

Proliferative Breast Disease Without Atypia

Morphology, clinical presentation, differential diagnosis, and risk

Usual ductal hyperplasia · Sclerosing adenosis · Radial scar · Papilloma

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Learning objectives

- Identify the four principal histologic patterns of proliferation without atypia.
- Explain how each lesion alters ducts, acini, or stromal architecture.
- Connect characteristic morphology to mammographic findings and symptoms.
- Distinguish risk indicators and carcinoma mimics from precursor lesions.

Three groups of benign epithelial breast changes

Group	Biologic interpretation	Cancer association
Nonproliferative changes	Common cystic, fibrotic, and adenotic changes	Baseline reference group
Proliferation without atypia	Epithelial proliferation with benign cytology	Small bilateral risk increase
Proliferation with atypia	Atypical, often clonal epithelial proliferation	Greater risk; precursor context

Classification is based on subsequent cancer risk, not on palpability.

Risk indicator does not mean direct precursor

- Carcinoma risk is increased in both breasts.
- The benign lesion need not evolve into carcinoma itself.
- The category predicts population-level risk; It is not a diagnosis of malignancy.

Either breast

And

Either breast

Bilateral risk association $\neq$ inevitable progression

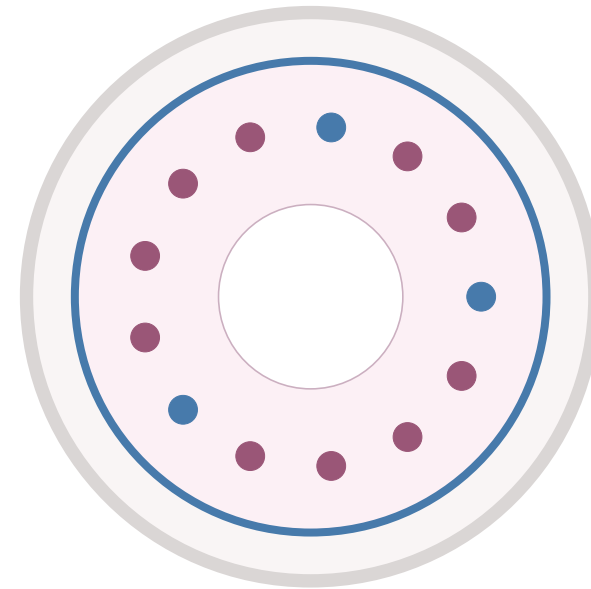
Schematic — not a histologic specimen

How these lesions enter the diagnostic pathway

- Mammographic densities may prompt evaluation.
- Calcifications may lead to biopsy.
- Some lesions produce a palpable mass or nipple discharge.
- Others are incidentally found in biopsies taken for unrelated findings.

Normal duct architecture is the morphologic reference

- A normal duct–lobular unit contains luminal epithelium and an outer myoepithelial layer.
- The distinction between lumen, lining cells, and surrounding stroma is essential.
- Proliferations are recognized by how they modify this baseline arrangement.



Normal duct (simplified cross-section)

Schematic — not a histologic specimen

Normal epithelial compartments

Luminal cells

- Face the duct or acinar lumen.
- Provide the epithelial lining.
- Appear larger and more open-nucleated in the Robbins example.

Myoepithelial cells

- Form the abluminal layer.
- Are relatively compact in the Robbins example.
- Their distribution provides architectural context.

Four proliferative patterns: First-pass recognition

Lesion	Dominant architectural alteration
Usual ductal hyperplasia	Mixed epithelial proliferation filling ducts/lobules
Sclerosing adenosis	Increased acini compressed by fibrosis
Radial scar	Central fibrous nidus with radiating glandular projections
Intraductal papilloma	Branching fibrovascular cores within a dilated duct

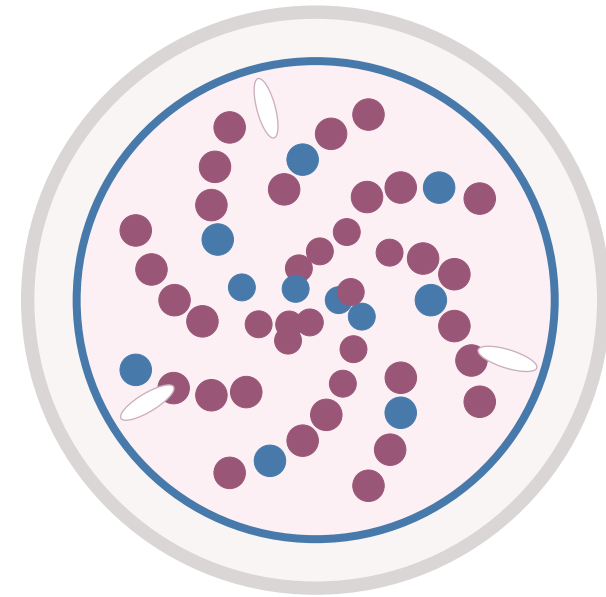
Breast epithelial change and subsequent invasive cancer risk

Textbook category	Relative risk (vs reference)
Nonproliferative breast changes	1.0
Proliferative disease without atypia	1.5–2
Proliferative disease with atypia	4–5
Carcinoma in situ	8–10

These are category-level epidemiologic associations Table 23.1, not individual patient predictions.

Usual ductal hyperplasia: Defining alteration

- Increased numbers of epithelial cells expand ducts or lobules.
- The population includes both luminal and myoepithelial cell types.
- Cytologic atypia is not the defining feature.

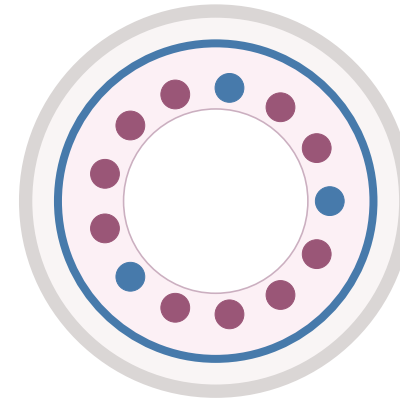


Mixed cells; Irregular peripheral fenestrations

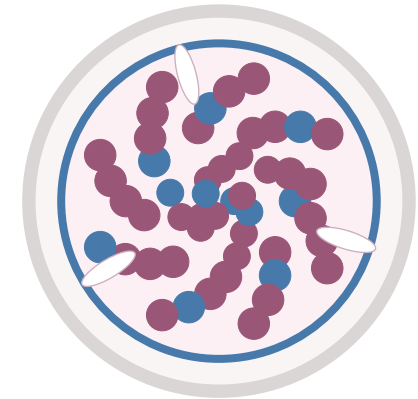
Schematic — not a histologic specimen

Usual ductal hyperplasia compared with normal

- Normal structure retains an open lumen and limited epithelial lining.
- Usual ductal hyperplasia fills and distends the space.
- Irregular residual spaces are often pushed toward the periphery.



Normal



UDH

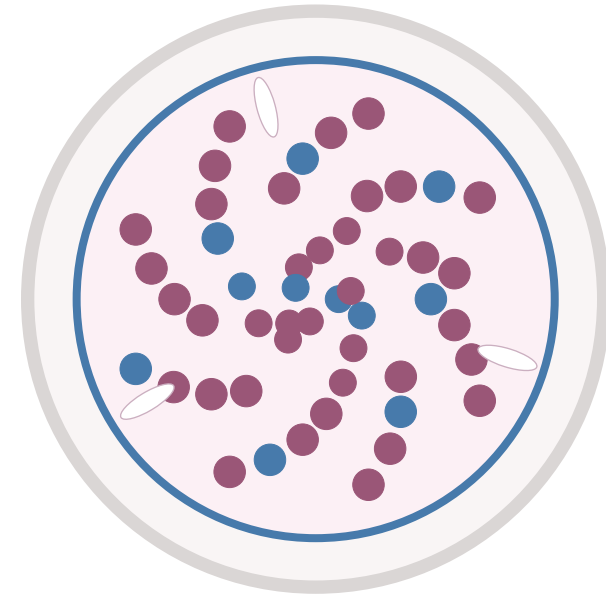
Schematic — not a histologic specimen

A heterogeneous cell population in usual hyperplasia

- The cellular proliferation contains luminal and myoepithelial elements.
- Cell types are intermingled rather than uniformly repeated.
- Heterogeneity is highlighted in the Robbins figure description.
- Assess architecture as well as individual nuclear appearance.

Peripheral slit-like lumens in usual hyperplasia

- Irregular slit-shaped openings may persist within the cellular mass.
- These openings are especially apparent around the periphery.
- They reflect the architecture of the expanding mixed-cell proliferation.



Mixed cells; Irregular peripheral fenestrations

Schematic — not a histologic specimen

Usual ductal hyperplasia: Immunostain correlation

- Robbins Fig. 23.6 demonstrates p63 in myoepithelial cells around a normal lobule.
- Its CK14 example of usual hyperplasia shows a mixed cell population.
- The teaching role of these stains is to support interpretation of cell distribution.
- Neither stain should substitute for examination of the overall H&E pattern.

Usual hyperplasia versus atypical ductal hyperplasia

Usual ductal hyperplasia

- Mixed luminal and myoepithelial cell population.
- Irregular slit-like fenestrations.
- Usually incidental; Risk category depends on degree.

Atypical ductal hyperplasia

- Monomorphic, regularly spaced cells.
- May exhibit cribriform or micropapillary structures.
- Resembles low-grade in situ carcinoma but has limited extent.

Why usual hyperplasia is often clinically silent

- The lesion often occurs as a microscopic proliferation within ducts/lobules.
- It is typically an incidental biopsy finding.
- Clinical sampling may instead be prompted by imaging findings associated with the specimen.
- Absence of symptoms does not determine the histologic category.

Extent matters when classifying usual hyperplasia

Morphologic degree	Placement in Robbins Table 23.1
Mild usual ductal hyperplasia	Nonproliferative / reference-risk group
Moderate or florid usual ductal hyperplasia	Proliferative disease without atypia

A diagnosis of “usual ductal hyperplasia” alone does not convey the grading distinction used in the risk table.

Usual hyperplasia: The structural reading sequence

- Identify the affected duct or lobule.
- Check whether it is filled or expanded by cells.
- Seek a heterogeneous epithelial population and slit-like peripheral spaces.



Schematic — not a histologic specimen

High-yield histologic checklist: Usual hyperplasia

- Increased epithelial cell count.
- Luminal and myoepithelial elements mixed within the proliferation.
- Ducts or lobules filled and distended.
- Residual irregular peripheral fenestrations.
- Correlate degree of hyperplasia with risk classification.

Case: An incidental crowded duct

A core specimen obtained for an unrelated imaging abnormality contains an expanded duct filled by mixed epithelial cells, with peripheral slit-like lumens.

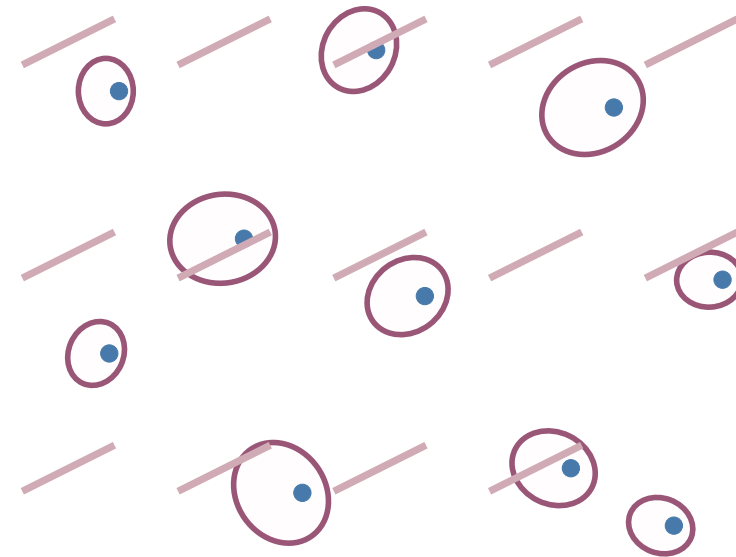
What benign proliferative pattern is represented?

Interpretation: Usual ductal hyperplasia

The combination of mixed cells, ductal distension, and irregular peripheral spaces supports the usual pattern.

Sclerosing adenosis: Proliferation of acini plus fibrosis

- The number of acini in a glandular unit increases.
- Stromal fibrosis compresses and distorts the expanded acinar population.
- Both the epithelial proliferation and its fibrotic environment define the lesion.

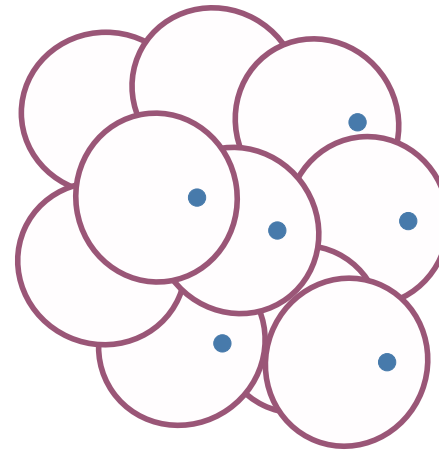


Schematic acini in fibrotic stroma

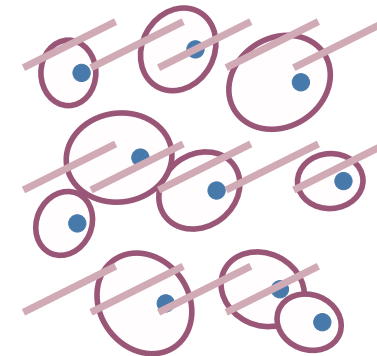
Schematic — not a histologic specimen

Adenosis is not the same as sclerosing adenosis

- Adenosis denotes increased acini per lobule.
- Sclerosing adenosis adds a pronounced fibrotic component.
- Fibrosis changes the shape and recognizability of glandular lumens.



Adenosis



Sclerosing adenosis

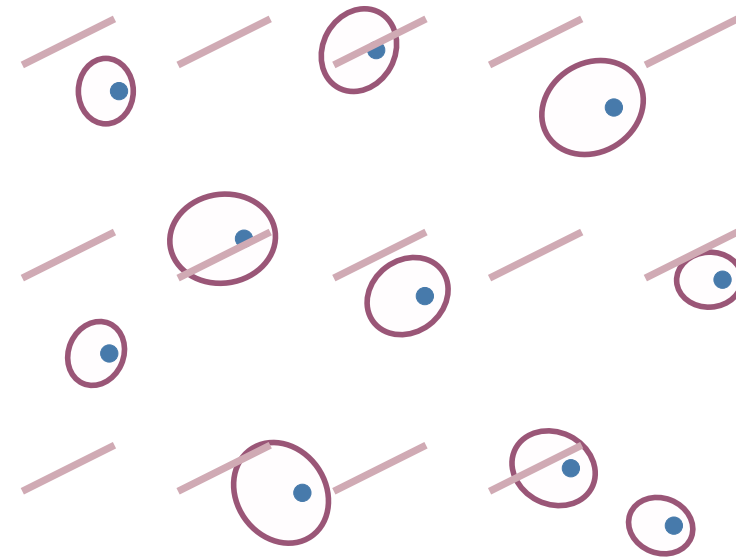
Schematic — not a histologic specimen

Sclerosing adenosis: The proliferative component

- More acini are present in the affected terminal duct–lobular unit.
- They remain glandular elements despite distortion.
- Architectural crowding should be interpreted together with surrounding stroma.

Dense stromal fibrosis is the sclerosing component

- Fibrous stroma increases around the acini.
- The stromal response physically compresses glandular structures.
- This produces tissue firmness and a deceptively complex microscopic pattern.



Schematic acini in fibrotic stroma

Schematic — not a histologic specimen

Compression may nearly obliterate acinar lumens

- Acini may become narrow and markedly distorted.
- Some lumens are completely compressed by surrounding fibrosis.
- The result can resemble paired cells or short epithelial strands in dense stroma.

The invasive-carcinoma mimic in sclerosing adenosis

Why it can resemble invasion

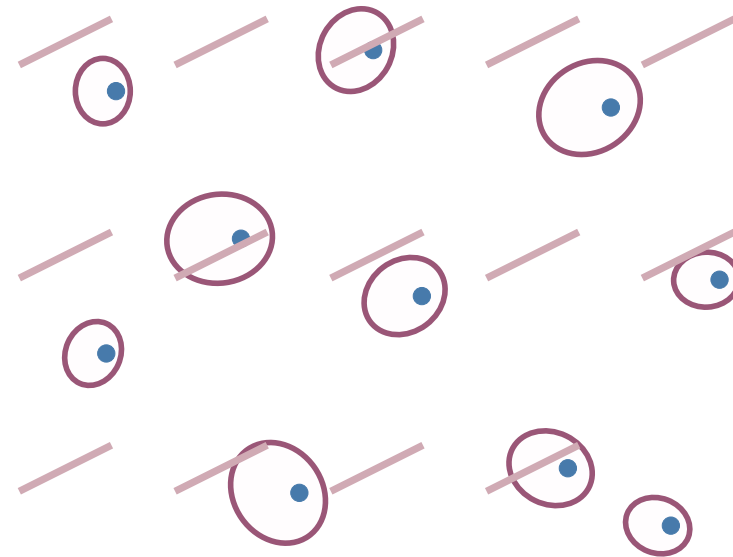
- Tiny compressed glands appear irregular.
- Lumens may be absent in individual profiles.
- Fibrosis increases the impression of infiltrative growth.

What the full pattern can reveal

- Glandular proliferation arranged in a lobular distribution.
- Swirling acinar arrangement.
- Relatively circumscribed external border in the Robbins illustration.

A swirling acinar arrangement is a useful clue

- The Robbins caption describes acini arranged in a swirling pattern.
- This pattern helps recognize a coherent benign glandular proliferation.
- Interpret the whole lesion instead of isolated compressed glandular profiles.



Schematic acini in fibrotic stroma

Schematic — not a histologic specimen

Circumscription changes the pattern interpretation

- The Robbins figure describes a well-circumscribed outer border.
- A recognizable boundary supports a localized lobular process.
- Evaluate the border alongside acinar multiplication and sclerosis.

Calcifications in sclerosing adenosis

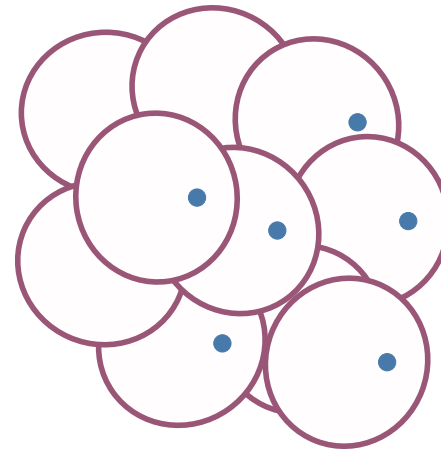
- Calcifications may occur within acinar lumens.
- They can create a mammographic finding requiring tissue sampling.
- A sampled calcification should be correlated with the glands actually present.

Sclerosing adenosis: Common routes to discovery

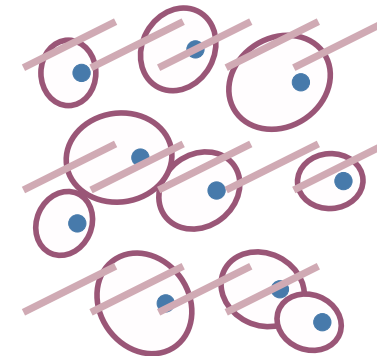
- Palpable mass.
- Radiologic density.
- Calcifications.
- The presenting abnormality can mimic cancer before histologic classification.

Sclerosing adenosis: Integrate gland and stroma

- Look for an increased number of acini.
- Determine whether fibrosis compresses or distorts lumens.
- Then assess the overall swirling, bounded glandular arrangement.



Adenosis



Sclerosing adenosis

Schematic — not a histologic specimen

Case: Compressed acini in a fibrotic mass

A breast mass contains numerous small acinar profiles, some reduced to paired cords of epithelium within dense fibrous stroma; The overall architecture is swirling.

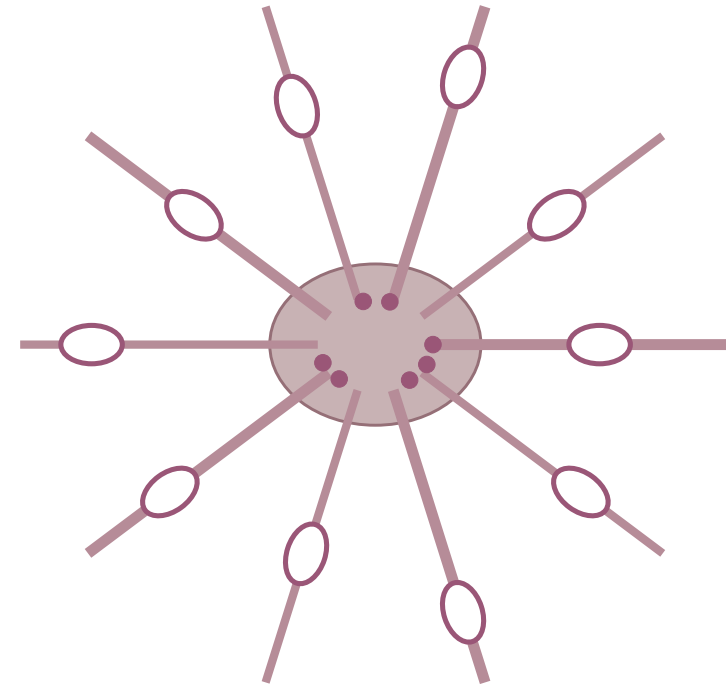
Which lesion best explains the combined findings?

Interpretation: Sclerosing adenosis

Acinar multiplication together with marked stromal compression explains the carcinoma-like microscopic appearance.

Radial scar: A small stellate sclerosing lesion

- The lesion contains a central fibrous focus and radiating glandular elements.
- Its overall stellate form can resemble an invasive carcinoma.
- The descriptive term “radial scar” refers to appearance, not an injury history.



Central fibrous nidus + radiating glands

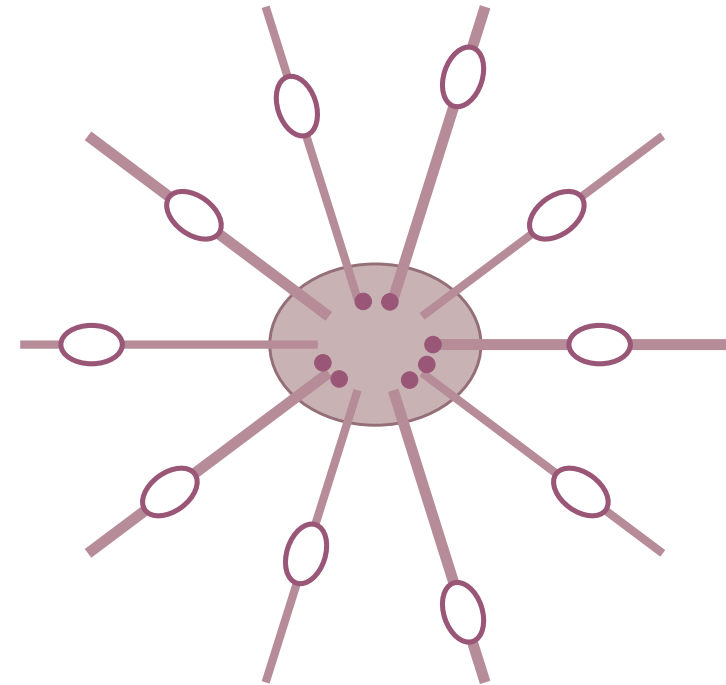
Schematic — not a histologic specimen

The term “radial scar” is a misnomer

- It does not imply preceding trauma.
- It is not defined by prior surgery.
- Name and appearance should not be mistaken for etiologic evidence.

Why a radial scar looks stellate on imaging

- A central area creates a focal density.
- Long projecting elements radiate into surrounding tissue.
- The overall radiographic silhouette can resemble malignancy.



Central fibrous nidus + radiating glands

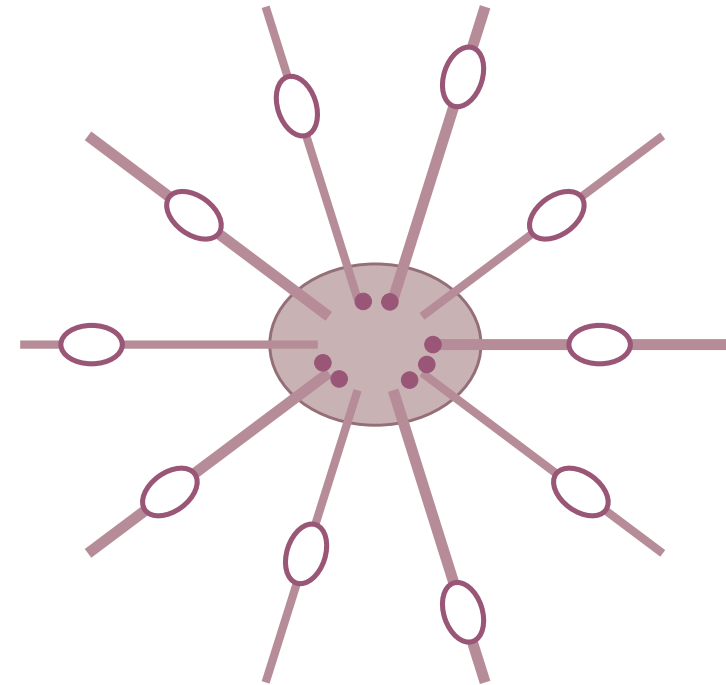
Schematic — not a histologic specimen

Gross resemblance to carcinoma

- A radial scar may be firm and irregular.
- The lesion has a radiating, scar-like configuration.
- That the mimicry spans imaging, gross, and microscopic examination.

The central nidus contains entrapped glands

- Small glands lie within central fibrous tissue.
- The stroma is hyalinized and elastotic.
- Central sclerosis and epithelial entrapment are defining morphologic features.



Central fibrous nidus + radiating glands

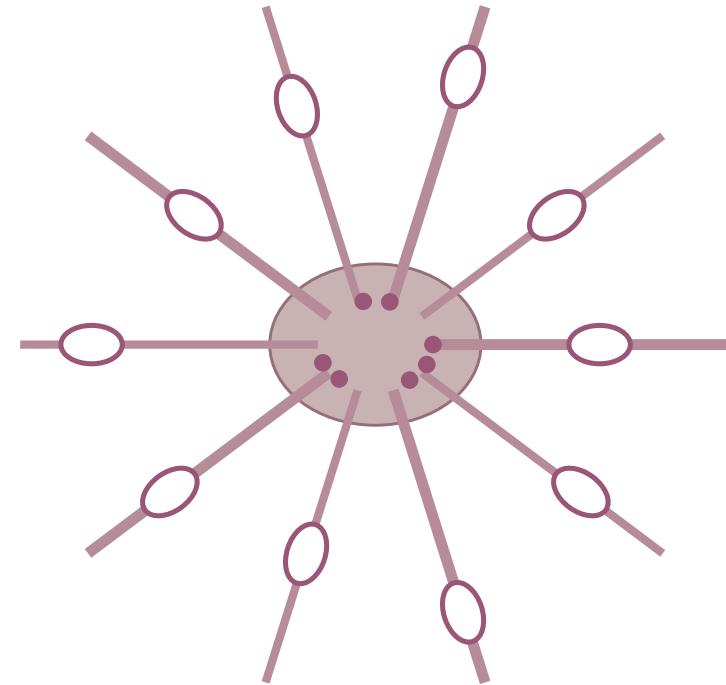
Schematic — not a histologic specimen

Hyalinized, elastotic stroma: Structural role

- The central stroma is dense and remodeled.
- Glandular elements become entrapped in this region.
- It forms the point from which the peripheral architectural projections extend.

Radiating projections contain glandular elements

- Peripheral projections extend outward from the central nidus.
- They contain epithelial / glandular structures.
- The entire lesion, not a single compressed gland, defines radial architecture.



Central fibrous nidus + radiating glands

Schematic — not a histologic specimen

A radial scar may combine several benign changes

- Sclerosing adenosis may be present in the projections.
- Cysts can contribute to the peripheral architecture.
- Papilloma and usual ductal hyperplasia may also coexist.
- Thus a single radial lesion can contain multiple benign patterns.

Radial scar and complex sclerosing lesion

Term	Size criterion in Robbins	Core architecture
Radial scar	Small radial sclerosing lesion	Central nidus + radiating glands
Complex sclerosing lesion	Radial scar larger than 1 cm	Same radial architecture, greater size

The >1 cm size criterion is explicitly stated in the primary source.

Radial scar versus sclerosing adenosis

Sclerosing adenosis

- Acinar proliferation with dense fibrosis.
- Swirling glandular arrangement.
- Compressed glands may resemble invasive structures.

Radial scar

- Central hyalinized–elastotic nidus.
- Long radiating epithelial projections.
- Often includes sclerosing adenosis and other benign changes.

Radial scar: The threefold carcinoma mimic

- Mammography: Irregular radiodense center with projections.
- Gross examination: Fibrotic, irregular stellate lesion.
- Microscopy: Epithelial structures trapped in dense stroma.
- Only integrated histologic assessment resolves this deceptive architecture.

Case: A stellate lesion with a central nidus

A small stellate breast lesion has a hyalinized center with entrapped glands and long peripheral gland-bearing projections. No history of trauma is known.

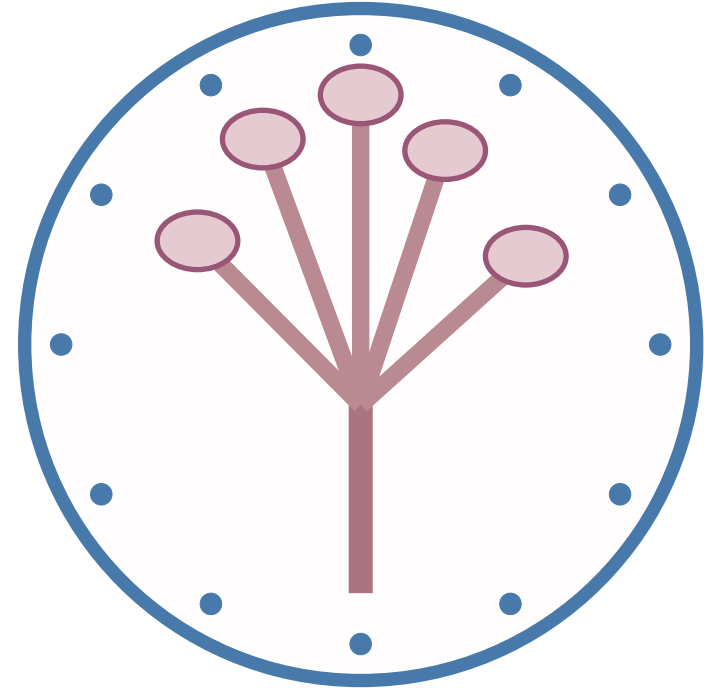
What is the pattern and why is the name misleading?

Interpretation: Radial scar (radial sclerosing lesion)

The lesion is defined by its central nidus and radiating elements; Trauma or surgery is not required.

Intraductal papilloma: Branching fibrovascular cores

- A papilloma grows within a dilated duct.
- Multiple branching fibrovascular cores form its architecture.
- This central structural feature distinguishes a true papillary proliferation from solid epithelial crowding.

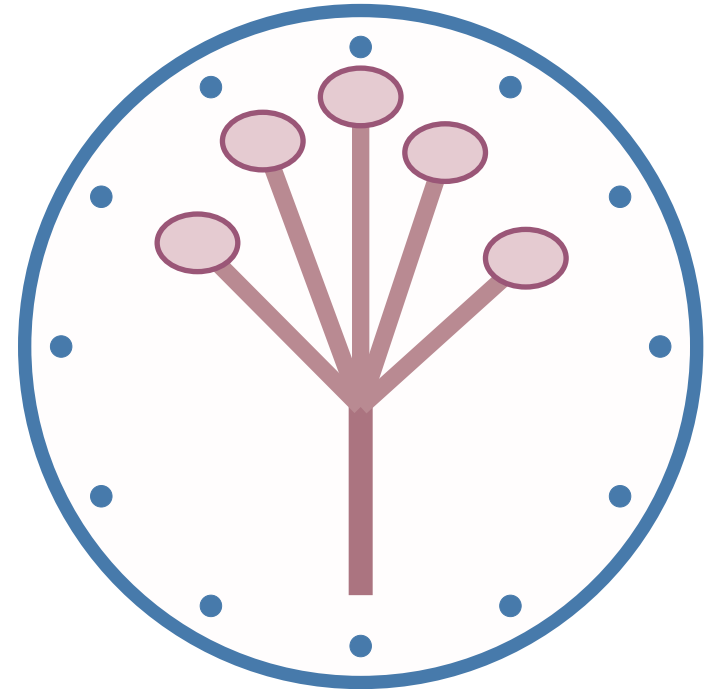


Duct lumen with branching fibrovascular cores

Schematic — not a histologic specimen

The papilloma occupies a dilated duct lumen

- The lesion develops inside a ductal space.
- Papillary projections arborize into that space.
- The duct wall remains the anatomic reference for orientation.



Duct lumen with branching fibrovascular cores

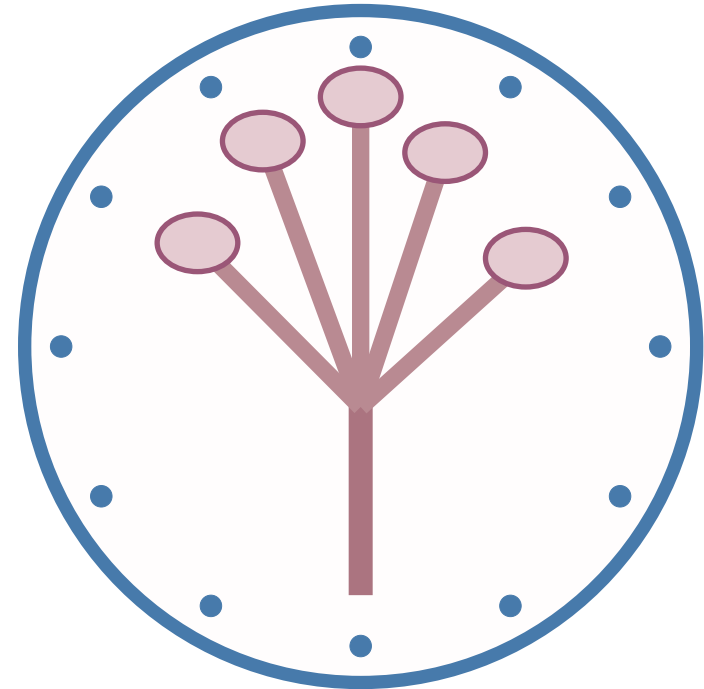
Schematic — not a histologic specimen

Fibrovascular cores are the organizing axis

- A fibrovascular stalk extends into the ductal lumen.
- It branches to support papillary fronds.
- The presence of true fibrovascular cores is the key morphologic descriptor.

Papilloma fronds have an epithelial covering

- The Robbins figure describes myoepithelial and luminal cells lining papillary fronds.
- These cells cover the branching fibrovascular architecture.
- Interpret a papillary structure in relation to its supporting core.



Duct lumen with branching fibrovascular cores

Schematic — not a histologic specimen

Associated epithelial changes within papillomas

- Usual ductal hyperplasia is frequently present.
- Apocrine metaplasia is also common.
- Both can alter the epithelial lining without changing the essential fibrovascular architecture.

Central and peripheral papillomas occupy different ducts

- Large duct papillomas usually occur centrally, in nipple lactiferous sinuses.
- Small duct papillomas typically involve the peripheral ductal system.
- Anatomic location correlates with symptoms and multiplicity.

Central / subareolar

Peripheral duct system



Schematic — not a histologic specimen

Large duct papillomas versus small duct papillomas

Large duct / central

- Usually solitary.
- Situated in lactiferous sinuses near the nipple.
- Commonly produce nipple discharge.

Small duct / peripheral

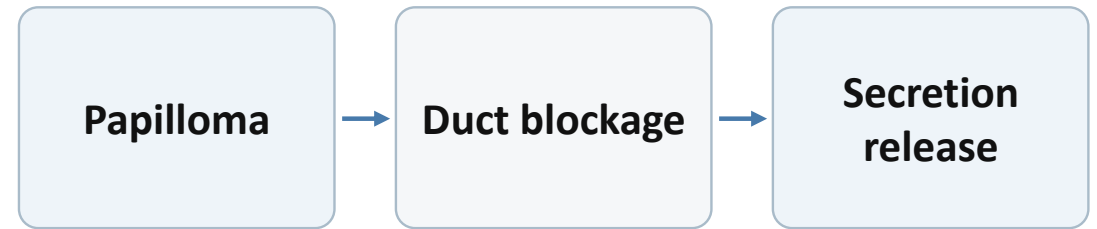
- Often multiple.
- Situated in the peripheral duct system.
- Usually clinically occult; May appear on imaging.

Bloody nipple discharge: The mechanism in papilloma

- The papillary stalk may undergo torsion.
- Torsion can lead to infarction of the lesion.
- Associated bleeding produces a bloody discharge.
- This is a mechanism described for large duct papillomas.

Serous discharge can arise by a different route

- Intermittent ductal blockage permits secretions to accumulate.
- Release of retained normal secretions may produce discharge.
- Direct irritation of the duct by the lesion is another stated explanation.



Schematic — not a histologic specimen

Discharge frequency must be assigned to the correct subtype

- More than 80% of large duct papillomas produce nipple discharge.
- This proportion is not stated for every papilloma subtype.
- The discharge may be bloody or serous.
- A symptomatic central lesion differs clinically from many peripheral papillomas.

Small duct papillomas may have no symptoms

- Most peripheral small duct papillomas are clinically occult.
- They may nevertheless produce a small palpable mass.
- They can also appear as mammographic density or calcifications.
- Multiplicity and peripheral location are useful contextual findings.

Papilloma versus papillary DCIS: Structure alone is insufficient

Intraductal papilloma

- Branching fibrovascular cores.
- Myoepithelial and luminal cells covering cores in the Robbins example.
- Usual hyperplasia/apocrine change may coexist.

Papillary ductal carcinoma in situ

- True papillae may also contain fibrovascular cores.
- Absence of myoepithelial lining in papillary DCIS.
- Assessment of the full epithelium is therefore essential.

Case: A central duct lesion and bloody discharge

A solitary intraductal mass in the subareolar region is composed of branching fibrovascular cores. The patient has spontaneous bloody nipple discharge.

What explains the morphology and the bleeding?

Interpretation: Large duct intraductal papilloma

The stalk-supported papillae define the lesion; Stalk torsion and infarction can produce blood in the discharge.

Architectural differential: The four hallmark patterns

Lesion	Most discriminatory structural finding
Usual ductal hyperplasia	Mixed cellular proliferation with irregular peripheral slits
Sclerosing adenosis	Numerous distorted acini within fibrotic stroma
Radial scar	Central elastotic focus with glandular radiations
Papilloma	True arborizing fibrovascular cores in a dilated duct

Clinical correlation across four benign lesions

Lesion	Characteristic way it may be detected
Usual ductal hyperplasia	Most often incidental
Sclerosing adenosis	Mass, radiologic density, or calcifications
Radial scar	Stellate abnormality resembling carcinoma
Large duct papilloma	Solitary central lesion with nipple discharge
Small duct papilloma	Often occult; mass or radiologic abnormality possible

An imaging mimic is not a microscopic diagnosis

- Sclerosing adenosis can appear invasive in tiny fibrotic gland profiles.
- Radial scar can mimic carcinoma on mammography, grossly, and histologically.
- The defining benign architecture must be recognized in the tissue.
- The radiologic finding and the tissue interpretation must describe the same lesion.

Risk marker versus precursor: Avoid category confusion

Without atypia

- A small elevation in subsequent cancer risk.
- Association affects both breasts.
- These lesions are considered predictors of risk, not direct precursors.

With atypia / in situ

- Atypical hyperplasia is a clonal, partly carcinoma-like proliferation.
- Carcinoma in situ is confined within duct–lobular structures.
- These are considered in the precursor-lesion framework.

Integrative case: Heterogeneous epithelial proliferation

A biopsy shows several expanded ducts containing mixed cell populations and slit-like residual spaces. The report states moderate usual hyperplasia.

How should this be classified for the textbook risk framework?

Interpretation: Proliferative breast disease without atypia

Moderate/florid usual hyperplasia is placed in this category; Mild usual hyperplasia is in the reference group.

Integrative case: A calcified sclerosing lesion

An imaging-driven core specimen contains closely packed, distorted acini with luminal calcifications; Dense stroma flattens some profiles into short strands.

Which diagnostic pattern should be considered first?

Interpretation: Sclerosing adenosis

Acinar multiplication, calcifications, and stromal compression explain the appearance without presuming invasion.

Integrative case: An irregular stellate density

A suspicious density corresponds to a fibrotic central nidus with surrounding radiating ducts and acini; Small cystic changes are also found in the projections.

What is the benign architectural mimic?

Interpretation: Radial scar

Its characteristic combination is a central elastotic core, outward glandular projections, and mixed benign components.

Integrative case: Clinically occult papillary lesion

An asymptomatic peripheral imaging finding contains several small ductal lesions with branching fibrovascular cores and an epithelial covering.

Which pattern fits location and morphology?

Interpretation: Small duct papillomas

Peripheral multiplicity and absence of symptoms fit Robbins' description of small duct papillomas.

Recognition summary: Four lesions, four morphologic anchors

Pattern	Must recognize	Main clinical connection
Usual hyperplasia	Mixed cells, irregular lumens	Often incidental
Sclerosing adenosis	Compressed acini + fibrosis	Mass/density/calcifications
Radial scar	Stellate central nidus + radiations	Carcinoma mimic
Papilloma	Arborizing fibrovascular cores	Duct location predicts presentation

Interpretive cautions for breast proliferations

- Morphologic resemblance to carcinoma does not establish malignancy.
- Usual hyperplasia and atypical hyperplasia are not interchangeable diagnostic terms.
- Papillary architecture requires attention to the epithelial and myoepithelial components.
- Category-level relative risk is not a probability of progression of an individual lesion.

Principal source and image status

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026), Chapter 23, The Breast.
- Topic text: “Proliferative Breast Disease Without Atypia,” p. 948.
- Morphologic corroboration: Fig. 23.6–23.9 captions, pp. 949–950.
- Epidemiologic classification: Table 23.1, p. 951.
- All displayed diagrams are editable teaching schematics; original textbook figures were not reproduced.