

Ductal carcinoma in situ

Pathology of an in situ breast epithelial neoplasm

Anatomic boundary • molecular pathways • morphology

Mammographic detection • clinicopathologic consequences

Dr Abu Suraih Sakhri

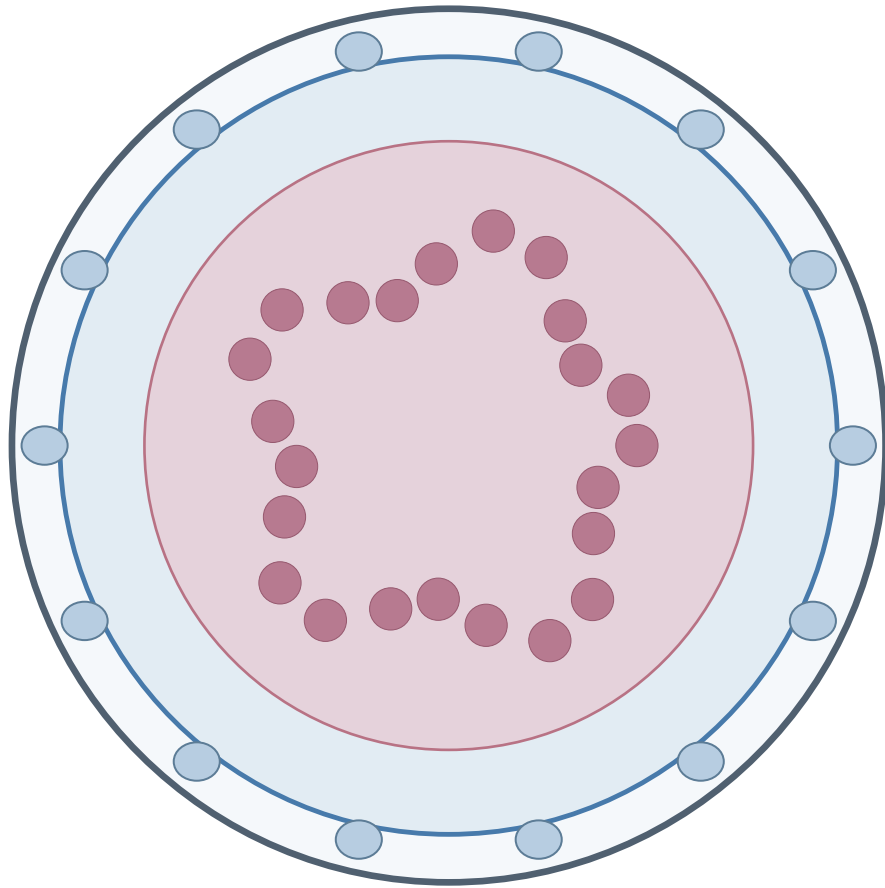
MBBS, MD (Pathology)

www.abusuraihsakhri.com

What this lecture should establish

- Define DCIS using epithelial confinement and basement-membrane integrity.
- Interpret nuclear grade, architectural pattern, necrosis, and calcification.
- Connect molecular phenotype to progression risk and local management.

Carcinoma in situ: The defining boundary



Schematic — not a histologic specimen

Neoplastic epithelial cells remain confined within duct-lobular structures.

The basement membrane separates the proliferation from adjacent stroma.

Crossing this boundary defines stromal invasion, not the degree of cytologic atypia.

DCIS arises in the terminal duct–lobular system



Ducts and lobules form a connected anatomic epithelial compartment.

Why “ductal” is not a cell-of-origin label

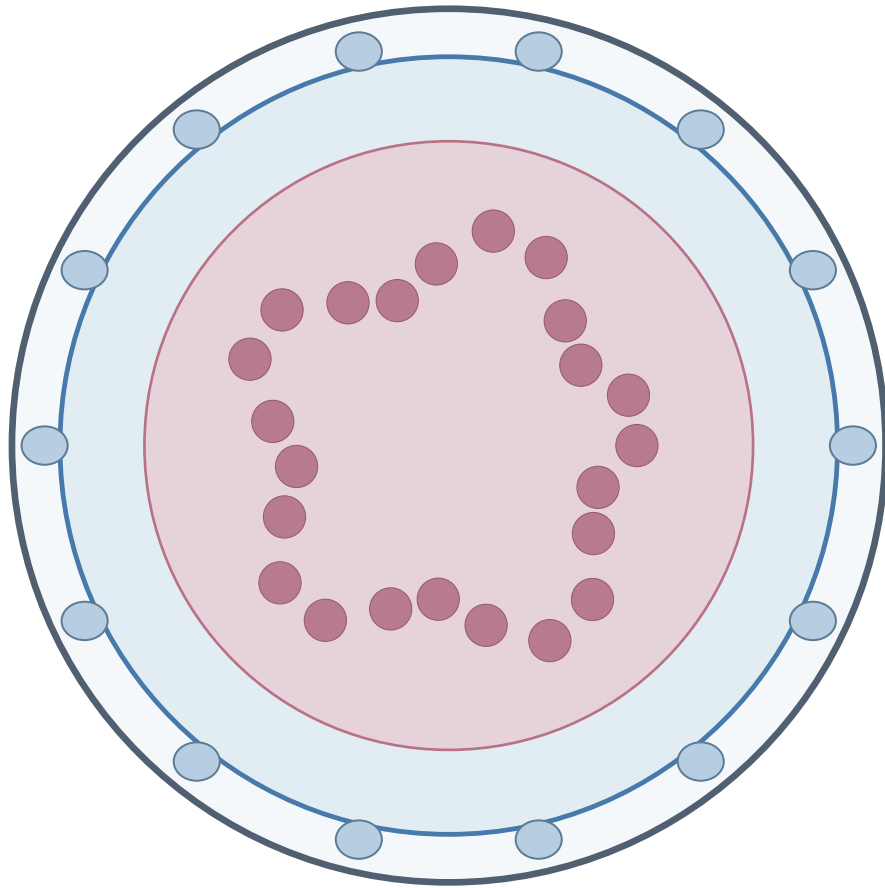
Historic terminology

- Ductal and lobular labels originally reflected involved-space appearance.
- Both major breast carcinoma groups are thought to originate in terminal duct–lobular units.

Contemporary meaning

- Patterns reflect distinctive tumor genetics and biology.
- The term DCIS describes a clinicopathologic phenotype, not a uniquely duct-derived progenitor.

DCIS: Epithelial proliferation with preserved containment



Schematic — not a histologic specimen

Ducts and lobules are expanded by neoplastic epithelial cells.

Myoepithelial cells are generally preserved along the involved spaces.

No unequivocal tumor nests are seen beyond the basement membrane.

In situ disease versus invasive carcinoma

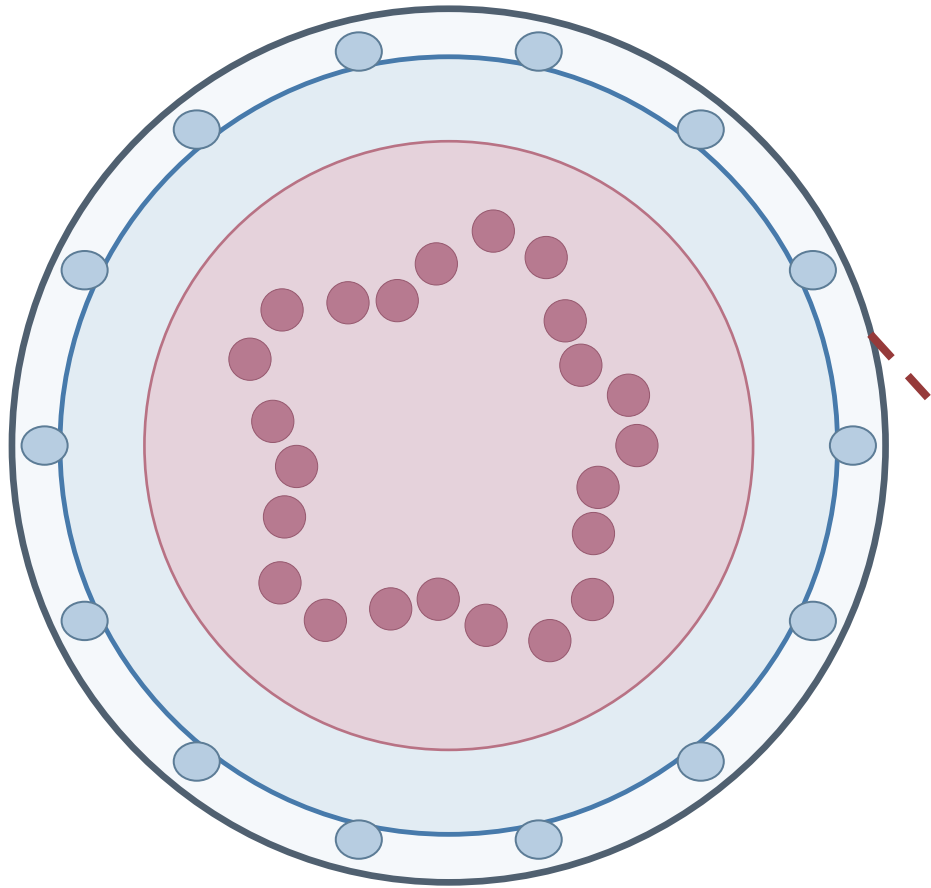
DCIS

- Malignant epithelial cells remain within duct-lobular boundaries.
- The myoepithelial compartment is generally preserved.

Invasive carcinoma

- Malignant cells infiltrate the surrounding breast stroma.
- Loss/disruption of the normal duct boundary must be assessed.

A boundary-based view of progression



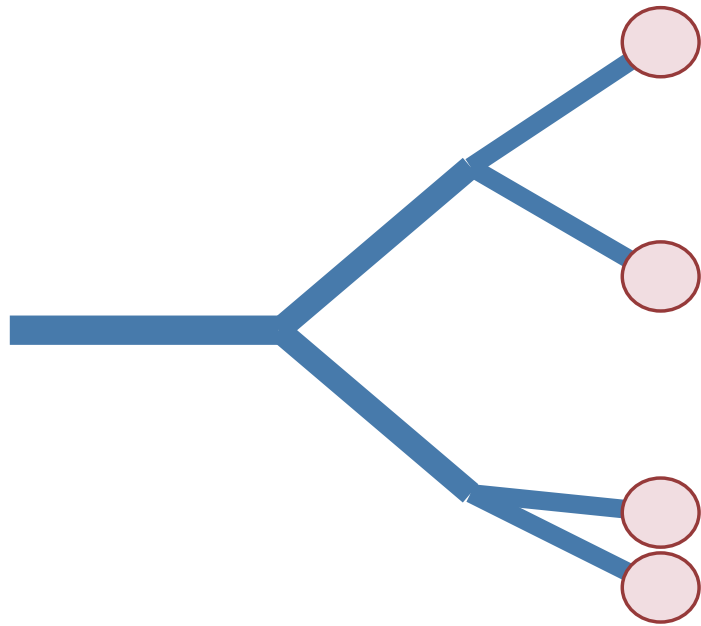
Schematic — not a histologic specimen

DCIS and invasive cancer can share many molecular changes.

Acquiring morphologic invasion is a separate step from acquiring cytologic malignancy.

The mechanisms permitting escape into stroma are incompletely understood.

Ductal spread explains extensive DCIS



Intraductal expansion along branching ducts

DCIS may spread along a connected ductal network.

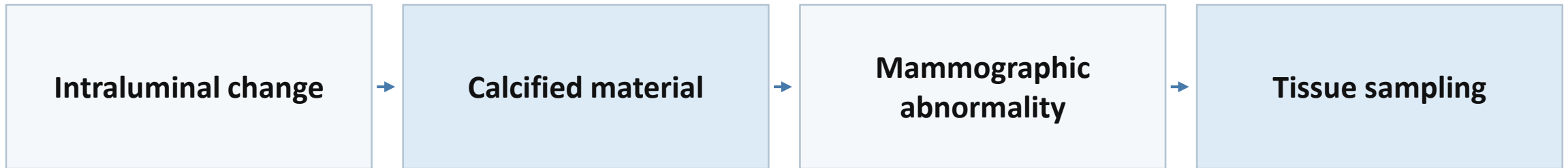
A single lesion can involve a large segment of breast tissue.

Segmental extent is not reliably inferred from a small core biopsy.

Why DCIS is often clinically occult

- DCIS usually produces no distinct gross mass.
- Detection often relies on screening mammography rather than palpation.
- A positive core biopsy does not establish the full breast extent.

Mammographic calcification is the common clue



Radiologic calcium localizes lesions; Histology establishes their nature.

Two morphologic sources of calcification

- Central necrotic material can calcify, especially in high-grade lesions.
- Secretory products may calcify in low-grade architectural patterns.
- Calcification supports localization but does not by itself determine histologic grade.

Calcification does not imply one DCIS phenotype

High-grade association

- Comedo necrosis can create central ductal calcium deposits.
- Specimen imaging may show linear or branching calcifications.

Low-grade association

- Cribriform spaces may contain calcifying secretory material.
- Calcification may occur without destructive central necrosis.

When DCIS appears as a mammographic density

- Periductal fibrosis may produce a density or vague palpable mass.
- The density reflects a stromal response adjacent to an in situ lesion.
- A density does not independently prove stromal invasion.

Uncommon modes of presentation

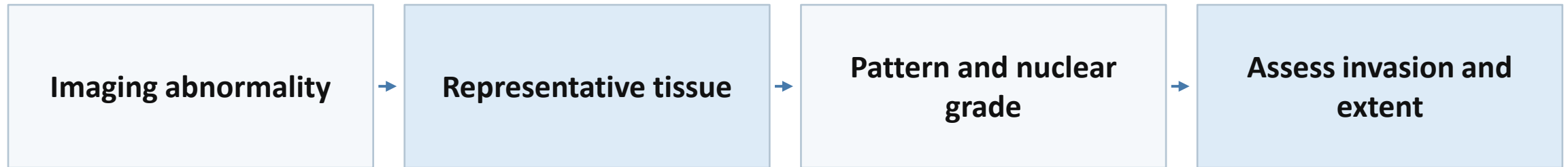
Nipple discharge

- Uncommon presentation; Often linked to micropapillary/papillary types.
- The discharge warrants ductal and clinical correlation.

Incidental detection

- DCIS may be discovered during biopsy of another lesion.
- Diagnosis rests on microscopic architecture and containment.

Image–pathology correlation as a diagnostic sequence



Sampling and microscopic assessment complement the imaging finding.

Why sampling is central to interpretation

- The radiographic target may contain calcified necrosis or secretions.
- Microscopic examination is necessary to classify the epithelial proliferation.
- Sampling may fail to capture a separate small invasive focus.

Nuclear grade governs DCIS classification

Nuclear size



**Nuclear shape /
pleomorphism**



Overall nuclear grade

The final grade reflects nuclear morphology, not a growth pattern.

Grade and architecture are different dimensions

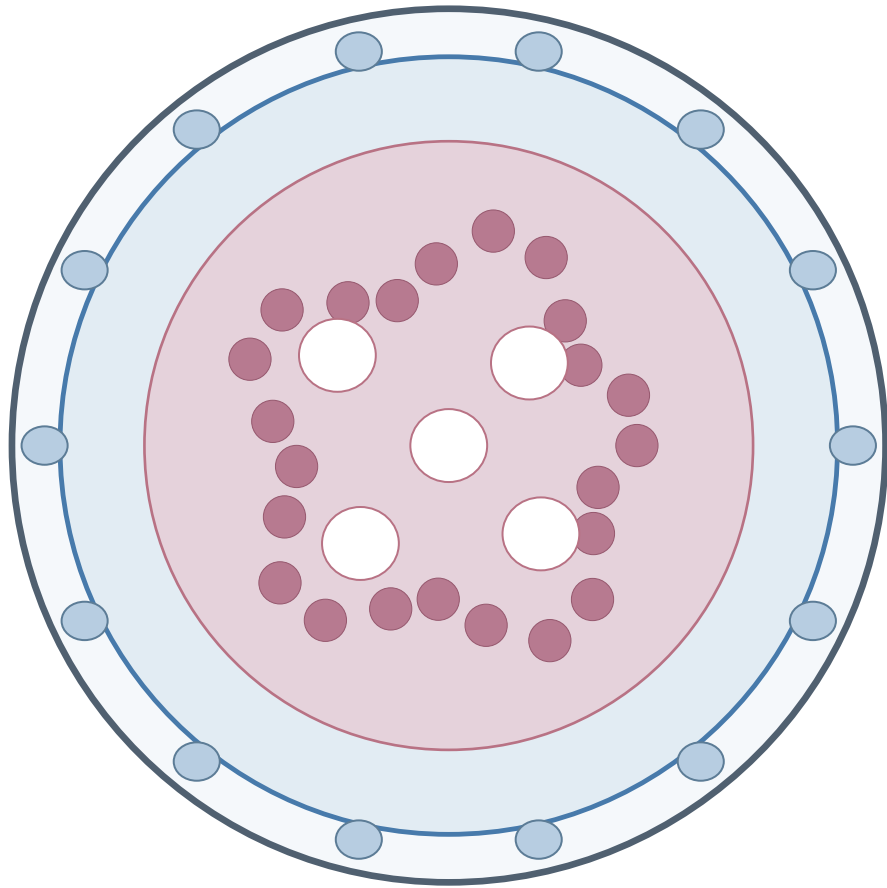
Nuclear grade

- Assessed from cytologic nuclear features.
- Robbins separates low- and high-grade biological pathways.

Architecture

- Describes the arrangement of epithelial growth.
- Cribriform, micropapillary and papillary patterns are examples.

Low-grade DCIS: Relatively uniform cytology



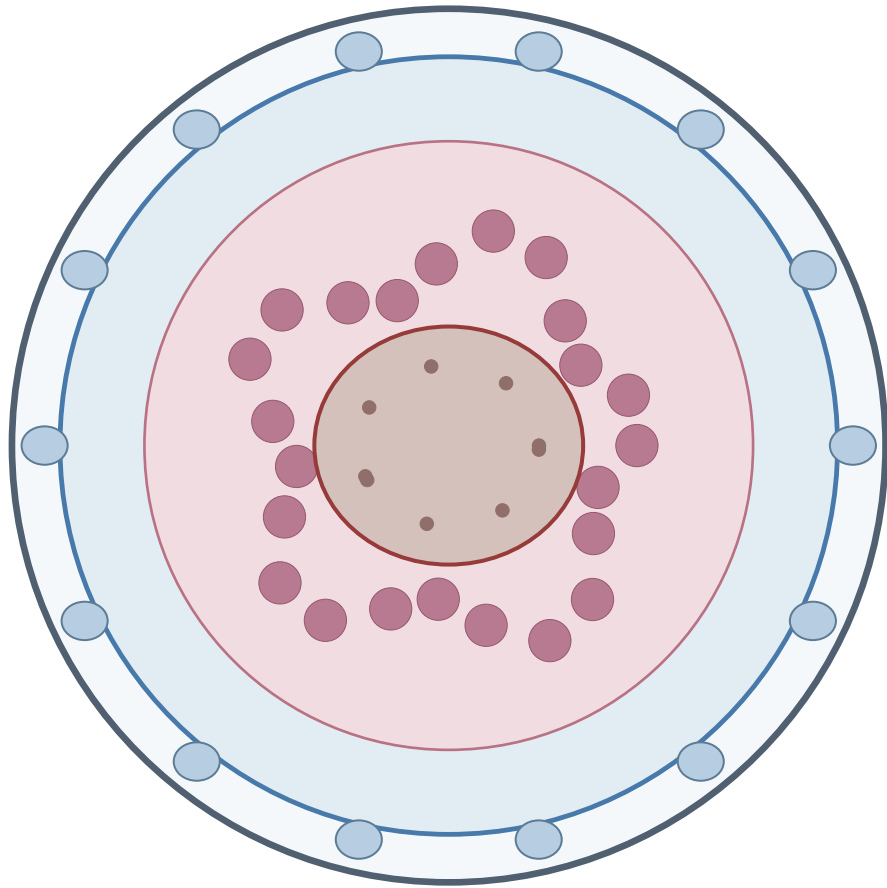
Schematic — not a histologic specimen

Nuclear uniformity supports a low-grade interpretation.

An involved duct may show orderly cribriform luminal fenestrations.

Low-grade biology is frequently associated with ER positivity.

High-grade DCIS: Pronounced nuclear atypia



Schematic — not a histologic specimen

High-grade lesions show greater nuclear abnormality.

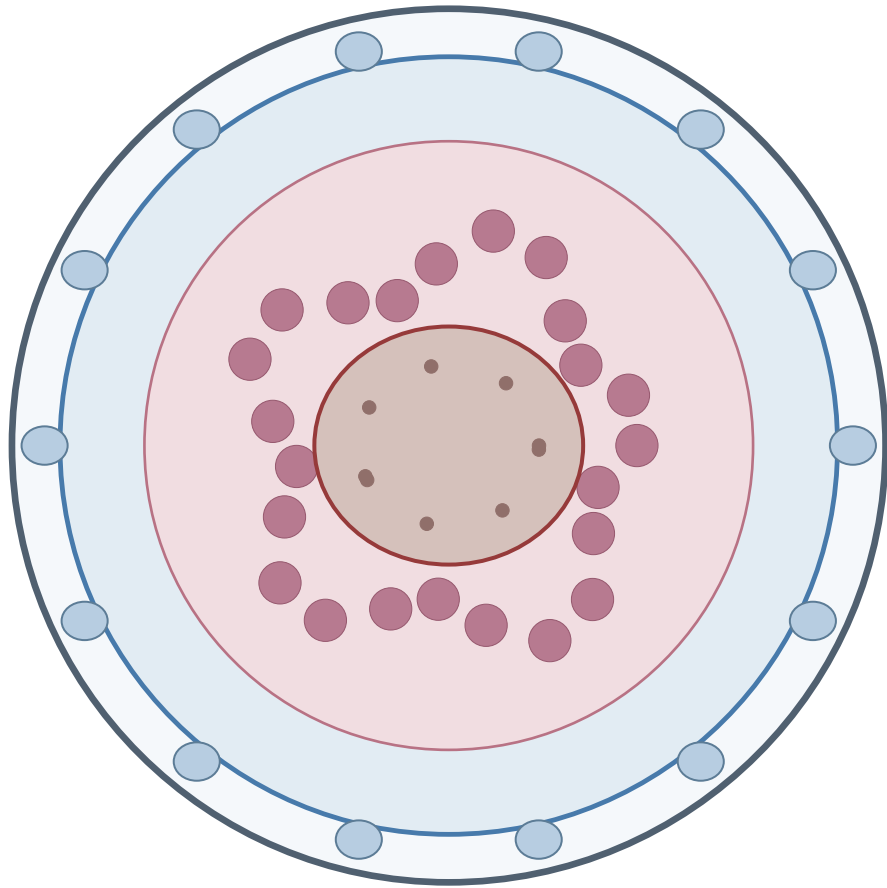
Comedo-type central necrosis is often associated with high-grade DCIS.

Some lesions show marked calcification within necrotic ducts.

Low-grade and high-grade DCIS at a glance

Feature	Low grade	High grade
Nuclei	More uniform	More pleomorphic
ER expression	Typically positive	May be negative
HER2 expression	Typically negative	May be positive
Molecular context	16q loss / 1q gain	Genomic instability / varied changes
Central comedo necrosis	Not defining	Common association

Comedo necrosis: Central death within filled ducts



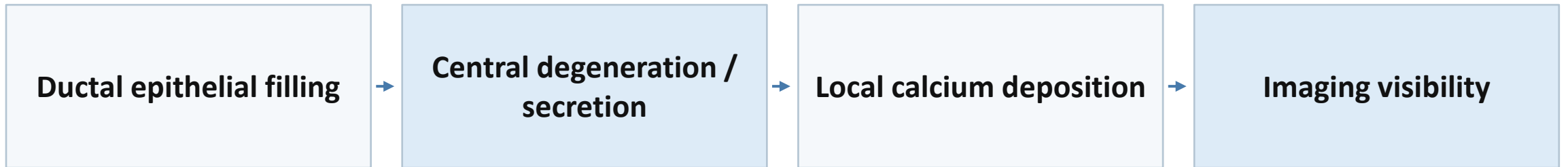
Schematic — not a histologic specimen

Necrotic debris occupies the center of the expanded duct.

DCIS remains in situ if the surrounding basement membrane is intact.

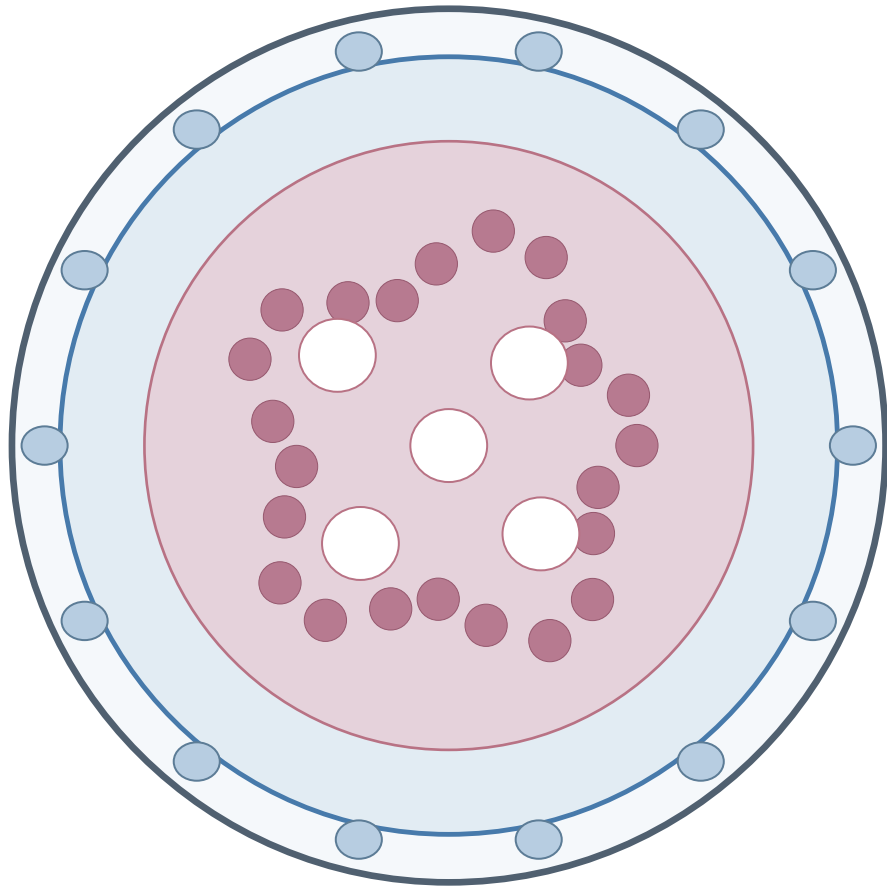
Necrosis and calcification are separable but often linked findings.

A plausible route to visible calcification



Calcification can follow necrosis or accumulation of secretory products.

Cribriform architecture: Punched-out lumina



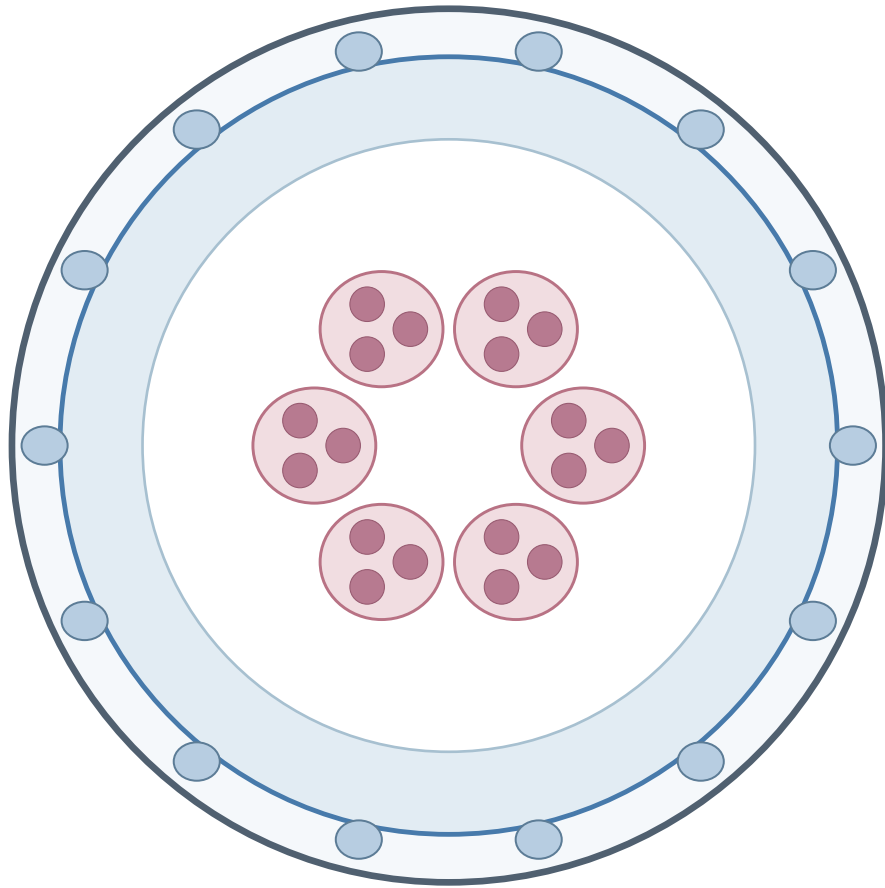
Schematic — not a histologic specimen

Multiple rounded regular spaces interrupt the epithelial proliferation.

The lumina may contain secretions or calcified material.

Cribriform pattern is architectural; Nuclear grade still requires separate assessment.

Micropapillary architecture: Projections without cores



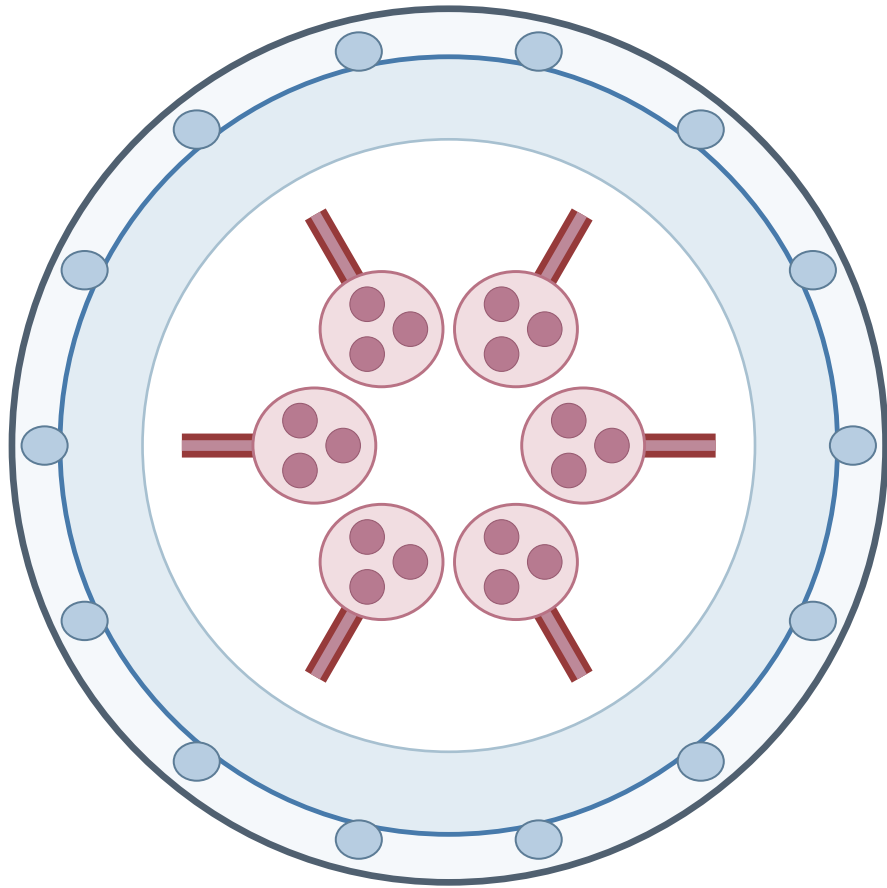
Schematic — not a histologic specimen

Bulbous epithelial tufts project into ductal lumina.

These tufts lack a fibrovascular stalk.

Micropapillary architecture can be associated with nipple discharge.

Papillary architecture: True fibrovascular cores



Schematic — not a histologic specimen

Papillary structures contain a genuine fibrovascular core.

Absent myoepithelial lining along neoplastic papillae.

The outer myoepithelial layer of the involved duct generally remains preserved.

Cribriform, micropapillary, and papillary patterns

Pattern	Principal architectural criterion	Important distinction
Cribriform	Round “cookie-cutter” lumina	Internal fenestrations
Micropapillary	Bulbous epithelial tufts	No fibrovascular core
Papillary	Papillae with fibrovascular cores	True stalks; Papillary myoepithelial cells absent

Papillary versus micropapillary DCIS

Micropapillary

- Tufts are supported by epithelial attachment to a duct wall.
- No vascularized connective-tissue core inside projections.

Papillary

- Fibrovascular stalks form branching supports.
- Outer ductal containment still determines whether the process is in situ.

Necrosis is not synonymous with invasion

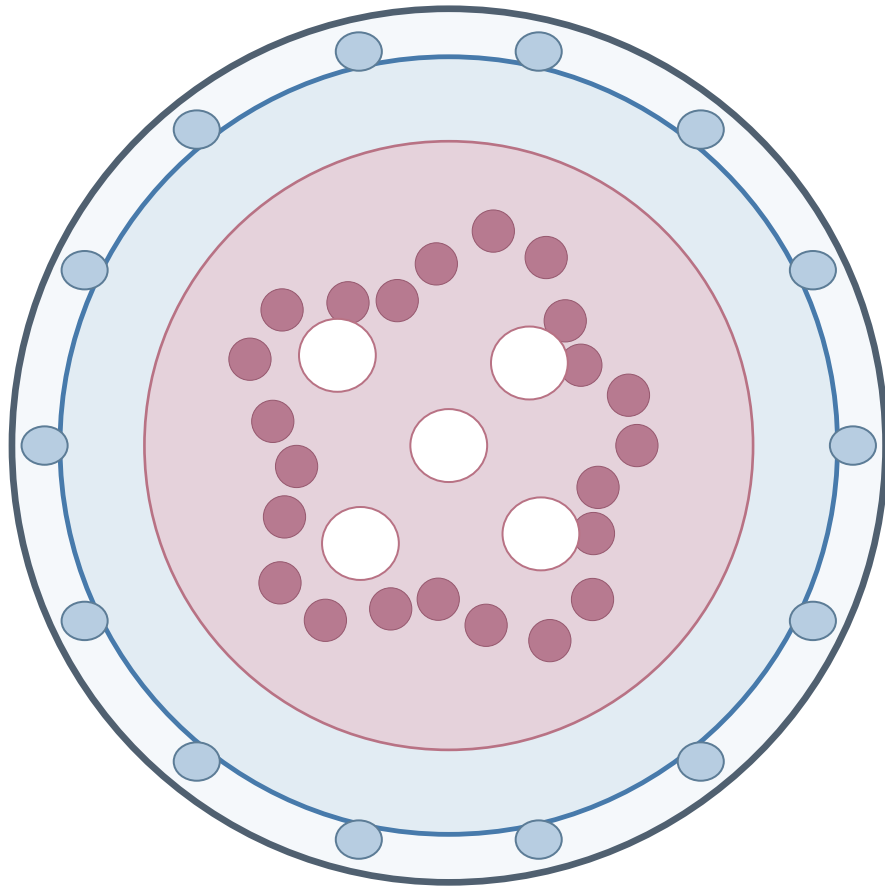
What necrosis tells us

- Cell death occurs within the tumor-filled duct.
- Can accompany high-grade DCIS and calcification.

What necrosis does not tell us

- Cannot prove penetration of basement membrane.
- Does not replace examination of peripheral ductal boundaries.

Reading an involved duct from outside inward



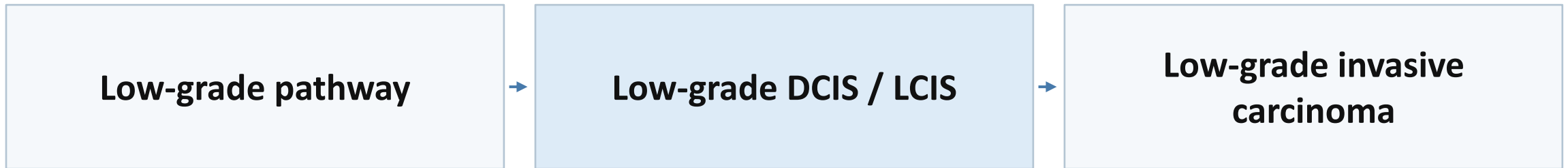
Schematic — not a histologic specimen

First identify stroma and the ductal boundary.

Then evaluate the myoepithelial layer and luminal proliferation.

Finally grade nuclei and describe pattern, necrosis, and calcification.

The low-grade breast neoplasia pathway

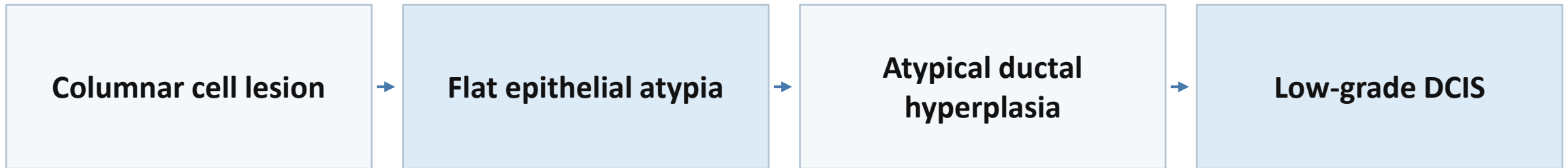


Low- and high-grade carcinomas are biologically divergent pathways.

Low-grade DCIS: Characteristic molecular profile

- Typically expresses estrogen receptor (ER).
- Typically lacks HER2 overexpression in the Robbins description.
- Common chromosomal alterations include loss of 16q and gain of 1q.

Recognizable low-grade precursor continuum

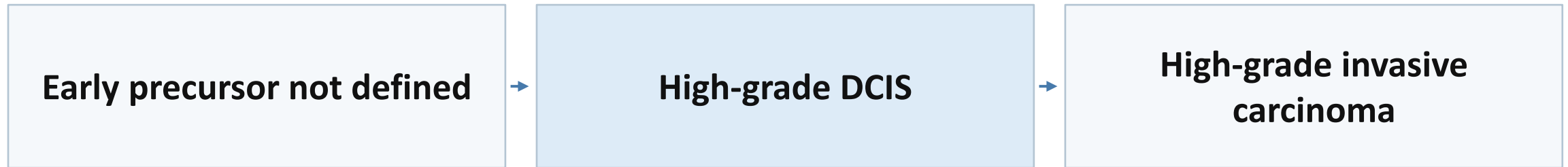


Conceptual continuum: Progression is neither inevitable nor strictly linear.

Low-grade lesions share a clonal background

- Earlier precursor lesions and low-grade DCIS show overlapping molecular changes.
- Low-grade DCIS may resemble atypical ductal hyperplasia architecturally.
- The morphologic boundary between ADH and DCIS often depends on extent.

The high-grade pathway has a different starting point



The earliest recognizable high-grade precursor remains undefined.

High-grade DCIS: Instability and heterogeneity

- ER may be negative, and HER2 may be positive.
- The genome can exhibit abnormalities shared with high-grade invasive tumors.
- 13q loss, 11q13 gain and 17q12 amplification as high-grade-pathway examples.

Grade-associated profiles are tendencies, not rules

Question	Interpretation
ER-positive?	Common in low-grade DCIS; Not proof of low grade by itself
HER2-positive?	May occur in high-grade DCIS; Not a substitute for nuclear grading
16q loss / 1q gain?	Support the low-grade molecular pathway
Genomic instability?	Characteristic of the high-grade pathway
Architecture?	Neither receptor status nor pattern replaces nuclear-grade assessment

Tumor genetics do not fully explain invasion

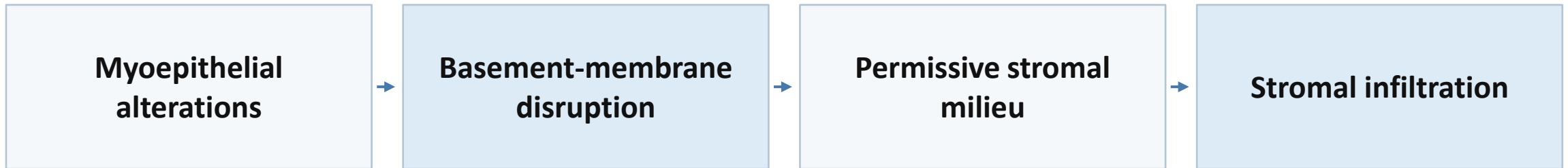
Genomic observation

- Many driver alterations exist before invasion.
- No universal invasion-specific genetic change has been identified in the cited chapter.

Mechanistic implication

- Tumor–microenvironment interactions may influence transition.
- The precise cause of invasion remains incompletely resolved.

Potential stromal contribution to invasion

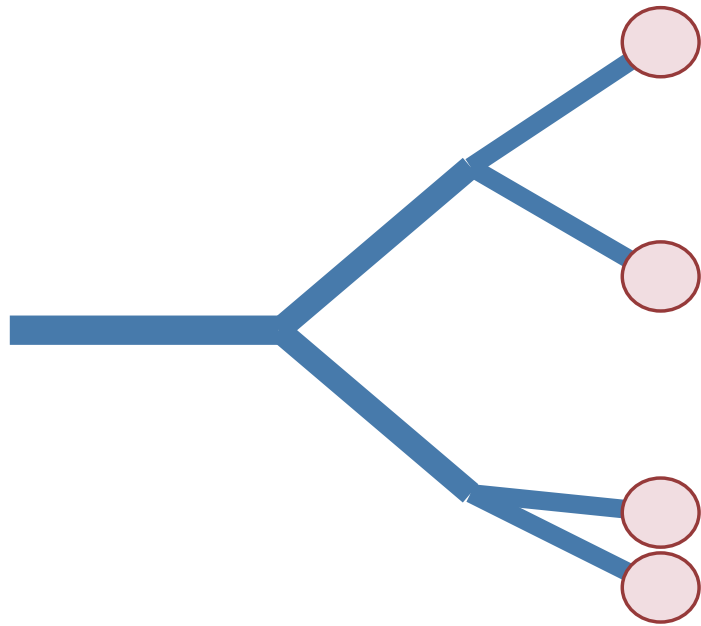


Proposed mechanism, not a clinically established deterministic sequence.

Microenvironmental hypotheses: Interpret cautiously

- Myoepithelial cells, stromal cells and extracellular matrix help maintain the duct barrier.
- Some in situ cancers show attenuation of the myoepithelium or gaps in basement membrane.
- These observations suggest mechanisms; They are not a deterministic clinical algorithm.

Spatial extent and biology are independent concerns



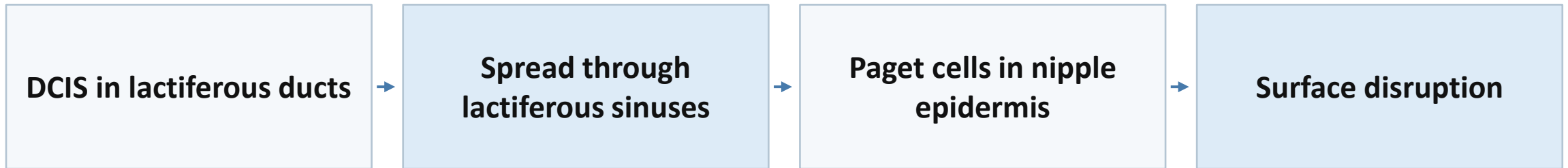
Intraductal expansion along branching ducts

A low-grade process may occupy a broad ductal network.

A high-grade focus may be relatively localized in a sampled region.

Both the biologic grade and anatomic extent affect clinical decisions.

Paget disease: Intraductal-to-epidermal spread

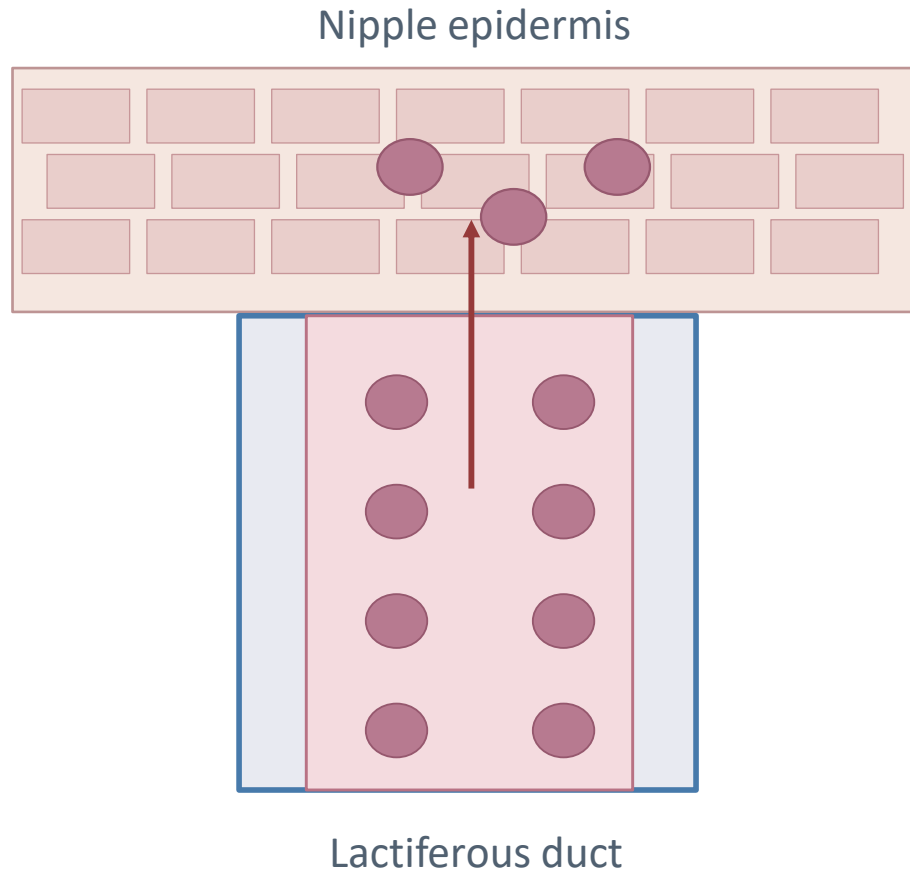


Epidermal extension can occur without crossing a basement membrane.

Paget disease: Characteristic presentation

- Rare breast cancer manifestation (1%–4% of cases).
- Typically unilateral, erythematous and scaly/crusted.
- Pruritus can lead to an initial impression of eczema.

Why Paget disease produces an oozing crust



Neoplastic cells extend into nipple epidermis without stromal invasion by that route.

Paget cells disrupt the squamous epithelial barrier.

Extracellular fluid reaches the surface, contributing to scale and crust.

Schematic — not a histologic specimen

Paget disease: With and without a palpable mass

No palpable breast mass

- Most patients have underlying DCIS.
- Staging usually reflects the underlying in situ process.

Palpable breast mass

- About half of patients have a detectable mass.
- The mass usually represents invasive carcinoma.

Paget disease: Microscopic confirmation

- Paget cells can be detected in nipple biopsy tissue.
- Cytologic preparations of nipple exudate may reveal malignant cells.
- The underlying breast lesion must be assessed for a separate invasive component.

Paget disease and dermatitis: A diagnostic trap

Possible clinical overlap

- Erythema, scale, crust and pruritus are nonspecific on appearance.
- A unilateral persistent nipple lesion deserves tissue evaluation.

Pathologic discriminator

- Malignant intraepidermal Paget cells establish neoplastic involvement.
- Assess for ductal DCIS and associated invasion, when present.

Why the untreated natural history is uncertain

- Most DCIS is treated shortly after detection.
- Observed progression therefore reflects selected untreated or residual disease.
- Rates from limited natural-history observations cannot be generalized to every grade and extent.

Progression in small, low-grade DCIS

- An invasive-cancer development rate near 1% per year.
- This estimate concerns small, low-grade lesions in the available data.
- It is not a prediction for an individual patient or for high-grade DCIS.

Concordance between DCIS and later invasive disease

Existing in situ clone



**Subsequent same-quadrant
invasion**



**Often similar grade and
ER/HER2 profile**

Concordant grade and receptor expression support a related lineage.

High-grade and extensive DCIS: Greater concern

- High-grade disease is believed to progress more rapidly.
- Extensive disease carries a higher estimated risk of later invasion.
- The source frames this as inference from incomplete natural-history data.

Metastatic breast cancer after a DCIS diagnosis

- Metastatic death in approximately 1%–3% after DCIS diagnosis.
- Possible origins include later invasive tumors in either breast.
- Occult invasion missed at the original diagnosis is another possible explanation.

Population survival must not be misread causally

Textbook observation

- Overall mortality among US females with diagnosed DCIS is lower than population mortality.
- The source discusses screening and care-access differences.

What cannot be concluded

- DCIS is not protective against death.
- The observation does not prove that DCIS treatment improves all-cause longevity.

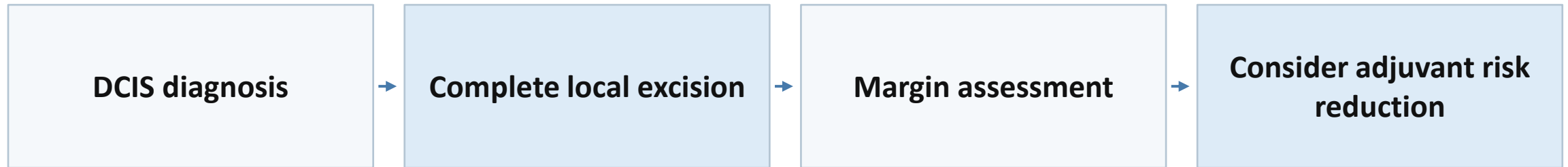
Why definitive extent assessment is difficult

- DCIS is commonly inapparent on gross inspection at surgery.
- Distribution may not correspond exactly to mammographic calcifications.
- Pathologic examination of the excision and margins is therefore critical.

Three major recurrence-risk features

Risk feature	Pathologic explanation
High grade and necrosis	More aggressive lesion biology
Extensive DCIS	Greater anatomic field of disease
Positive surgical margins	Potential residual neoplastic epithelium remains

Local treatment targets persistence or recurrence



Excision extent and margin status inform residual local disease risk.

Mastectomy is highly effective for DCIS

- Cure in more than 95% of patients.
- Local treatment is rational because DCIS is confined to breast duct–lobular units.
- Occult invasive disease and later contralateral cancers explain why risk never becomes absolutely zero.

Radiation reduces local recurrence after surgery

- Postoperative radiation is described as reducing recurrence risk.
- Its contribution concerns local disease control, not proof of preexisting invasion.
- The source excerpt does not supply a patient-level indication rule or effect size.

Endocrine risk reduction with tamoxifen

- Tamoxifen reduces recurrence clinical discussion.
- This is especially biologically relevant to ER-expressing neoplastic epithelium.
- The source does not define a complete contemporary endocrine-treatment algorithm.

Surveillance trials versus established local treatment

Current textbook account

- Trials are ongoing to identify DCIS subgroups safe for observation.
- Progression estimates are heterogeneous and uncertain.

Teaching interpretation

- Do not equate indolent biology with guaranteed harmlessness.
- Do not present observation as universally proven equivalent to excision.

DCIS versus lobular carcinoma in situ

Feature	DCIS	Classic LCIS
Imaging	Usually calcification-associated	Often incidental finding
Cell growth	Cohesive architectural patterns	Dyscohesive cells
E-cadherin	Usually retained in ductal phenotype	Usually lost
Clinical orientation	Local ipsilateral recurrence/precursor	Risk to either breast

Atypical ductal hyperplasia versus DCIS

Shared features

- Uniform cells with cribriform or micropapillary pattern.
- Both belong to the low-grade neoplasia pathway.

Distinguishing consideration

- ADH is limited in size and extent.
- More extensive proliferation with characteristic features supports DCIS.

Common interpretive errors in DCIS

- Calling an architectural pattern a histologic grade.
- Mistaking central necrosis for proof of stromal invasion.
- Assuming the full lesion extent can be read from one core sample.

Case study: Calcifications with punched-out lumina

Clinical–pathology scenario

- Screening mammography prompts biopsy of segmental calcifications.
- Ducts contain relatively uniform epithelial cells and round fenestrations.

What pattern is present, and which separate feature still requires grading?

Case analysis: Cribriform DCIS

Mechanism-based interpretation

- Cribriform pattern is identified by regular round intratumoral spaces.
- Assign nuclear grade by nuclear features, not by naming the pattern.
- Determine absence or presence of invasion separately.

Case study: Unilateral scaly nipple change

Clinical–pathology scenario

- A patient develops pruritic unilateral scaling and crusting of the nipple.
- A biopsy identifies malignant epithelial cells in the epidermis.

What ductal route is possible, and what underlying lesion must be assessed?

Case analysis: Paget disease

Mechanism-based interpretation

- DCIS may extend through lactiferous ducts into nipple epidermis.
- Paget cells impair epithelial barrier function and cause crusting.
- Assess underlying breast tissue for DCIS versus an associated invasive mass.

Case study: A focal excision with positive margin

Clinical–pathology scenario

- An excision contains high-grade DCIS with comedo necrosis.
- The epithelial proliferation reaches the inked resection margin.

Which independent features increase concern for subsequent recurrence?

Case analysis: Recurrence-risk assessment

Mechanism-based interpretation

- High nuclear grade and necrosis are major adverse factors.
- Positive margin suggests possible residual disease after excision.
- Overall disease extent remains another critical variable.

Synthesis: Six durable concepts

- DCIS is malignant epithelial proliferation without demonstrable stromal invasion.
- Mammographic calcification often reveals otherwise occult disease.
- Grade is primarily nuclear; Architecture is a separate descriptor.
- Low- and high-grade DCIS follow biologically different pathways.
- Paget disease may reflect epidermal extension of an underlying DCIS.
- Risk assessment depends on grade, necrosis, extent and margins.

Source and interpretation boundaries

- Primary teaching source: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th edition.
- Chapter 23: The Breast — carcinoma in situ, precursor lesions, and breast-cancer pathogenesis.
- All histology-like drawings in this lecture are editable conceptual schematics; no diagnostic specimen images were embedded.

Scope: Robbins text and parent context; no external treatment guidelines incorporated.