



Apocriene laesies
Celien Vreuls

15:55-16:00

Welkom en opening

Deel I - Apocriene laesies

Celien Vreuls

16:00-16:45

Presentatie

16:45-17:30

Coupe sessie

17:30-18:00

Pauze

Deel II - Fibroepitheliale laesies

Paul van Diest

18:00-18:45

Presentatie

18:45-19:30

Coupe sessie

19:30-20:00

Afsluiting

Disclosure belangen spreker

Geen (potentiële)
belangenverstrengeling



Inhoud

- Apocriene metaplasie
- Apocriene adenosis/ apocriën adenoom
- Atypische apocriene adenosis
- Apocriene ADH/DCIS
- Apocriën carcinoom



Apocriene metaplasie



Apocrine metaplasie (AM)

Etiologie: ?

“apocrine differentiation precursor cells” versus
metaplasie

Virchows Arch (1997) 431:205–209

© Springer-Verlag 1997

ORIGINAL ARTICLE

Paolo Viacava · Antonio Giuseppe Naccarato
Generoso Bevilacqua

Apocrine epithelium of the breast: does it result from metaplasia?



UMC Utrecht

Apocriene metaplasie (AM)

- Meest voorkomende “metaplasie” in de mamma
- Apocriene klieren niet aanwezig in normale mamma
- Etiologie onbekend; hormonale disbalans
- Palpabele cysten meestal AM (78%)
- AM vanaf 25 jaar aanwezig, piek na 50 jaar
- Kan in benigne en maligne afwijkingen voorkomen



Apocriene metaplasie (AM)

- Radiologie: cyste, microcalcificaties
- Prognostisch: geen relatie ontwikkelen carcinoom

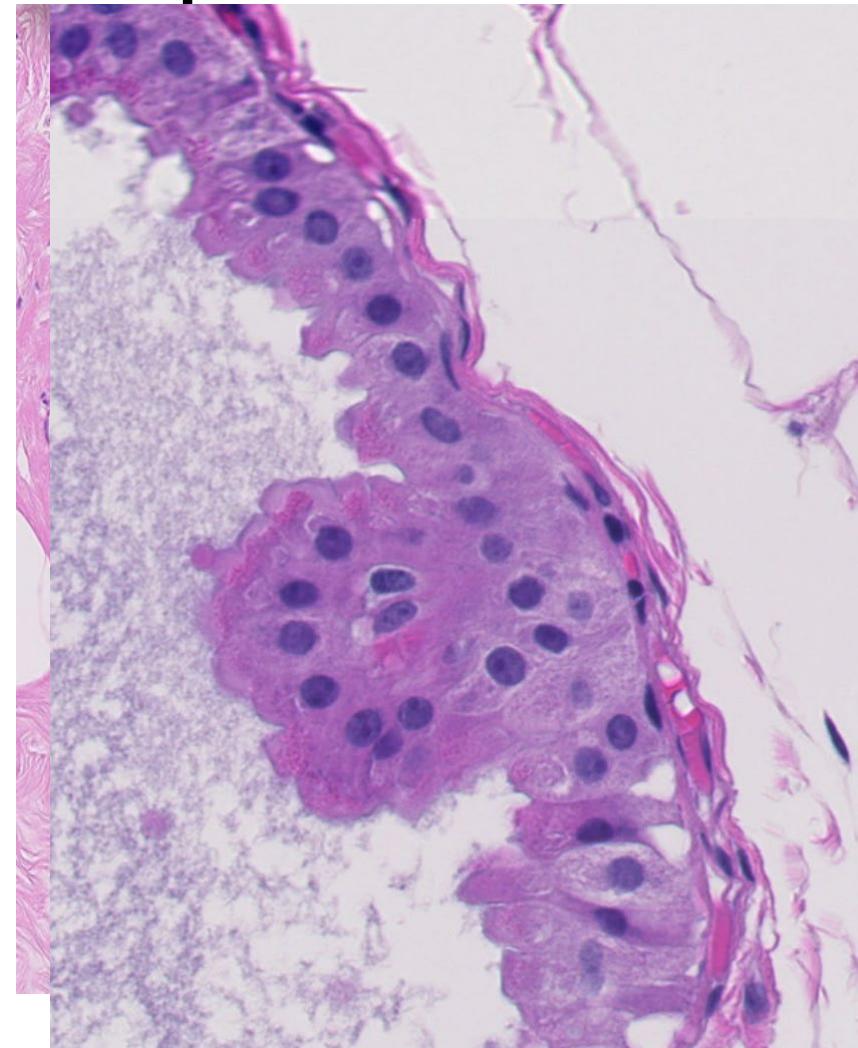


Apocriene metaplasie

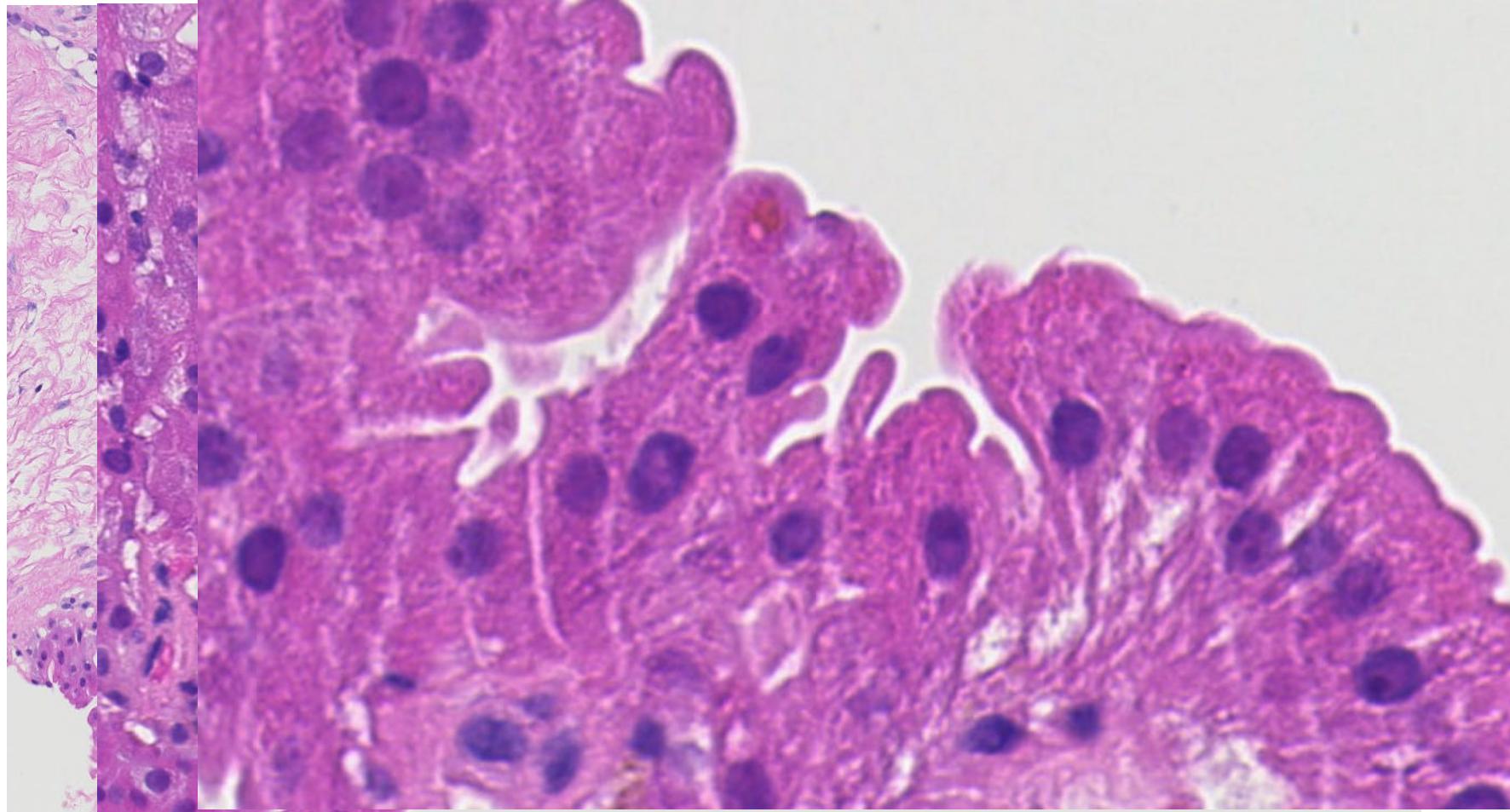
Microscopie

Architectuur

- Epitheel van een simpele cyste
- Enkele laag tot papillaire proliferatie
micropapillair tot papillair
- Myoepitheel meestal duidelijk aanwezig
- Aanwezig in veel (benigne) afwijkingen



Papillaire apocriene veranderingen



UMC Utrecht

Apocriene metaplasie

Microscopie

Detail

- Vergrote epitheliale cellen
- Ruim eosinofiel cytoplasma
- Apicale blebbing of snouting
- Supranucleaire vacuole of eosinofiele granules in het cytoplasma
- Kern is rond, variërend in vorm, dens chromatine en een enkele, centraal gelegen nucleool



Calcium oxalate crystallen

The American Journal of Surgical Pathology 14(10): 961-968, 1990

© 1990 Raven Press, Ltd., New York

Calcium Oxalate Crystals in Breast Biopsies The Missing Microcalcifications

The American Journal of Surgical Pathology 15(6): 586-591, 1991

© 1991 Raven Press, Ltd., New York

Calcium Oxalate Crystals in the Breast Pathology and Significance

Jose Edmundo G. Gonzalez, M.D., Richard G. Caldwell, M.D.,
and Jonas Valaitis, M.D.

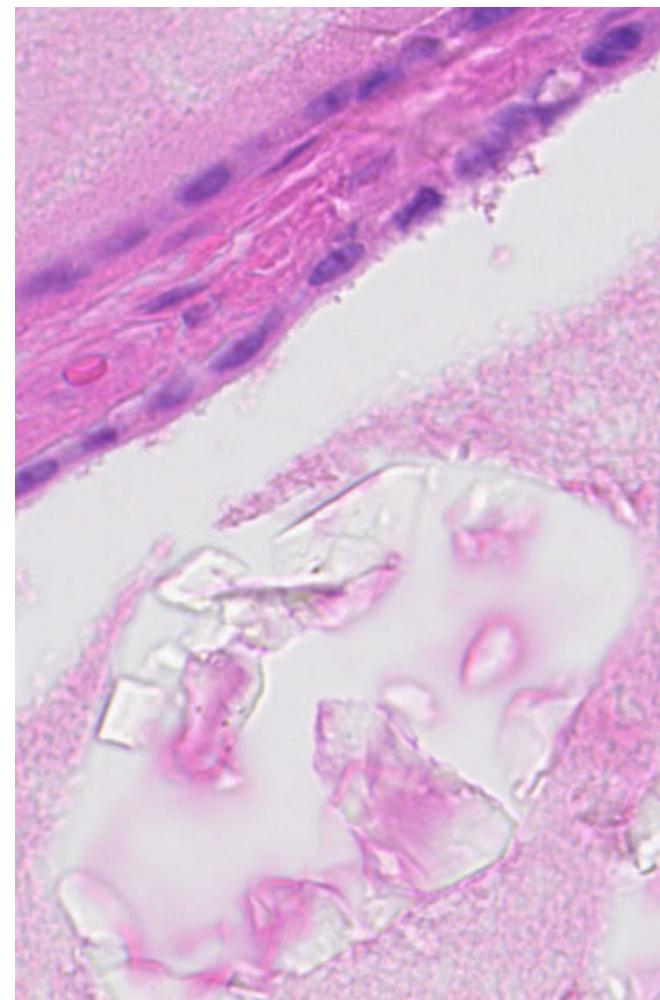
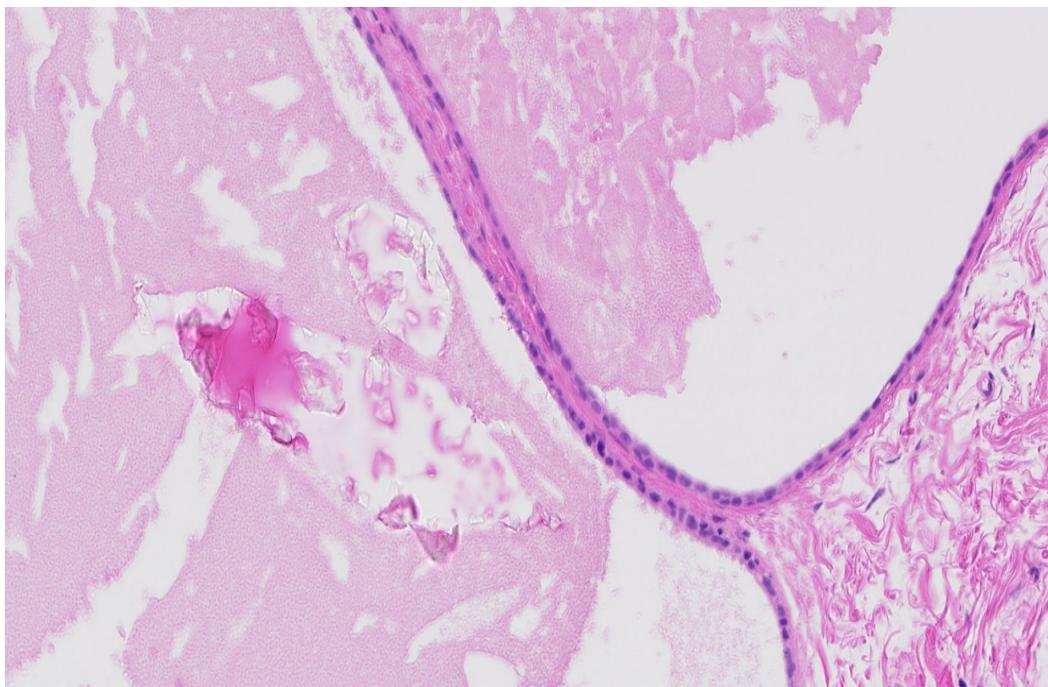
Calcium oxalate cr澀allen

- Calcium fosfaat vs. calcium oxalaat cr澀allen
- Polarisatie
- Secretoir product
- Apocrine metaplasie

TABLE 2. *Lesions found in 16 breast biopsies with calcium oxalate deposits (one or more lesion/biopsy)*

| Lesion | No. of biopsies |
|---|-----------------|
| Cystic or papillary apocrine metaplasia | 14 |
| Simple apocrine metaplasia | 4 |
| Lobular carcinoma in situ | 4 |
| Atypical lobular hyperplasia | 4 |
| Moderate/florid ductal hyperplasia | 3 |
| Mild ductal hyperplasia | 3 |
| Sclerosing adenosis | 3 |
| Inflammation | 3 |
| Papilloma | 3 |
| Atypical ductal hyperplasia | 2 |
| Fibroadenoma | 2 |
| Infiltrating ductal carcinoma | 1 |
| Atrophy | 1 |

Calcium oxalate crystallen

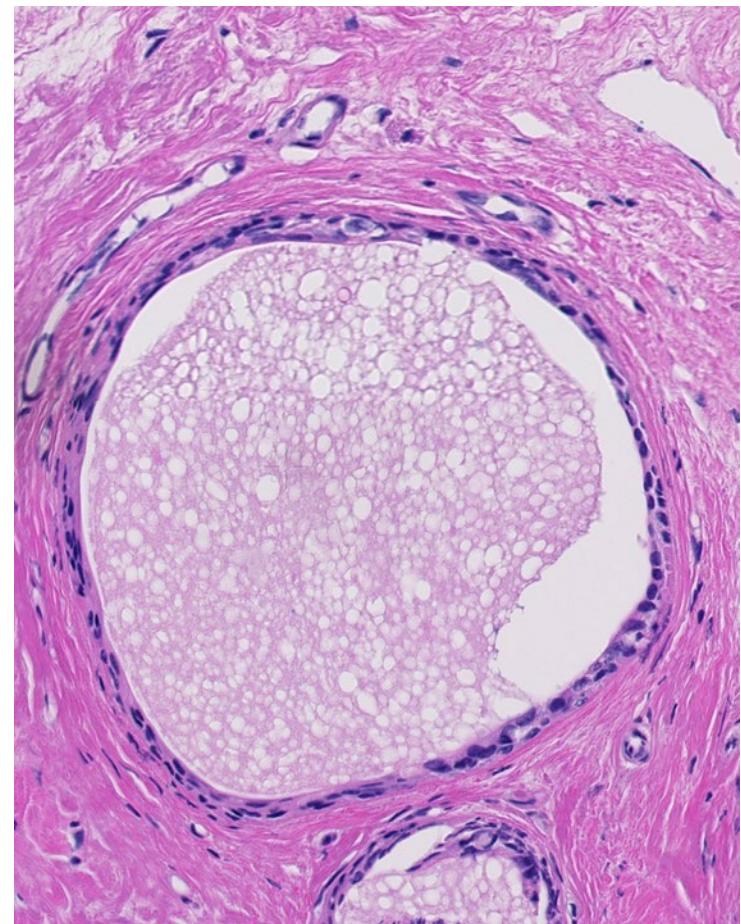


Apocriene metaplasie

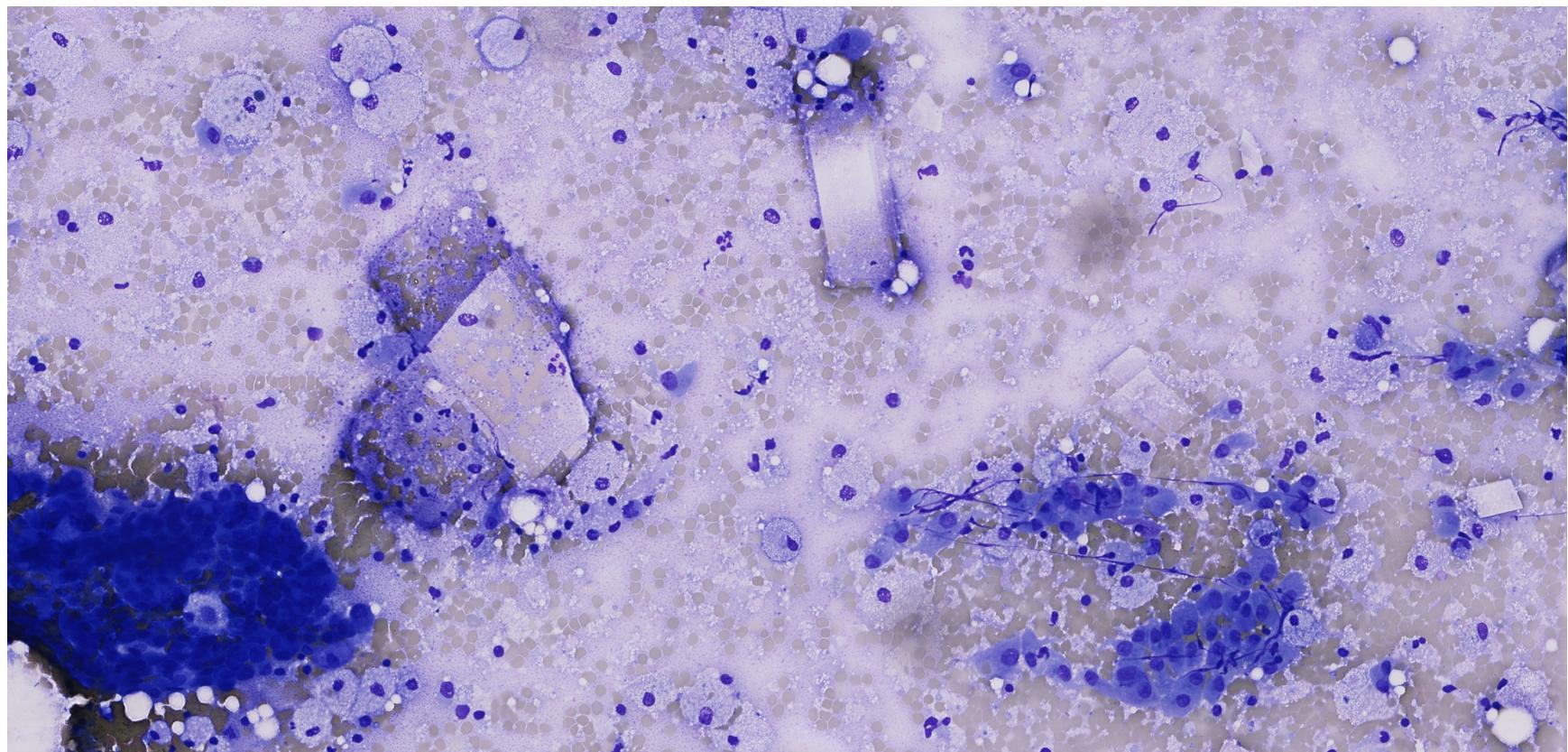
Verschillende fases

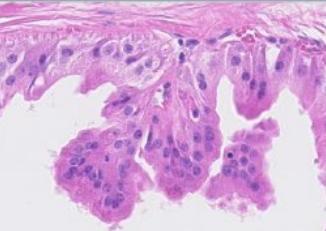
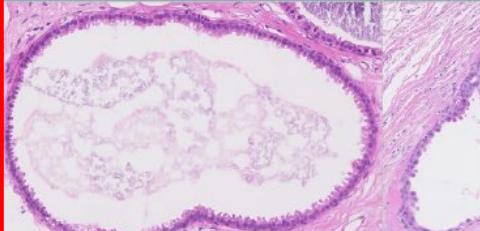
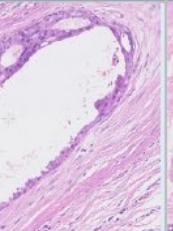
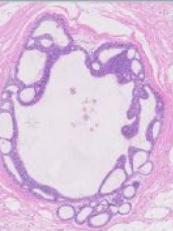
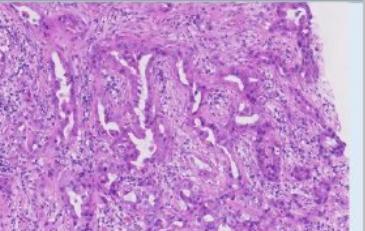
Proliferative fase →
zoals we het kennen

Regressive fase →
afgeplat epitheel



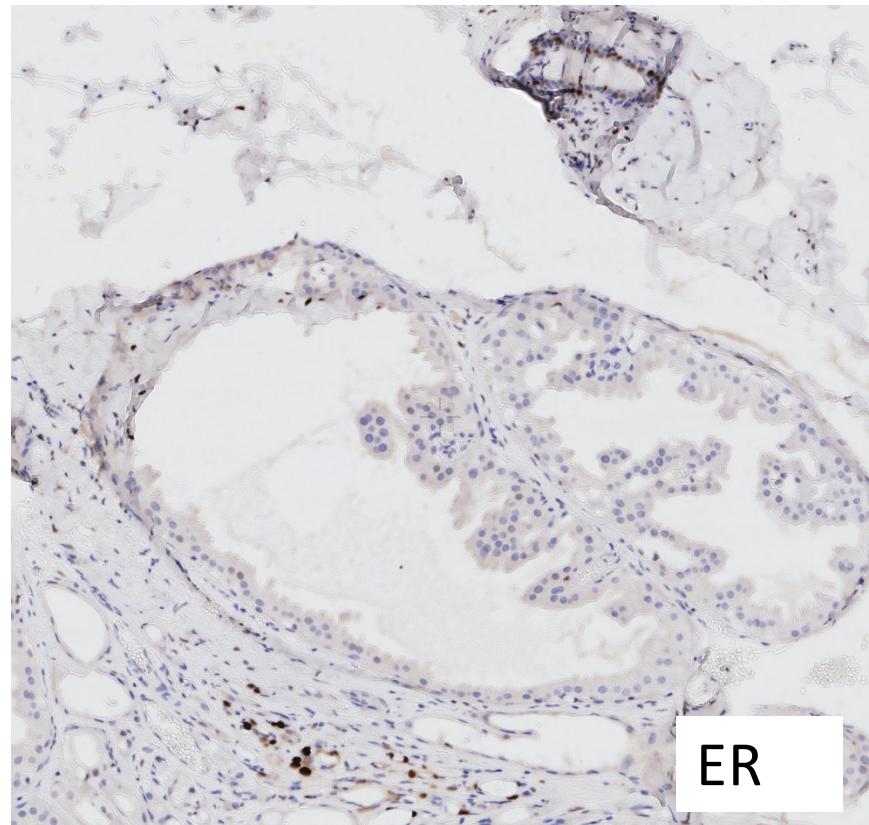
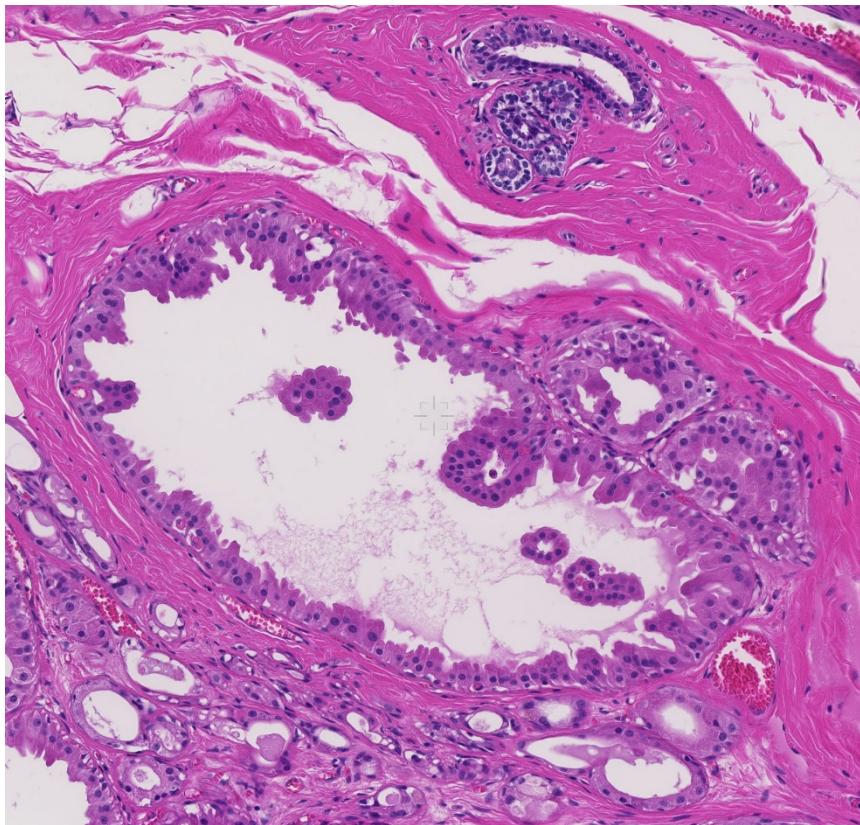
Apocriene metaplasie - cytologie



| Marker | (Papillaire) apocriene metaplasie | Cilinder cel veranderingen | (Laaggradige) apocriene DCIS | Laaggradige DCIS | Carcinoom met apocriene differentiatie |
|---------------------|---|--|---|---|---|
| FOTO |  |  |  |  |  |
| ER | - | + | - | + | - |
| PR | - | + | - | + | - |
| Her neu | + / - | - | + | - | + / - |
| AR | + | + / - | + | + | + |
| CK5 | - | - | - | - | - |
| GCDFP-15 (BRST2) | + | + / - | + | -/+ | + |

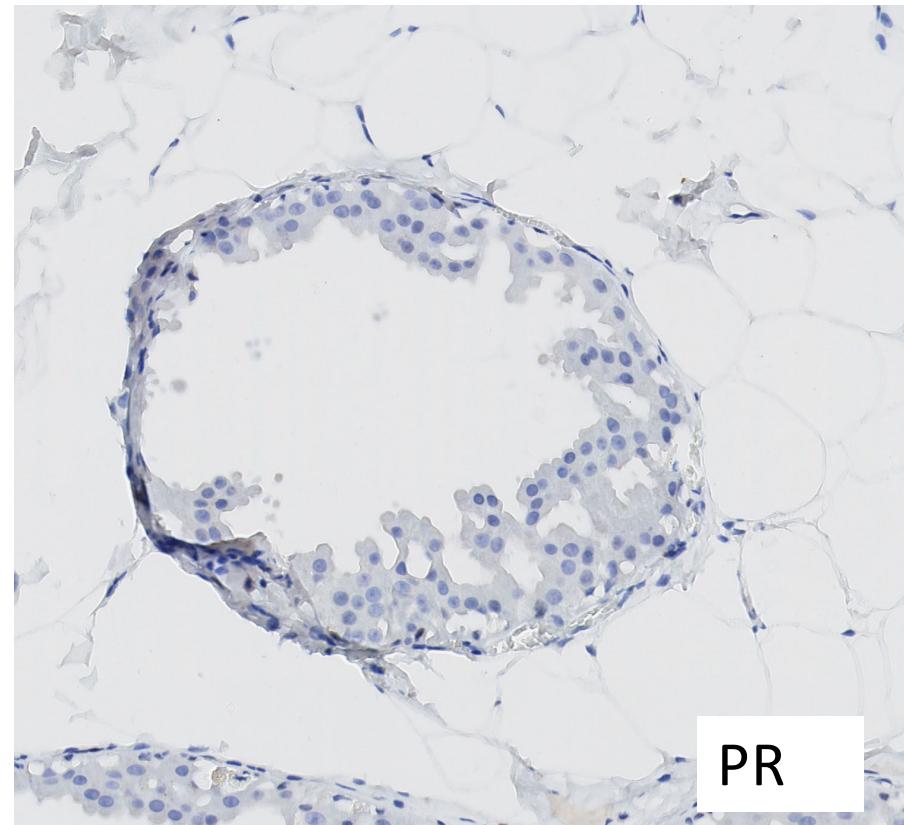
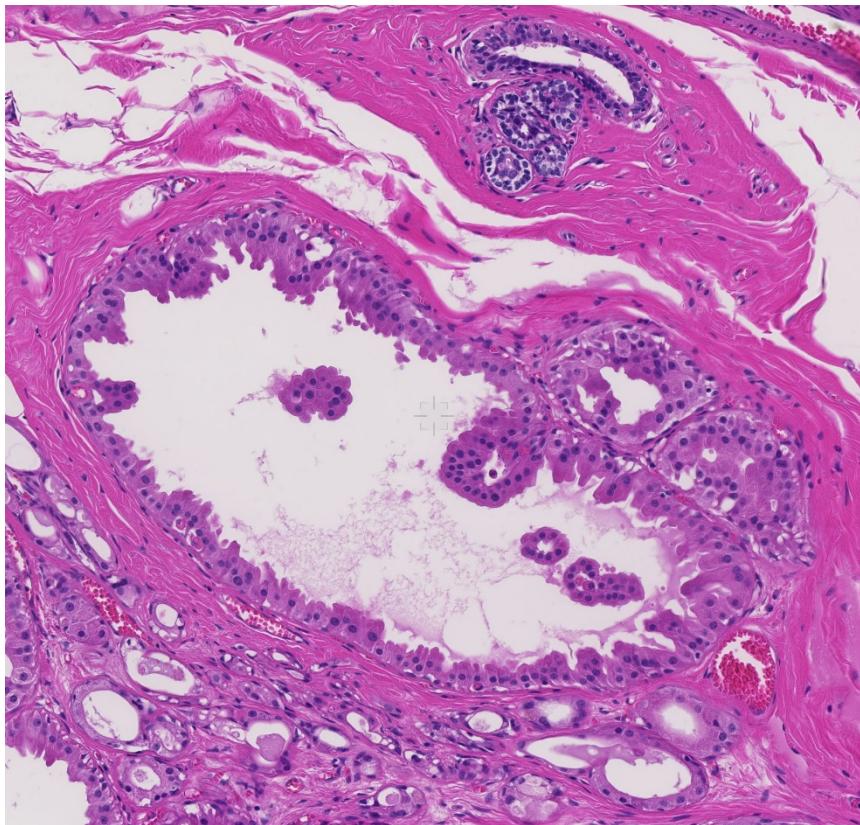


Apocrine metaplasie



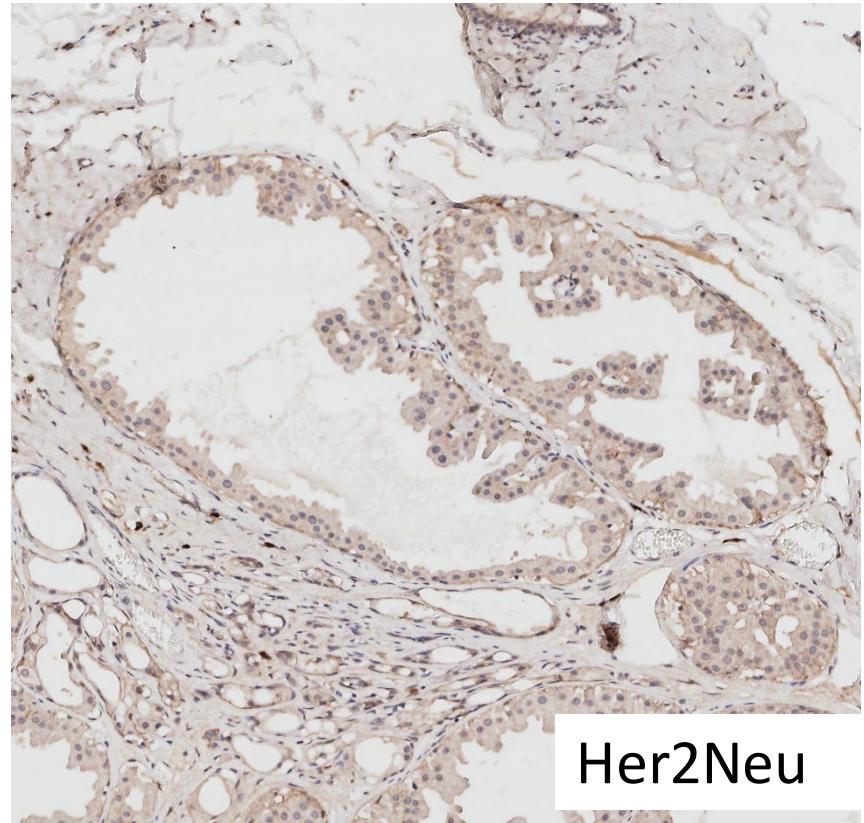
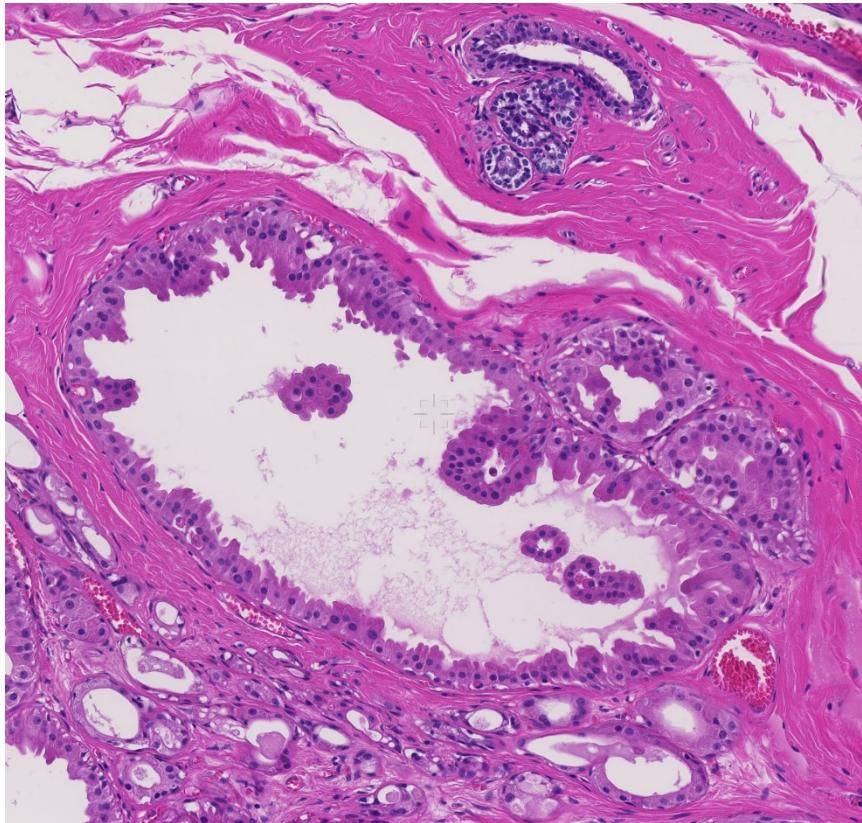
UMC Utrecht

Apocrine metaplasie

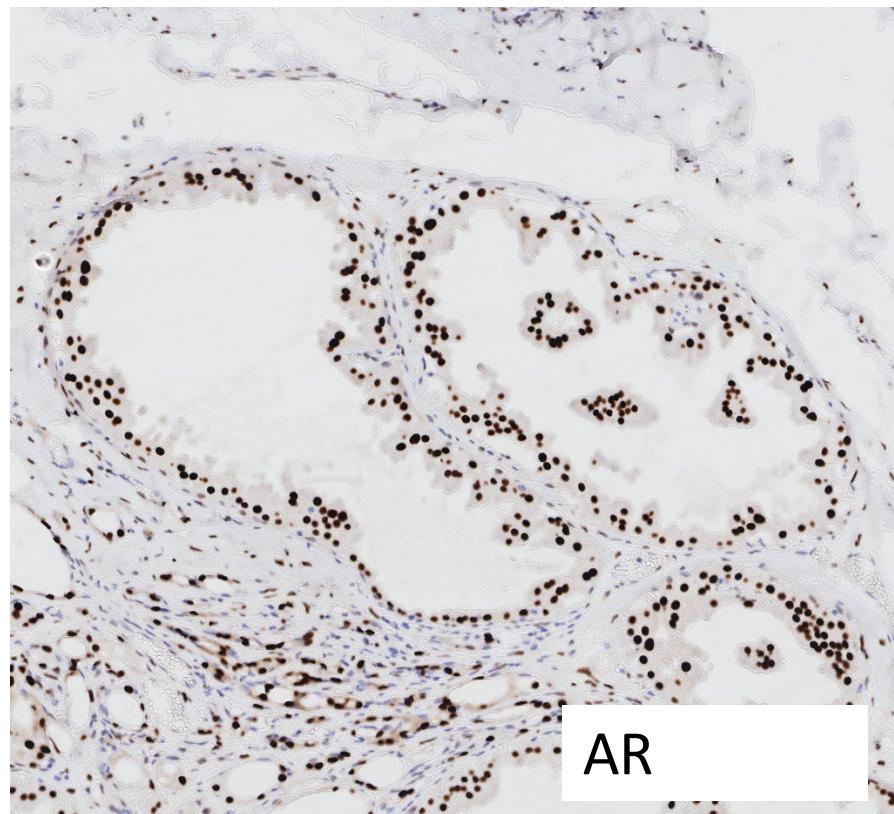
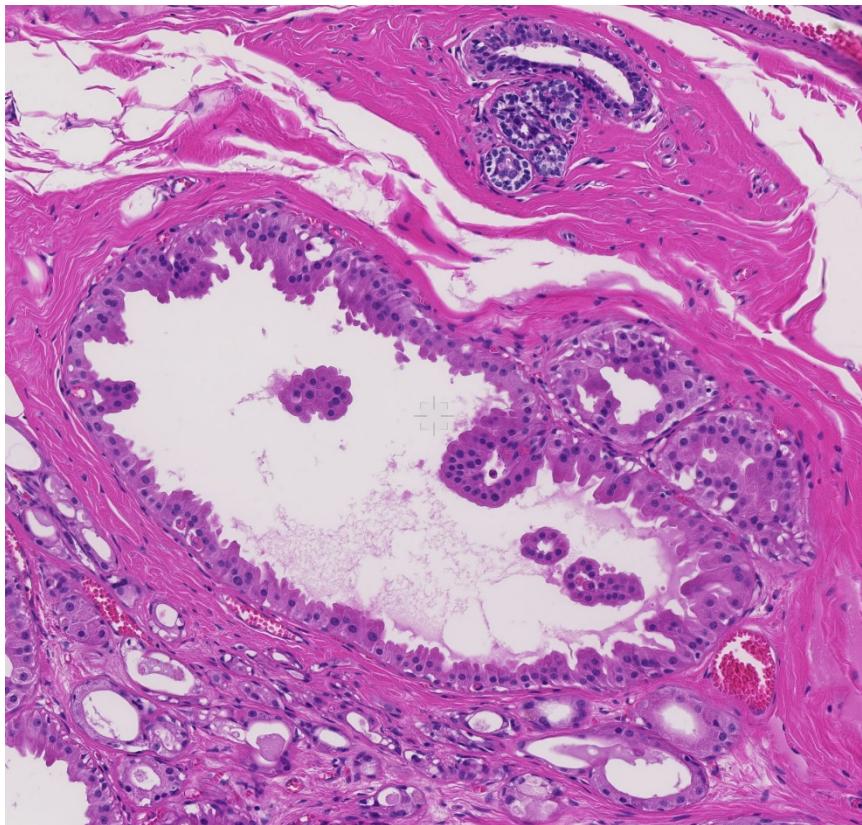


UMC Utrecht

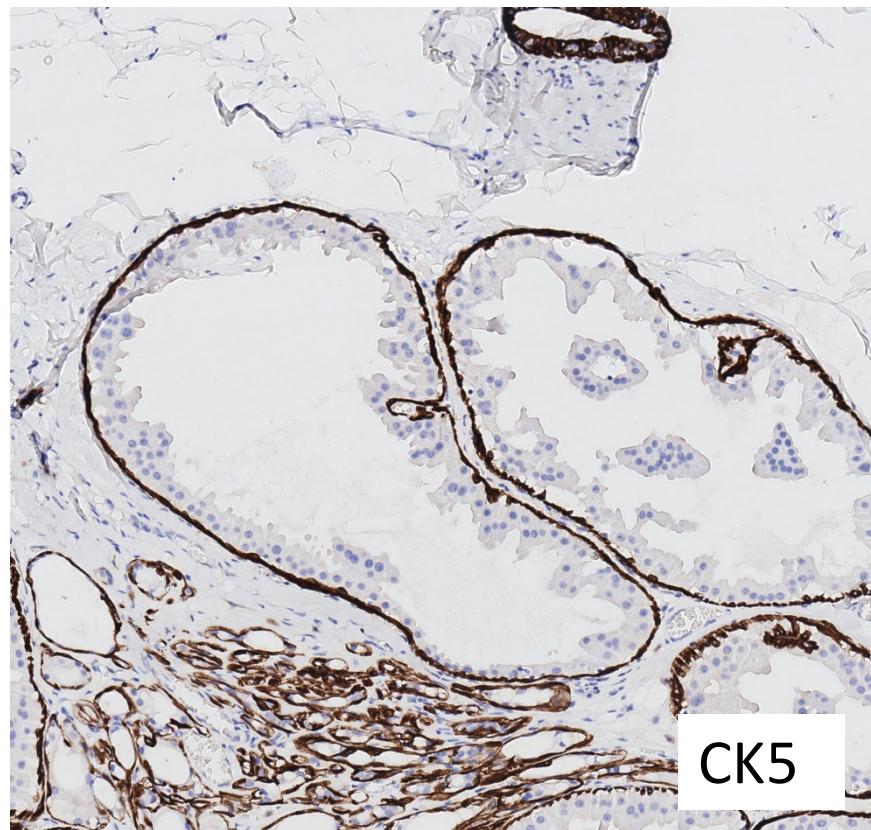
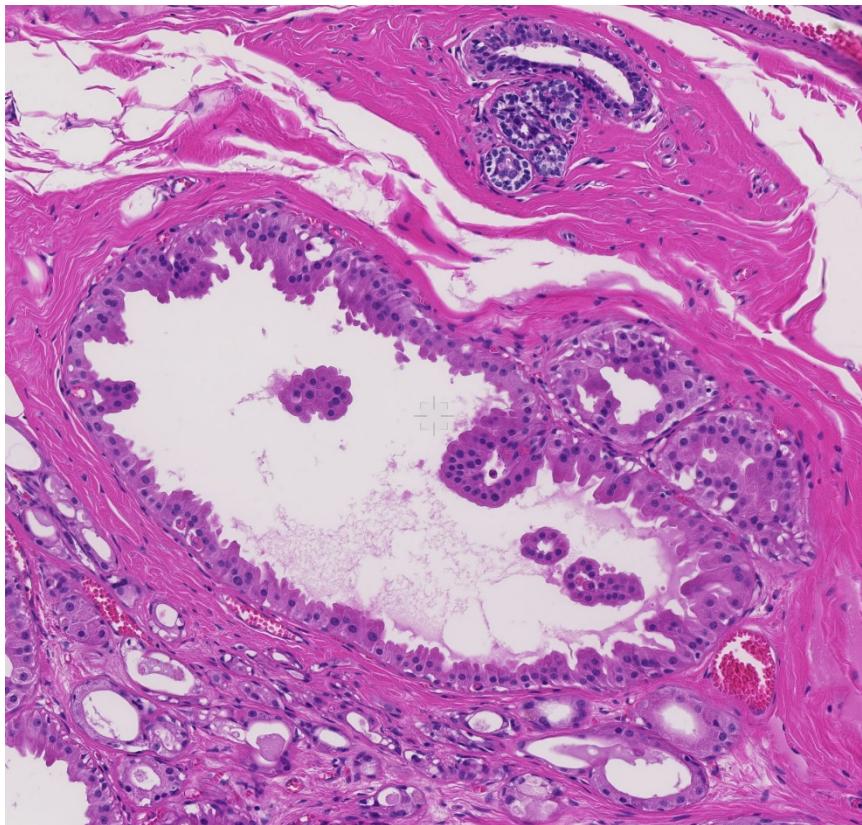
Apocrine metaplasie



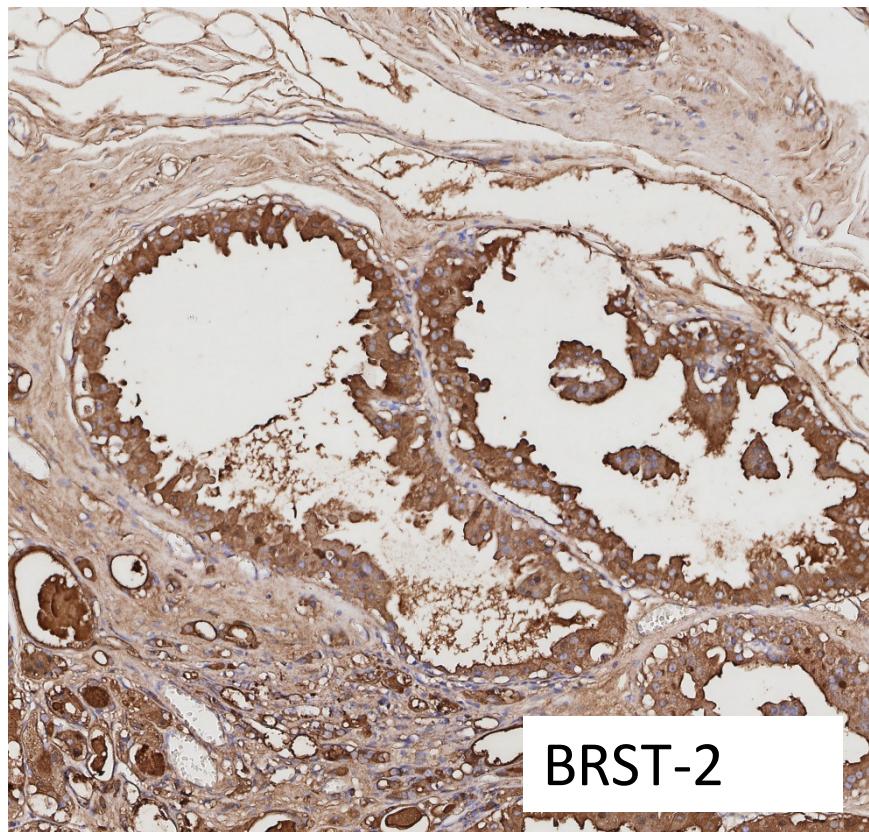
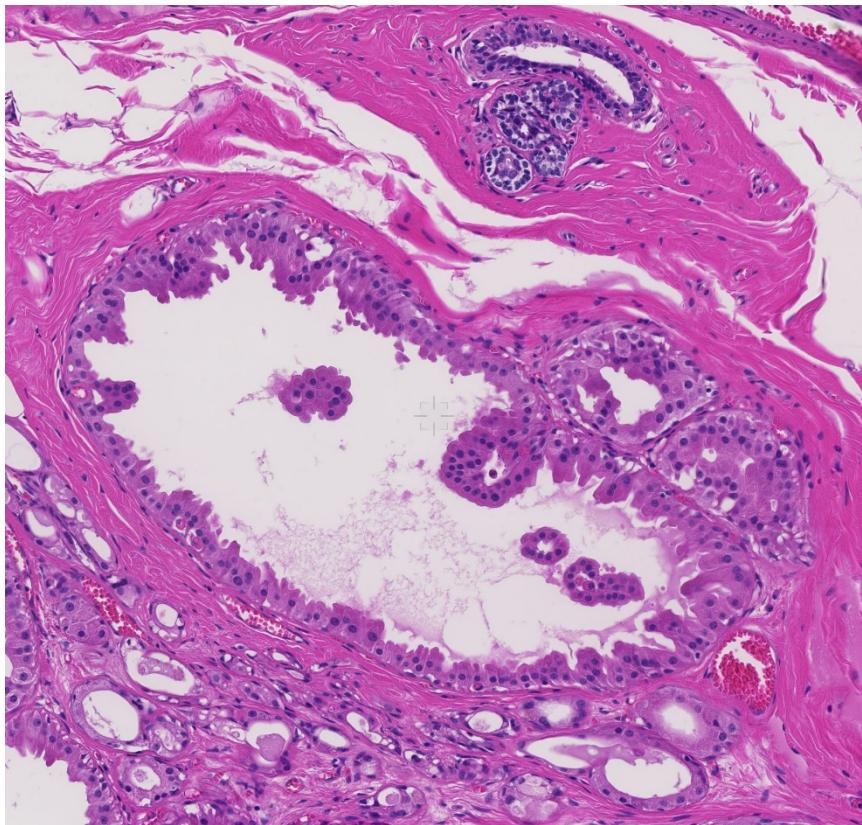
Apocrine metaplasie



Apocrine metaplasie

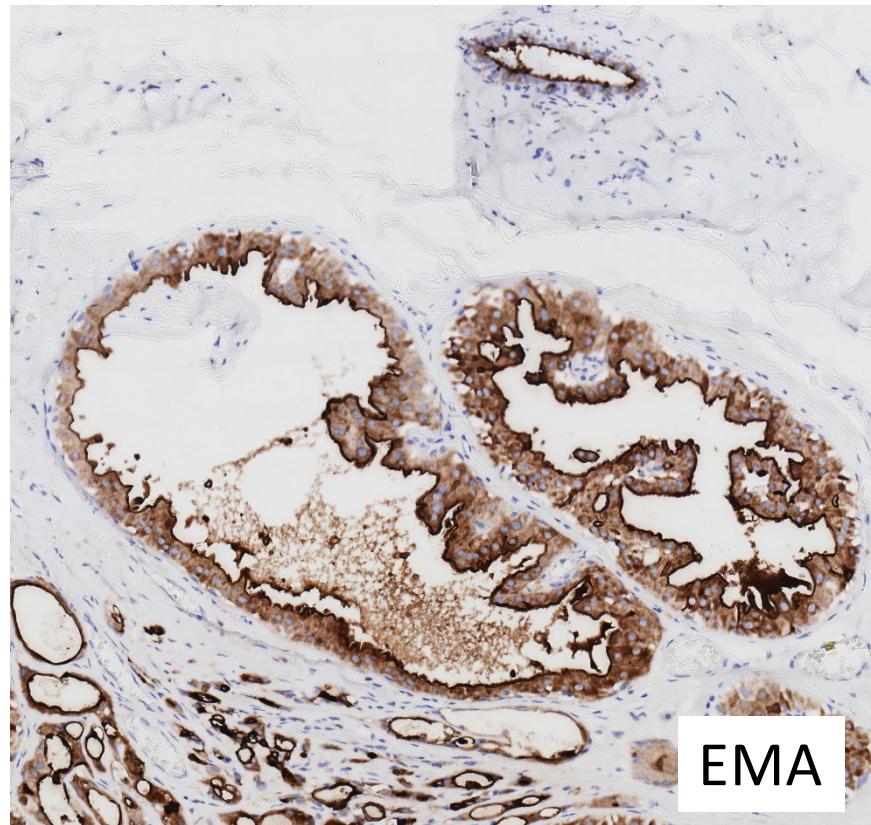
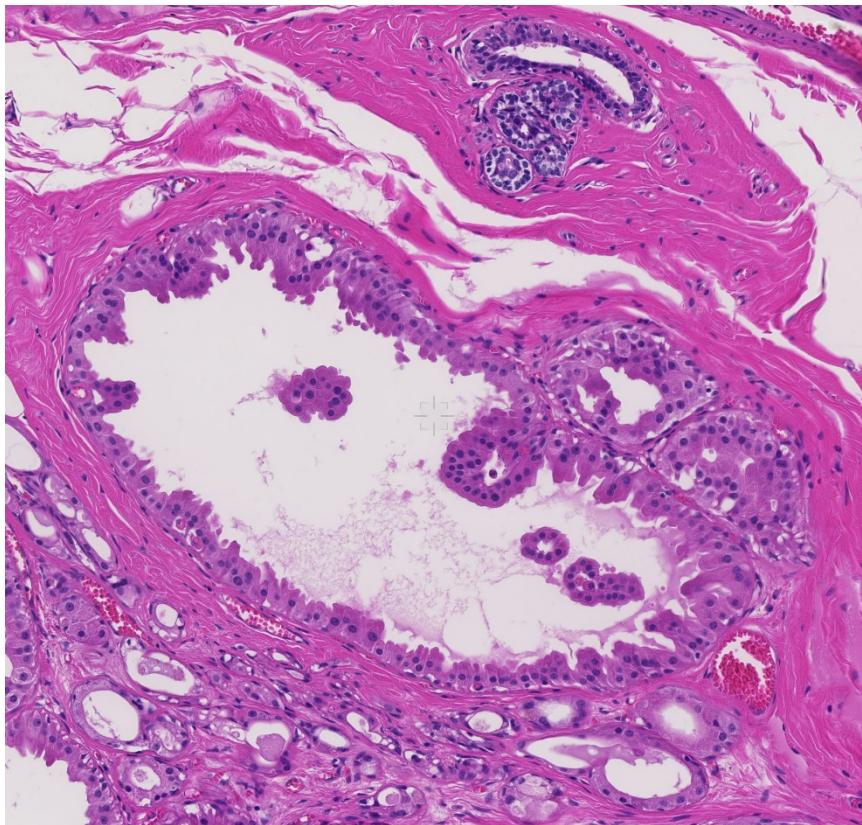


Apocrine metaplasie



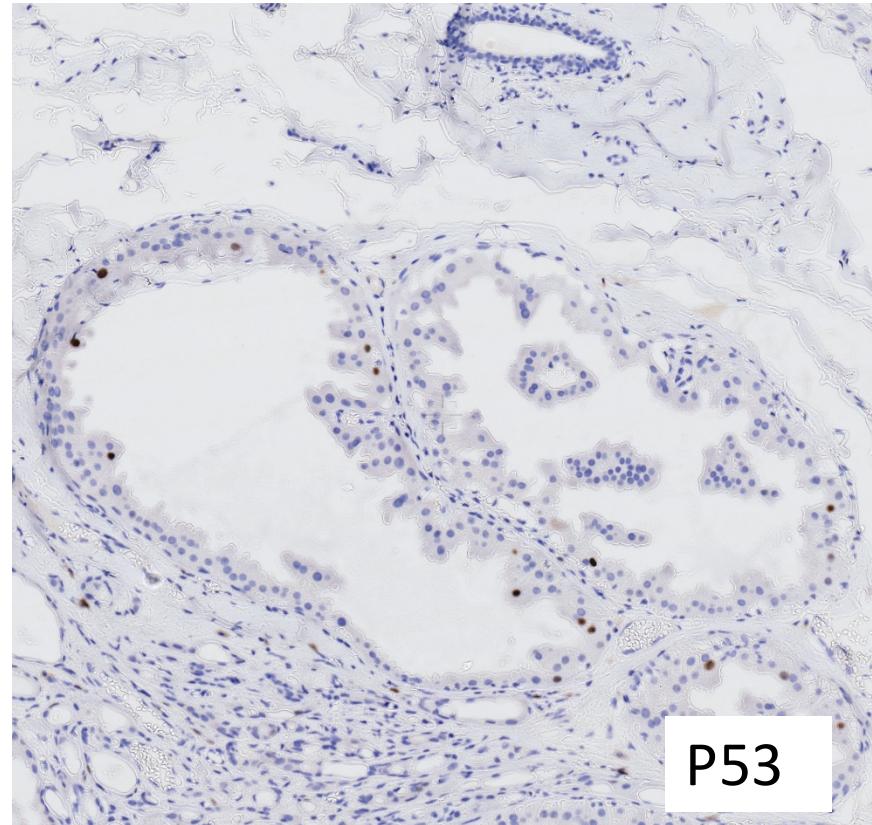
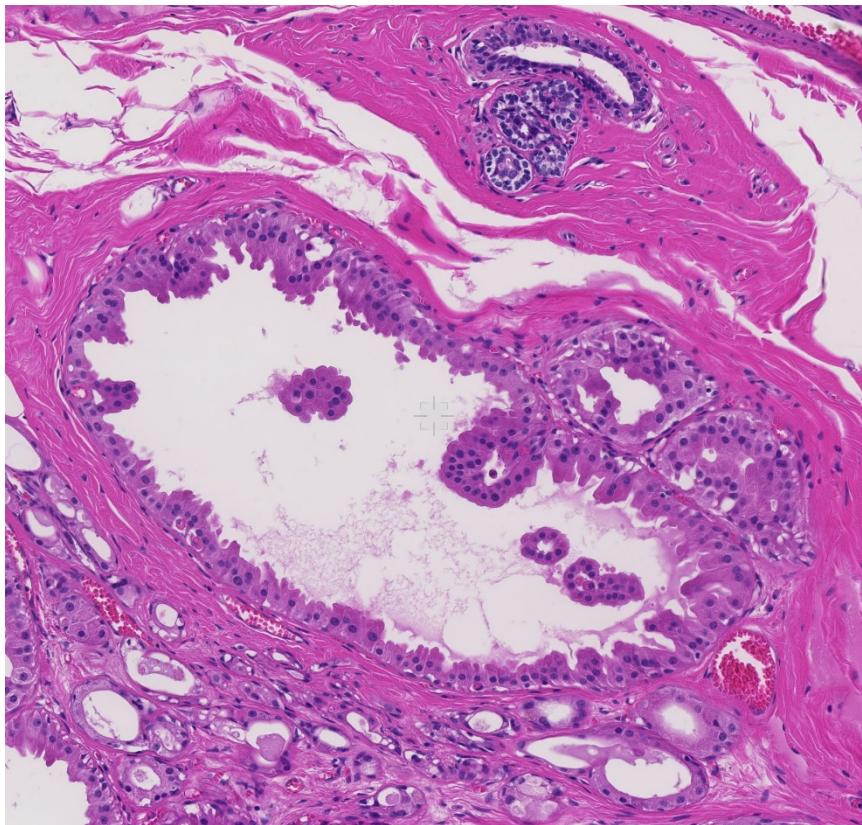
UMC Utrecht

Apocrine metaplasie



UMC Utrecht

Apocrine metaplasie



UMC Utrecht

Apocriene adenosis en apocrien adenoom



Apocrine adenosis en apocrine adenoom

Essential and desirable diagnostic criteria

Essential

Apocrine adenosis: a lobulocentric proliferation of benign glandular structures, distorted by fibrosis and lined by apocrine cells characterized by eosinophilic granular or vacuolated cytoplasm containing a prominent nucleolus.

Apocrine adenoma: a well-delineated benign tumour characterized by a dense, diffuse proliferation of round and oval tubular structures with luminal apocrine cells and an outer attenuated basal myoepithelial cell layer with little background stroma.

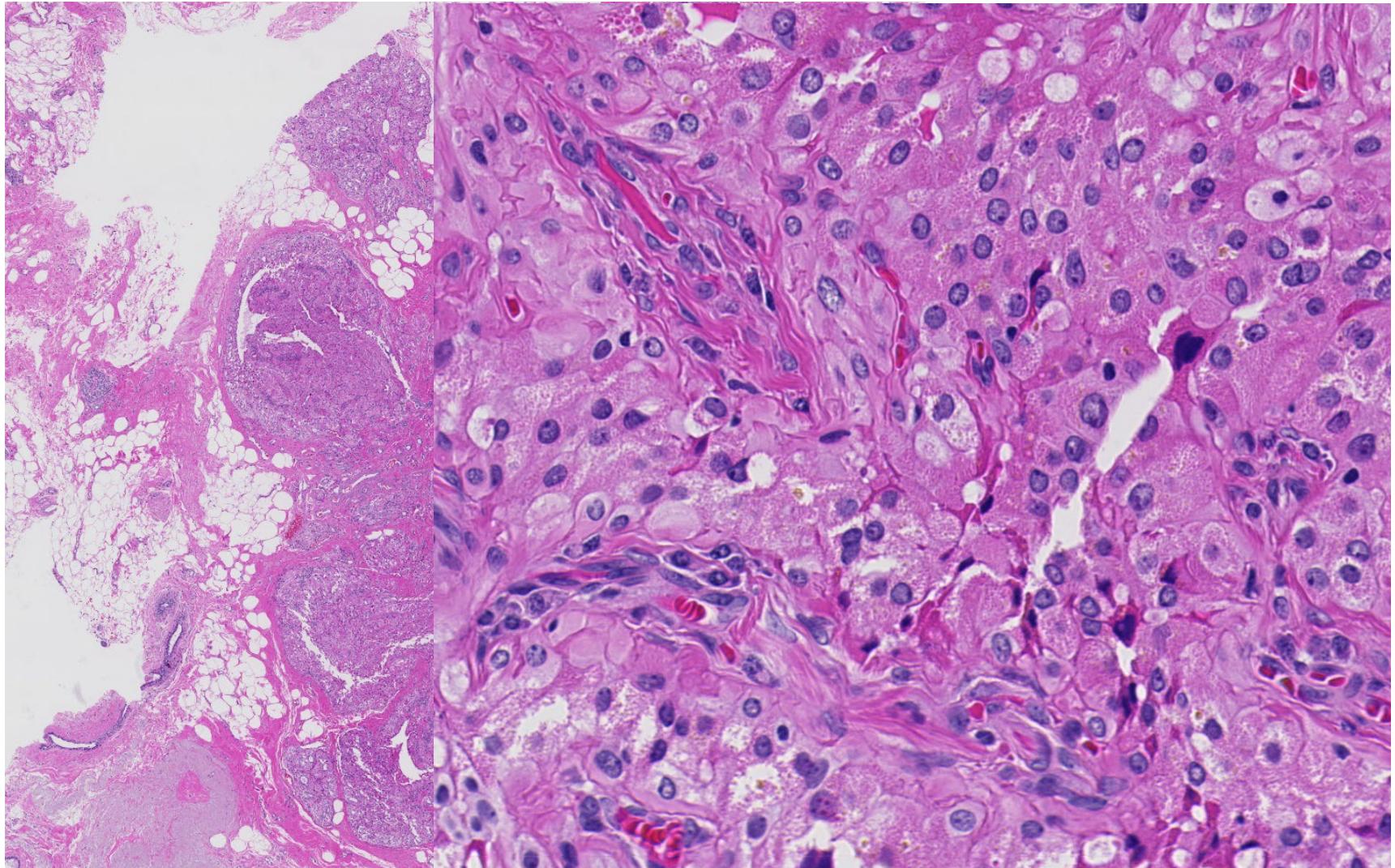


Apocriene adenosis en apocriën adenoom

- (scleroserende) adenosis + apocriene metaplasie
- Benigne laesie
- Behandeling vergelijkbaar met fibroadenoom
- Geen maligne transformatie



Apocrine adenosis



Atypische apocriene adenosis



Atypische apocriene adenosis

Morfologische kenmerken:

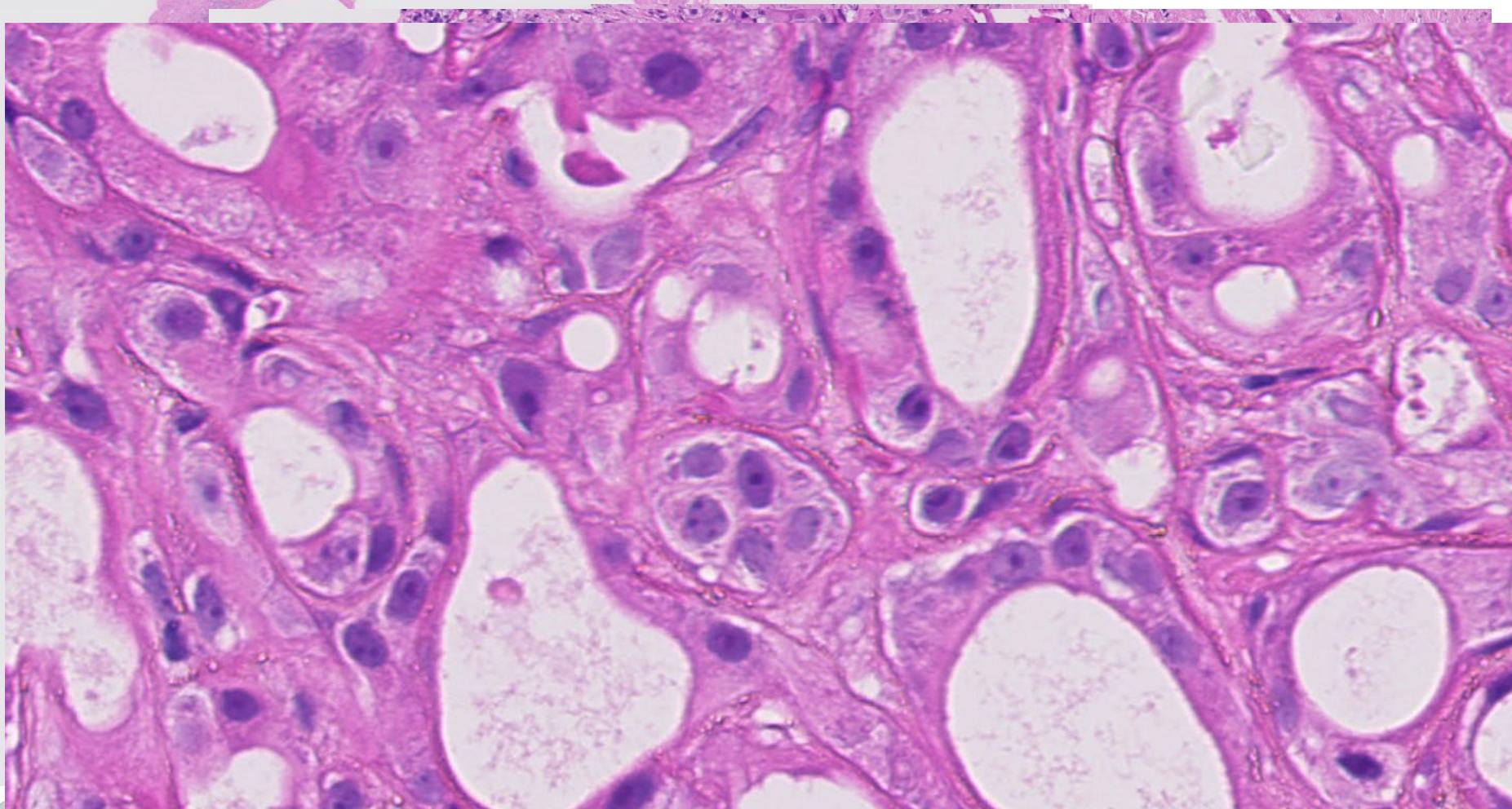
- Kern 3 x vergroot
- Cytoplasmatische opheldering/ vacuolisatie
- Irregulaire kernmembraan
- Kernpleomorfie

Geen hoog-risico precursor laesie

DD: apocriene DCIS



Atypische apocriene adenosis



Apocrine ADH/DCIS



UMC Utrecht

Apocriene ADH/DCIS

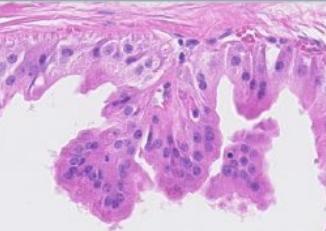
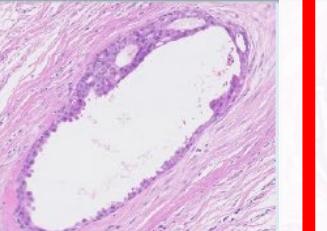
Architecturele atypie

- Cribiforme, solide of (micro)papillaire groei

Cytonucleaire atypie

- Kernen niet basaal georiënteerd
- Nucleoli zijn minder uniform, excentrisch gelegen en multiple
- Cytoplasma gevacuoliseerd
- ‘decapitatie’ verdwijnt

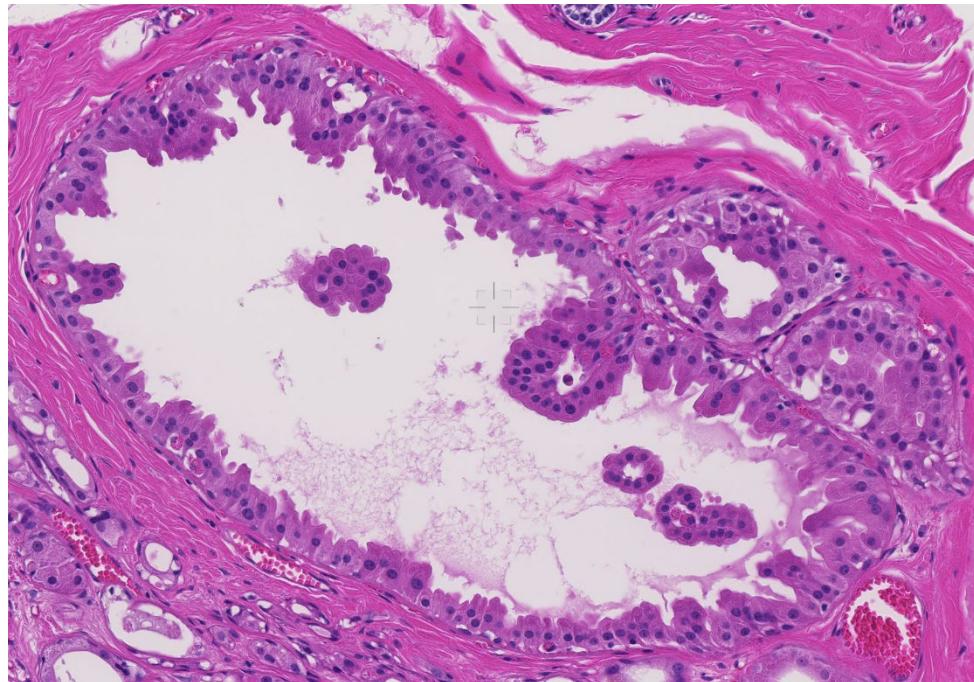


| Marker | (Papillaire) apocriene metaplasie | Glijder cel veranderingen | (Laaggradige) apocriene DCIS | Hogegradijte DCIS | Carcinoom met apocriene differentiatie |
|---------------------|---|---|--|---|---|
| FOTO |  |  |  |  |  |
| ER | - | + | - | + | - |
| PR | - | + | - | + | - |
| Her neu | + / - | - | + | - | + / - |
| AR | + | + / - | + | + | + |
| CK5 | - | - | - | - | - |
| GCDFP-15 (BRST2) | + | + / - | + | - / + | + |

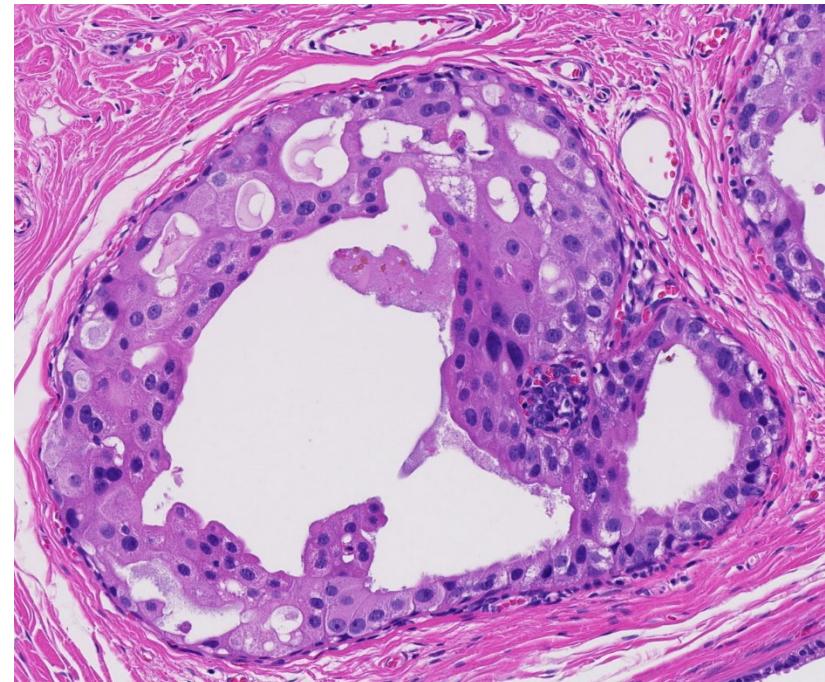


Diagnostisch dilemma

Apocriene metaplasie



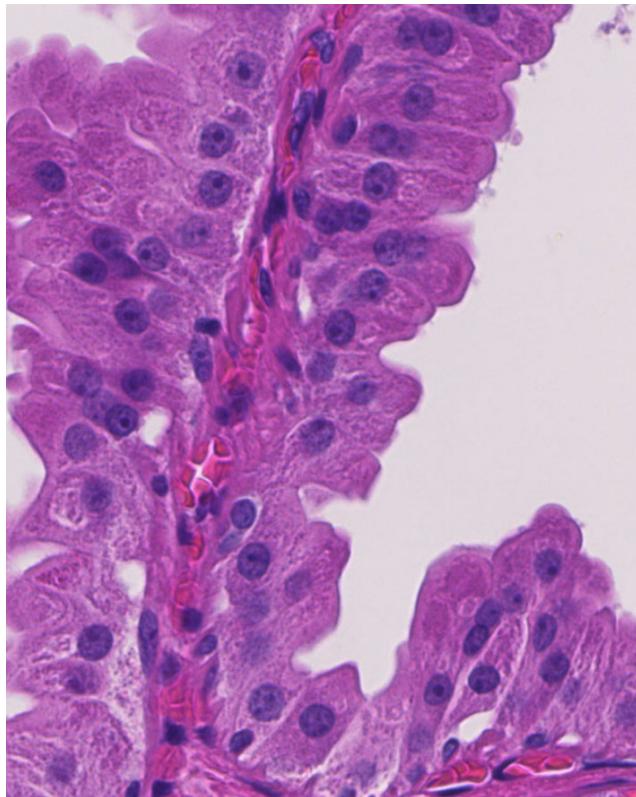
ADH/ laaggradige
apocriene DCIS



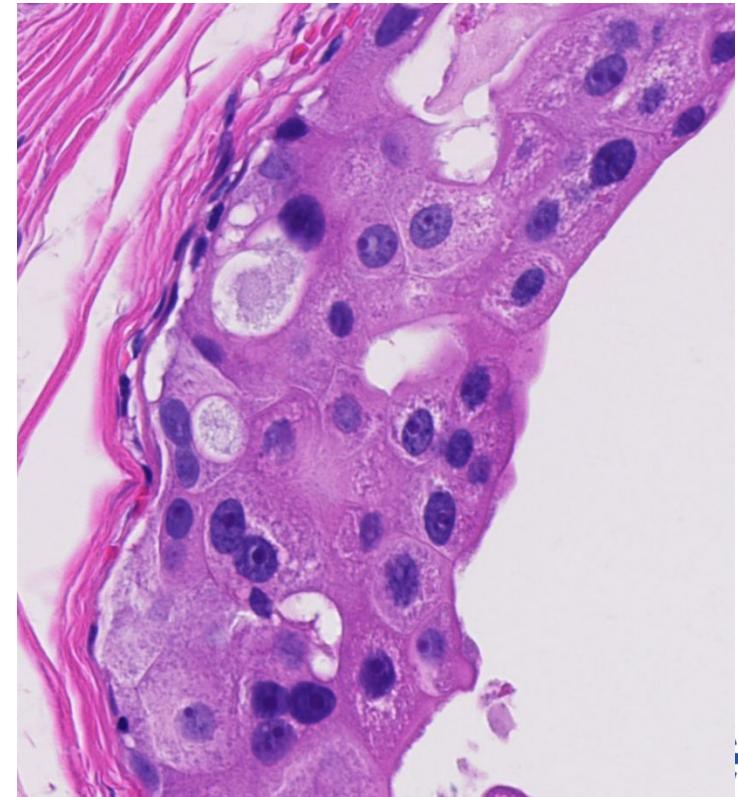
UMC Utrecht

Diagnostisch dilemma

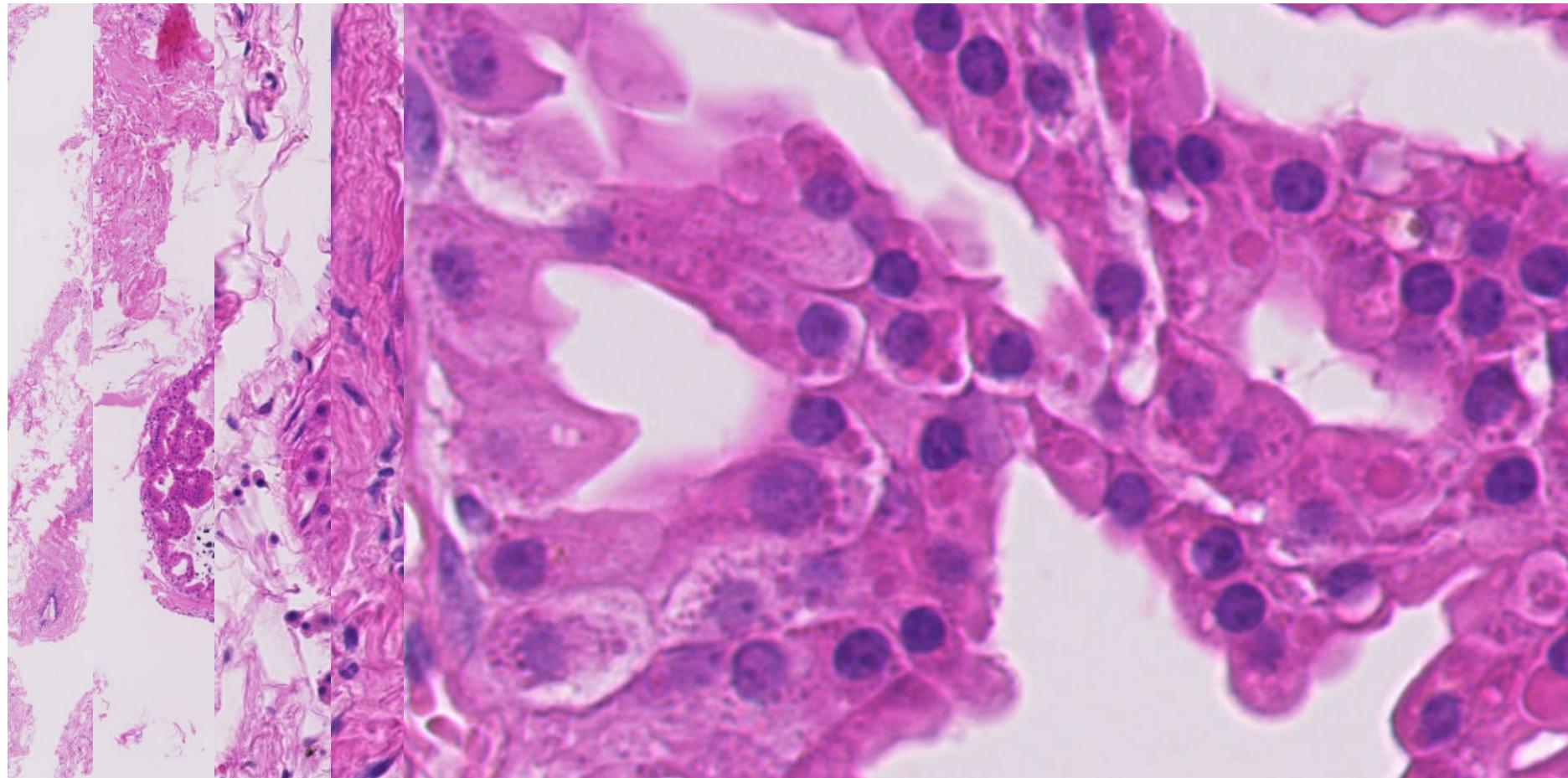
Apocriene metaplasie



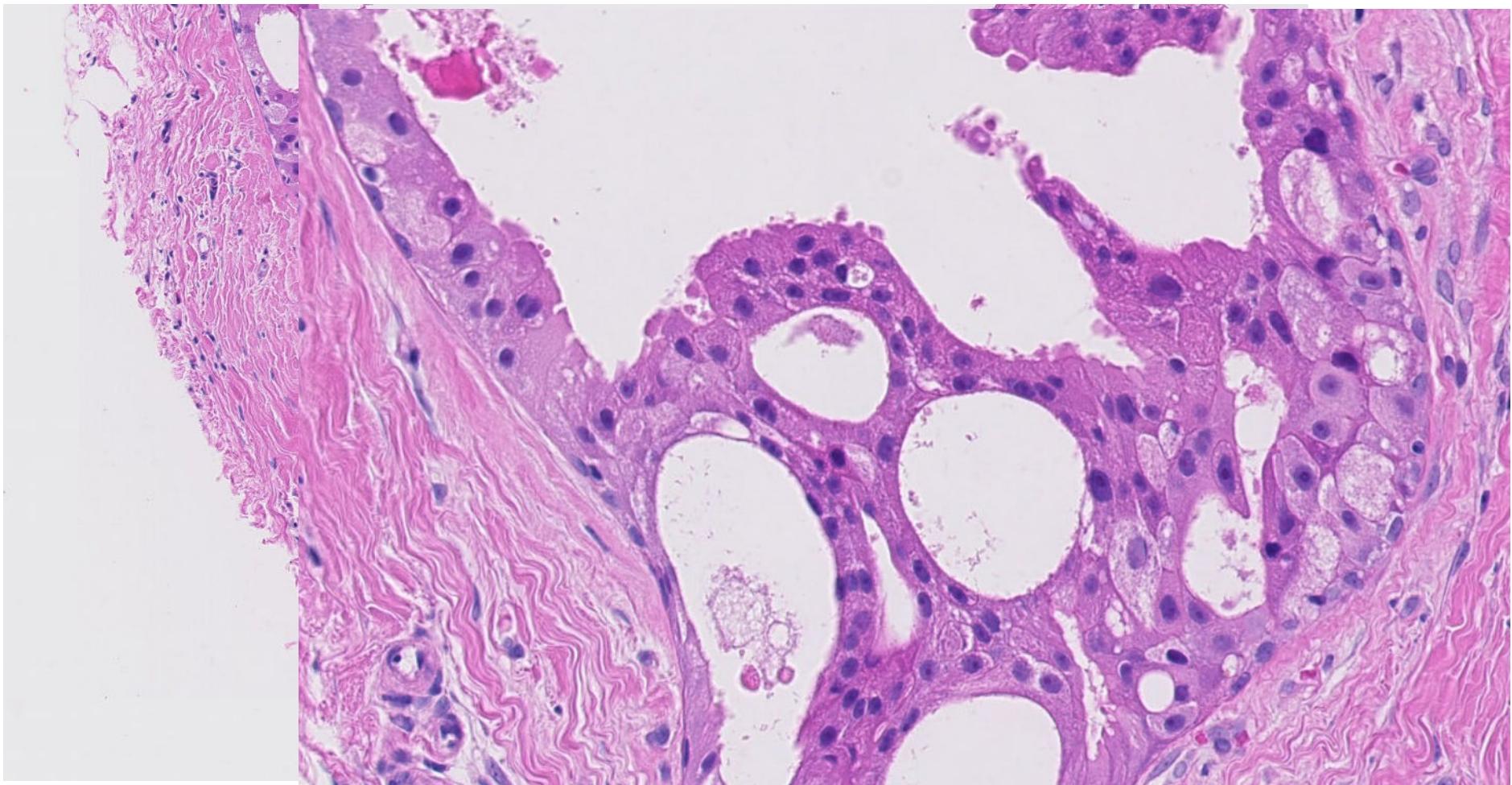
ADH/ laaggradige
apocriene DCIS



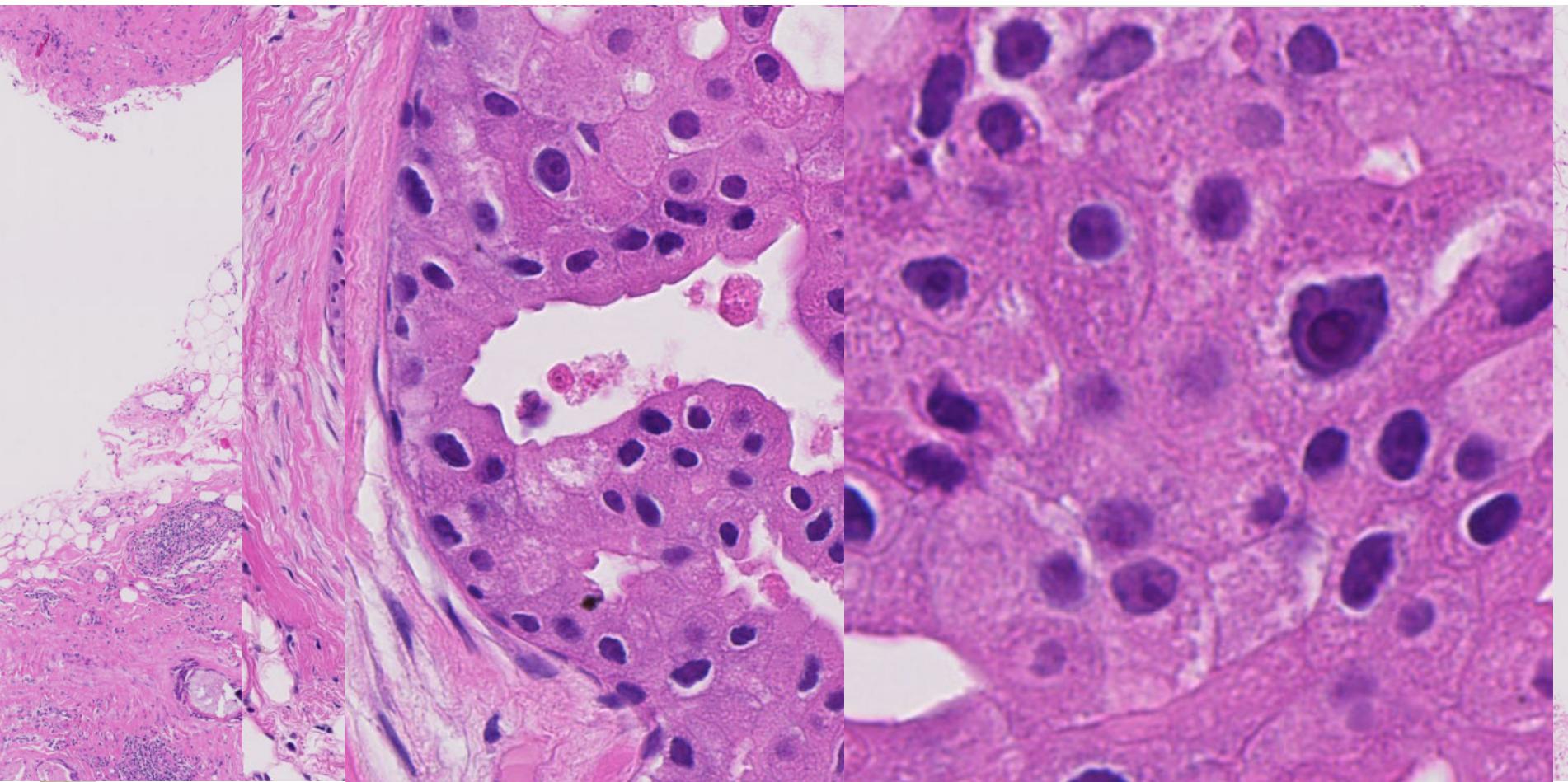
Apocriene DCIS graad 1



Apocriene DCIS graad 1/2



Apocriene DCIS graad 3



Carcinoom met apocriene differentiatie



Carcinoma with apocrine differentiation

Provenzano E
Gatalica Z
Vranic S

Definition

Carcinoma with apocrine differentiation is an invasive carcinoma characterized by large cells with abundant eosinophilic granular cytoplasm and enlarged nuclei with prominent nucleoli, resembling apocrine sweat glands.

ICD-O coding

8401/3 Apocrine adenocarcinoma

ICD-11 coding

2C61 & XH4GA3 Invasive carcinoma of breast & Adenocarcinoma with apocrine metaplasia

Related terminology

Acceptable: invasive apocrine carcinoma; apocrine carcinoma.

Subtype(s)

None

Localization

The localization is similar to that of invasive breast carcinoma of no special type (NST).

Clinical features

The clinical features are similar to those of invasive breast carcinoma NST. Carcinoma with apocrine differentiation usually presents as a firm, poorly circumscribed mass. Microcalcifications may be seen on mammography, in particular if associated ductal carcinoma in situ (DCIS) is present.

Epidemiology

Apocrine carcinoma is a rare subtype, constituting about 1% of all breast carcinomas [1376]. Patients tend to be older than those with invasive carcinoma NST [1377,2351,917,478].

Etiology

Most carcinomas with apocrine differentiation are sporadic. Some carcinomas in patients with germline *PTEN* mutation (Cowden syndrome) may have apocrine morphology [115].

Pathogenesis

There is no definitive information regarding the pathogenesis of carcinoma with apocrine differentiation. The relationship between apocrine metaplasia, atypical apocrine adenosis, and carcinoma with apocrine differentiation remains controversial. One group found similar genetic alterations in papillary apocrine metaplasia and adjacent DCIS and invasive carcinoma with apocrine morphology, including loss at 1p, 16q, and 17q and gains at 2q and 13q, raising the possibility that some apocrine metaplasia might be a non-obligate precursor of a subset of carcinomas with apocrine differentiation [956]. Reports of early oncogenic events – overexpression of the ERBB2 (HER2) and MYC (c-myc) oncogenes without alterations of the corresponding genes – in apocrine metaplasia and apocrine adenosis may also support this hypothesis [1892,1862,1891]. However, most of the genetic alterations found in carcinoma with apocrine differentiation are also present in invasive carcinoma NST. Overall, carcinomas with apocrine differentiation have heterogeneous gene expression profiles [2249], but they constitute a more

Carcinoom met apocriene differentiatie

Essential and desirable diagnostic criteria

Essential: apocrine morphology in > 90% of tumour cells.

Desirable: ER-negative, PR-negative, and AR-positive immuno-profile.

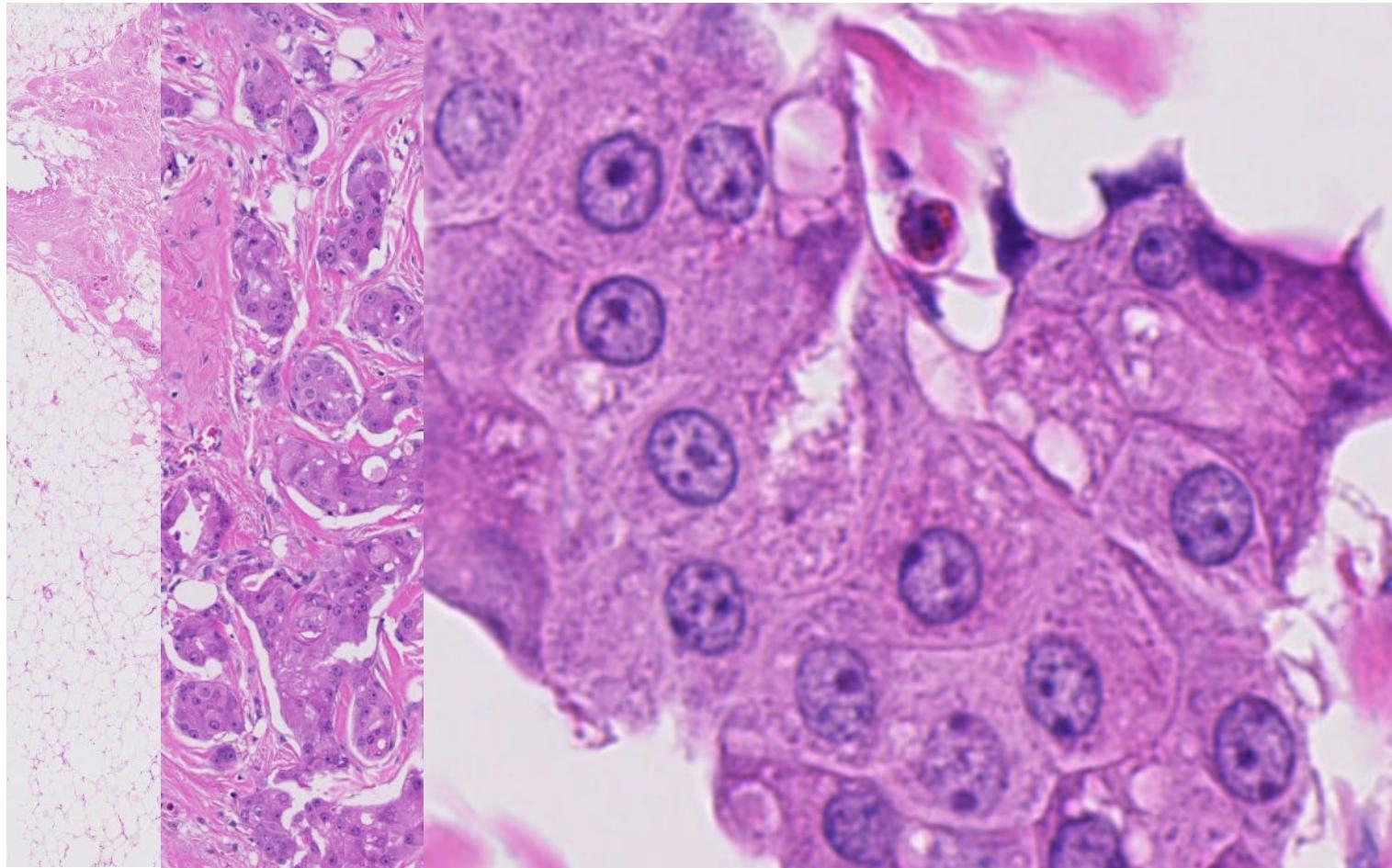
- Pathogenese: ?
- 1-4% van de mammacarcinomen
- (ouder dan de gemiddelde patiënt met invasief carcinoom NST)
- Meeste zijn sporadisch, sommige in kader PTEN mutatie
- Prognose en behandeling gelijk aan invasief carcinoom NST

Carcinoom met apocriene differentiatie

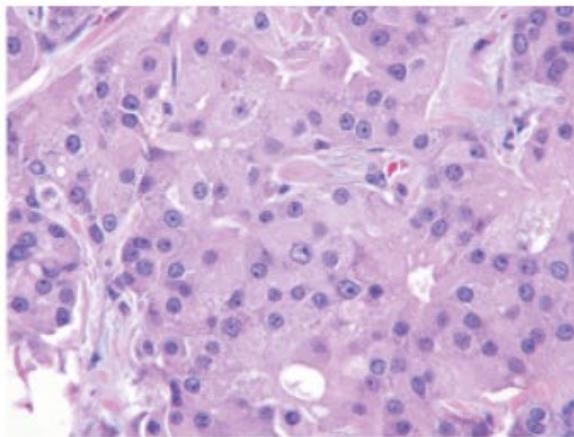
Microscopie

- Ruim eosinofiel cytoplasma of gevacuoleerd cytoplasma met duidelijke celgrenzen
- Kernen vergroot, rond-ovaal, matige atypie, prominente nucleoli, matige-hoge mitotische activiteit, solide groeipatroon
- DCIS met apocriene morfologie

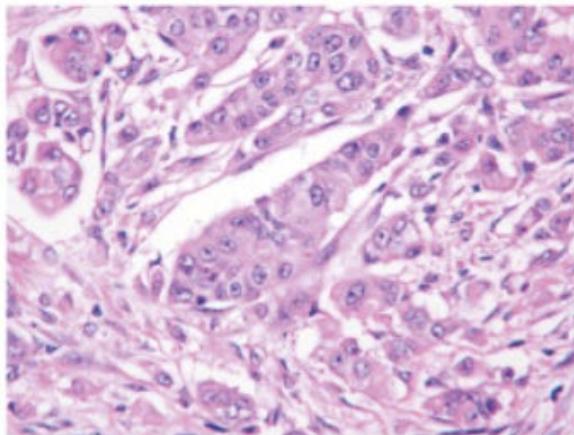
NST met apocriene differentiatie



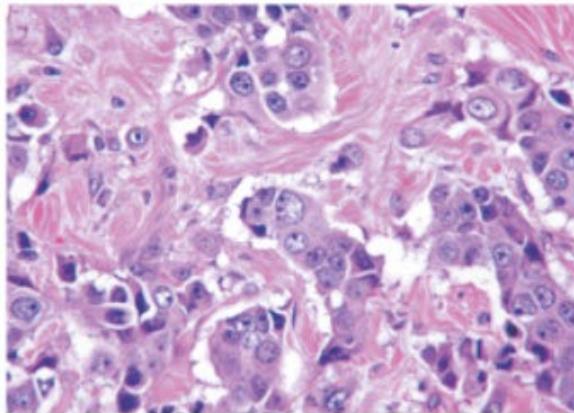
ER-/PgR-
HER2-
[Triple Neg]
Apocrine
diff in ~30%



ER+(w/m)
HER2-
[Luminal]
Apocrine
diff in ~10%

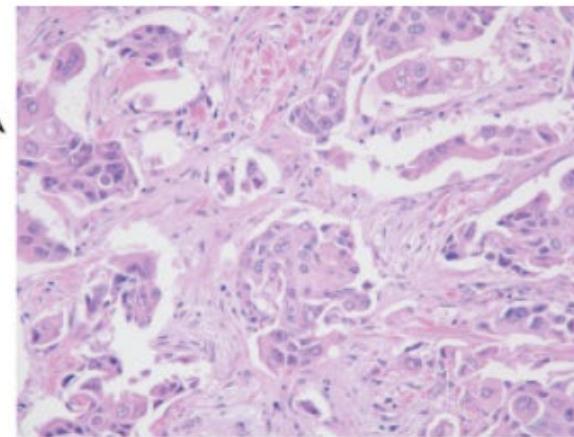


ER+(s)
HER2-
[Luminal]
Apocrine
diff in ~5%

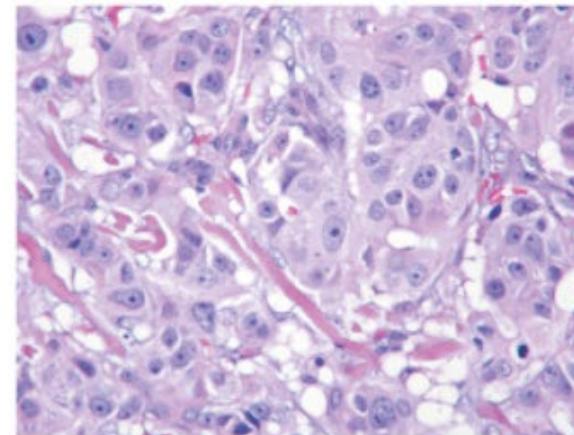


Apocrine differentiation

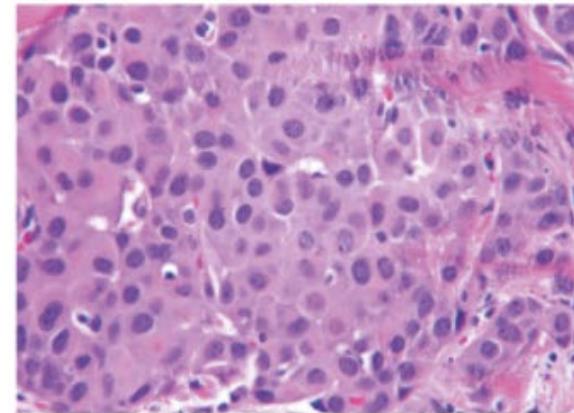
ER-/PgR-
HER2+
[ERBB2]
Apocrine
diff in ~80%

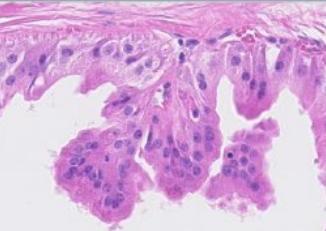
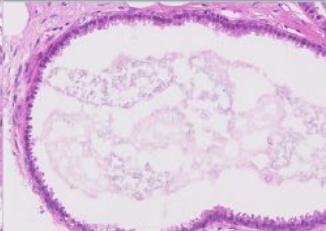
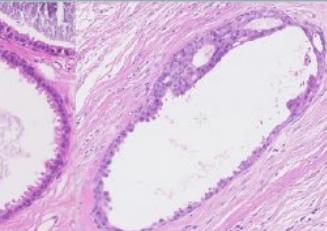
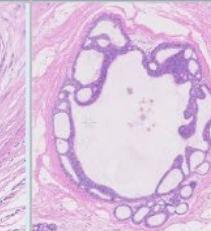
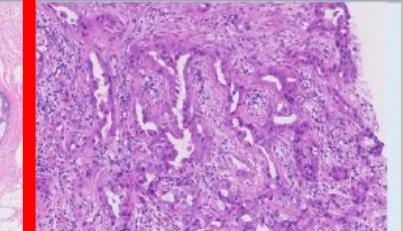


ER+(w/m)
HER2+
Apocrine
diff in ~25%

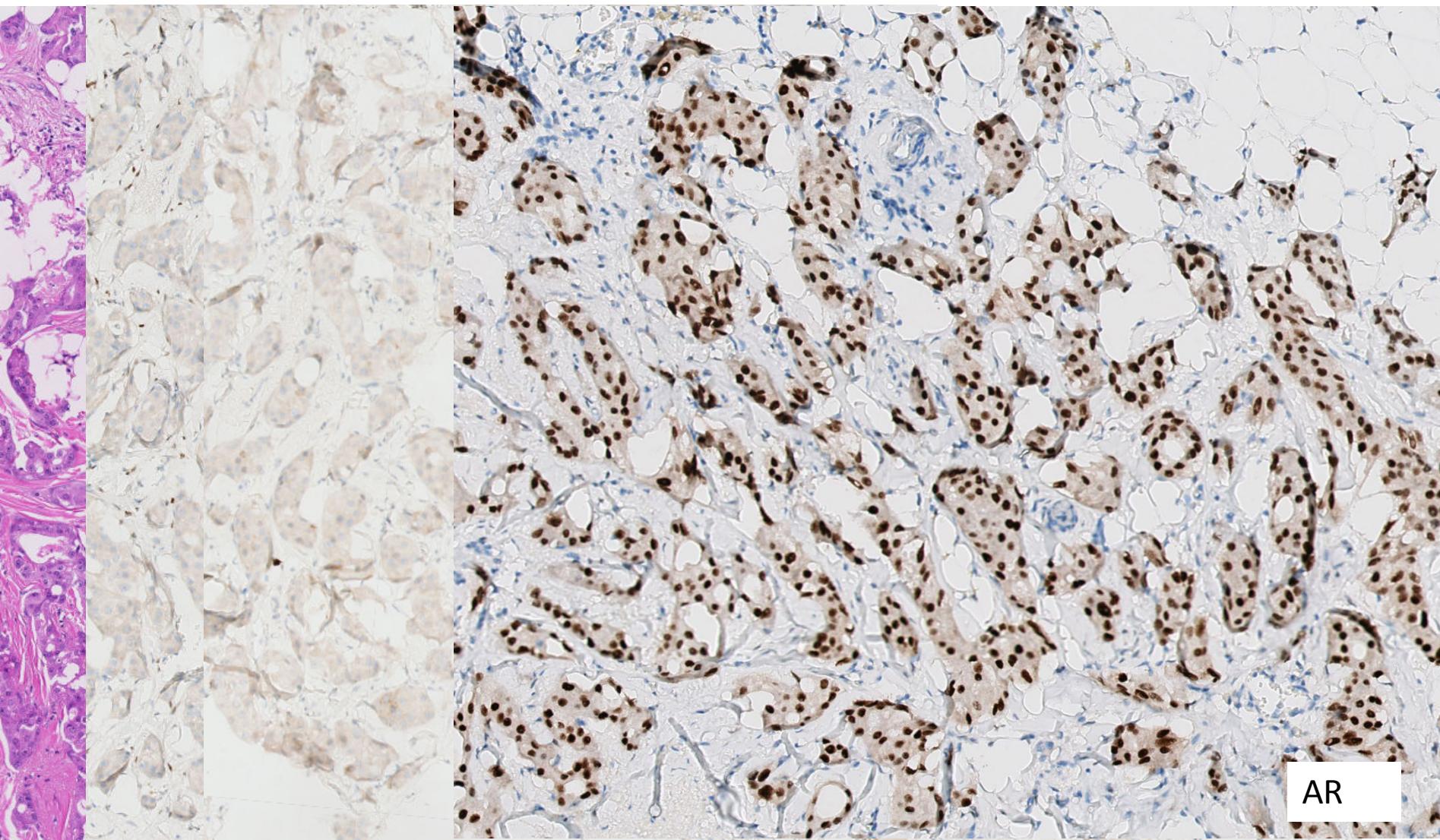


ER+(s)
HER2+
Apocrine
diff in ~20%



| Marker | (Papillaire) apocriene metaplasie | Cilinder cel veranderingen | (Laaggradige) apocriene DCIS | Laaggradige DCIS | Carcinoom met apocriene differentiatie |
|---------------------|---|---|--|---|---|
| FOTO |  |  |  |  |  |
| ER | - | + | - | + | - |
| PR | - | + | - | + | - |
| Her neu | + / - | - | + | - | + / - |
| AR | + | + / - | + | + | + |
| CK5 | - | - | - | - | - |
| GCDFP-15 (BRST2) | + | + / - | + | -/+ | + |





AR

Cowden Syndroom

Banneau *et al.* *Breast Cancer Research* 2010, **12**:R63
<http://breast-cancer-research.com/content/12/4/R63>



RESEARCH ARTICLE

Open Access

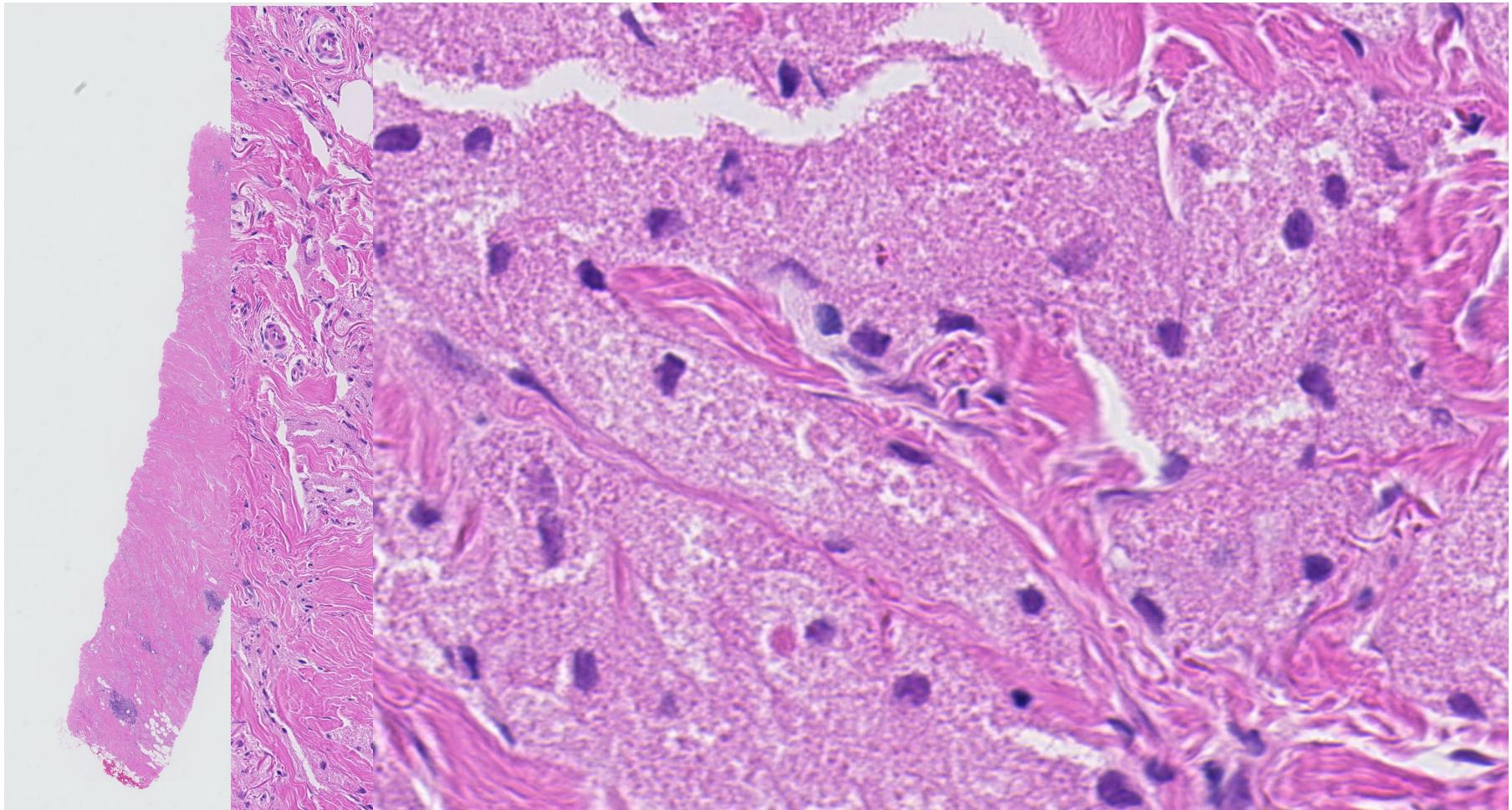
Molecular apocrine differentiation is a common feature of breast cancer in patients with germline *PTEN* mutations

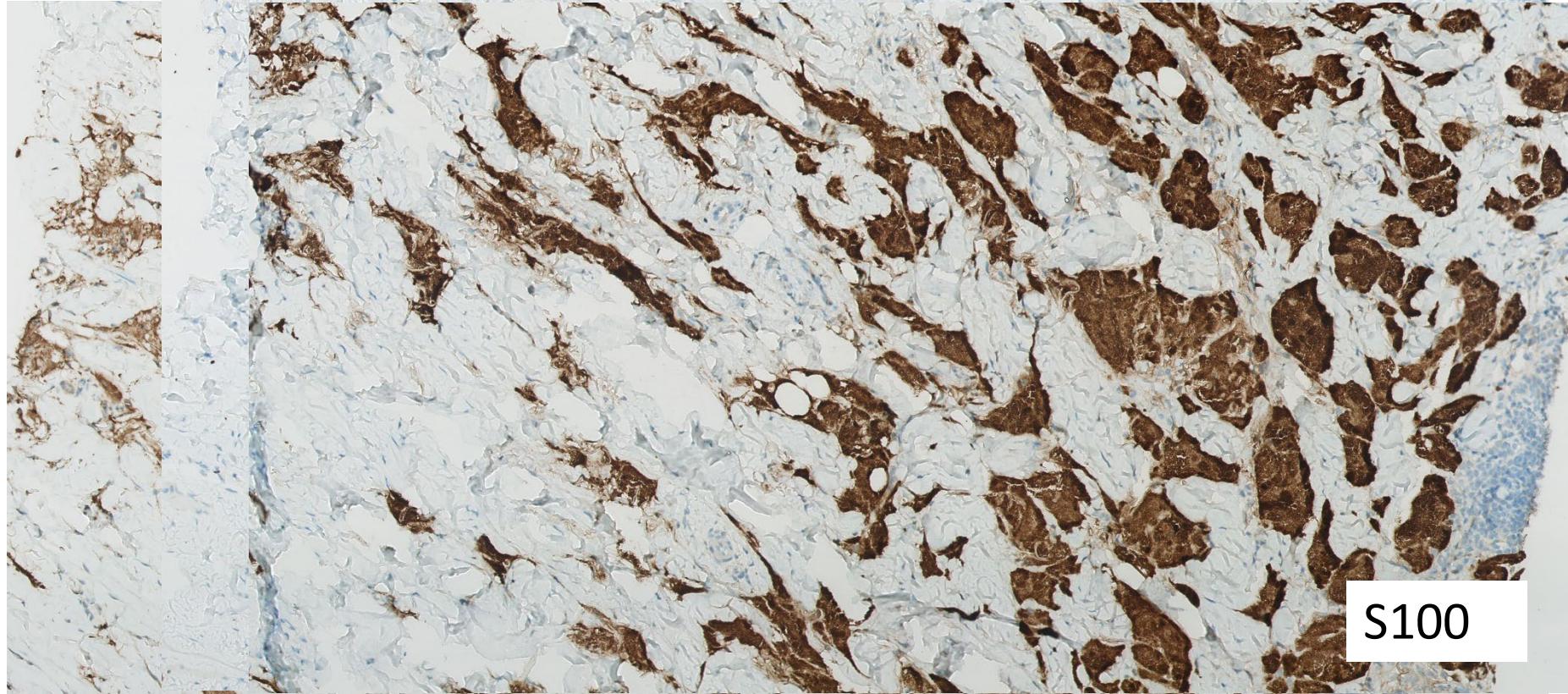
Guillaume Banneau¹, Mickaël Guedj², Gaëtan MacGrogan^{1,3}, Isabelle de Mascarel³, Valerie Velasco³, Renaud Schiappa², Valerie Bonadona⁴, Albert David⁵, Catherine Dugast⁶, Brigitte Gilbert-Dussardier⁷, Olivier Ingster⁸, Pierre Vabres⁹, Frederic Caux¹⁰, Aurelien de Reynies², Richard Iggo¹, Nicolas Sevenet^{1,11}, Françoise Bonnet^{1,11}, Michel Longy^{1,11*}



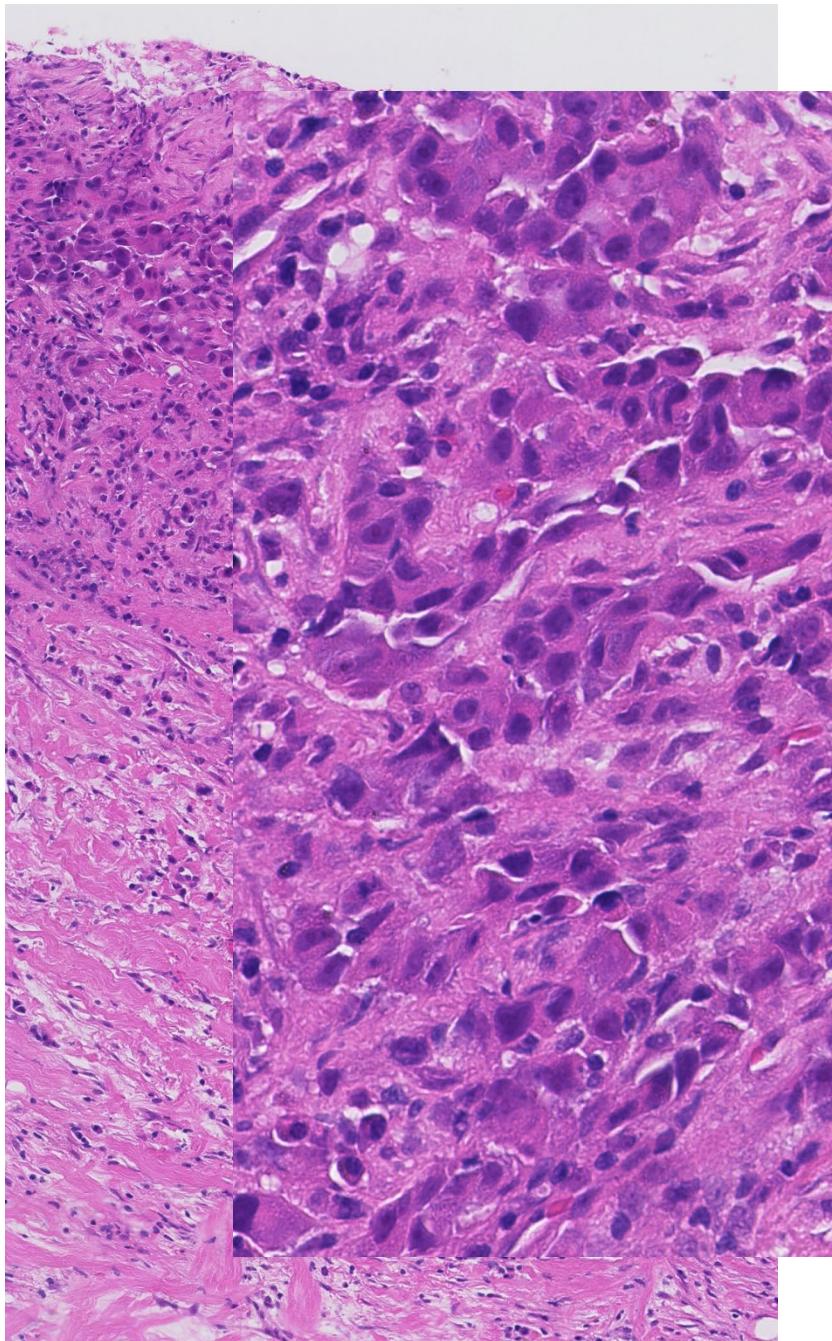
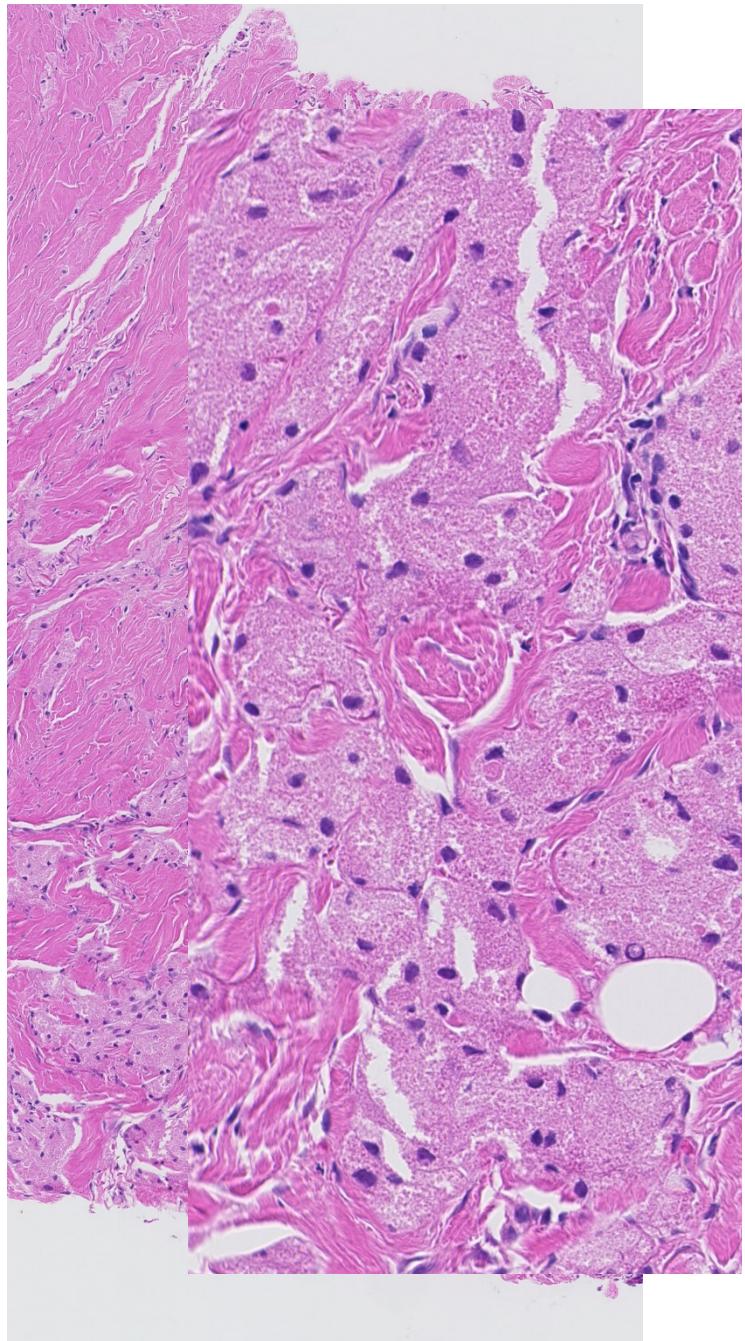
UMC Utrecht

Differentiaal diagnose met ...

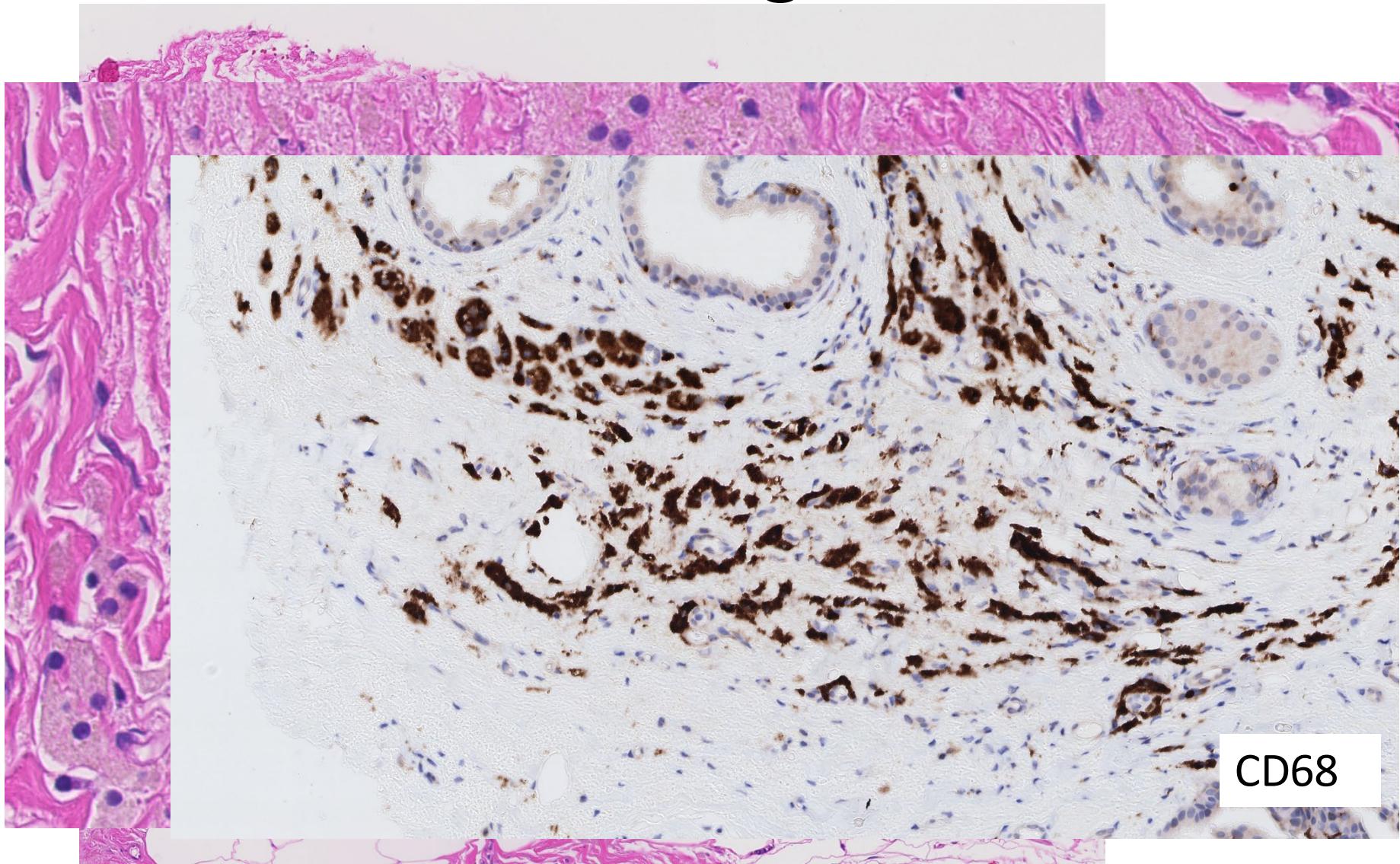




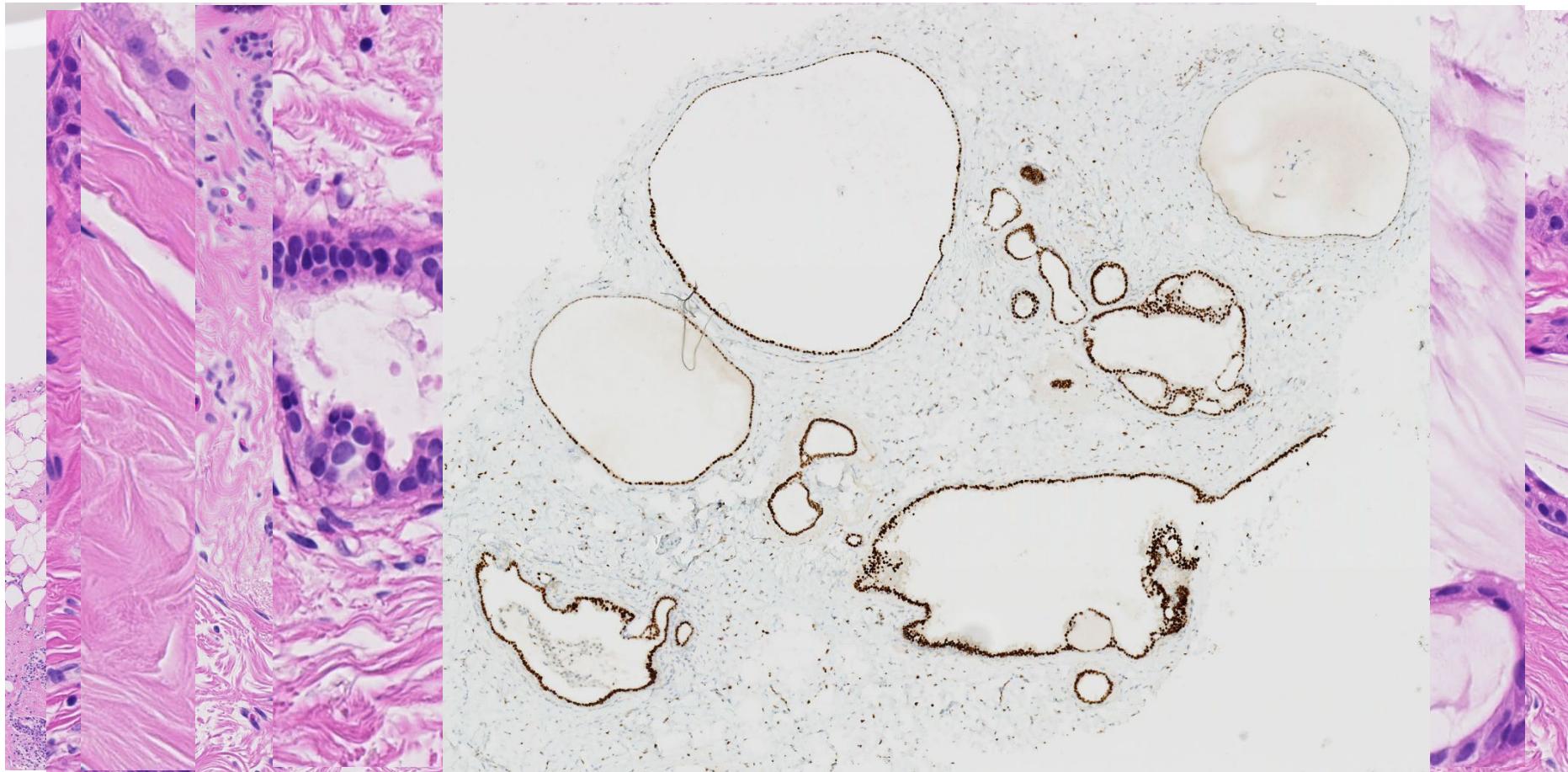
S100



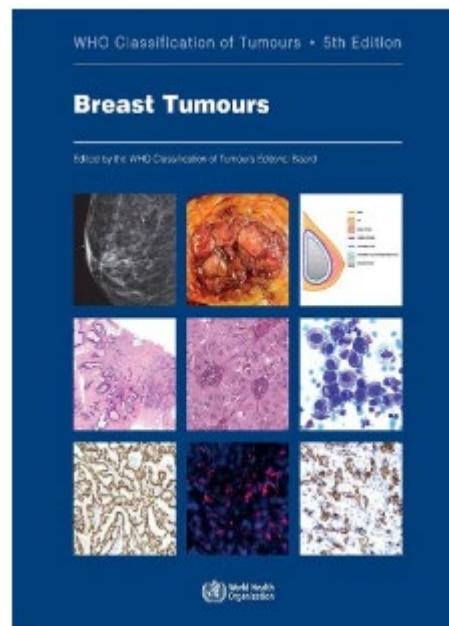
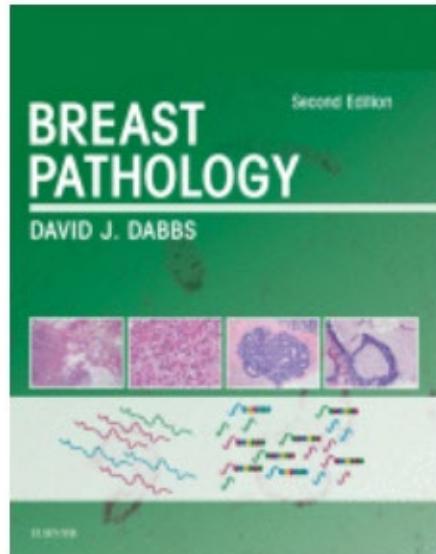
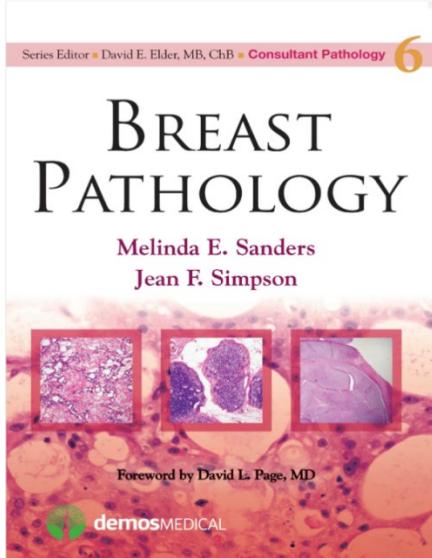
Differentiaal diagnose met ...



Differentiaal diagnose met ...



Literatuur



Met dank aan:

Natalie ter Hoeve

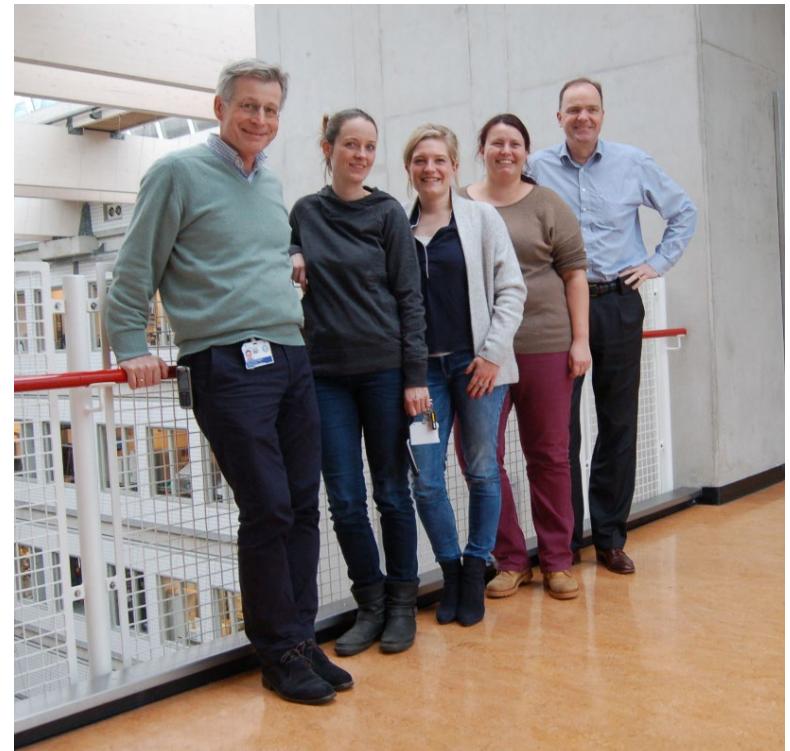
Willy van Bragt

Nikolas Stathonikos

Roel Goldschmeding

Mirthe de Boer

Paul van Diest



15:55-16:00

Welkom en opening

Deel I - Apocriene laesies

Celien Vreuls

16:00-16:45

Presentatie

16:45-17:30

Coupe sessie

17:30-18:00

Pauze

Deel II - Fibroepitheliale laesies

Paul van Diest

18:00-18:45

Presentatie

18:45-19:30

Coupe sessie

19:30-20:00

Afsluiting

Coupesessie



PAUZE

