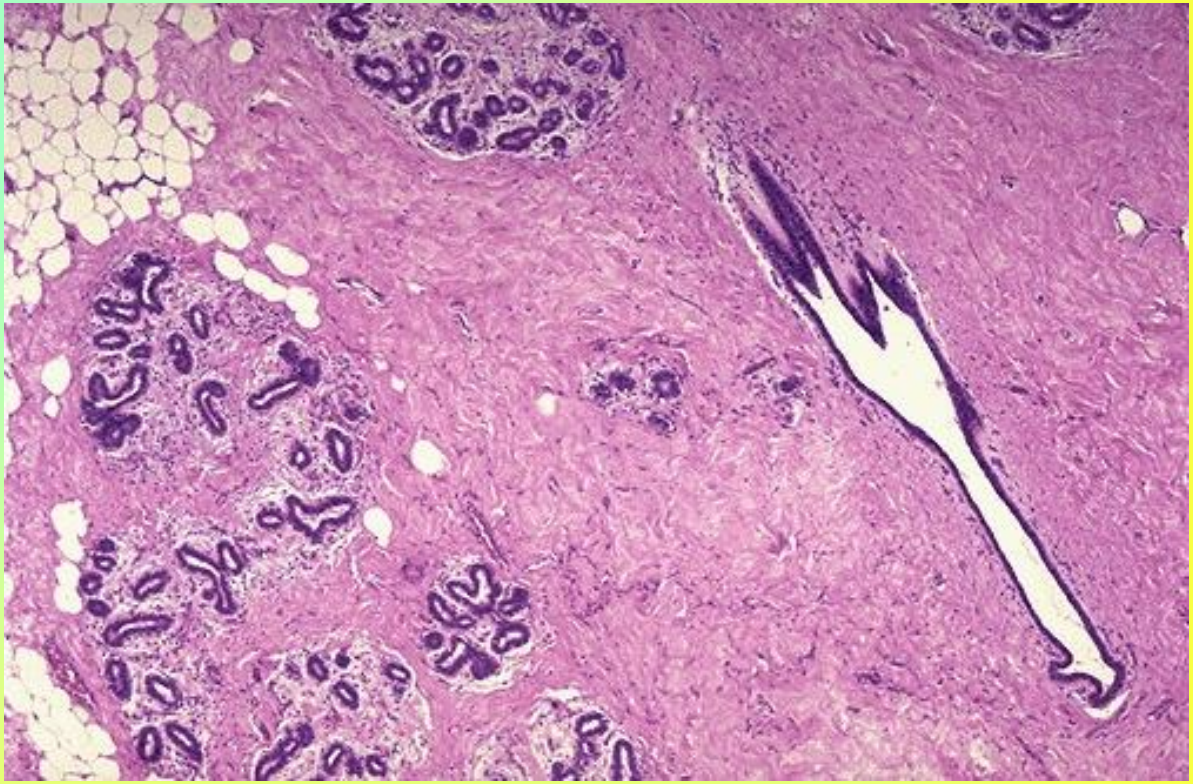
BREAST PATHOLOGY

- INFLAMMATORY DISEASES
- BENIGN EPITHELIAL LESIONS
- FIBROEPITHELIAL LESIONS
- MALIGNANT TUMORS

http://core.ecu.edu/som/strausbauchp/webpath/breshtml/brest020.htm



Histology / **Normal breast tissue**: most of the breast is composed of stromal tissue, largely mature adipose and fibrous tissue. Within stroma lie the important breast epithelial structures, from which most breast lesions are derived: the lobules form well-defined islands of small tubular structures (acini) surrounded by intralobular stroma.

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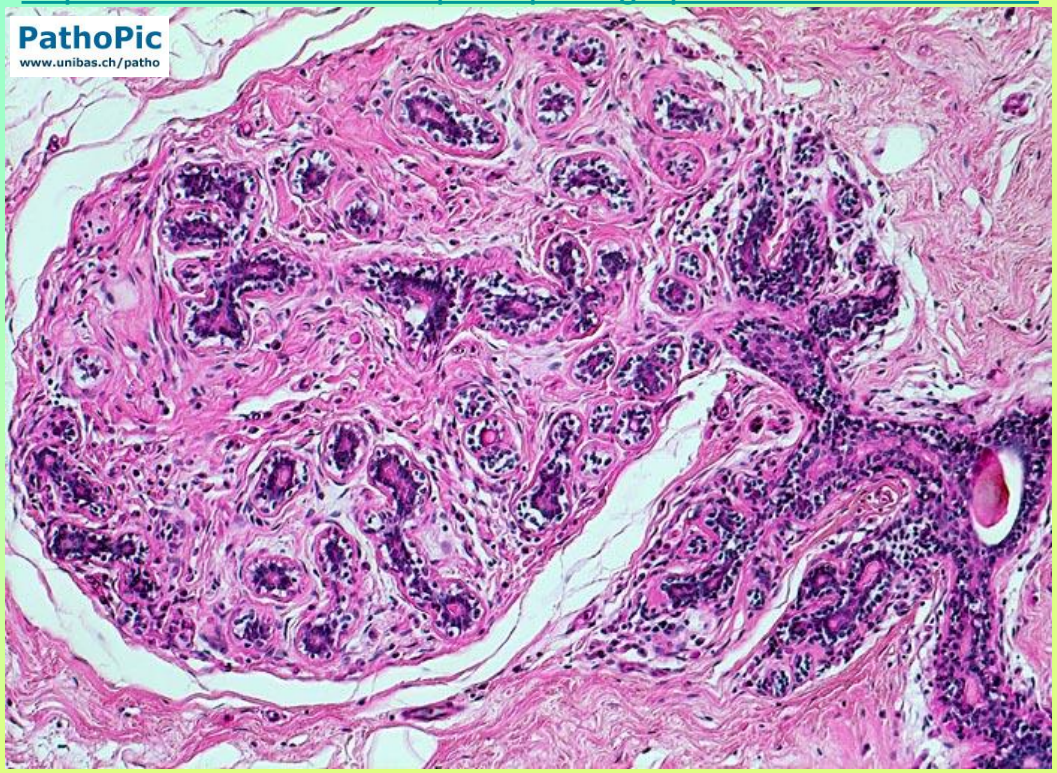
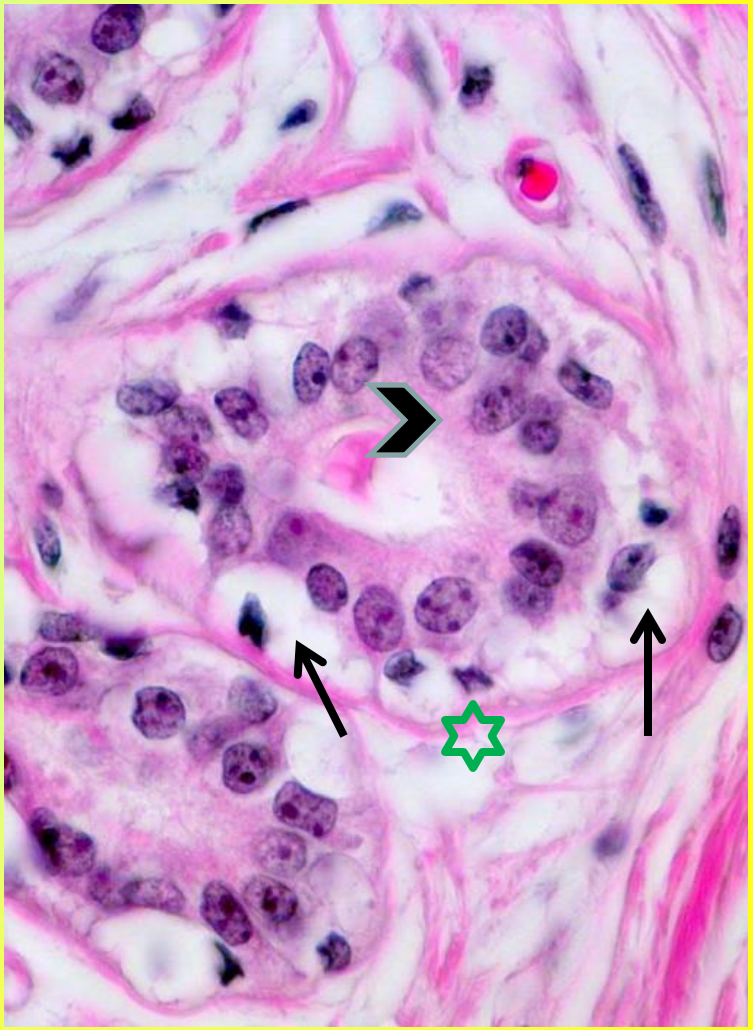
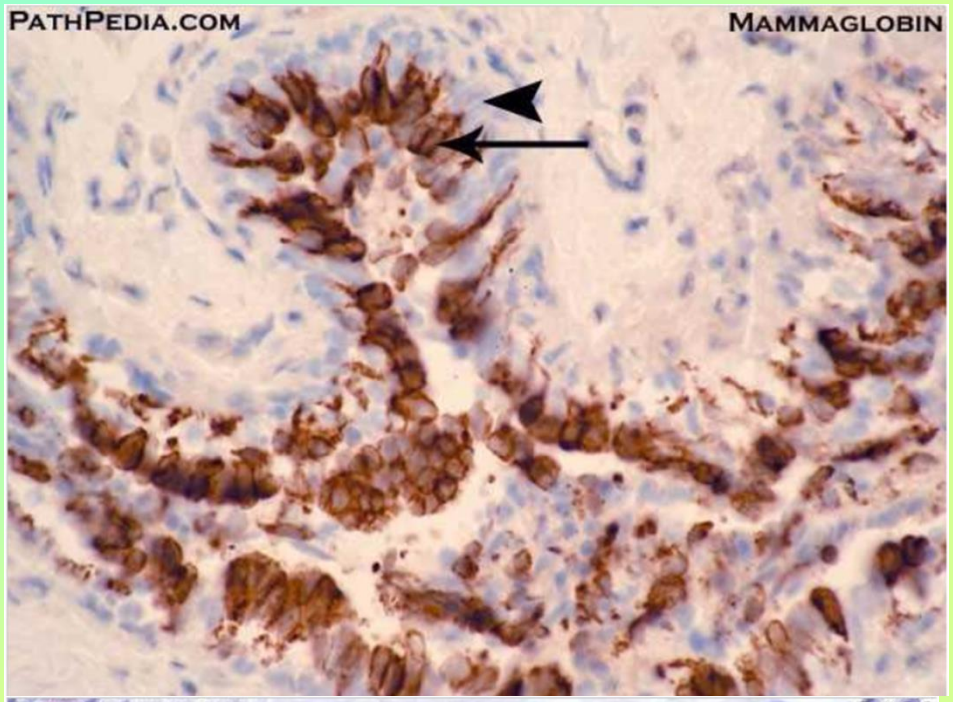
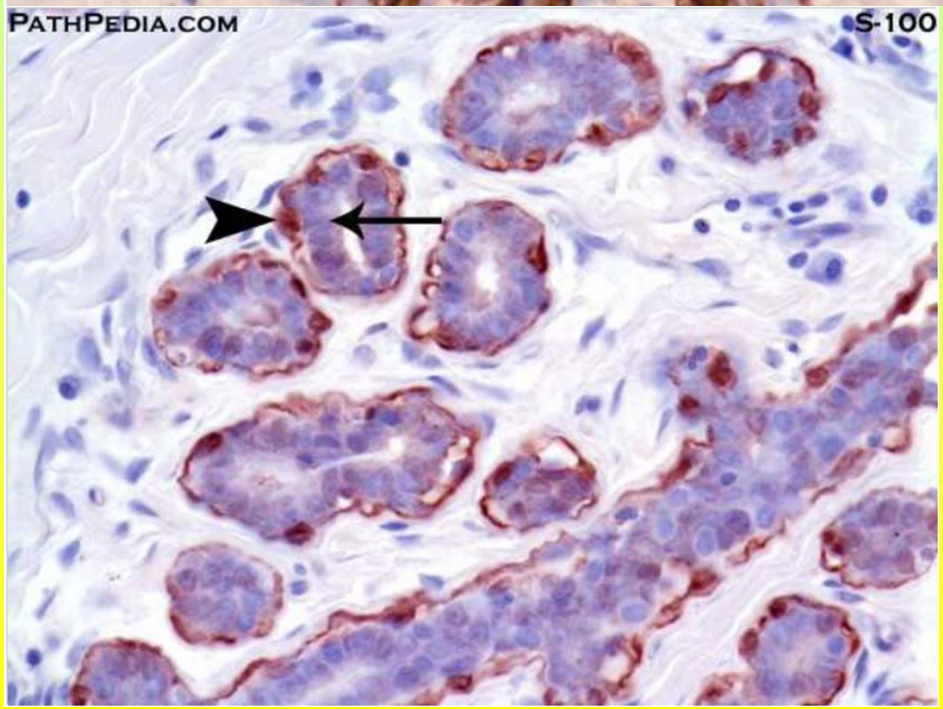


The **terminal duct lobular unit (TDLU)** consists of small ductules arrayed around an intralobular duct.



Detail: the ducts are lined by a double layer of inner / luminal epithelium of secretory cells (arrowhead) over a basal layer of myoepithelial cells (arrows), against the basement membrane (star).

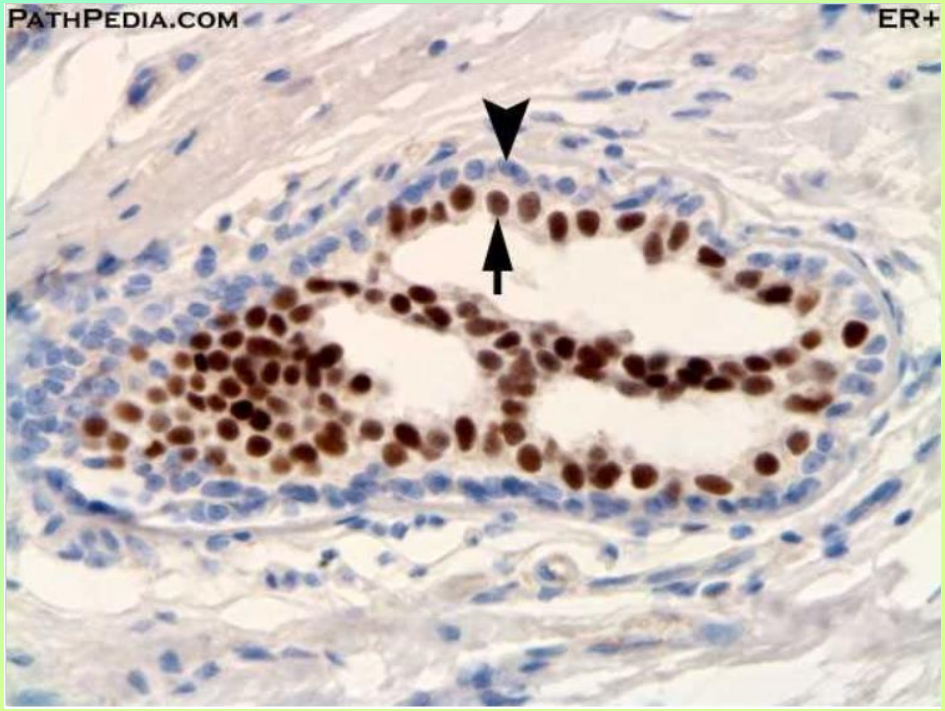


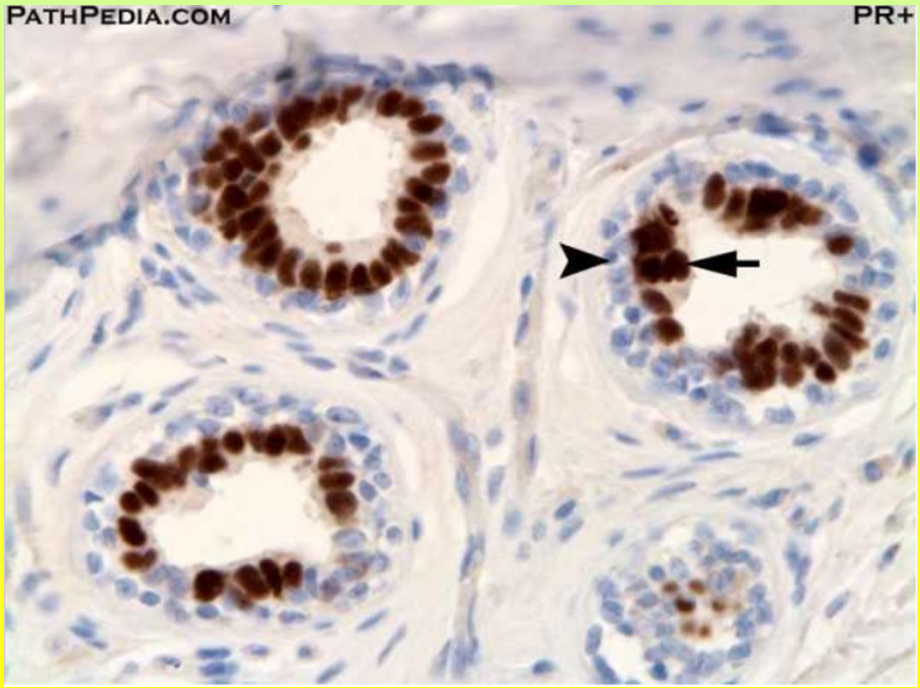


Different imunoprofile:

Epithelial luminal cells (arrow): mammaglobin+; S100-

Myoepithelial cells (arrowhead): mammaglobin-; S100+



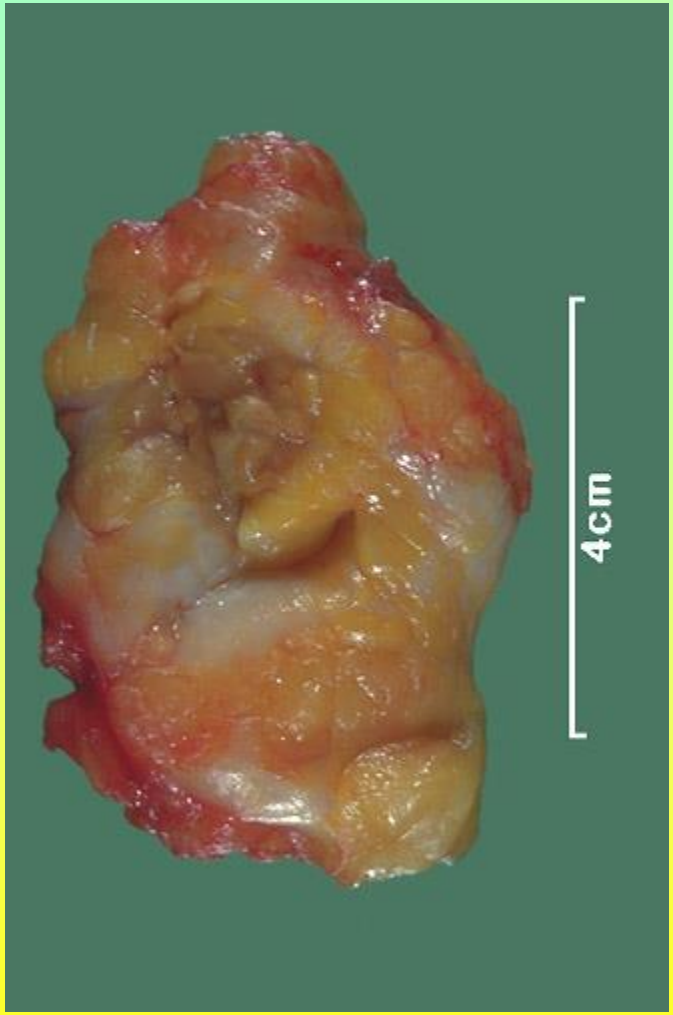


Different imunoprofile:

Epithelial luminal cells (arrow): estrogen receptors (ER) +; progesterone receptors (PR) +

Myoepithelial cells (arrowhead): ER-; PR-

INFLAMMATORY DISEASES OF THE BREAST

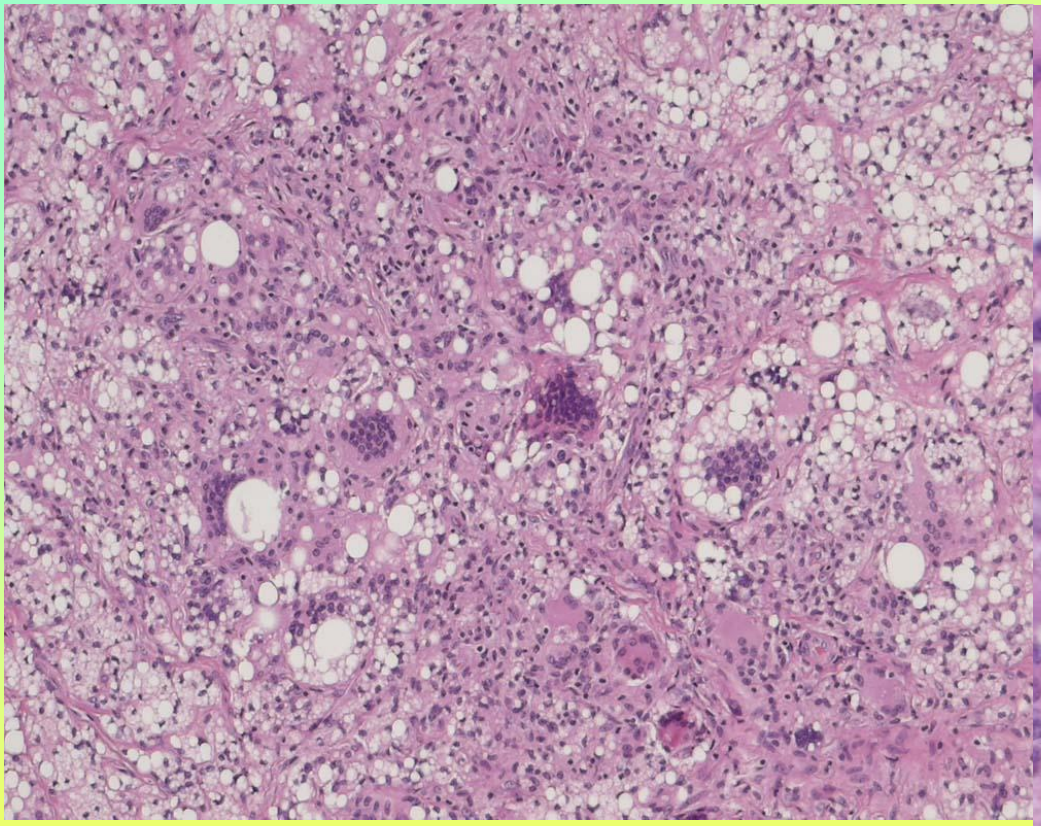


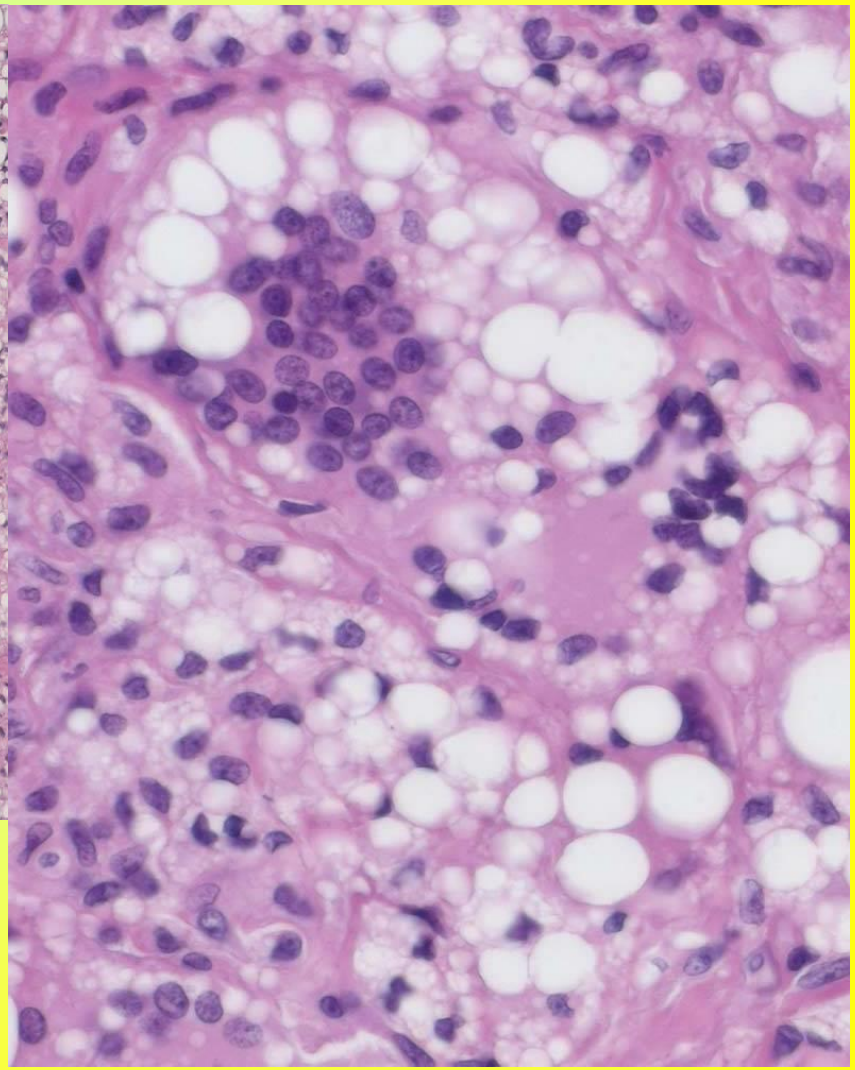
Breast **abscess**, gross.

http://core.ecu.edu/som/strausbauchp/webpath/breshtml/brest090.htm

- **Acute mastitis and abscess**
  - pyogenic bacteria (Staphylococcus, Streptococcus)
  - postpartum lactating
  - involuting breast
- **Chronic granulomatous mastitis:** the terminal duct lobular unit shows an intense granulomatous and chronic inflammatory process with conspicuous giant cells
  - idiopathic
  - foreign material
  - sarcoidosis
  - tuberculosis (Mycobacterium)

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009629





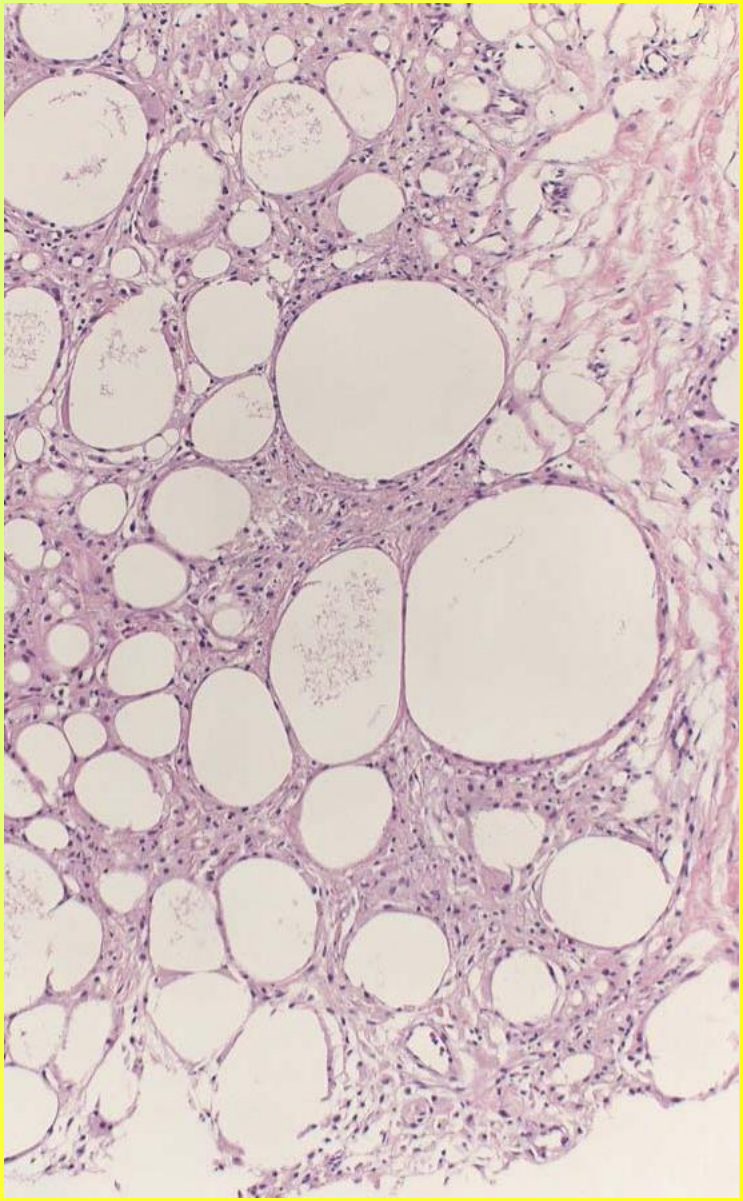
https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009627

Foreign body reaction to silicone leakage: Foamy macrophages and giant cells with round transparent vacuoles corresponding to phagocytized silicone.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009372

Traumatic fat necrosis

- arises in the fatty tissue of the breast and may present as a hard lump mimicking cancer
- necrosis is accompanied by haemorrhage and followed by an acute inflammatory reaction
- becomes heavily infiltrated by foamy macrophages containing lipid and often haemosiderin, and crystals of lipid may be deposited stimulating a foreign-body giant cell reaction
- Granulation tissue forms around the lesion and gradually matures into a thick layer of fibrous tissue



Breast, **fat necrosis**: lipid cysts are surrounded by foamy macrophages

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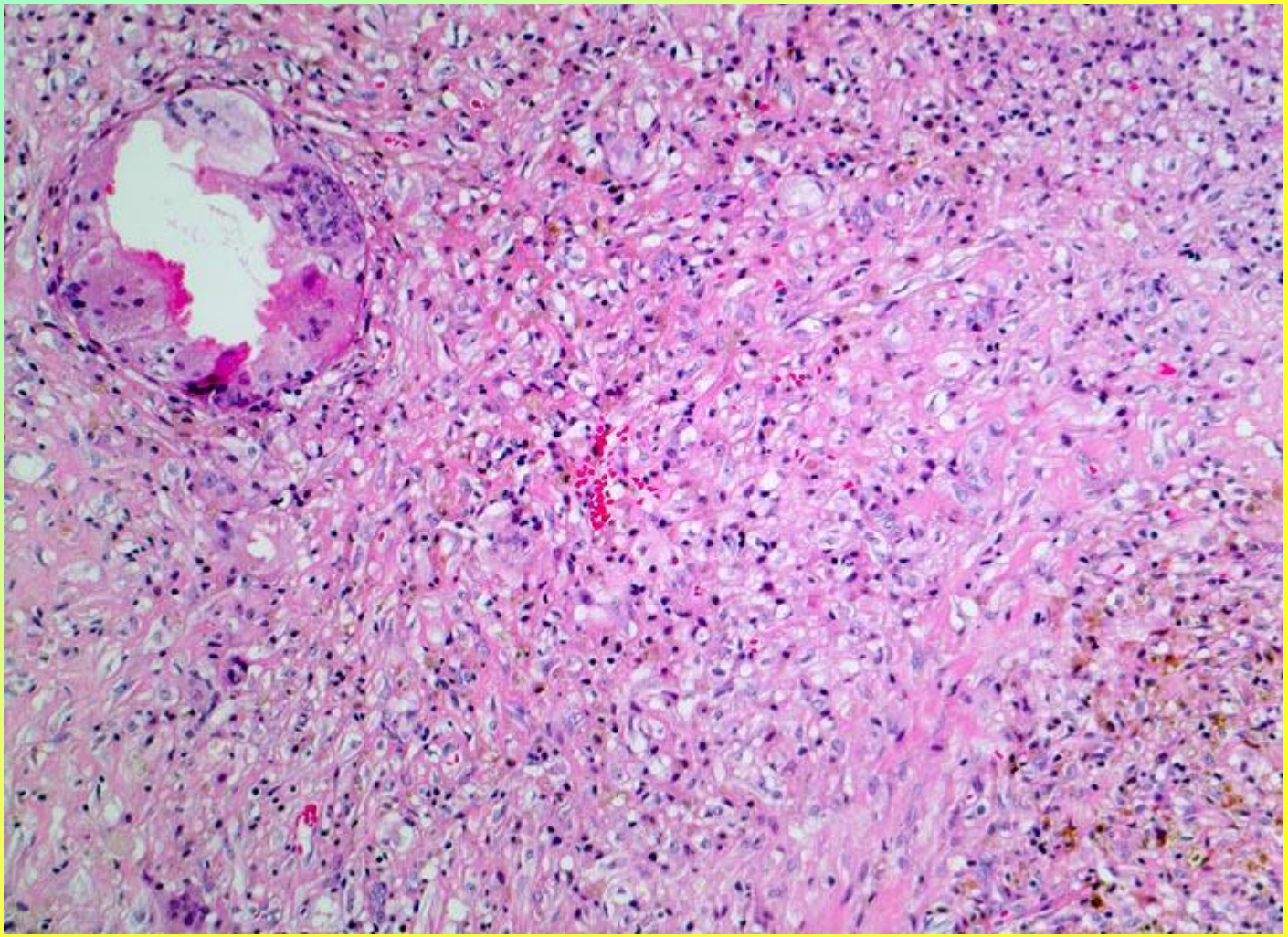


Breast, granulation tissue secondary to **fat necrosis**, foamy macrophages and haemosiderin; larger crystals of lipid stimulate foreign-body giant cell reaction (upper left corner).

BENIGN EPITHELIAL LESIONS:

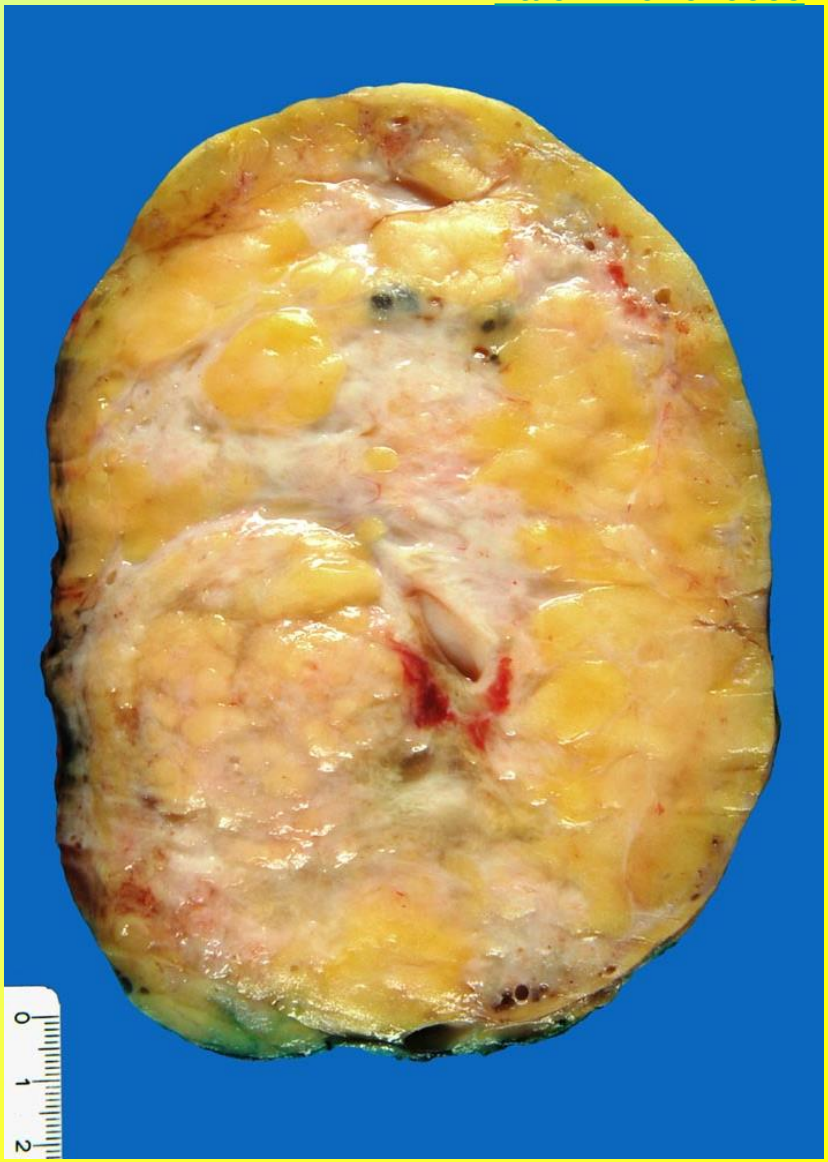
~ risk of developing breast cancer

- *nonproliferative breast changes* (fibrocystic change) **0 risk**
- *proliferative breast disease without (epithelial) atypia* ***1.5*** **–** ***2****x* **risk**
- *proliferative breast lesions with (epithelial) atypia (atypical hyperplasia)* ***4*** **–** ***5****x* **risk**

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=010069

NONPROLIFERATIVE BREAST CHANGE / FIBROCYSTIC CHANGE

- unknown cause
- 10% of adult women [35 – 55] years old
- Asymptomatic / clinical evident
- **Hallmarks:**
  - Fibrous stroma
  - Δ cystic dilatation of terminal ducts (> 5 cm dark fluid gross)



Fibrocystic change, gross: irregular fibrosis and small cysts (some are blue)

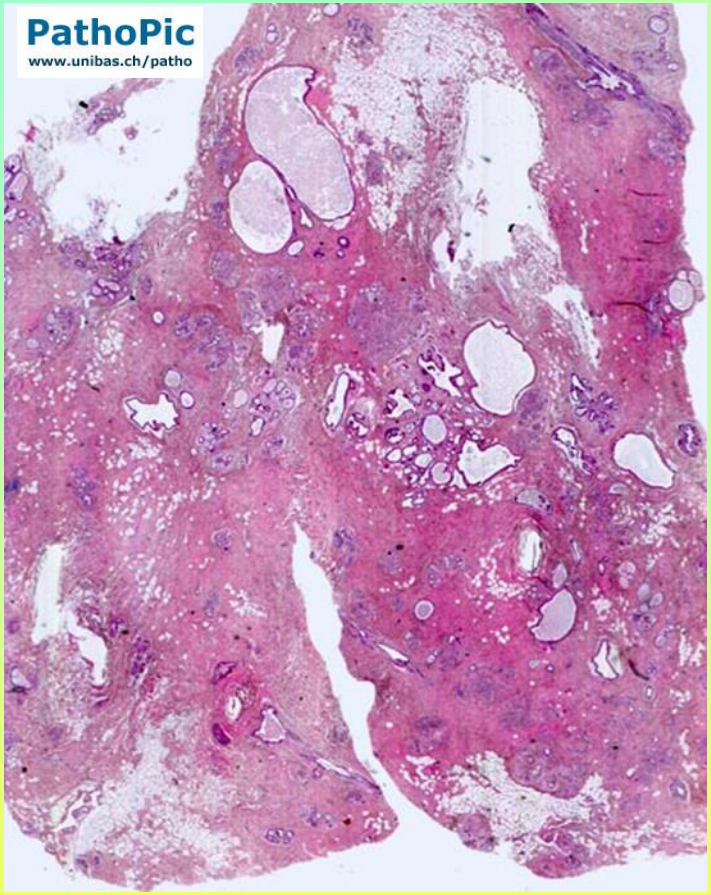
https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=002896

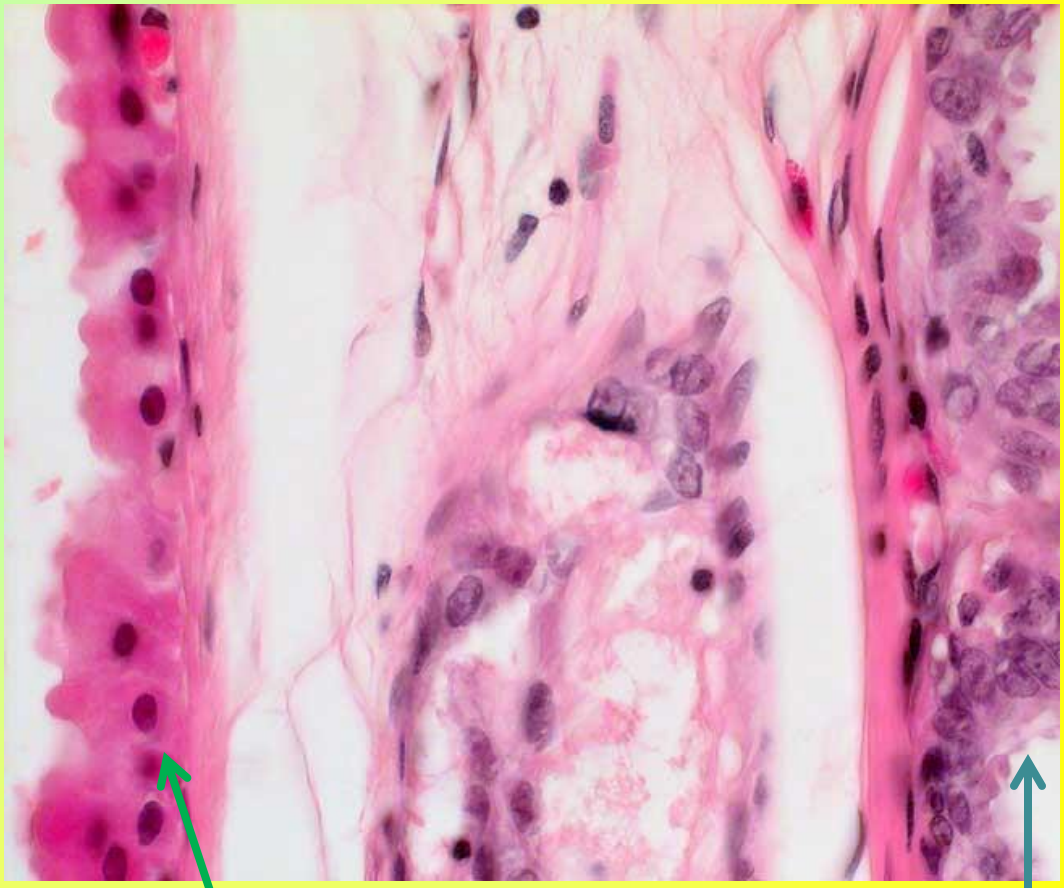
Fibrocystic change, gross: fibrosis and dilated ducts.

NONPROLIFERATIVE BREAST CHANGE / FIBROCYSTIC CHANGE

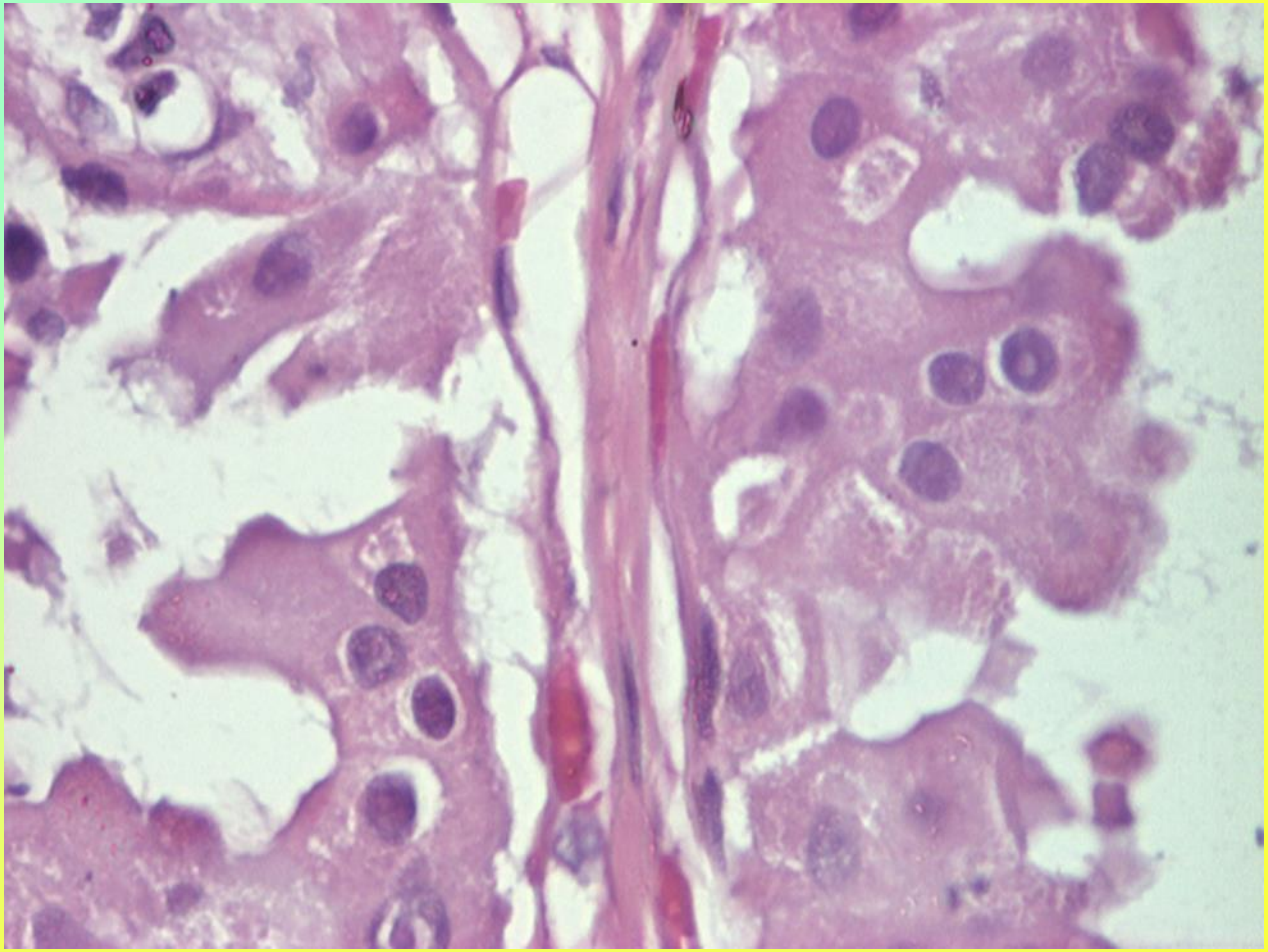
- **MICROSCOPY:**
- cystic dilatation of terminal ducts
  - simple
  - apocrine metaplasia
- relative increase in fibrous stroma
- variable proliferation of terminal duct epithelial elements: adenosis

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=005707

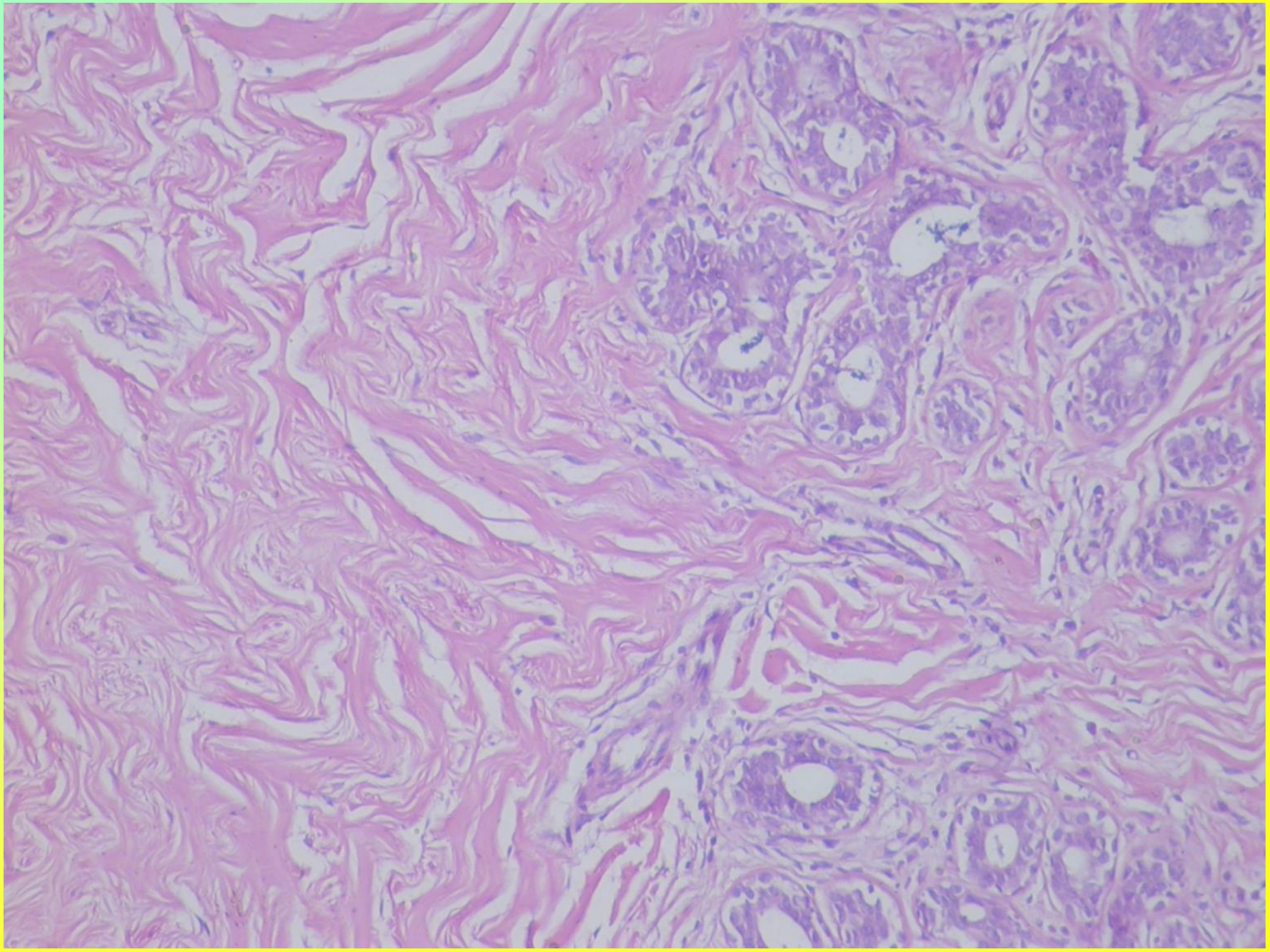




Fibrocystic change: cystically dilated ducts are lined by apocrine (apocrine metaplasia) or usual epithelium.

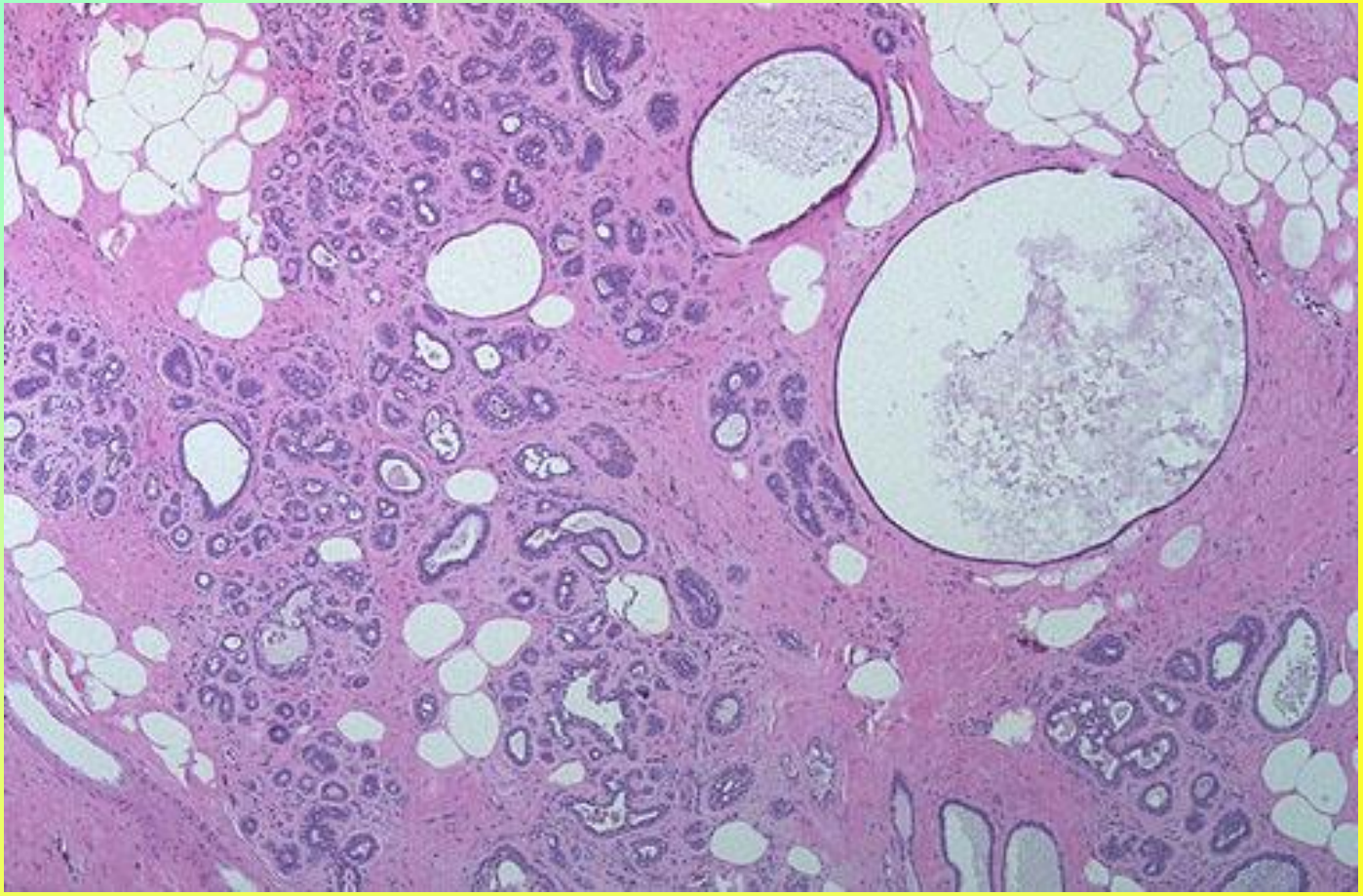


Fibrocystic change: apocrine metaplasia, higher magnification, slide from discipline archive.

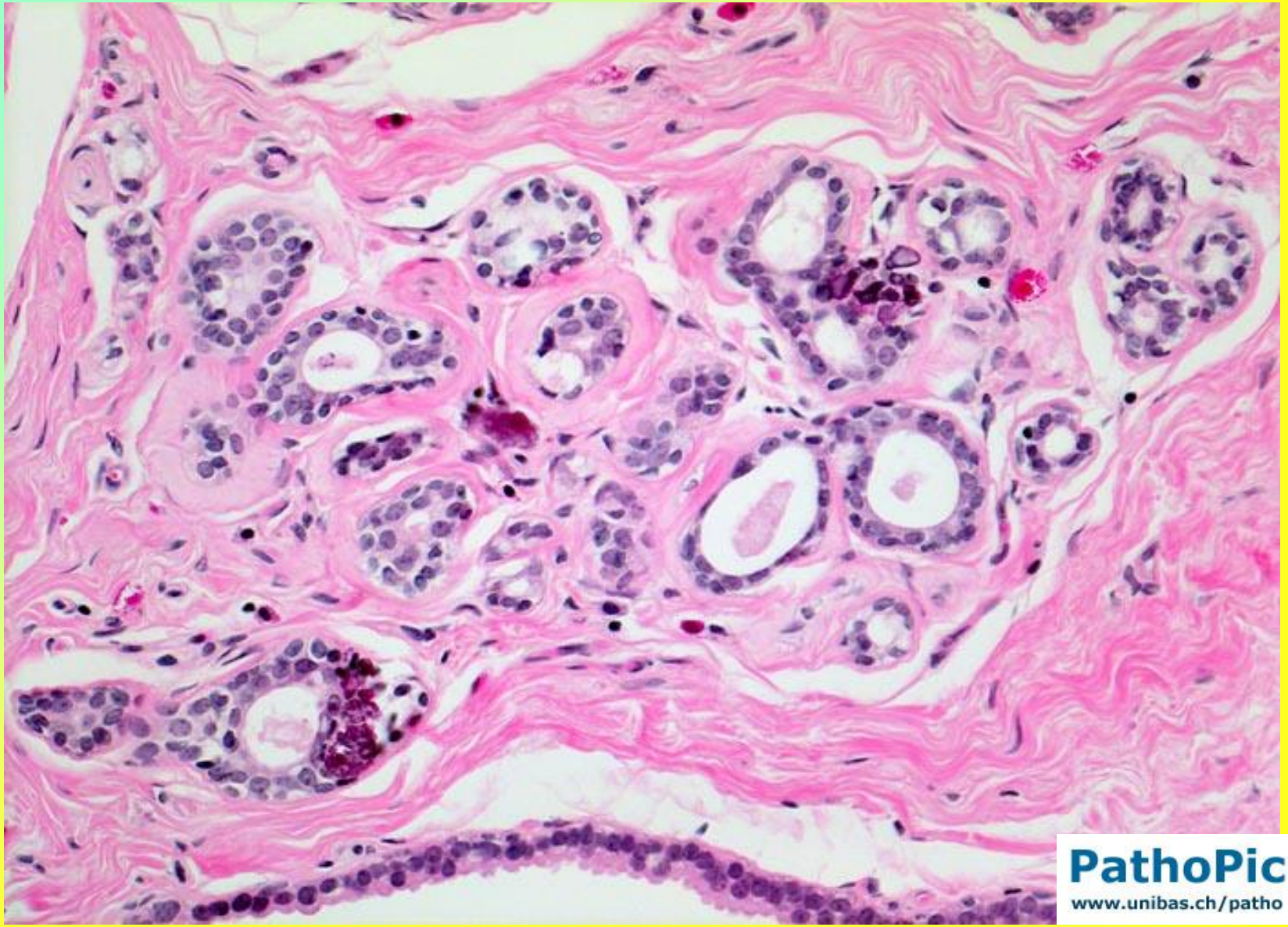


Fibrocystic change: interstitial (stroma) fibrosis, slide from discipline archive.

http://core.ecu.edu/som/strausbauchp/webpath/breshtml/brest047.htm



Fibrocystic change: adenosis an increase in the number of acini per lobule



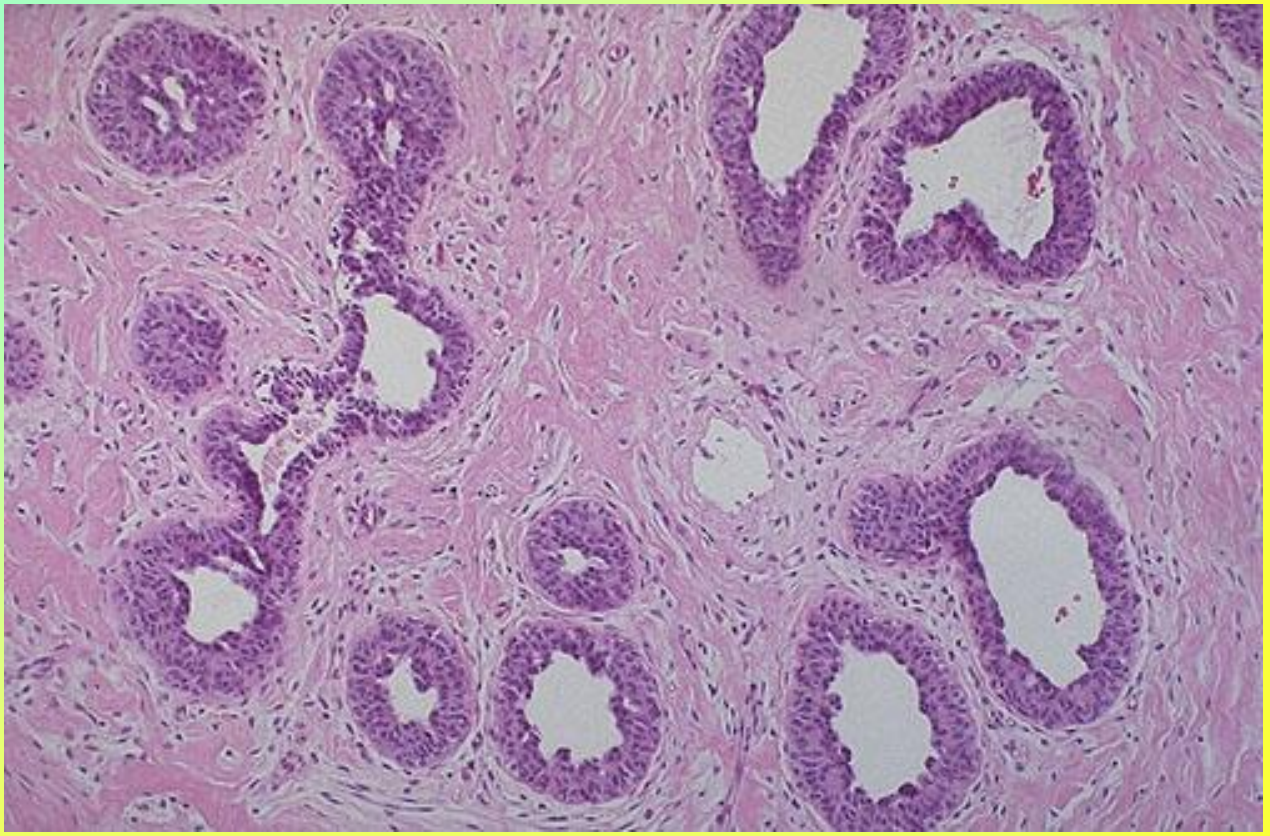
Fibrocystic change: adenosis **+** dystrophic calcification (amorphous purplish material) + fibrosis

Proliferative breast disease without atypia:

- one or more of several forms of epithelial proliferation that are not clonal
- mammographic densities, calcifications, incidental findings in biopsies

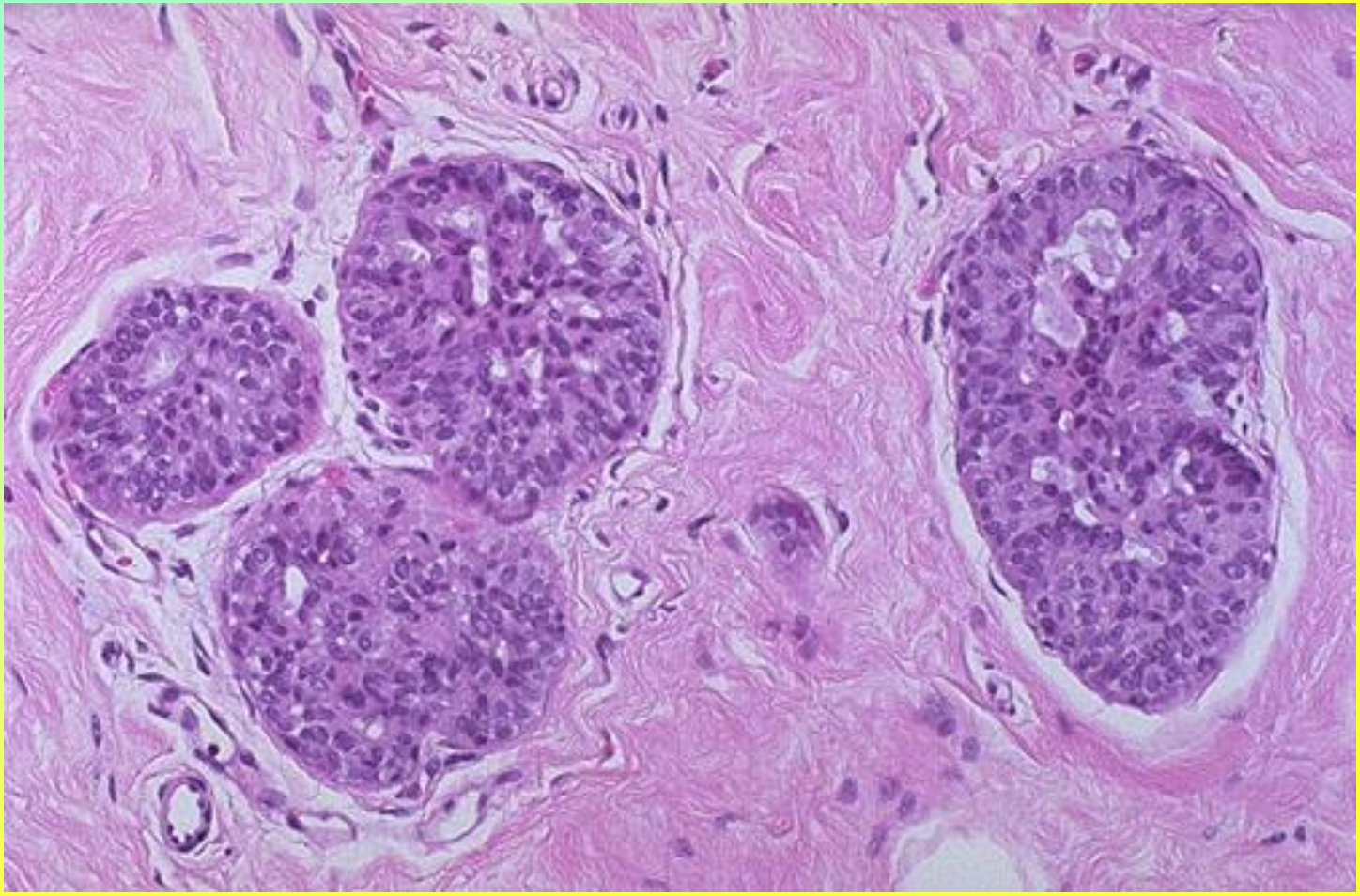
- **usual (ductal) epithelial hyperplasia / UDH** both luminal and myoepithelial cell types fill and distend ducts and lobules
- **sclerosing adenosis** proliferation of epithelial, myoepithelial and intralobular stromal cells, resulting in distortion and expansion of lobules and obliterating duct spaces
- **papilloma** within a dilated duct, multiple branching papillae with fibrovascular cores
  - Solitary large duct papilloma (central papillomas)
  - Multiple small duct papillomas (peripheral papillomas)

http://core.ecu.edu/som/strausbauchp/webpath/breshtml/brest043.htm

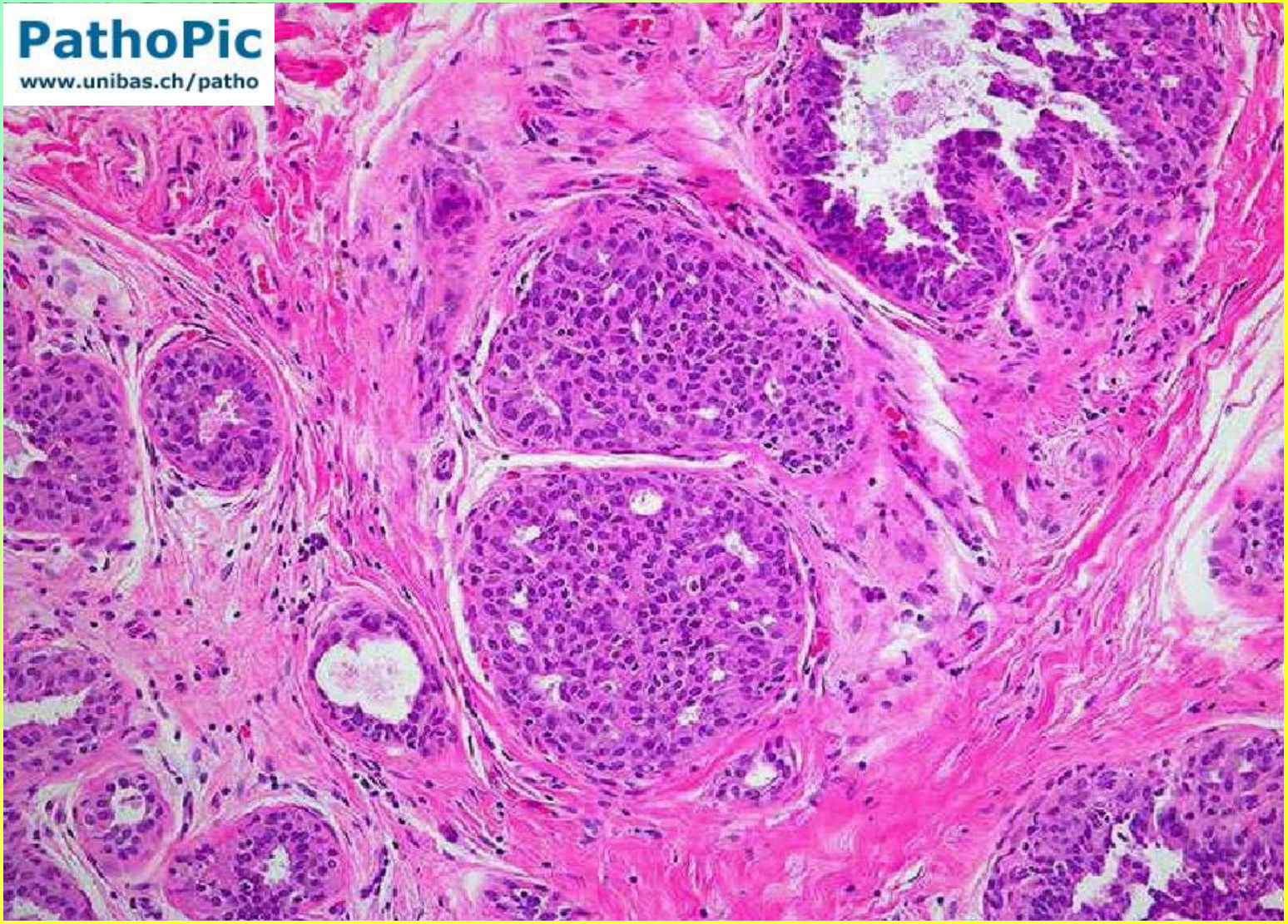


Usual (ductal) epithelial hyperplasia, aka UDH: increased numbers of both luminal and myoepithelial cells that fill and distend ducts and lobules. There is no cytological atypia.

http://core.ecu.edu/som/strausbauchp/webpath/breshtml/brest044.htm

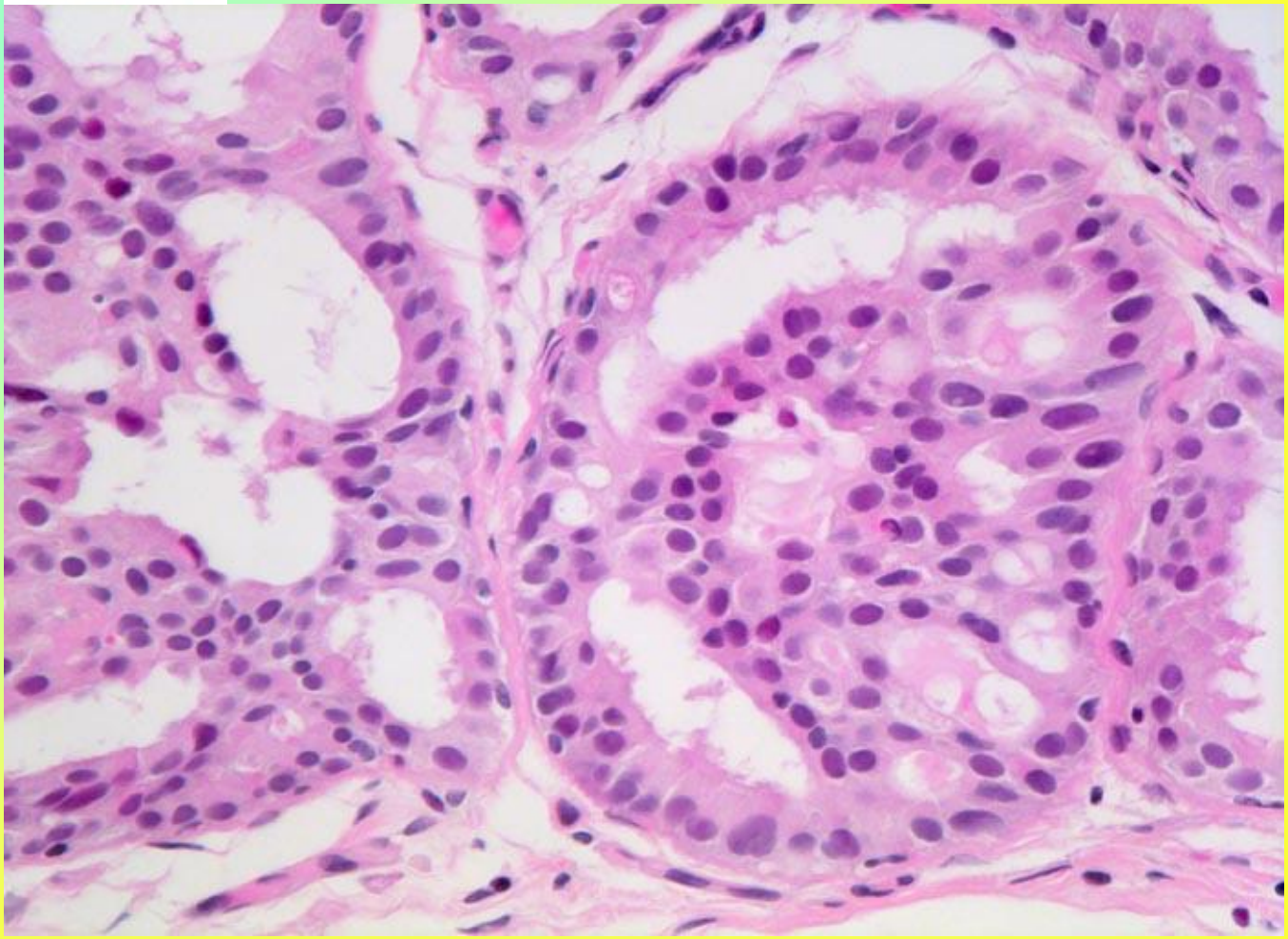


UDH: more than 4 cell layers of luminal and myoepithelial cells, bridging across duct lumina; slit-like, peripheral secondary spaces. Nuclei present a streaming pattern, but no atypia.



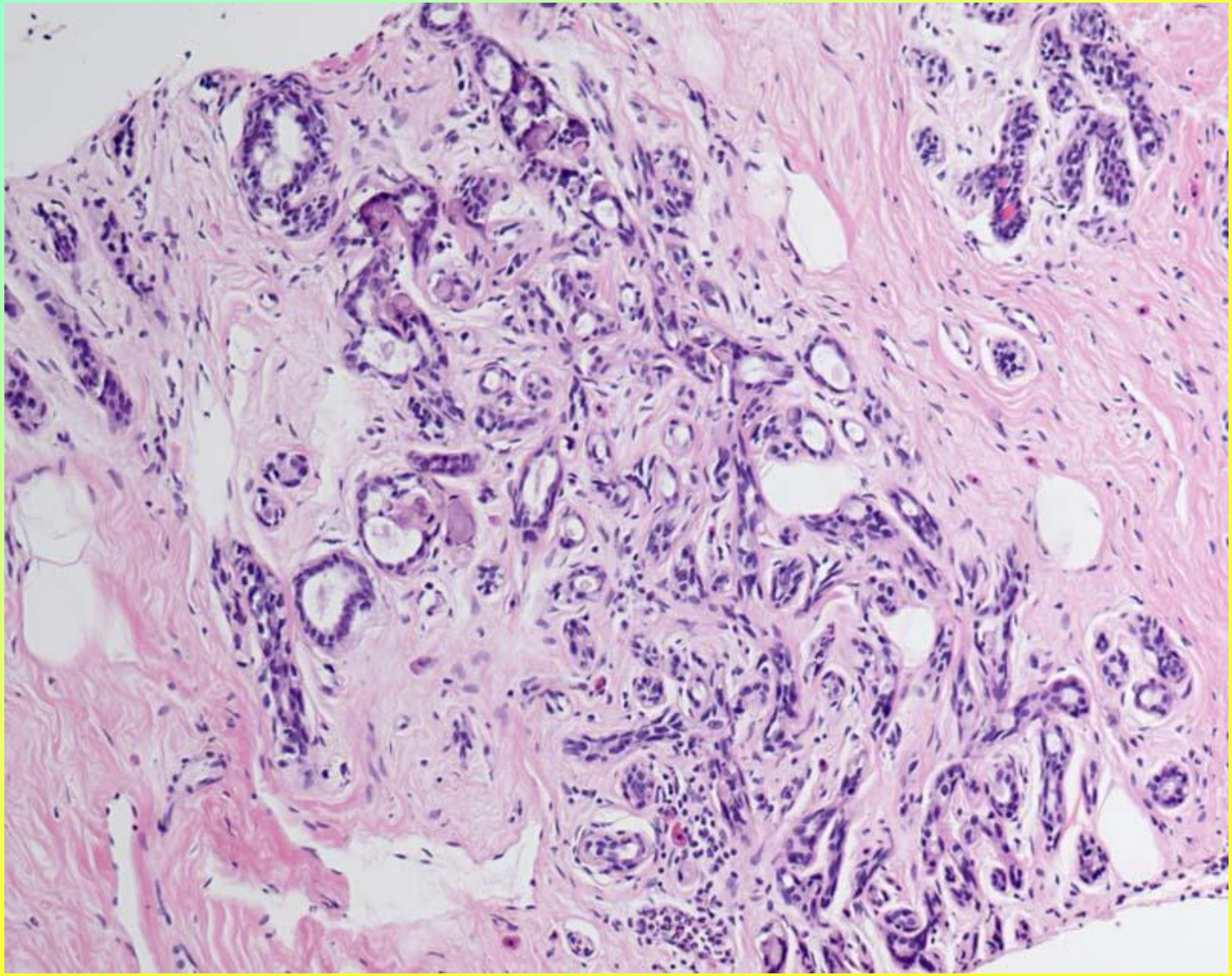
Usual (ductal) epithelial hyperplasia: more than 4 cell layers, often bridging across duct lumens; nuclei present a streaming pattern; secondary spaces are slit-like, irregular and typically peripheral in location.

PathoPic
www.unibas.ch/patho



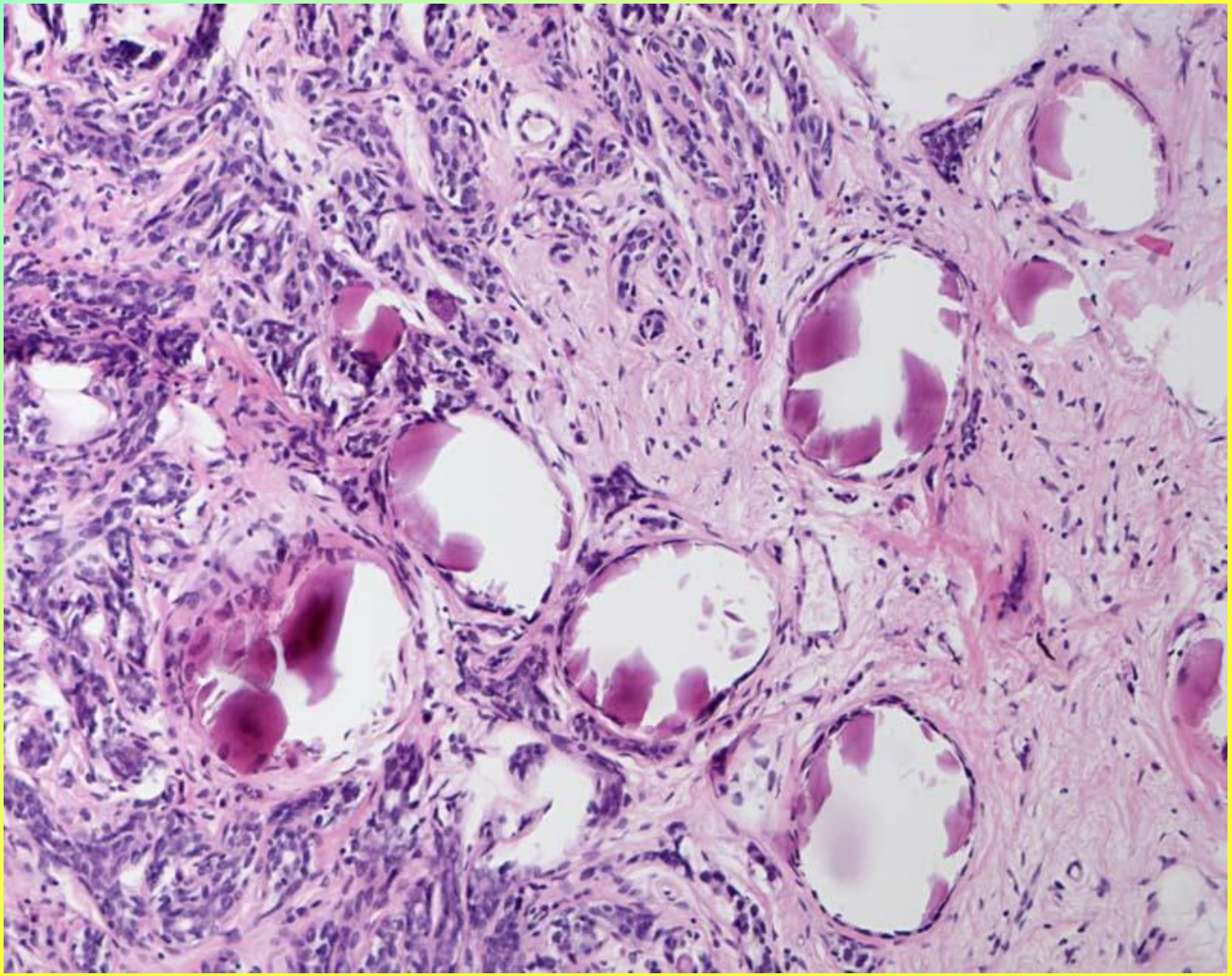
Detail for breast UDH: variable cyto-morphology (= not clonal proliferation), no nuclear atypia.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=008070



Sclerosing adenosis: disorderly proliferation of epithelial, myoepithelial and intralobular stromal cells, resulting in distortion and expansion of lobules and obliterating duct spaces.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=008231



Sclerosing adenosis calcifications present within the lumina (intraductal calcifications).

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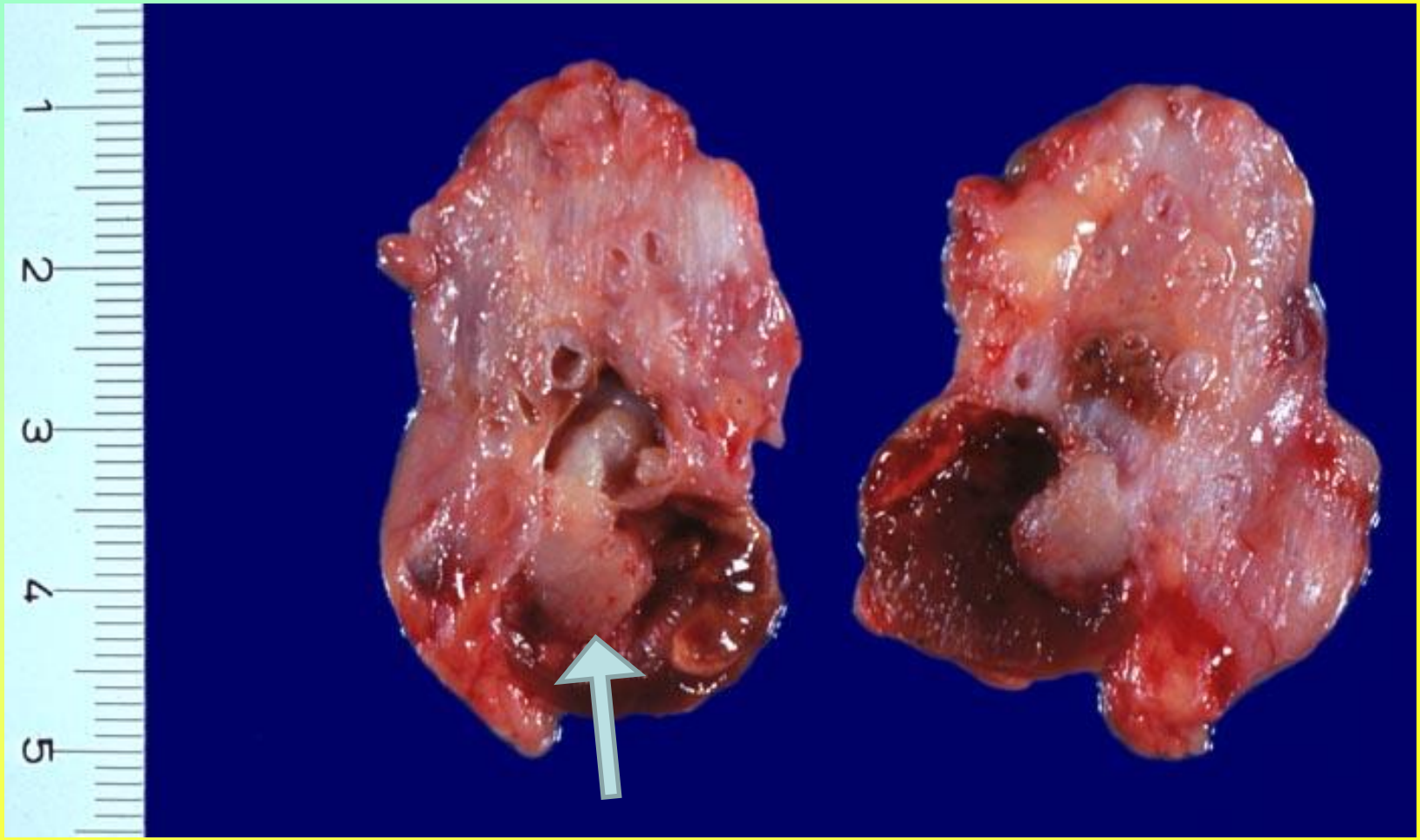
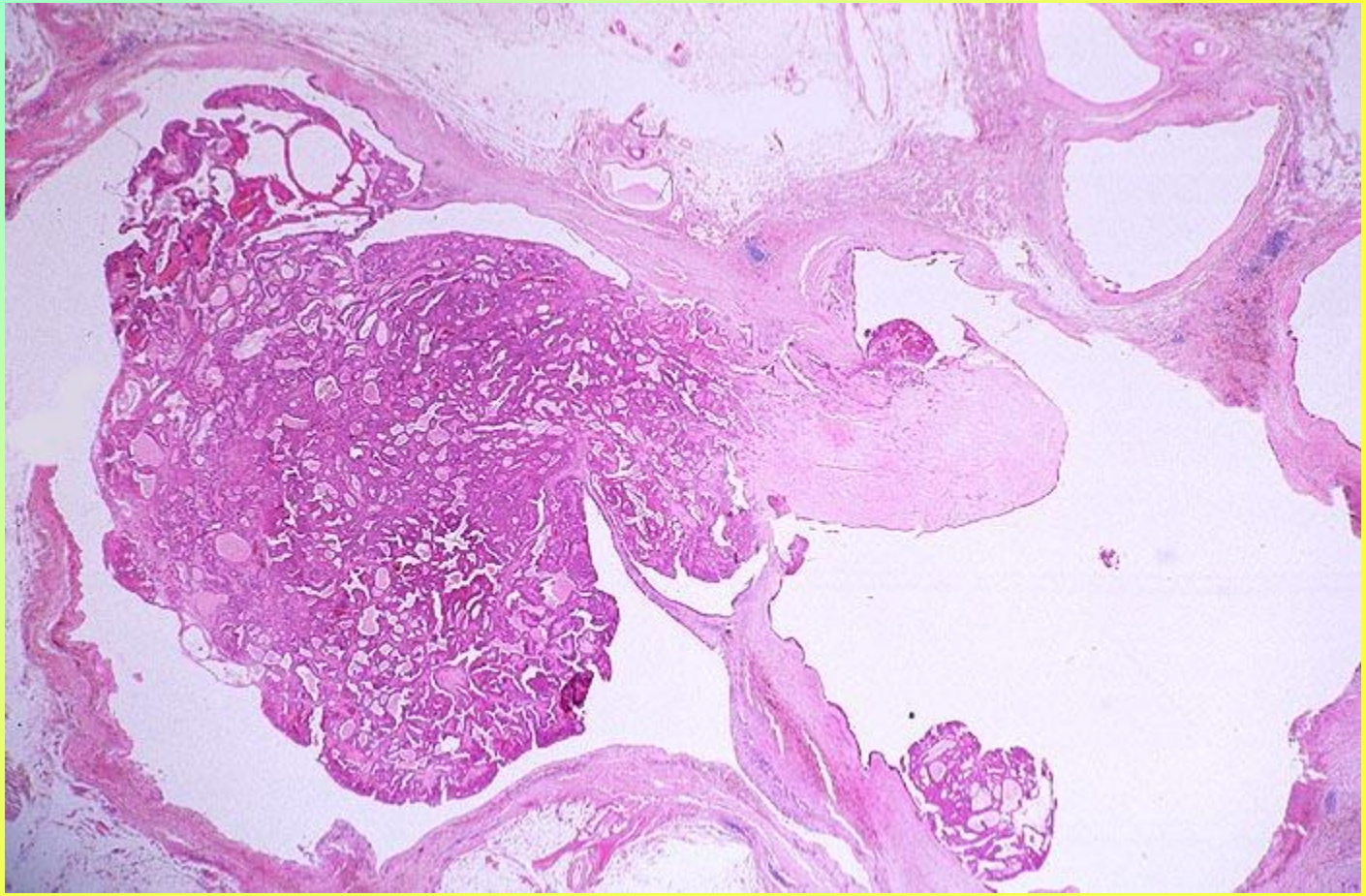


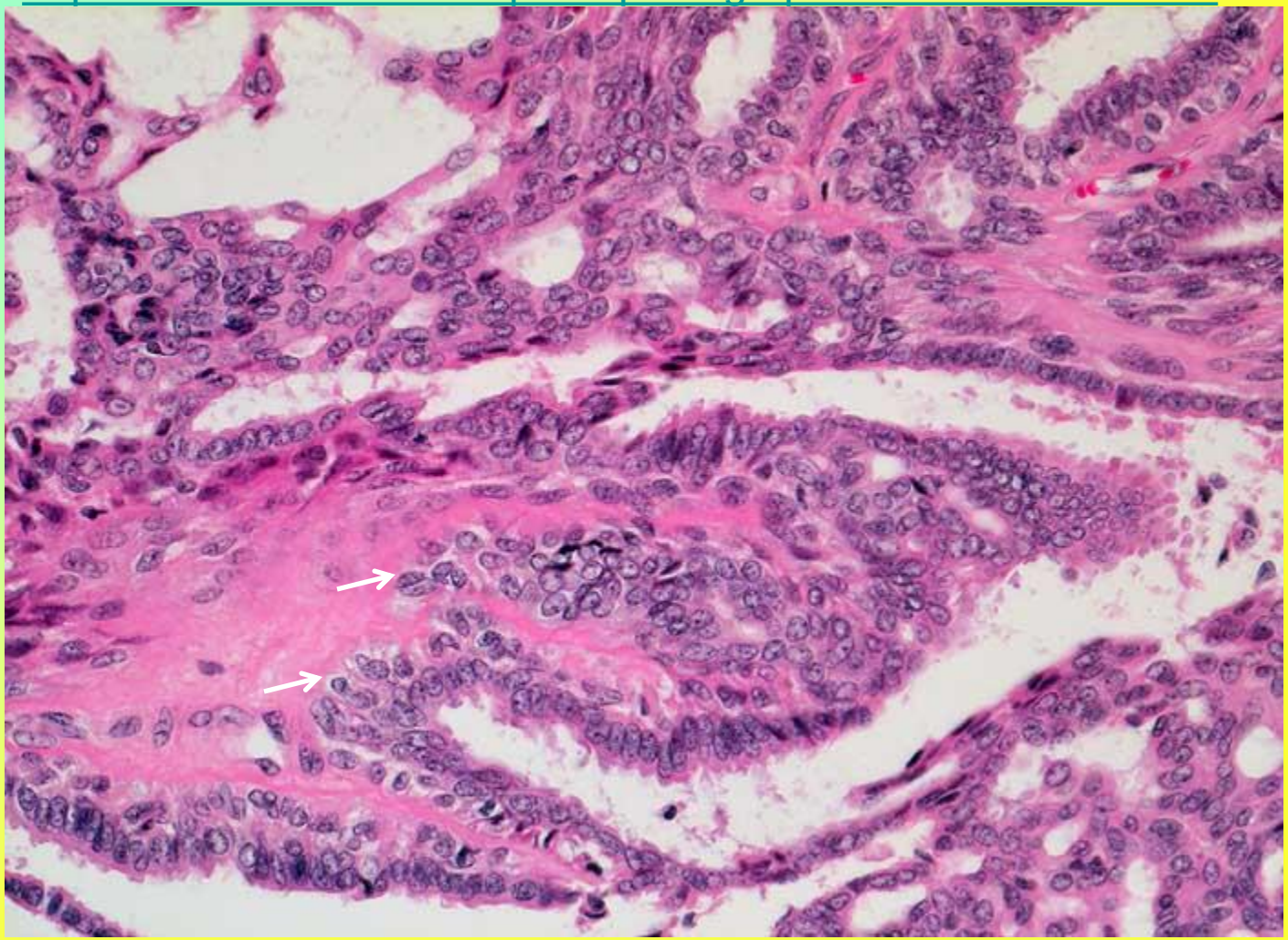
Large duct **papilloma** (central papilloma, usually solitary) within a lactiferous sinus of the nipple – cut section: a hemorrhagic cyst with protruding tan tumor (arrow).

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=003642

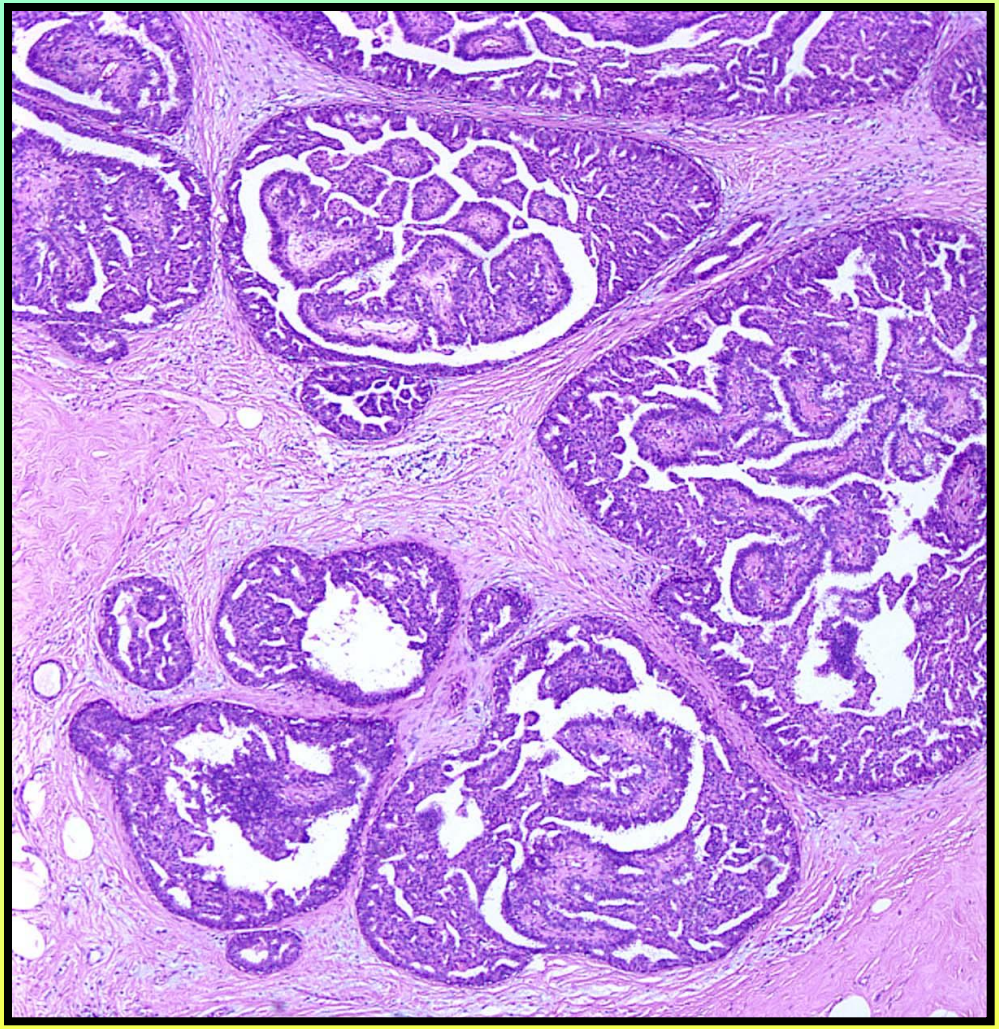


Large duct **papilloma** (central papilloma): the dilated duct contains multiple branching papillae with fibrovascular cores.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=005697



Large duct **papilloma** (central papillomas) detail of fibrovascular cores lined by inner / luminal layer of columnar cells and an outer / basal myoepithelial cell layer (arrows).



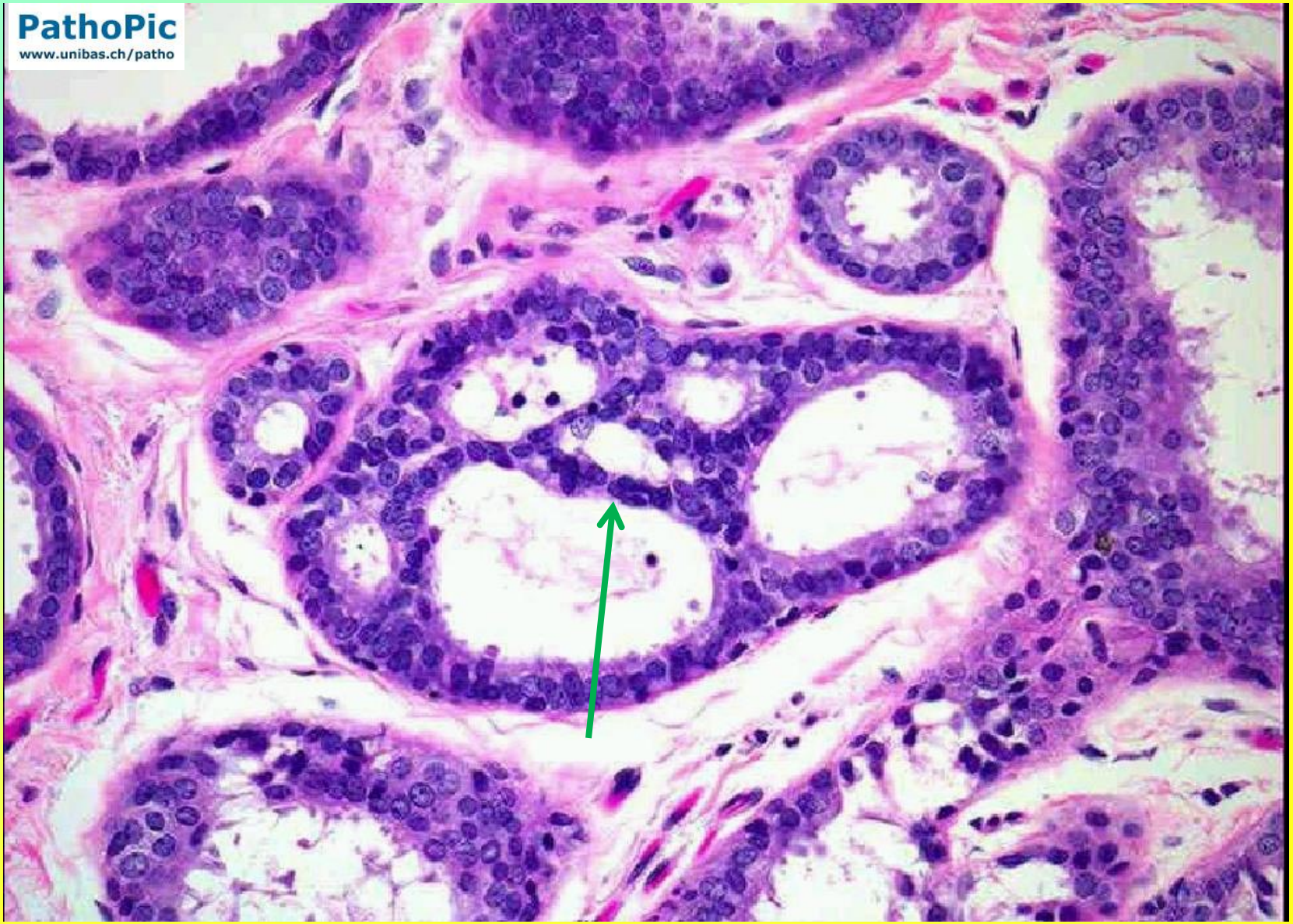
Small duct papillomas (peripheral papillomas) are commonly multiple (papillomatosis).

http://www.asl5.liguria.it/Portals/0/AnatomiaPatalogica2014/Collins

Proliferative breast disease with atypia = atypical hyperplasia:

- is a clonal proliferation having some, but not all, of the histologic features that are required for the diagnosis of carcinoma in situ
- mammographic Ca

- **atypical ductal hyperplasia (ADH)** intraductal epithelial proliferation with a dual population of low-grade neoplastic epithelial cells and benign cells; neoplastic population = monomorphic small cells evenly spaced, with well-defined cytoplasmic borders and round, hyperchromatic, uniform nuclei forming complex structures, such as micropapillae, rigid bridges, bars, solid sheets or cribriform arrays
- **atypical lobular hyperplasia (ALH)** proliferation of monomorphic small, round, loosely cohesive cells < 50% of the acini within a lobule
- **flat epithelial atypia (FEA)** acini are variably dilated, lined by one or several layers of epithelial cells, with low-grade cytologic atypia; cell polarity is lost, but the architectural complexity is absent.



Atypical ductal hyperplasia (ADH) monomorphic small cells evenly spaced, with round, hyperchromatic, uniform nuclei forming complex structures, such as rigid bridges, bars, cribriform arrays (arrow).

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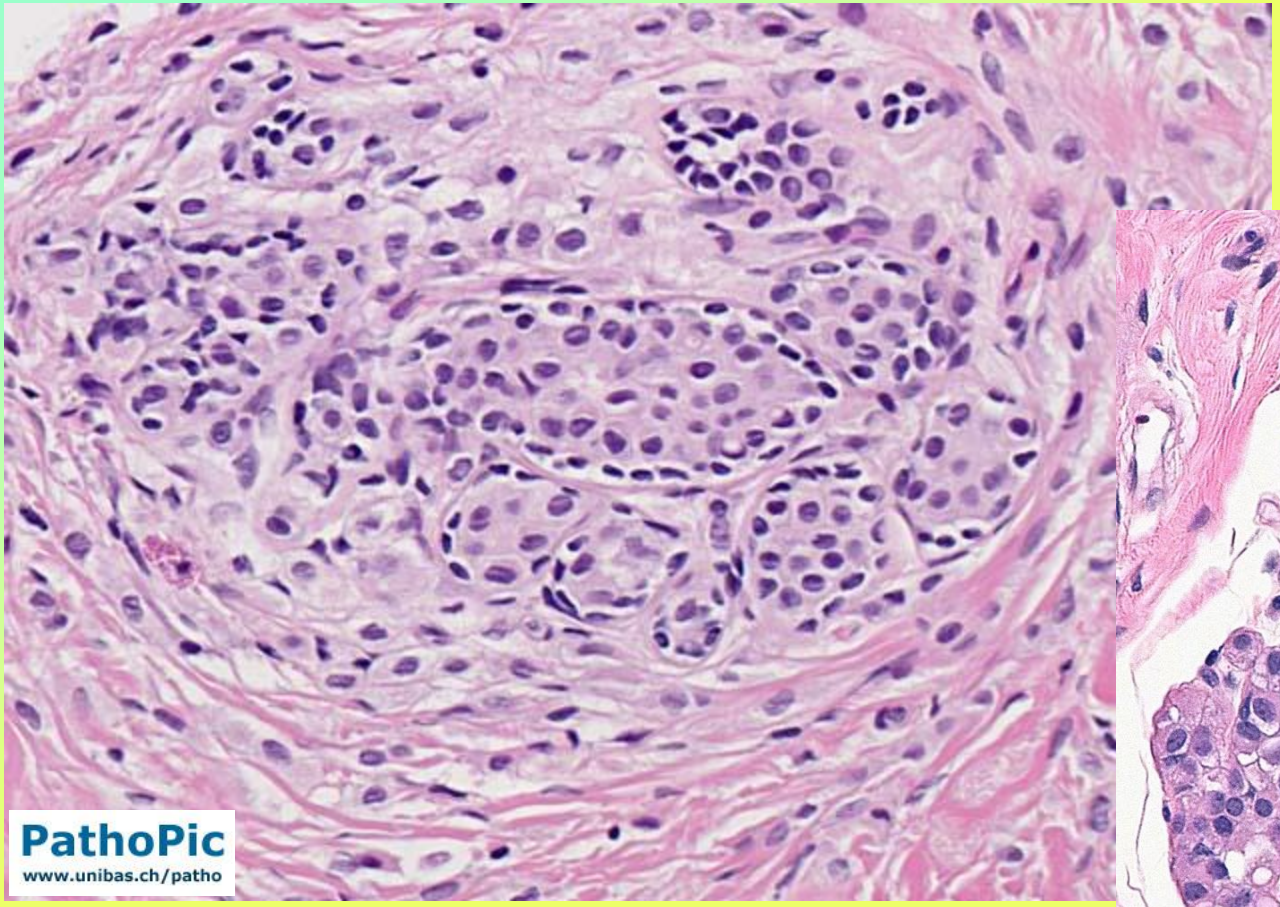
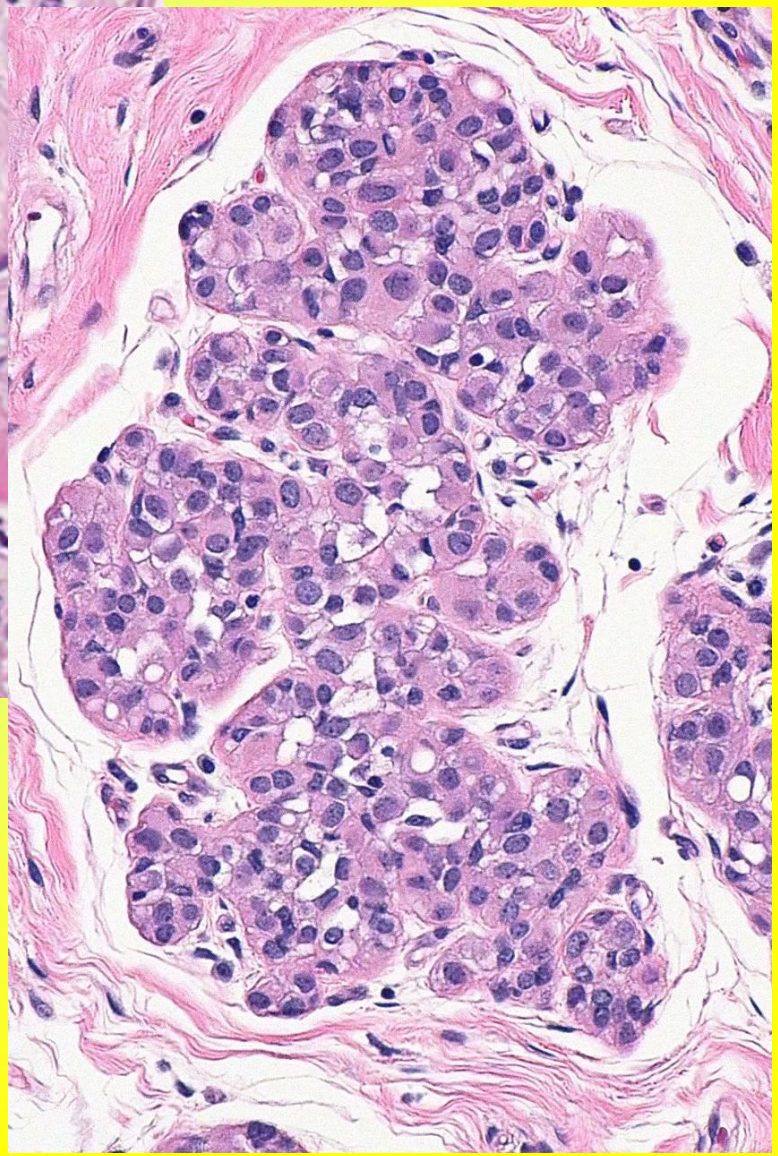
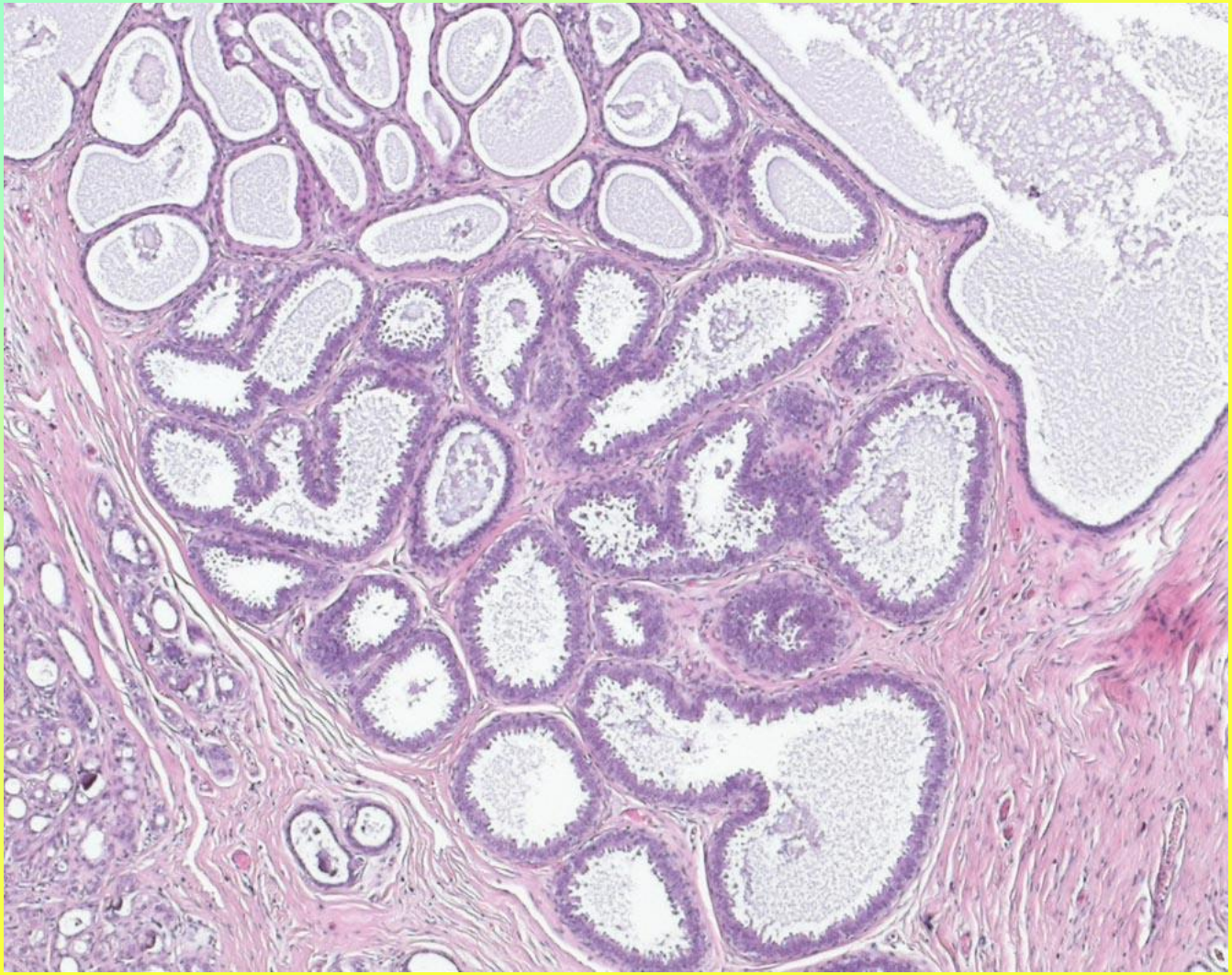




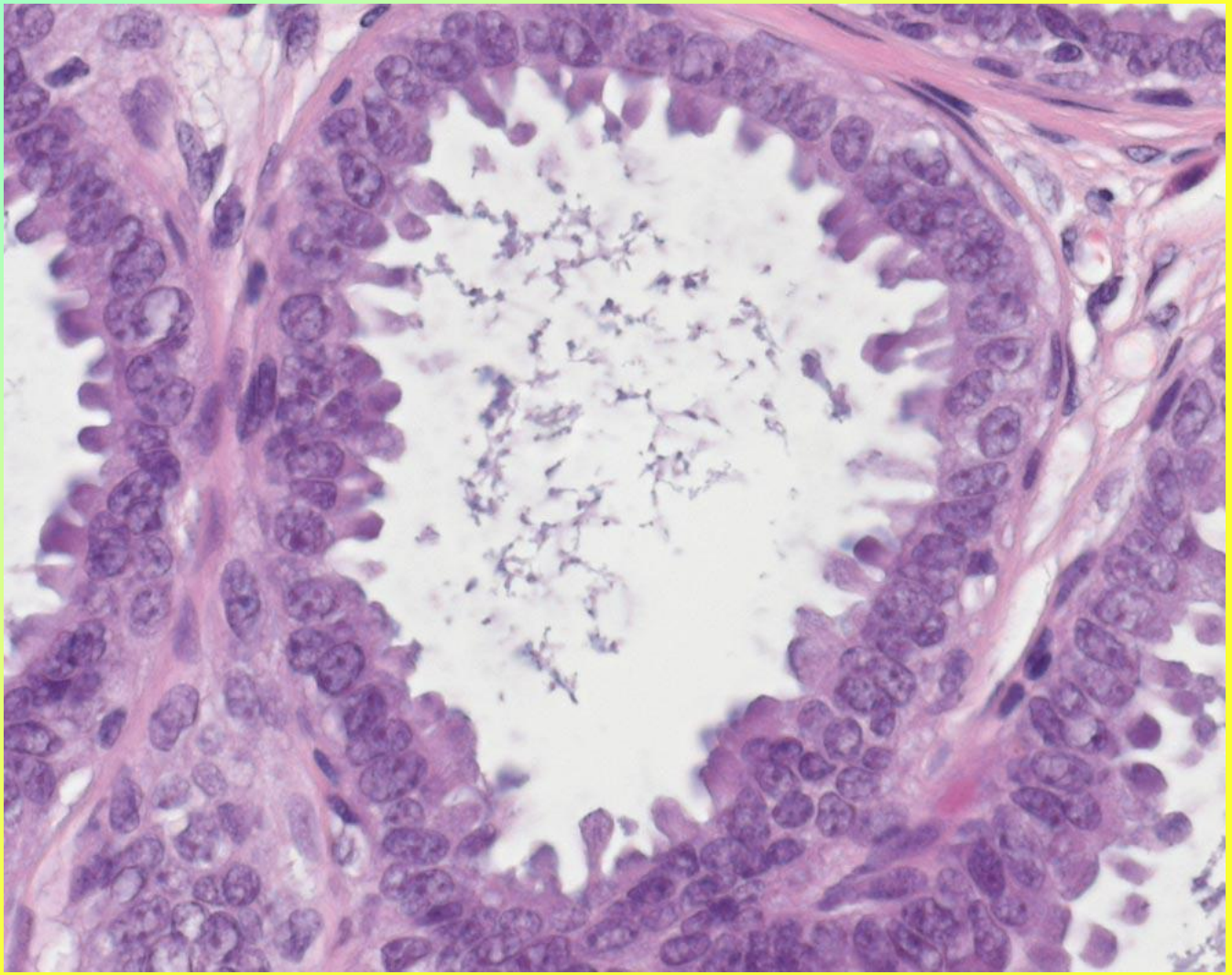
Atypical lobular hyperplasia / ALH: monomorphous cells within the lobules.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009976



Flat epithelial atypia (FEA): Terminal ductulolobular unit consisting of dilated acini with undulating contour. Acini are lined by columnar cells with apical snouts.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=009977



Flat epithelial atypia (FEA): Dilated acinus lined by columnar cells with apical snouts. Nuclei are round, enlarged, and not oriented perpendicular to the basement membrane. They have prominent nucleoli.

FIBROEPITHELIAL LESIONS

Origin: ntralobular stroma and contain both stromal and epithelial elements:

- **Fibroadenoma** round, rubbery tumor, which is sharply demarcated from the surrounding breast and is thus freely movable;
  - mixture of fibrous connective tissue and ducts simple and round (pericanalicular pattern) or elongate and branching (intracanalicular pattern).

- **Phyllodes tumor** few cm to massive lesion involving the entire breast sharply circumscribed. Its cut surfaces is firm, glistening and grayish white;
  - hypercellular stroma lead to formation of leaf-like structures, which project into cystic spaces lined by a dual layer of benign epithelium and myoepithelium

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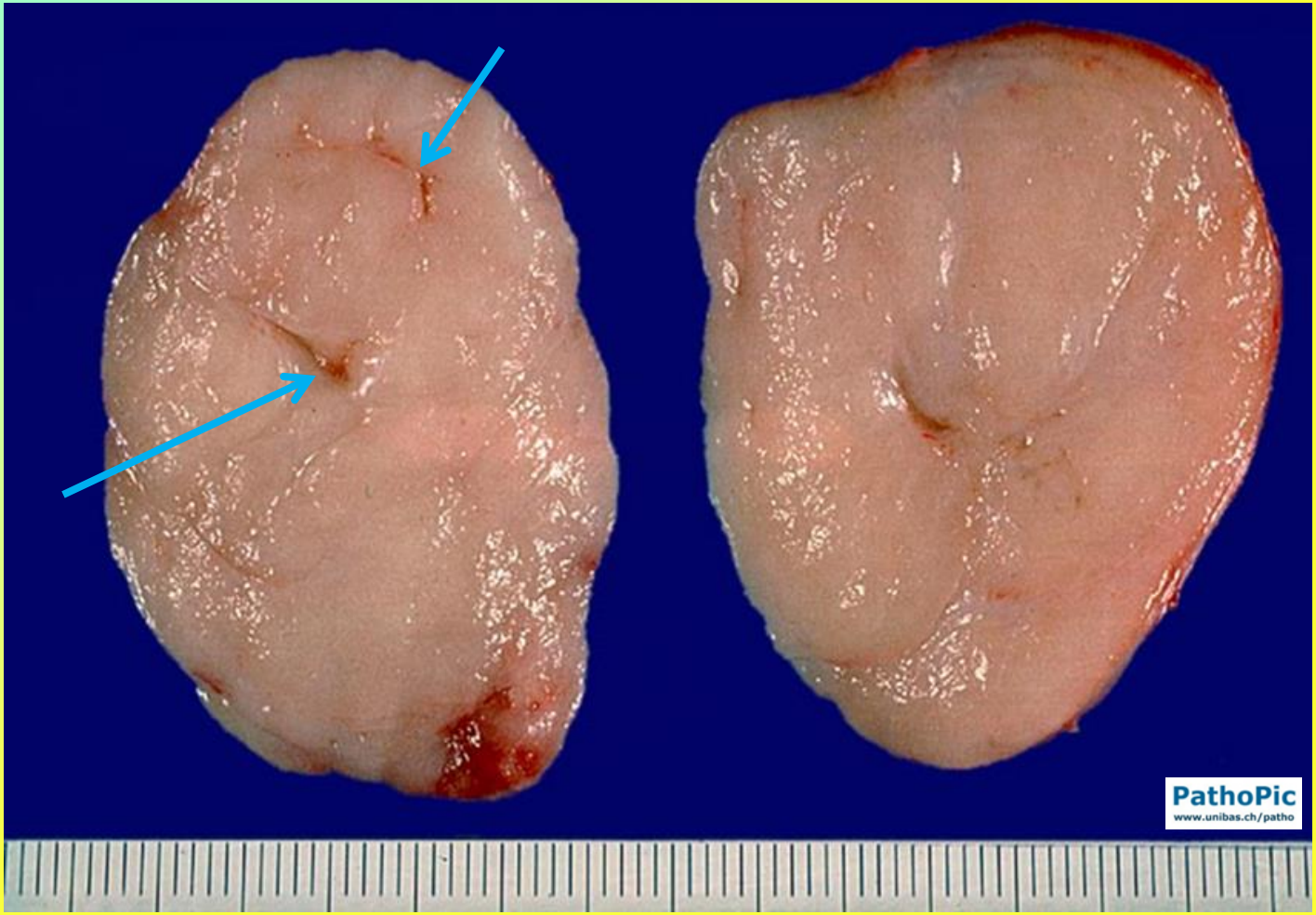

Fibroadenoma. A rubbery, white, well-circumscribed mass is clearly demarcated; compressed slit-like glands (arrows).

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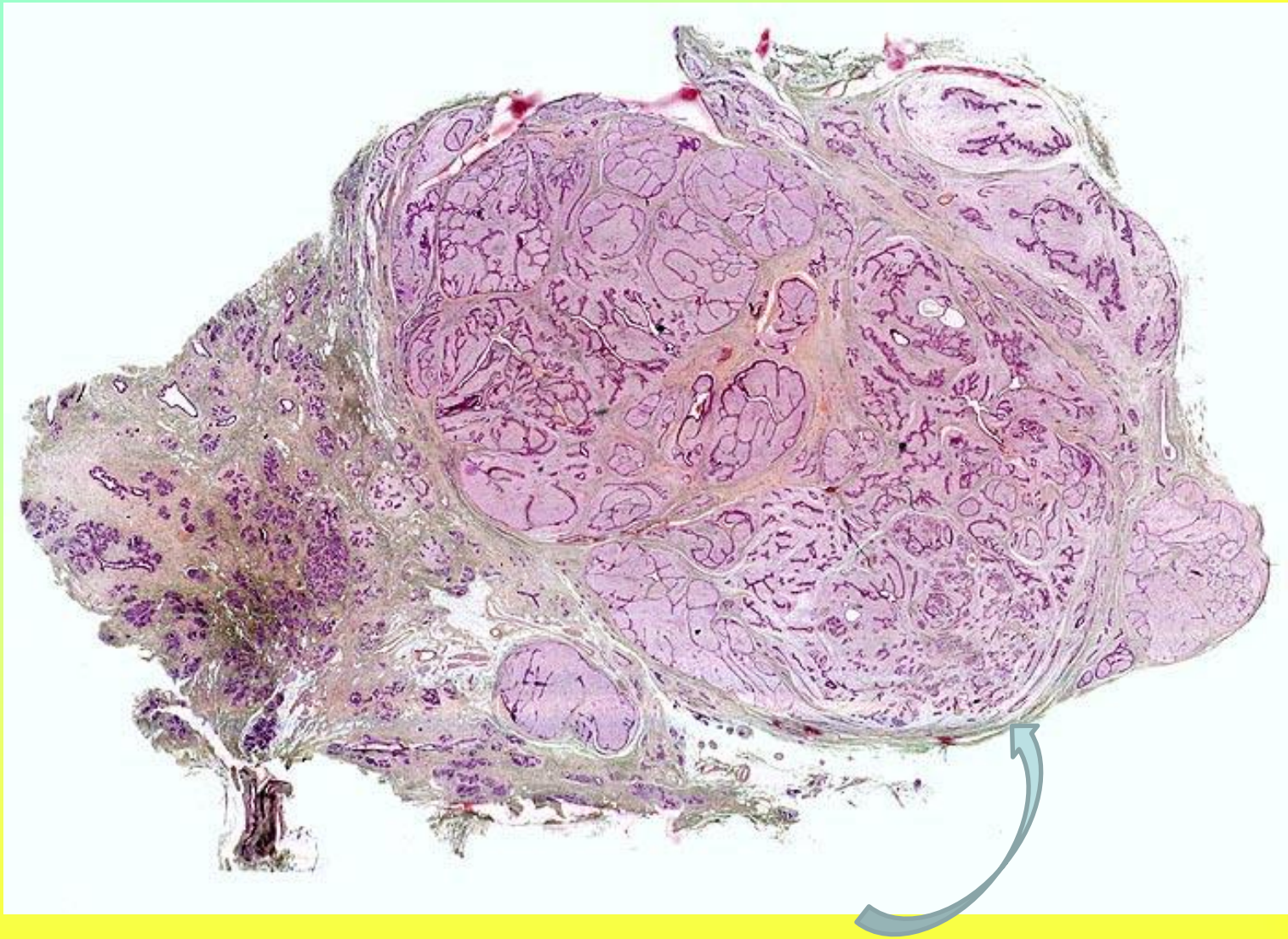
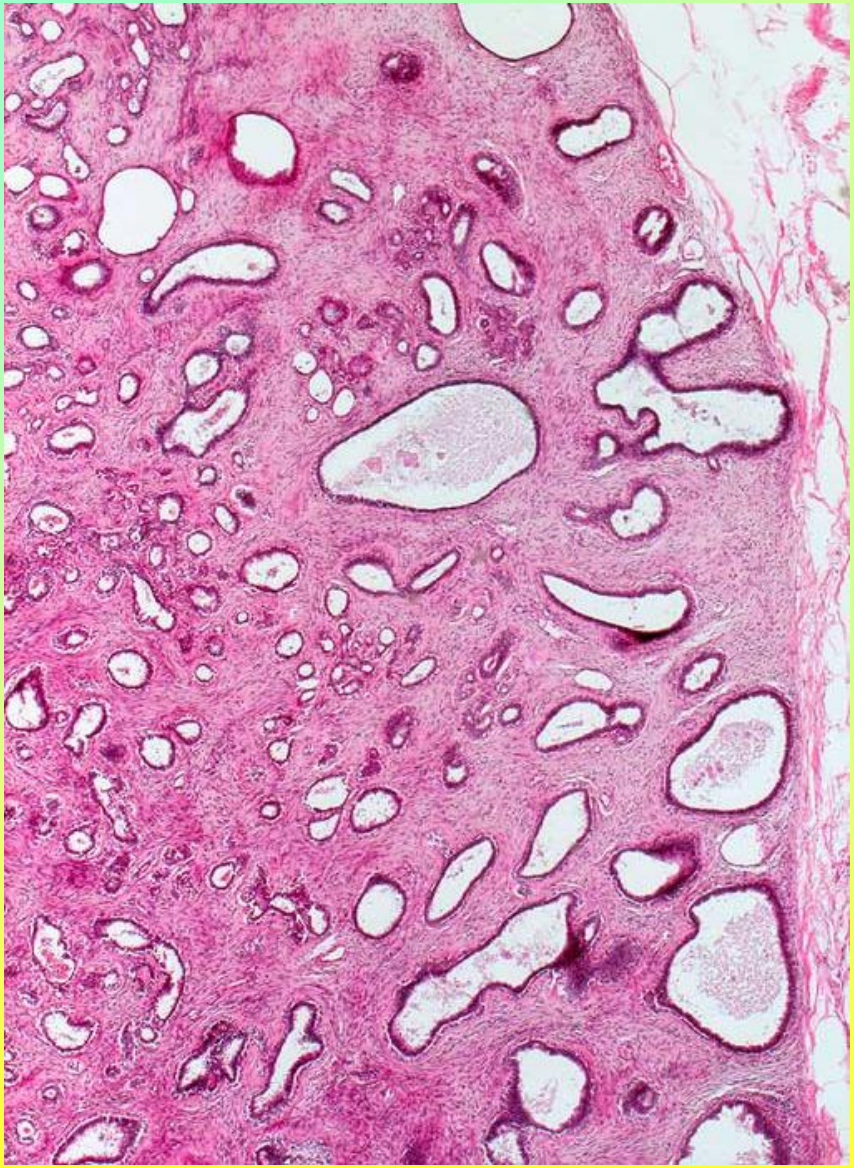
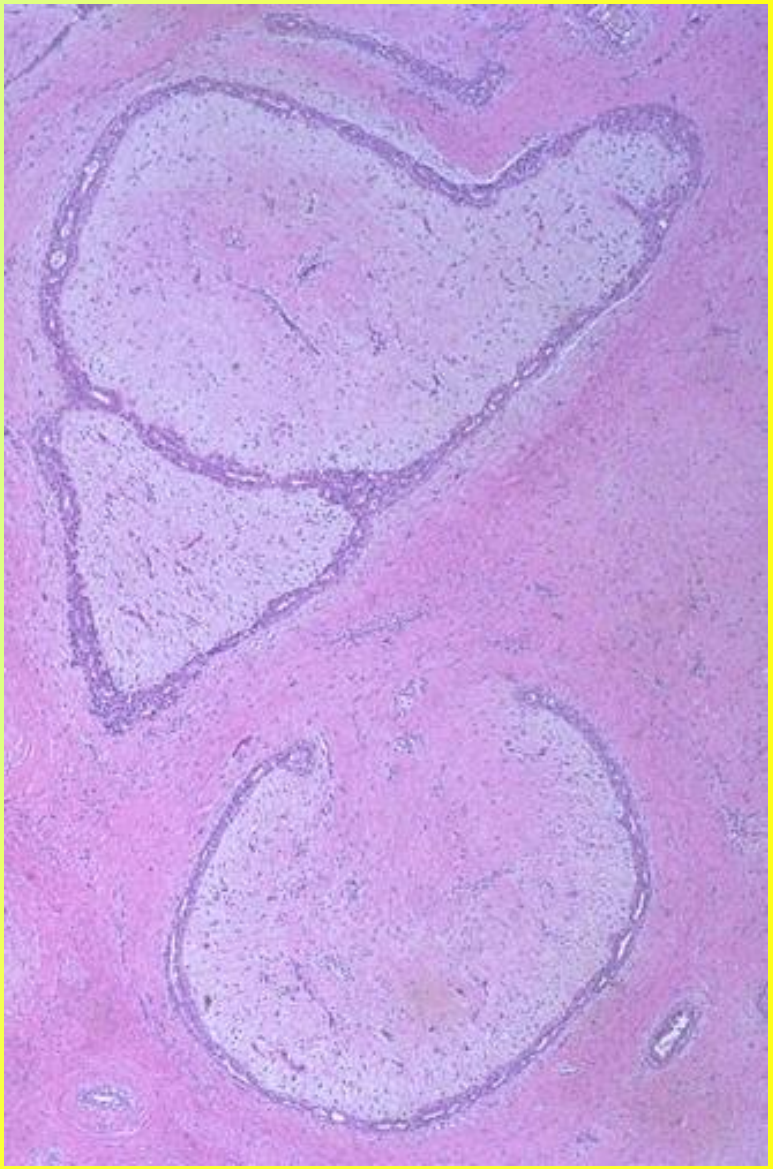


Whole mount of **fibroadenoma**: fibrous capsule; within the fibroconnenctive tissue stroma, glandular structures have a slit-like appearance.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=005698

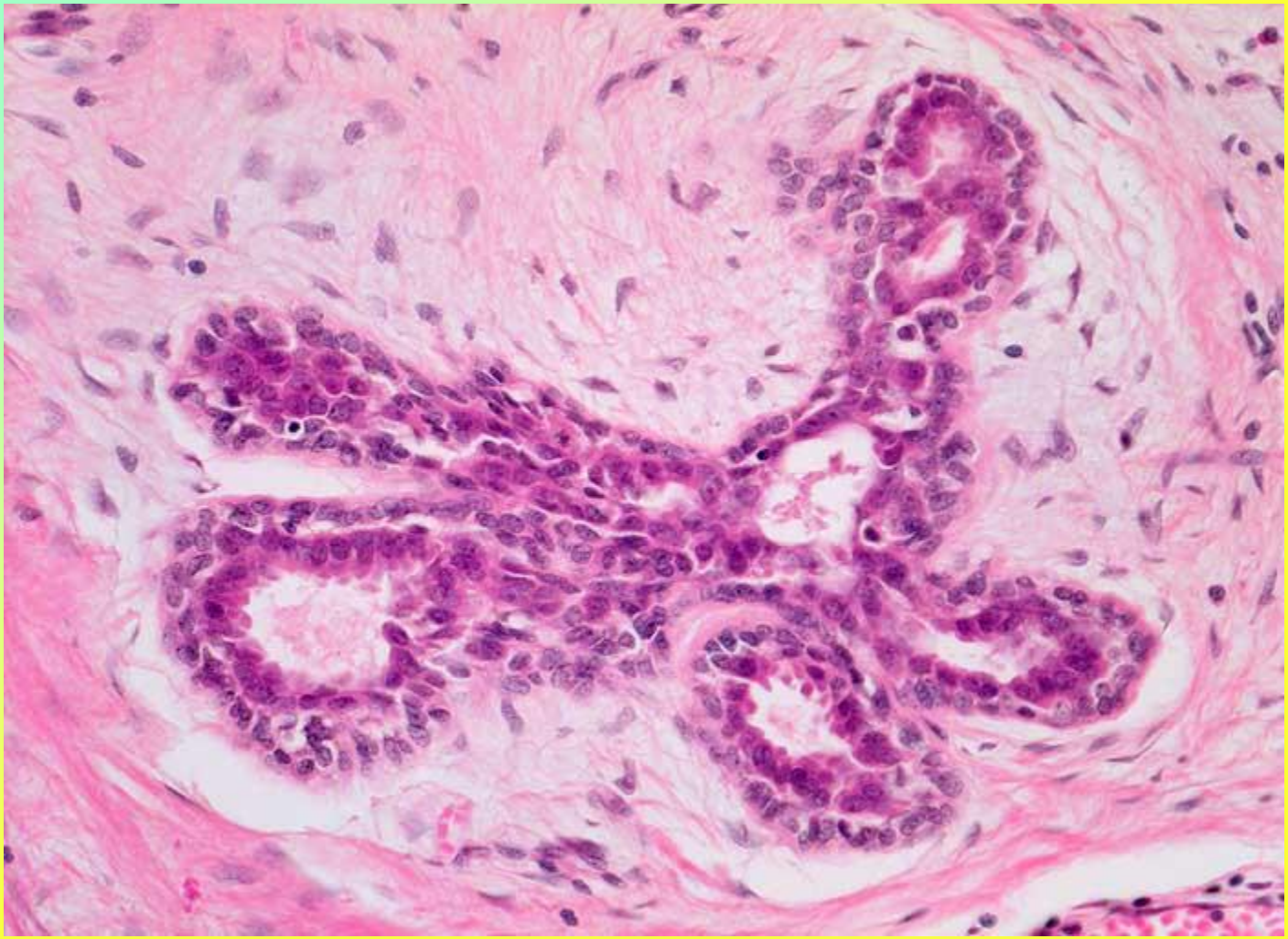


Pericanalicular fibroadenoma: glandular structures, uncompressed by the stroma, have a round to oval lumen.



Intracanalicular fibroadenoma: fibrous tissue compresses the proliferated ducts, reducing them to curvilinear slits.

https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=005670



double layer of epithelium: luminal / secretory
+ basal / myoepithelial

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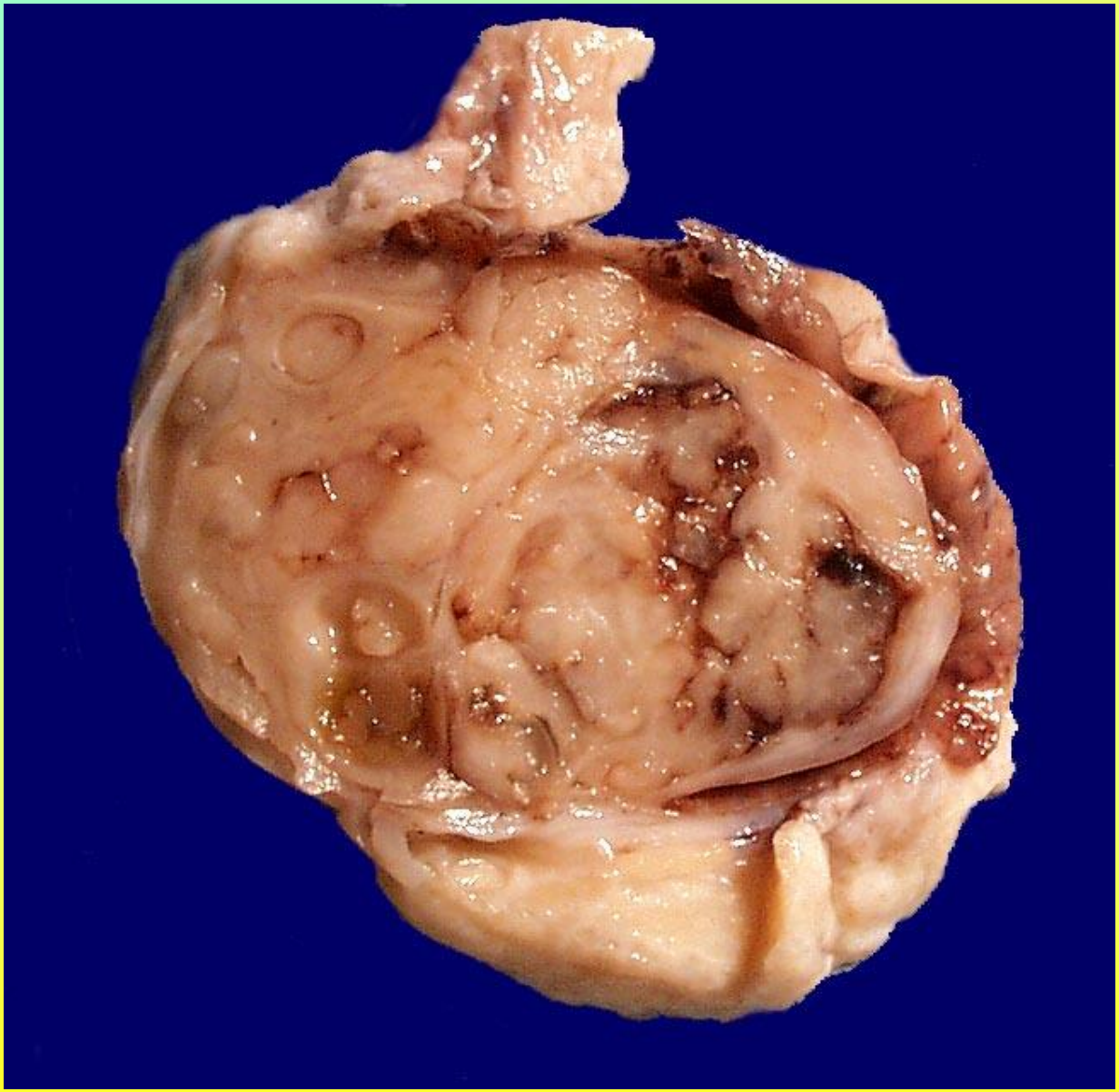
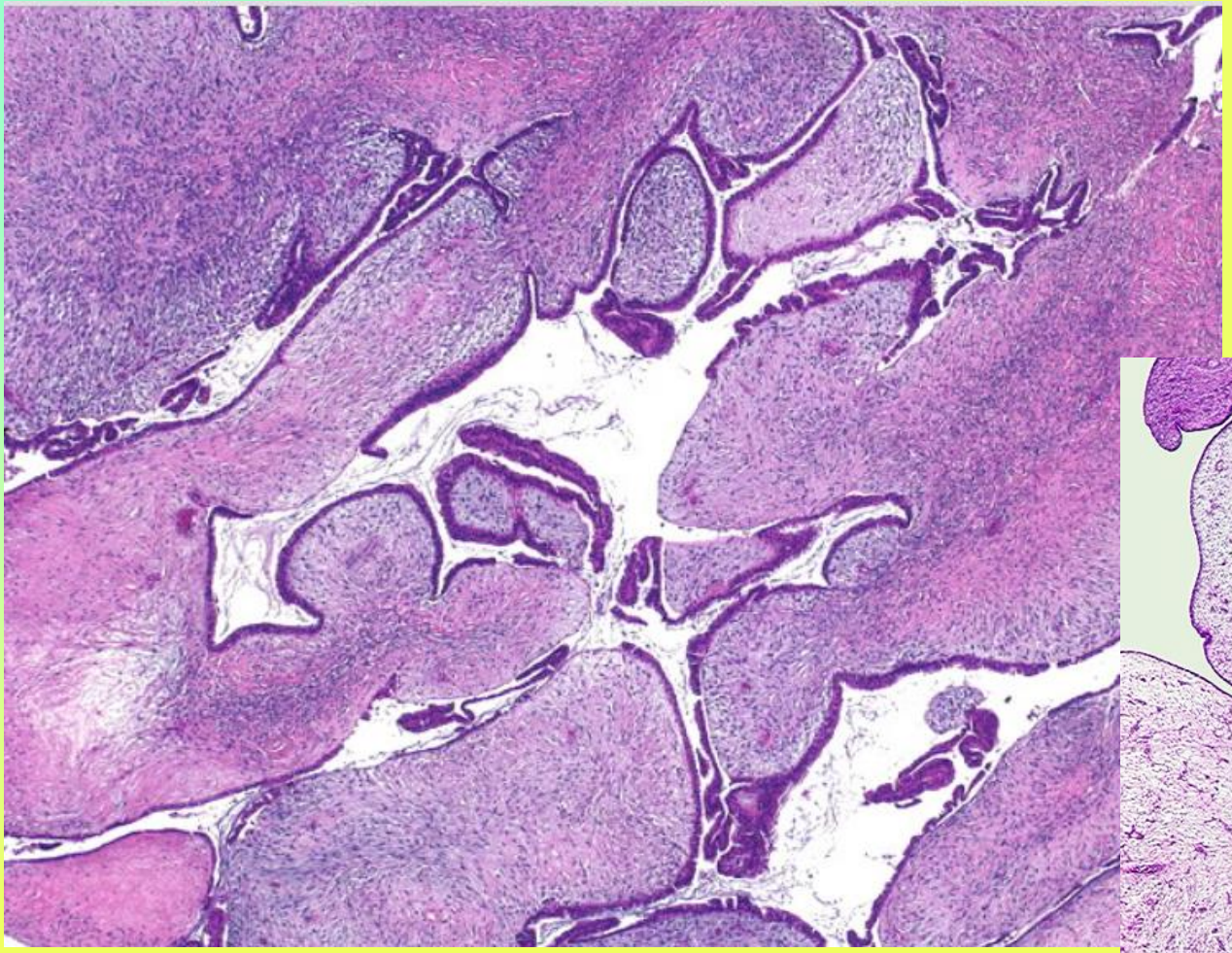
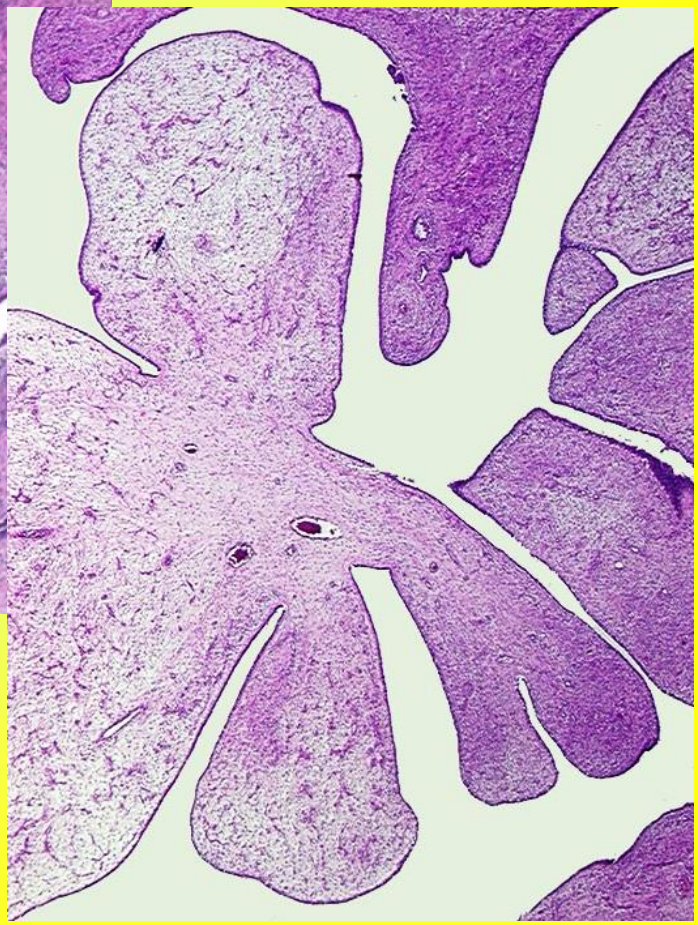


Phyllodes tumor: sharply circumscribed lesion; the cut surface is firm, glistening and grayish-white / tan and shows several **cleft-like spaces.**





Phyllodes tumor: fronds of hypercellular stroma lead to formation of leaf-like structures, which project into cystic spaces.

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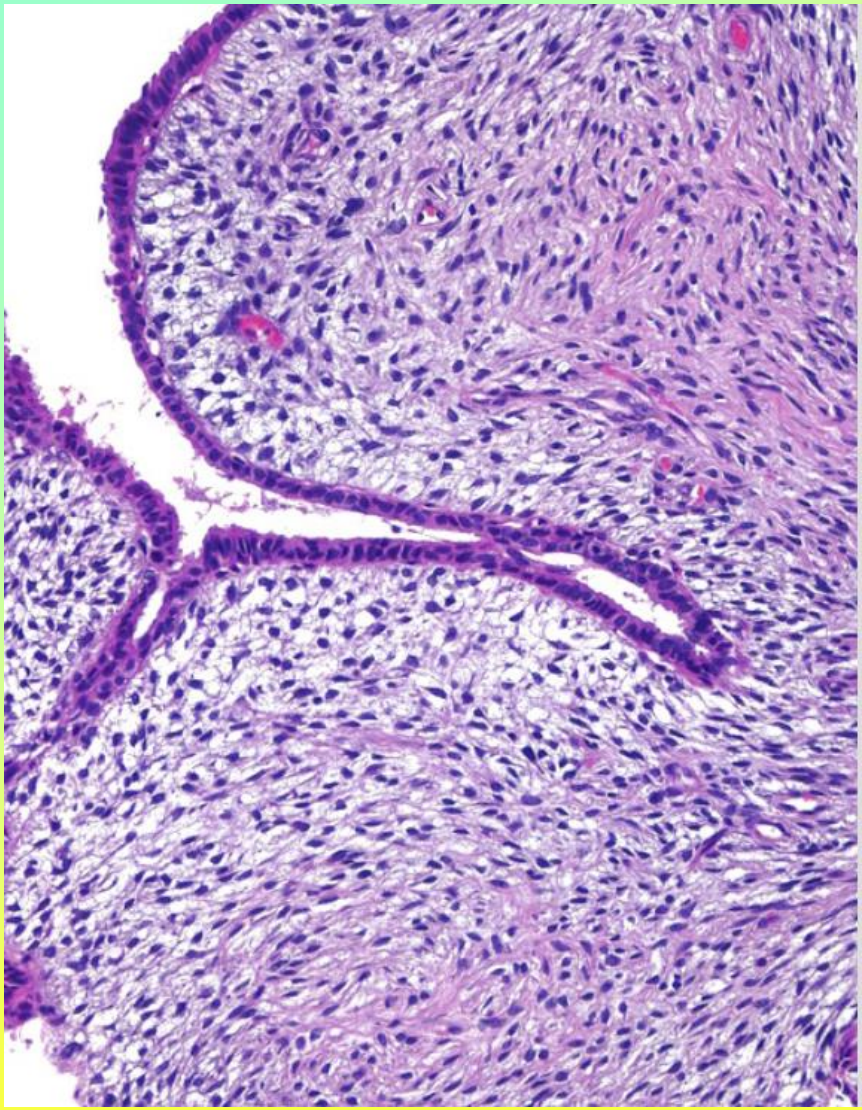
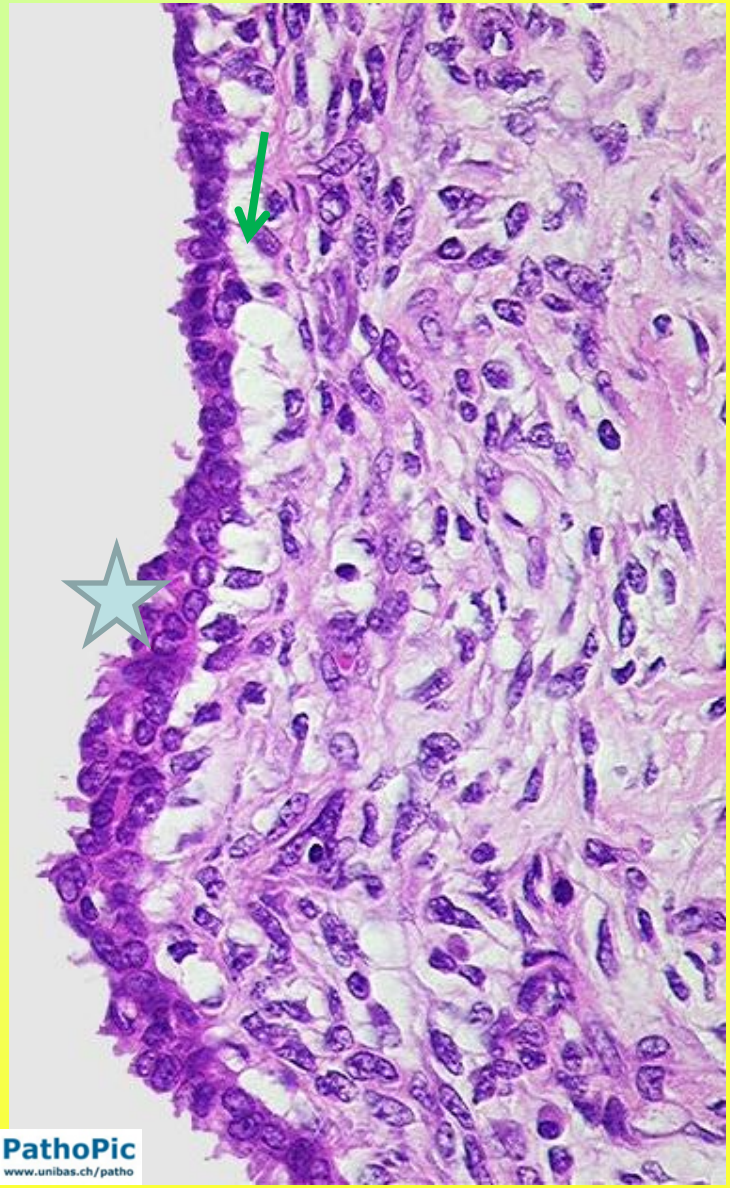
https://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=000820





Phyllodes tumor: hypercellular stroma underneath the cleft-like spaces lined by dual layer: benign glandular epithelium (star) and myoepithelium (arrow).

MALIGNANT TUMORS OF THE BREAST

- the most common malignancy of women
- second cause of cancer deaths
- incidence increases after age 30 (woman who lives 90 years has a one in eight chance for BC)
- **Risk factors**
- almost all (>95%) are adenocarcinomas, from the glandular epithelium of the terminal duct lobular unit TDLU

- **hereditary factors**:
  - *germline mutations*: 5% to 10% of breast cancers occur in persons with germline mutations in tumor suppressor genes: BRCA1, BRCA2, TP53 and CHEK2.
  - *first-degree relatives with breast cancer*. (mother, sister or daughter)
- **age**: breast cancer risk rises throughout a woman's life-time, peaking at 70 to 80 years
- **hormonal status** – cumulative lifetime exposure to estrogen: early menarche, late menopause, and older age at first-term pregnancy, menopausal hormone therapy
- **breast density:** women with very dense breasts on mammography have 4-to 6-fold risk
- benign breast disease: a prior breast biopsy revealing *atypical hyperplasia* or *proliferative changes*
- **radiation exposure**: radiation to the chest, for cancer therapy (Hodgkin lymphoma)
- other as diet, obesity, environmental toxins

MALIGNANT TUMORS OF THE BREAST

- **Symptoms**: often none, sometimes: pain, “lumpiness” (almost always discovered by the patient) and nipple discharge
- **Imagistics** highly important: in United States more than half of breast cancers are asymptomatic and are detected by **mammographic screening**

- At time of clinical detection:
  - 70% are **Invasive carcinoma** (“infiltrating” carcinoma) with penetration of carcinoma cells through the basement membrane within stroma = vessels, regional lymph node, remote dissemination possible
  - 30% **carcinoma in situ** = neoplastic proliferation of epithelial cells that is confined to ducts and lobules by the basement membrane
- terms *ductal* and *lobular* are used to describe subsets of both in situ and invasive carcinomas based on the resemblance of the involved space to normal ducts or lobules
- these growth patterns are **not** related to the cell of origin, because both arise from cells in the terminal duct lobular unit, but rather reflect differences in tumor cell genetics and biology

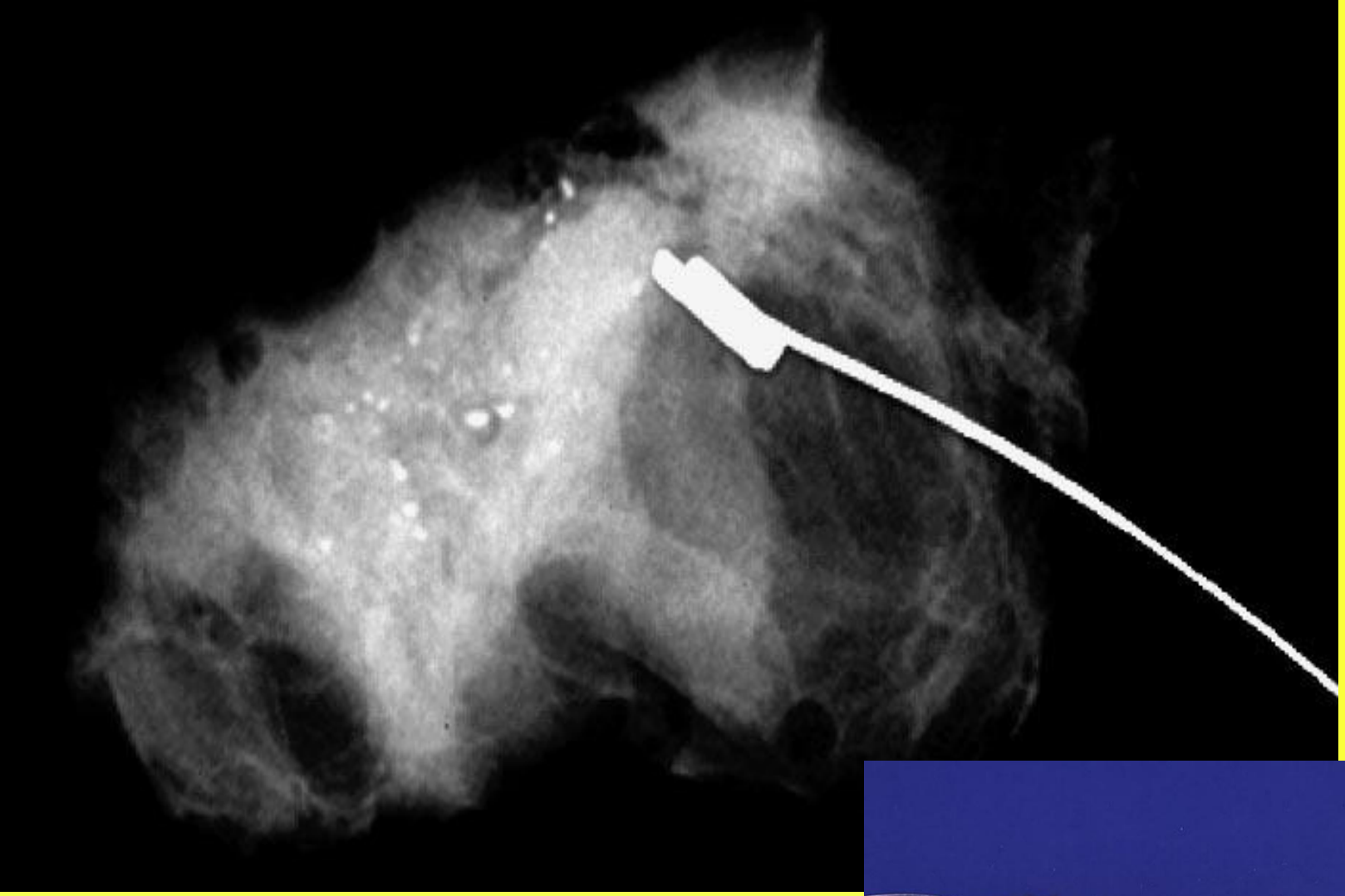
Carcinoma in situ (noninvasive carcinoma)

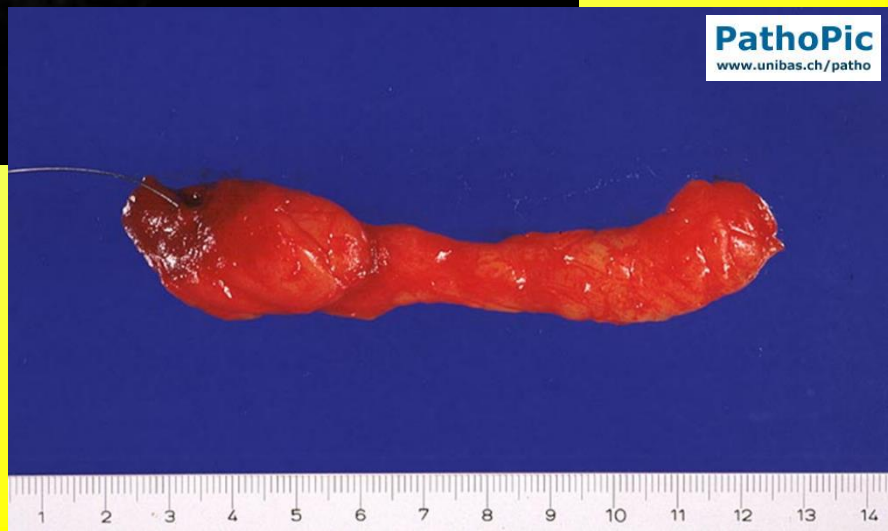
the preinvasive form of cancer = malignant clonal proliferation of epithelial cells limited to ducts and lobules by the basement membrane

histologic types:

- architectural type
- the nuclear grade of malignant cells

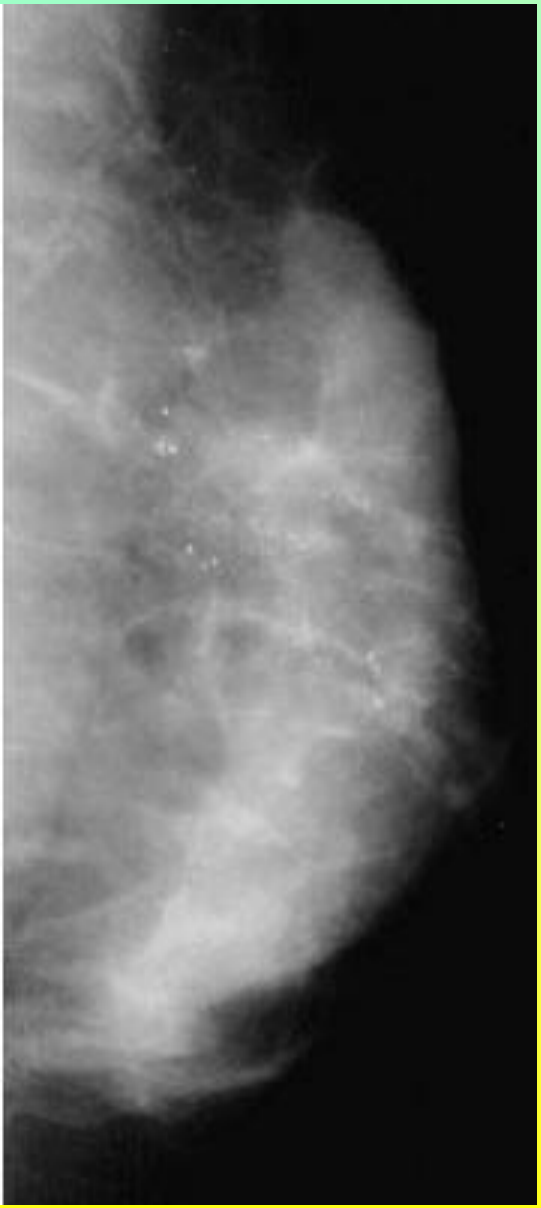
- *Ductal carcinoma in situ (DCIS)* arises in the terminal duct lobular unit which may become markedly enlarged, thereby resembling large ducts
  - *Comedo DCIS* grows in a solid pattern and often becomes centrally necrotic (intraductal necrosis) cells very large, pleomorphic, with abundant eosinophilic cytoplasm and irregular nuclei, prominent nucleoli (nuclear high-grade)
  - *Noncomedo DCIS* papillary structures and small, regular fenestrations (cribriform pattern) cells and nuclei are smaller and more regular (nuclear low-grade)
- *Lobular carcinoma in situ (LCIS)* cells within ducts and lobules grow in a discohesive fashion, with an acquired loss of the tumor suppressor protein **E-cadherin**

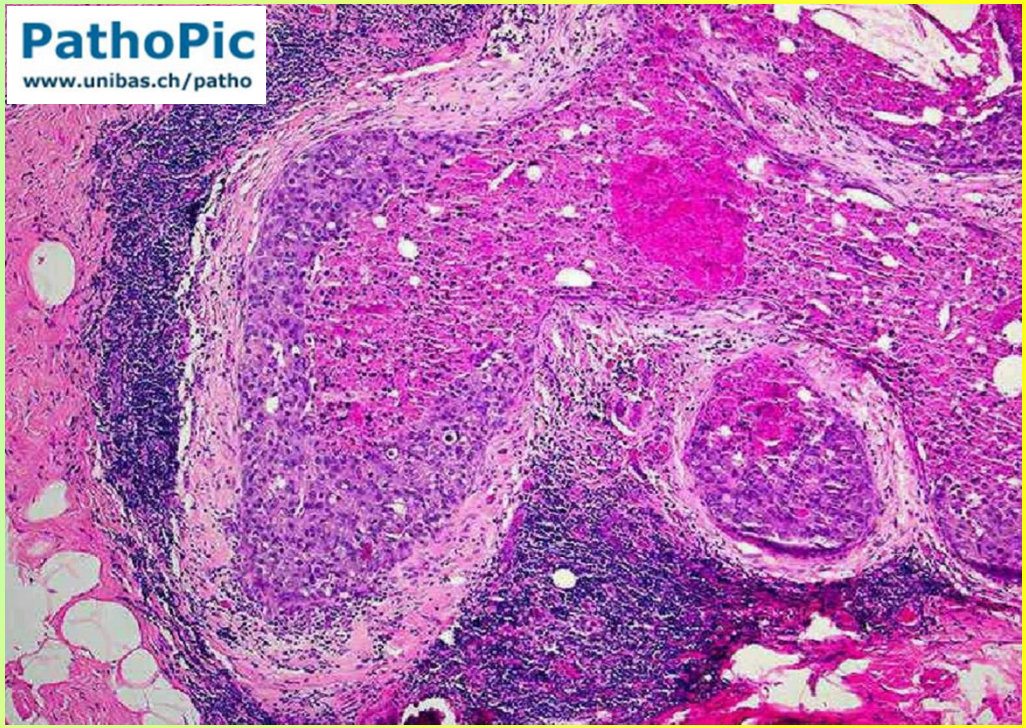




Mammography: suspicious (for malignancy) microcalcifications;

Next (mandatory) step: **core biopsy**

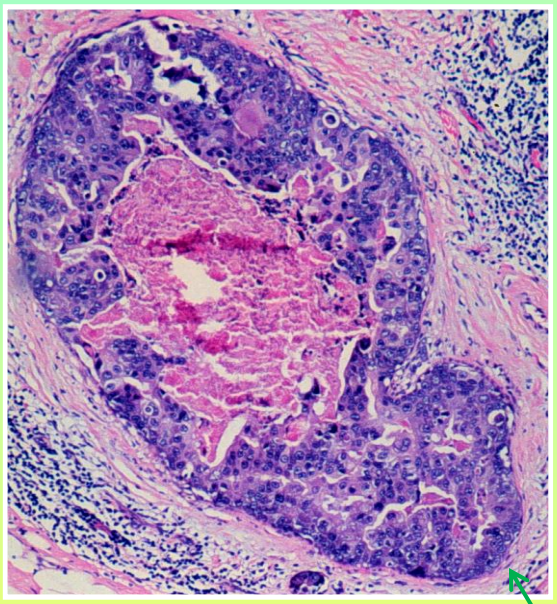


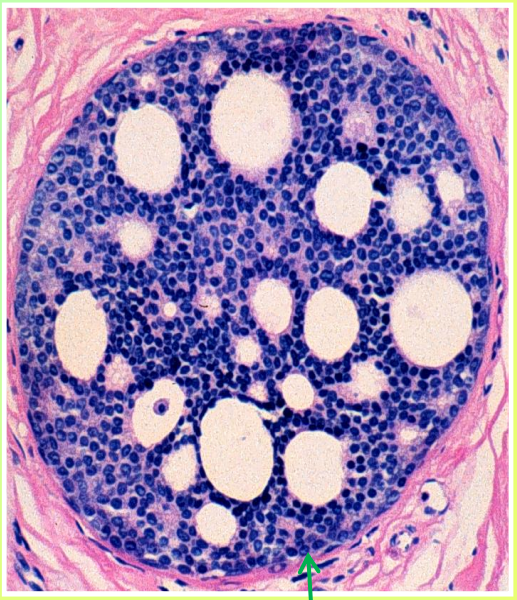


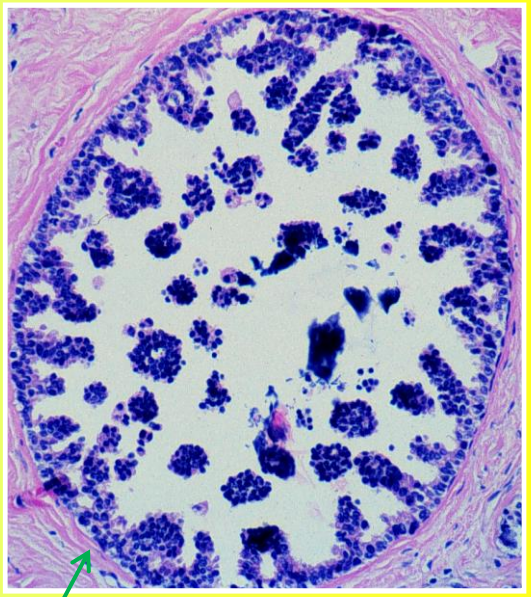
Comedo DCIS fills several adjacent ducts (or completely replaced lobules) and is characterized by large central zones of necrosis with calcified debris. This type of DCIS is most frequently detected as radiologic calcifications.

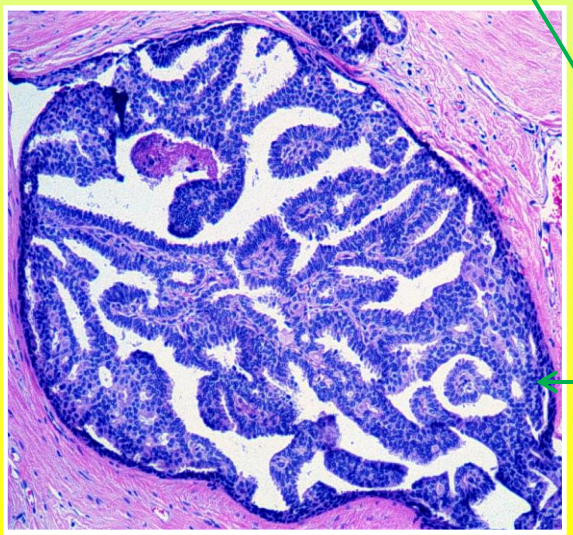
This mammogram reveals multiple clusters of small, irregular calcifications in a segmental distribution. Suspicious calcifications must be biopsied, as 20% to 30% will prove to be due to DCIS.

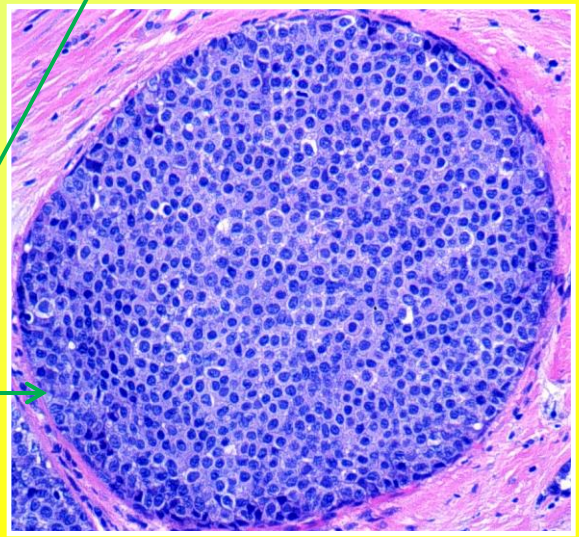
DCIS can have many architectural patterns









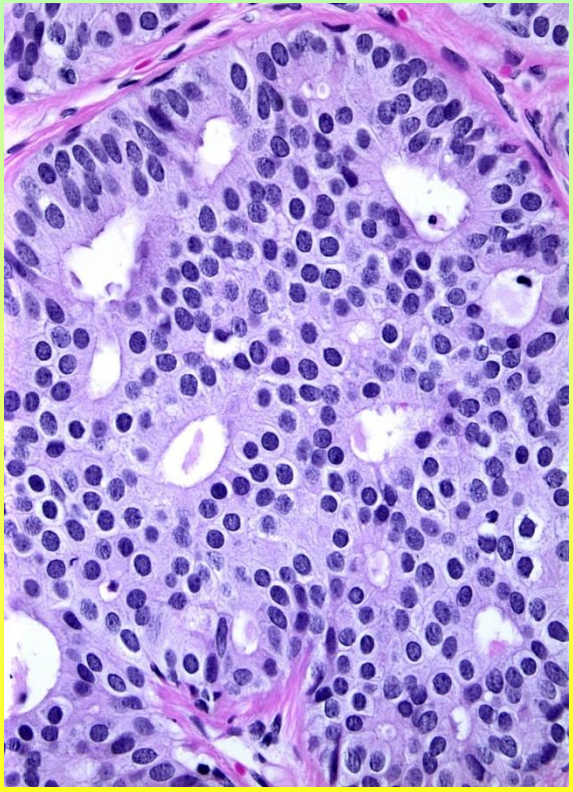


DCIS: architectural heterogeneity

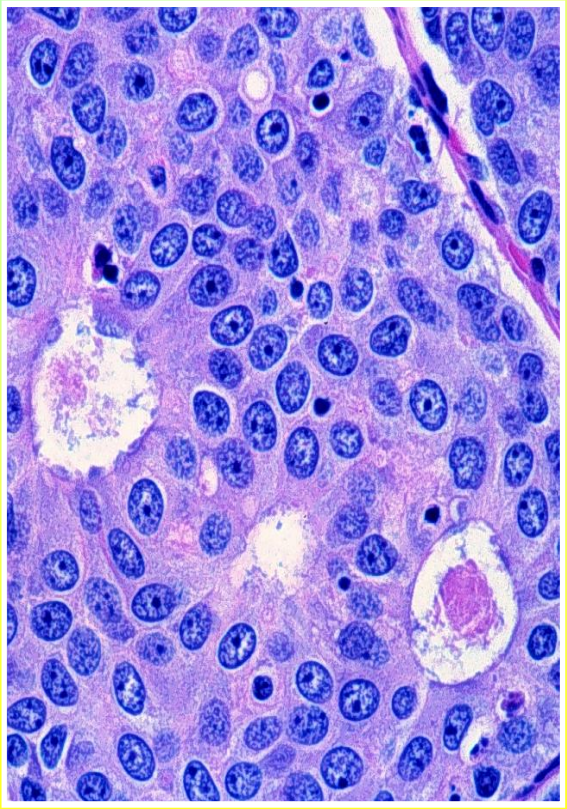
comedo, cribriform, micropapillary, papillary and solid patterns

Because the **nuclear grade** of malignant cells and the presence of necrosis are better predictors of local recurrence and progression to invasion than architectural type, DCIS is classified according to nuclear grade parameter

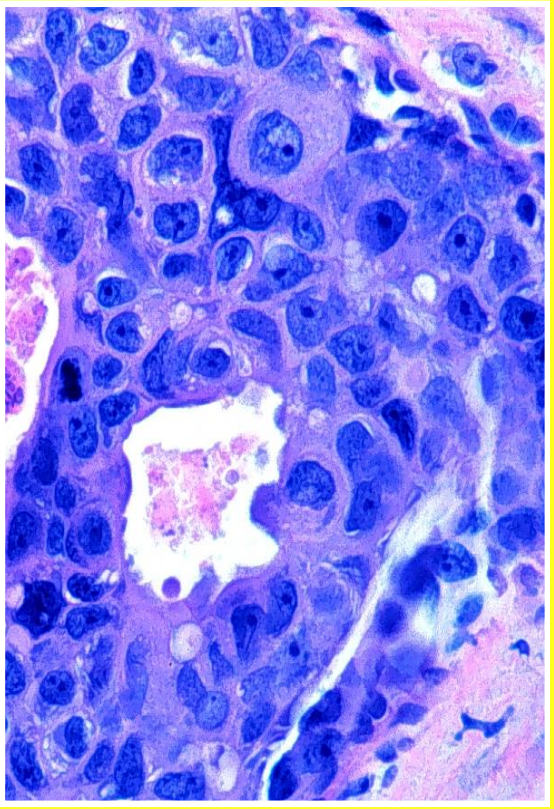
Low



Intermediate

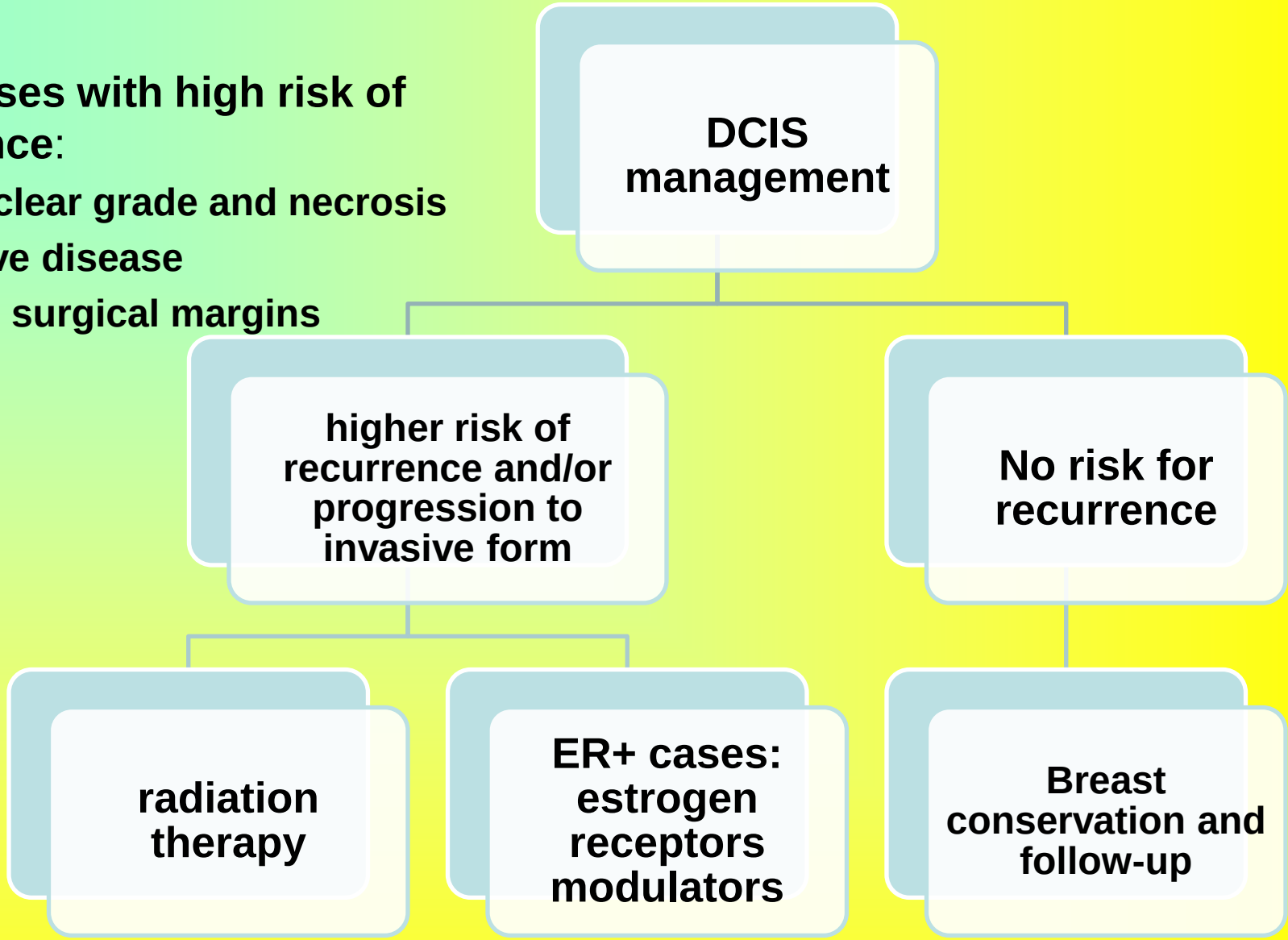


High



DCIS cases with high risk of recurrence:

- high nuclear grade and necrosis
- extensive disease
- positive surgical margins



Lobular carcinoma in situ (LCIS)

- the cells expand but do not distort involved spaces hence the underlying lobular architecture is preserved
- is always an incidental biopsy finding (no suspicious mammogram
  - no calcifications
  - no densities)

- Cancer cells:
  - tend to be smaller and more monotonous than those of the ductal type
  - do not form papillary or cribriform structures
  - almost always express hormone receptors (ER and PR)
  - lack of E-cadherin expression = discohesive fashion of grow within ducts and lobules

- LCIS is a risk factor for invasive carcinoma, in the ipsilateral breast as well as in the contralateral breast
- ! Bilateral disease most cases

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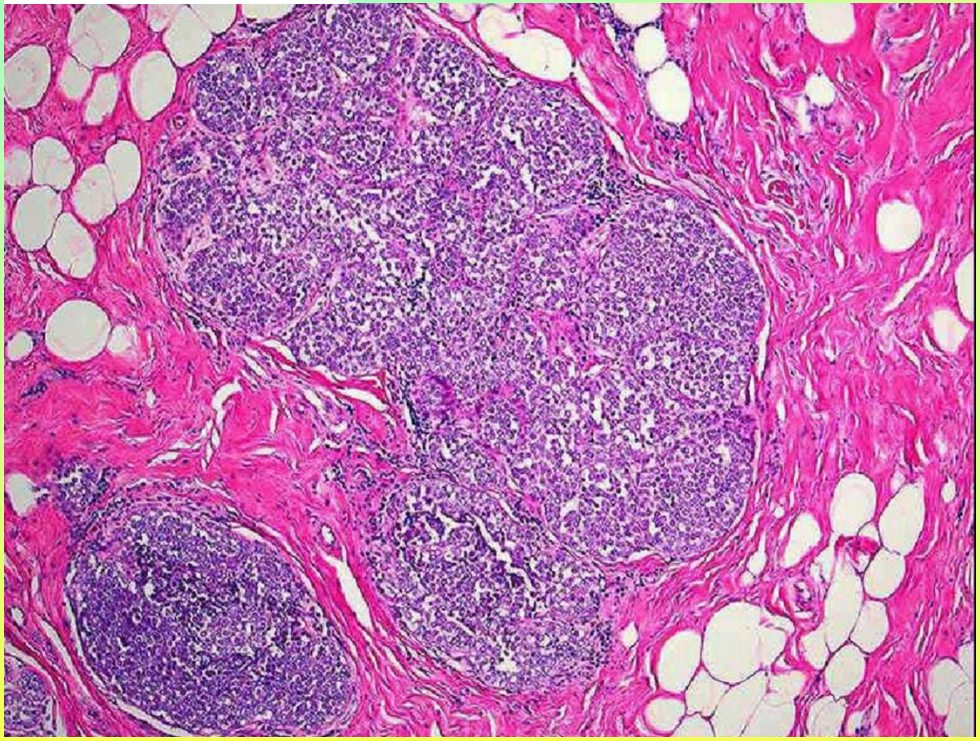
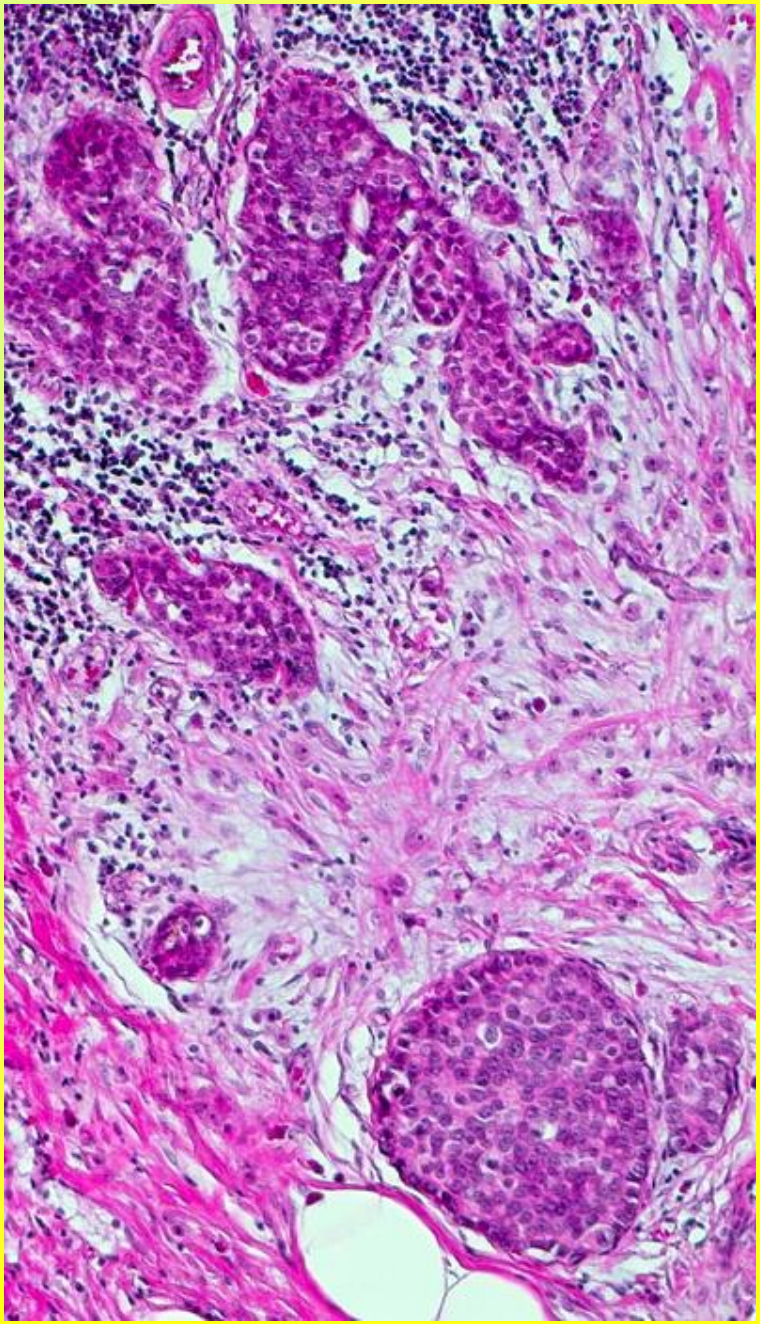
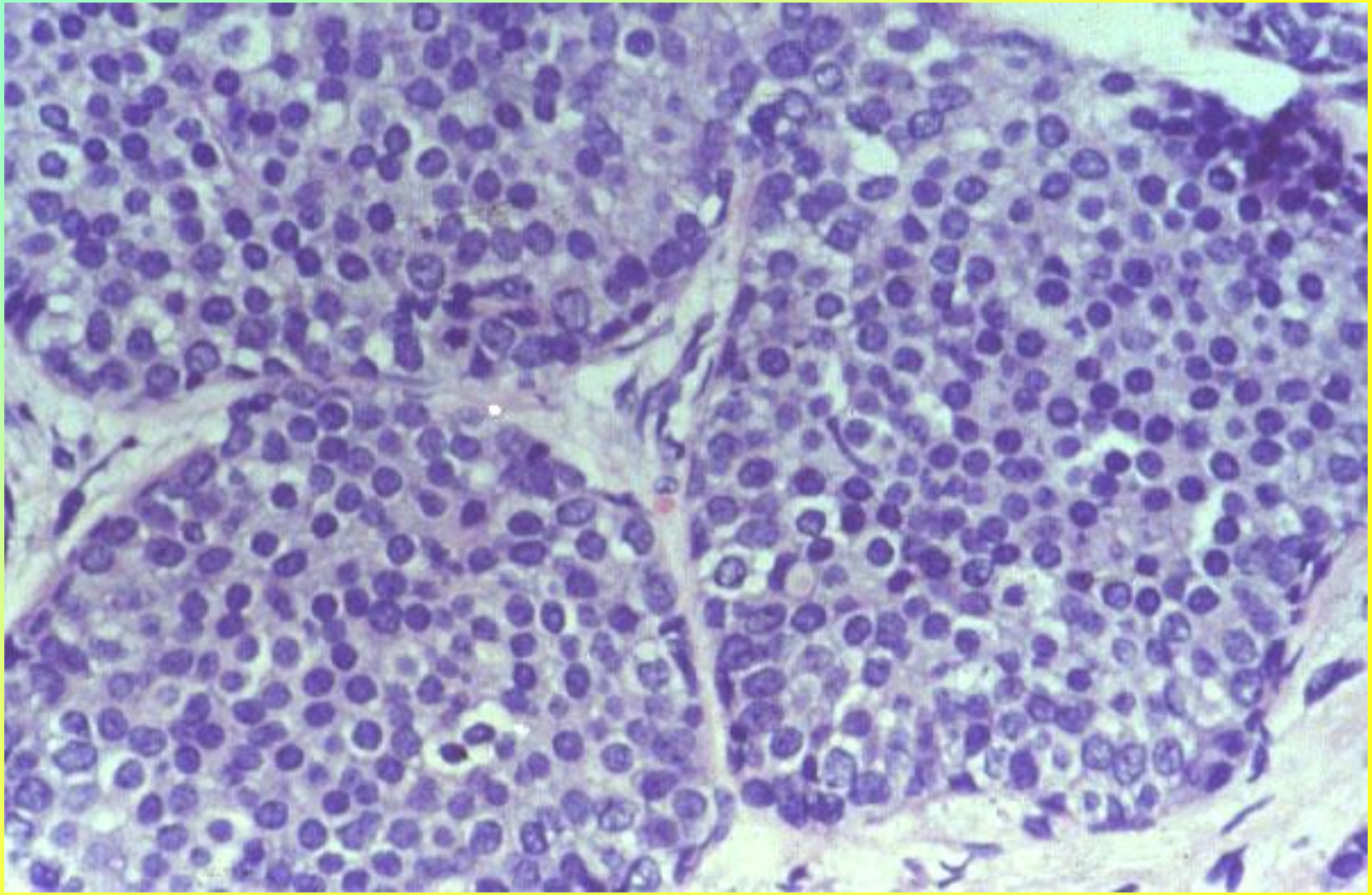
PathoPic
www.unibas.ch/patho



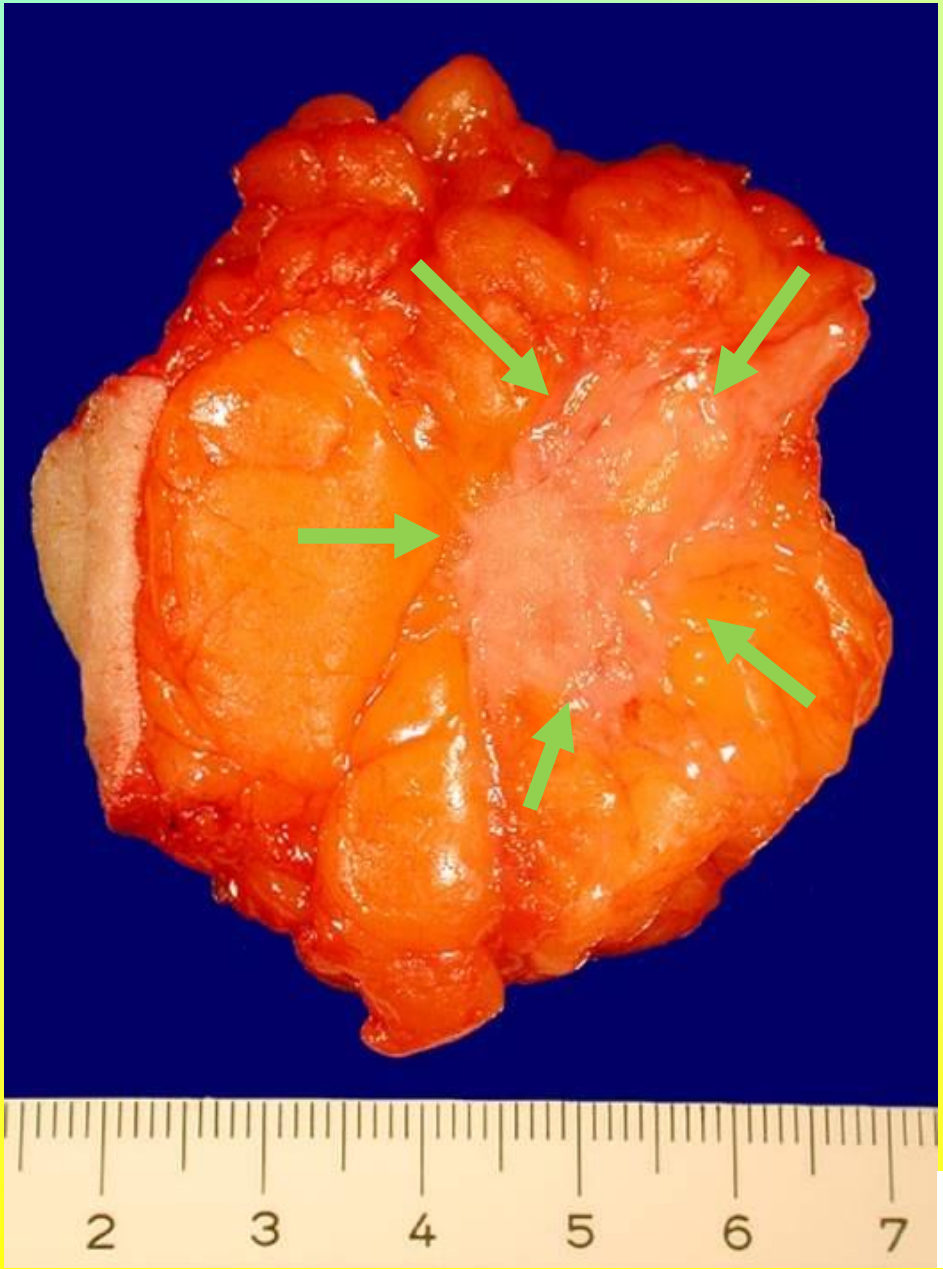


Marked expansion of a lobular unit by **lobular carcinoma in situ (LCIS)**.



Lobular carcinoma in situ: showing fairly monotonous small round, discohesive cells filling the ducts.

Breast invasive (infiltrating) carcinoma



In the absence of mammographic screening (for early detection), most breast invasive carcinoma presents as a mass of at least 2 to 3 cm in size, hard, irregular whitish lesion associated with a desmoplastic stromal reaction; when cut or scraped, such tumors typically produce a characteristic grating sound.

Invasive breast carcinoma (microscopically):

- 2/3 of cases **ductal no special type** NST

- 1/3 of cases special type:

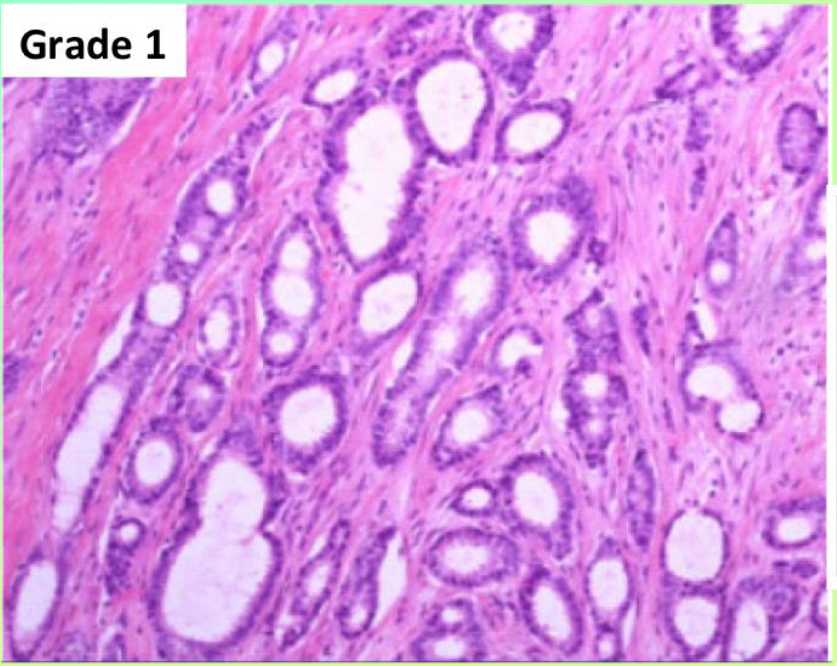
  - ✓ **Invasive lobular carcinoma**
  - ✓ **Tubular carcinoma**
  - ✓ **Mucinous / colloid carcinoma**
  - ✓ Classic **medullary carcinomas**
  - ✓ **Micropapillary carcinoma**
  - ✓ **Papillary carcinoma**
  - ✓ **Apocrine carcinoma**
  - ✓ **Metaplastic carcinomas**

Nottingham histologic score (also called the modified Bloom and Richardson method) imparts points accordingly to:

tubule formation	1 to 3 points
nuclear pleomorphism	1 to 3 points
mitotic rate	1 to 3 points

The added points (for each category) divide carcinomas into grade I (well differentiated / G1), grade II (moderately differentiated / G2), and grade III (poorly differentiated / G3) types.

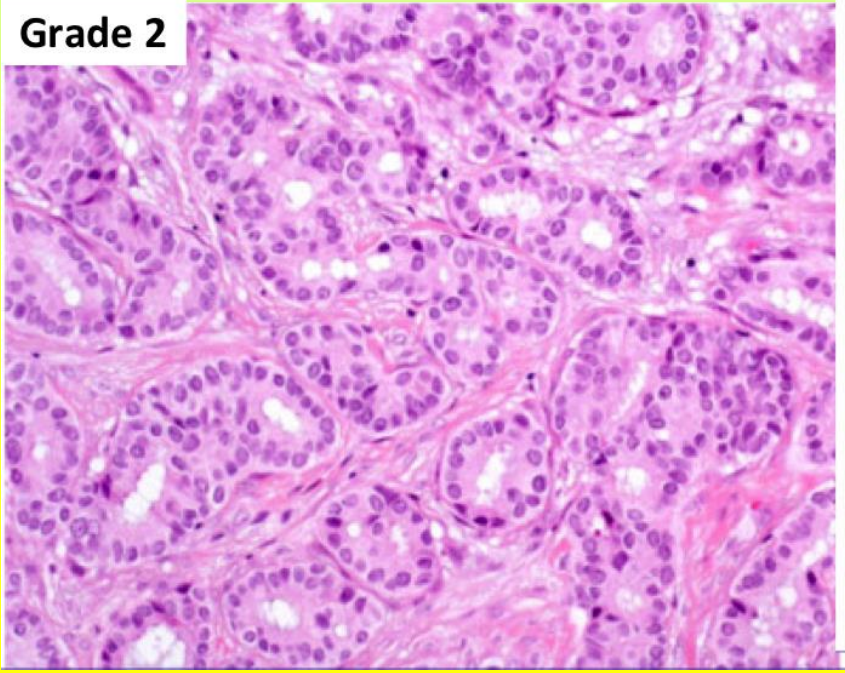
Grade 1



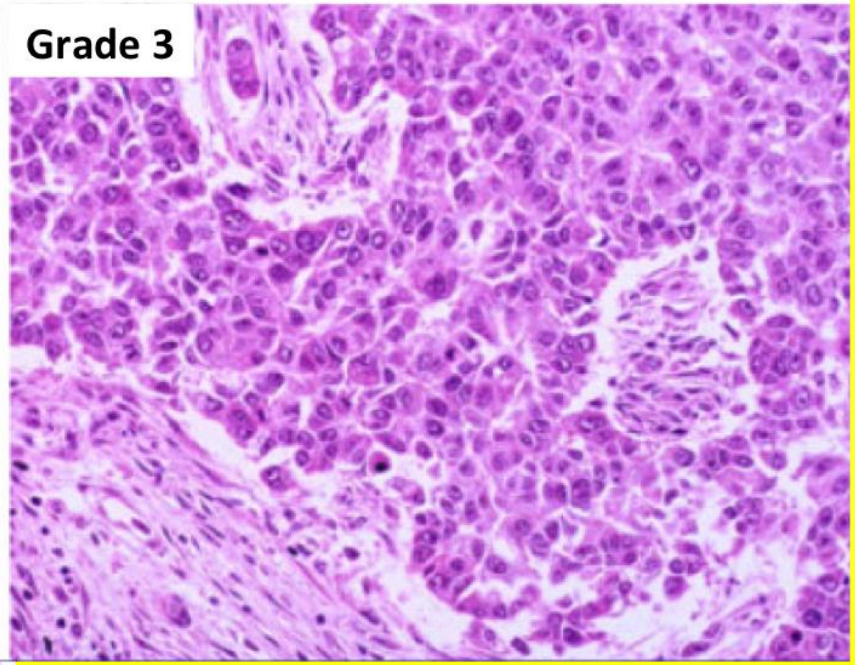
Nottingham Breast Cancer Grade

Total Feature Score	Tumor Grade	Appearance of Cells
3-5	Grade 1 Tumor	Well-differentiated (appear normal, growing slowly, not aggressive)
6-7	Grade 2 Tumor	Moderately-differentiated (semi-normal, growing moderately fast)
8-9	Grade 3 Tumor	Poorly-differentiated (abnormal, growing quickly, aggressive)

Grade 2



Grade 3



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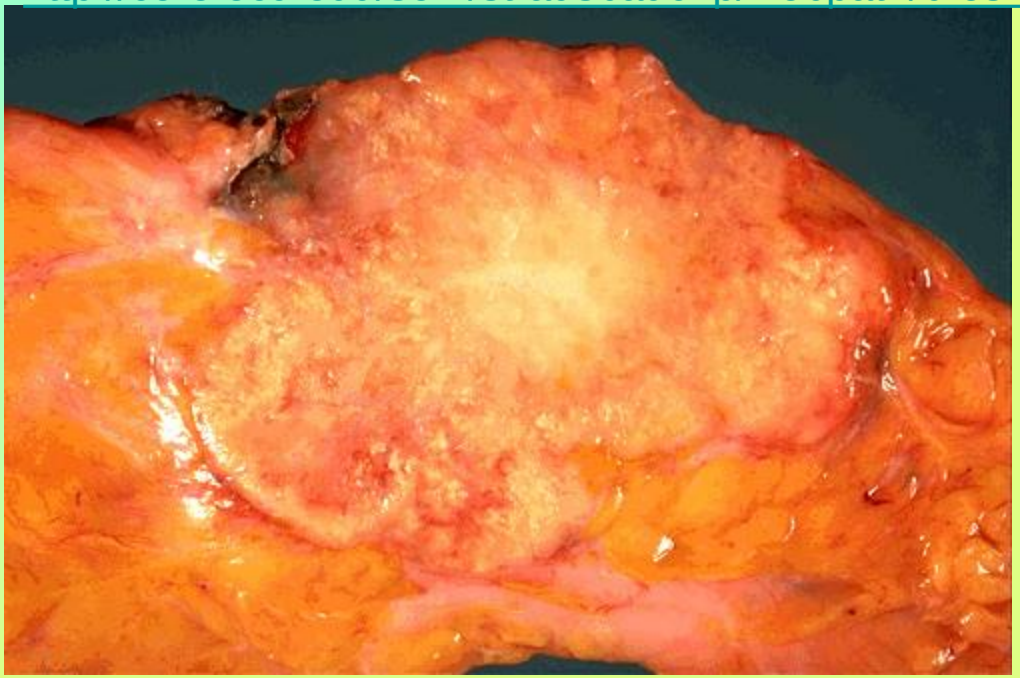
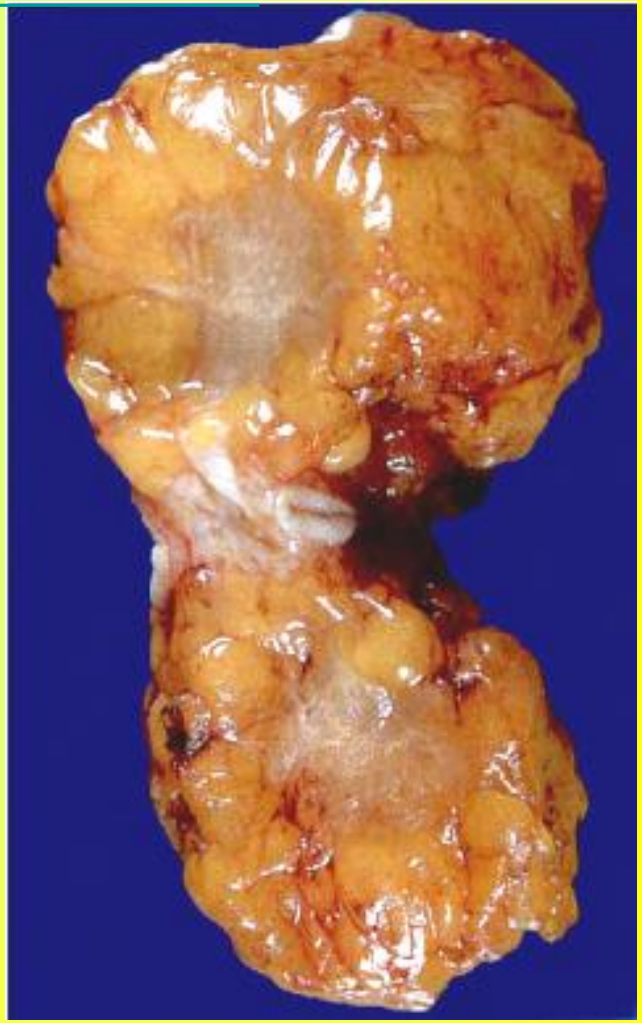
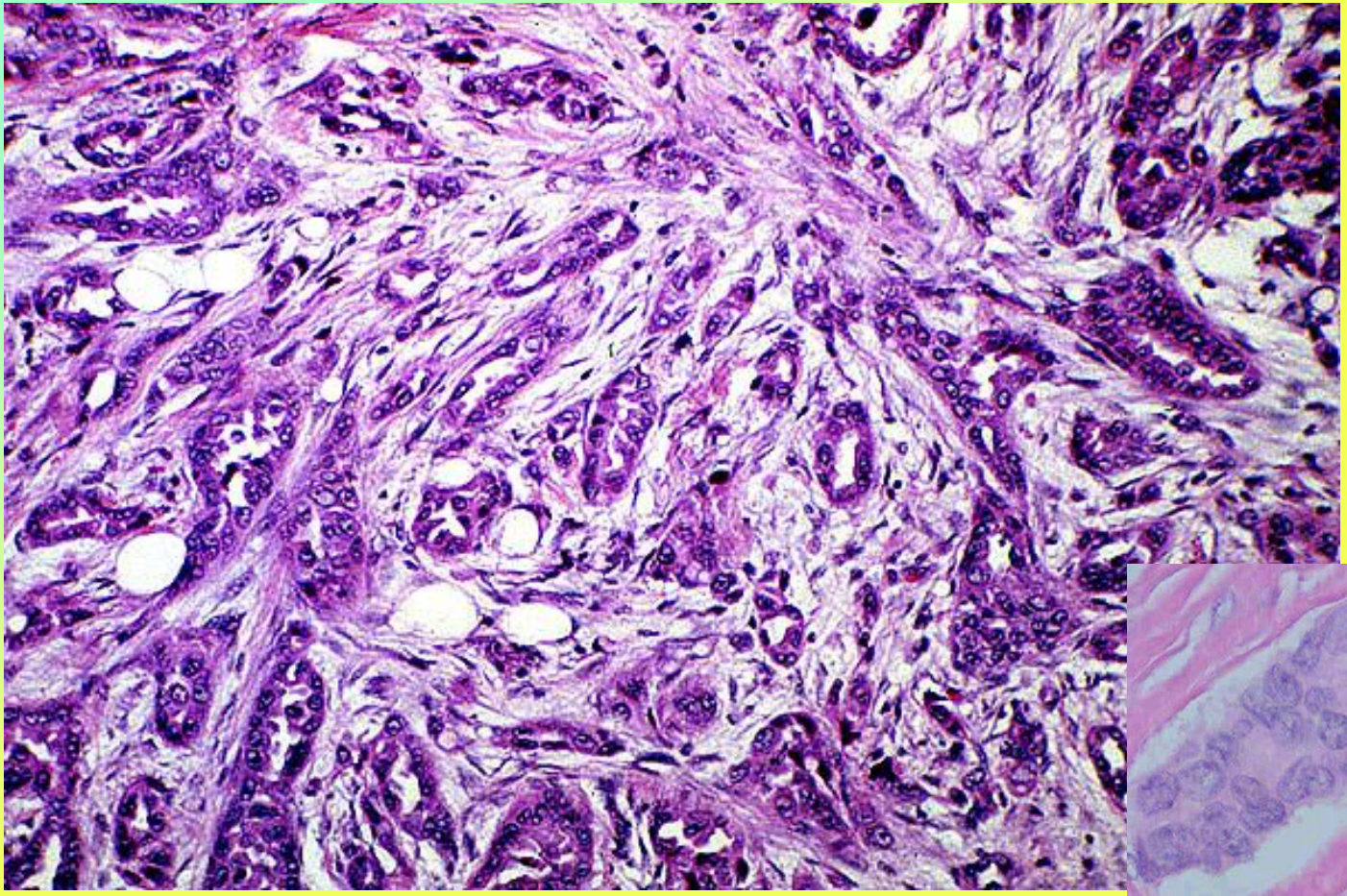


Infiltrating ductal carcinoma of breast: the center is very firm (scirrhous) and white because of the desmoplasia. There are areas of yellowish necrosis in the portions of neoplasm infiltrating into the surrounding tissue.

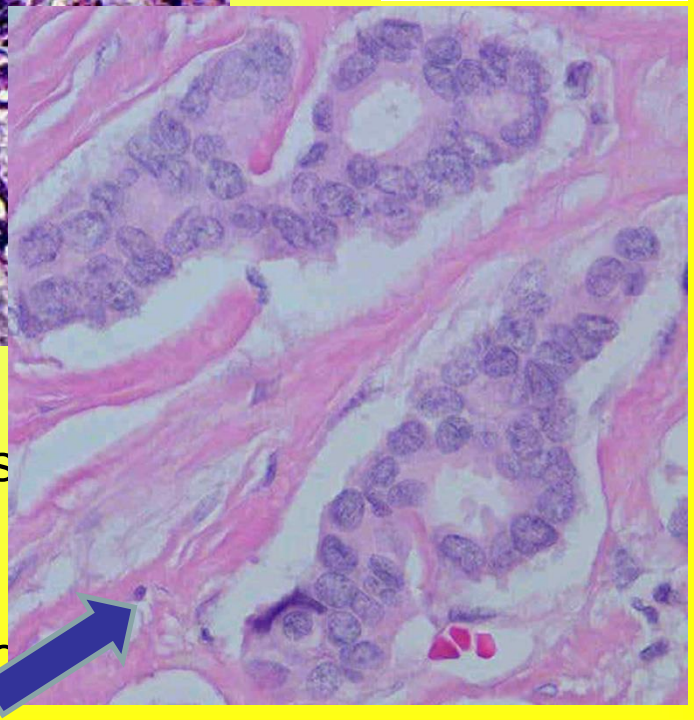


The most common form of **breast invasive carcinoma: ductal / no special type (NST),** gross

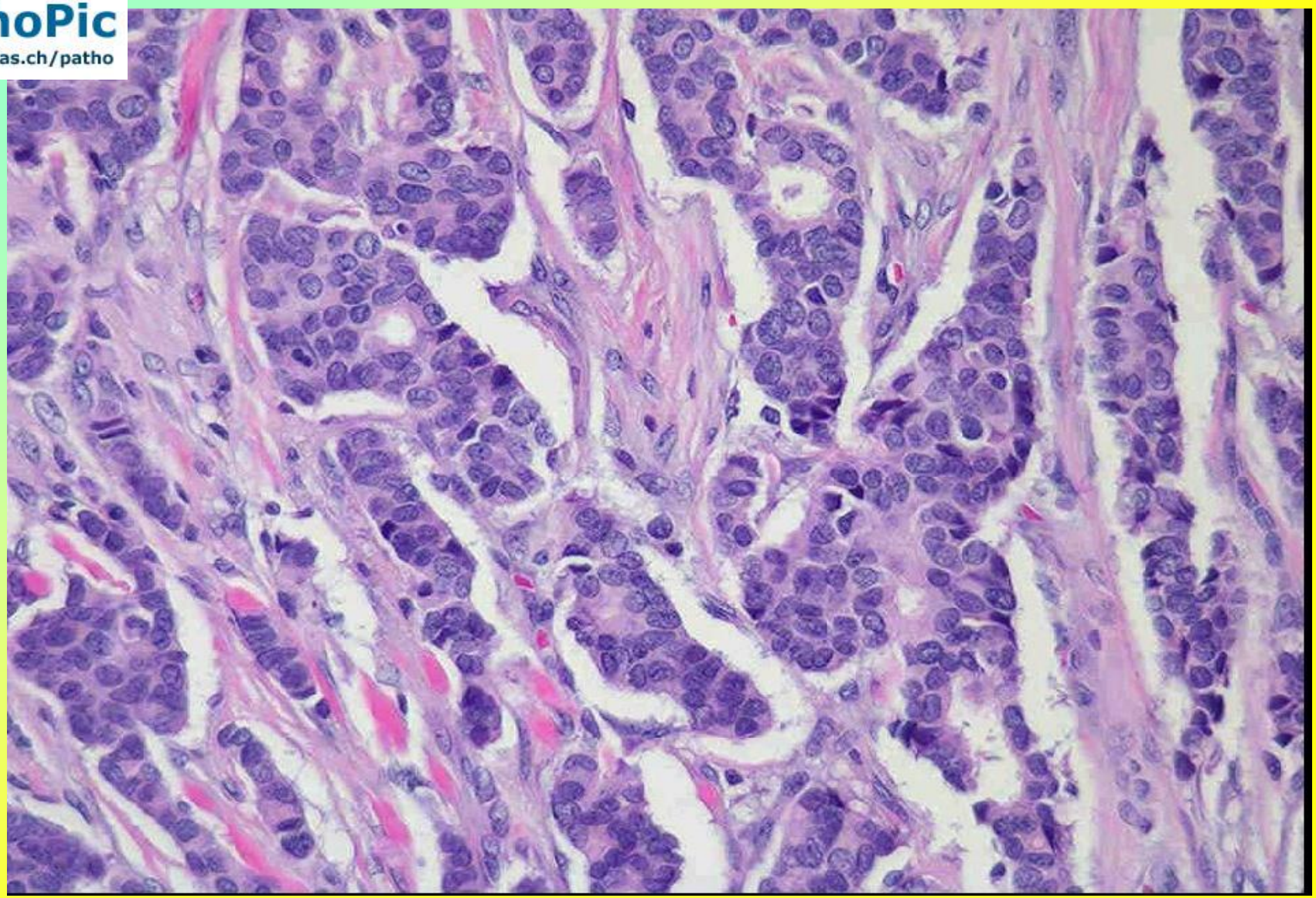
Carcinoma of the breast. A breast lump removed for **frozen section**. When cut across, it was hard and gritty and the cut surface bulged inwards.



PathoPic
www.unibas.ch/patho



Infiltrating ductal carcinoma well-differentiated (G1) of **no special type** of the breast: tumor cells form trabeculae, sheets, nests and glands. Nuclear pleomorphism and mitotic counts vary; also the tumor stroma from loose to desmoplastic



Moderately-differentiated (G2) **invasive carcinoma** of **no special type**: tubules and nests of cells with small monomorphic nuclei invade into the stroma with a desmoplastic response

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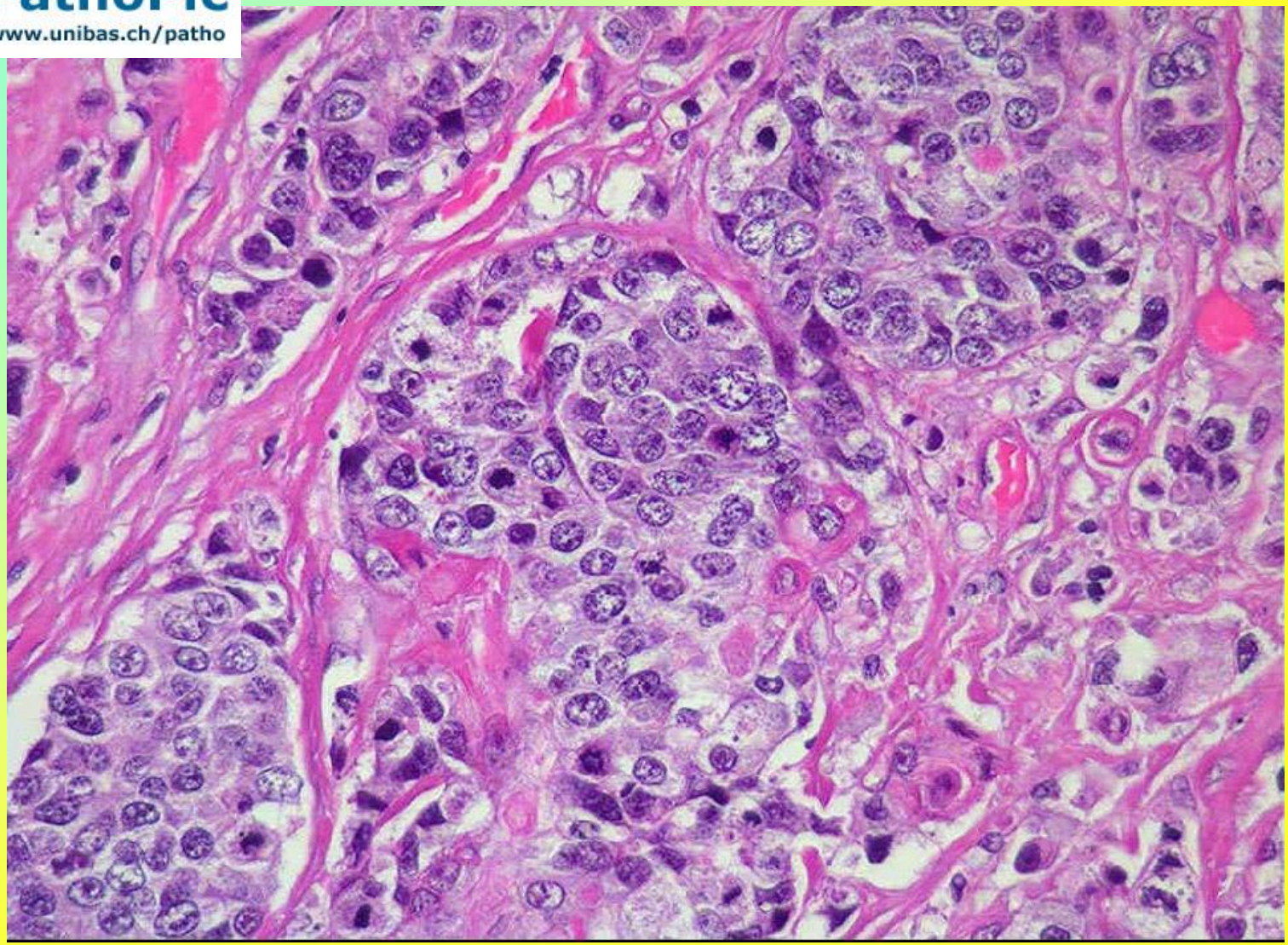
www.unibas.ch/patho



Poorly-differentiated (G3) **invasive carcinoma** of **no special type**: irregular nests of cells with large pleomorphic nuclei and brisk mitotic activity invade into the stroma with a desmoplastic response.

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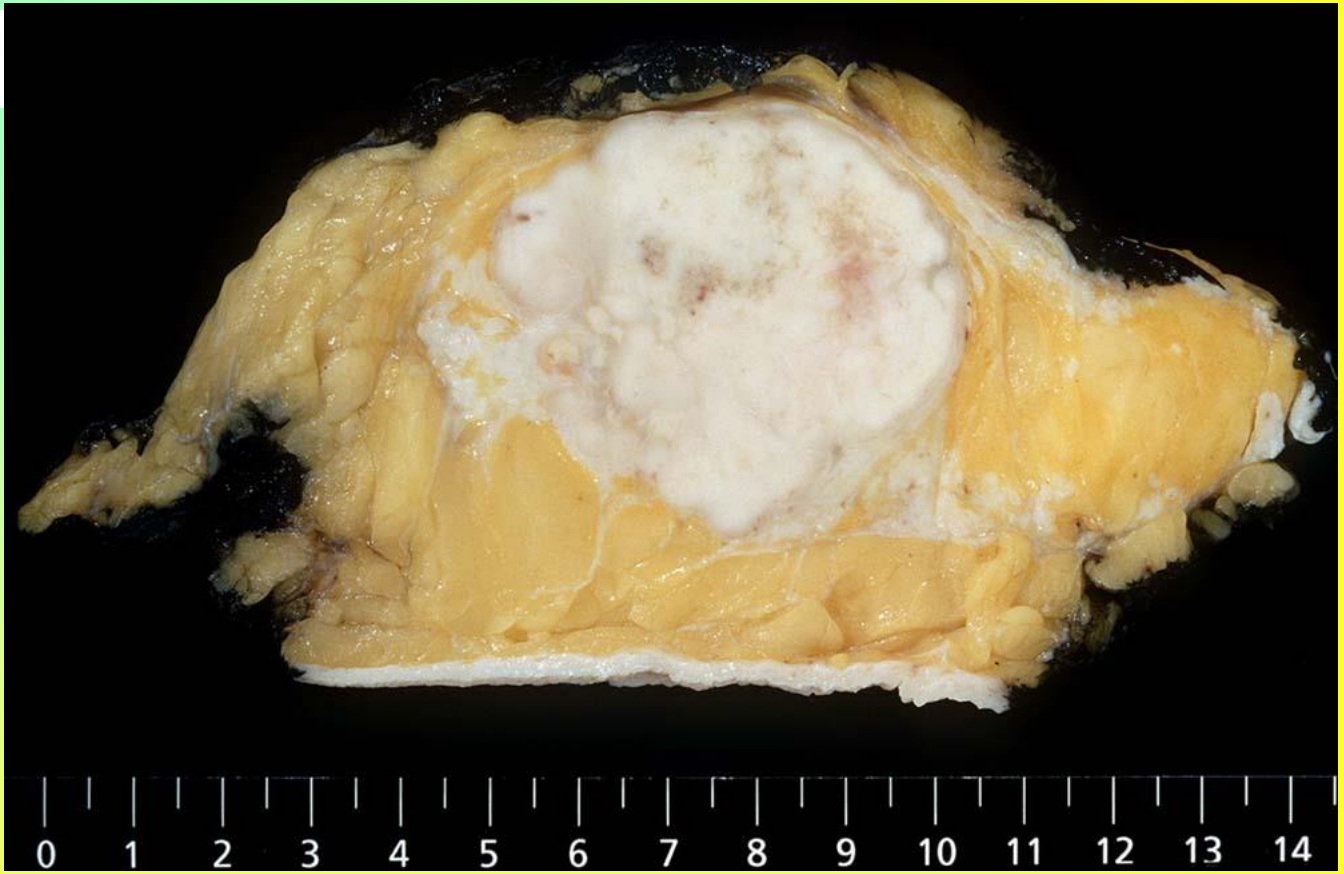
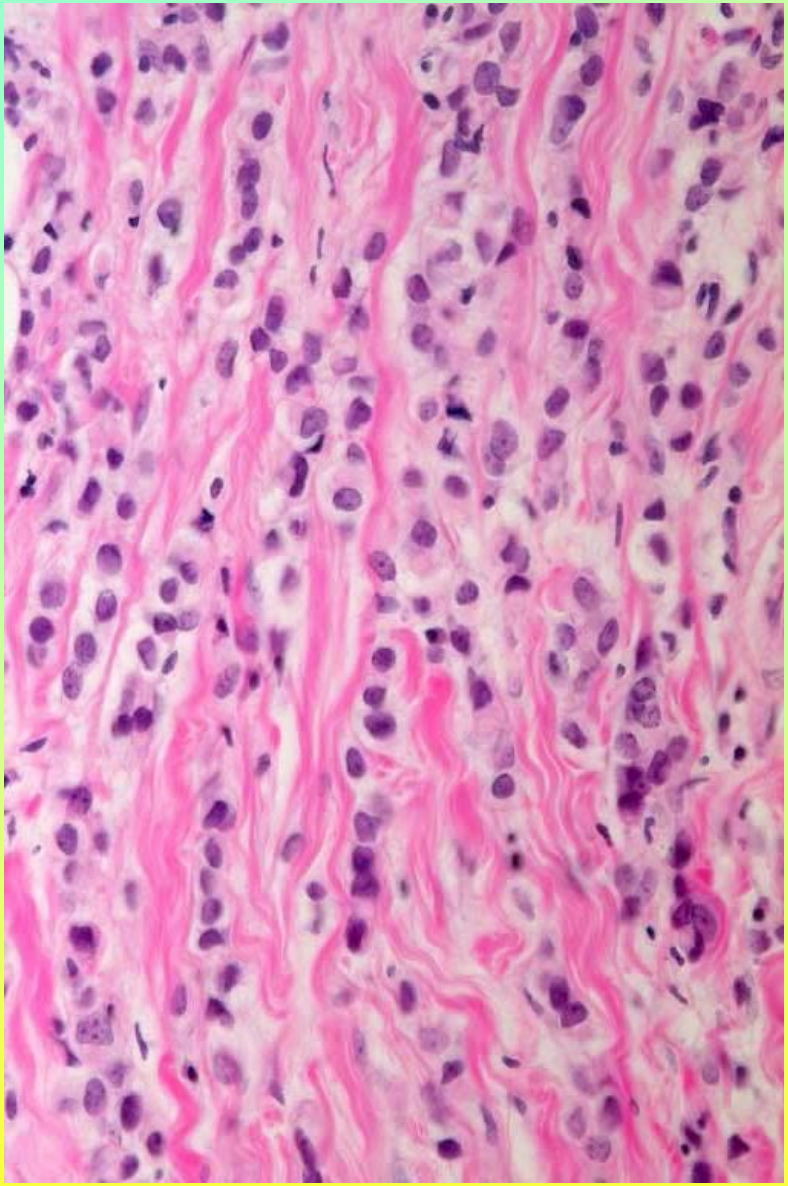
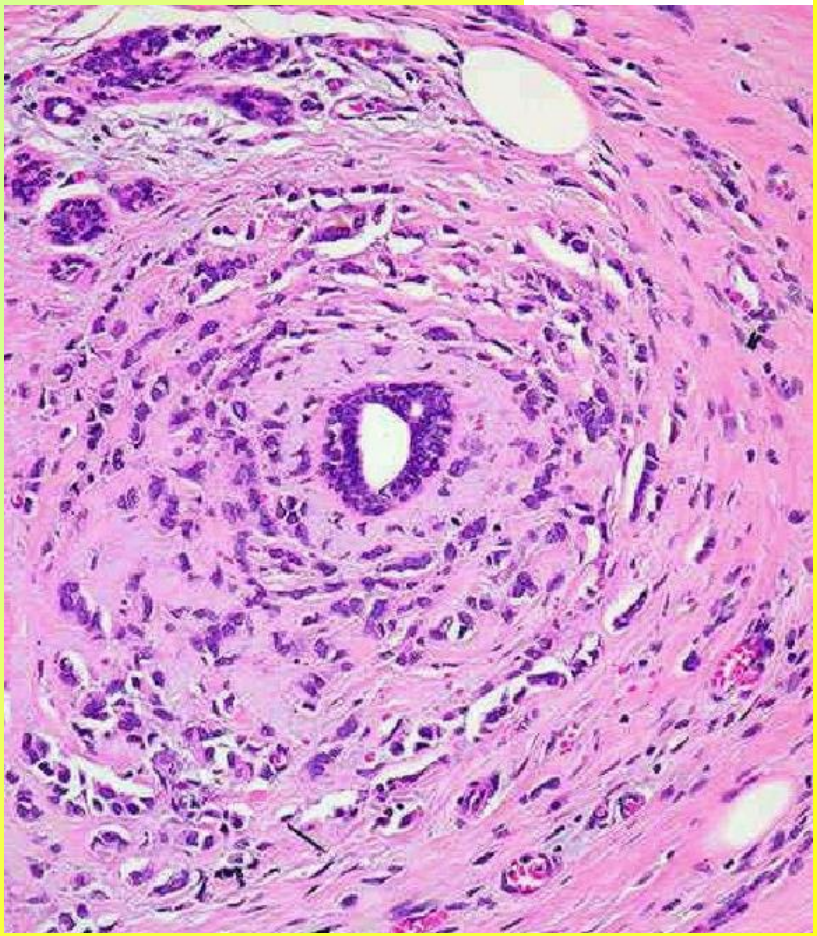
PathoPic
www.unibas.ch/patho

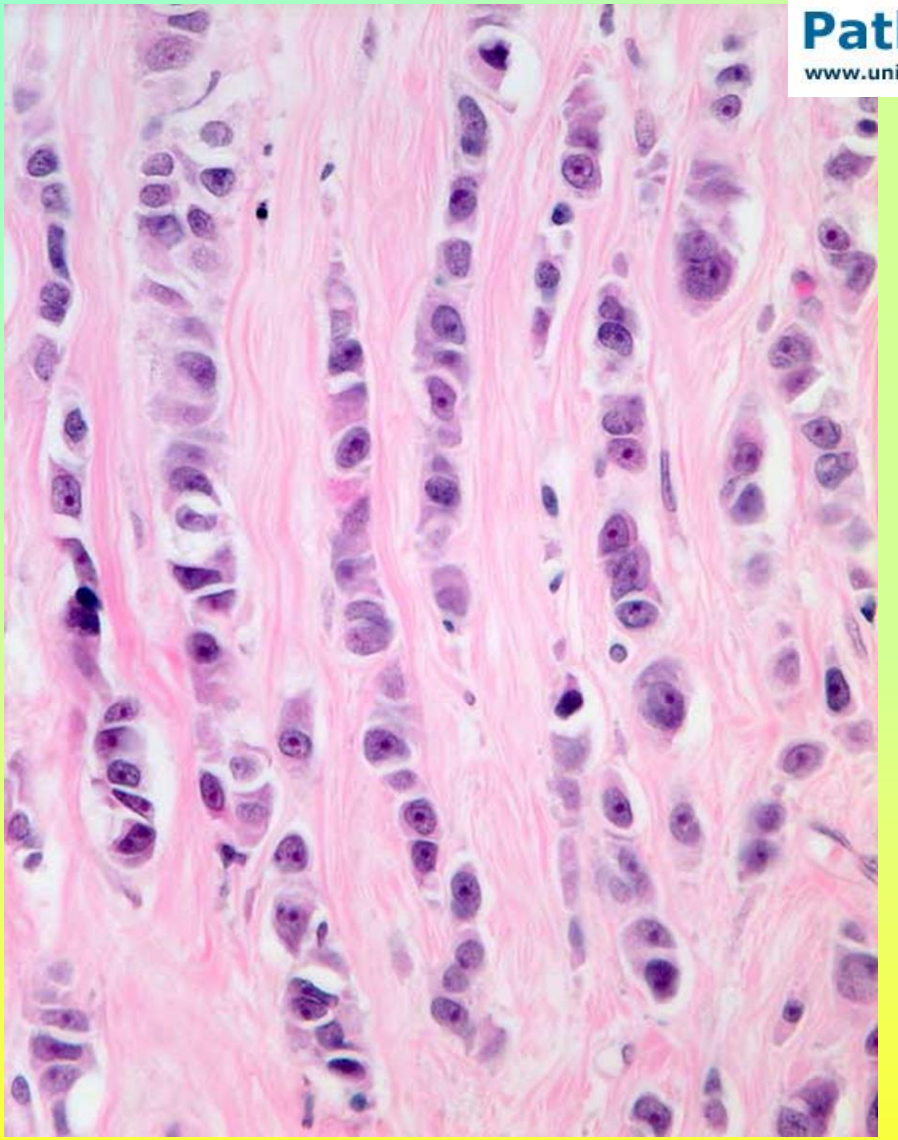


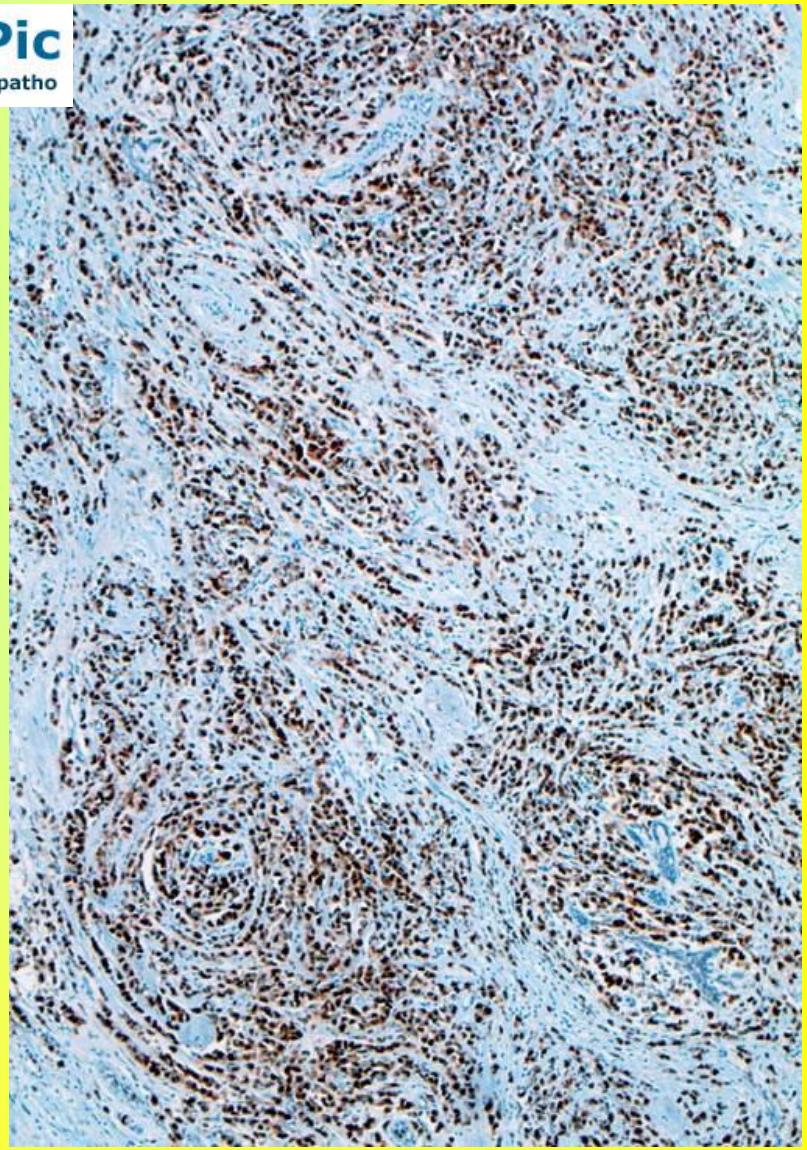
Invasive lobular carcinoma the second most common form of invasive breast cancer, patients often have clinically silent disease grossly until such size (~6 cm).





Invasive lobular carcinoma discohesive malignant epithelial cells infiltrate the stroma diffusely. They often line up in a row „Indian filling” (right) and may show a periductal “targetoid” arrangement (left).





Invasive lobular carcinoma the discohesive malignant epithelial cells that infiltrate the stroma are lined up in „Indian files” (right) and are positive for estrogen receptors ER ~ 100% (left).

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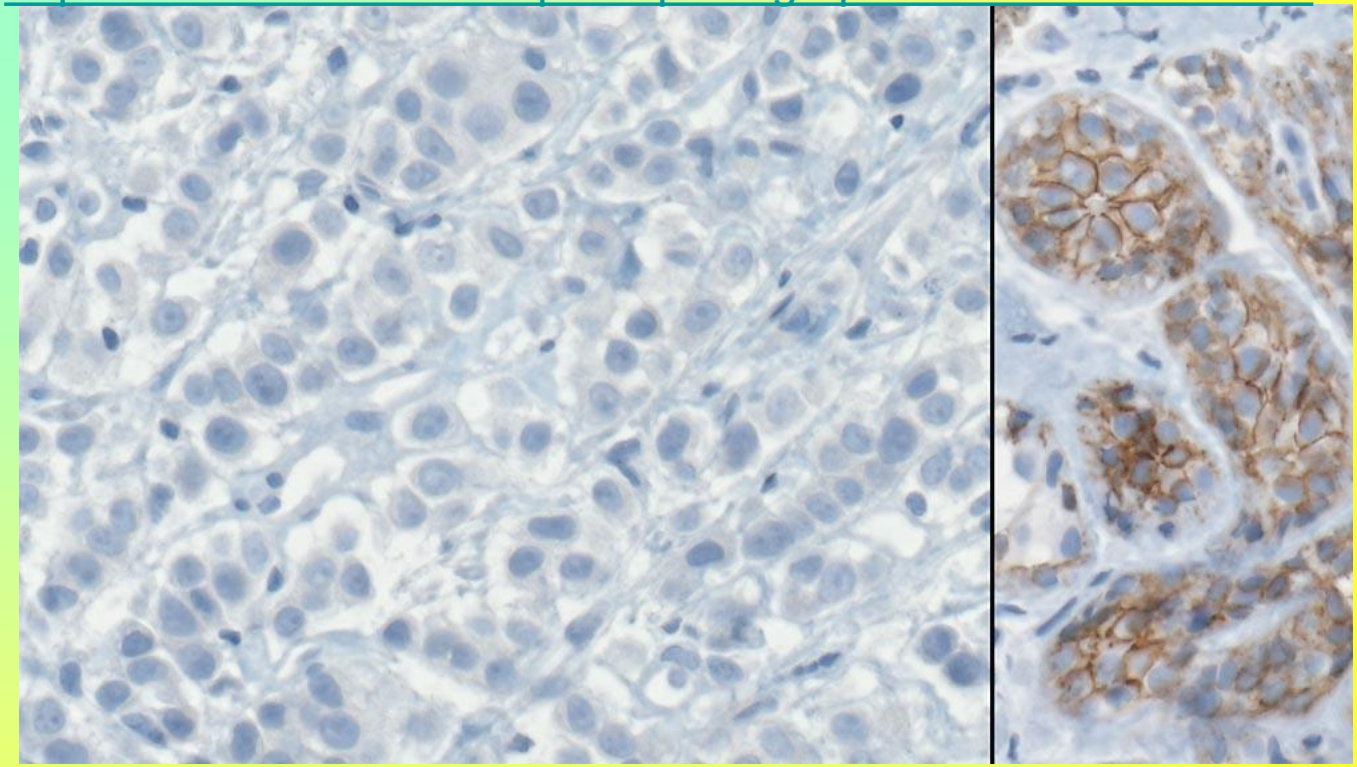


Invasive lobular carcinoma: *E-cadherin negative* in malignant cells (on the left); on the right, internal positive control of a normal breast lobule on the same section with membranous E-cadherin positivity.

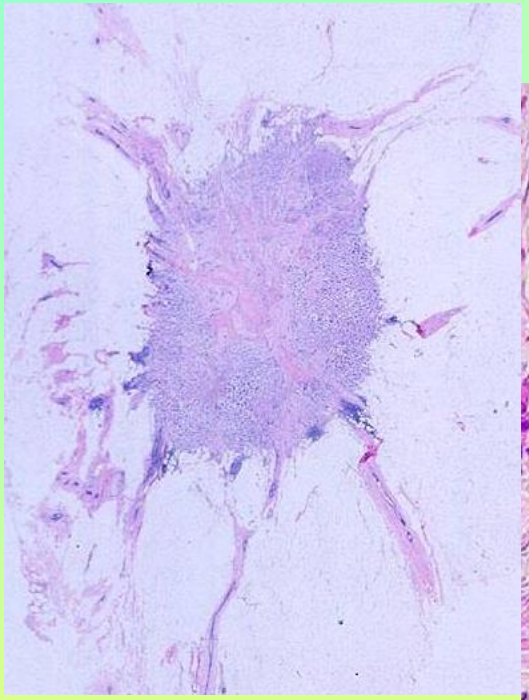
Invasive breast carcinoma (microscopically):

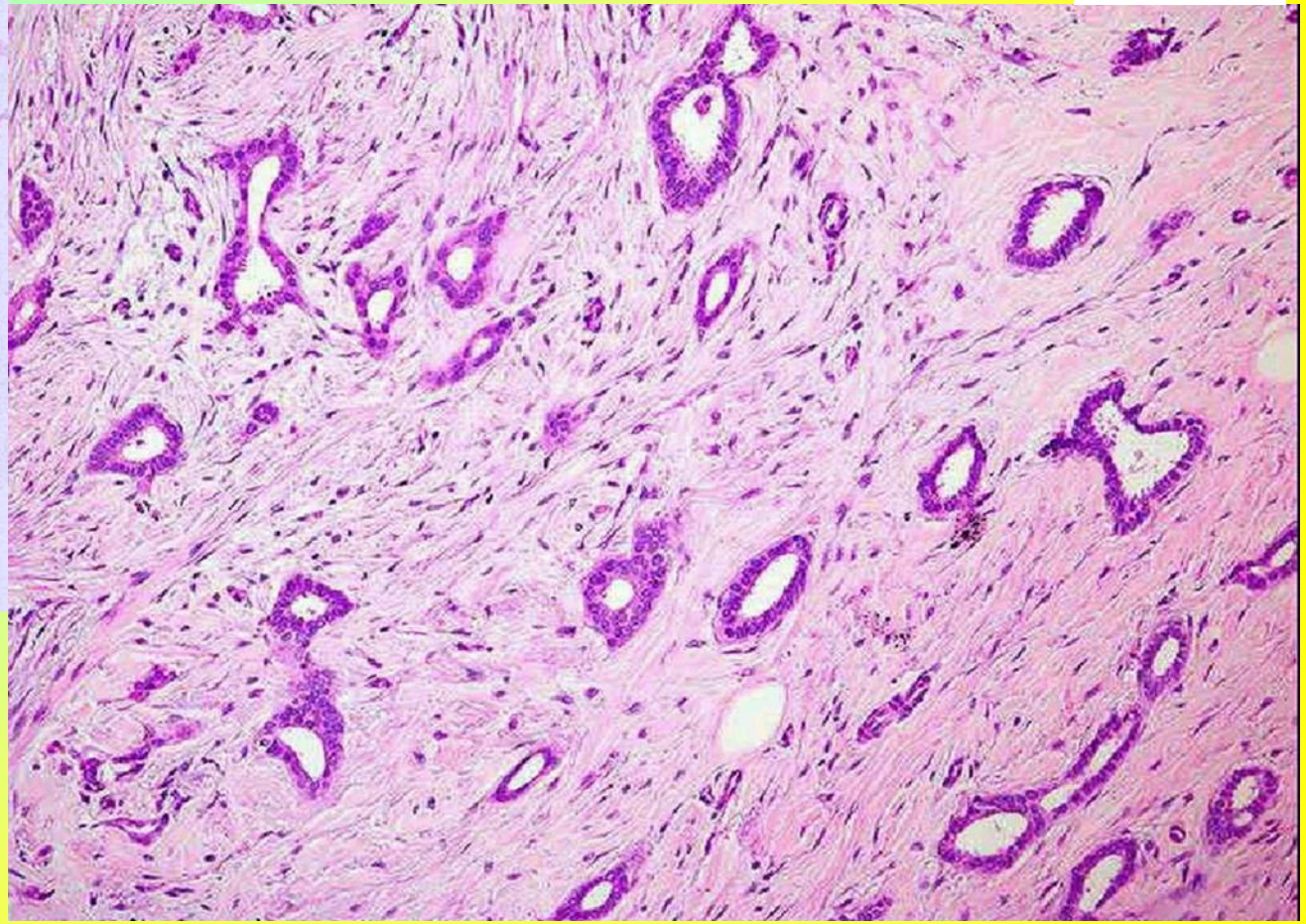
- 2/3 of cases **ductal no special type** NST

- 1/3 of cases special type:
  - ✓ **Invasive lobular carcinoma**

- **Tubular carcinoma**
- **Mucinous / colloid carcinoma**
- Classic **medullary carcinomas**
- **Micropapillary carcinoma**
- **Papillary carcinoma**
- **Apocrine carcinoma**
- **Metaplastic carcinomas**

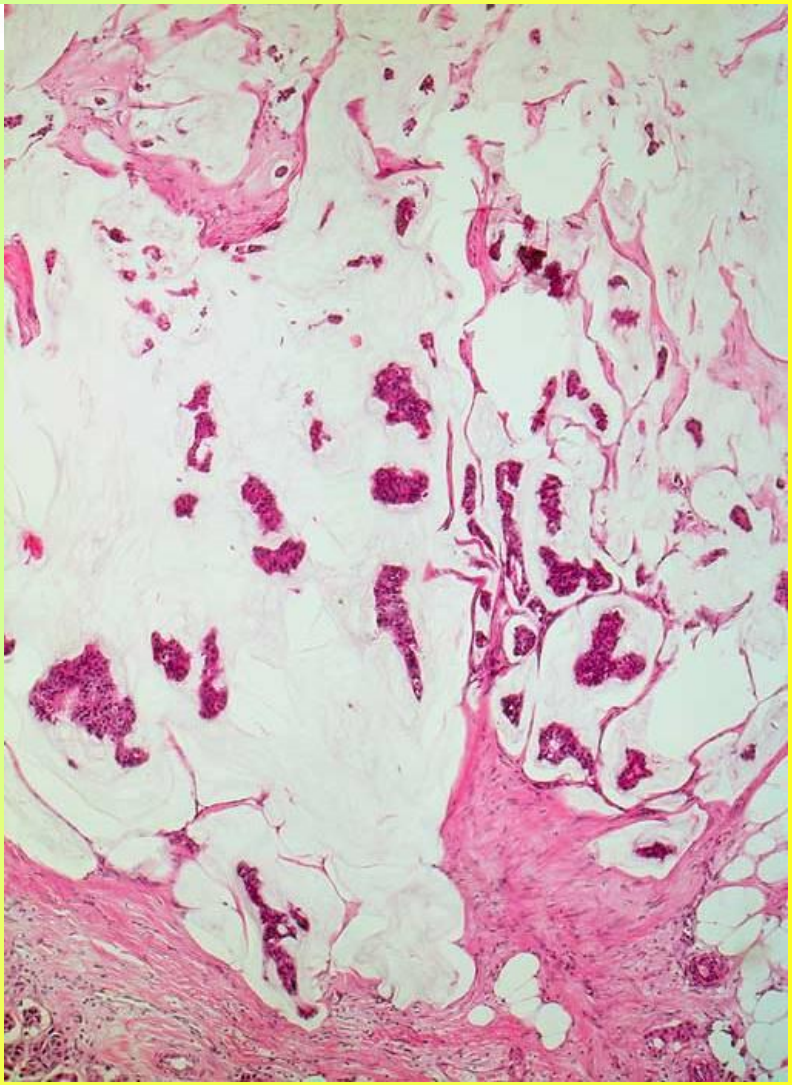
} **less common encountered in practice**



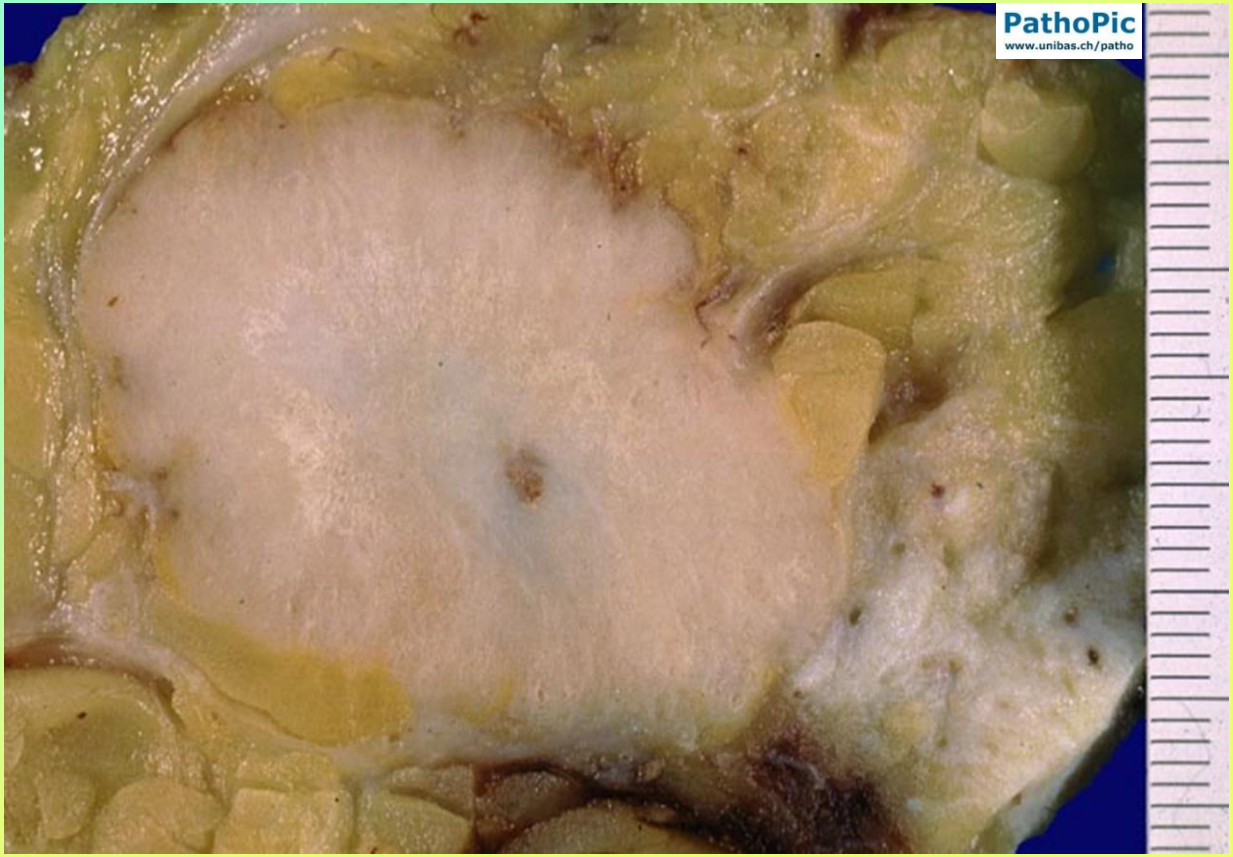


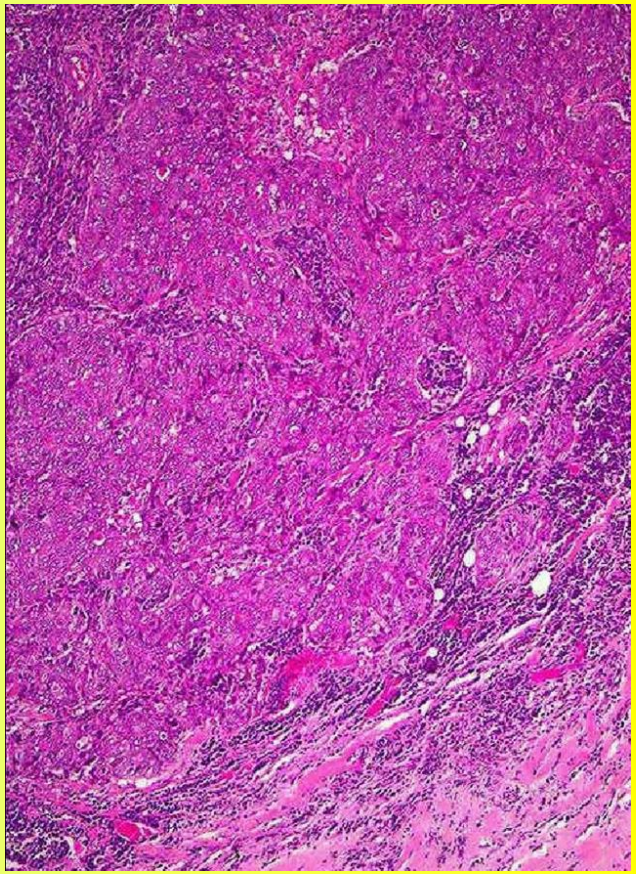
Tubular carcinoma is a well-defined stellate mass whose cellular composition is almost entirely round-open and angulated tubules, lined by a single layer of mildly atypical epithelial cells. Being a *well-differentiated carcinoma (G1)*, the *prognosis is excellent*, and it is virtually always cured by mastectomy.

Typical gelatinous gross appearance of **pure mucinous / colloid carcinoma**. On cut section, colloid carcinoma has a glistening surface and mucoid consistency.



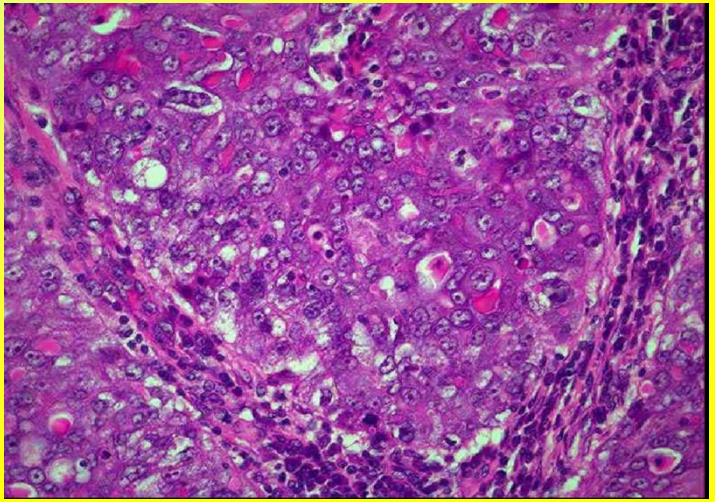
Low-grade malignant epithelial cells form acini, nests or trabeculae, which appear to float in pools of extracellular mucin.



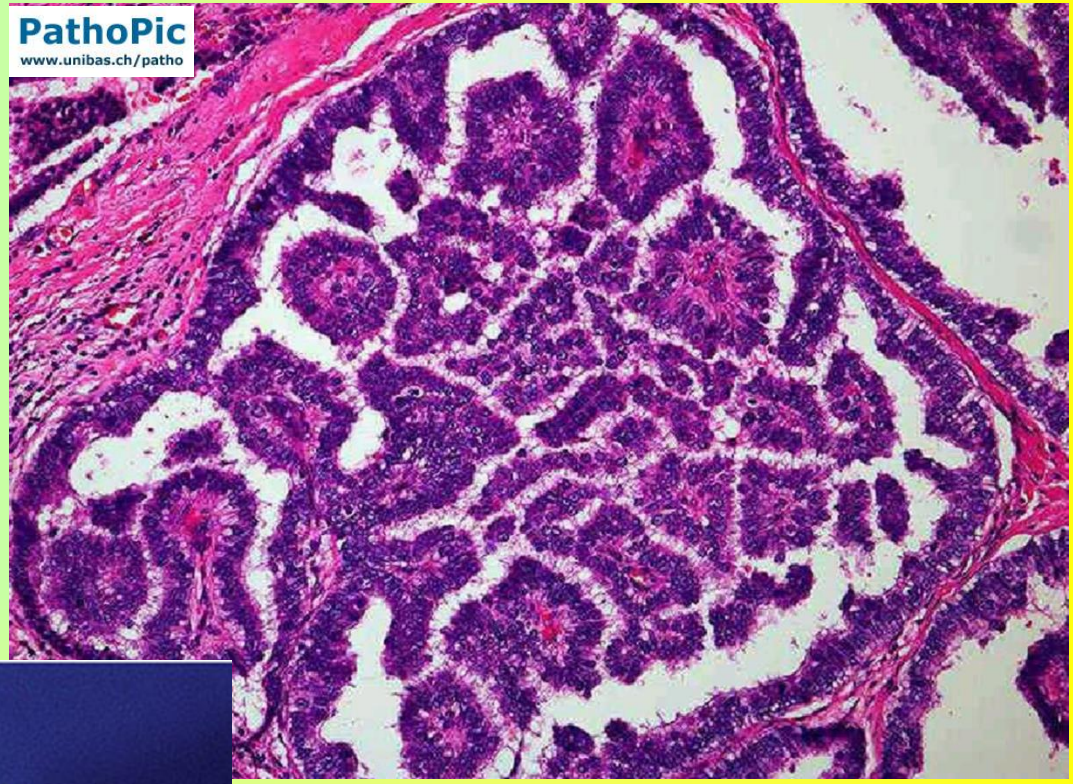


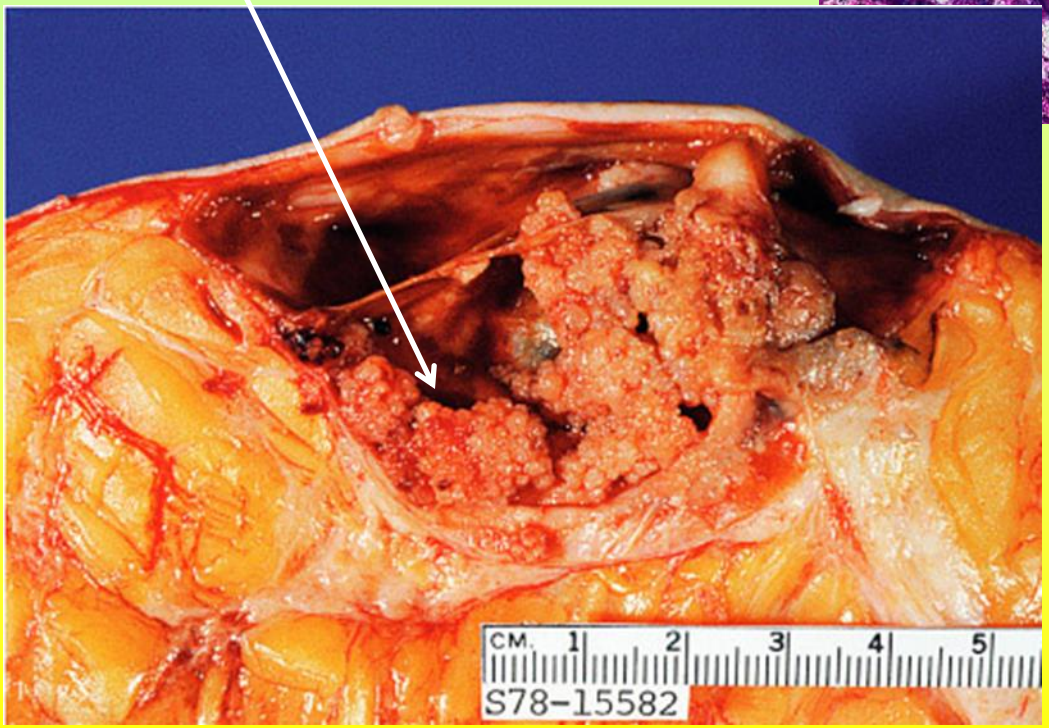
Medullary carcinoma is well circumscribed and soft, with pushing margins, gross.

Microscopy: high nuclear grade; syncytial growth pattern in more than 75% of the tumor; a moderate or marked lympho-plasmacytic infiltrate; and no tubule formation.

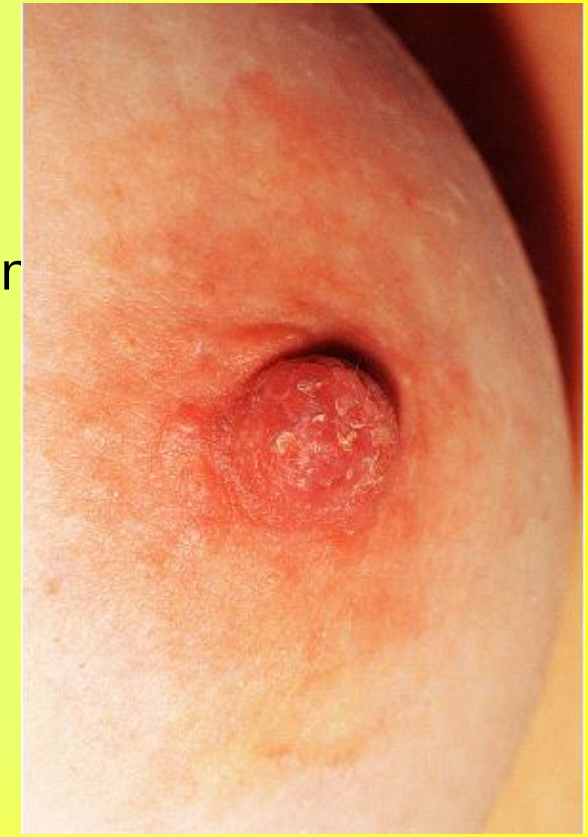


Papillary intracystic carcinoma of the breast. The papillary configuration of the tumor is already grossly evident.





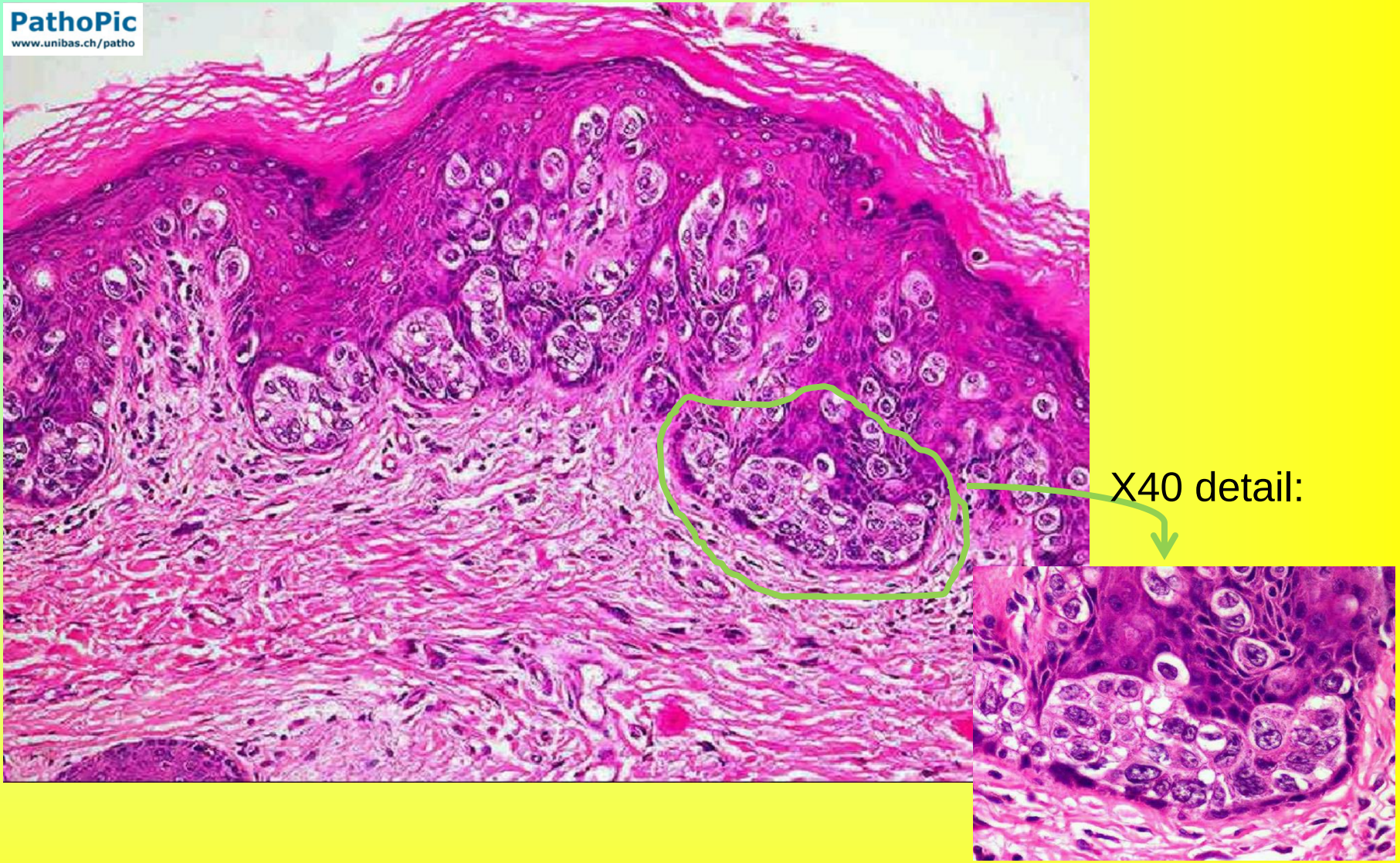
Paget disease of the nipple is a rare manifestation of breast cancer (1% to 4% of cases) that presents as a unilateral erythematous eruption with a scale crust.



Malignant cells (**Paget cells**) from DCIS / invasive carcinoma arising within the ductal system of the breast extend up the lactiferous ducts into nipple skin without crossing the basement membrane (an intraepithelial pattern of spreading). The malignant cells disrupt the normally tight squamous epithelial cell barrier, allowing extracellular fluid to seep out and form an oozing scaly crust over the nipple skin.

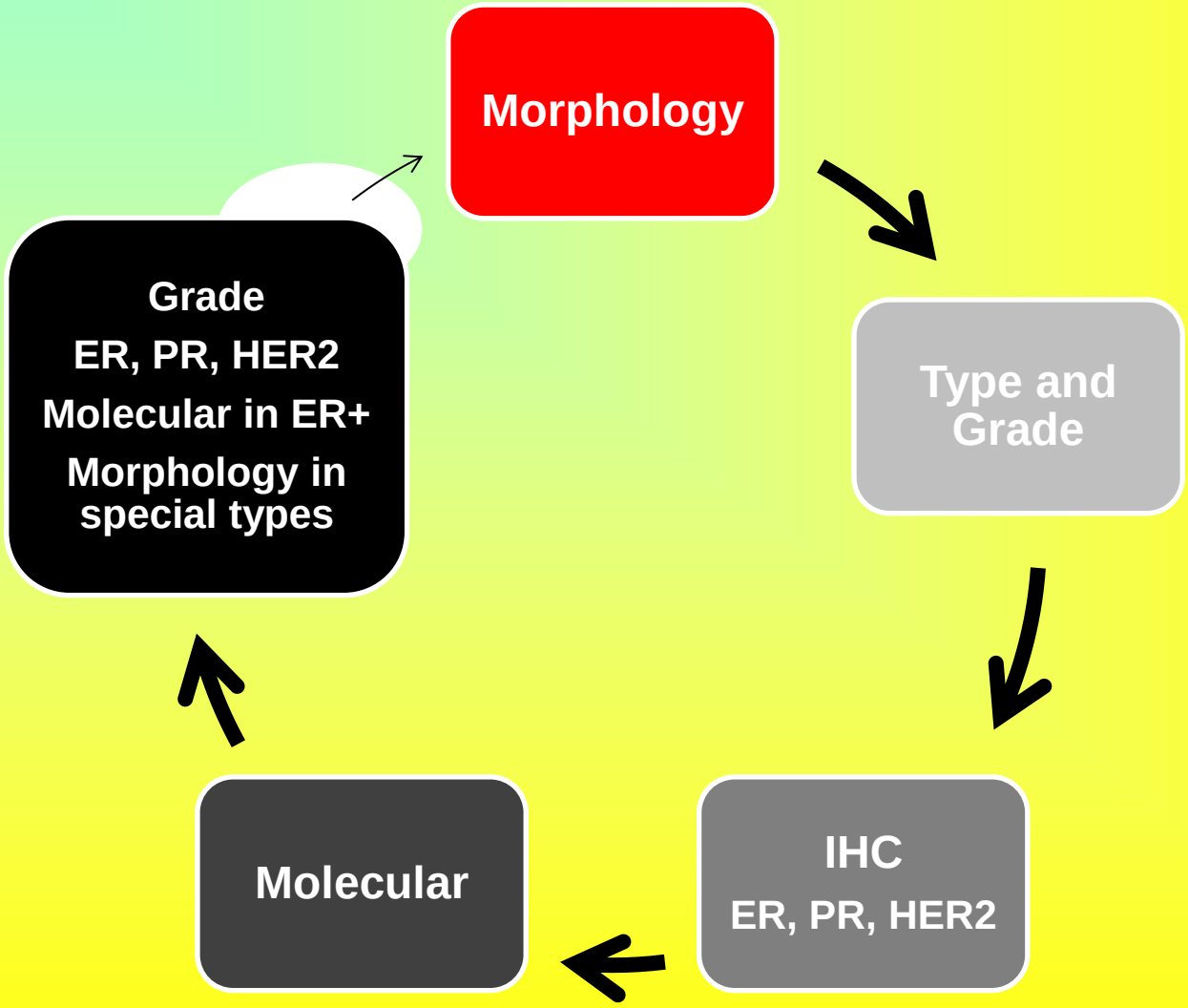
- A **palpable mass** is present in 50% to 60% of women with Paget disease, and almost all of these women have an underlying **invasive carcinoma**, usually **poorly differentiated**.
- The remainder group of women **without a palpable mass** have “only” **DCIS.**

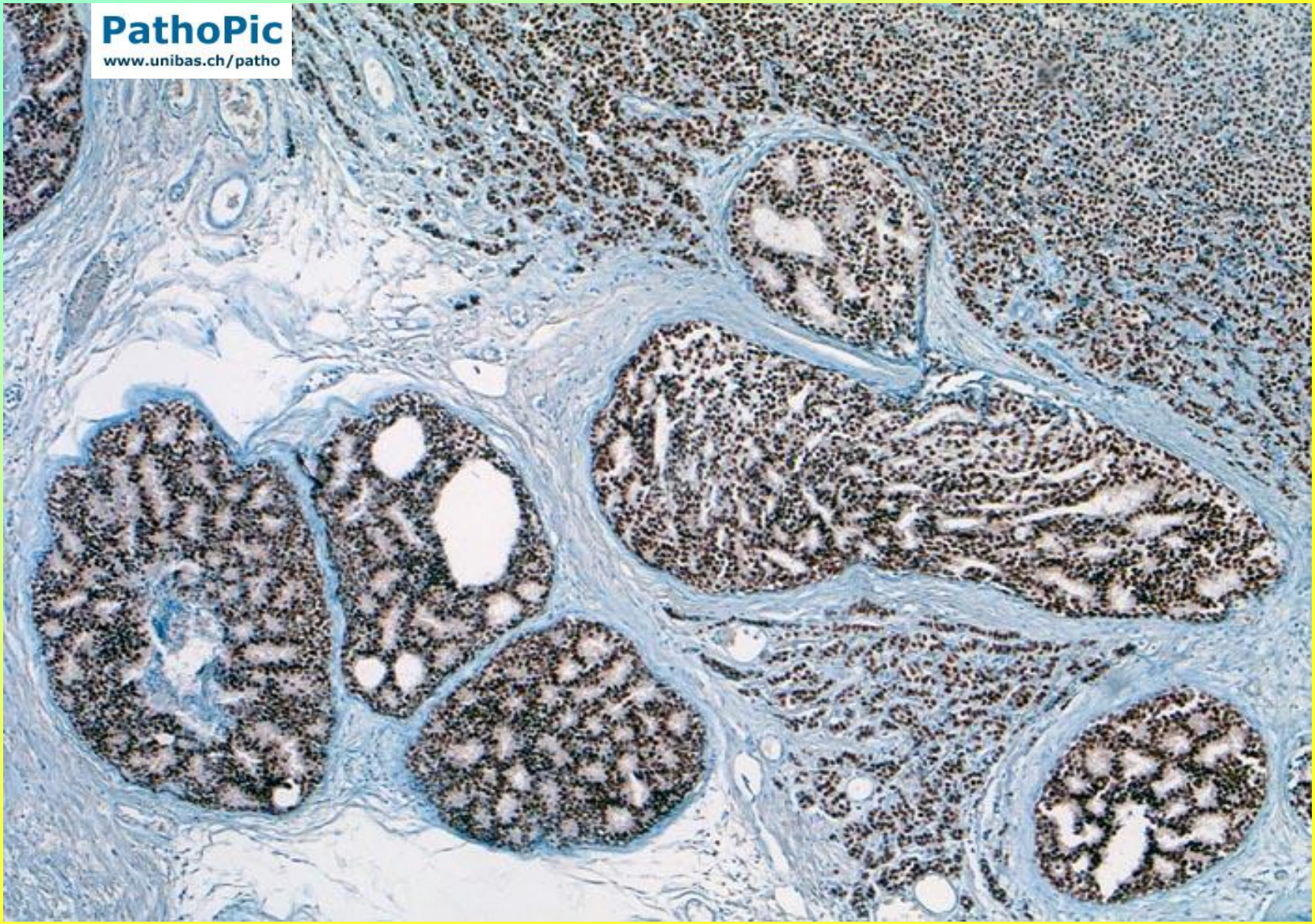
!Prognosis of Paget disease depends on the features of the underlying carcinoma



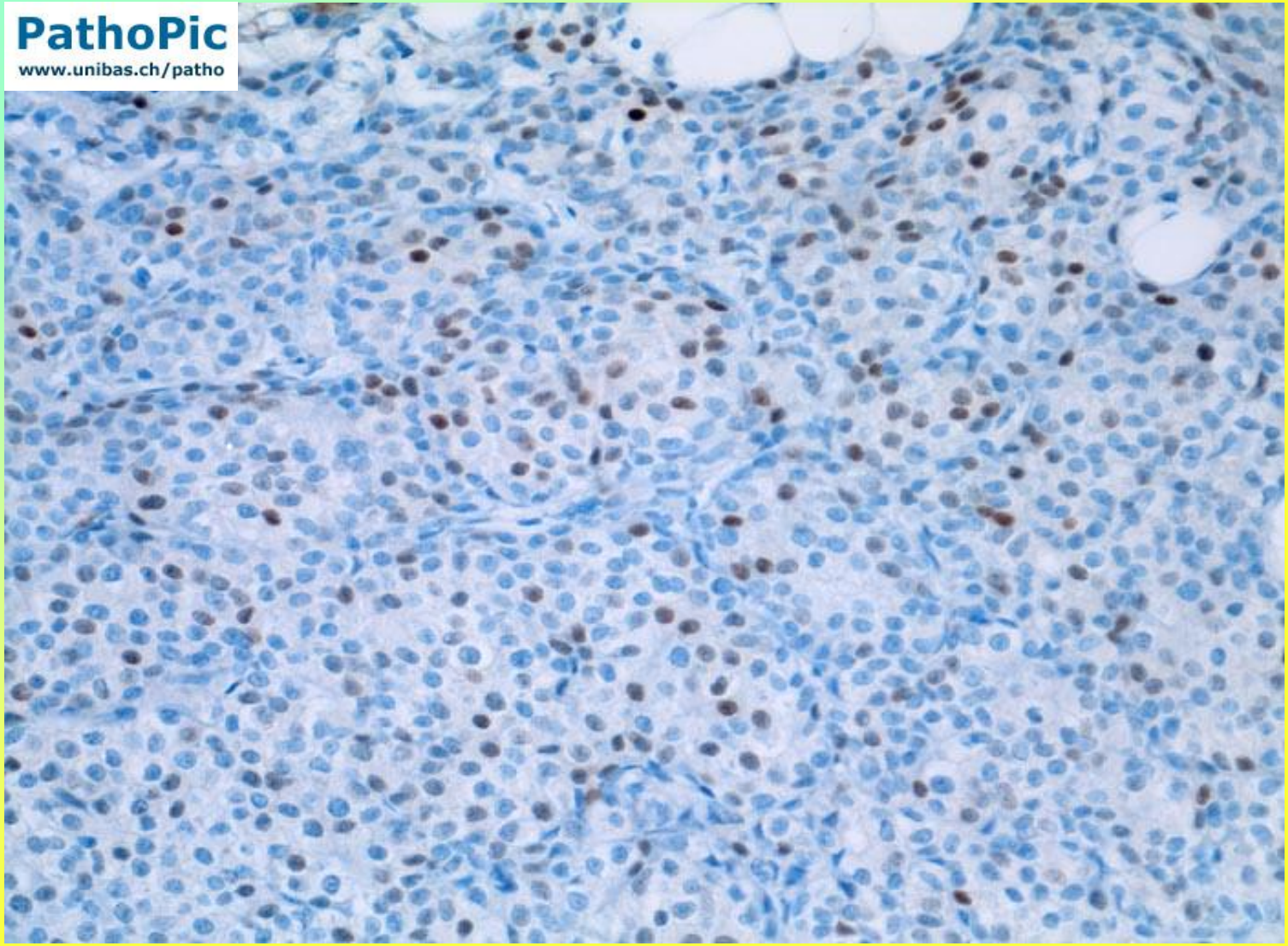
Paget's disease of the nipple. The large cells infiltrating into the epidermis represent intraepithelial extension of an underlying **ductal carcinoma in situ** or **invasive ductal carcinoma**. At high magnification, the Paget's cells have abundant clear cytoplasm, atypical nuclei and appear in the epidermis either singly or in clusters.

Life Cycle of Breast Cancer Classification

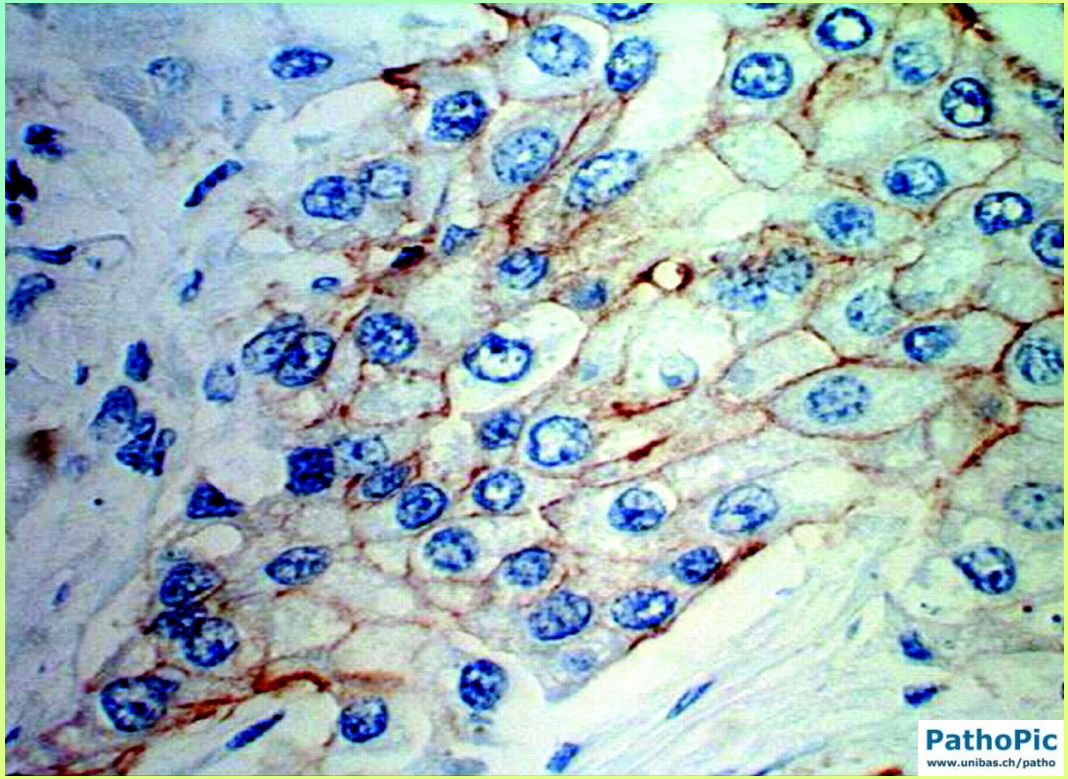




Breast carcinoma predictive markers: **Estrogen receptors** (**ER+**) detected in the nucleus (brown = positive) by immunohistochemical studies. DCIS & invasive, NST



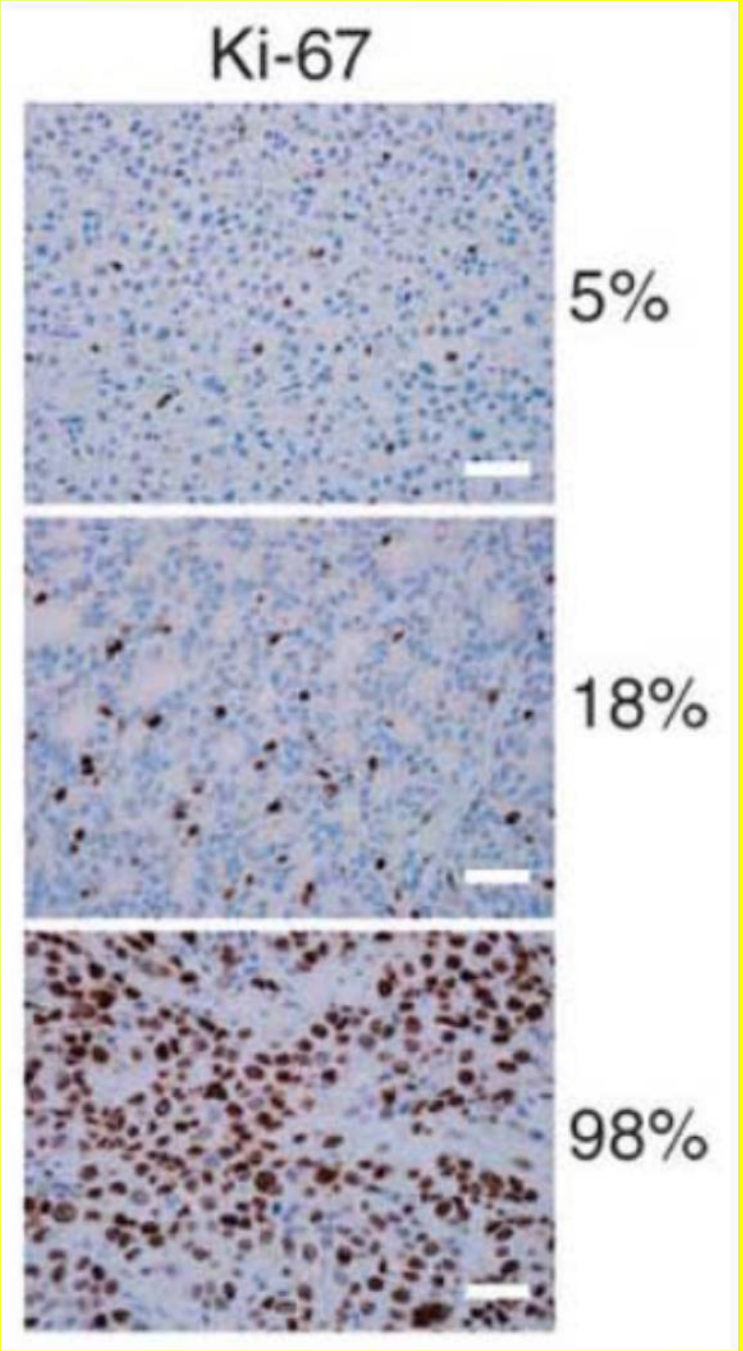
Breast carcinoma predictive markers: **Progesterone receptors** (**PgR+**) detected in the nucleus (brown = positive) by immunohistochemical studies. Ductal invasive, NST



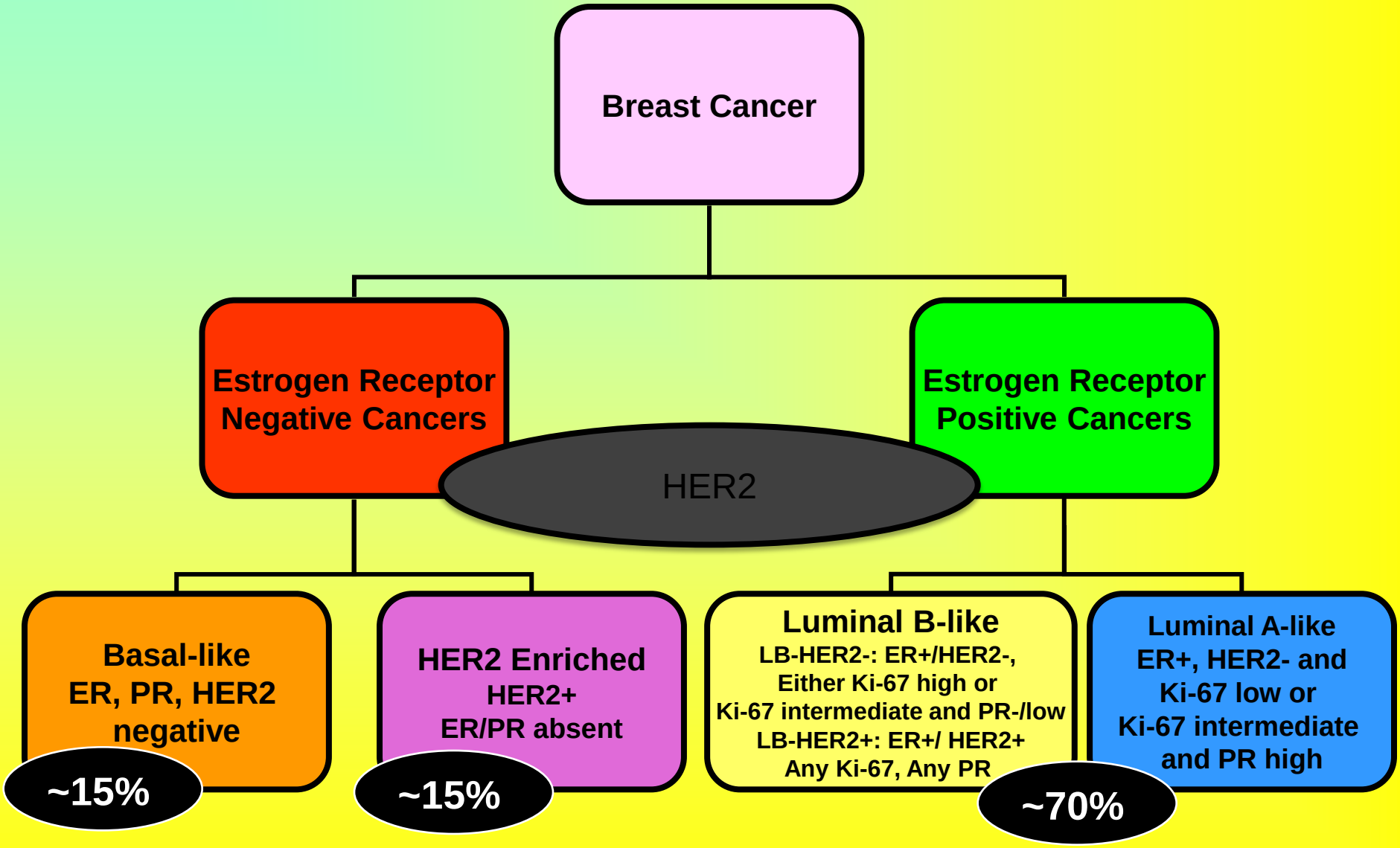
Breast carcinoma predictive markers:
HER2/neu expression is detected on the cell membrane by immunohistochemistry (scored 0 ⇒ 3+).

Proliferative rate – mirrored by Ki-67 antigen, nuclear brown stain by IHC:

- low-intermediate ≤ 20%
- high > 20% (of malignant cells).



Molecular Classification

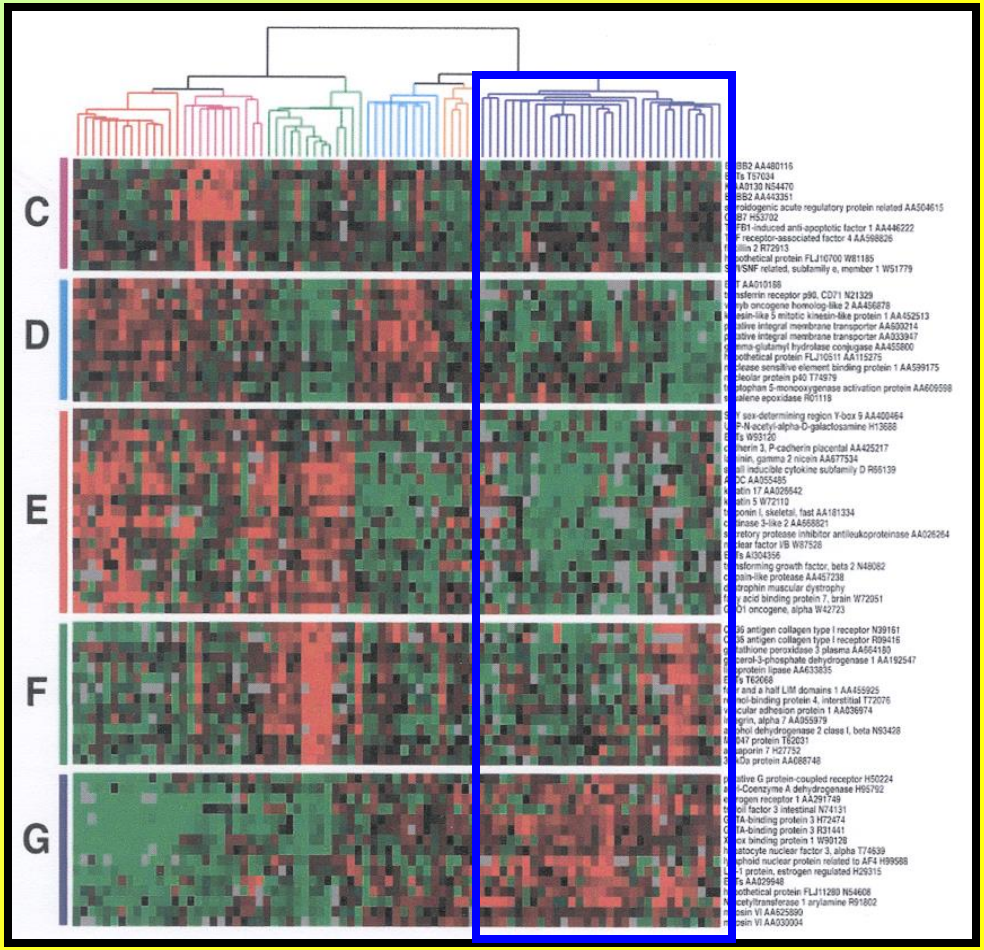


Luminal A-like Breast Carcinoma

- **~60% of breast cancers**
- **ER and PR positive**
- **Tend to be low grade (Ki-67 low)**
- **Do not overexpress HER2**
- Includes ER positive special type cancers

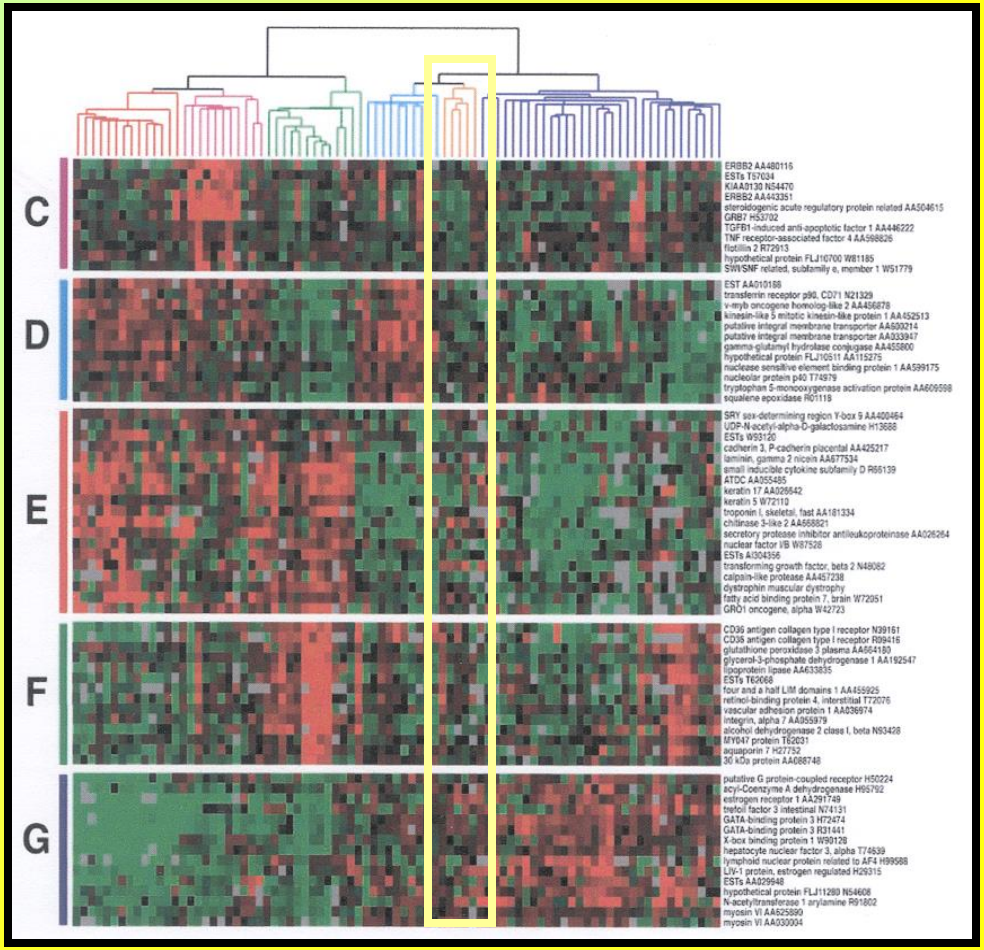
- **High expression of hormone receptors and associated genes (Lum A > Lum B)**

- **Respond to endocrine therapy**
- **Chemotherapy generally not indicated**
- **Good prognosis**



Luminal B-like Breast Carcinoma

- **~10% of breast cancers**
- **ER positive**
- **Tend to be higher grade and/or have a higher proliferation index**
- **May overexpress HER2 (Luminal B, HER2+)**
- **High expression of hormone receptors and associated genes**
- **Respond to endocrine and chemotherapy**
- **Prognosis not as good as for Luminal A**

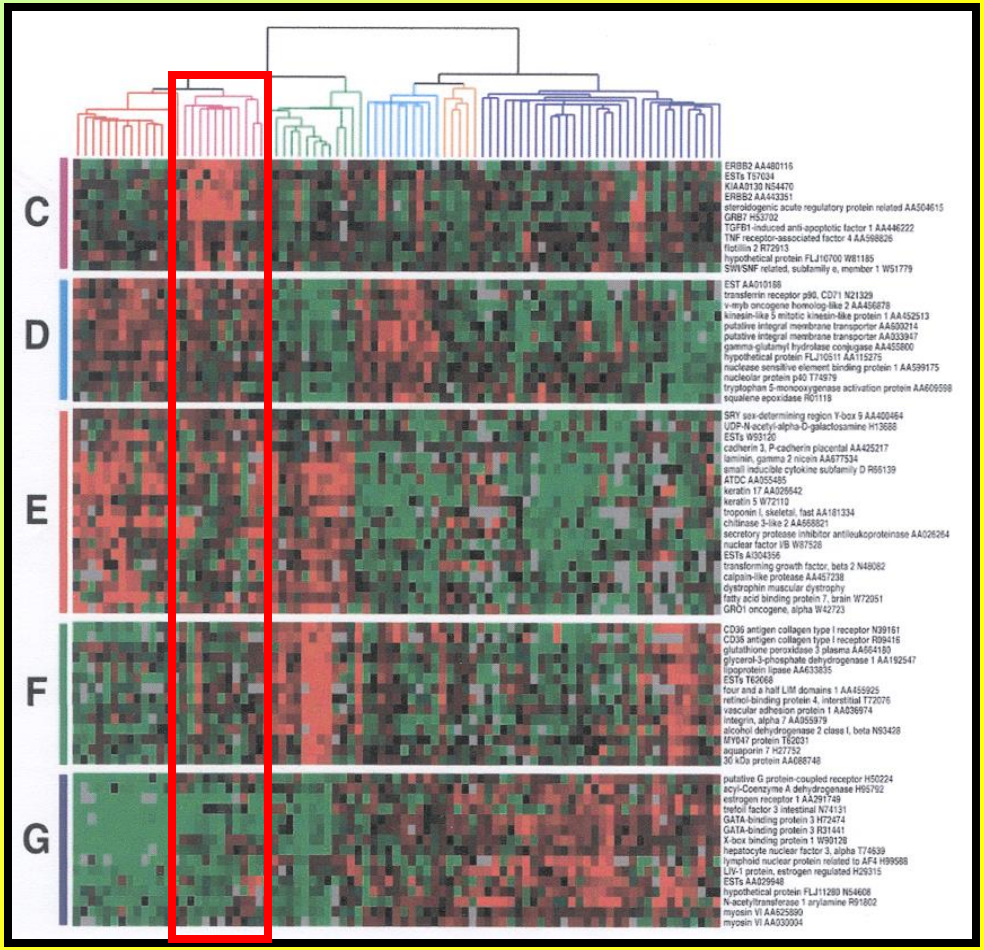


HER2-enriched (positive) Breast Carcinoma

- ~15% - 20% of breast cancers
- ER/PR negative
- More likely high grade and lymph node +

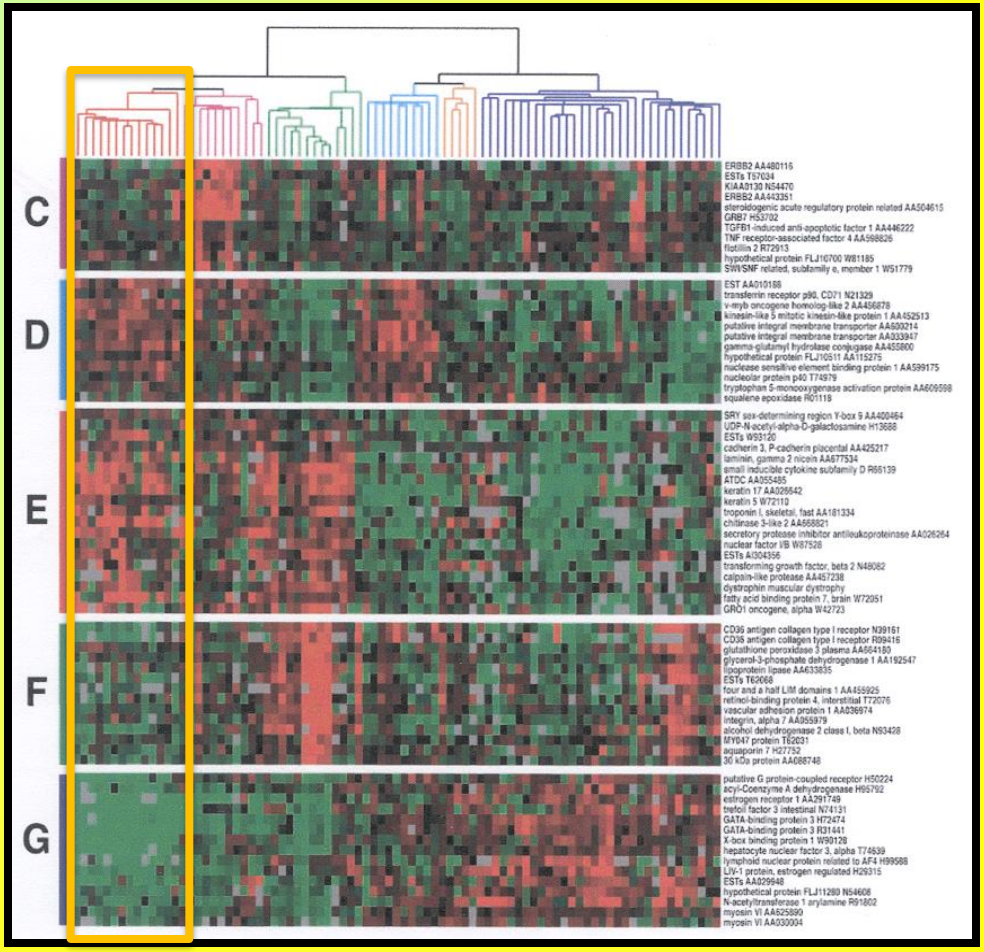
- High expression of HER2 and other genes in amplicon
- Low expression of ER and associated genes

- Respond to Herceptin
- Respond to anthracycline-based chemo
- Generally poor prognosis

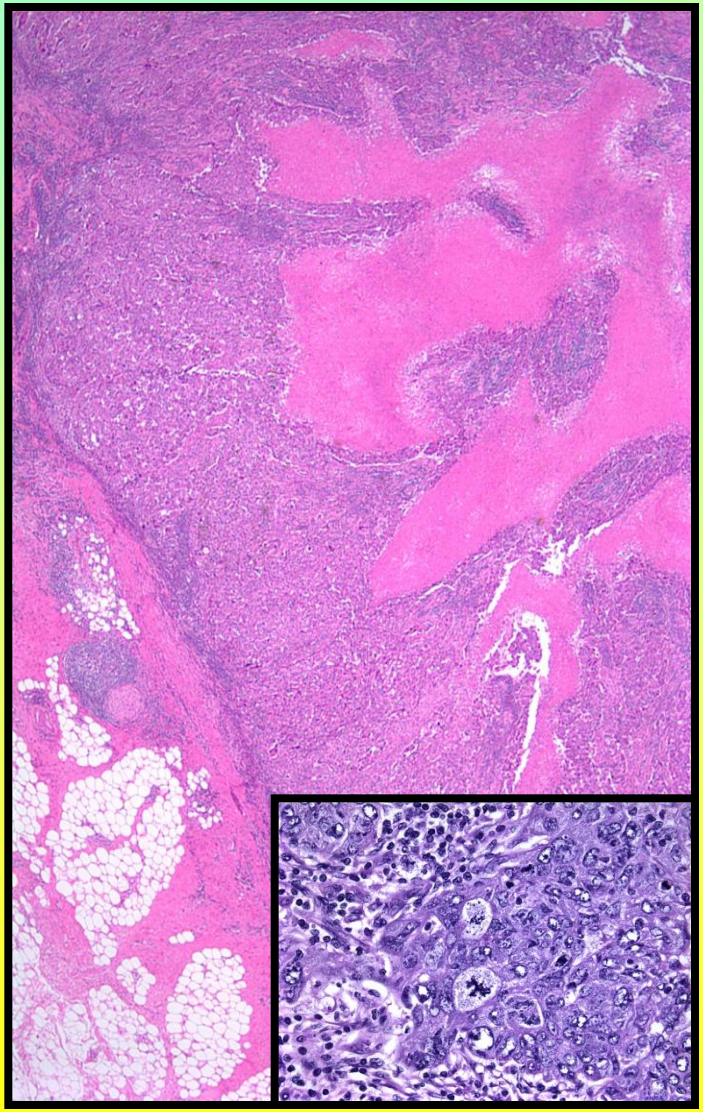


Basal-Like Carcinoma

- **Subtype of invasive breast cancer identified through gene expression profiling studies**
- **Express genes characteristic of basal epithelial cells**
- **Comprise ~ 15% of invasive breast cancers**
- **Includes high grade TNBC (triple negative breast carcinoma) and ER negative special type cancers**



Basal-Like Carcinoma/TNBC



- **Most high grade invasive ductal carcinomas, often with circumscribed borders, geographic necrosis and/or fibrotic foci, lympho-plasmacytic infiltrates, very high mitotic rate**
- **Associated with *BRCA1* germline mutations**
- **More common in African and African-American women**
- **Lack conventional therapeutic targets (ER, HER2)**
- **Poor prognosis**

Immunophenotyping to Approximate Molecular Subtype

Luminal A-like	**ER+, HER2-,** **Ki-67<14% or Ki-67 intermediate (14-19%) and PR≥20%,**
Luminal B-like	**ER+, HER2-** **Ki-67 intermediate (*14-19%) and PR- or low (<20%) or Ki-67≥20%** **HR+, HER2+**
HER2-enriched	**ER-, PR-, HER2+**
Basal-like	**ER-, PR-, HER2-, [CK5/6+ and/or EGFR+]**

Prognostic factors & the **outcome** for women with breast cancer are related to:

- ✓ **extent of carcinoma / pathological stage = pTNM:**
  - ➢ ***Invasive carcinoma vs. carcinoma in situ***
  - ➢ ***Distant metastases***
  - ➢ ***Lymph node metastases, Lymphovascular invasion***
  - ➢ ***Tumor size***

- ✓ **biologic features of the carcinoma**:
  - ➢ **Molecular subtypes and histologic grade**
  - ➢ **Special histologic types**
  - ➢ **Hormone status**

Stages of breast cancer			
	T	N	M
Early Breast Cancer Stage 1 or 2	T1-2 Tumour up to 5cm	No – None N1 – Up to 3 involved nodes	No metastases
Locally Advanced Stage 3	(Any size)	N2 – 4 or more nodes, or fixed nodes N3 – Nodes other than in axilla	No metastases
Blank	T3 – More than 5cm T4 – Fixed to skin or chest wall	(Any nodes)	No metastases
Metastatic Stage 4	(Any Size)	(Any nodes)	Metastases

IMPORTANT NOTES BREAST CARCINOMA

- **TUMOR SIZE: GROSSING**
- **MICROSCOPY:**
  - **H&E: ▪ SURGICAL MARGINS ± malignant cells**
    - **HISTOLOGICAL TYPE**
    - **HISTOLOGICAL GRADE**
    - **TUMOR CELLS EMBOLI**
    - **REGIONAL LYMPH NODE METASTASES (!sentinel lymph node if possible technically)**
  - **IMMUNOHISTOCHEMISTRY:**
    - **HORMONE STATUS (ER, PR)**
    - **RATE OF PROLIFERATION (Ki67 antigen)**
    - **HER2 ONCOPROTEIN SCORE (0 ⇒ 3+)**
- **IMAGISTIC MRI: REMOTE METASTASES?**
- **PATHOLOGICAL STAGE TNM = or ≠ CLINICAL STAGE**