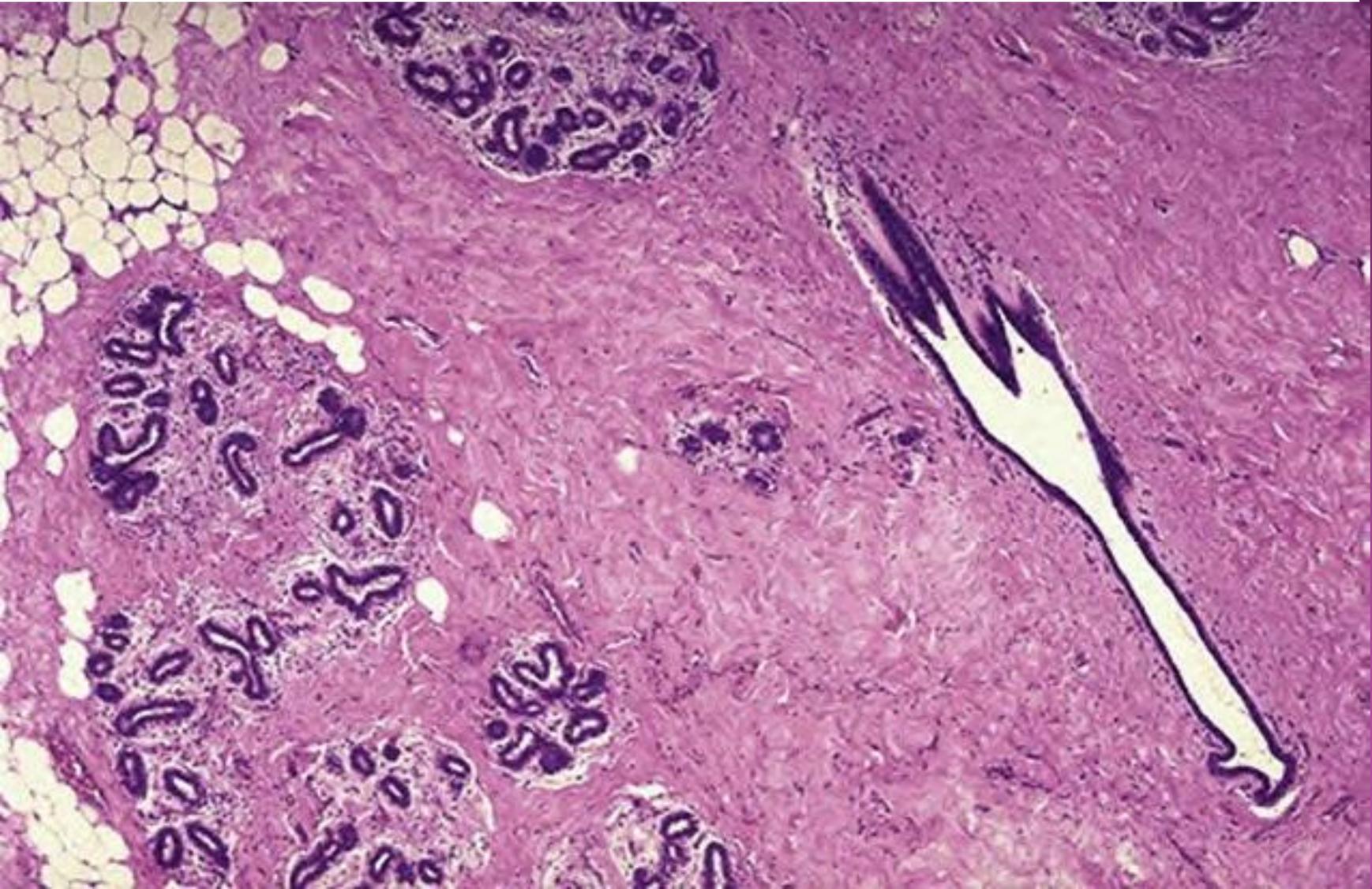


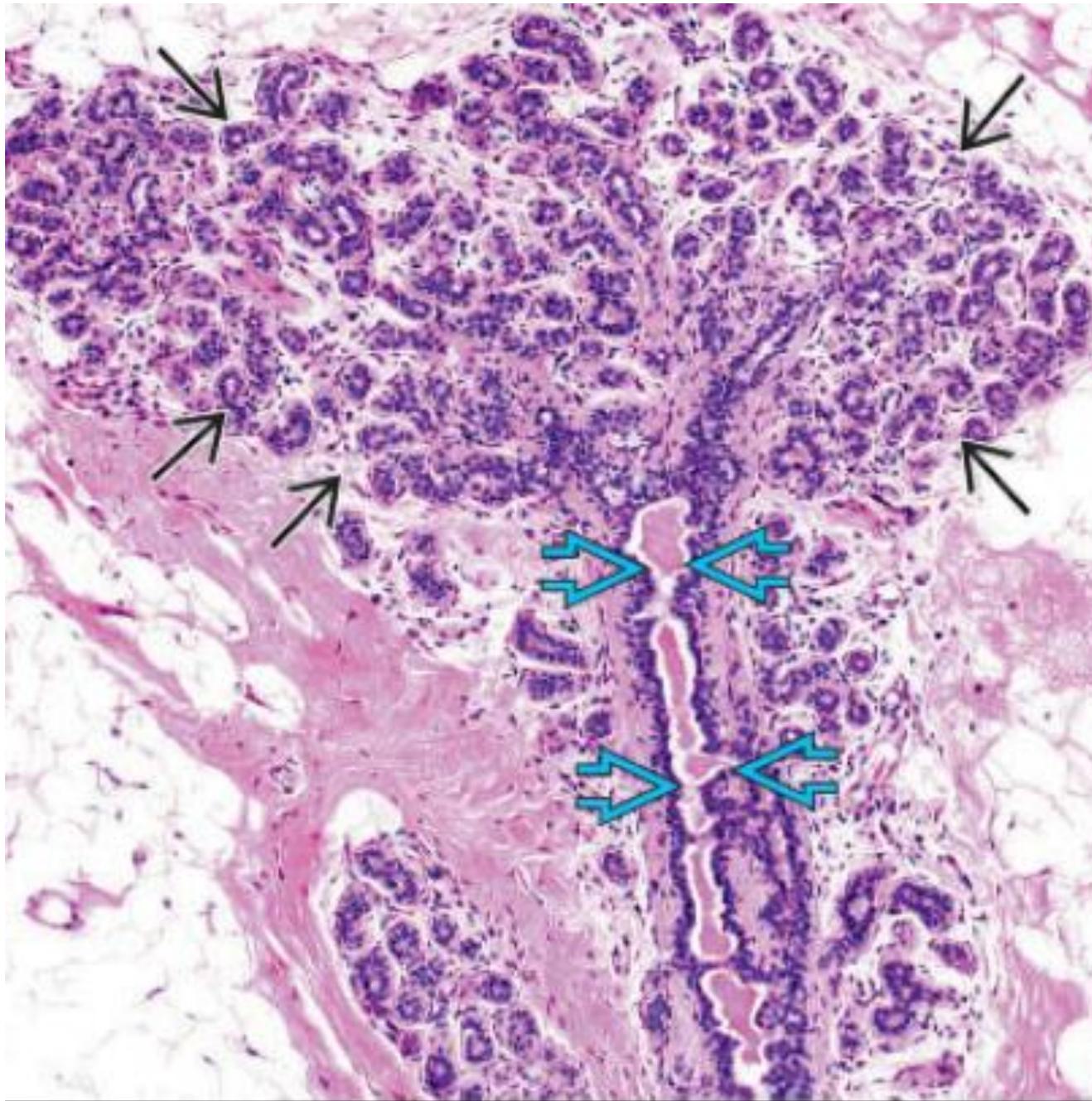
BREAST; STROMAL TUMORS, BENIGN EPITHELIAL LESIONS AND CARCINOMA IN SITU

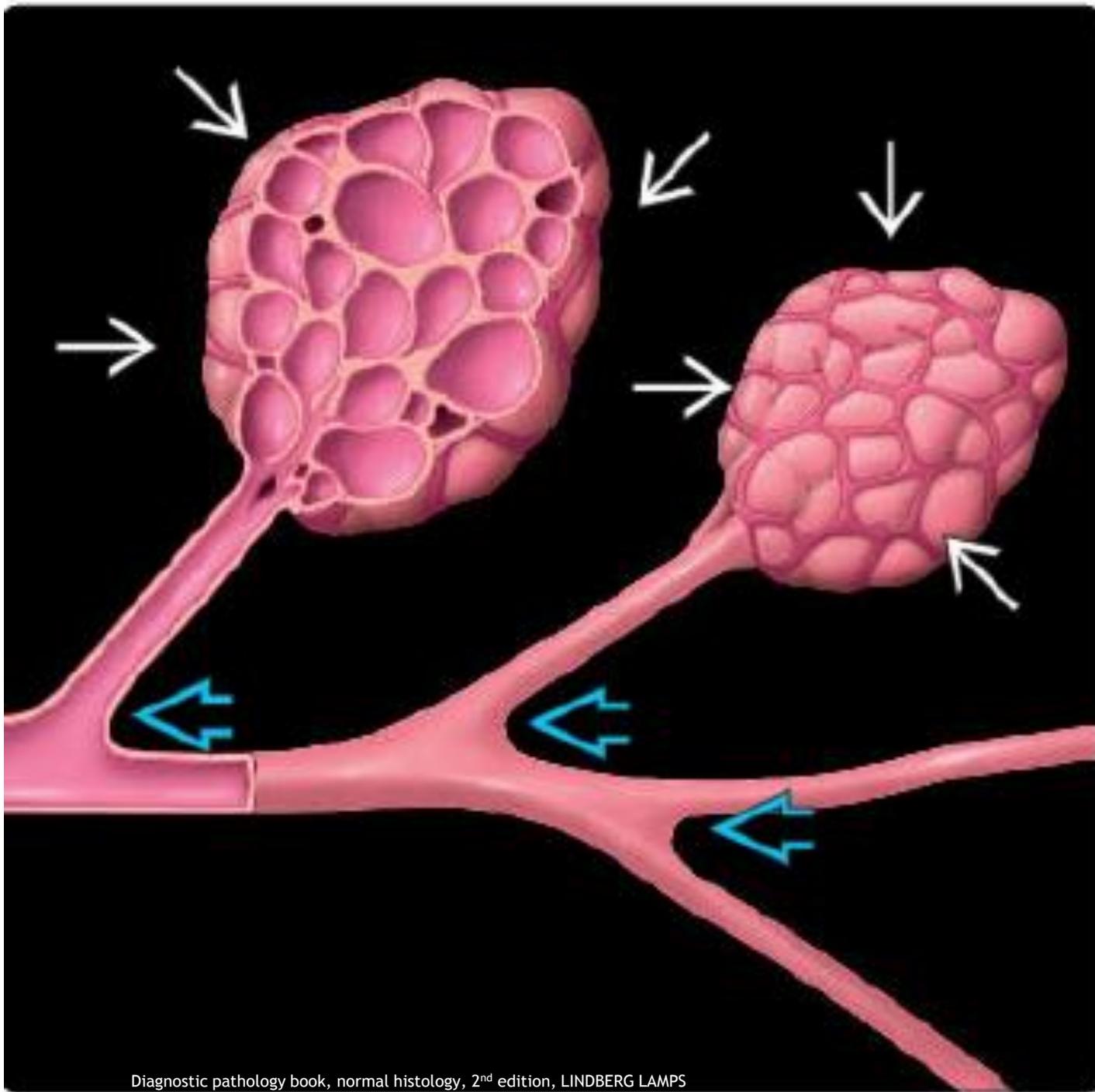
Maram Abdaljaleel, MD

Dermatopathologist and Neuropathologist
University of Jordan, School of Medicine

NORMAL BREAST, MICROSCOPIC







REGARDLESS OF THE SYMPTOM:

- The underlying cause is **benign** in >90% of cases.
- The likelihood of malignancy increases with **age**:
 - the risk of nipple discharge being due to cancer increases from 7% in women <60 years vs. 30% in women >60.
 - only 10% of palpable masses in women <40 years are carcinomas vs. 60% in women >50.

○ Of women with cancer:

- about 45% have symptoms
 - Palpable mass>>>> pain> nipple discharge > inflammatory changes
- the remainder come to attention through screening tests

MAMMOGRAPHIC SCREENING:

- ◉ detects early, nonpalpable asymptomatic breast carcinomas before metastasis.
- ◉ the average size of invasive carcinomas detected by mammography is about 1 cm, at this stage only 15% will have metastasized to regional lymph nodes
- ◉ The sensitivity and specificity of mammography increase with age → due to replacement of the fibrous, radiodense tissue of young women with the fatty, radiolucent tissue of older women

CLINICAL PRESENTATIONS OF BREAST DISEASE:

□ Pain:

- cyclic: diffuse, premenstrual edema and swelling.
- noncyclic: Localized, ruptured cyst or physical trauma, or infection
- Almost all painful masses are **benign** except for 10% of cases that relates to cancers

□ Inflammation:

- causes edematous and erythematous breast.
- most often caused by infections (during lactation and breastfeeding).
- An important mimic of inflammatory breast cancer

□ ***Nipple discharge:***

- **Normal:** when small in quantity and bilateral.
- **Milky discharges (galactorrhea):**
 - are associated with elevated prolactin levels (pituitary adenoma), hypothyroidism, or endocrine anovulatory syndromes, patients taking OCPs, tricyclic antidepressants, methyldopa, or phenothiazines.
- **Bloody or serous discharges:**
 - commonly due to large duct papillomas and cysts.
 - During pregnancy, result from the rapid growth and remodeling of the breast.
- **BUT spontaneous, unilateral, and bloody discharge increases concern for malignancy.**

□ ***Palpable masses:***

- 95% are benign
- all palpable masses require evaluation.
- **The most common palpable lesions are cysts, fibroadenomas, and invasive carcinomas**
- generally detected when they are 2 to 3 cm in size.

□ ***Gynecomastia:***

- The only common breast symptom in **males**.
- resulting from an imbalance between estrogens, which stimulate breast tissue, and androgens, which counteract these effects.

INFLAMMATORY PROCESSES:

- rare
- caused by infections, autoimmune disease, or foreign body-type reactions.
- Clinically: erythema, edema, pain and focal tenderness.
- The only infectious agent is ***Staphylococcus aureus***
- Enters via fissures in nipple skin during the first weeks of breastfeeding → lactational abscesses
- If untreated, tissue necrosis → fistula tracks opening onto the skin.

- **Treatment:** antibiotics and continued expression of milk. Rarely, surgical incision and drainage is required.
- **Note:** Because inflammatory diseases are rare, the possibility that the symptoms are caused by inflammatory carcinoma **should always be considered**

STROMAL NEOPLASMS:

- ⦿ The two types of stroma: intralobular and interlobular
- ⦿ tumors arising from **Intralobular** stroma:
 - specialized stroma may elaborate growth factors resulting in proliferation of the non-neoplastic epithelial component of these tumors
 - **biphasic tumors:** comprised of both stromal cells and epithelial cells
 - **fibroadenoma and phyllodes tumor**

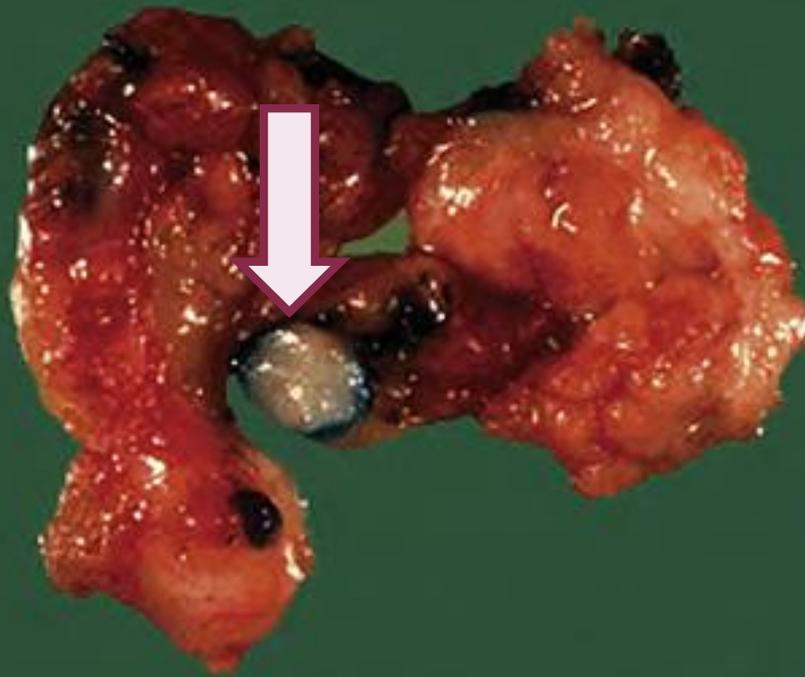
- Tumors arising from **Interlobular** stroma:
 - Monophasic tumors (only mesenchymal cells)
 - same types of tumors found in **other sites** of the body (lipomas and angiosarcomas) as well as tumors **arising more commonly in the breast** (pseudoangiomatous stromal hyperplasia and myofibroblastomas,).

- The only malignancy derived from **interlobular** stromal cells of note is **angiosarcoma**

FIBROADENOMA

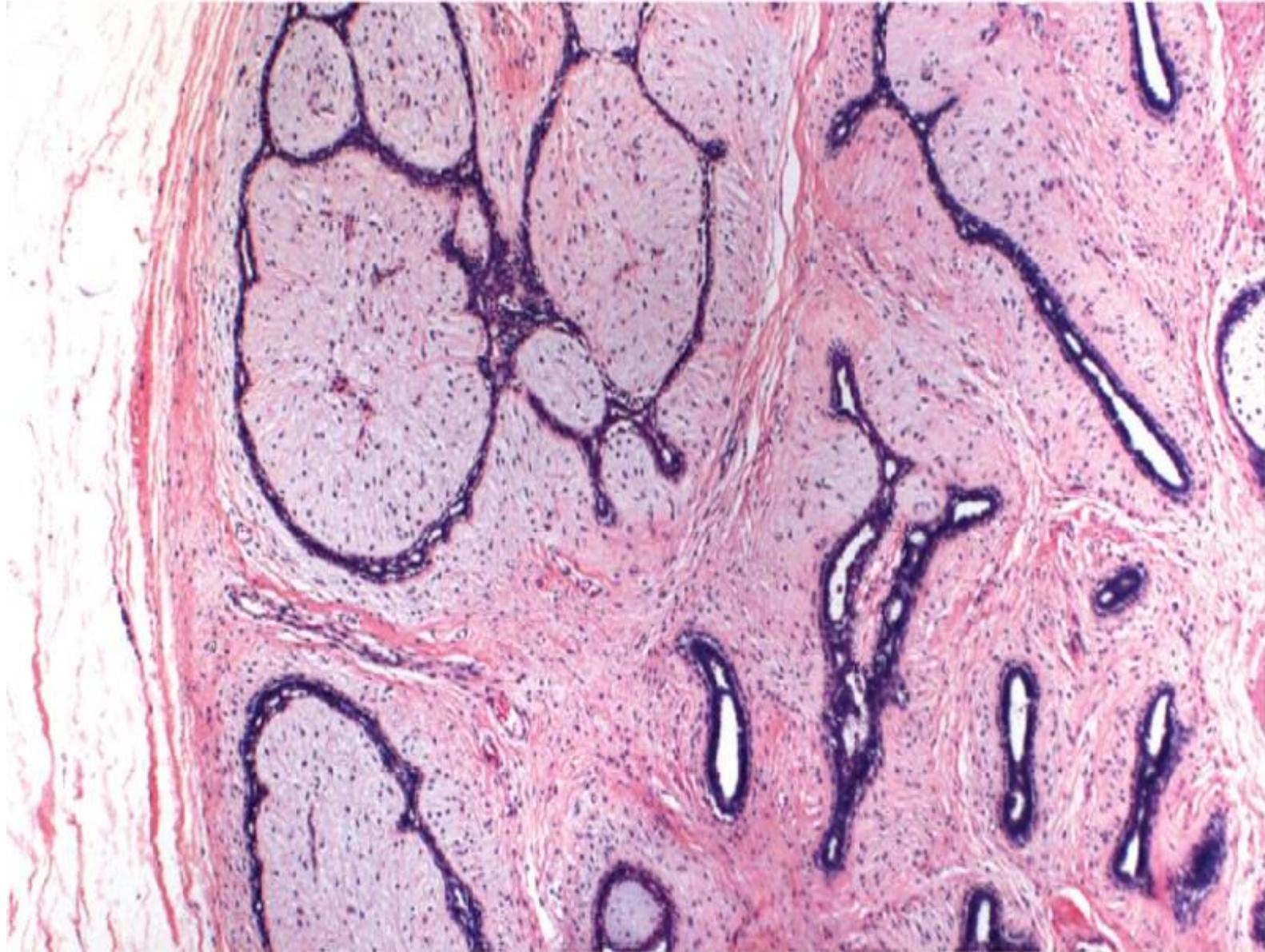
- The **most common benign neoplasm** of the female breast.
- Related to **estrogen activity**:
 - may enlarge late in the menstrual cycle and during pregnancy.
 - After menopause they usually regress and calcify.
- 20s and 30s women
- frequently multiple and bilateral
- discrete, solitary, freely movable nodule, (1-10 cm).
- usually easily "shelled out" surgically.

FIBROADENOMA, GROSS



4 cm

FIBROADENOMA



PHYLLODES TUMOR

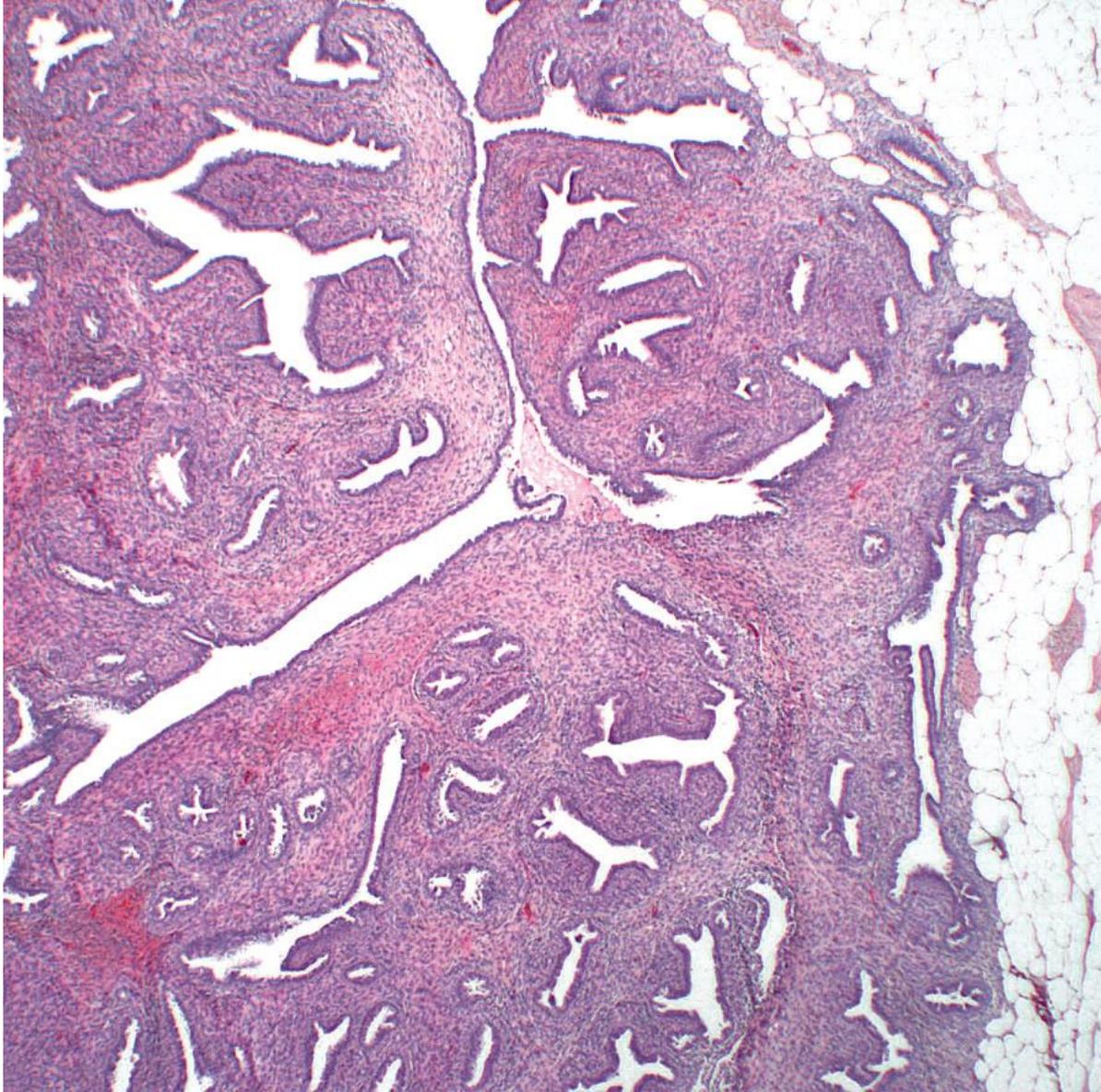
- Much less common than fibroadenomas
- Arise from the intralobular stroma and not from preexisting fibroadenomas.
- most present in the sixth decade
- Leaf-like clefts and slits →
 - due to the presence of nodules of proliferating stroma covered by epithelium
 - they have been designated phyllodes (Greek for "leaflike")

⊙ phyllodes tumors:

- Mostly low-grade → occasionally recurrence locally & do not metastasize.
 - Intermediate grade → often recur locally unless they are treated with wide excision or mastectomy.
 - high-grade → uncommon, give rise to distant hematogenous metastases in 1/3 of cases.
- ⊙ 70% are benign and tend to remain localized and cured by excision.

- The most worrying change → higher cellularity, higher mitotic rate, nuclear pleomorphism, stromal overgrowth, and infiltrative borders.

PHYLLODES TUMORS



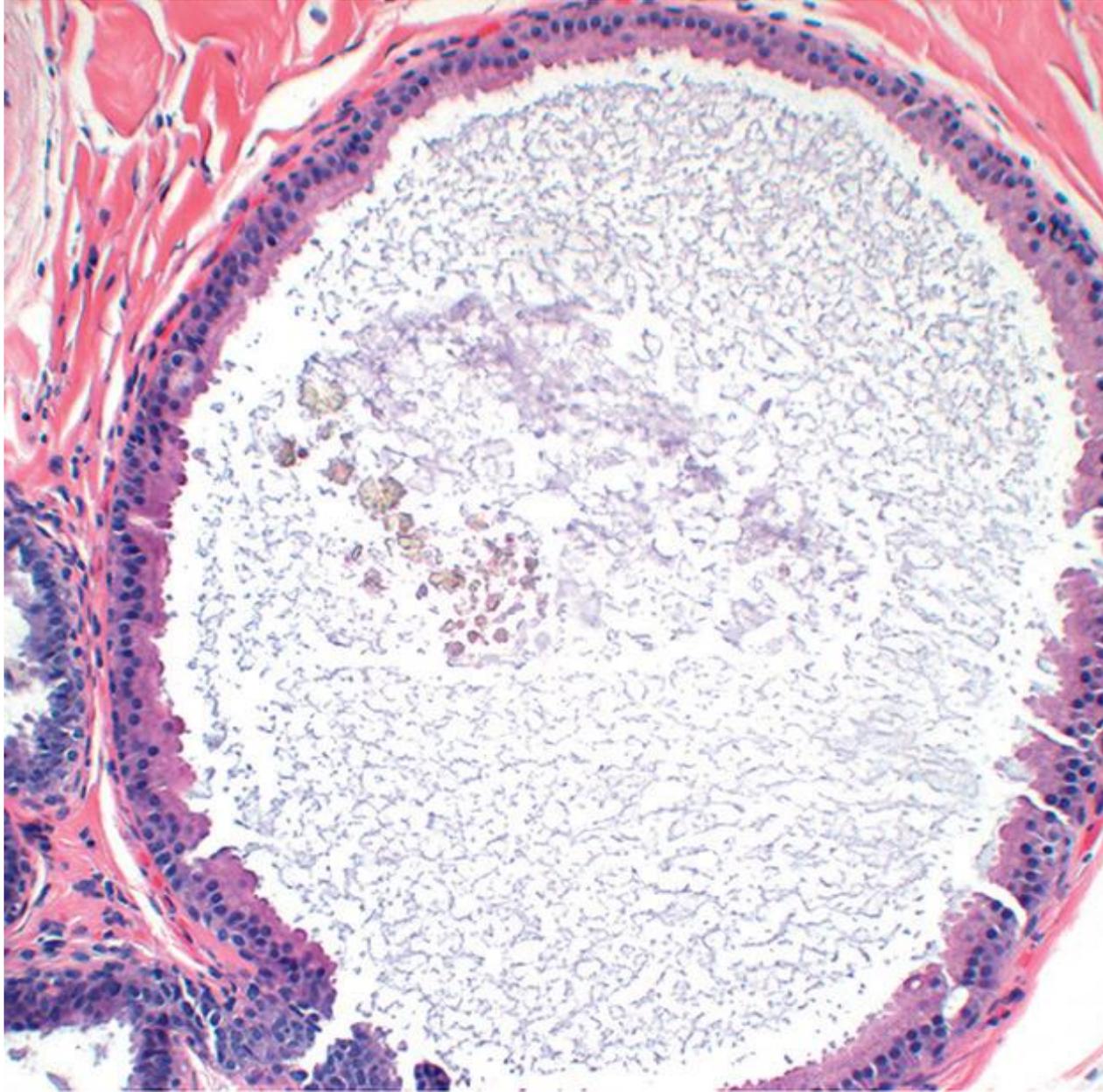
BENIGN EPITHELIAL LESIONS:

- ◉ The majority are incidental findings detected by mammography.
- ◉ Benign changes are divided into three groups:
 - **Nonproliferative changes:** is not associated with an increased risk of breast cancer.
 - **Proliferative disease without atypia:** polyclonal hyperplasias & associated with 1.5-2 folds increase risk of breast cancer.
 - **Proliferative disease with atypia:** monoclonal “**precancers**” & associated with 4-5 folds increase risk of breast cancer in **both** breast

NONPROLIFERATIVE BREAST CHANGES (FIBROCYSTIC CHANGES)

- ◉ Common
- ◉ There are three principal morphologic changes:
 - (1) cystic change, often with apocrine metaplasia (most common)
 - (2) Fibrosis
 - (3) adenosis
- ◉ H/P: Those lesions contain single layers of epithelial

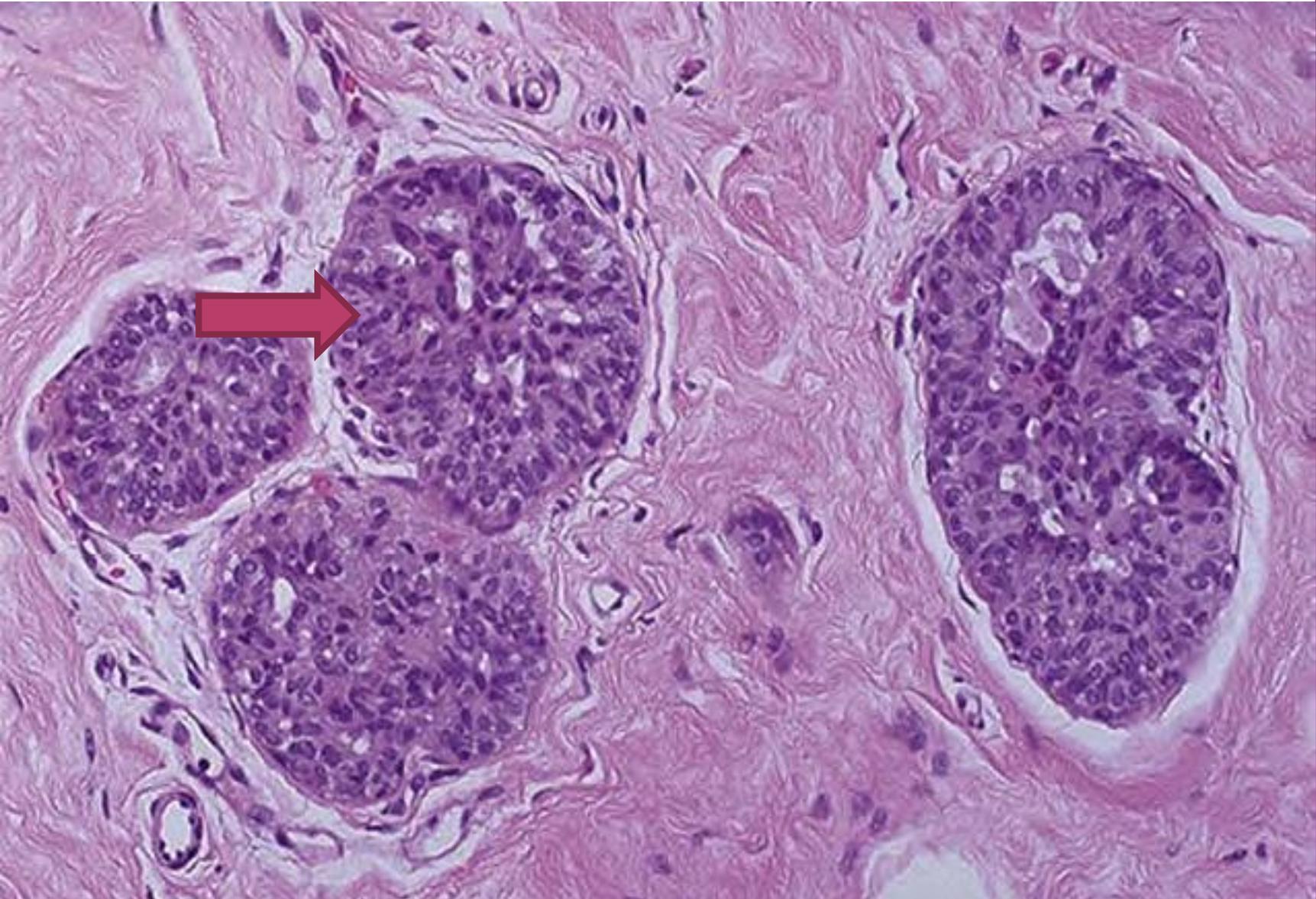
NONPROLIFERATIVE DISEASE. AN APOCRINE CYST



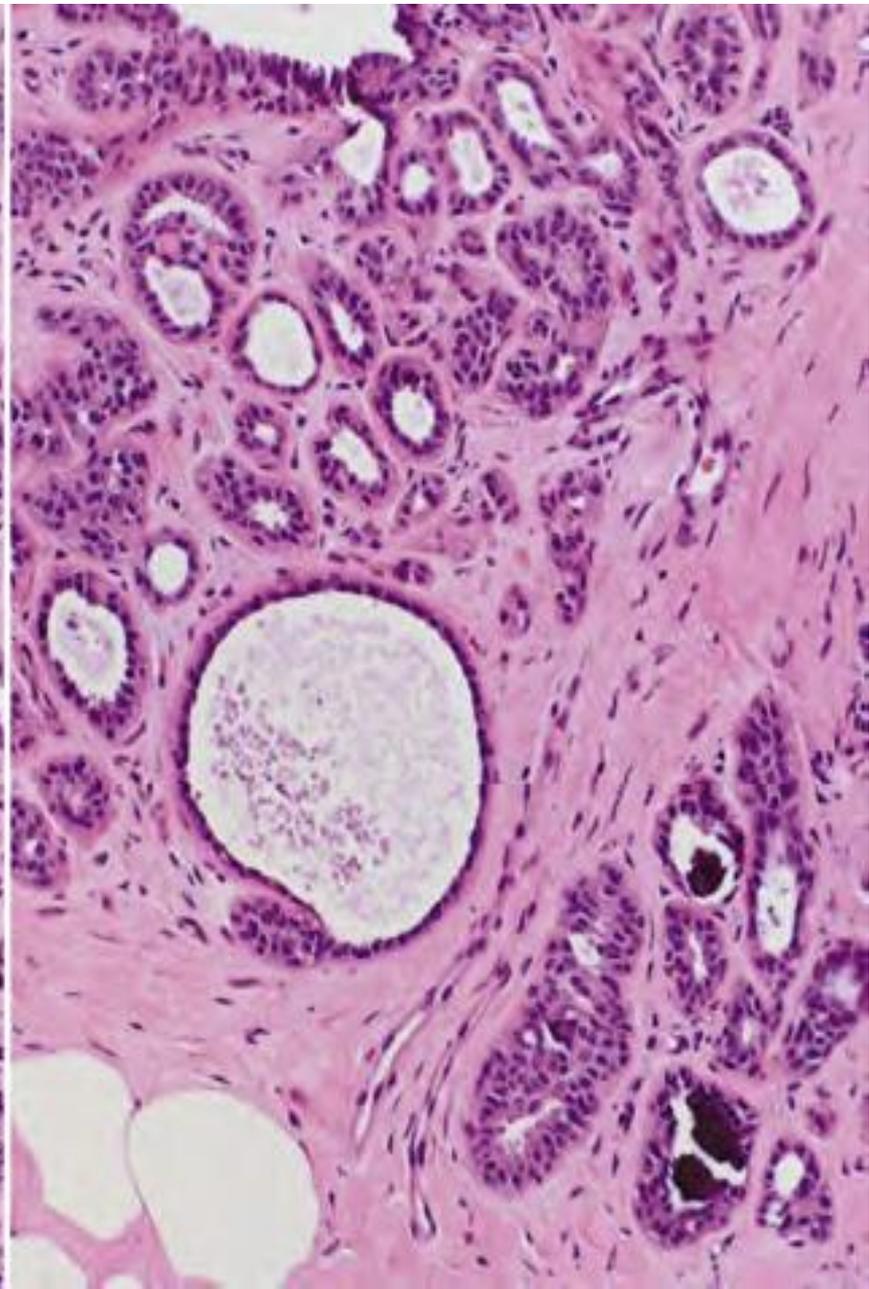
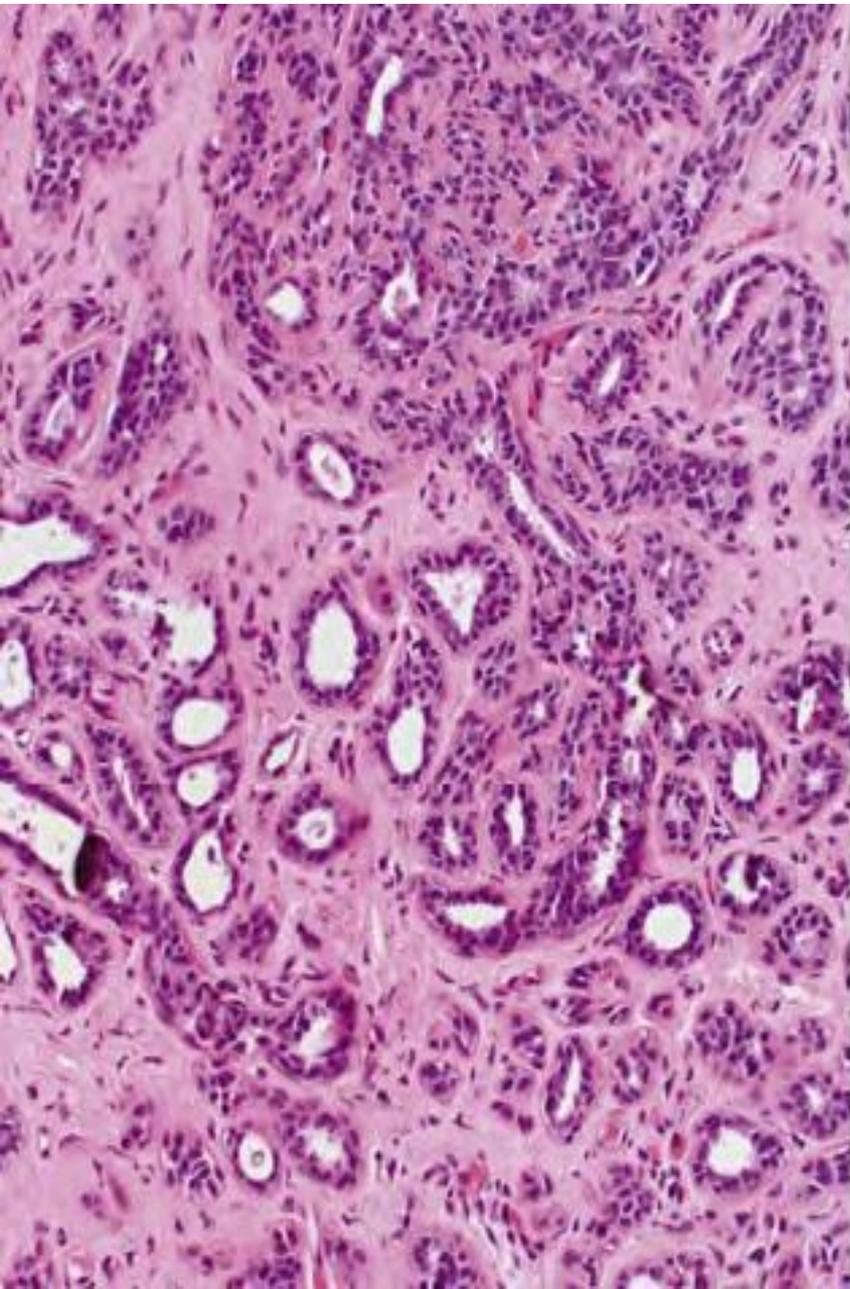
PROLIFERATIVE DISEASE WITHOUT ATYPIA

- Includes:
 - epithelial hyperplasia
 - sclerosing adenosis
 - complex sclerosing lesion
 - papilloma
- associated with varying degrees of epithelial cell proliferation.
- **associated with a small increase in the risk of subsequent carcinoma in either breast.**
- not clonal and are not commonly found to have genetic changes.
- are predictors of risk but unlikely to be true precursors of carcinoma.

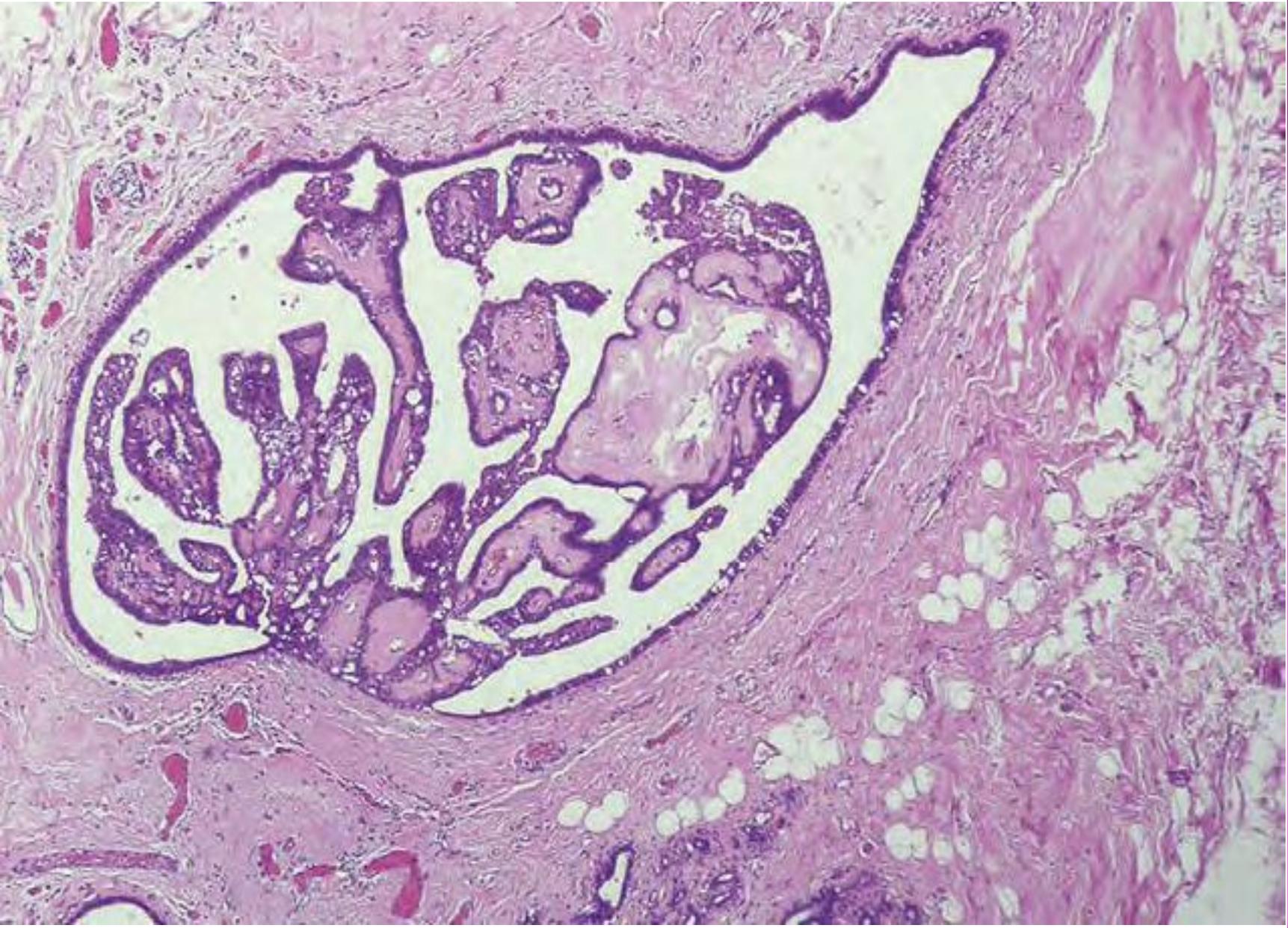
epithelial hyperplasia → the epithelial cells are multilayered, filling the ducts or acini; myoepithelial cells are increased. there is no epithelial cell atypia



Sclerosing adenosis:



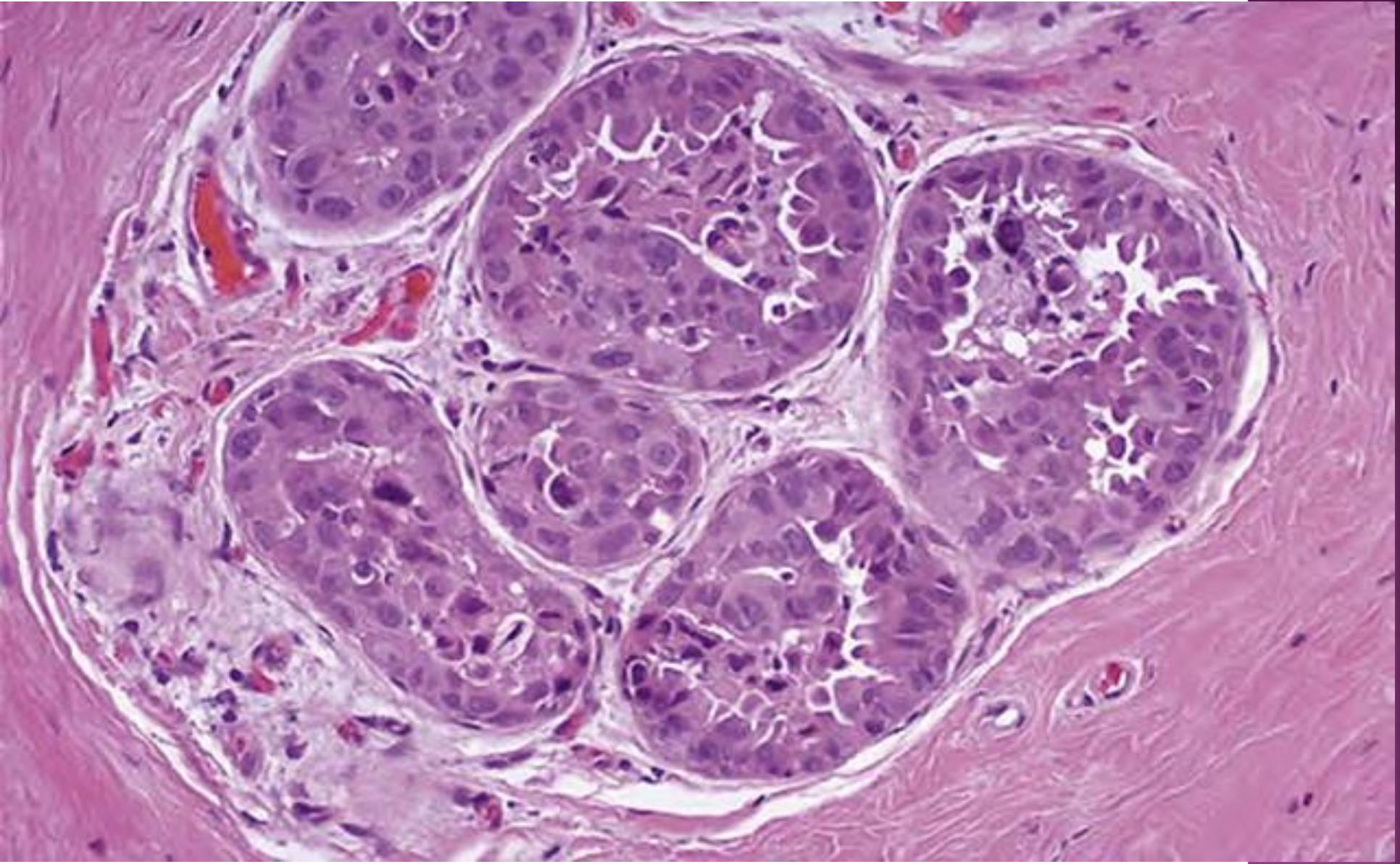
intraductal papilloma in a breast duct.



PROLIFERATIVE DISEASE WITH ATYPIA

- ⦿ **atypical lobular hyperplasia (ALH):** resembles lobular carcinoma in situ (LCIS)
- ⦿ **atypical ductal hyperplasia (ADH):** resembles ductal carcinoma in situ (DCIS)
- ⦿ are clonal proliferations having some, but not all, histologic features that are required for the diagnosis of carcinoma in situ.
- ⦿ Associated with a moderately increased risk of carcinoma

atypical ductal hyperplasia →



NONINVASIVE (IN SITU) CARCINOMA

- ◉ **include:**
 1. Ductal carcinoma in situ, DCIS
 2. Lobular carcinoma in situ, LCIS
- ◉ both types arise from cells in the terminal duct that give rise to lobules.
- ◉ LCIS usually expands involved lobules, whereas DCIS distorts lobules into duct like spaces
- ◉ **By definition both confined by a basement membrane and do not invade into stroma or lymphovascular channels**

LOBULAR CARCINOMA IN-SITU (LCIS)

- Malignant clonal proliferation of cells within ducts and lobules
- Cells grow in a discohesive fashion → an **acquired loss of the tumor suppressive adhesion protein E-cadherin.**
- The term “lobular” was used to describe this lesion because the cells expand but do not distort involved spaces and, thus, the underlying lobular architecture is preserved.

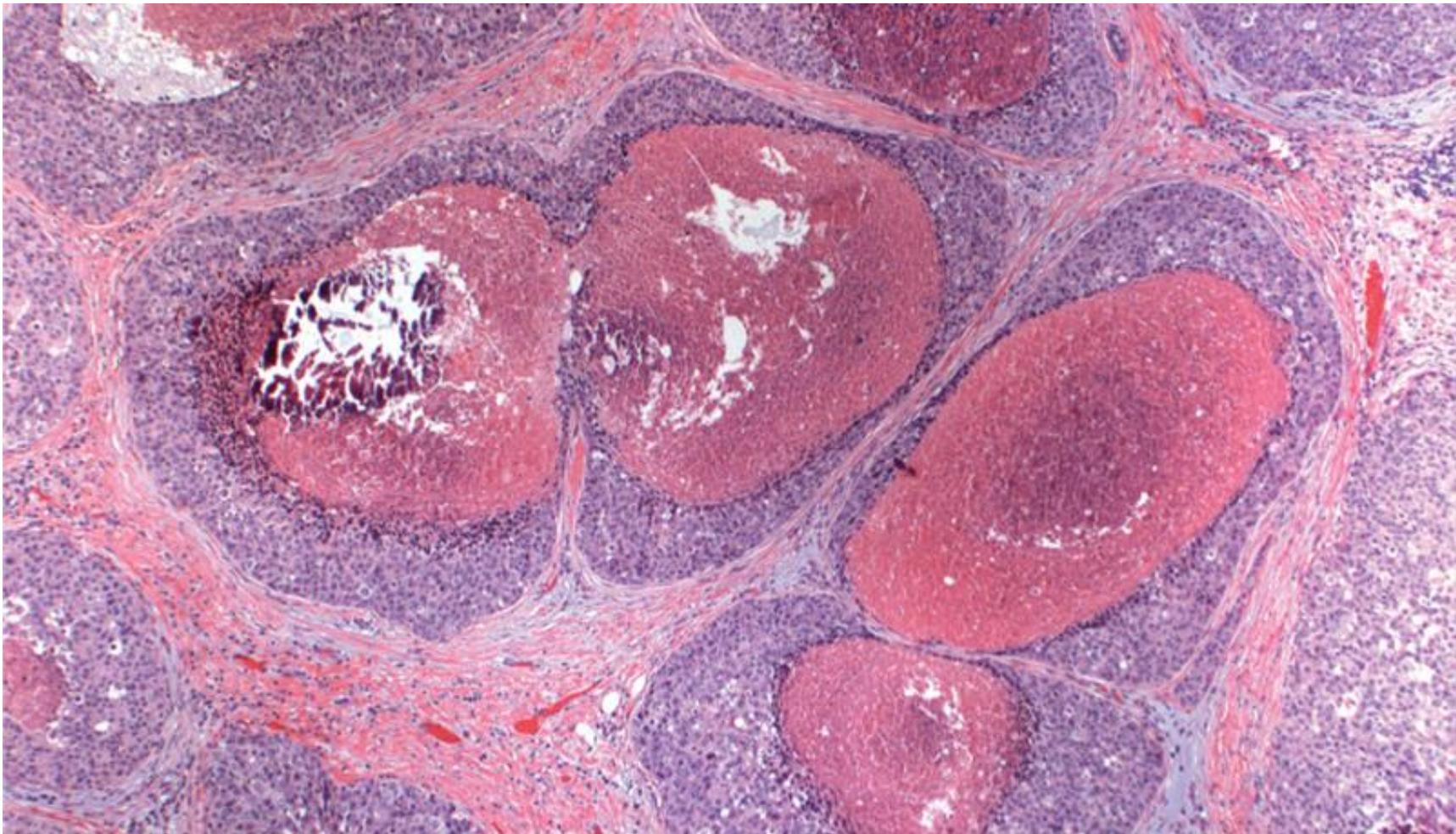
DUCTAL CARCINOMA IN-SITU (DCIS)

- malignant clonal proliferation of epithelial cells within ducts and lobules.
- DCIS has a wide variety of histologic appearances including:
 - solid, comedo, cribriform, papillary, and micropapillary
- Ranges from low to high nuclear grade (pleomorphic).
- **comedo** subtype:
 - *extensive central necrosis*. (The name derives from the toothpaste-like necrotic tissue).
 - **Frequently associated with Calcifications** → detected by mammography

DCIS MANAGEMENT:

- The prognosis : excellent (97% long-term survival **after** simple mastectomy)
- Current treatment strategies: surgery and irradiation, tamoxifen
- Significance: adjacent invasive CA; become invasive if untreated (1/3 of cases)

COMEDO DCIS: HIGH-GRADE PROLIFERATION ASSOCIATED WITH LARGE CENTRAL ZONES OF NECROSIS AND CALCIFICATIONS FILLS SEVERAL DUCTS.



REFERENCES:

- ◉ Diagnostic pathology book, normal histology, 2nd edition, LINDBERG LAMPS
- Robbins basic pathology, 10th edition
- Robbins and Cortan Atlas of Pathology, 3rd edition

THANK YOU