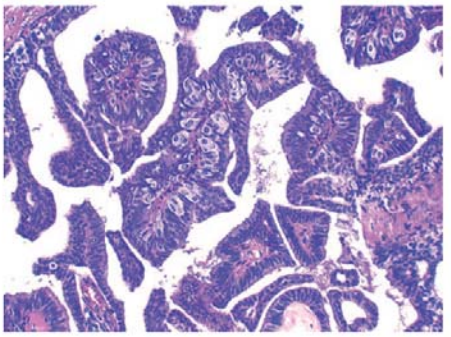
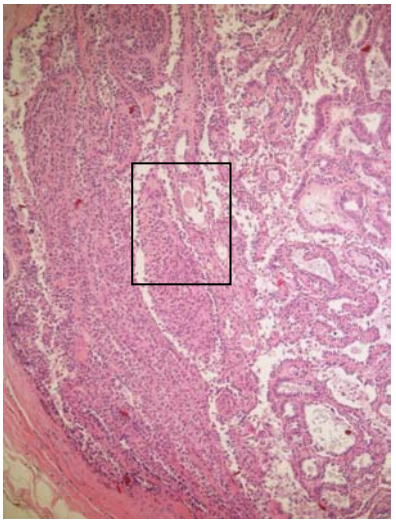
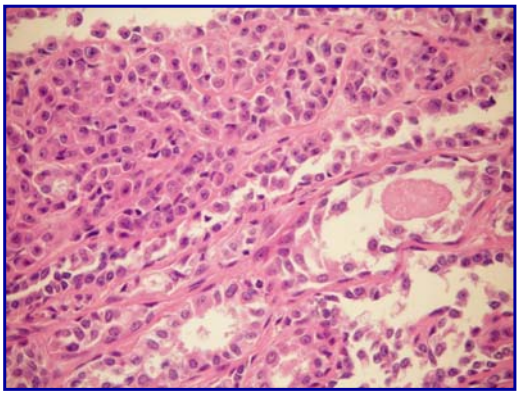


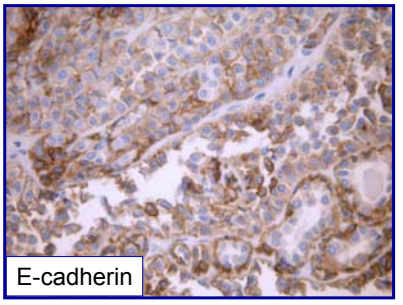
Figure 8. Papillary ductal carcinoma *in situ* with dimorphic cell population. In addition to the neoplastic columnar epithelial cells covering the papillae, a second population of cells with pale cytoplasm is evident, primarily in a basal location. These cells ('globoid' cells) should not be mistaken for myoepithelial cells.

Singola fila di cellule epiteliali



Lesione papillare con LIN (13%)



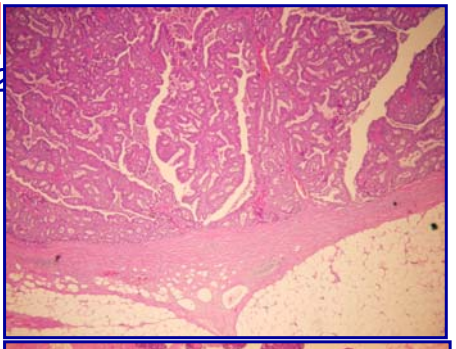


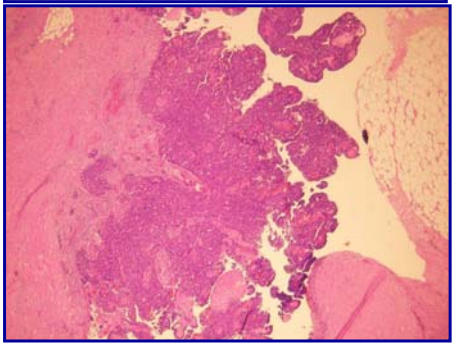
E-cadherin

Intracystic papillary carcinoma

Am J Surg Pathol 2006;30:1002

Solitary, circumscribed tumor,
arborizing papillary fronds surrounded by a fibrotic rim.

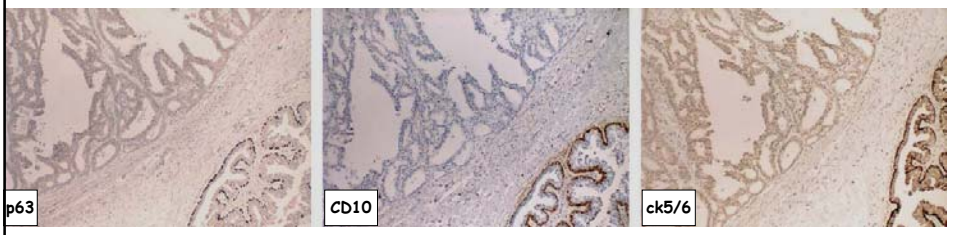




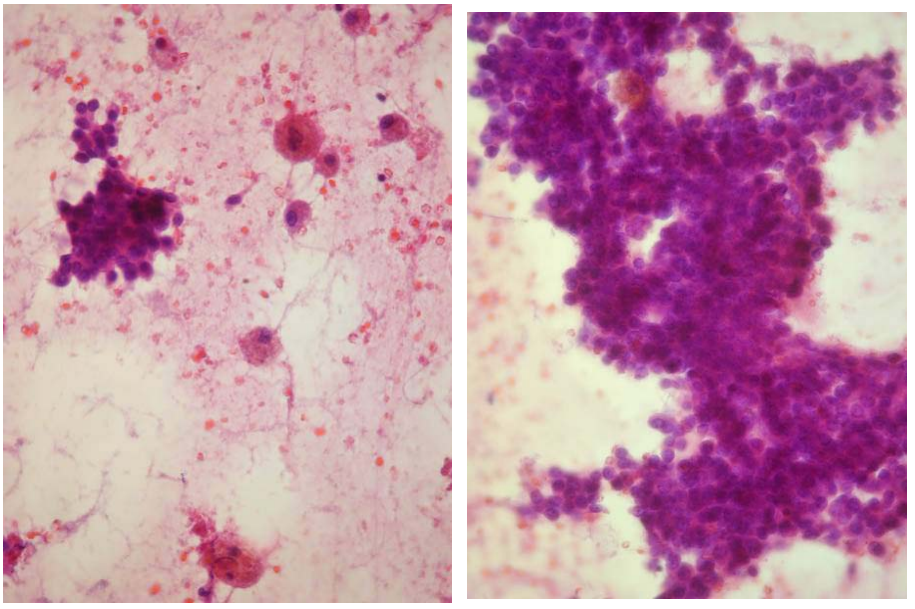
Solid or cribriform pattern of growth of monomorphic epithelial cells.

Intracystic Papillary Carcinomas of the Breast: A Reevaluation Using a Panel of Myoepithelial Cell Markers
Laura C. Collins, et al.

Am J Surg Pathol 2006;30:1002–1007



"Encapsulated Papillary Carcinoma"
circumscribed nodules of papillary carcinoma surrounded by a fibrous capsule in which a peripheral layer of
MEC is not identifiable.

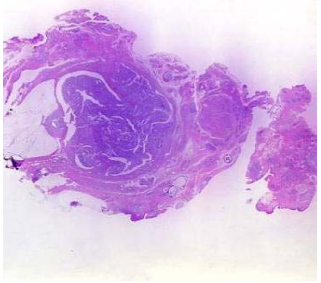


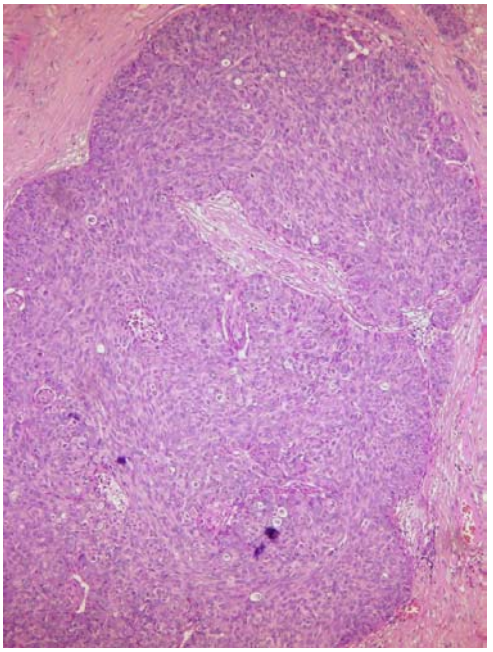
FNA: Carcinoma papillare intracistico/incapsula

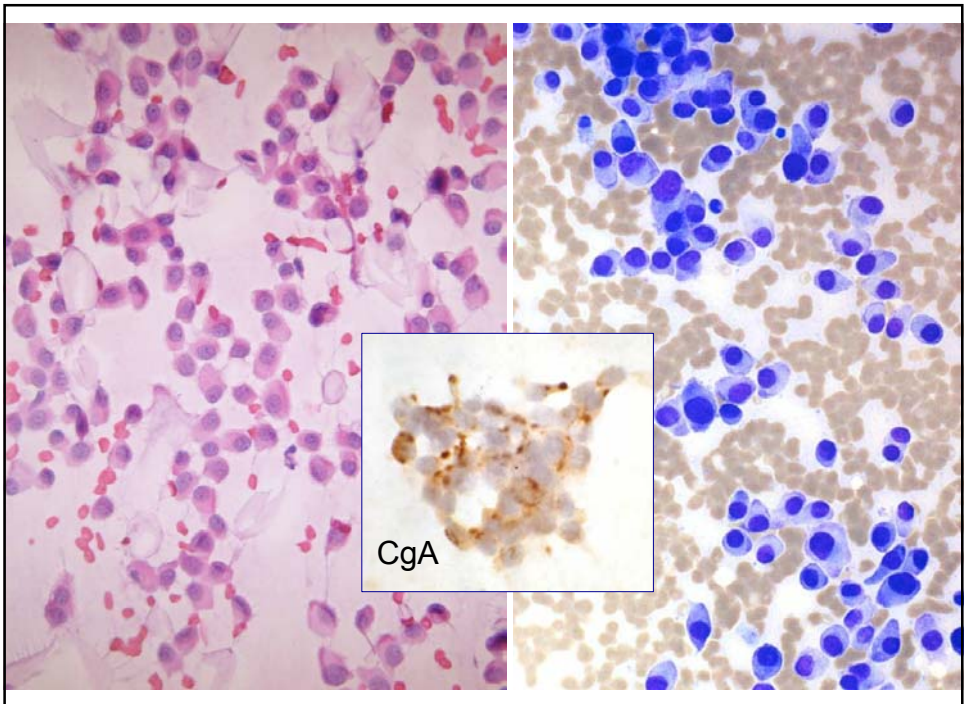
Solid Papillary Carcinoma

aged women

Expansive lesions, forming solid sheets and festoons, lined by delicate fibro-vascular stroma.







Fine needle aspiration cytology of papillary lesions of the breast: how accurate is the diagnosis?

G M K Tse, T K F Ma, P C W Lui, D C H Ng, A M C Yu, J S L Vong, Y Niu, B Chaiwun, W W M Lam and P H Tan

J Clin Pathol 2008;61:945-949

- The overall cellularity of the aspirate.
- The presence of cohesive epithelial cells clusters in the form of cell balls and the presence and degree of nuclear atypia of these cells.
- The presence of single background epithelial cells and the presence and degree of nuclear atypia of these cells.
- The presence of papillae, and their shapes.
- The presence of necrosis and background.

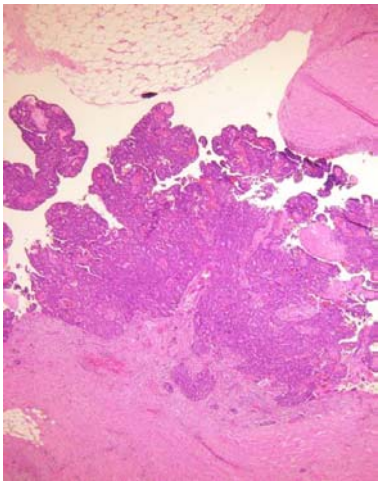
Take-home messages

- Cytological diagnosis of papillary lesions of the breast is difficult, with low sensitivity and specificity.
- If a papillary lesion is suspected in the fine needle aspiration cytology, prompt histological evaluation is warranted for accurate diagnosis.

How important is the differential diagnosis for patient management?

Intracystic/encapsulated papillary carcinoma

Am J Surg Pathol 2006;30:1002–1007

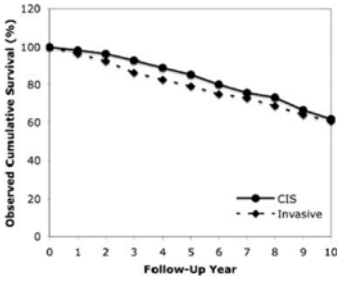


Available outcome data indicate that **they have an excellent prognosis with adequate local therapy alone.**
We believe it is most prudent to continue to manage patients with these lesions as they are currently managed (ie, similar to patients with DCIS) and **to avoid categorization of such lesions as frankly invasive papillary carcinomas.**

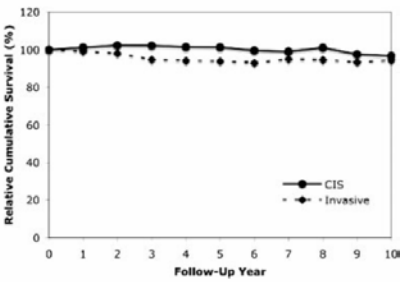
Intracystic Papillary Carcinoma

A Review of 917 Cases

Cancer 2008;113:916–20



this overall survival rate may be influenced by the older age of patients (mean age 69.5 years-range27 years-99 years)and consequent comorbidities



It is obtained by adjusting observed survival for the normal life expectancy of the general population of the same age, the relative survival rate is an estimate of the chance of surviving the effects of cancer.

The addition of radiation to the treatment of patients did not change the incidence of local recurrence or likelihood of death compared with those who did not receive radiation

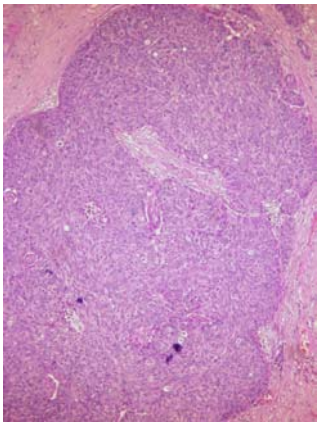
Am J Surg. 2002;184:364-368

There has been no clear indication for adjuvant endocrine therapy, even among patients with estrogen receptor–positive tumors.
Furthermore, the addition of hormonal treatment does not appear to have impacted outcome.

Br J Surg. 1999;86:1274.

Clinicopathologic Analysis of Solid Papillary Carcinoma of
the Breast and Associated Invasive Carcinomas

Nassar H et al. Am J Surg Pathol 2006;30:501–507



SPC has an indolent behavior.

Lymph node and distant metastases are uncommon and generally limited to cases with (conventional) invasive components.