1e Utrechtse Interactieve Mamma Cursus

Thema: Premaligne laesies

UMC Utrecht

Voorloperlaesies in de laaggradige nucleaire mammaneoplasie familie

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Patholoog UMCU

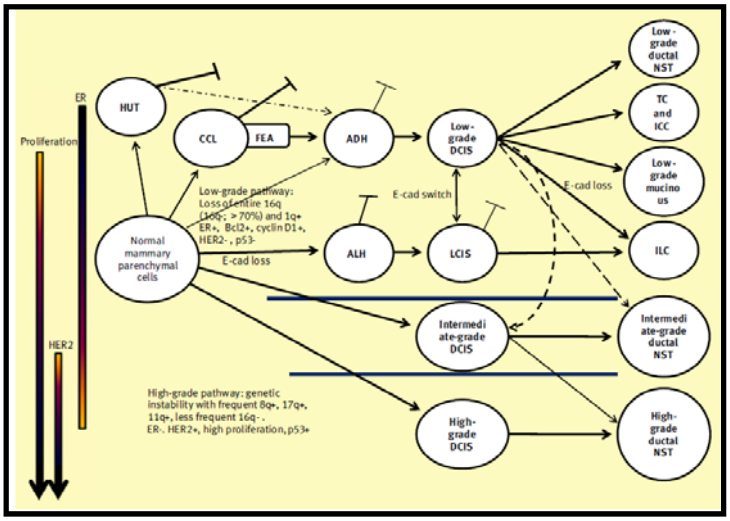
Universitair Medisch Centrum Utrecht

Low-grade breast neoplasia family

- Laag gradige tumoren hebben overeenkomsten[1]
  - Kernmorfologie
  - Immuunhistoschemisch profiel
    - ER/PR positief
    - Her2 negatief
    - CKHMW/CK5/6 negatief [2]
    - Cycline D1 positief
    - P53 negatief
  - Genetisch
    - Weinig chromosomale abberaties
    - Vaak chromosoom 16q loss en chromosoom 1q gain

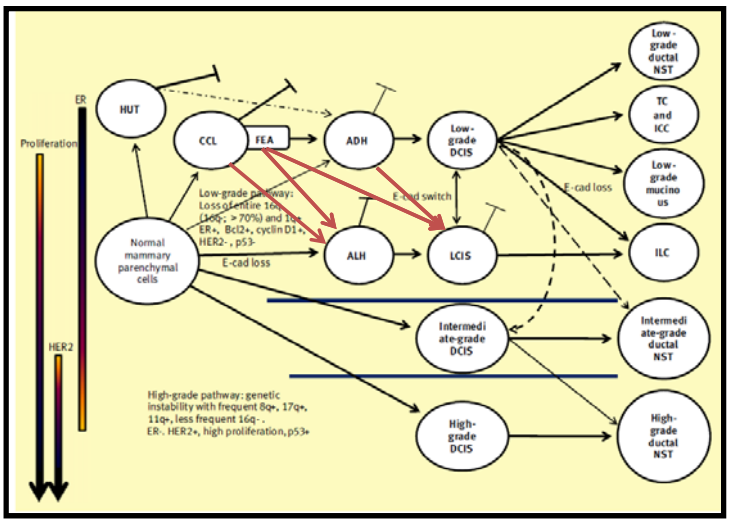
[1]Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012
[2]Abdel-Fatah TMA, Morphologic and moleculair Evolutionary Pathways of Low Nuclear Grade Invasive Breast Cancers, Am J Surg Pathol 2008

Low-grade breast neoplasia family



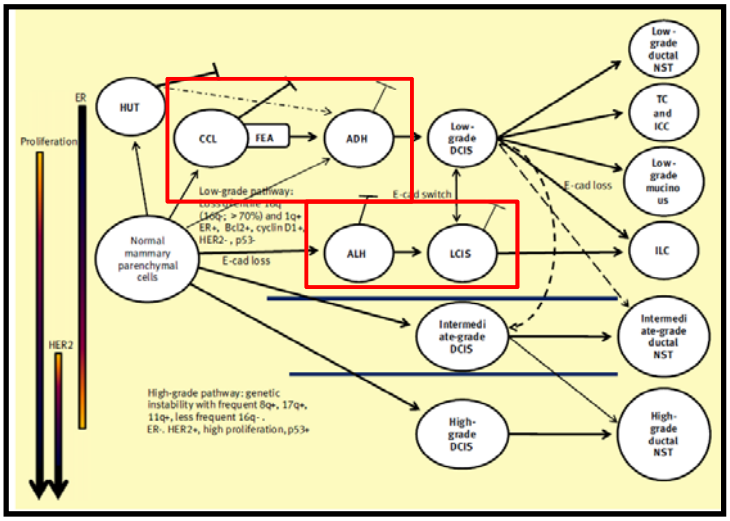
Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

Low-grade breast neoplasia family



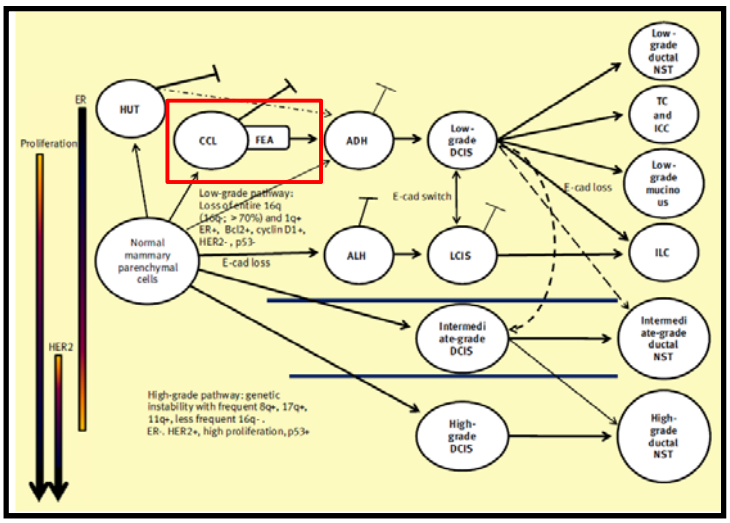
Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

Inhoud van de presentatie



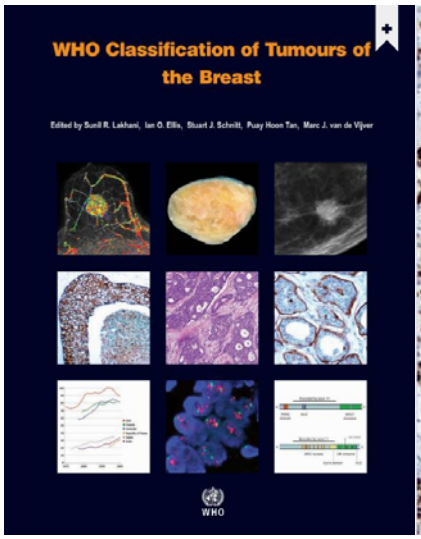
Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

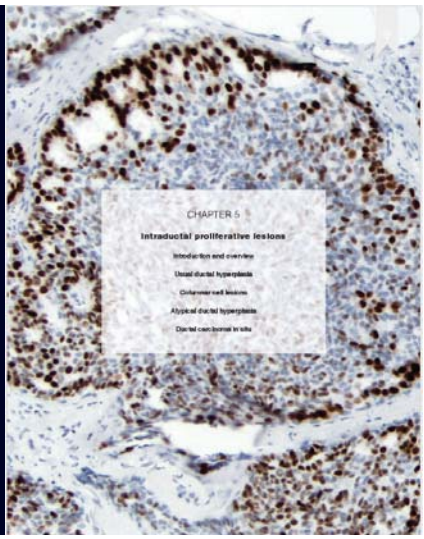
Cilindercellaesies



Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

Cilindercellaesies - terminologie





- Cilindercellaesie
  - Cilindercel-veranderingen en hyperplasie
  - Flat epithelial atypia

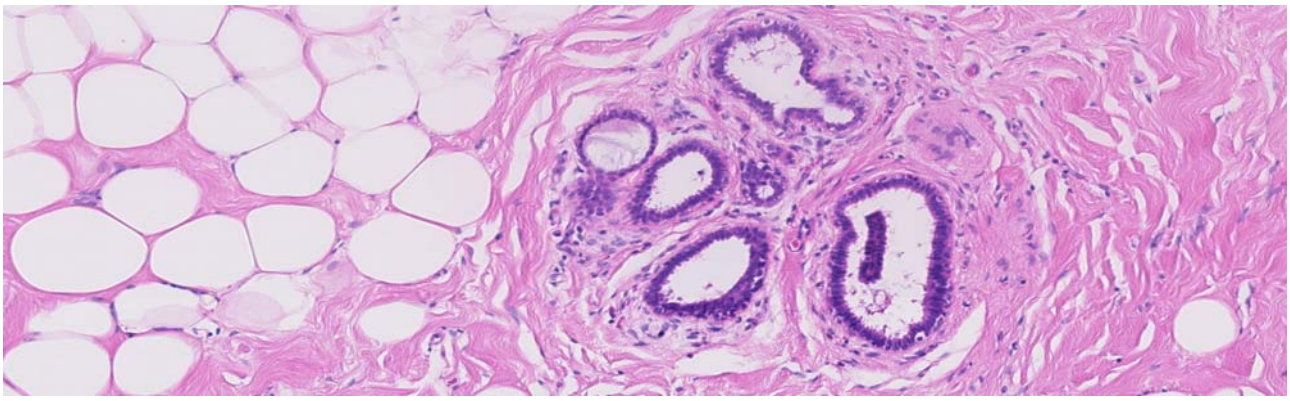
Cilindercelveranderingen

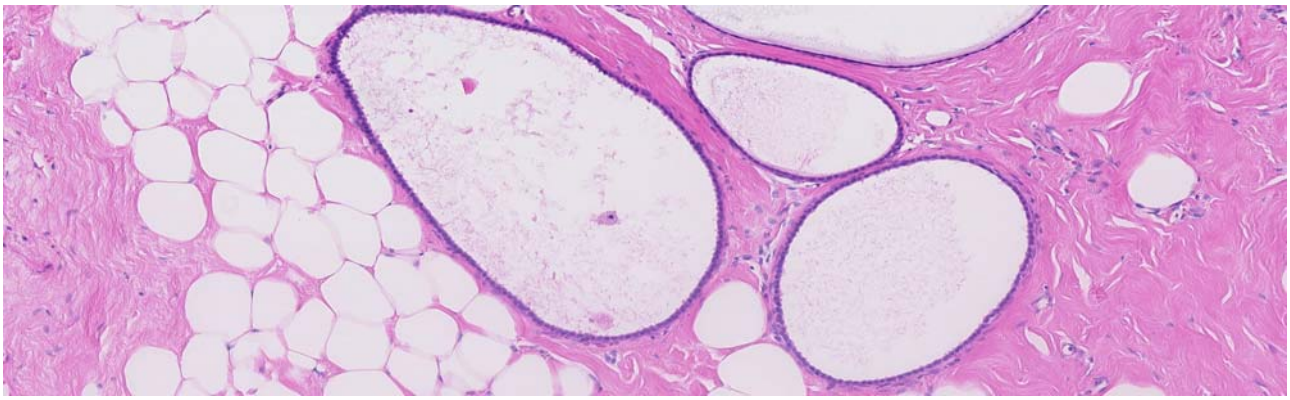
- Synoniemen:
  - Blunt duct adenosis (BDA)
  - Columnar alteration of lubules
  - Columnar metaplasia
  - Hyperplastic unfolded lobules
  - Hyperplastic enlarged lobular units
  - Enlarged lobular units with columnar alterations
  - Columnar cell hyperplasia (meer dan 2 lagen cilindrische cellen)

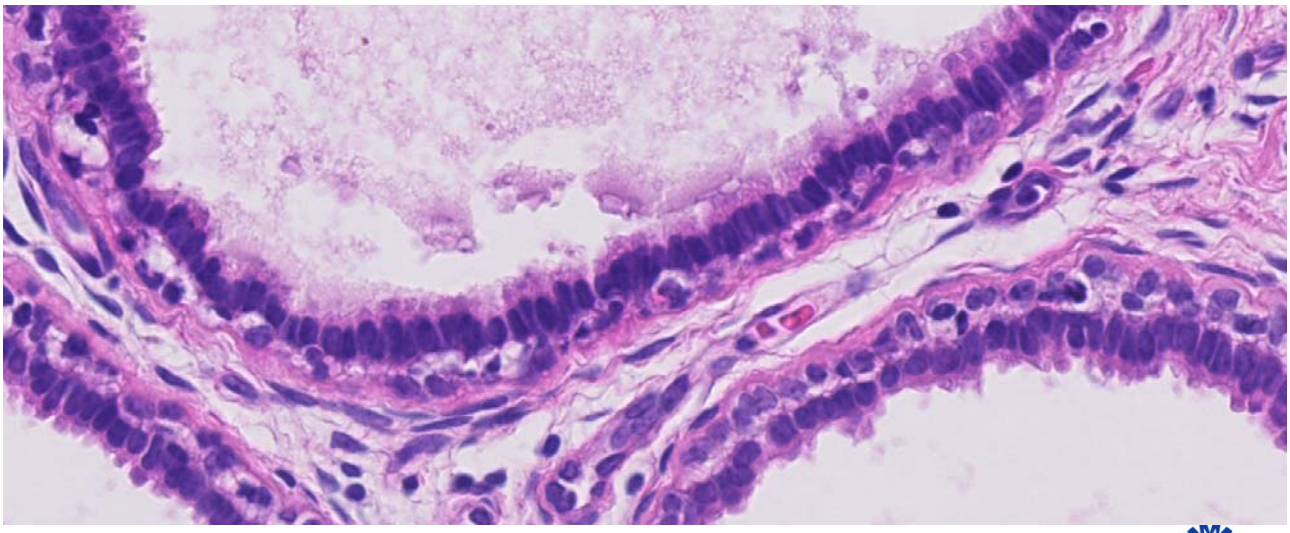
WHO Classification of Tumours of the Breast

Cilindercelveranderingen

- Histologische karakteristieken
  - Gedilateerde acini, vaak irregulaire contouren
  - Bekleding met cilindrische cellen met apicale snouts
  - Regelmatige perpendiculaire oriëntatie van cel en kern ten opzichte van het basaalmembraan
  - Kernen ovaal, fijn chromatine, onopvallende nucleoli
  - Luminale secreties en of microcalcificaties
  - Eventueel prominent myoepitheel
  - Eventueel gespecialiseerd stroma
  - GEEN CYTONUCLEAIRE ATYPIE



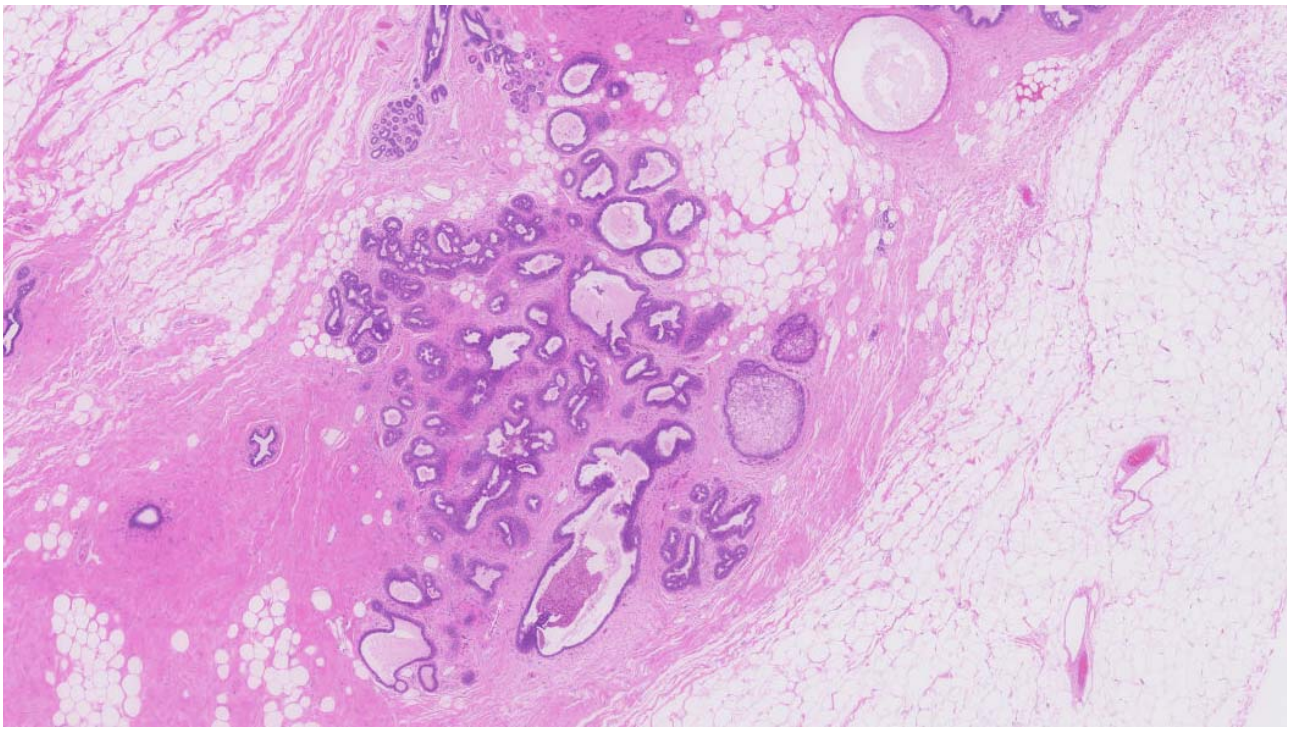


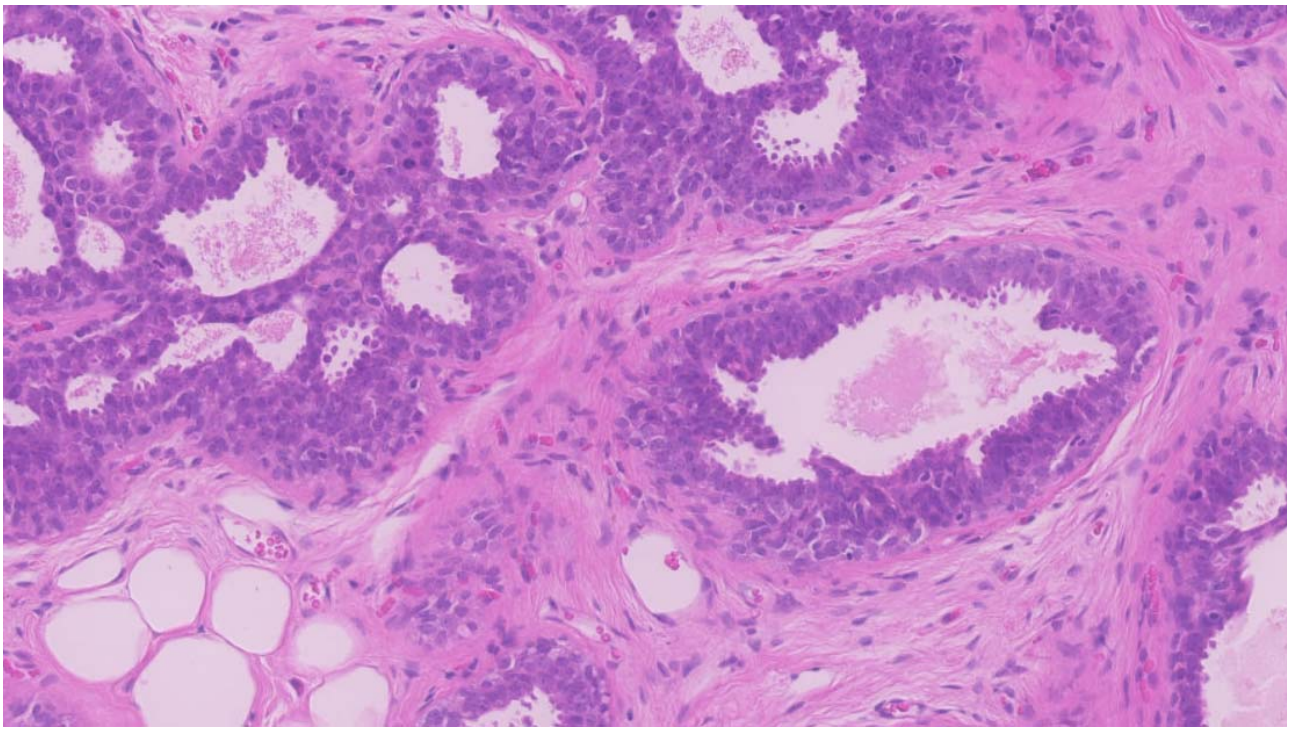


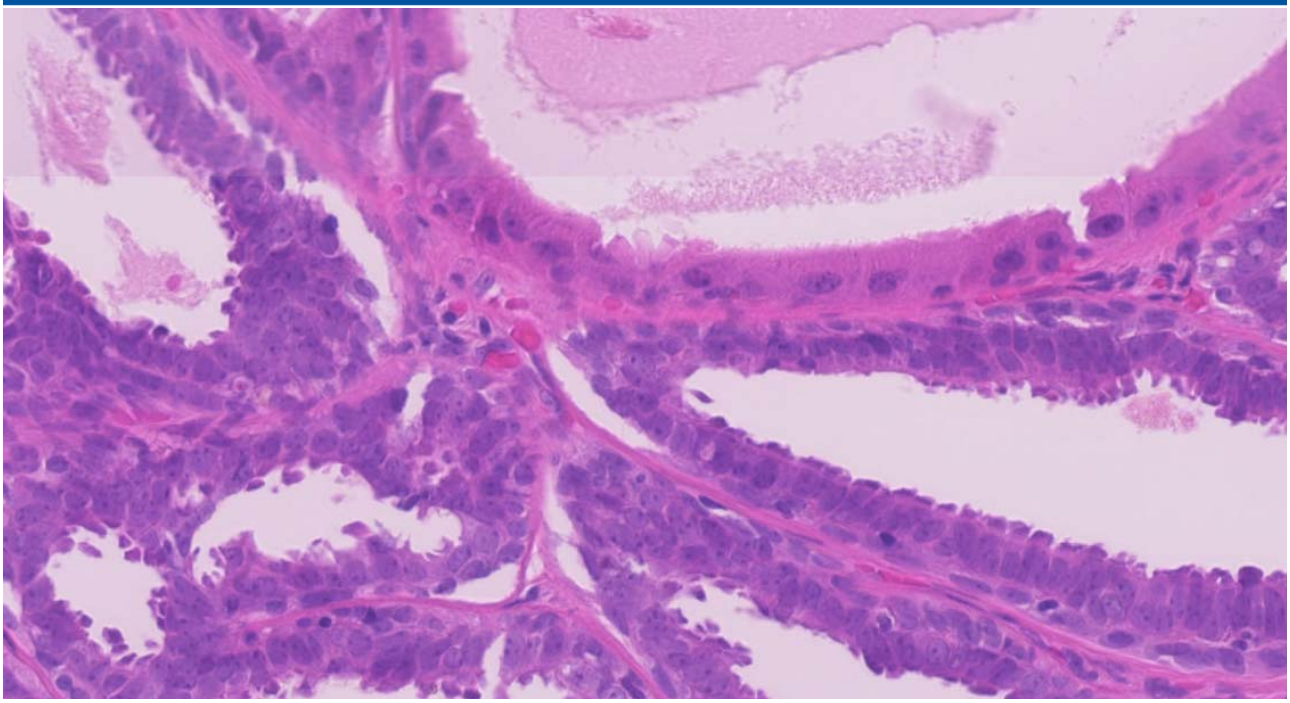
Blunt Duct Adenose (BDA)

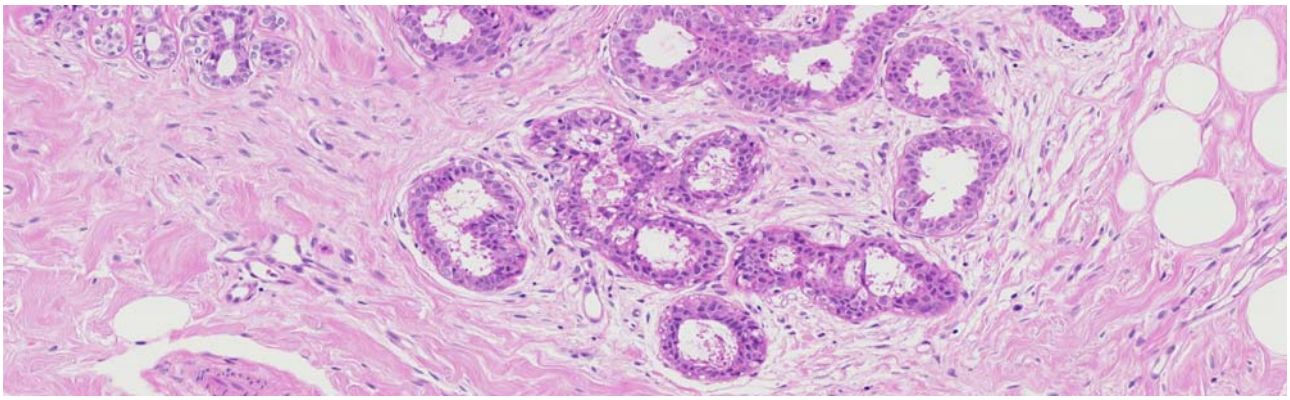
- Definitie en criteria niet duidelijk

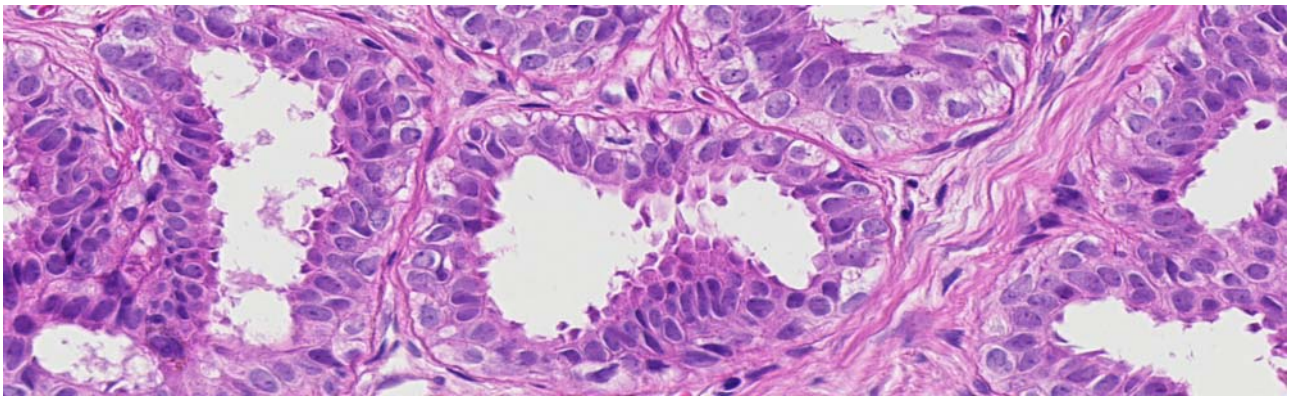
- Histologische karakteristieken
  - Gedilateerde acini, vaak irregulaire contouren
  - Prominent myoepitheel
  - Opvallend en celrijk stroma
  - Luminale cellen hebben overlappende kenmerken met hyperplasie (UDH)
    - Kernoverlap
    - Weinig opvallende celgrenzen
    - Nucleoli soms aanwezig









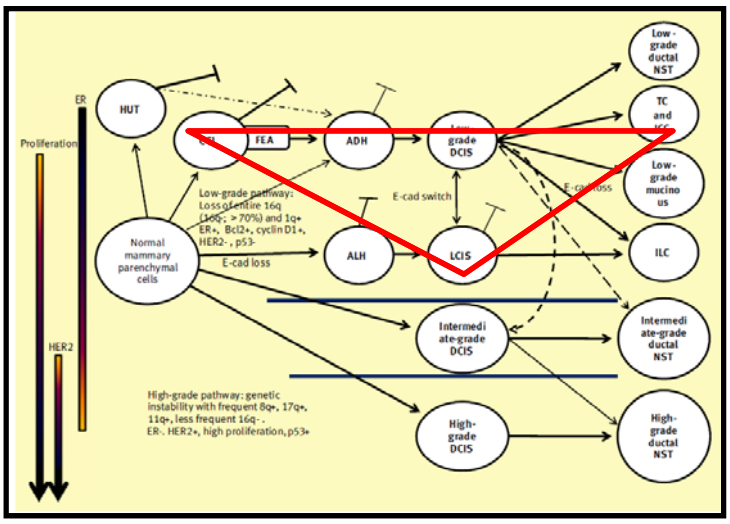


Cilindercelveranderingen

- Immuunhistochemie:
  - ER/PR positief
  - CK5/6 negatief (mogelijk wel frequenter residuale cellen)
- Klinische implicaties
  - Laag risico op het vervolgens ontwikkelen van borstkanker (RR 1,5)[1]
  - Geen behandelconsequenties

1 WHO Classification of Tumours of the Breast

"Rosen Triad"



Flat epithelial atypia (FEA)

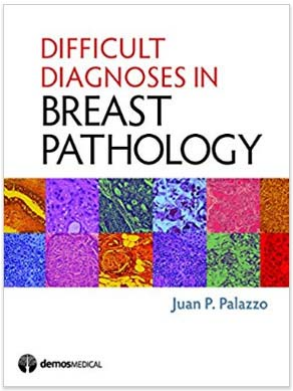
- Neoplastische verandering van de terminale duct lobulaire unit met bekleding met epitheel met laag-gradige (monomorfe) cytologische atypie
- Synoniemen:
  - Cilinder cell verandering met atypie
  - Cilinder cell hyperplasie met atypie
  - Cilinder cell laesie met atypie

WHO Classification of Tumours of the Breast

Flat epithelial atypia (FEA)

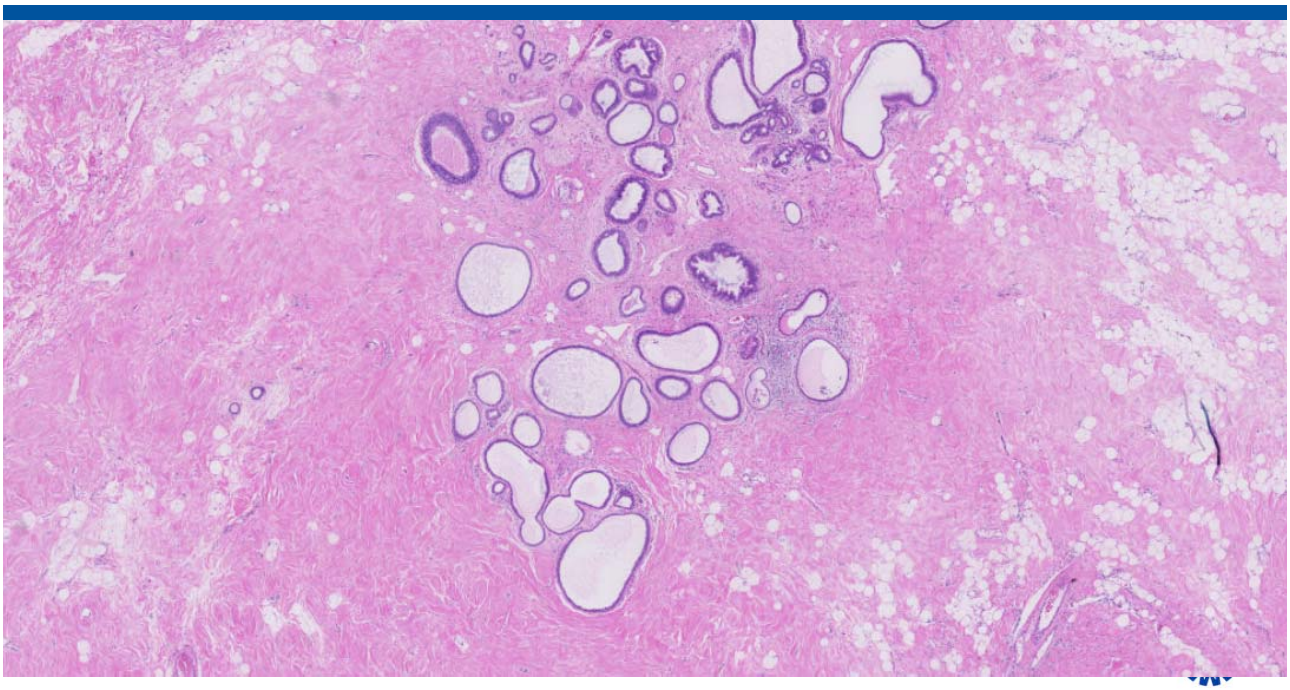
- Histologische karakteristieken
  - Gedilateerde acini vaak met gladde contour
  - Bekleedt met cilindrische of cubische cellen, vaak apicale snouts, eventueel verlies van polariteit
  - Geringe cytonulceaire atypie (monomorf)
    - Ronde, uniforme kernen
    - Nucleoli (varierend van onopvallend tot matig vergroot)
    - Grotere kernen en verstoorde kern/cytoplasma ratio?
  - Er mogen wel “tufts”en “mounds” zichtbaar zijn, echter geen architecturele atypie
  - Vaak aanwezigheid luminale secreties en/of microcalcificaties

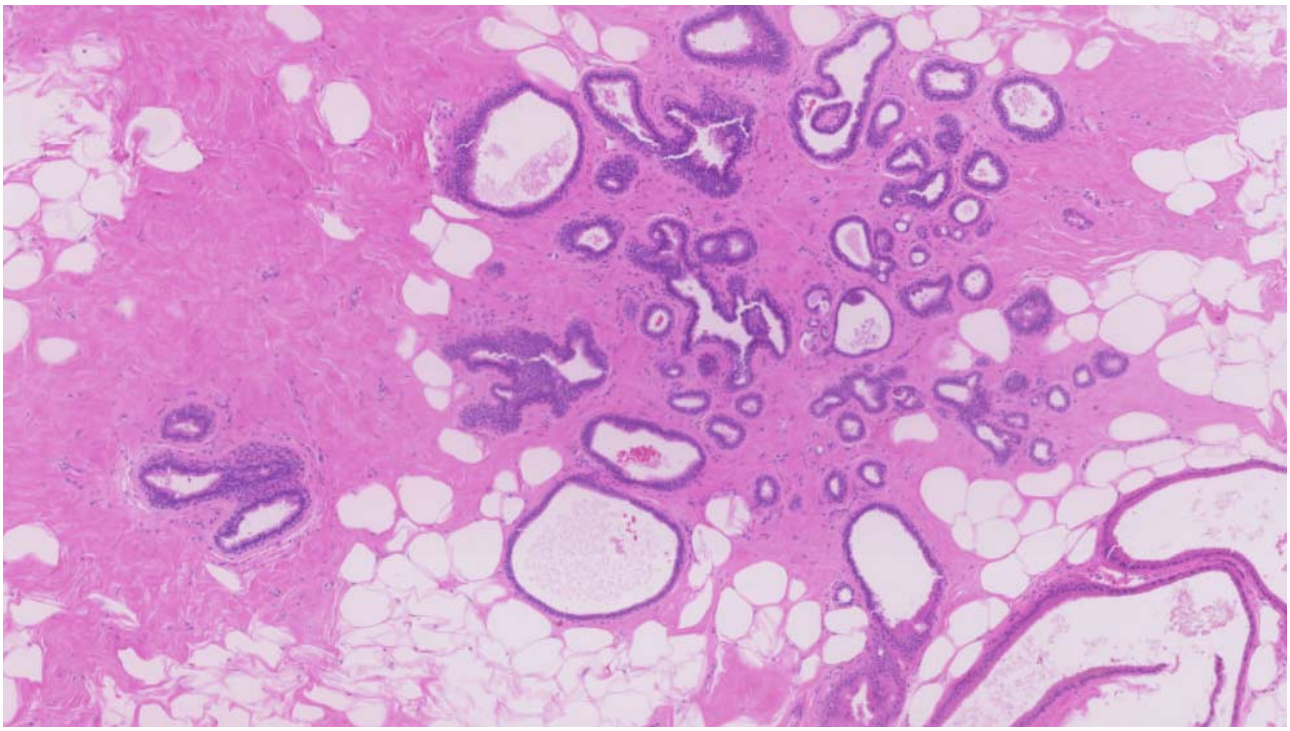
Cytologische karakteristieken van laaggradige atypie

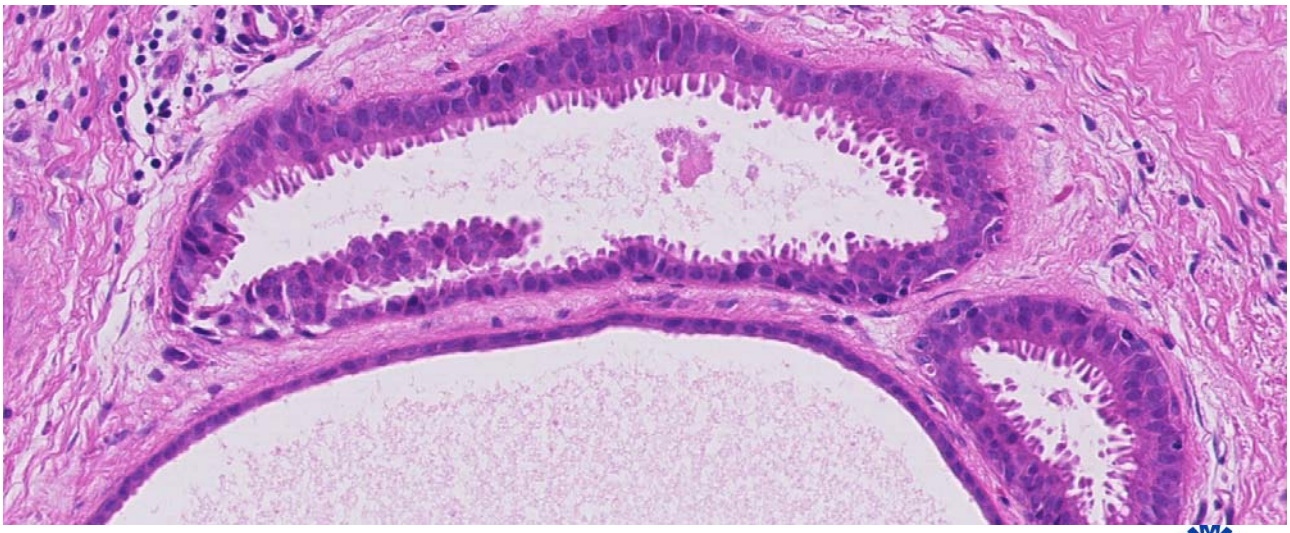


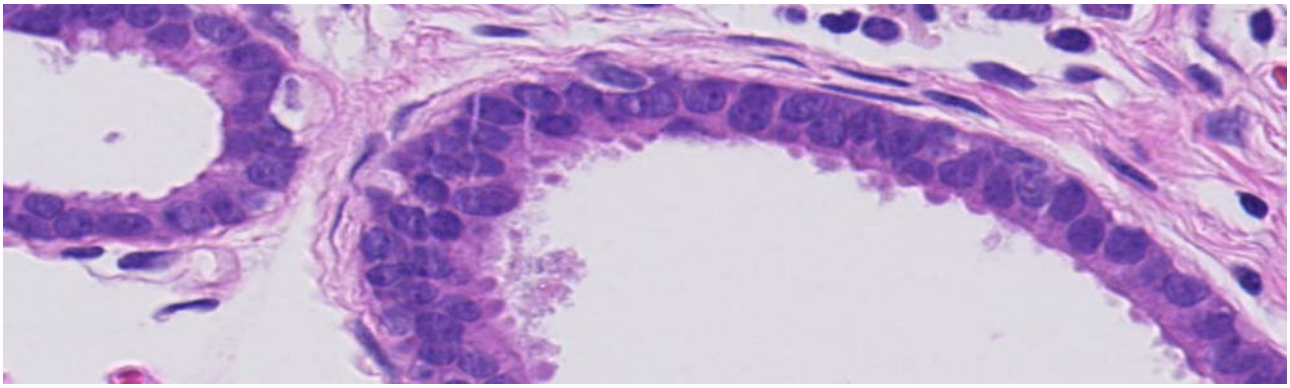
■ **Table 4.1** Cytologic features of low-grade ductal atypia

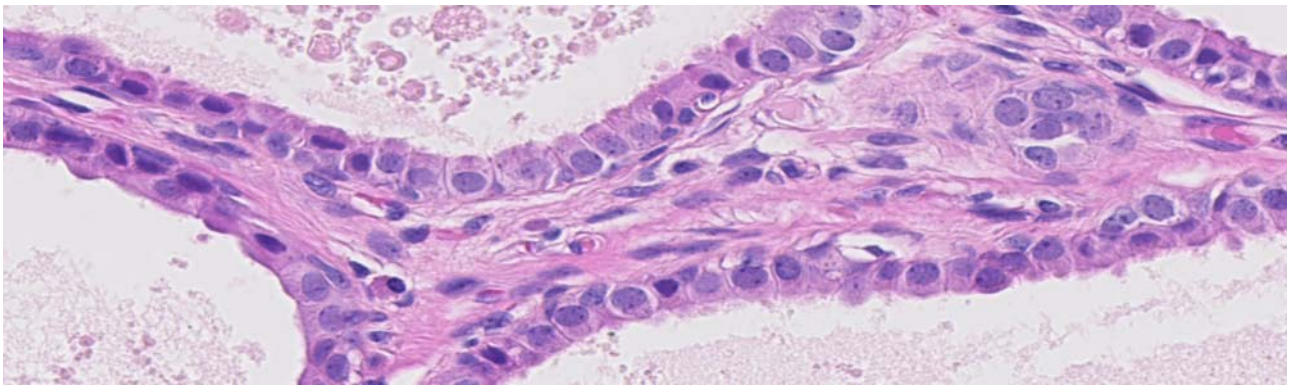
Cell population	Monomorphic
Nuclear shape	Round or oval
Nuclear contours	Smooth
Chromatin	Homogeneous, fine, hyperchromatic
Nucleoli	Often inconspicuous
Nuclear pseudoinclusions	Absent
Cytoplasm, amount	Increased
Cytoplasm, staining quality	Eosinophilic or amphophilic, pallorous
Cell borders	Sometimes distinct

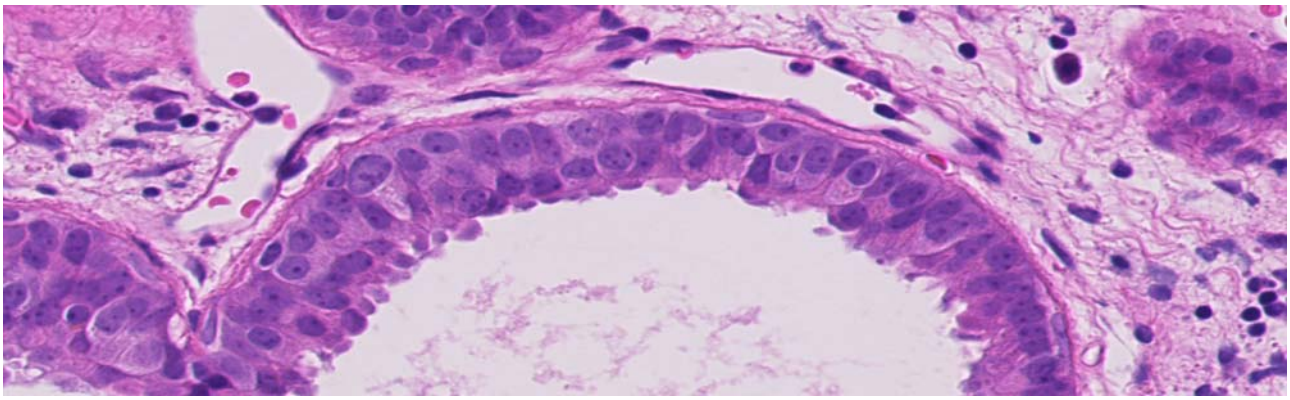


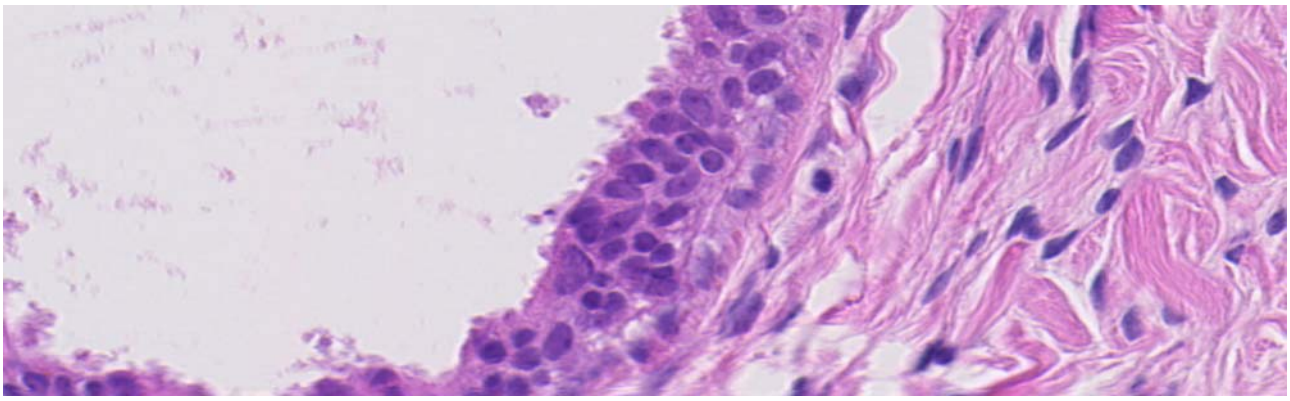


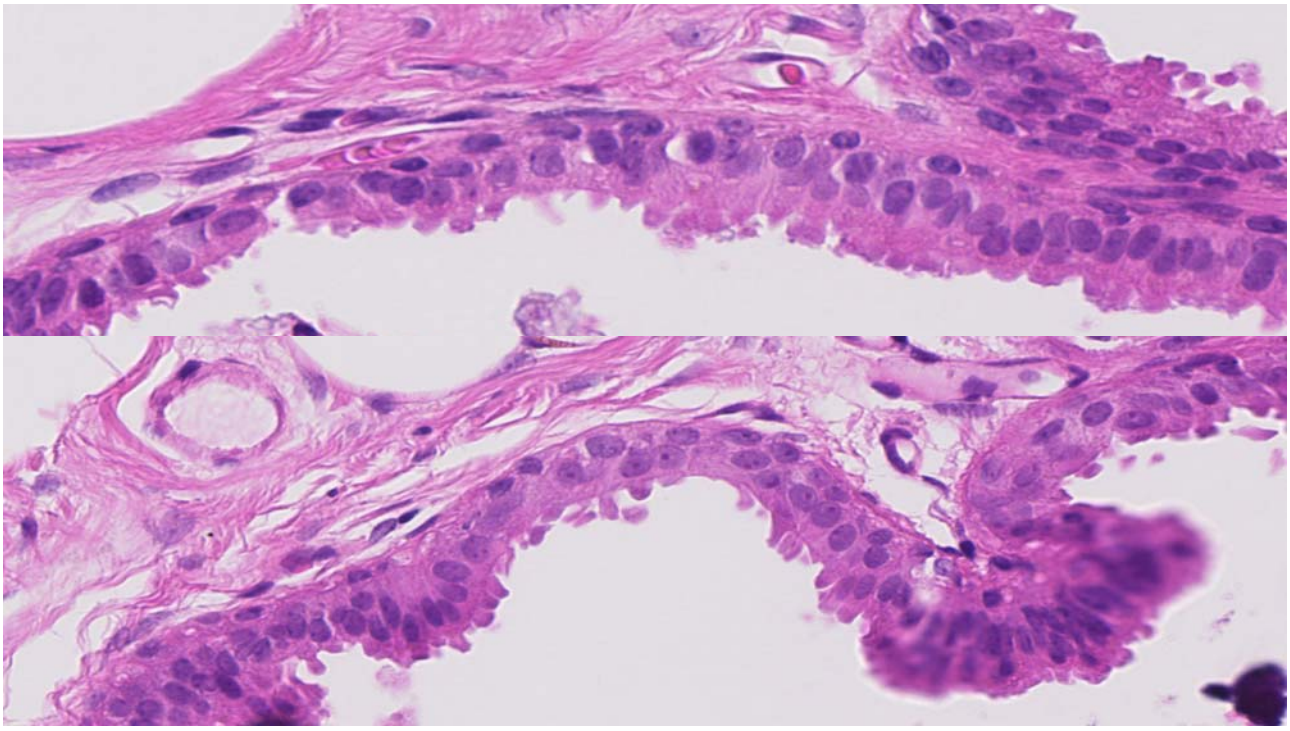


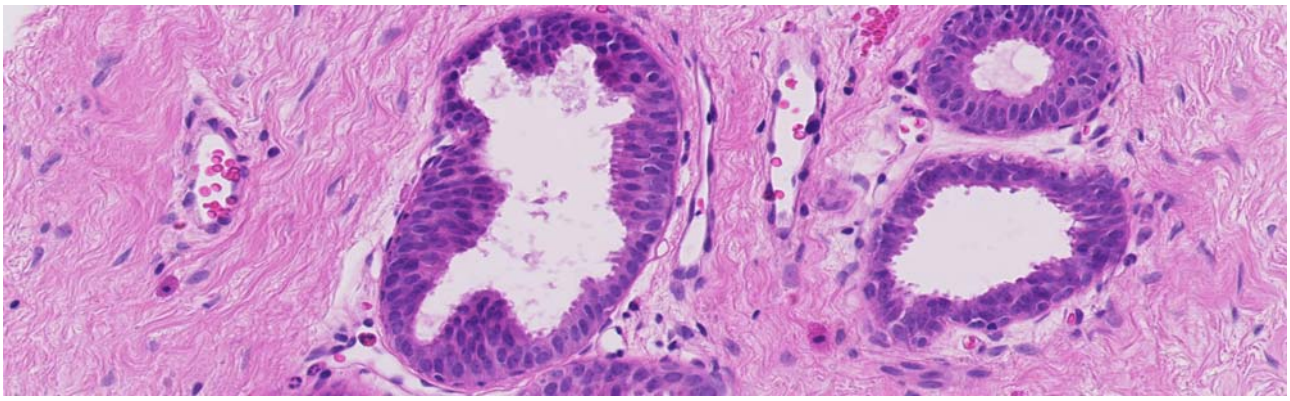


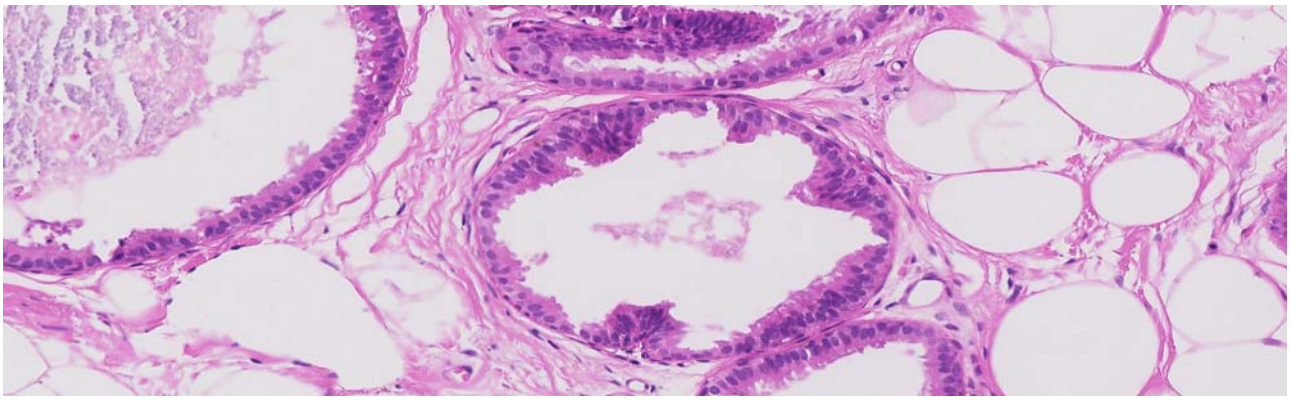


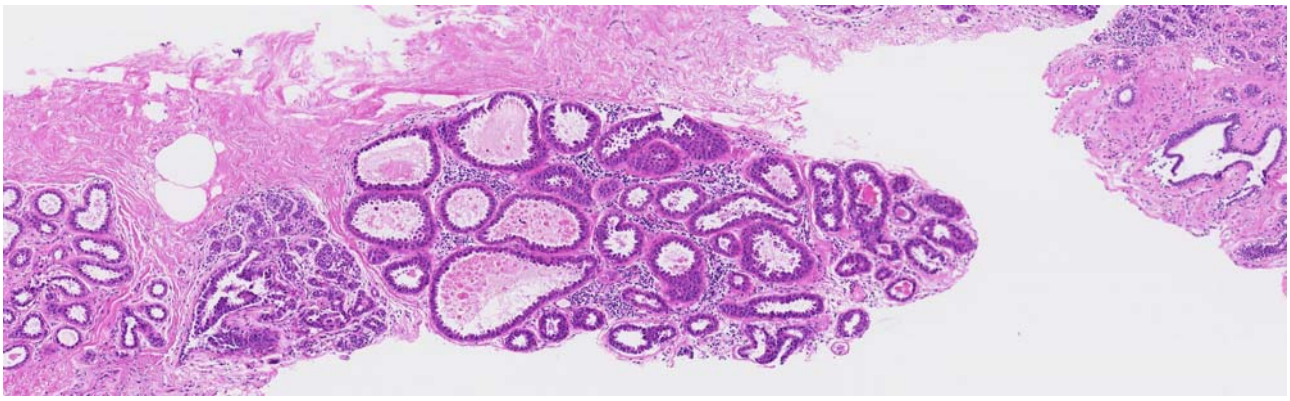


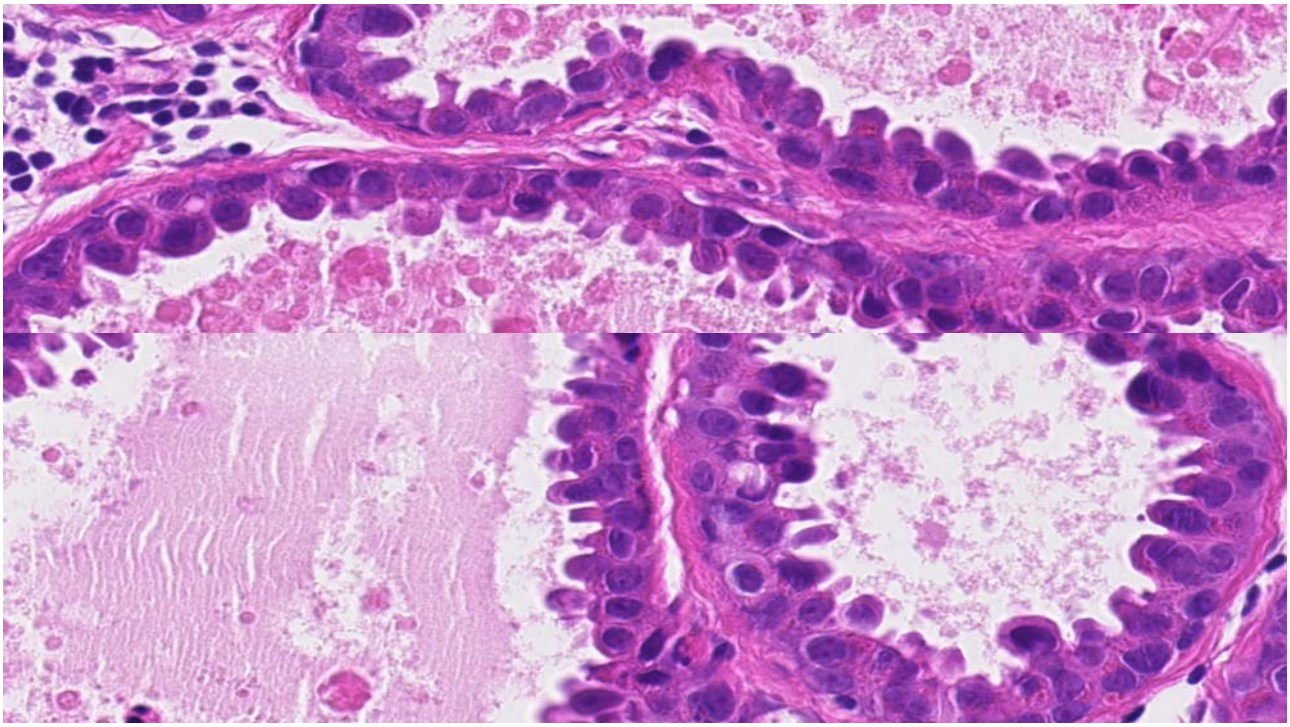


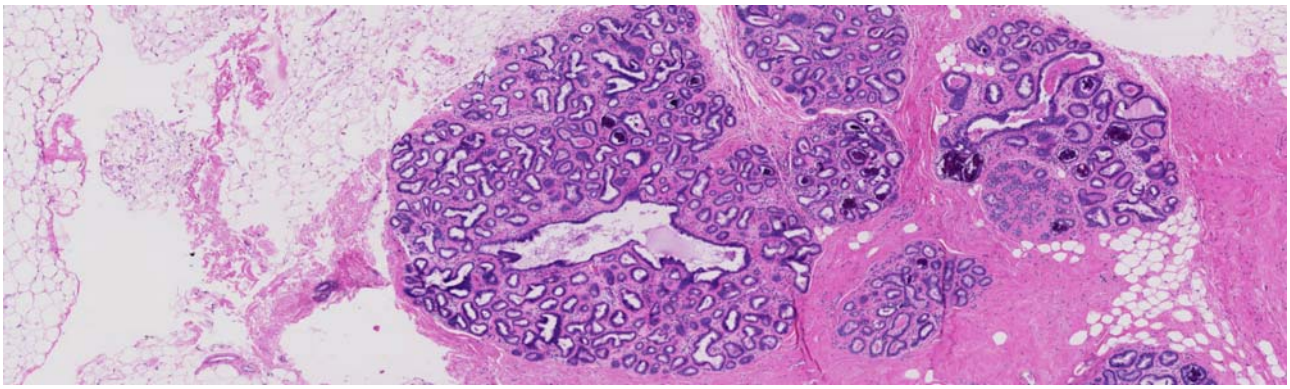


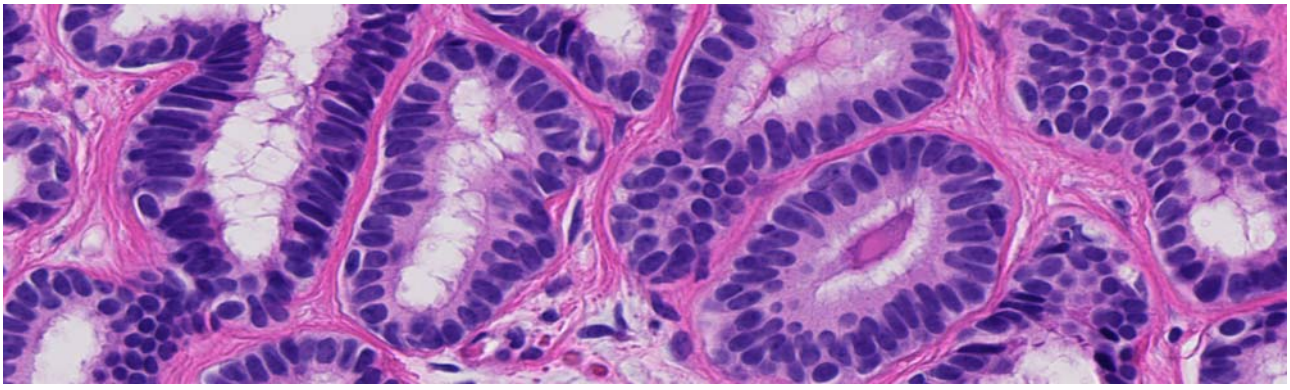


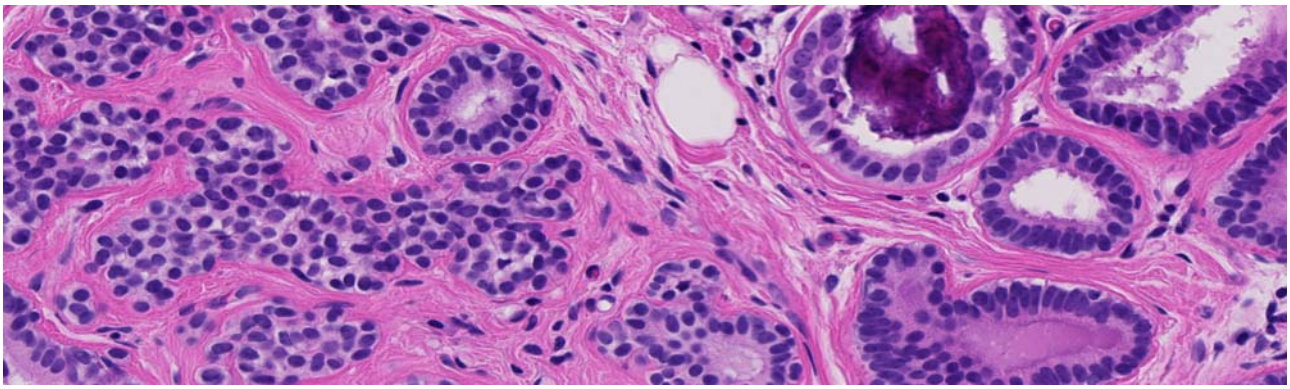


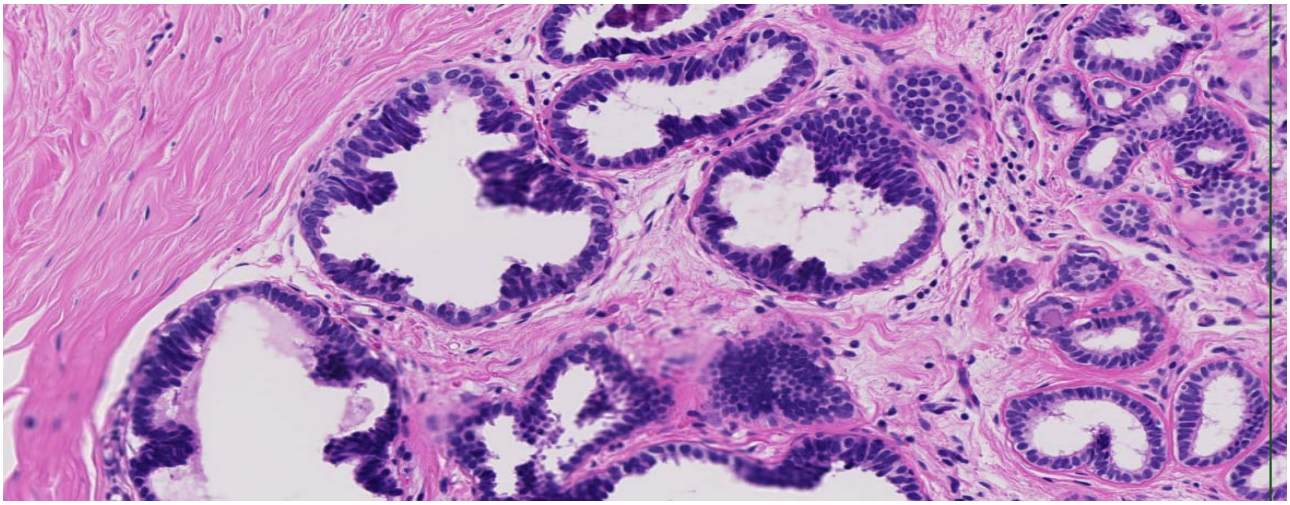












Flat epithelial atypia (FEA)

- Immuunhistochemie
  - ER/PR positief (sterk diffuus)
  - Her2 negatief
  - CK5/6 negatief
- Klinische implicaties

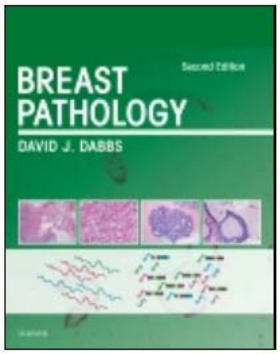


TABLE 19.4 Comparison of Pure FEA on Core Biopsy-Complete Versus Variable Surgical Excision Rates

Upstage Rate%	FUE-FEA %	FUE-ADH %	FUE-LN %
8.5% (All excised)	21	16	4
7.8 (Variable excised)	34	23	98. 7

ADH, Atypical ductal hyperplasia; *FEA,* flat epithelial atypia; *FUE,* follow-up excision; *LN,* lobular neoplasia

REVIEW AND META-ANALYSIS

Columnar Cell Lesions on Breast Needle Biopsies: Is Surgical Excision Necessary?

A Systematic Review

Anoek H. J. Verschuur-Maes, MD, Carolien H. M. van Deurzen, MD, PhD,† Evelyn M. Monninkhof, PhD,‡ and Paul J. van Diest, MD, PhD§*

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Progression risk of columnar cell lesions of the breast diagnosed in core needle biopsies

Anoek H.J. Verschuur-Maes[1], Arjen J. Witkamp[2], Peter C. de Bruin[3], Elsken van der Wall[4] and Paul J. van Diest[1]

[1] Department of Pathology, University Medical Centre Utrecht, The Netherlands

Flat epithelial atypia (FEA) – Differentiaal Diagnose

- CCL zonder atypie (kappa value 0,27 - 0,83[1-3])
  - Blunt duct adenose
- Apocriene metaplasie
- Atypische Ductale Hyperplasie (ADH)
- DCIS (hooggradig)
  - Hooggradige cytonulceaire atypie

1 Gomes, Inter-observer variability between general pathologists and a specialist in breast pathology in the diagnosis of lobular neoplasia, columnar cell lesions, atypical ductal hyperplasia and ductal carcinoma in situ of the breast. *Diagn Pathol.* 2014.
2 Tan, Pathological diagnosis of columnar cell lesions of the breast: are there issues of reproducibility? *J Clin Pathol.* 2005
3 O'Malley, Interobserver reproducibility in the diagnosis of flat epithelial atypia of the breast. *Mod Pathol.* 2006

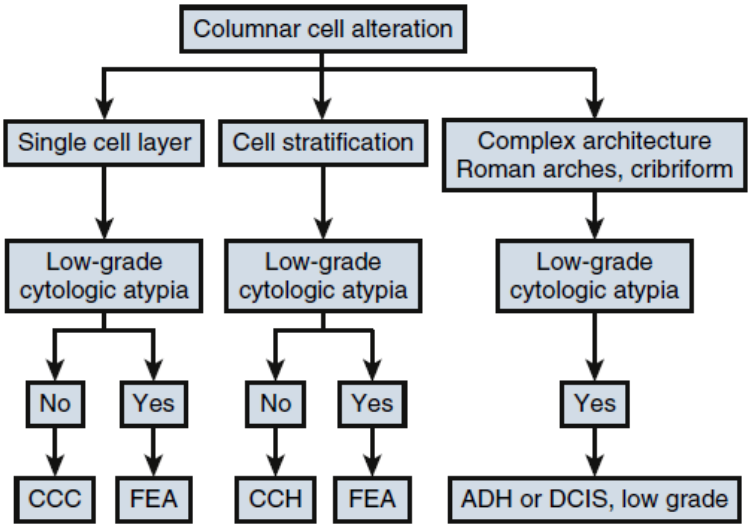
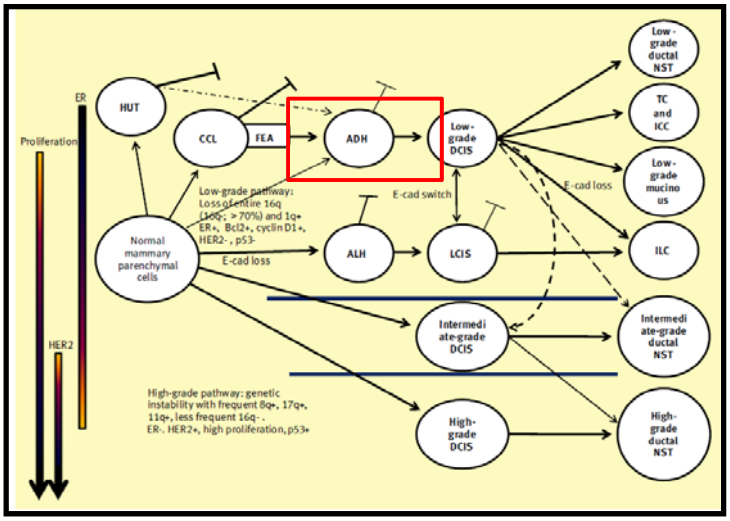


FIG. 19.16 Algorithmic approach to morphologic assessment of columnar-related lesions. *ADH,* Atypical ductal hyperplasia; *CCC,* columnar cell change; *CCH,* columnar cell hyperplasia; *DCIS,* ductal carcinoma in situ; *FEA,* flat epithelial atypia.

Atypische ductale hyperplasie (ADH)

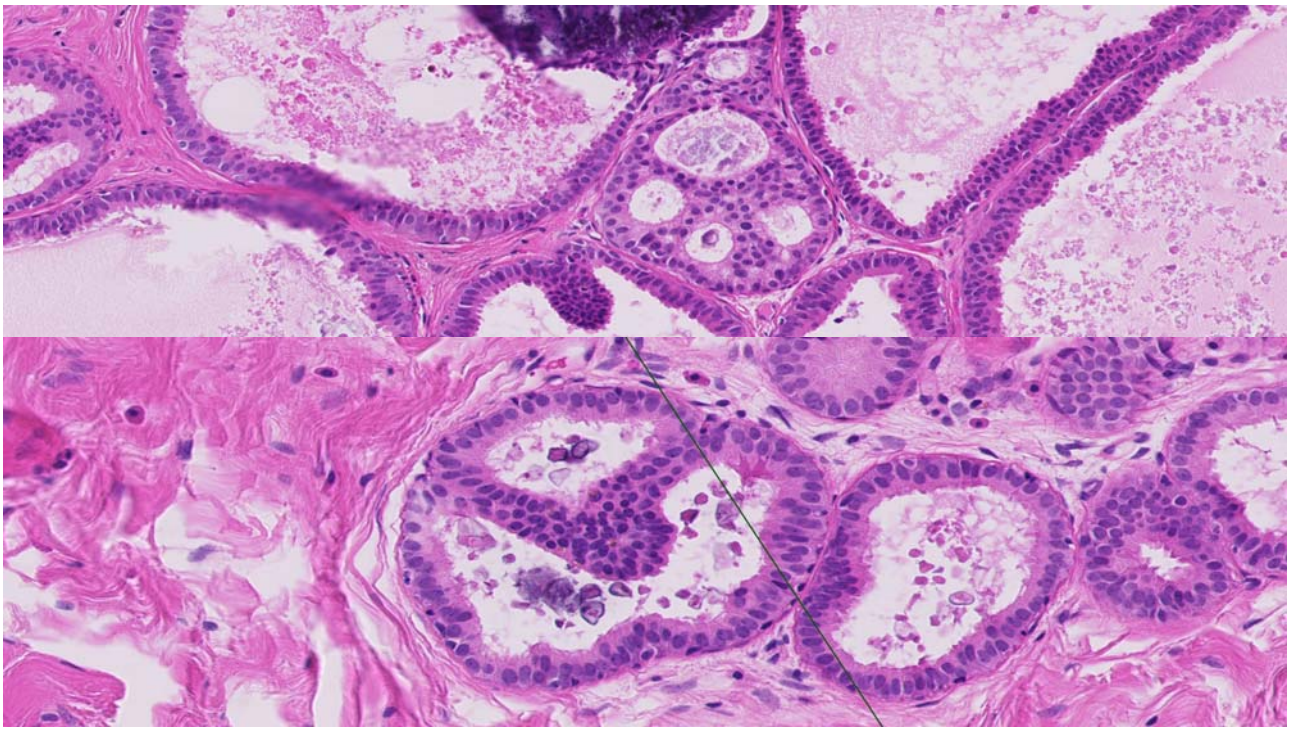


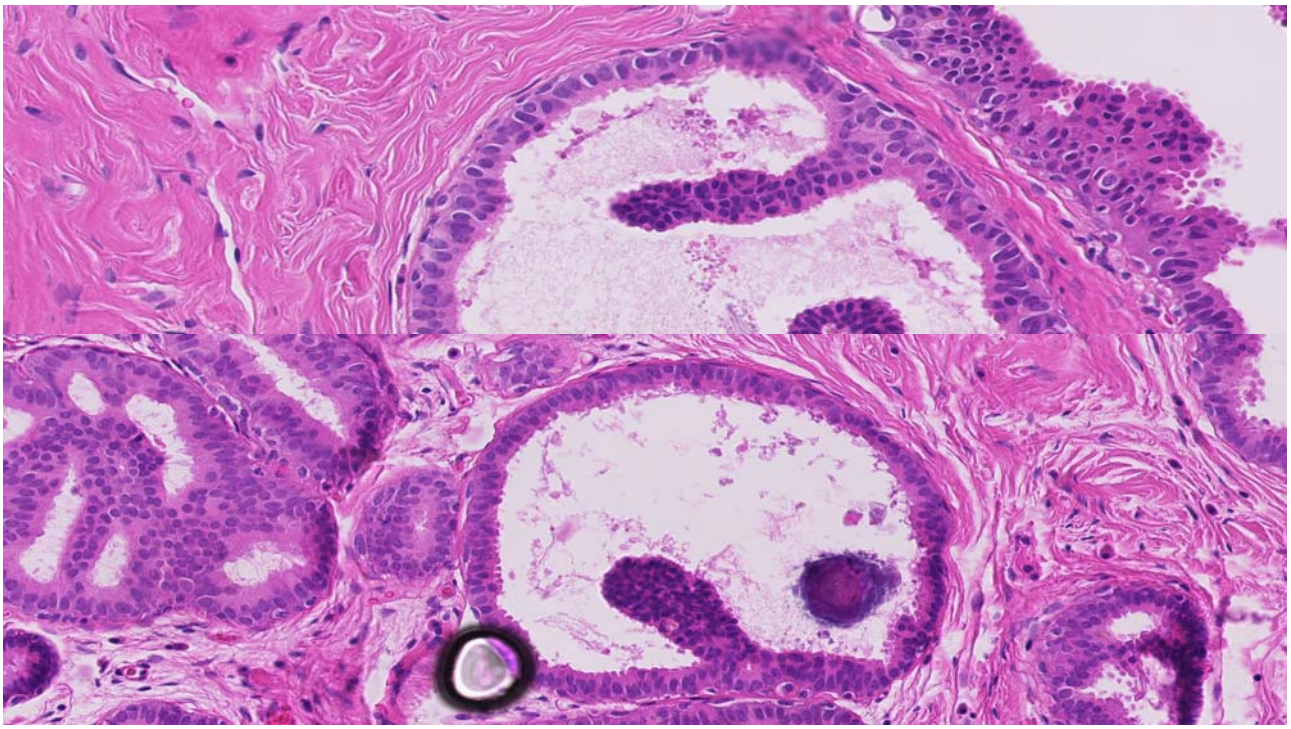
Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

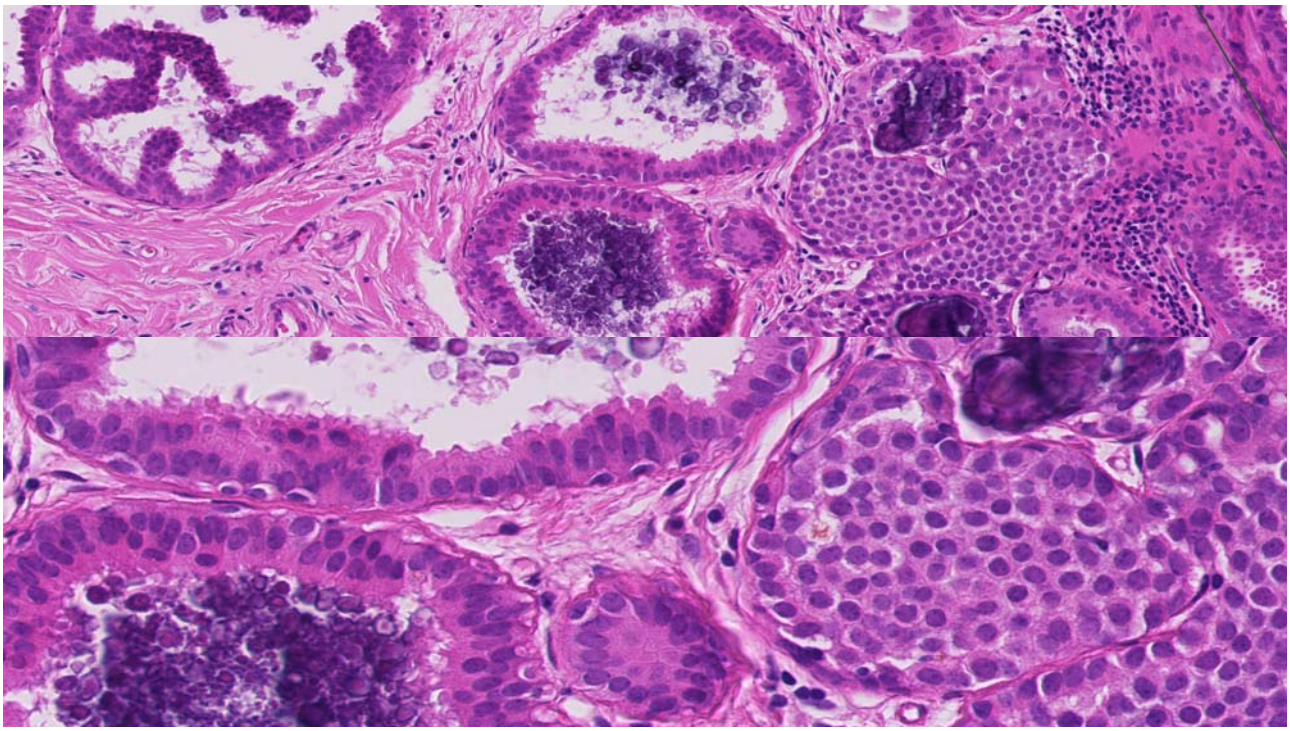
Atypische ductale hyperplasie

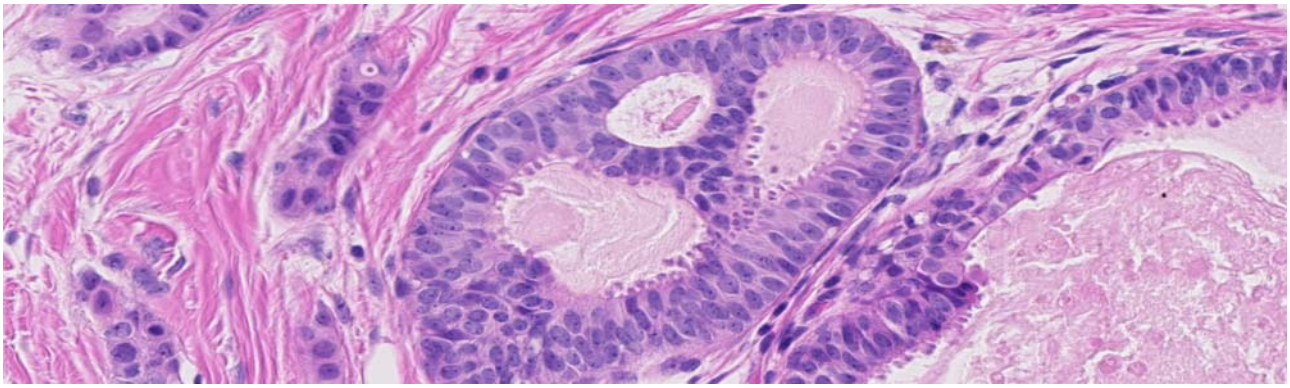
- Proliferatie van monoforfe epitheliale cellen in de TDLU. Per definitie is er een combinatie van architecturele en (geringe) cytologische atypie.

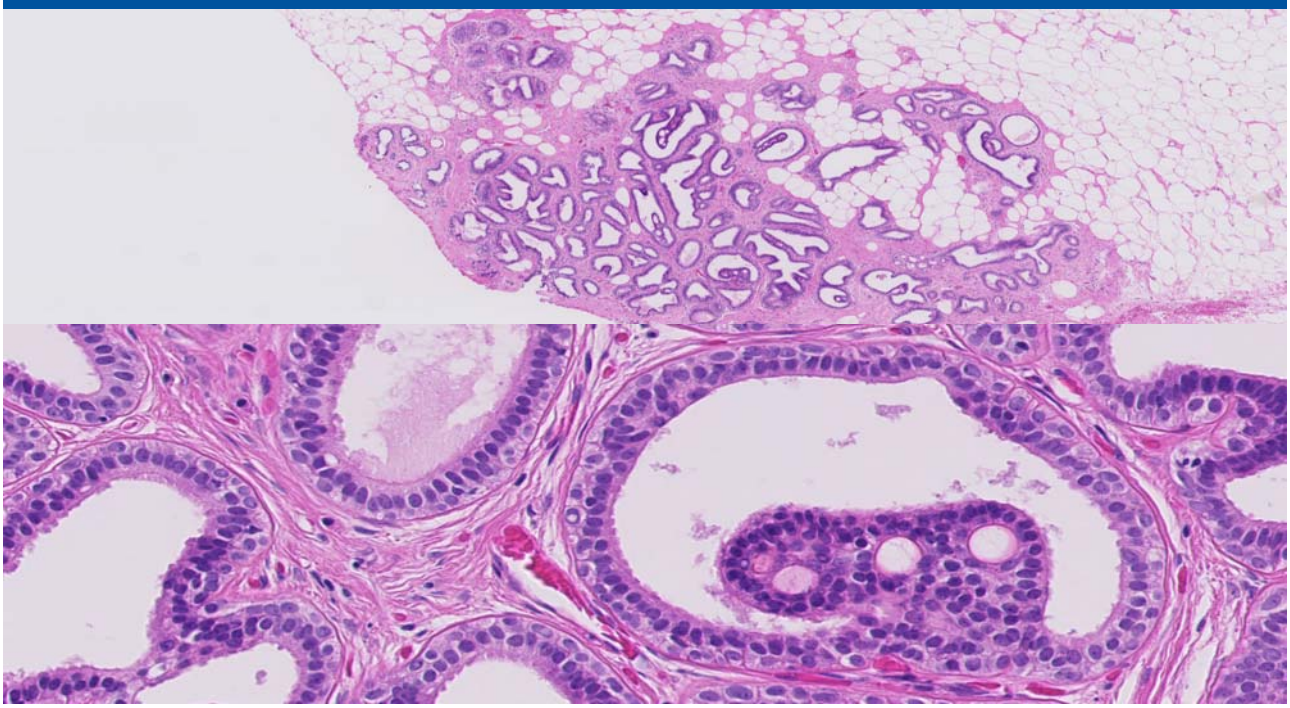
- Histologische kenmerken
  - Geringe cytonulceaire atypie (vergelijkbaar met DCIS graad 1)
  - Regelmatige ligging van luminale cellen met scherpe celgrenzen, geen streaming en overlap
  - Architecturele atypie (solide, cribriform, micropapillen en bruggen)











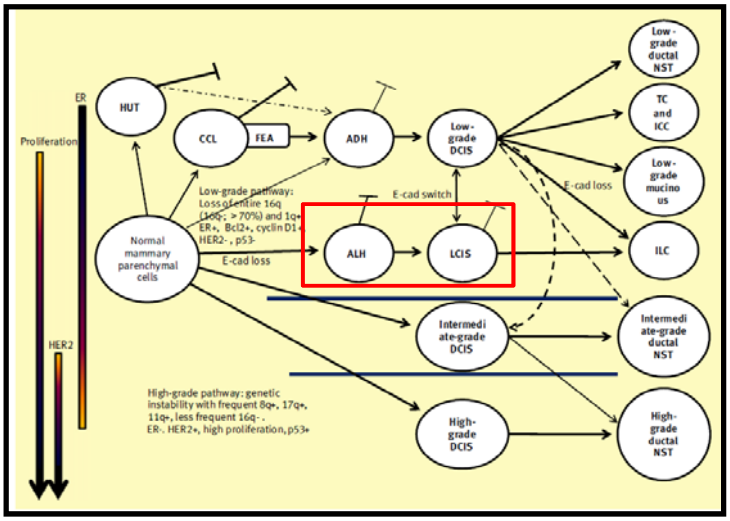
Atypische ductale hyperplasie

- Klinische implicaties
  - RR maligniteit 3-5 (bilateraal)
  - Diagnose op naaldbiopten lastig
    - Advies: atypische intranductale proliferatie, differentiaal diagnostisch ADH of DCIS graad 1
- Differentiaal diagnose
  - Benigne hyperplasie (UDH)
  - Laaggradig DCIS
    - Diameter > 2mm, homogene betrokkenheid van ≥ 2 membraan gebonden ruimten
  - Collagene spherulose

Atypische ductale hyperplasie versus hyperplasie

UDH	ADH
Cellulaire streaming	Behoud cellulaire oriëntatie
Slit like lumina	Uitgeponste lumina
Kernoverlap	Regelmatige celverdeling, geen kernoverlap
Onduidelijke celgrenzen	Duidelijke celgrenzen
CK5/6 mozaiek aankleuring	CK5 negatief
ER wisselende aankleuring	ER uniform en sterk positief

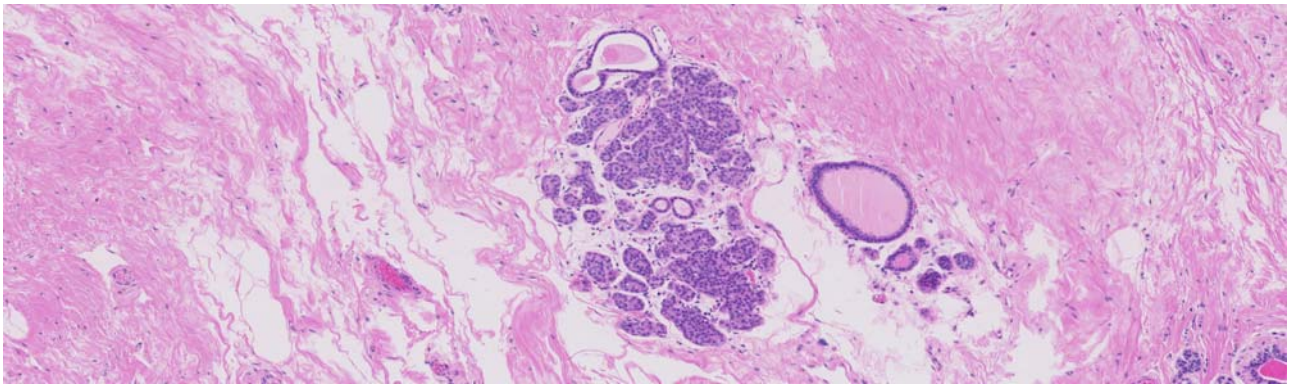
Lobulaire neoplasie

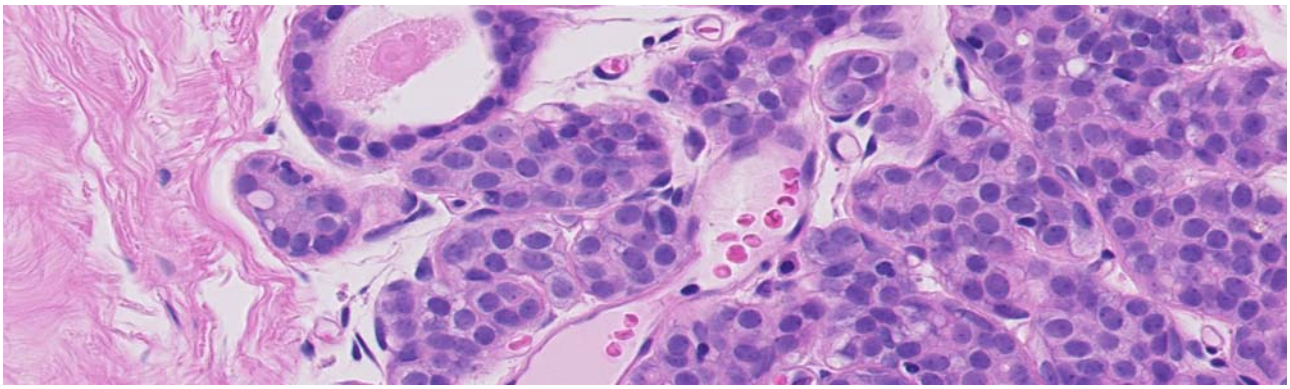


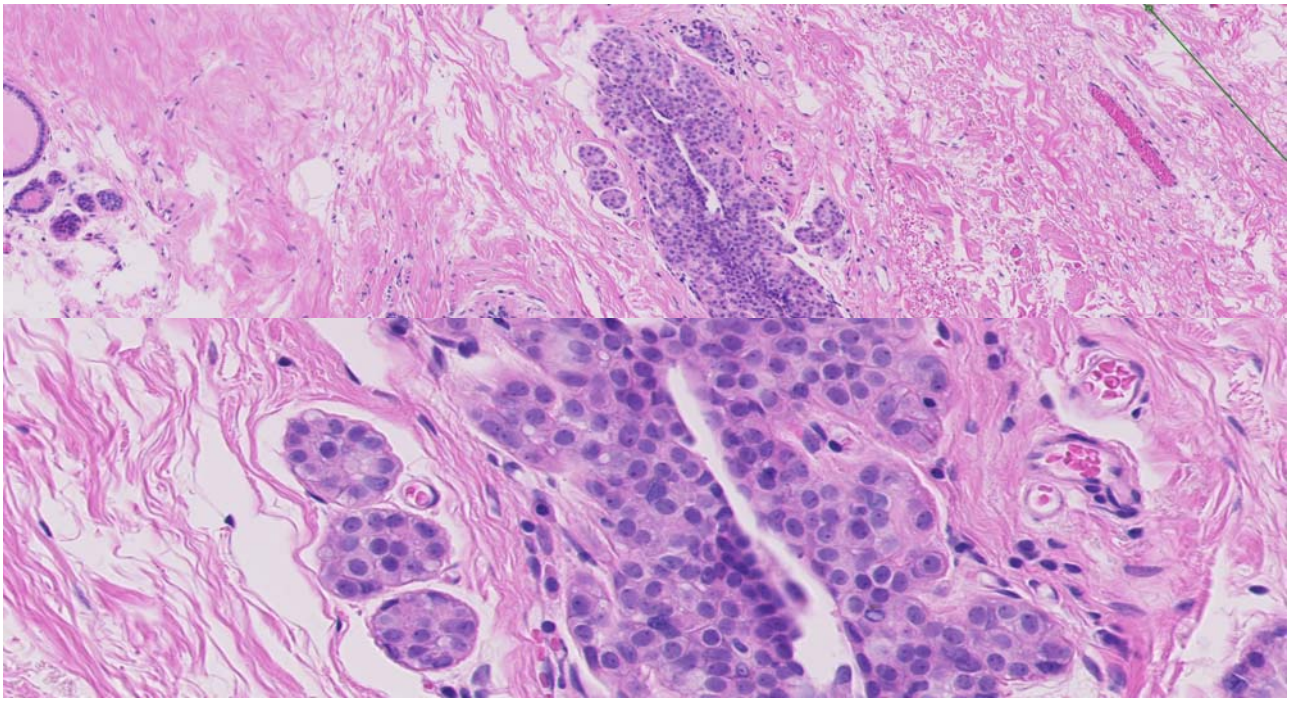
Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012

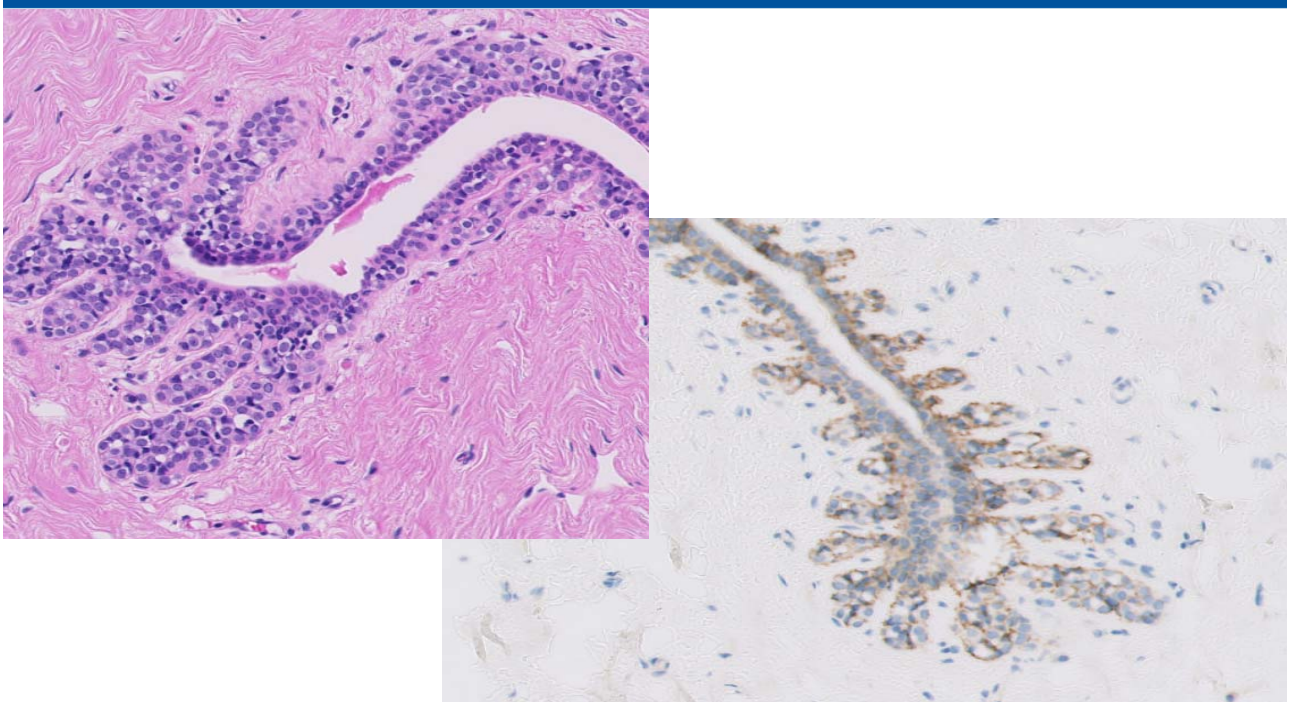
Lobulaire neoplasie

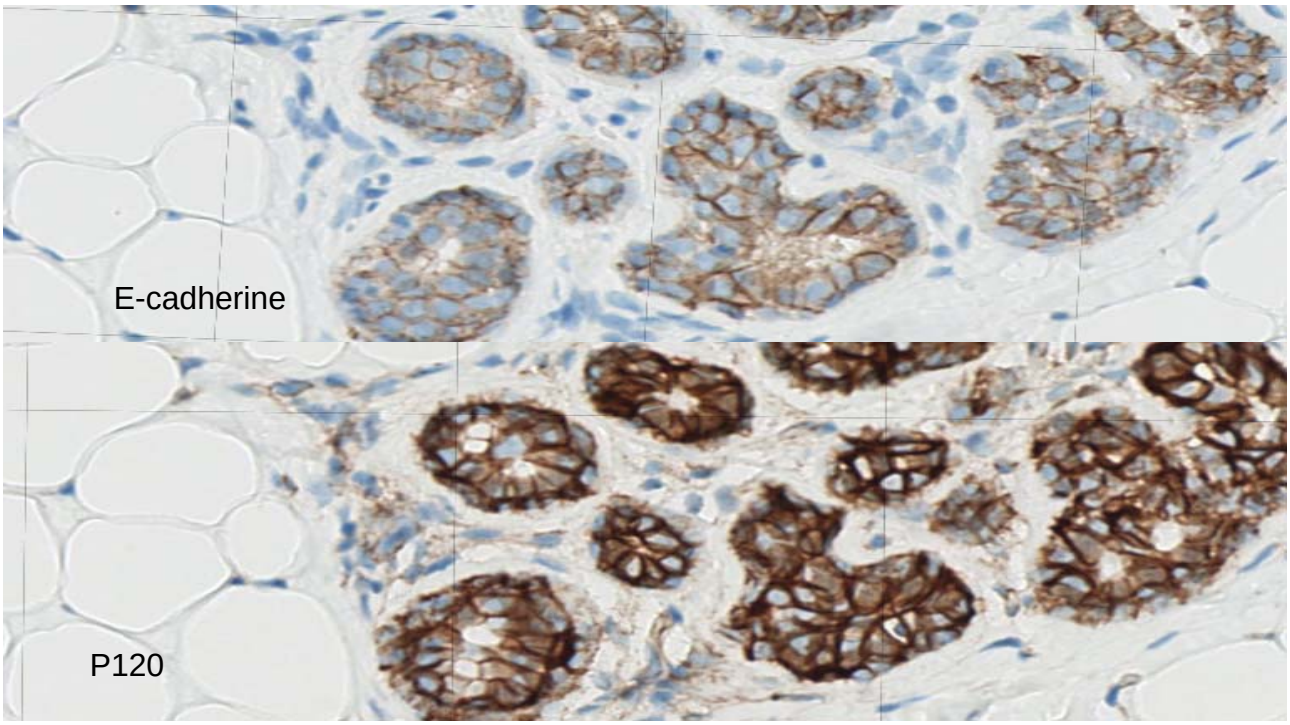
- Lobulaire neoplasie
  - ALH: ≤ 50% van de acini van een lobulaire unit zijn gedilateerd
  - LCIS: > 50% van de acini van een lobulare unit zijn gedilateerd
- Histologische kenmerken
  - Mogelijk pagetoid
  - Monomorfe proliferatie van discohesieve cellen
  - Uniforme ronde kernen
  - Vaak intracytoplasmatische vacuolen
  - Milde tot matige cytonucleaire atypie -) classiek LCIS (onderscheid maken met pleiomorf LCIS)

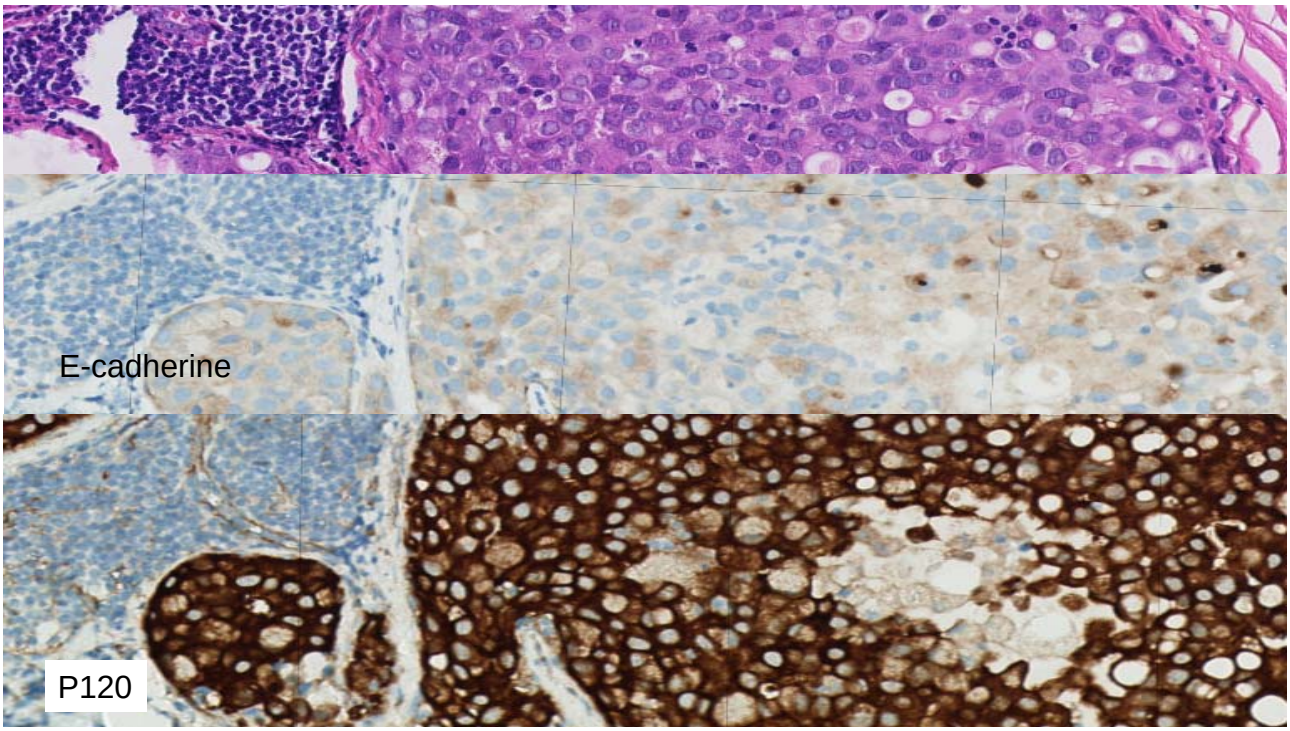








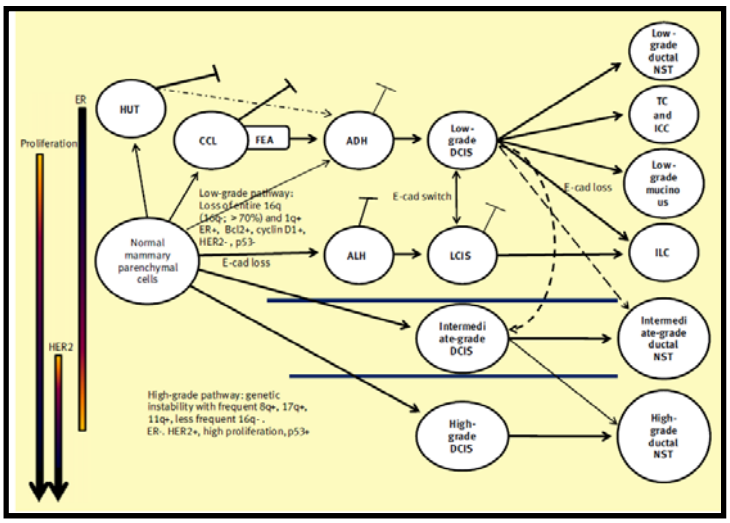

E-cadherine
P120



Lobulaire neoplasie

- Immuunhistochemisch profiel
  - E-cadherine verlies (80-90%)/ cytoplasmatische aankleuring P120
- Klinische implicaties
  - Het betreft meestal een toevalsbevinding
  - RR maligniteit 4-12
    - 2/3e van de volgende carcinomen ontstaan ipsilateraal
    - Jaarlijkje follow-up mammagrografie bij klassieke lobulaire neoplasie
    - Excisie voor LCIS met necrose, massa vormende LCIS en pleiomorfe LCIS
- Differentiaal diagnose
  - Solide DCIS of DCIS met lobulaire cancerisatie

Vragen?



Rakha EA, The low nuclear grade breast neoplasia family, Diagnostic Histopathology, 2012