Breast pathology

2nd Department of Pathology

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Breast pathology - Summary

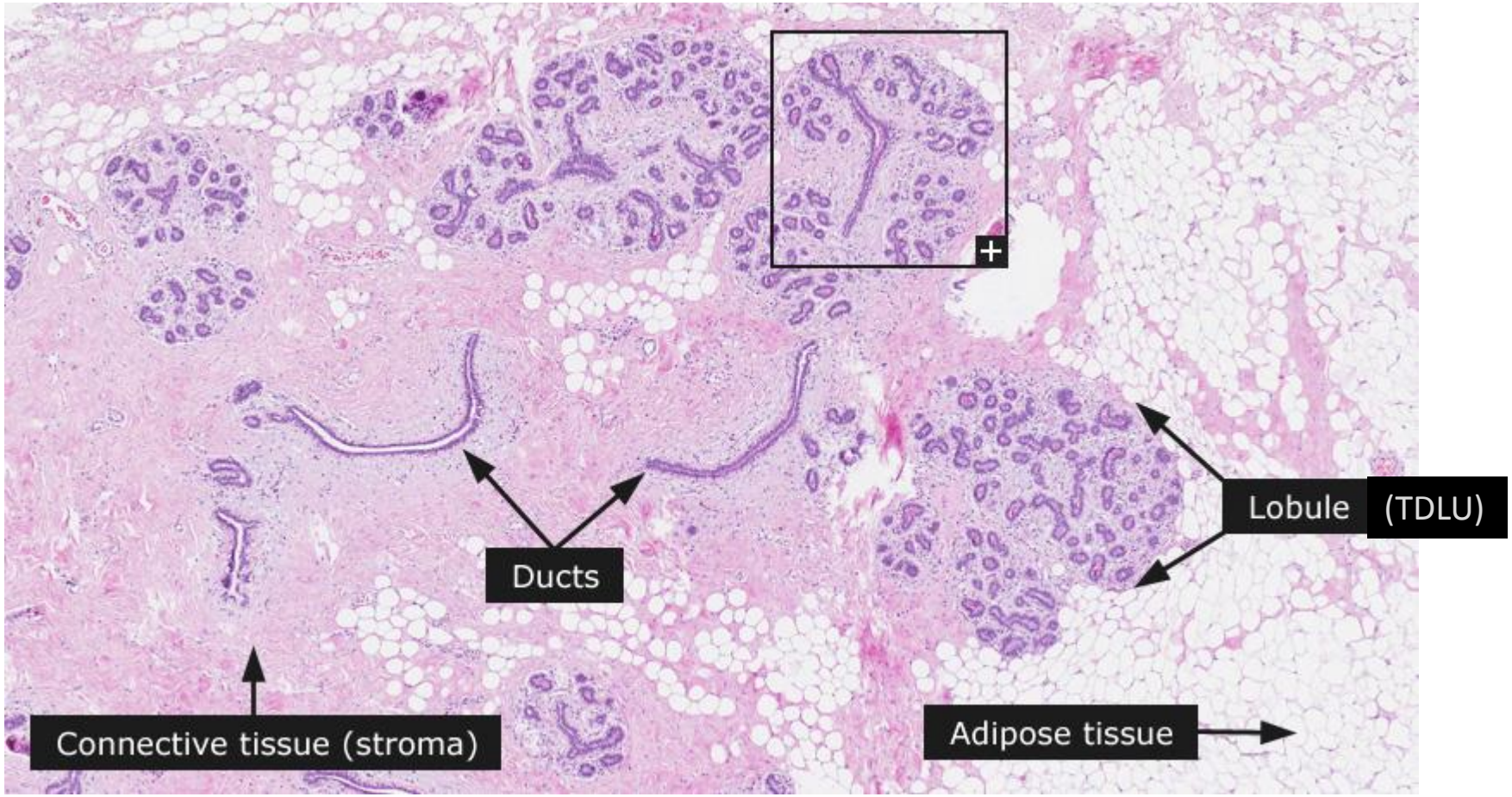
- Benign lesions
  - Acute mastitis
  - Plasma cell mastitis / duct ectasia
  - Fat necrosis
  - **Fibrocystic change/ benign proliferative lesions**
  - Intraductal papilloma
  - **Fibroadenoma**
  - Benign phyllodes tumor
  - Gynecomastia (male breast)

Breast pathology - Summary

- Malignant lesions
  - In situ carcinomas: DCIS, LCIS, Paget's disease
  - Invasive carcinomas
    - Invasive carcinoma NOS (not otherwise specified) – 80%
    - Invasive lobular carcinoma – 10%
    - Tubular carcinoma
    - Mucinous carcinoma
    - Other rare types of carcinomas

    } 10%
  - Malignant phyllodes tumor
  - Other malignant tumors: angiosarcoma, lymphoma, metastases

Normal histology of the breast



TDLU: terminal duct lobular unit

Fibrocystic change/mastopathy

- Most common between ages of 20 and 50, >50% of women is affected
- **Clinically**: palpable nodule(s), tension, pain, the consistency of the affected area can change (by menstrual cycle), nipple discharge, increased density and calcification by mammography, it could be incidental finding (minimal changes)

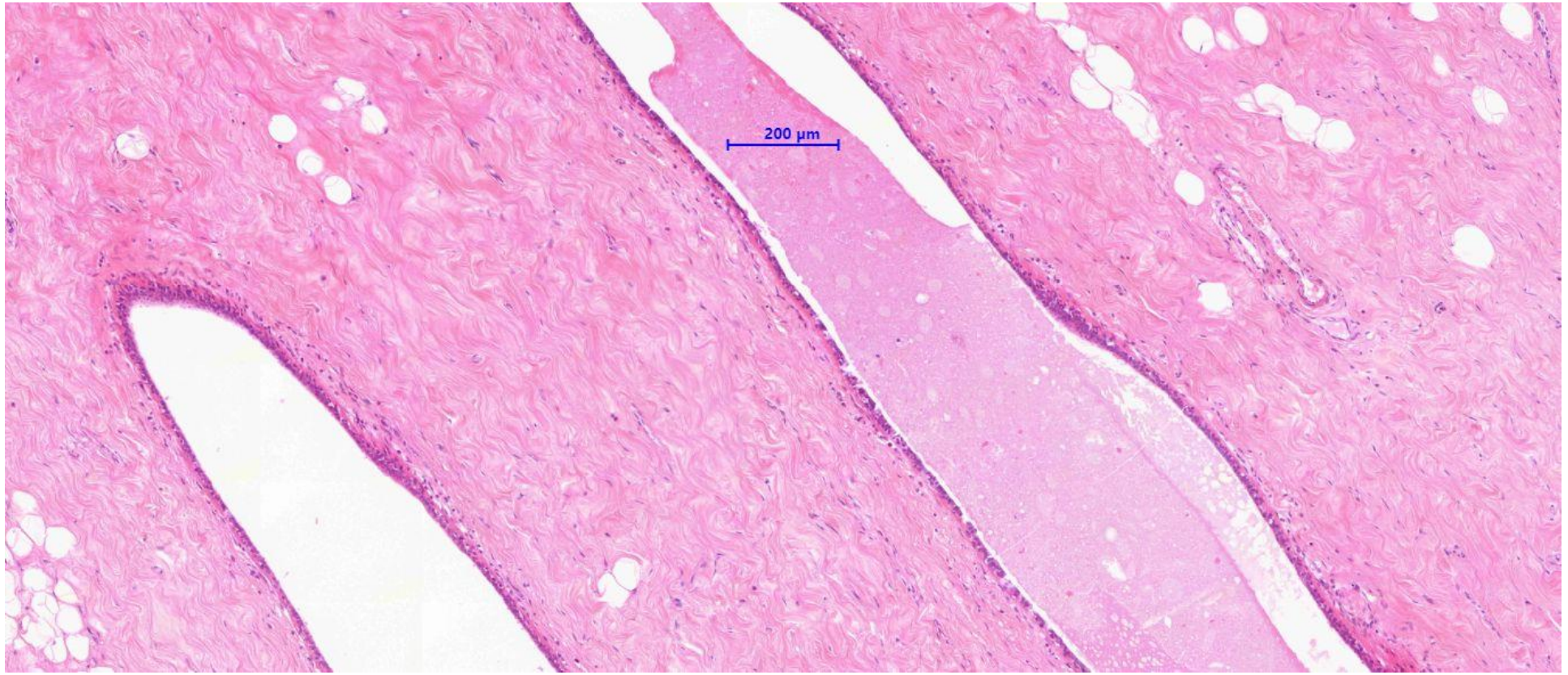
Fibrocystic change/mastopathy microscopy

Heterogenous morphological changes

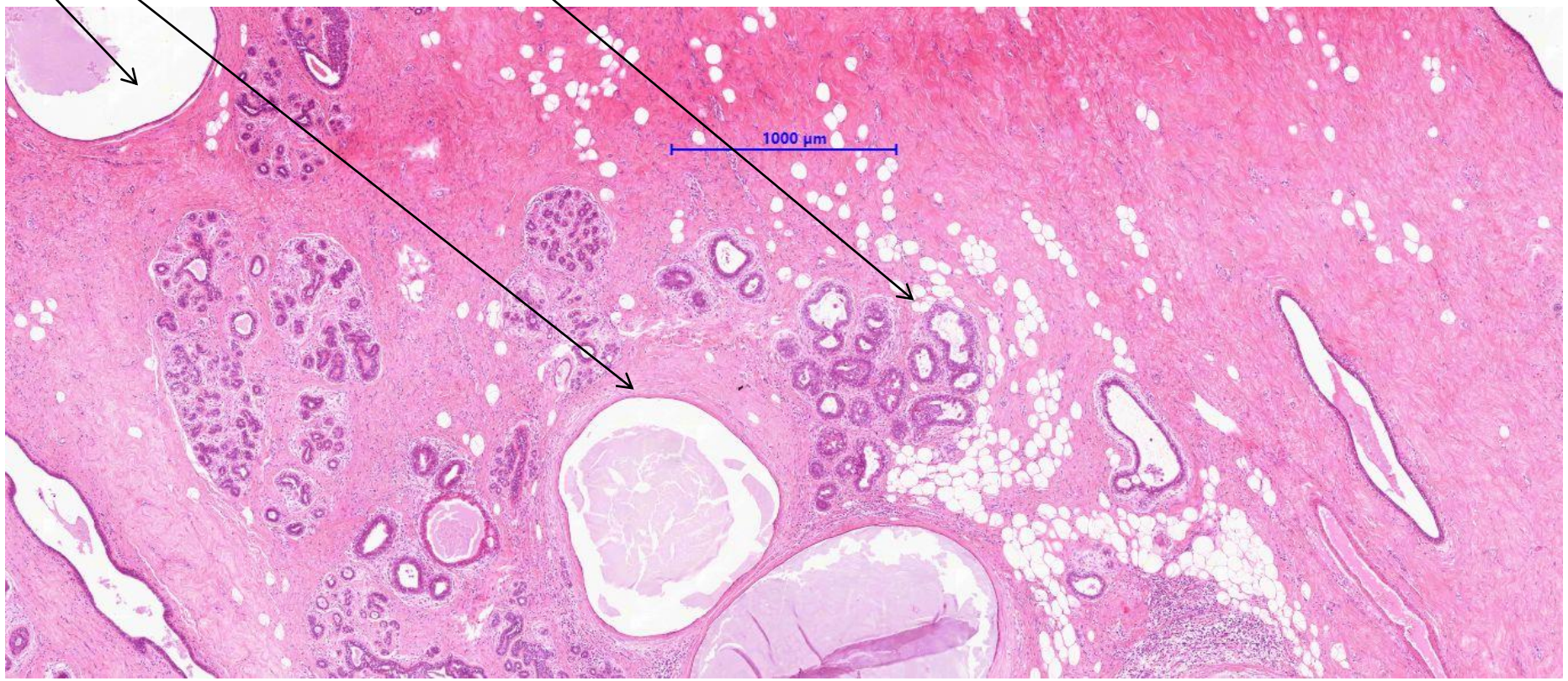
- **Fibrosis**: increase of stroma / adipose tissue ratio
- **Structural changes**: cyst, adenosis, sclerosing adenosis etc..

  can be associated with: radial scar/complex sclerosing lesion
- Alteration of **ductal epithelium:**
  - **Benign**: apocrine metaplasia, usual type and/or florid intraductal epithelial hyperplasia, columnar cell lesions
  - **„Risk" lesions**: atypical ductal hyperplasia or atypical lobular hyperplasia

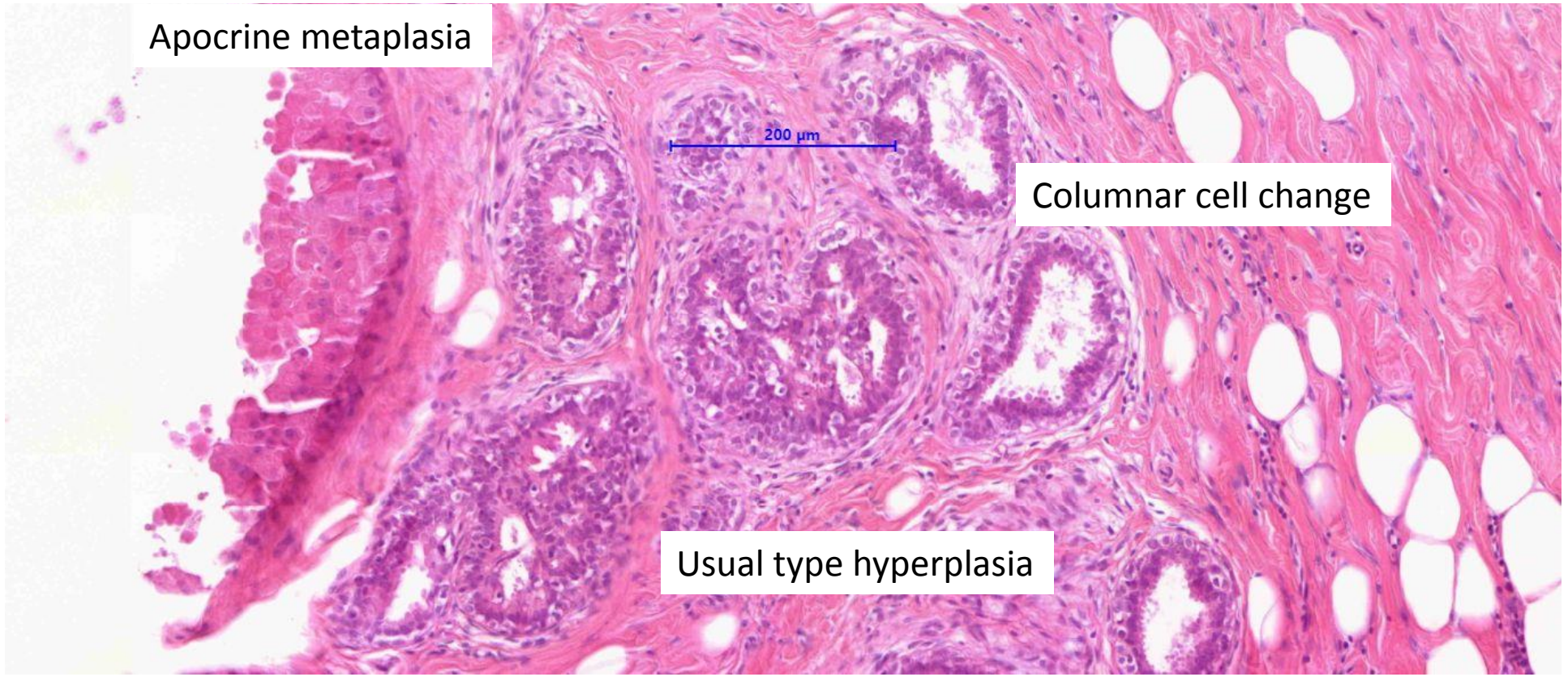
Fibrosis: increased amount of collagen in the extralobular stroma



Cysts, adenosis



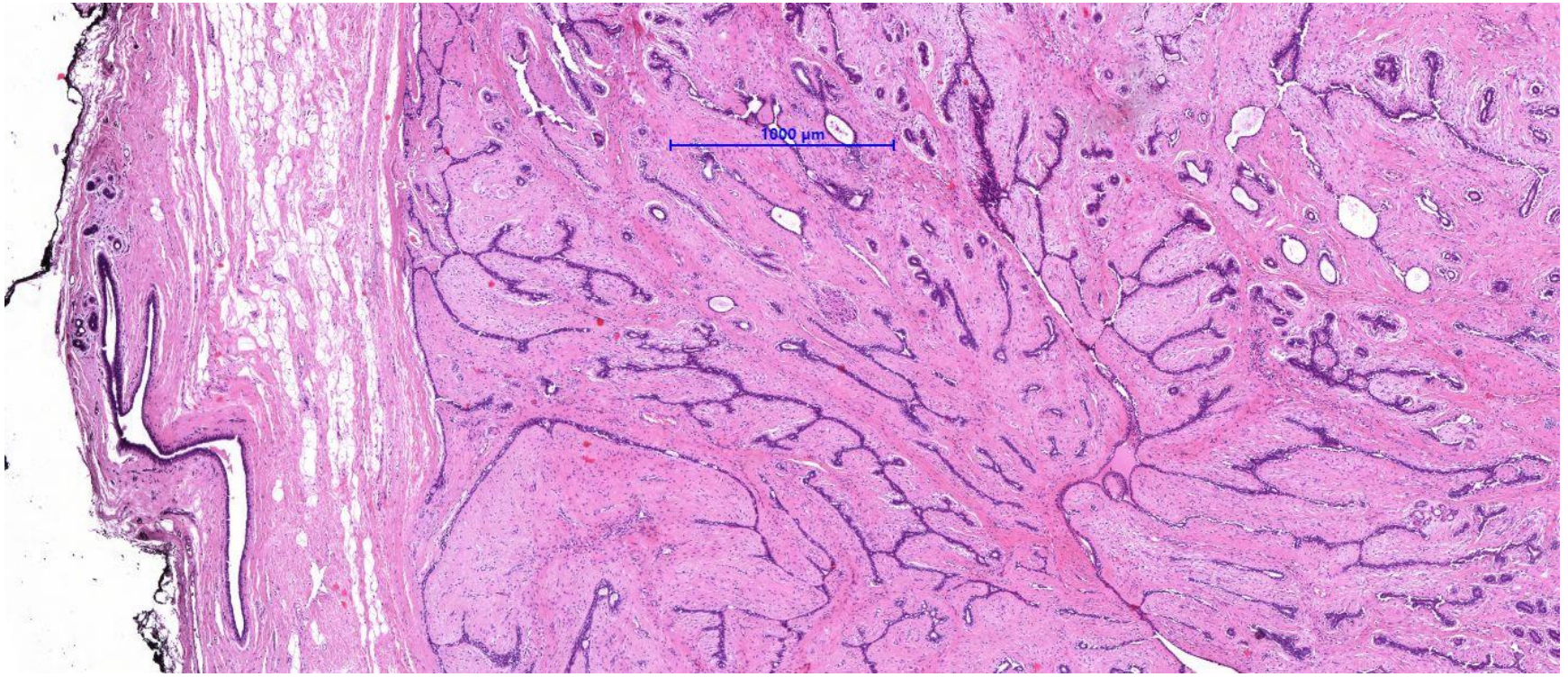
Common alteration of ductal epithelium



Fibroepithelial tumors

- **Biphasic tumors: epithelial and stromal component**
- **Most common: fibroadenoma** (young women): **Well circumscribed**, most commonly solitary nodule, rubbery
- „nodule in the breast”, it can grow rapidly, it can change, in can be painful

Fibroadenoma: Two components: **fibrous stroma + benign ductal epithelium** (compressed, branching ducts)



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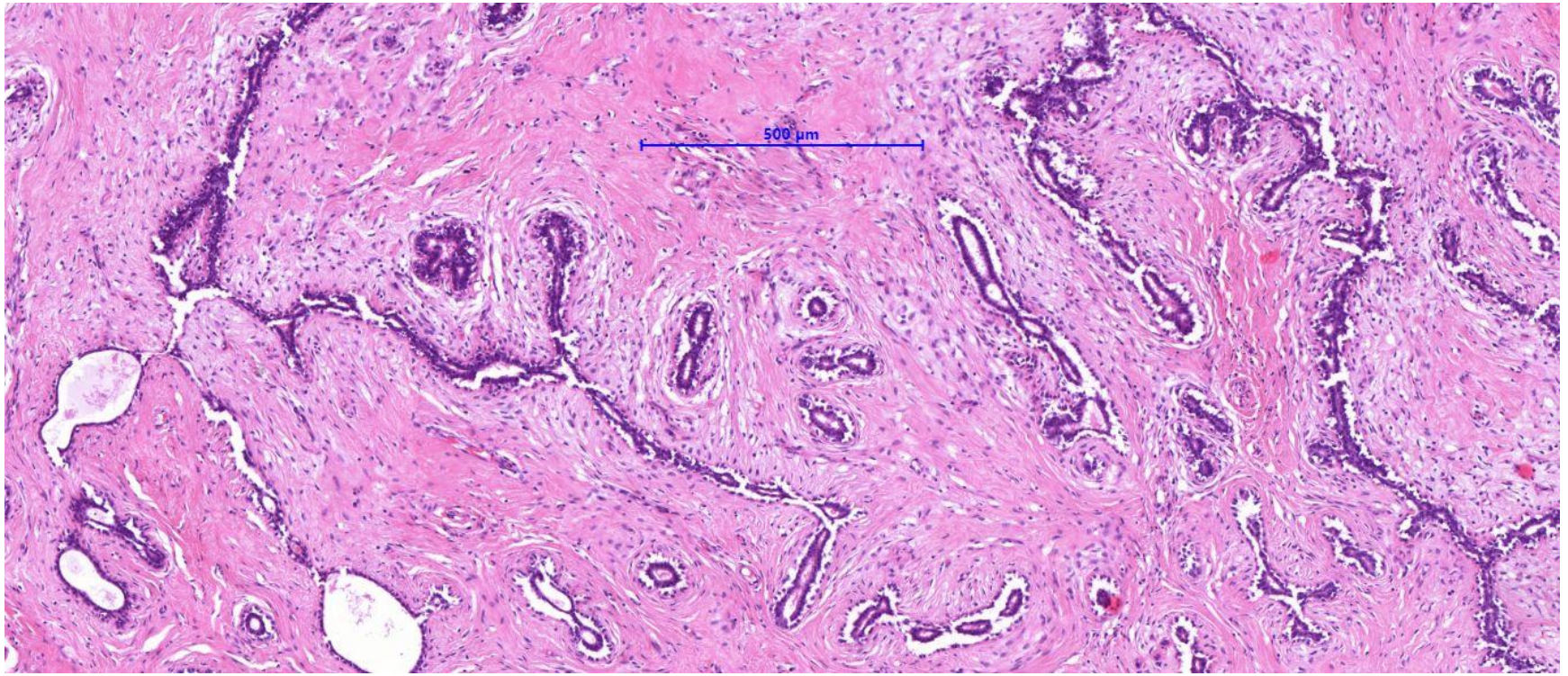
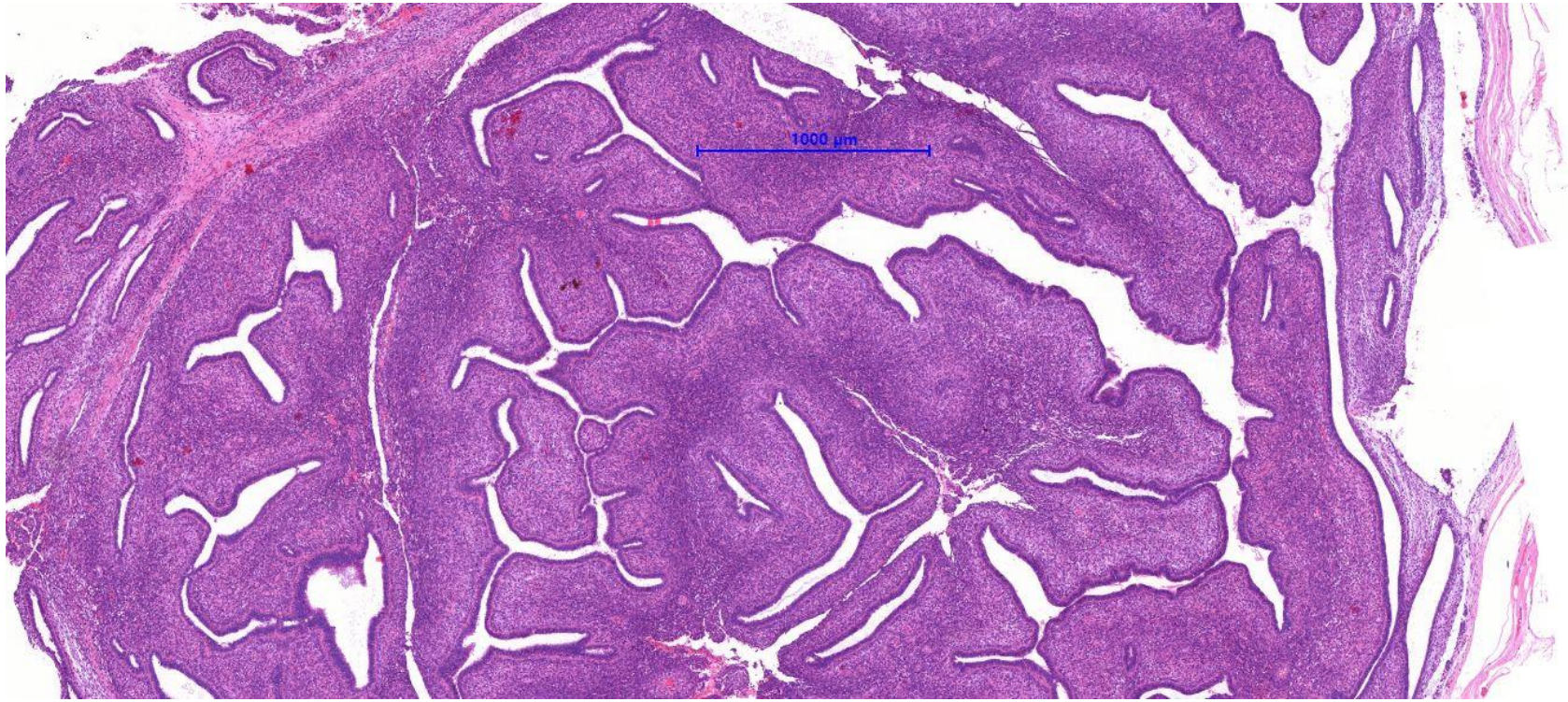
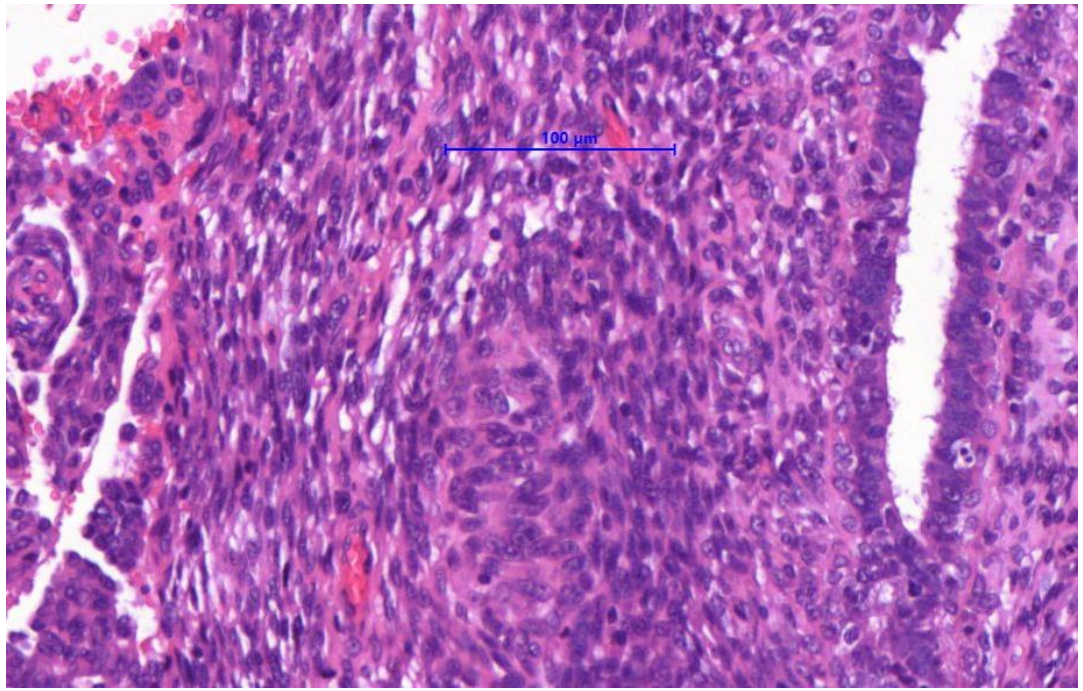


Phyllodes tumor (rare): cellular stroma and leaf like pattern



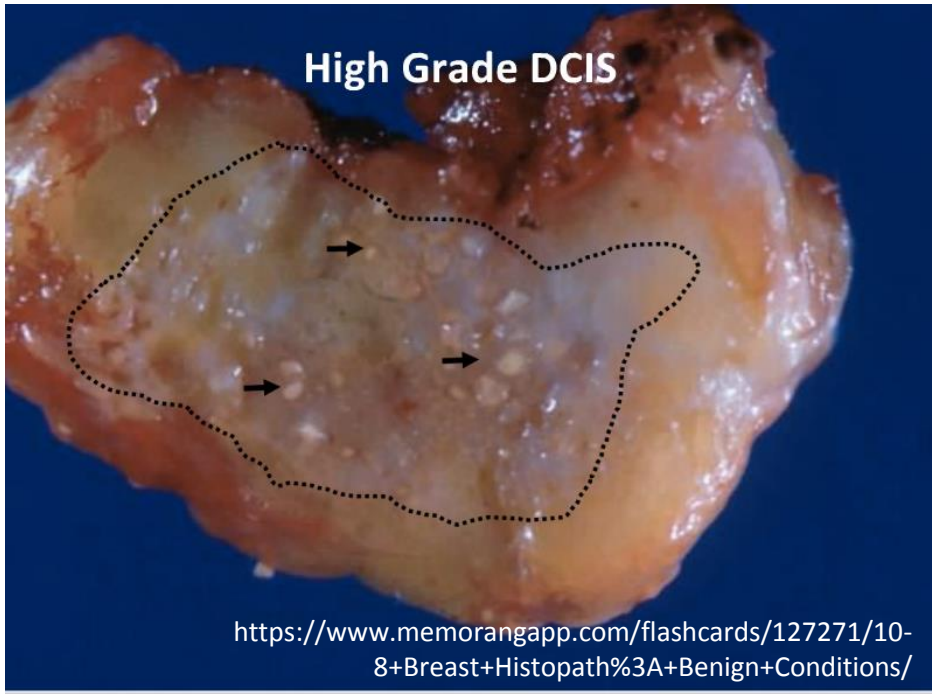
Biological behavior of phyllodes tumor

- **Benign (most common) > Borderline > Malignant**
  (low grade – intermediate grade – high grade)
- Signs of malignancy
  - Overgrowth of stromal component
  - Pleomorphism of stromal cells
  - Mitotic activity of stromal cells
  - Heterologous elements in the stroma
  - Invasive growth pattern (periphery)
  - Metastases



Intraductal carcinoma / Carcinoma in situ mammae (DCIS)

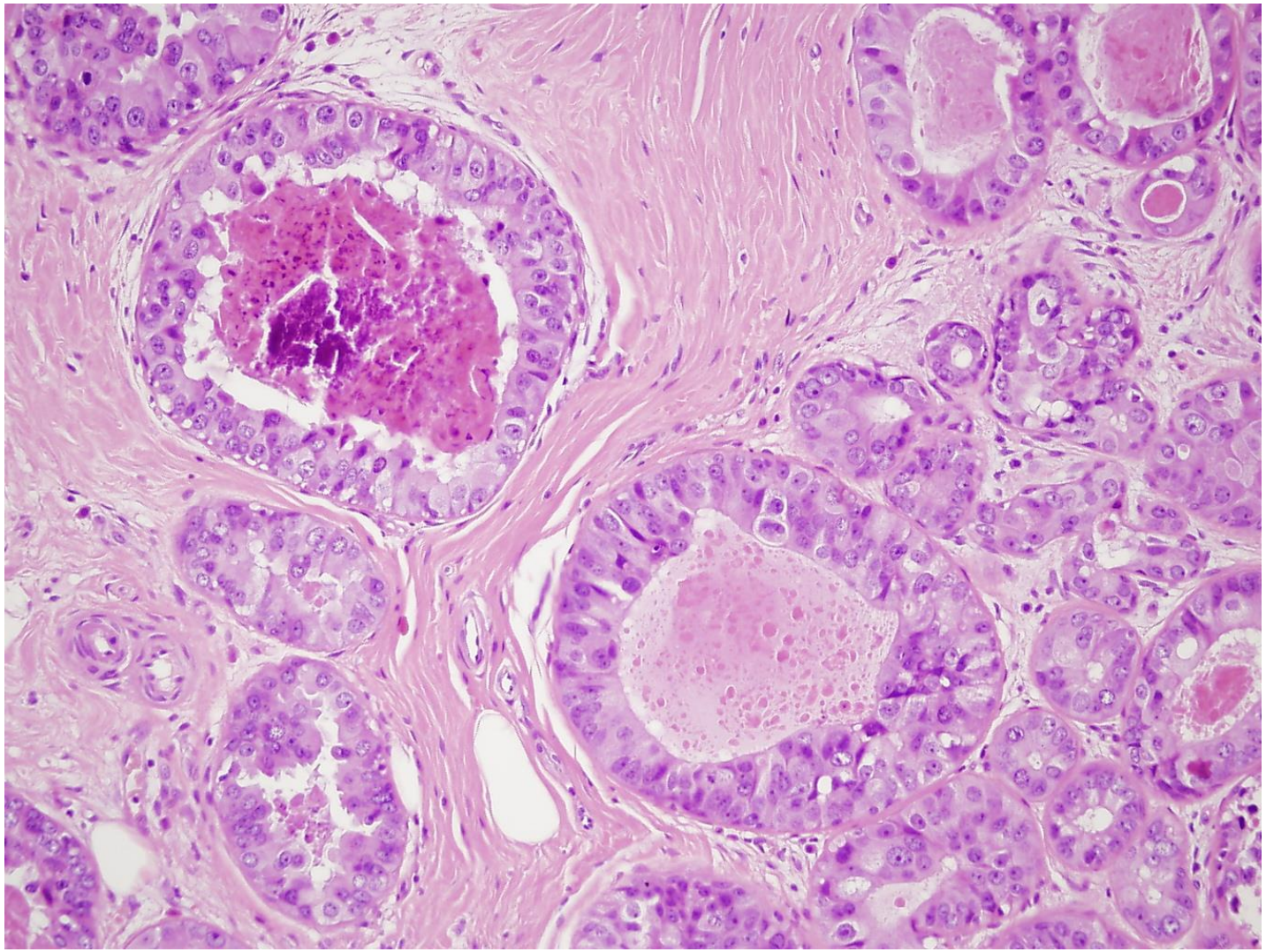
- **Microcalcification is characteristic** (mammography can reveal it – screening!)
- **Macroscopically invisible or difficult to detect:** the whole breast can be affected
- It can be detectable by *comedo necrosis*



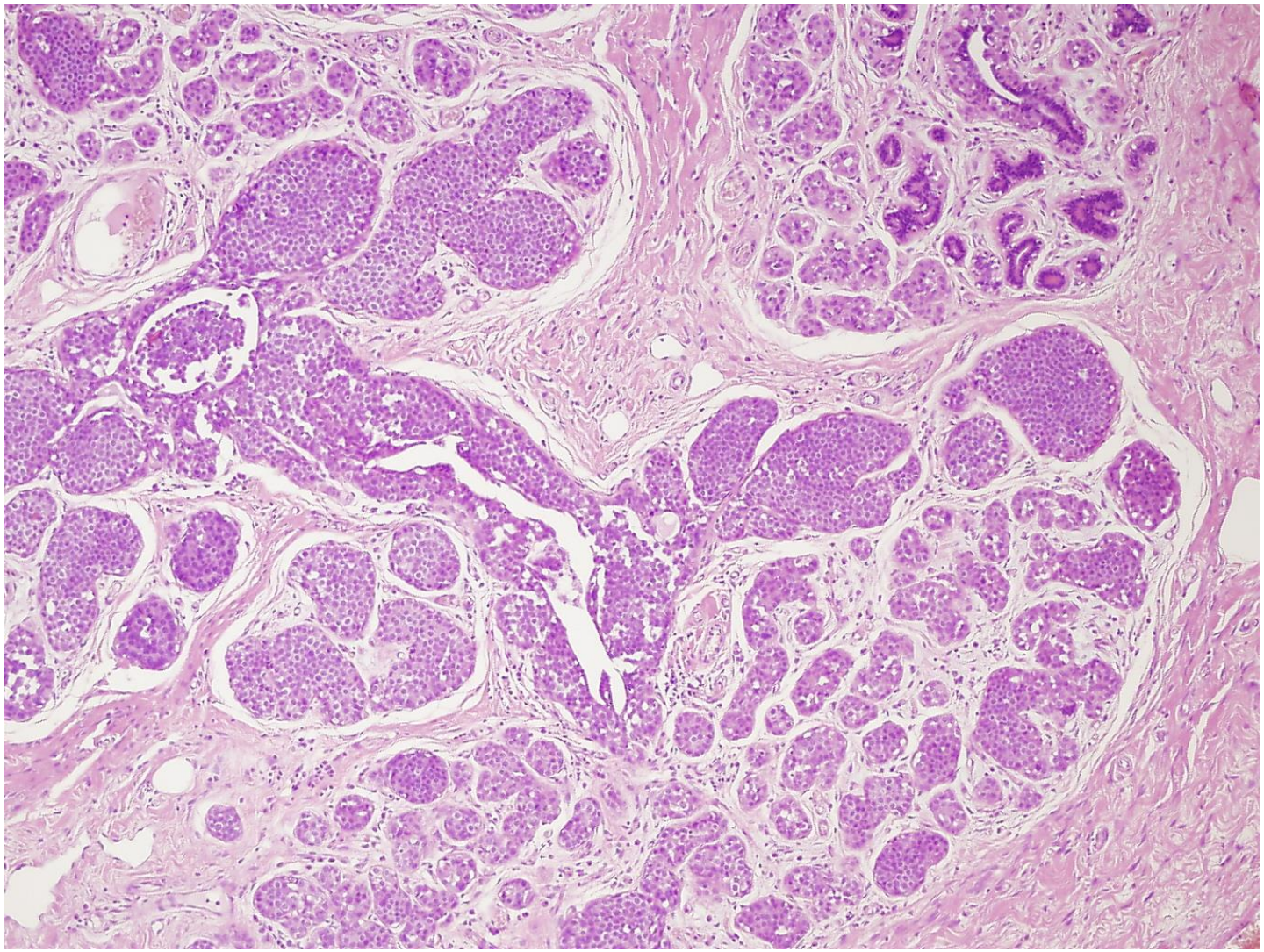
Intraductal carcinoma/ductal carcinoma in situ (DCIS)

- **Malignant cells proliferate within acini (in TDLUs) and in ducts**
- Myoepithelial cells and basal membrane present at the periphery of affected, distended acini and ducts
  - Types according to morphology:
    comedo, cribriform, solid, papillary, flat
  - Types according to nuclear morphology:
    Low – Intermediate – High grade

- **Intraductal proliferation** of tumor cells! **Dilated ducts, comedo necrosis**

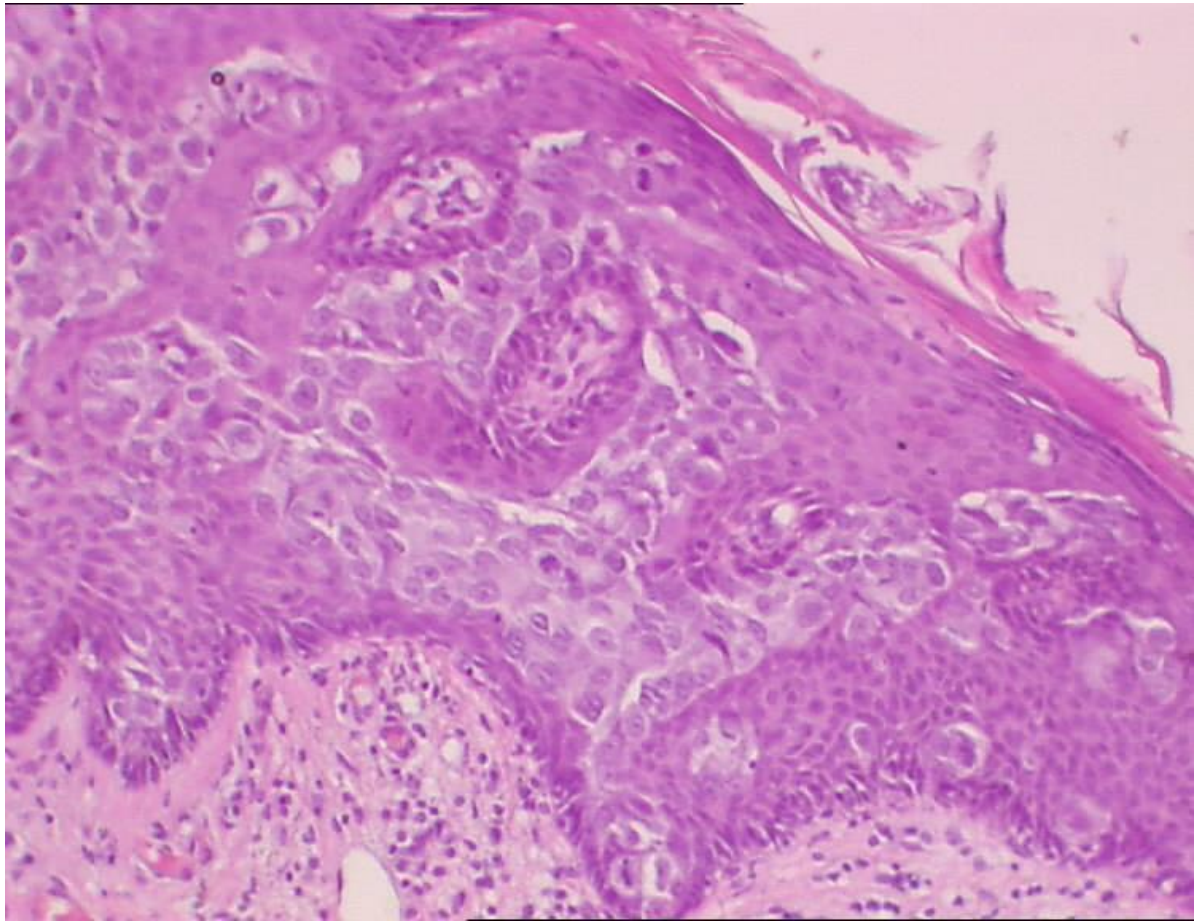


In situ lobular carcinoma (LCIS)



Paget’s disease of the nipple

- **Eczematoid appearance of the nipple, ulceration!!**
- Malignant „ductal” type cells in the epidermis of the nipple-areola complex
- May complicate DCIS or invasive carcinoma



Invasive breast cancer

- **Clinical presentation**: nodule in the breast, or in the axillary tissue, inflammation, exulceration of the skin of the breast, symptoms caused by distant metastases *(bone pain, neurological disorders because of intracranial metastases, incidental finding of lung and liver metastases)*
- **Macroscopically: infiltrative; solitary, diffuse or multifocal**, rarely well-circumscribed (differential diagnosis: fibroadenoma)
- Grey, firm,irregular

Invasive breast cancer – histological types

- Invasive breast carcinoma NST*(IBC NST) (ca. 80%)
  - (Formerly: Invasive Ductal Carcinoma NST, IDC NST)
- Invasive lobular carcinoma (ca. 10%)
- Tubular carcinoma (ca. 6%)
- Mucinous carcinoma (ca. 2%)
- Other, rare types

* No special type

Breast cancer – main prognostic factors

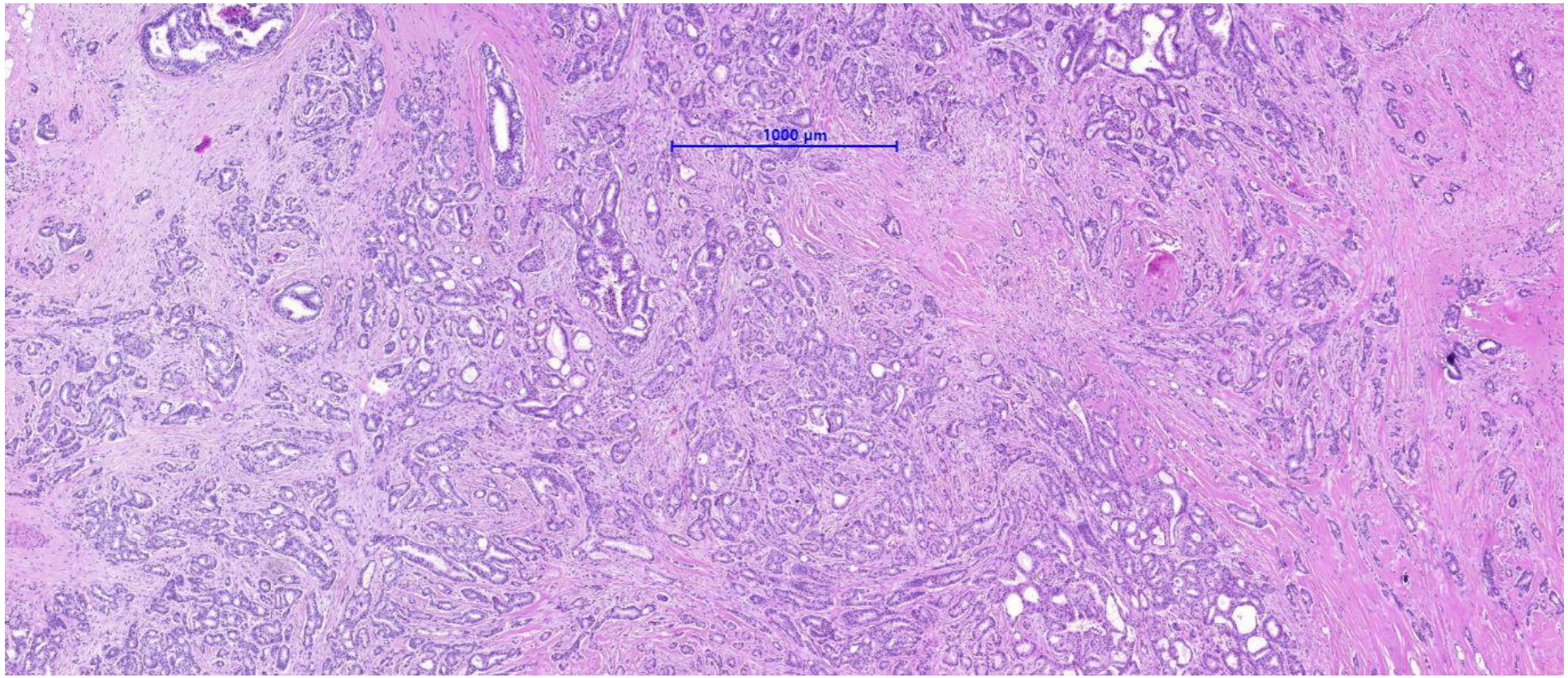
- **Size of the tumor**
- **Tumor stage** (lymph node metastases, distant metastases)
- **Histological and molecular subtypes**
  - Presence of estrogen and progesterone receptors
  - HER2 amplification
- **Histological grade** (structure + cytomorphology + mitotic rate)
- **Lymphovascular invasion**

Breast cancer – Microscopy

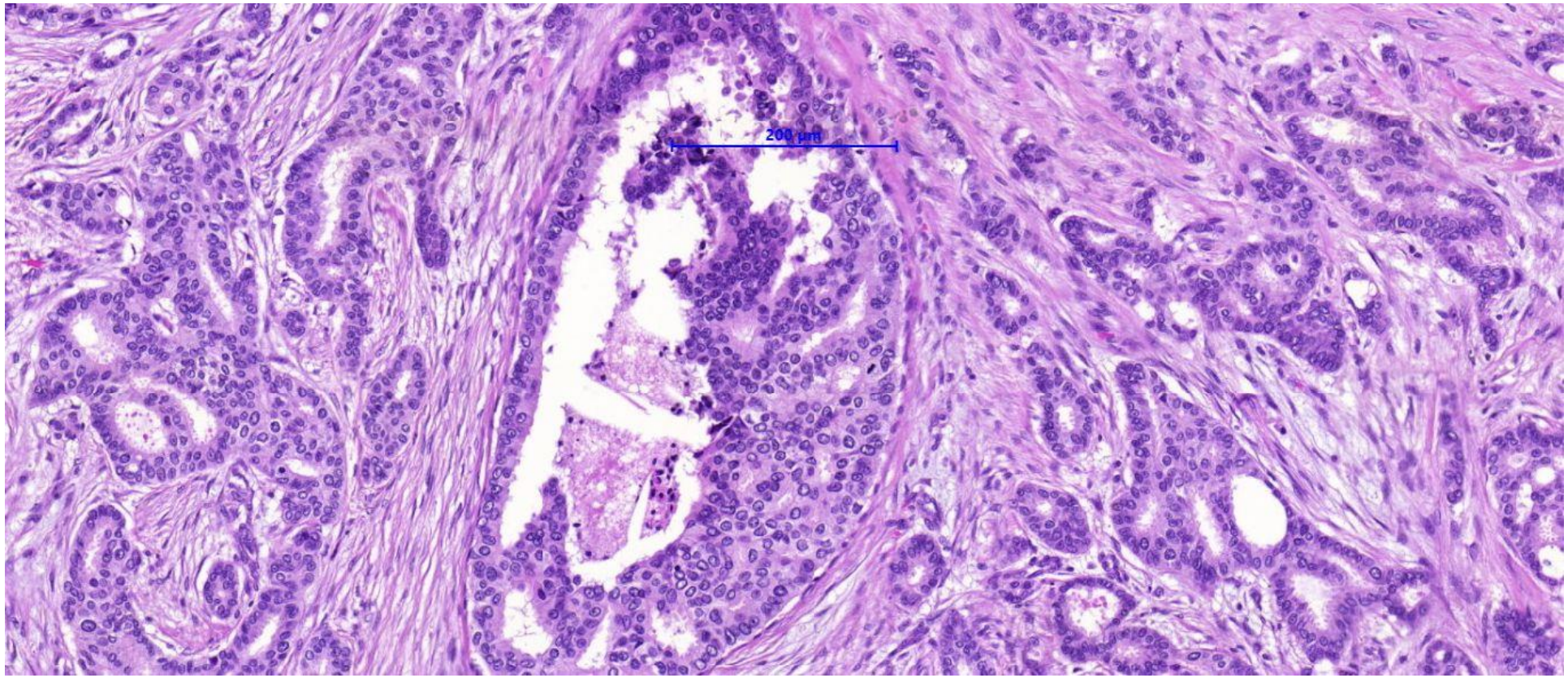
- **Infiltrative** growth
- **Desmoplasia**
- **Grade**: *structure+cytomorphology+mitotic rate*
- **Cytomorphology**
  - **Carcinoma NST** (Ductal): variable atypia
  - **Lobular**: small, round tumor cells, usually slight/moderate polymorphism
- **Structure**:
  - **Carcinoma NST** (Ductal) type (tubules)
  - **Lobular** type (single-file infiltrating pattern, *„Indian file”*)

Invasive breast carcinoma NST

- Tumor cells form tubules, cribriform structures, nests and cords.

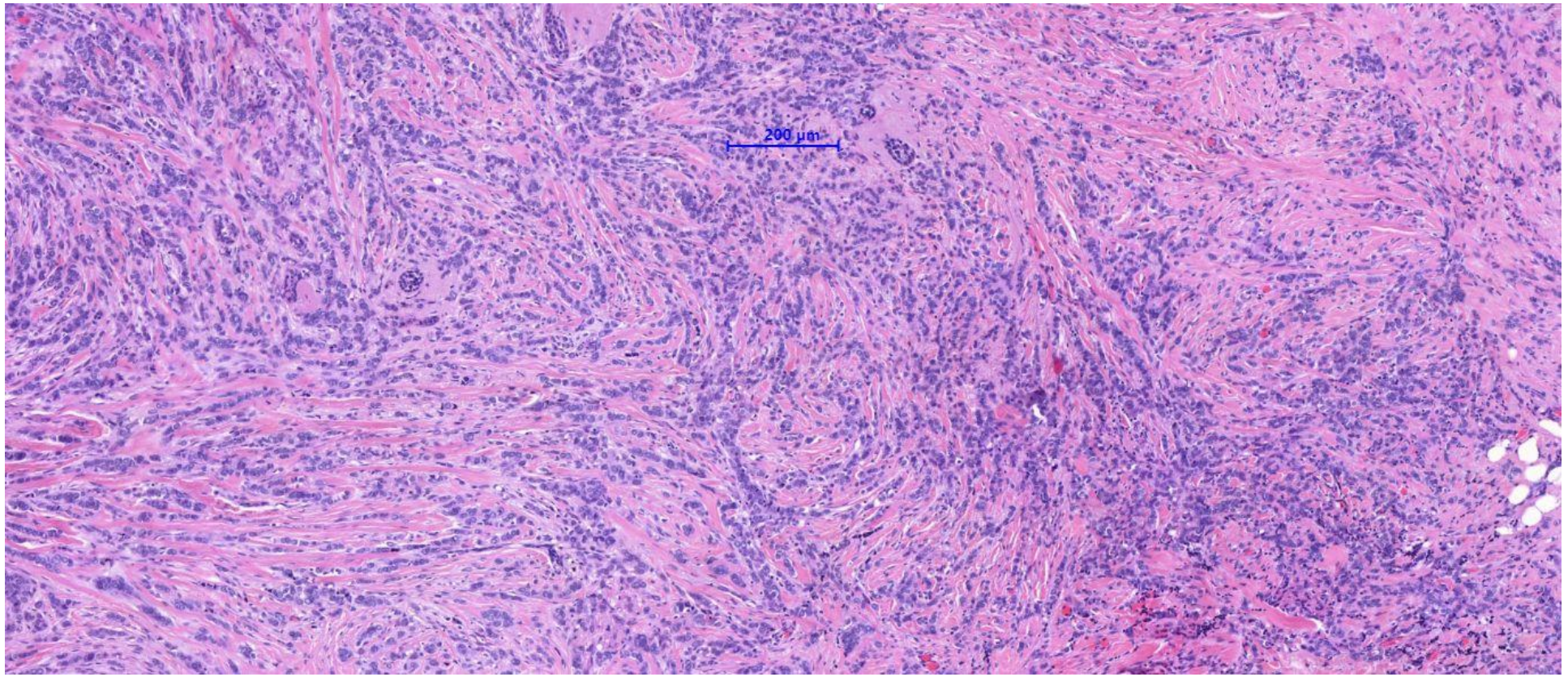


Invasive breast carcinoma NST

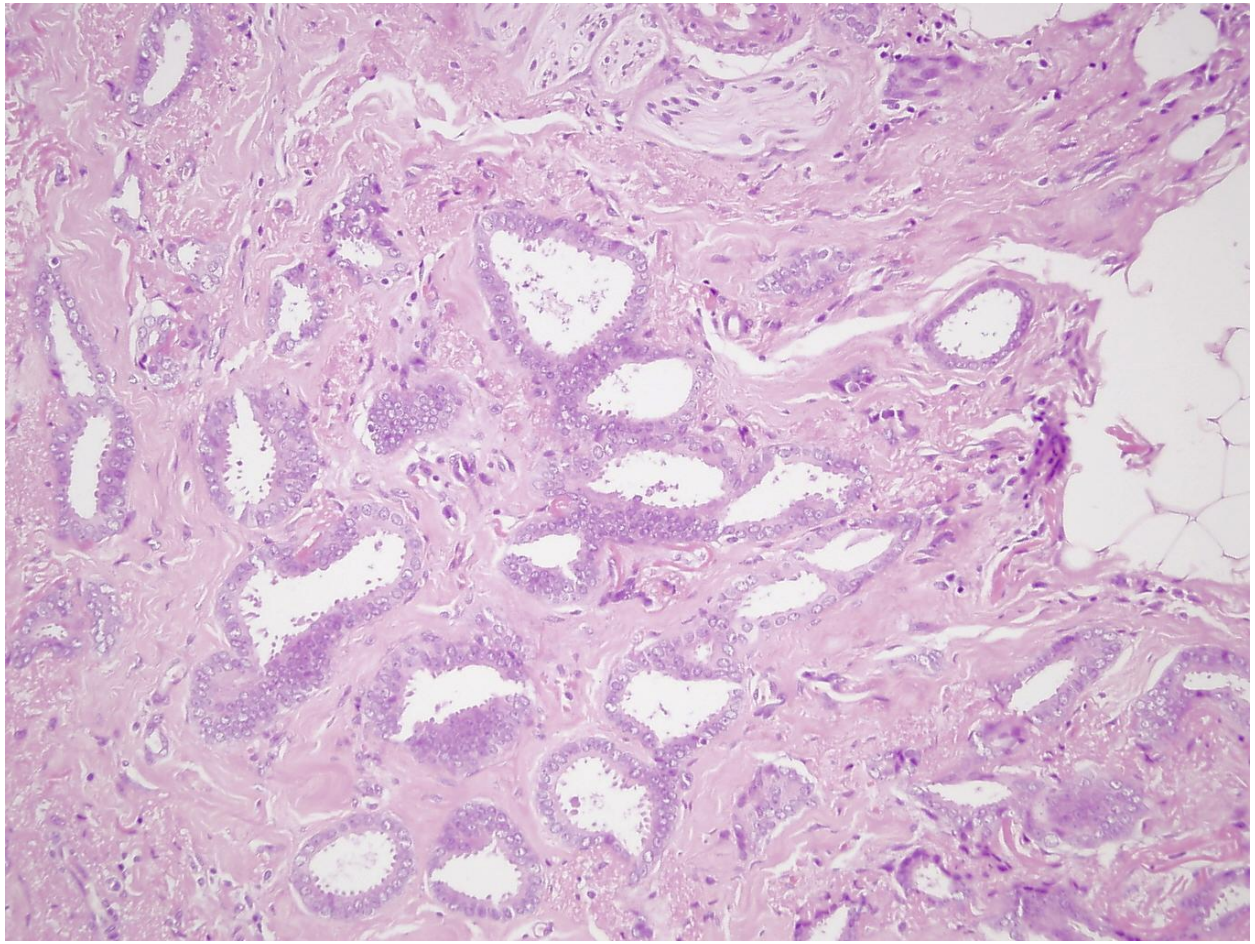


Invasive lobular carcinoma

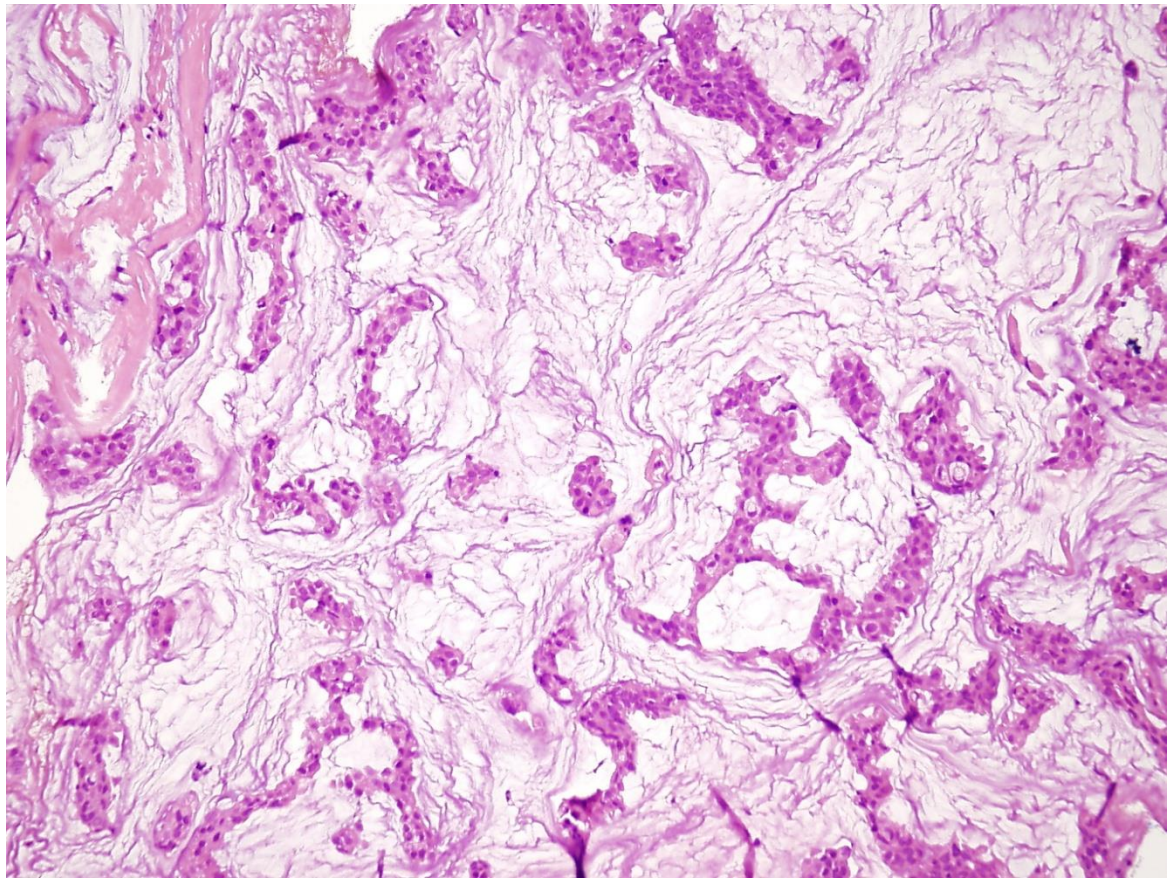
- Discohesive cells, single-file infiltrating pattern (*„Indian file")*, often targetoid (target like) pattern around enclosed normal ducts.

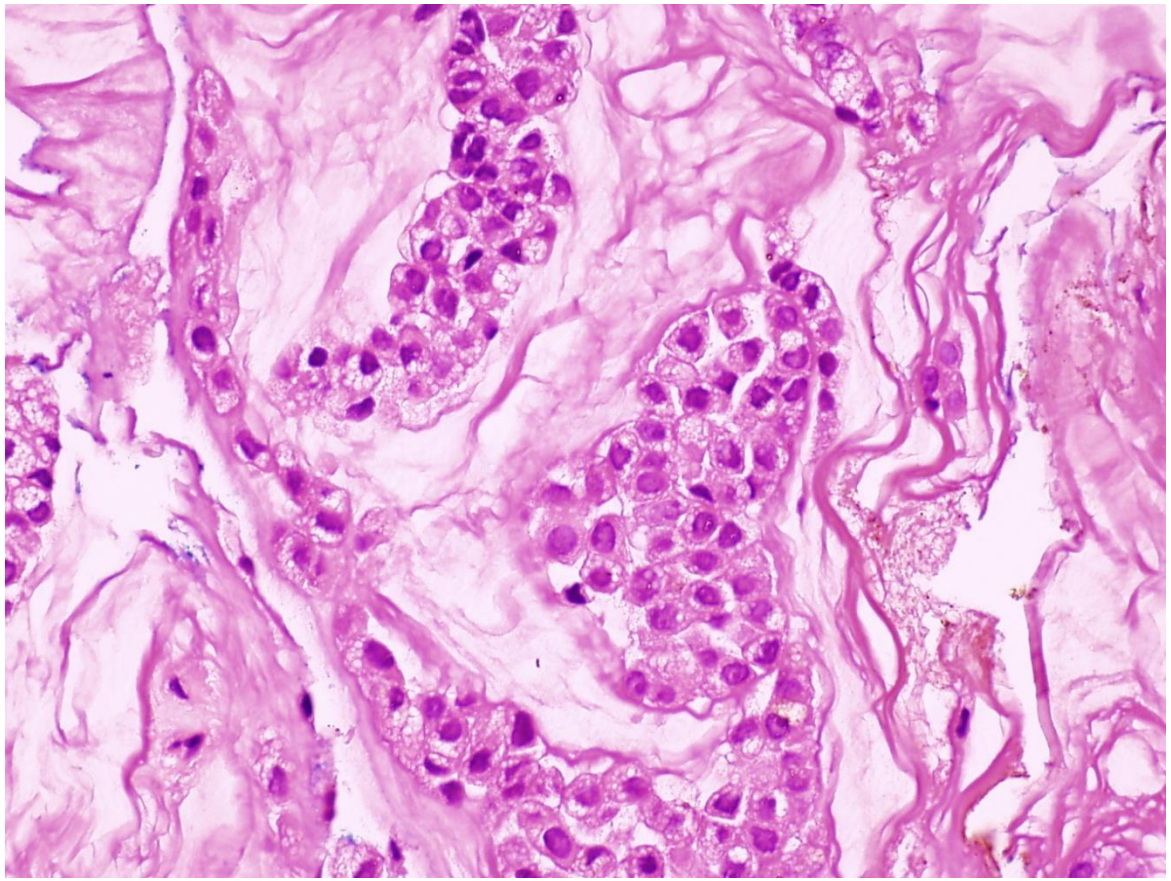


Tubular breast cancer: best prognosis



Mucinous breast cancer (colloid carcinoma)





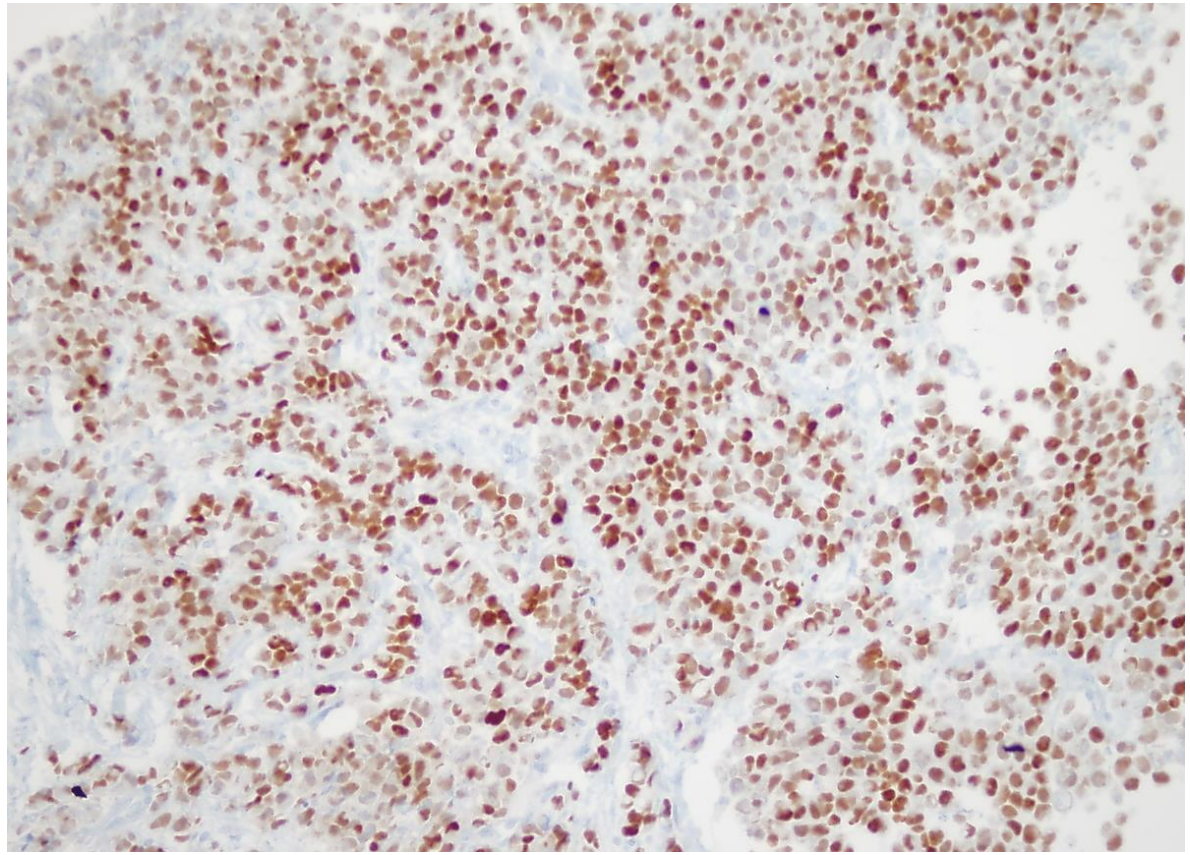
Immunohistochemistry

- Prognostic and predictive markers, always assessed during routine histological examination
  - **Estrogen**
  - **Progesterone**
  - **HER2**
  - **(Ki-67** (proliferation marker)

  Short-term and long-term therapy are based on these results!

Immunohistochemistry

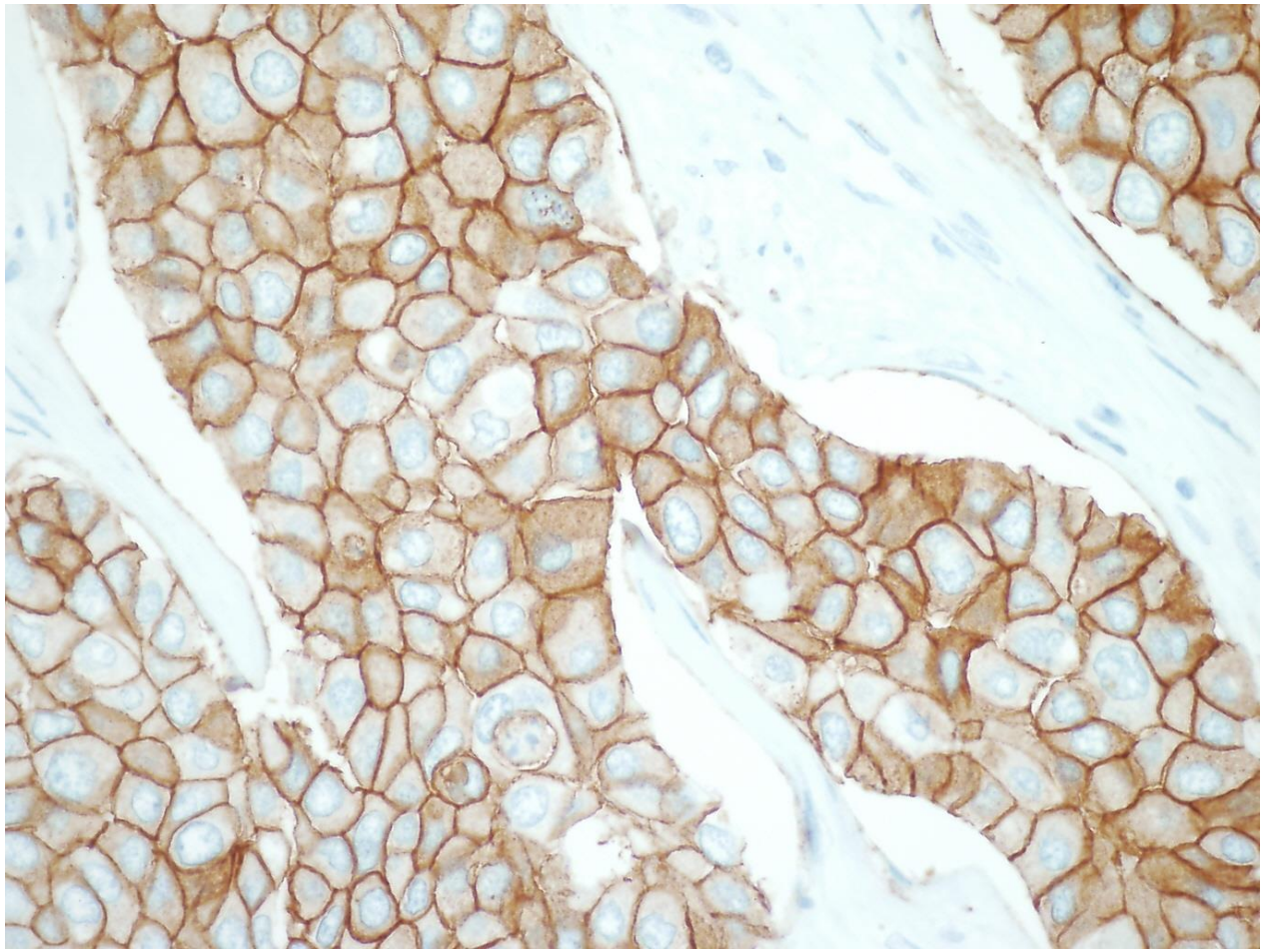
Estrogen and progesterone:
nuclear reactions
(Clinical significance: hormone therapy can be applied!)



Immunohistochemistry

HER2

In equivocal cases FISH examination can verify the HER2 status
Clinical significance: targeted antibody therapy (trastuzumab = Herceptin) or tyrosine kinase inhibitor therapy (Pertuzumab, etc.) can be applied



Immunohistochemistry

- **Ki-67: shows the degree of proliferation**
- Clinical significance: high Ki-67 index (fast-growing tumor) predicts high sensitivity to chemotherapy. (Chemotherapy affects proliferating cells!)