

Carcinoma in Situ

Breast pathology: biologic boundaries and diagnostic distinctions

Ductal and lobular patterns in their clinicopathologic context

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

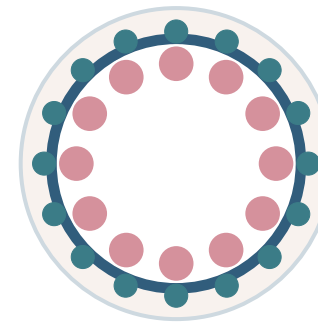
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Learning outcomes

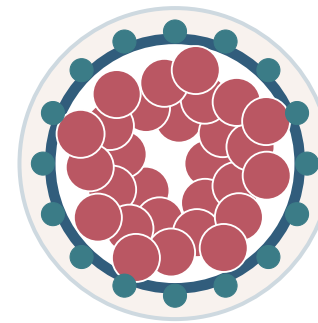
- Define breast carcinoma in situ using its tissue boundary.
- Explain why “ductal” and “lobular” do not identify separate cells of origin.
- Recognize the dominant diagnostic features of DCIS and LCIS.
- Connect in situ morphology to detection, subsequent cancer risk, and management.

“In situ” describes an anatomical constraint

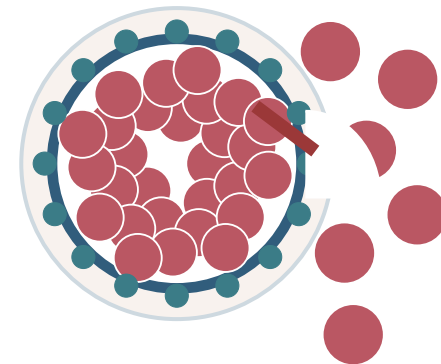
- Neoplastic epithelial cells remain within ducts and lobules.
- An intact basement membrane separates involved spaces from stroma.
- The term denotes a location and invasion boundary—not benignity.
- The distinction is established by the relationship of tumor to surrounding structures.



Normal duct



In situ

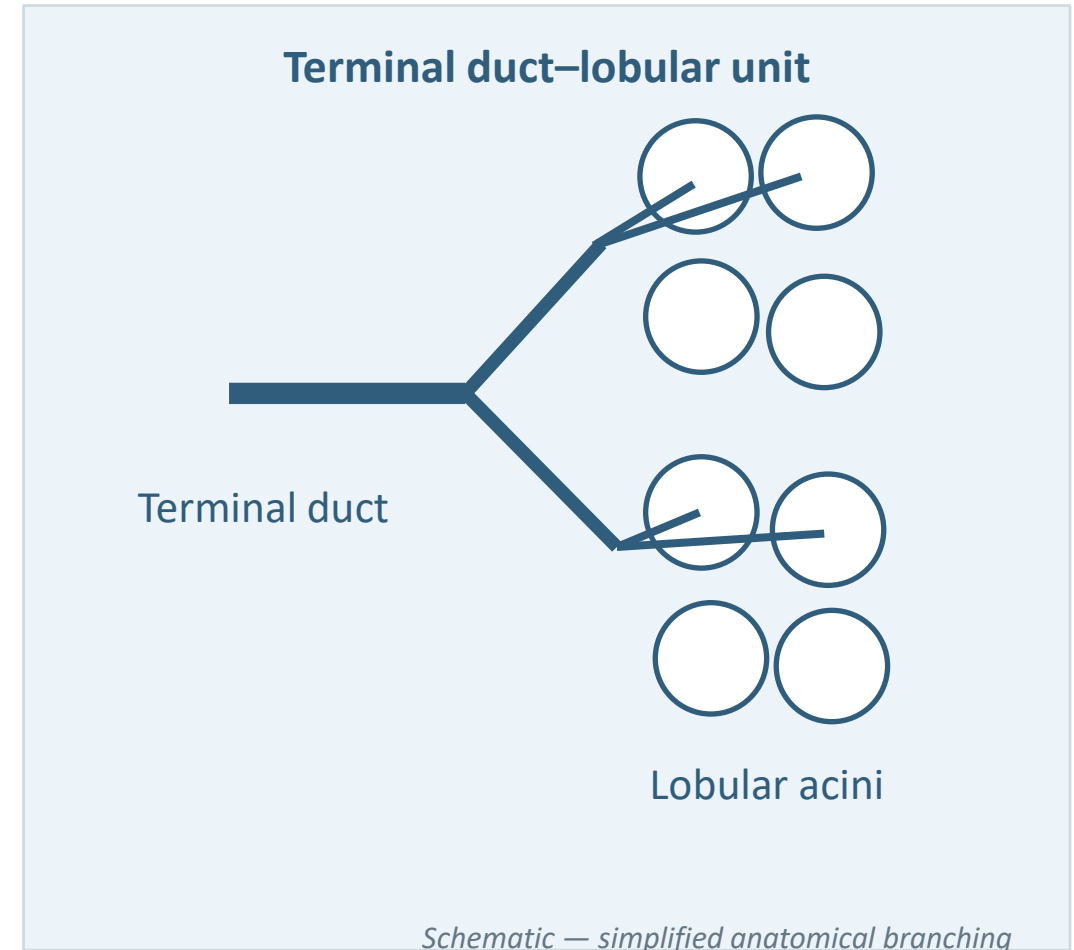


Invasive

Schematic — not a tissue section

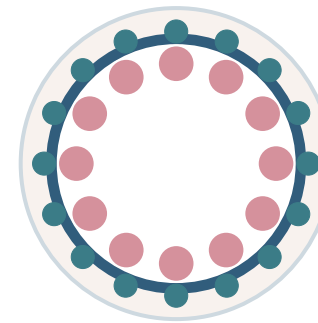
The terminal duct–lobular unit is the shared origin

- The terminal duct–lobular unit contains terminal ducts and associated acini.
- Evidence indicates that both major carcinoma patterns originate here.
- A ductal-type lesion may populate lobules; A lobular-type lesion may populate ducts.
- Anatomic distribution should not be mistaken for the cell of origin.

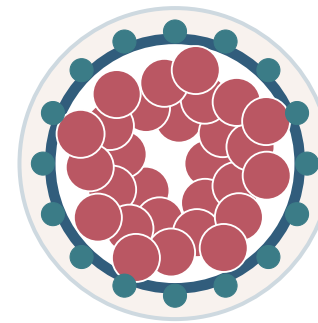


Two boundaries organize the diagnosis

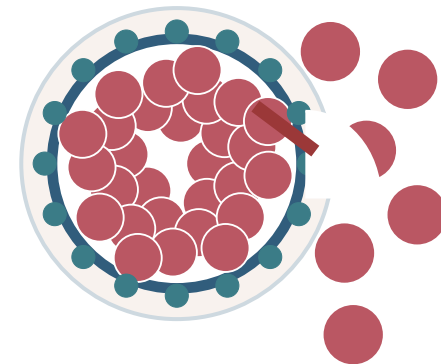
- Luminal epithelial proliferation forms the neoplastic component.
- A basement membrane marks confinement versus invasion.
- Myoepithelial cells are generally preserved around DCIS-involved spaces.
- Cells beyond the boundary require assessment for invasive carcinoma.



Normal duct



In situ

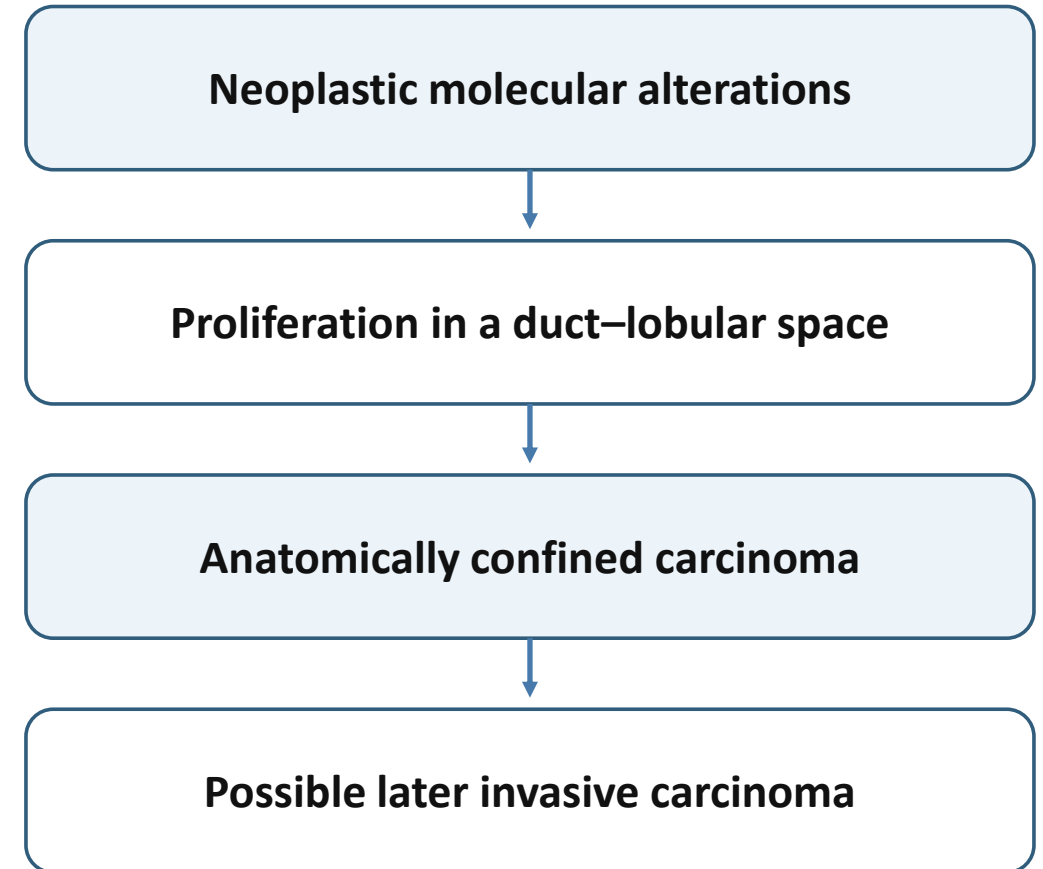


Invasive

Schematic — not a tissue section

Confinement does not imply molecular normality

- Carcinoma in situ carries many molecular alterations seen in invasive cancer.
- The lesion can be genetically neoplastic despite an intact tissue boundary.
- The phrase “carcinoma in situ” therefore reflects both malignant biology and location.
- Whether—and when—progression occurs varies among lesions.



Historical “ductal” and “lobular” terminology

Historical interpretation

- Terms originally described which normal spaces a lesion resembled.
- The patterns were taken as clues to the anatomical site of origin.
- This view was primarily morphological.

Current biologic interpretation

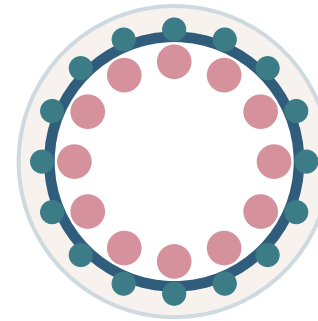
- Most breast carcinomas arise from terminal duct–lobular epithelium.
- Architectural differences reflect tumor genetics and biology.
- Names remain useful diagnostic categories, not origin maps.

The two major in situ patterns

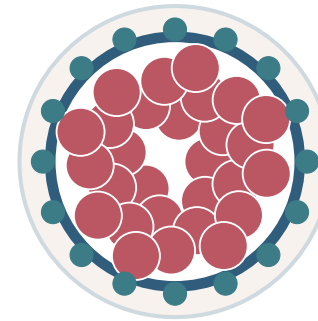
Feature	DCIS	LCIS
Cohesion	Usually cohesive	Typically dyscohesive
Detectability	Often calcification-associated	Usually incidental biopsy finding
Main grade framework	Nuclear grade	Classic versus aggressive variants
Clinical pattern	Usually local recurrence concern	Risk affecting either breast

The architectural relationship is diagnostic

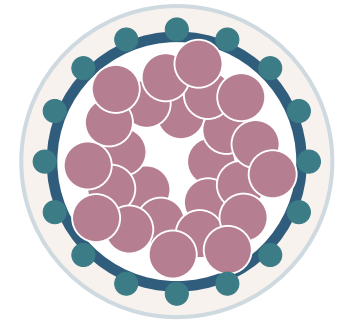
- DCIS involves ducts and lobules while generally maintaining myoepithelial cells.
- LCIS also involves ducts and lobules, often with reduced cell-to-cell cohesion.
- The intact boundary is shared; Patterns and molecular programs differ.
- Do not infer invasiveness from the adjective “carcinoma” alone.



Normal duct



In situ



Lobular-type

Schematic — not a tissue section

Detection begins before a microscopic label

- DCIS most often comes to attention on mammography.
- Calcification is its dominant radiologic clue.
- LCIS usually lacks calcification and a stromal response.
- Sampling supplies the microscopic distinction that imaging cannot establish alone.

How the lesions are encountered

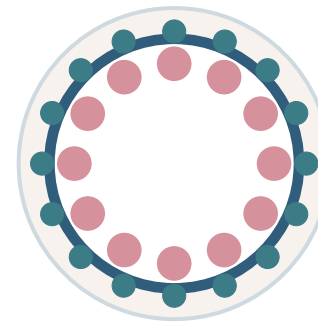
DCIS → mammographic finding

LCIS → incidental biopsy finding

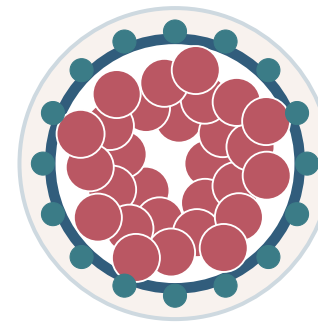
Morphology → final pattern recognition

DCIS: A proliferation confined to epithelial spaces

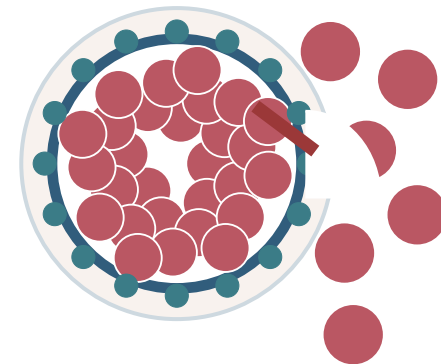
- Neoplastic cells remain limited to ducts and lobules.
- Myoepithelial cells are generally maintained in affected structures.
- Neoplastic cells may extend through connected ductal spaces.
- Extensive involvement can occupy an entire breast segment.



Normal duct



In situ

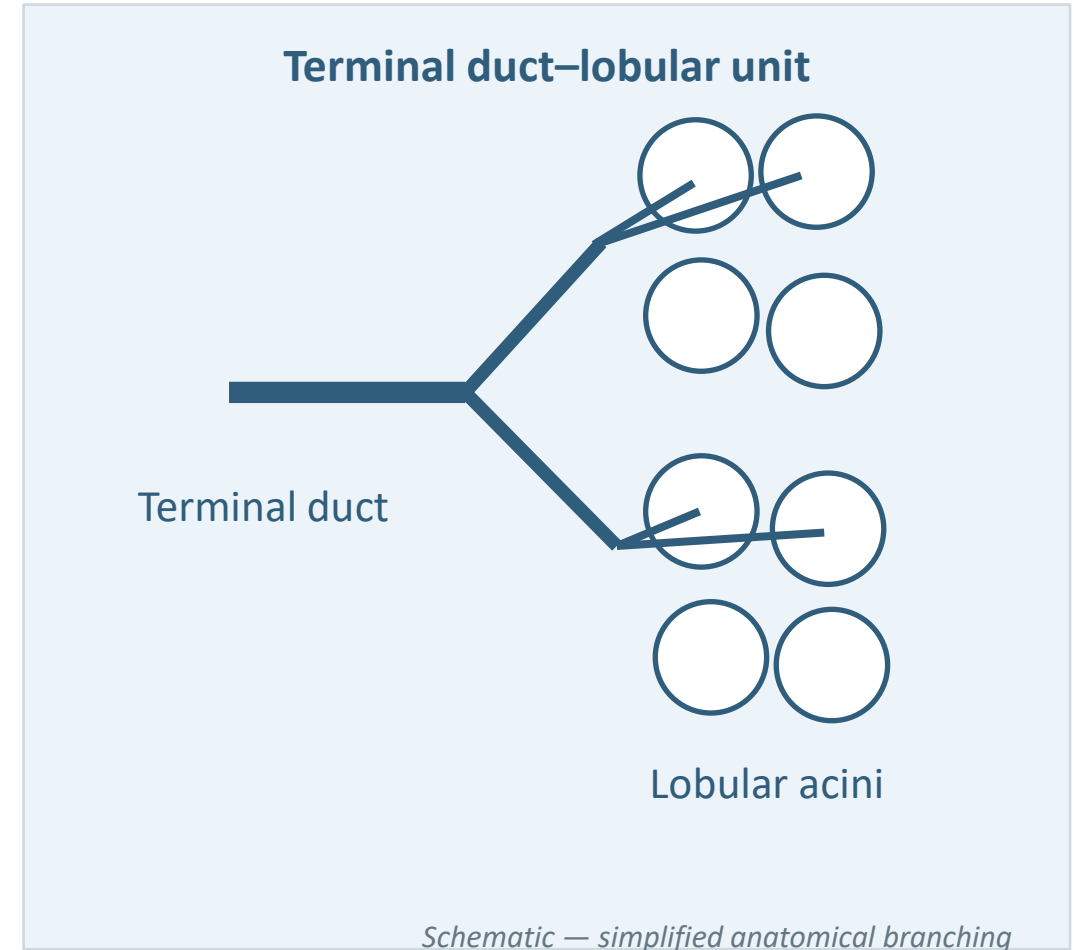


Invasive

Schematic — not a tissue section

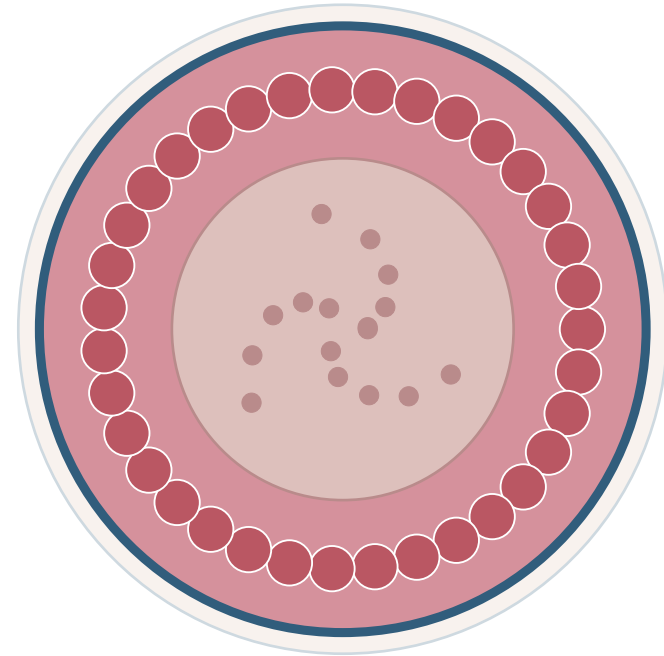
Segmental ductal extension explains hidden extent

- The ductal tree permits contiguous spread through branching epithelial spaces.
- Imaging may underestimate how much of the system contains DCIS.
- The lesion may not be grossly visible at operation.
- Extent becomes relevant to complete surgical excision.



Why mammography frequently detects DCIS

- Intraductal calcifications form a conspicuous imaging clue.
- Mineralization may accompany necrotic cell debris.
- Secretory material can also calcify in the involved lumen.
- The finding is a radiologic manifestation, not proof of stromal invasion.



Schematic — not a photomicrograph

DCIS can produce a density or a palpable abnormality

- Periductal fibrosis sometimes produces mammographic density.
- A vaguely palpable mass is less common than calcification-only detection.
- Nipple discharge occurs rarely, often with papillary patterns.
- Incidental detection on biopsy is also possible.

Presentations mentioned by Robbins

Calcifications (predominant)

Density / subtle palpable mass

Discharge / incidental finding

DCIS is graded chiefly by nuclear features

- Nuclear size and shape are central to nuclear-grade assessment.
- The architectural pattern is not the primary grading criterion.
- Low-grade and high-grade groups differ in associated biology.
- Report logic should not substitute “comedo” or “cribriform” for nuclear grade.

Two separate descriptive axes

Nuclear grade → cytologic features

Architecture → growth pattern

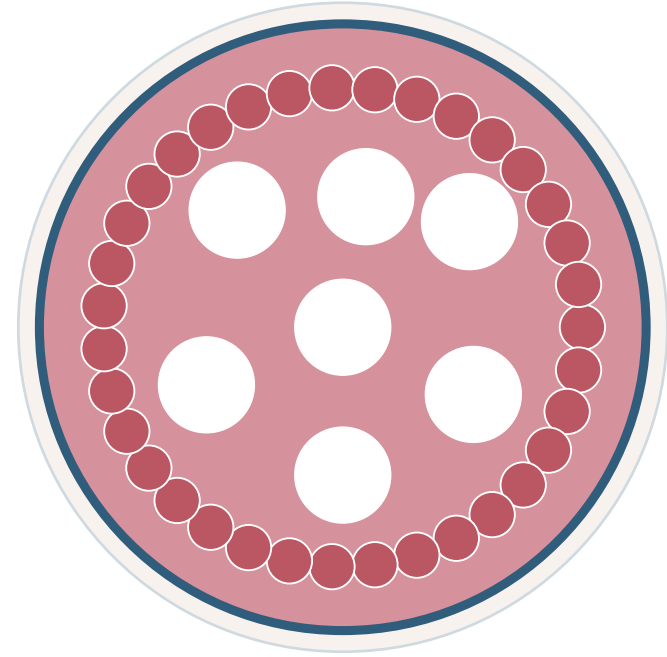
Necrosis → additional feature

Grade and architecture answer different questions

Descriptor	What it captures	What it does not establish
Nuclear grade	Size and shape of nuclei	The architectural pattern
Cribriform	Punched-out intraluminal spaces	A unique grade by itself
Micropapillary	Bulbous projections, no core	The degree of nuclear atypia
Comedo necrosis	Central necrotic material	A separate cell of origin

Cribriform DCIS: Rounded internal lumina

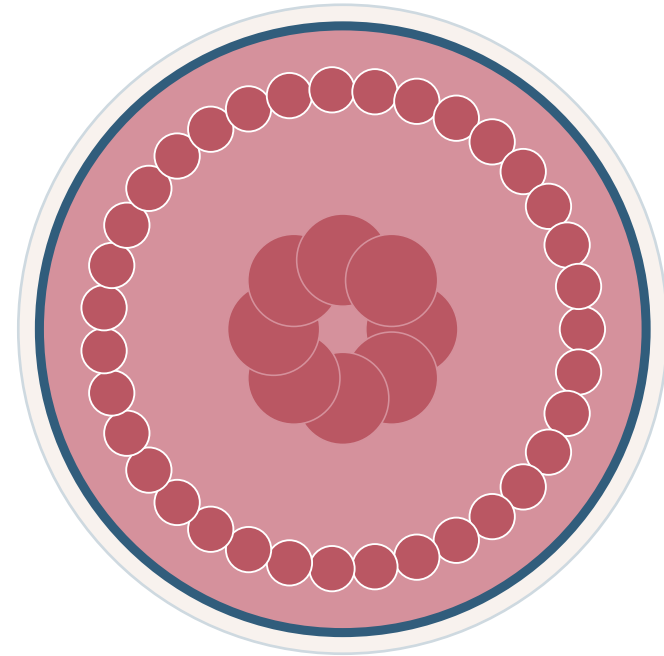
- The involved space contains neoplastic epithelium with repeated rounded holes.
- The “cookie-cutter” configuration describes architecture.
- Secretory material within spaces may undergo calcification.
- The appearance is one possible pattern of DCIS.



Schematic — not a photomicrograph

Micropapillary DCIS: Projections without cores

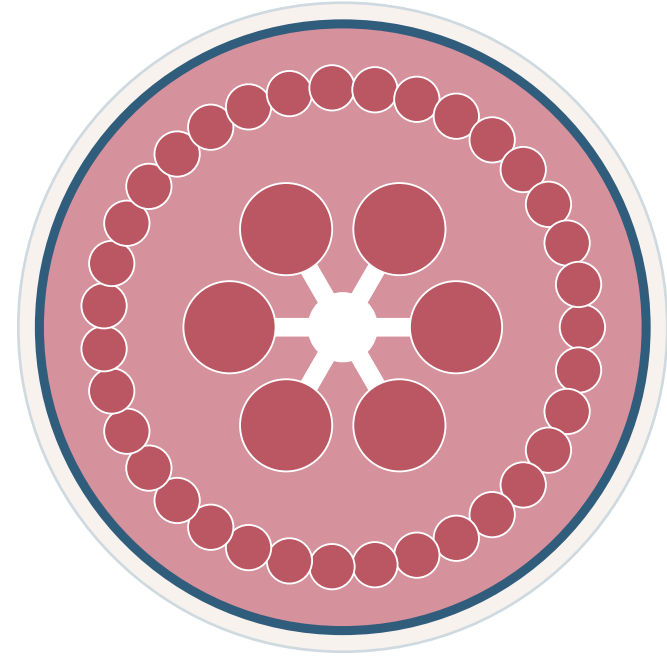
- Tumor forms bulbous intraluminal protrusions.
- The projections lack fibrovascular cores.
- Architecture must be distinguished from a true papillary lesion.
- Micropapillary architecture may occasionally accompany nipple discharge.



Schematic — not a photomicrograph

Papillary DCIS: True fibrovascular cores

- True papillae have fibrovascular cores.
- The cores in papillary DCIS lack a myoepithelial layer.
- This is not equivalent to micropapillary protrusion.
- Location and lining characteristics support correct lesion classification.



Schematic — not a photomicrograph

Micropapillary versus papillary architecture

Micropapillary DCIS

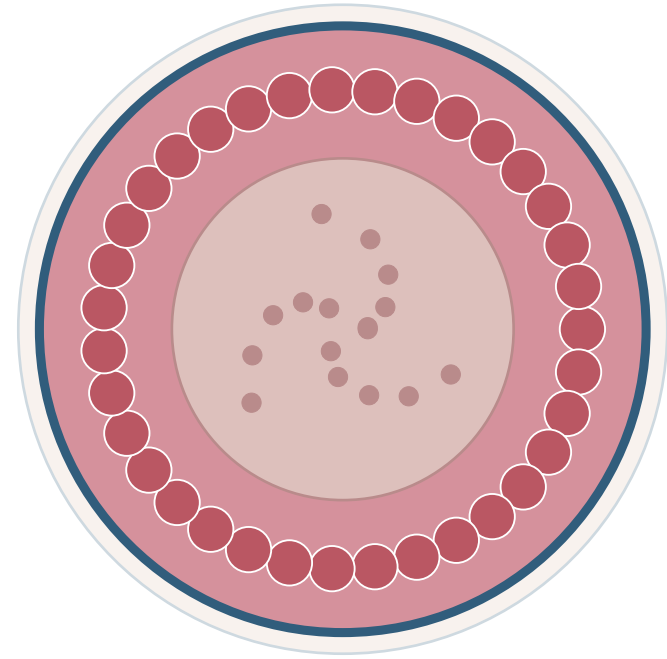
- Bulbous projections of neoplastic epithelium.
- No fibrovascular stalk within protrusions.
- Architecture alone does not determine nuclear grade.

Papillary DCIS

- True projections built around fibrovascular stalks.
- Papillary cores lack an associated myoepithelial layer.
- Architecture alone does not determine invasive status.

Comedo necrosis: Central cell breakdown

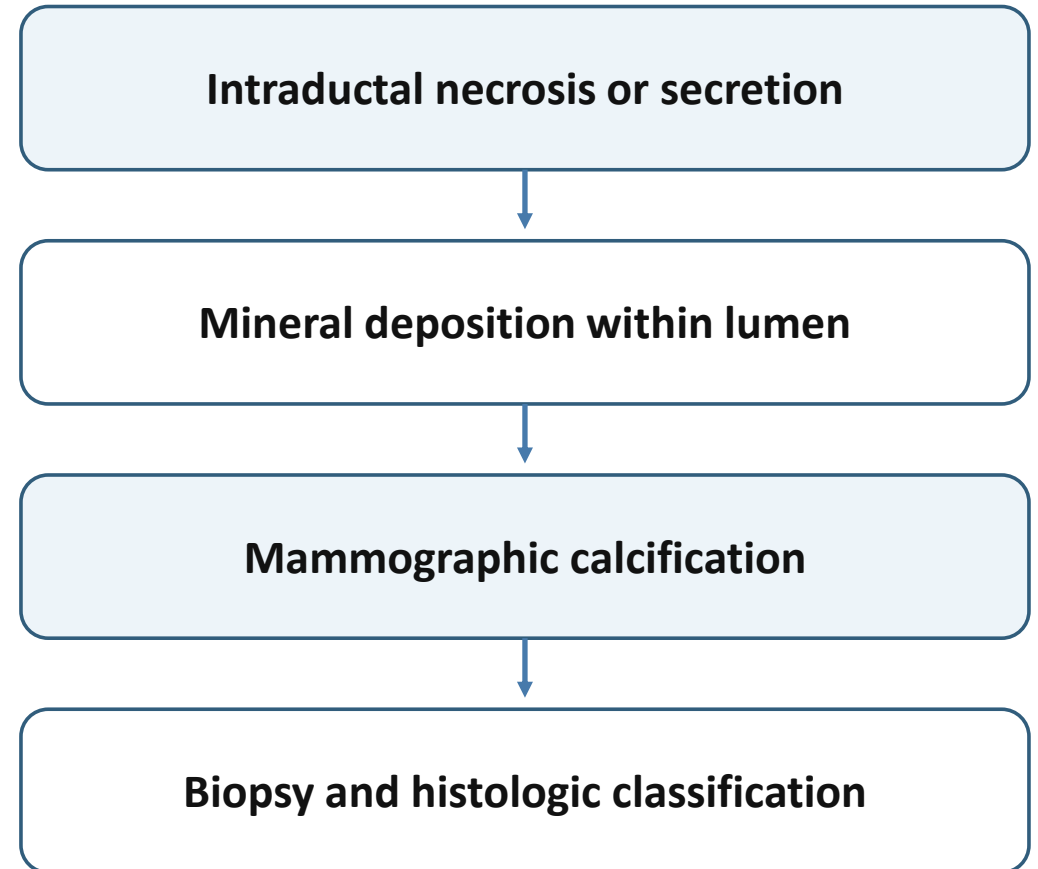
- Necrotic material accumulates in the central ductal lumen.
- This feature is mainly associated with high-grade DCIS.
- Calcification may accompany central necrosis.
- Its presence is relevant to recurrence-risk assessment.



Schematic — not a photomicrograph

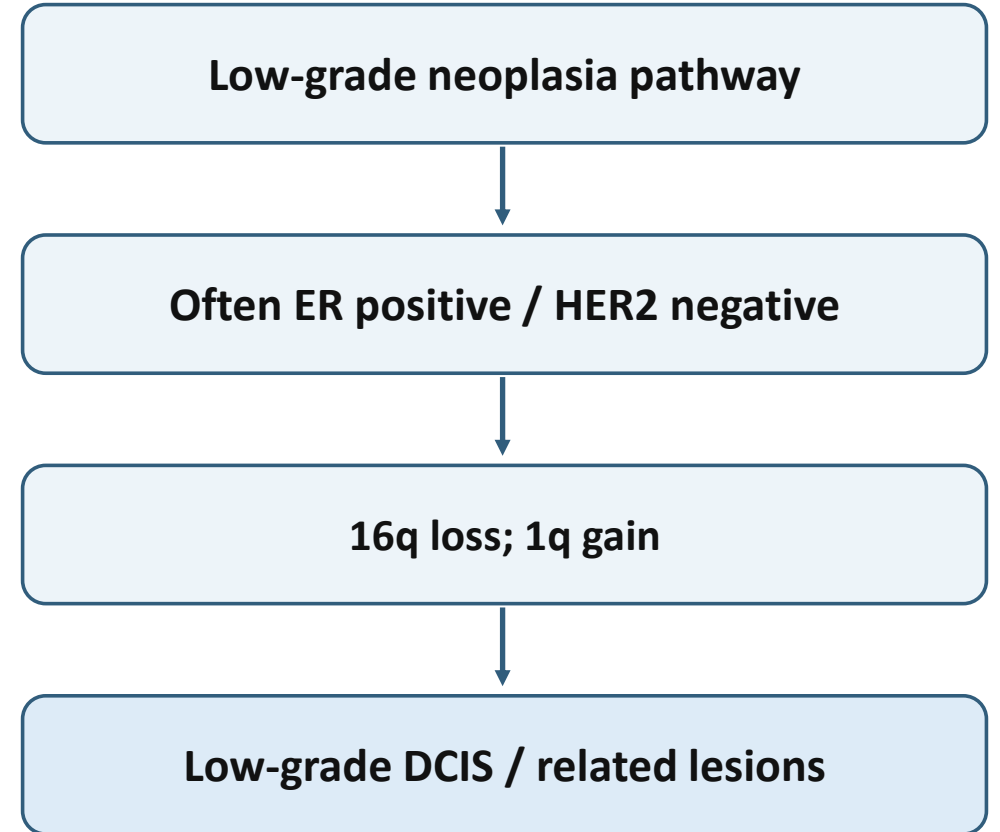
Calcification and necrosis are related, not synonymous

- Necrotic central material can calcify.
- Secretions in otherwise intact lumina may also calcify.
- Calcification is the imaging signal; Microscopic examination defines the lesion.
- The same mammographic clue can accompany different DCIS architectures.



Low-grade DCIS: A characteristic pathway

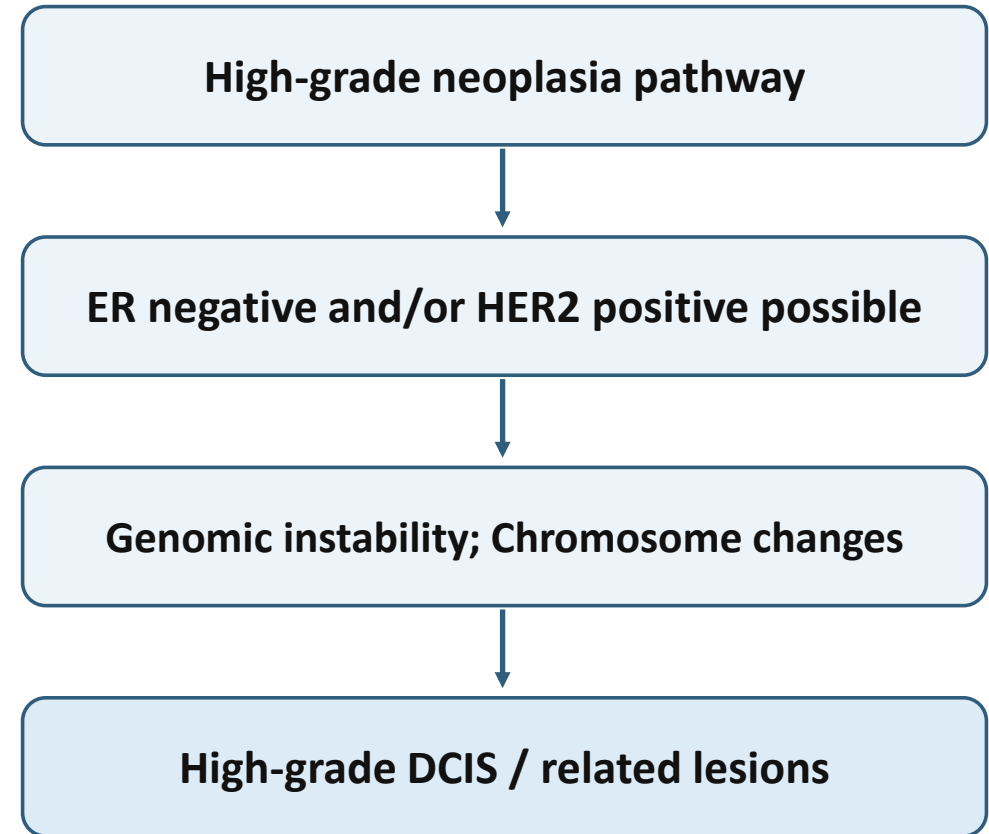
- Low-grade lesions are typically estrogen-receptor positive.
- They are commonly HER2 negative.
- Loss of 16q and gain of 1q exemplify the low-grade molecular pathway.
- These features connect in situ lesions with related invasive carcinomas.



Simplified source-grounded relationship

High-grade DCIS: A different biological program

- High-grade DCIS may lack ER expression.
- HER2 positivity is possible in this group.
- Greater genomic instability and chromosomal alterations occur.
- Molecular patterns resemble those of high-grade invasive carcinomas.



Simplified source-grounded relationship

Biologic contrast between DCIS grades

Property	Low-grade DCIS	High-grade DCIS
ER	Typically positive	May be negative
HER2	Typically negative	May be positive
Molecular changes	16q loss; 1q gain	Genomic instability
Pathway	Low-grade neoplasia	High-grade neoplasia

DCIS progression is not a single uniform sequence

- Low- and high-grade DCIS appear biologically distinct.
- They may follow separate pathways toward invasive carcinoma.
- A subsequent invasive lesion often resembles the associated DCIS phenotype.
- Neither histology nor receptors alone predicts an exact date of invasion.

Parallel source-described pathways

Low-grade DCIS → related invasion

High-grade DCIS → related invasion

**Timing in an individual remains
uncertain**

Natural history: Treatment obscures observation

- Most diagnosed DCIS is treated, limiting untreated follow-up.
- The full untreated trajectory cannot be observed directly in most cases.
- Source estimates apply to groups, not a particular patient.
- Higher-grade and extensive lesions are believed to progress faster.

Question for interpretation

Interpret rates as cohort estimates.

Do not imply every DCIS becomes invasive.

Distinguish biological risk from observed outcomes.

Small low-grade DCIS: Reported invasive risk

- Invasive cancer development of approximately 1% per year.
- The estimate refers specifically to small low-grade DCIS.
- Invasive disease often emerges in the same breast quadrant.
- Grade and ER/HER2 pattern commonly resemble antecedent DCIS.

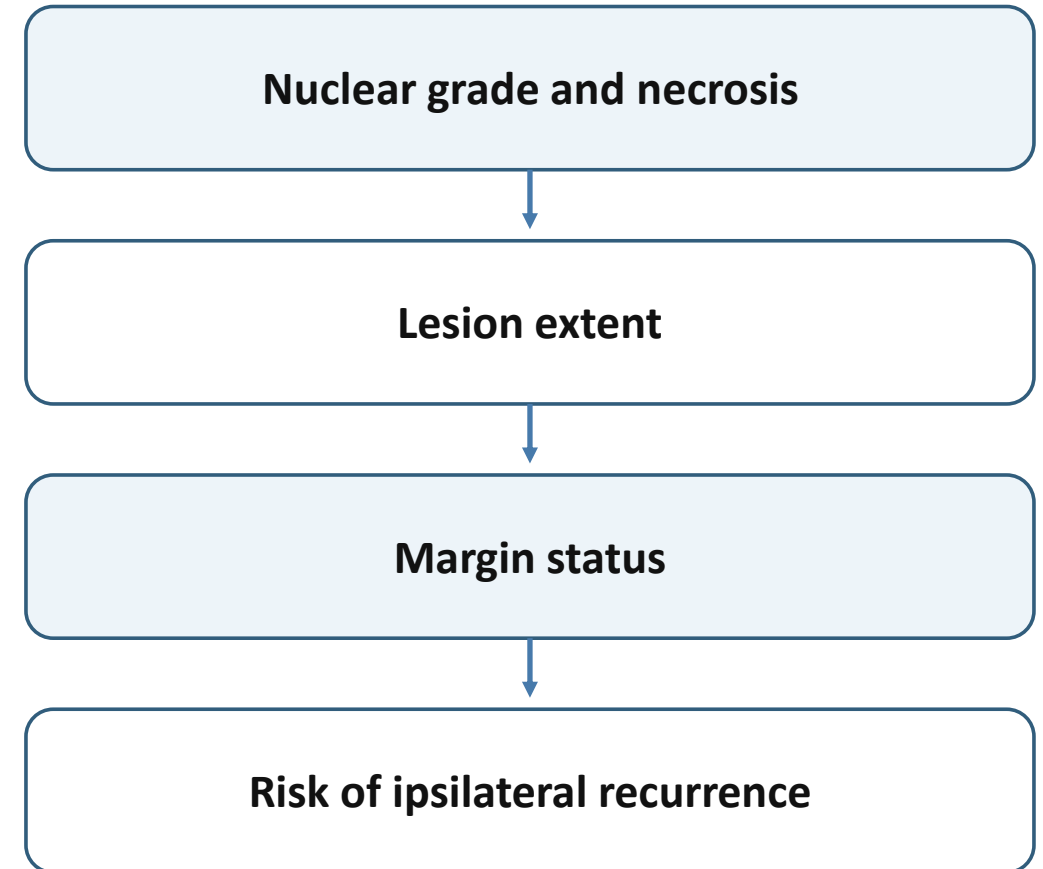
Clinical distribution

DCIS: Usually same site

LCIS: Risk in either breast

DCIS recurrence risk: Three major features

- High nuclear grade with associated necrosis increases recurrence concern.
- Extensive intraductal distribution increases the chance of residual disease.
- A positive surgical margin indicates incomplete local clearance.
- These are source-described recurrence factors, not an individual risk calculator.



DCIS treatment logic is primarily local

- Mastectomy cure in more than 95% of patients with DCIS.
- Complete excision can be difficult when extent is not grossly apparent.
- Postoperative radiation reduces recurrence risk.
- Tamoxifen also reduces recurrence in appropriate circumstances.

What local therapy targets

Remove anatomically confined lesion

Reduce residual-local recurrence

Consider future ipsilateral disease risk

Clinical decisions must preserve uncertainty

- Confinement does not guarantee the absence of occult invasion.
- Metastatic deaths after an initial DCIS diagnosis are uncommon.
- Possible origins include later invasive carcinoma or initially occult invasion.
- Active investigation of surveillance for selected DCIS.

Question for interpretation

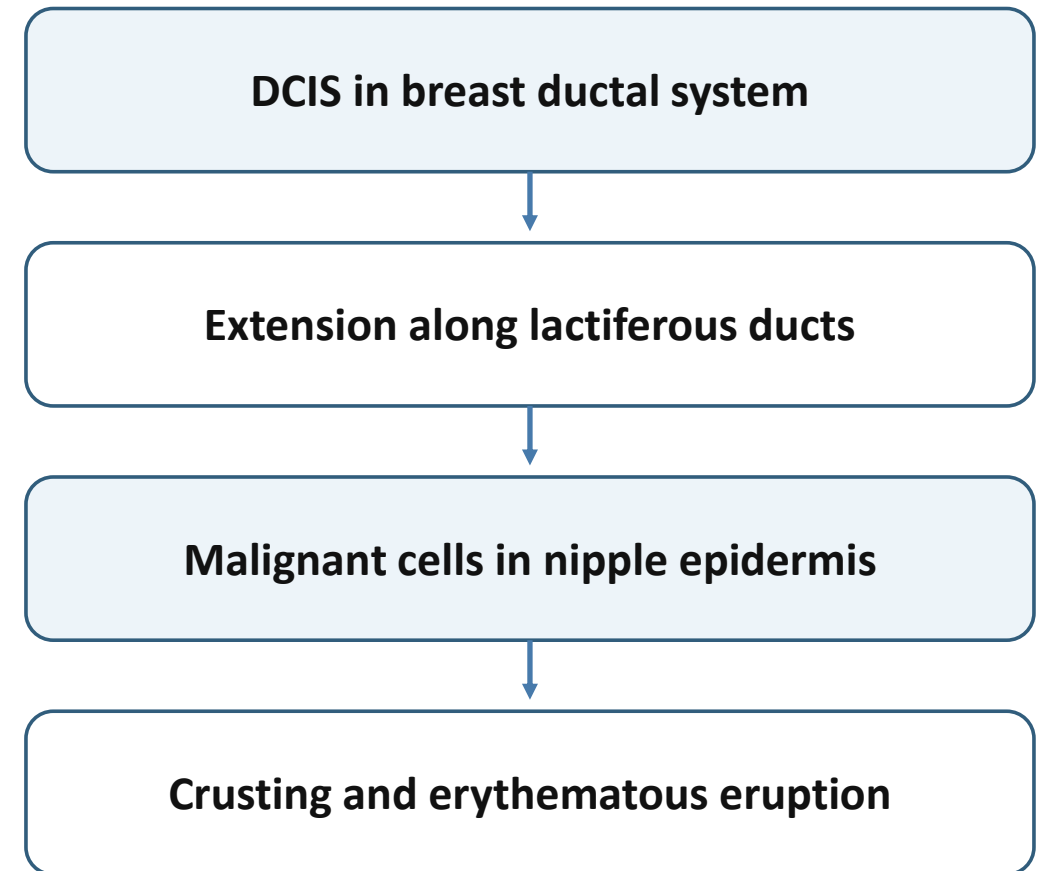
Pathologic diagnosis $\neq$ certainty of future course.

Sampling limitations remain important.

Management trials were ongoing in source edition.

Paget disease: Extension to the nipple epidermis

- Tumor cells can move from DCIS along lactiferous ducts.
- They reach the nipple epidermis without crossing the basement membrane.
- The resulting epithelial disruption permits fluid leakage.
- An in situ ductal process can therefore generate a visible skin lesion.



Paget disease can mimic unilateral eczema

- Clinical appearance includes erythema and a scaling crust.
- Itching is common.
- The unilateral nipple pattern should prompt pathologic evaluation.
- Paget cells may be identified on nipple biopsy or exudate cytology.

Clinicopathologic reasoning

Unilateral itchy, crusted nipple

Paget cells within epidermis

Evaluate underlying breast lesion

An underlying mass changes the Paget scenario

- Without a palpable mass, Paget disease frequently accompanies DCIS.
- With a palpable mass, invasive carcinoma is often present.
- Prognosis reflects the invasive component if one is identified.
- The presence of Paget disease itself is not the key prognostic driver.

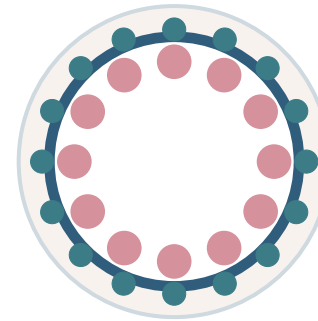
Clinical distribution

DCIS: Usually same site

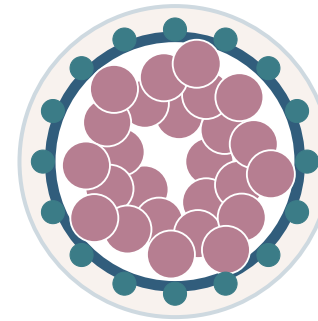
LCIS: Risk in either breast

LCIS: In situ growth with cellular dyscohesion

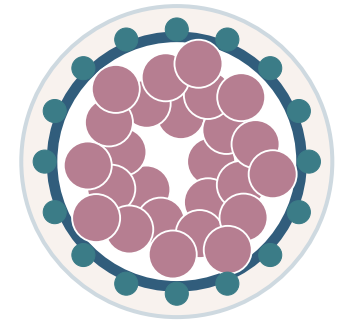
- Neoplastic epithelial cells grow within ducts and lobules.
- Unlike typical DCIS, the cells are loosely cohesive.
- The lesion is usually detected incidentally on biopsy.
- This phenotype is linked to impaired E-cadherin-mediated adhesion.



Normal duct



Lobular-type

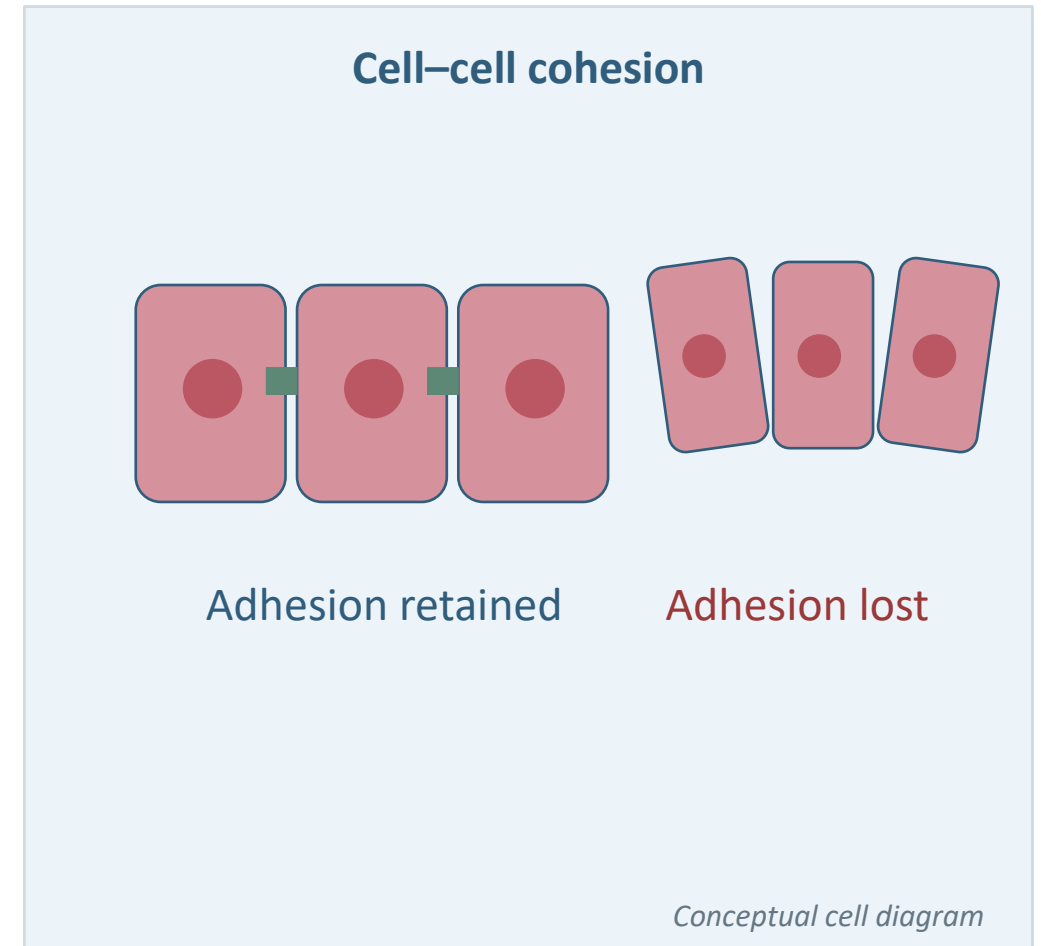


Lobular-type

Schematic — not a tissue section

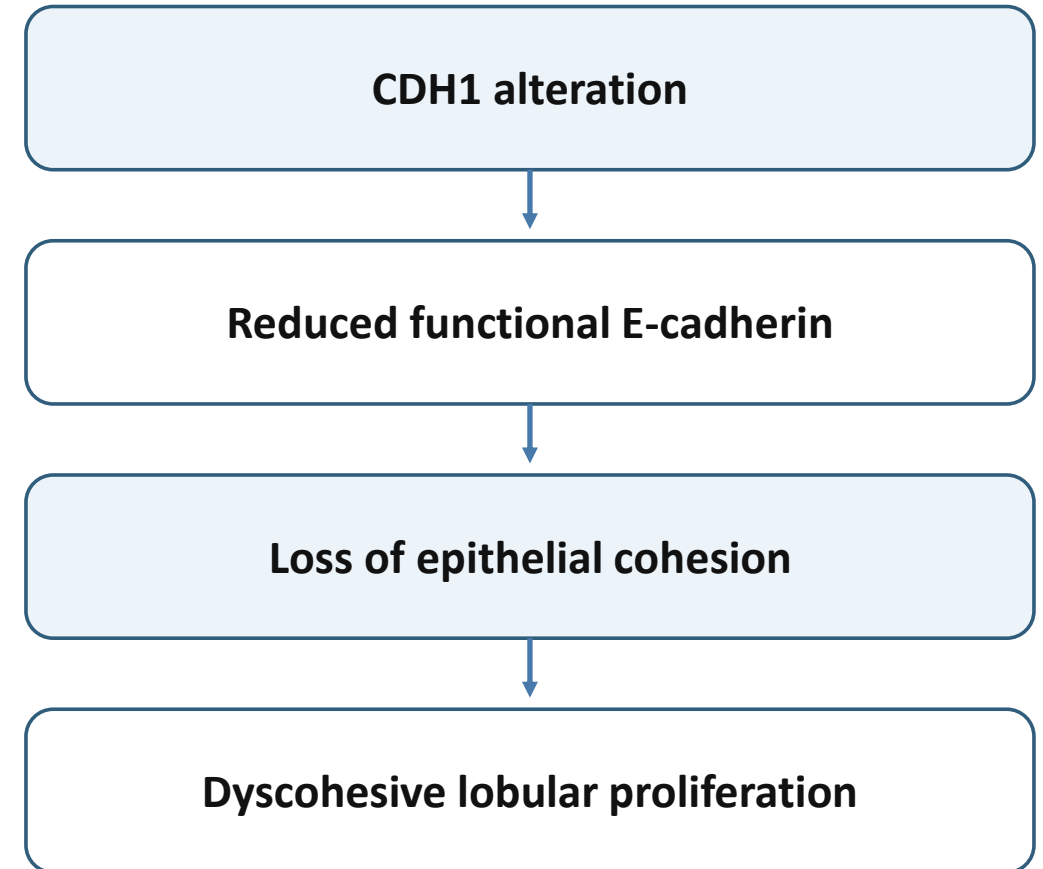
E-cadherin helps adjacent epithelial cells adhere

- E-cadherin is a transmembrane epithelial adhesion protein.
- It contributes to cell-to-cell attachment in glandular tissues.
- Functional loss permits the rounded, separate-cell pattern of LCIS.
- Loss of cohesion is biological, not proof of stromal invasion.



CDH1 is a major route to E-cadherin loss

- The E-cadherin gene is CDH1 on chromosome 16q22.1.
- Mutation or deletion is a common cause of its loss in lobular lesions.
- Adhesion failure helps explain dyscohesive morphology.
- The pathway overlaps with low-grade breast neoplasia alterations.



Not every lobular lesion loses CDH1 itself

- Other adhesion-complex proteins are sometimes dysfunctional.
- Robbins specifically mentions β -catenin as an alternative.
- The diagnostic phenotype reflects compromised adhesion.
- A single protein result must be interpreted with morphology and context.

Alternative molecular routes

E-cadherin loss (commonly CDH1)

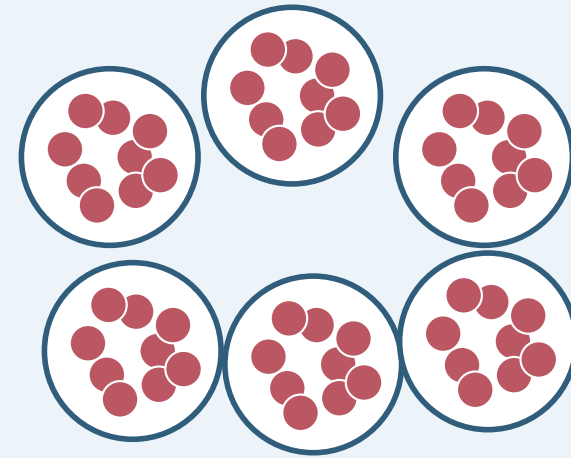
Other adhesion component dysfunction

Shared effect: Cellular dyscohesion

Classic LCIS: Uniform cells within lobular units

- Rounded or oval nuclei with small nucleoli are characteristic.
- Cells tend to be monomorphic and loosely connected.
- Affected acini become filled and expanded.
- The source describes more than half of acini in a unit involved.

Classic LCIS: Expanded acini



Rounded, separated cells expand multiple acini

Schematic — not a photomicrograph

Classic LCIS may contain signet-ring cells

- Intracytoplasmic mucin can create a signet-ring appearance.
- Signet-ring cells may occur within otherwise classic LCIS.
- The observation does not by itself establish invasive carcinoma.
- Interpret individual cells in the architecture of the involved unit.

Question for interpretation

Cell morphology and compartment are separate questions.

Mucin positivity can occur in classic LCIS.

Preserve the in situ/invasive distinction.

Pagetoid lobular spread is not nipple Paget disease

- Lobular neoplastic cells may extend beneath the luminal duct epithelium.
- This distribution is termed pagetoid spread.
- It occurs between basement membrane and overlying luminal cells.
- Nipple epidermal Paget disease is a different phenomenon.

Two unrelated uses of “Paget”

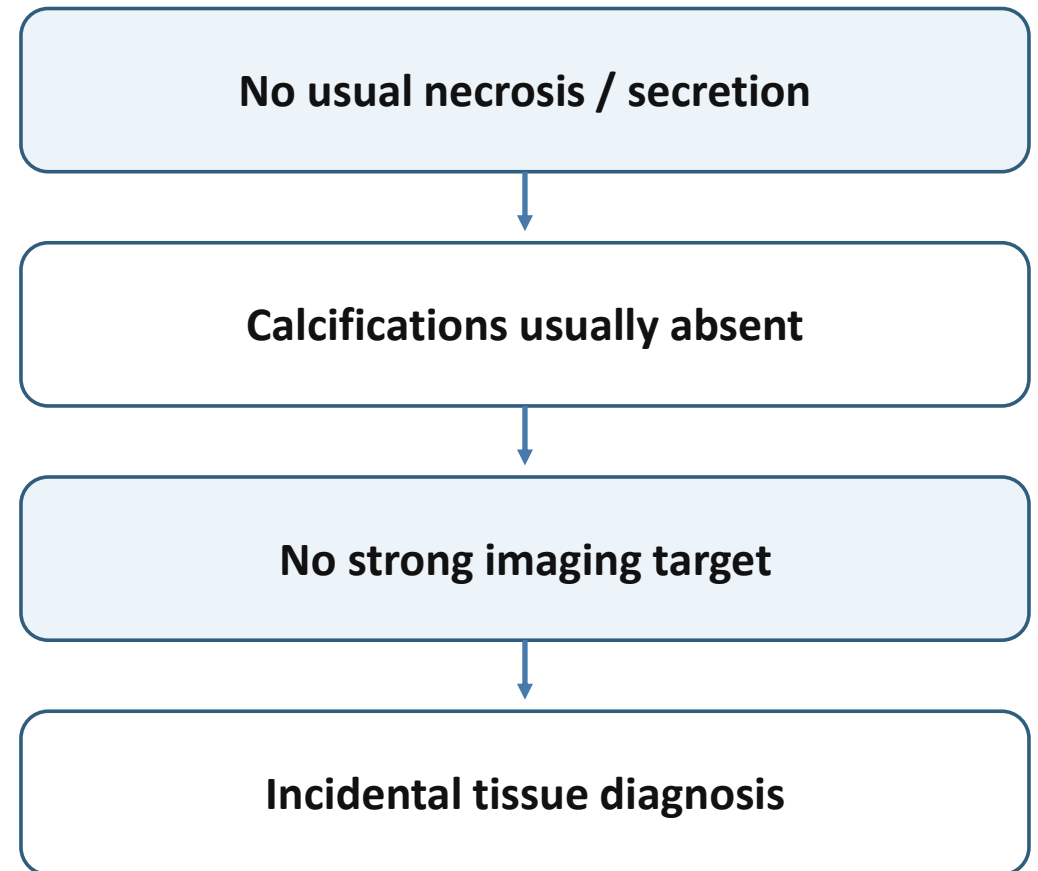
LCIS pagetoid spread: Duct wall

Paget disease: Nipple epidermis

Do not equate the two diagnoses

LCIS is usually occult on breast imaging

- Classic LCIS rarely produces calcifications.
- Necrosis and secretory activity are generally absent.
- There is usually no stromal reaction causing a density.
- Diagnosis commonly follows biopsy obtained for another reason.



Pleomorphic LCIS is an important exception

- Aggressive lobular in situ variants can show necrosis.
- Associated calcifications may make these lesions image-detectable.
- Their behavior and management differ from classic LCIS.
- “Lobular” does not automatically mean indolent morphology.

Question for interpretation

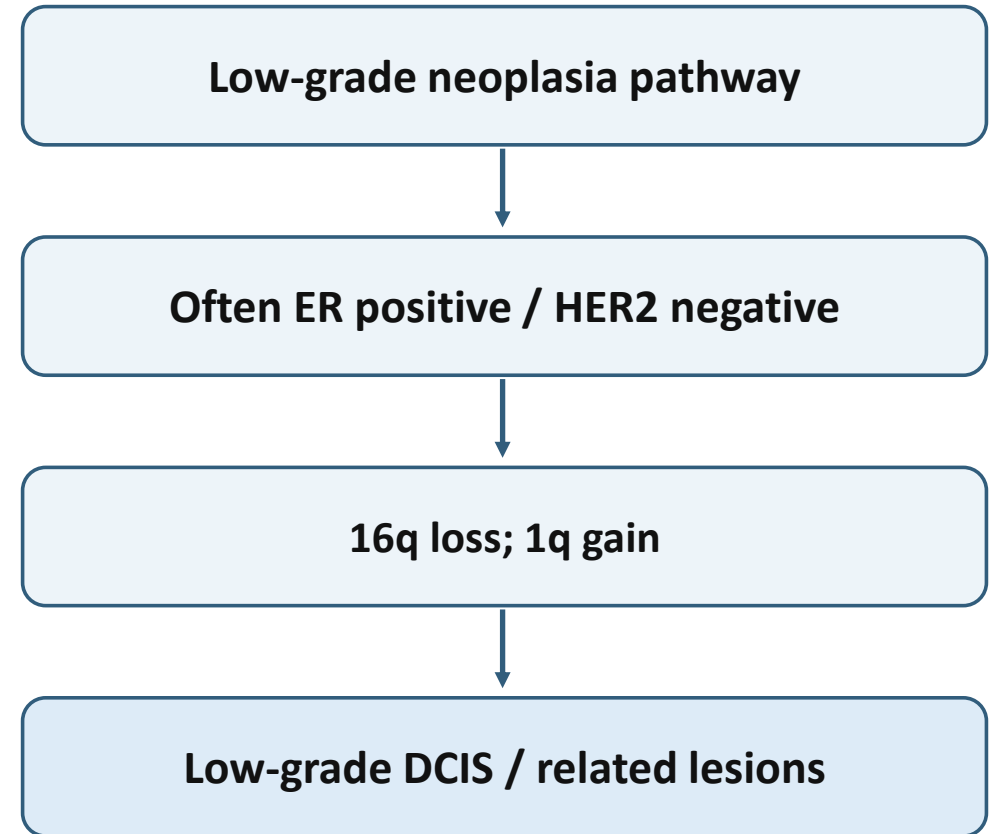
Classic phenotype ≠ all variants.

Assess necrosis, nuclear appearance, and context.

Variant recognition changes management.

LCIS receptor phenotype

- LCIS almost always expresses estrogen receptor.
- Progesterone-receptor expression is also usual.
- Most lesions are HER2 negative.
- This phenotype is consistent with a low-grade neoplasia pathway.



Simplified source-grounded relationship

LCIS can occur in both breasts

- Bilateral LCIS in 20%–40% when both breasts are biopsied.
- The analogous reported proportion for DCIS is 10%–20%.
- These are observed biopsy-distribution figures, not population prevalences.
- Bilateral potential is relevant to future risk assessment.

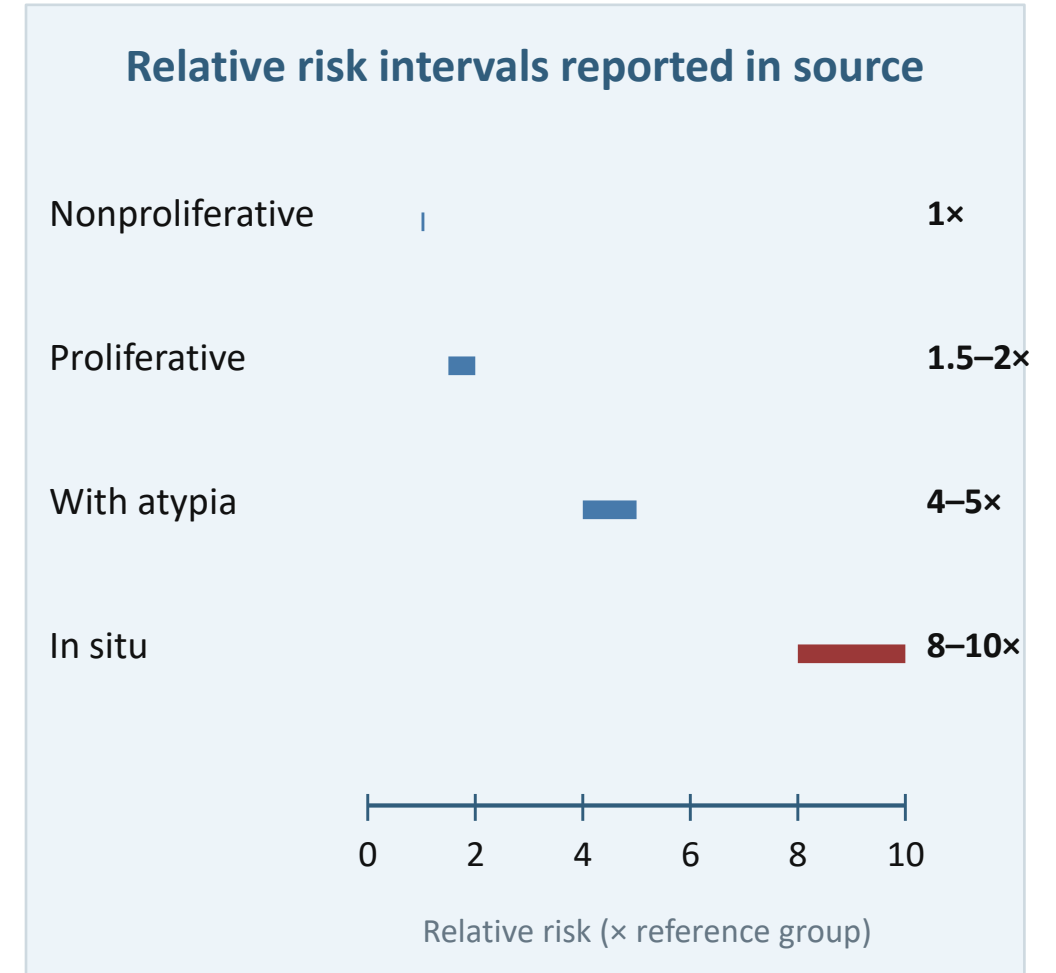
Clinical distribution

DCIS: Usually same site

LCIS: Risk in either breast

Classic LCIS indicates bilateral invasive-cancer risk

- The risk applies to either breast, somewhat higher ipsilaterally.
- An 8- to 10-fold increased relative risk.
- A subsequent invasive cancer occurs at about 1% per year.
- This is not the same clinical model as local DCIS recurrence.



Classic and aggressive LCIS variants are managed differently

- Classic LCIS on a concordant core biopsy may be surveilled.
- The source associates concordance with a low chance of missed invasive disease.
- Pleomorphic LCIS and other aggressive variants merit surgical excision.
- Endocrine strategies or mastectomy are options in selected circumstances.

Risk-adapted source framework

Classic + concordant → surveillance possible

Aggressive variants → excision

Individualized risk-reduction options

Relative risk across breast epithelial lesions

Lesion category	Relative risk of invasive breast carcinoma
Nonproliferative change	1.0
Proliferation without atypia	1.5–2
Proliferation with atypia	4–5
Carcinoma in situ (DCIS / LCIS)	8–10

Atypical ductal hyperplasia is not automatically DCIS

- Atypical ductal hyperplasia can partly involve a duct.
- The Robbins figure describes cytologically monotonous cells and cribriform spaces.
- Architectural resemblance does not by itself establish full DCIS.
- Lesion extent and diagnostic assessment must be integrated.

Source-illustrated relationship

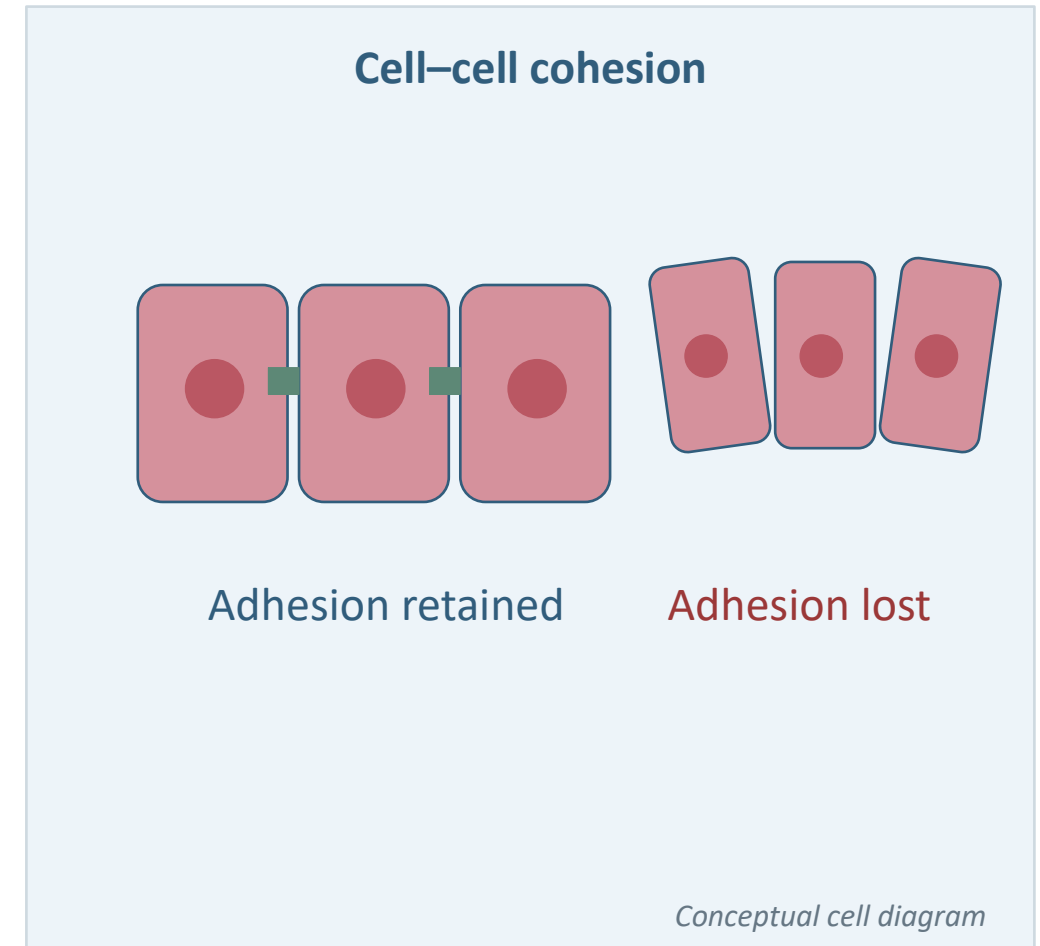
ADH: Partial duct involvement

DCIS: Defined in situ neoplastic lesion

Avoid diagnosis from one motif alone

Atypical lobular hyperplasia and LCIS share a phenotype

- Atypical lobular hyperplasia contains monomorphic dyscohesive cells.
- LCIS cells are morphologically identical to cells in ALH.
- Extent of lobular-unit involvement distinguishes diagnostic categories.
- Adhesion biology supports their relationship.



Microscopic differentiation: DCIS versus LCIS

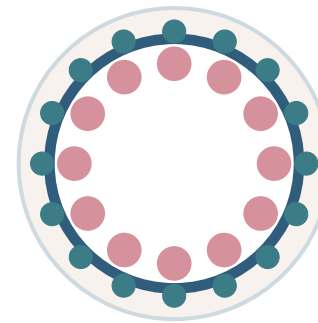
Criterion	DCIS	Classic LCIS
Cell arrangement	Usually cohesive	Dyscohesive
Dominant classification	Nuclear grade	Lobular phenotype / variant
Necrosis	Comedo necrosis possible	Typically absent
Calcifications	Common	Usually absent
E-cadherin	Generally retained	Usually lost

Clinical interpretation: DCIS versus LCIS

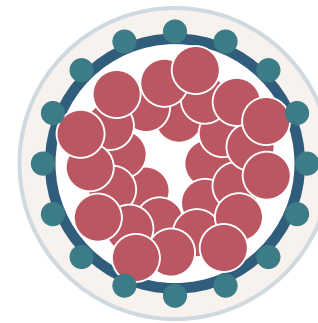
Question	DCIS	Classic LCIS
How found?	Usually mammography	Usually incidental biopsy
Later risk	Often same region of breast	Either breast
Local therapy?	Commonly treated locally	Concordant lesions may be observed
Important exception	High-grade / extensive disease	Pleomorphic variants

Histologic boundaries depend on adequate sampling

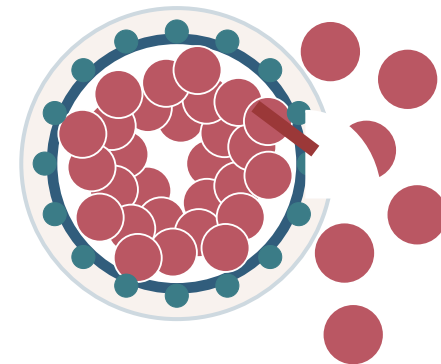
- Imaging cannot demonstrate a basement membrane directly.
- Involvement may extend beyond the radiologic abnormality.
- When invasion is suspected, the sampled tissue must be examined carefully.
- An initial in situ diagnosis does not eliminate the possibility of unsampled invasion.



Normal duct



In situ



Invasive

Schematic — not a tissue section

Case 1 — mammographic calcifications

Clinical / pathology vignette

Screening detects branching calcifications in one segment of the breast.

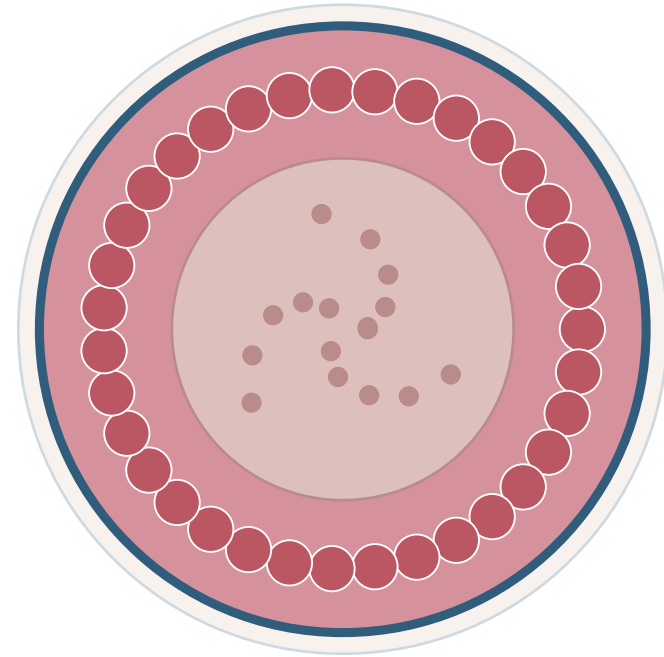
Core biopsy shows enlarged atypical nuclei in ducts with central necrosis.

The involved duct periphery remains bounded; No definite stromal invasion is sampled.

Question: Which in situ phenotype is most strongly suggested?

Case 1 — interpret the full feature set

- Intraductal cells with comedo necrosis support DCIS.
- High nuclear grade is compatible with prominent atypia and necrosis.
- Calcification helps explain the mammographic presentation.
- Sampling still determines whether an invasive component is identified.



Schematic — not a photomicrograph

Case 2 — incidental lobular epithelial proliferation

Clinical / pathology vignette

Biopsy for an unrelated imaging finding shows expanded acini.

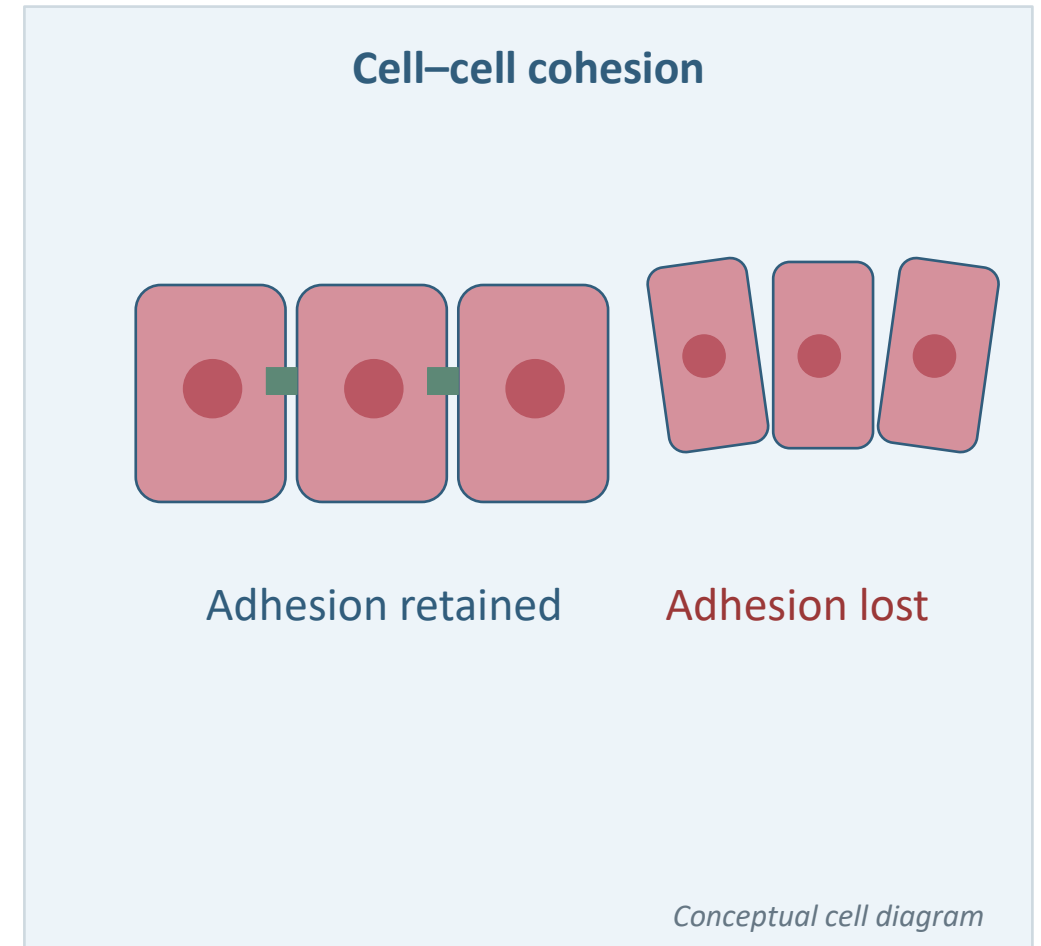
Small monomorphic cells are round, separated, and lack strong cohesion.

No significant necrosis or calcifications are identified within the proliferation.

Question: What molecular change would explain the phenotype?

Case 2 — connect cell shape to adhesion

- A lobular in situ proliferation is favored by dyscohesive cell morphology.
- E-cadherin function is commonly lost through CDH1 alteration.
- Other adhesion-component defects can yield a similar phenotype.
- Morphology and specimen context remain necessary for classification.



Case 3 — persistent unilateral nipple eruption

Clinical / pathology vignette

A patient reports unilateral nipple pruritus with a recurrent scaly crust.

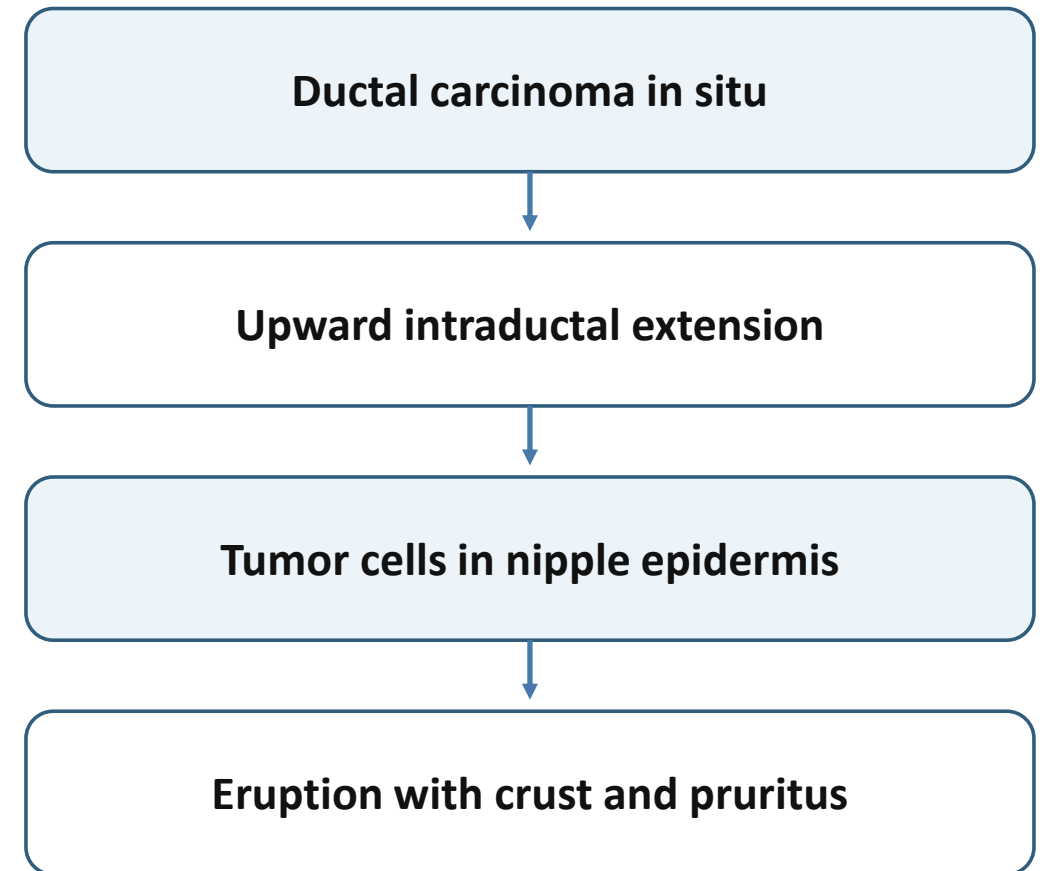
Biopsy finds malignant cells among squamous epidermal cells.

Breast sampling identifies an associated ductal in situ lesion.

Question: How can an in situ breast carcinoma affect nipple skin?

Case 3 — epidermal spread without stromal invasion

- Paget cells can track along lactiferous ducts to the nipple epidermis.
- Disruption of the epidermal barrier produces ooze and crusting.
- A palpable mass should raise concern for underlying invasive disease.
- The prognosis is determined by any invasive component.



Three critical distinctions prevent category errors

- In situ versus invasive refers to the basement membrane boundary.
- Ductal versus lobular describes growth phenotype and tumor biology.
- Nuclear grade versus architecture are different DCIS descriptors.
- Classic LCIS versus pleomorphic variants changes clinical interpretation.

Four questions at diagnosis

Is tumor confined?

Ductal or lobular phenotype?

Nuclear grade and architecture?

Variant and lesion extent?

Synthesis: What the pathologist must establish

- Identify a neoplastic epithelial proliferation within the duct–lobular unit.
- Evaluate confinement by the basement membrane and epithelial boundary.
- Classify the ductal or lobular pattern with morphology and biology.
- Communicate lesion grade/variant, extent, and clinically relevant risk.

Recommended reading

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).
- Chapter “The Breast”: introductory section, “Carcinoma in Situ.”
- “Ductal Carcinoma In Situ”: morphology, molecular distinctions, and clinical course.
- “Lobular Carcinoma In Situ”: cohesion biology, morphology, and clinical course.