

Types of Invasive Breast Carcinoma

Histologic patterns, biologic associations, and diagnostic distinctions

Invasive carcinoma of no special type • Special histologic subtypes • Clinicopathologic correlations

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Learning objectives

- Distinguish invasive carcinoma of no special type from special histologic subtypes.
- Explain the three morphologic variables used in Nottingham histologic grading.
- Recognize characteristic invasive architectures and their diagnostic mimics.
- Relate selected subtypes to receptor groups, dissemination, and clinical presentation.
- Separate inflammatory carcinoma as a presentation from histologic classification.

The organizing principle: Architecture before label

Identify invasion

Recognize malignant epithelial cells infiltrating breast stroma.

Classify pattern

No special type, or a definable special morphology.

Characterize biology

Assess grade and relevant receptor phenotype.



Most invasive breast malignancies are adenocarcinomas

- Approximately 20 morphologically defined subtypes of invasive carcinoma.
- Histologic type reflects tumor architecture, growth pattern, and cellular morphology.
- Special types have distinctive morphologic phenotypes; Not every pattern is a separate type.
- Type, grade, and receptor expression describe different dimensions of a carcinoma.

No special type dominates the classification

Invasive breast carcinoma of no special type (NST) accounts for approximately 75% of invasive cases.

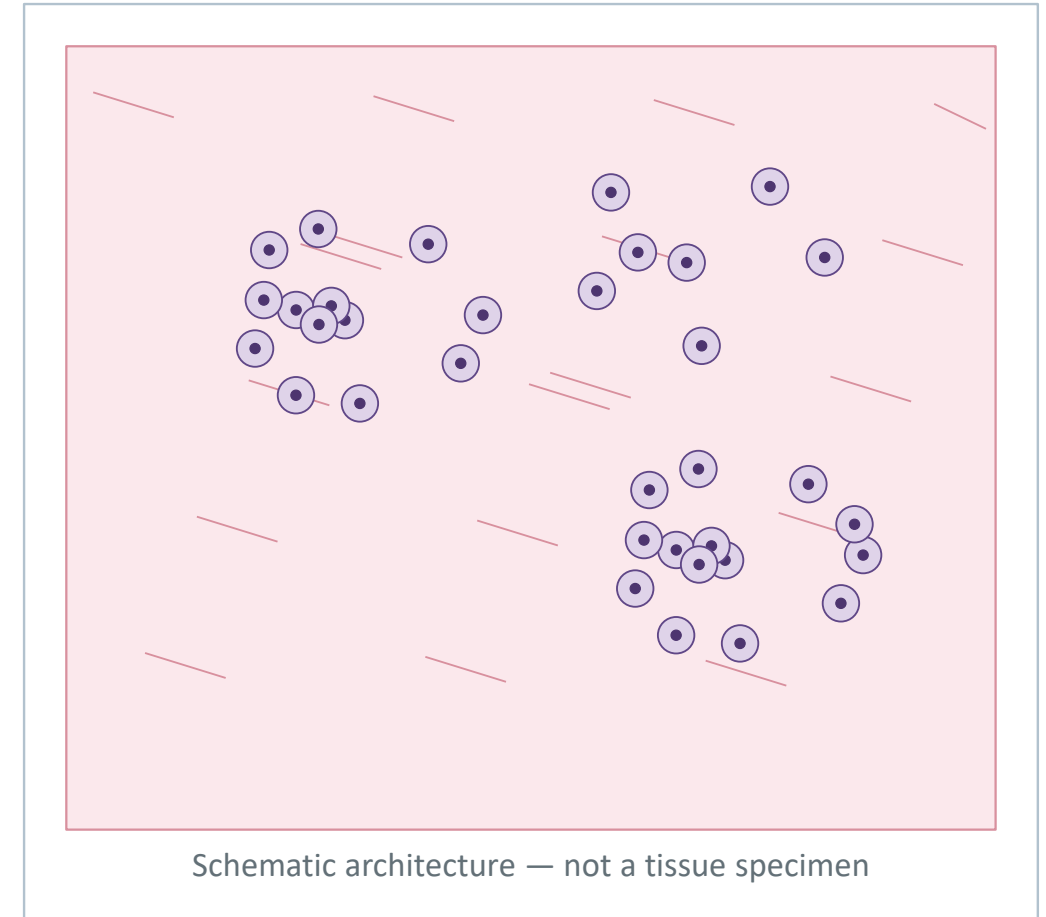
A heterogeneous category • Not one uniform microscopic architecture

A special type must have distinctive morphology

- Special types are separated from NST by characteristic tumor architecture or cytomorphology.
- Some have recognizable genomic or receptor associations.
- A specific pattern should not be equated automatically with a single molecular profile.
- The source emphasizes selected informative subtypes rather than all named rare entities.

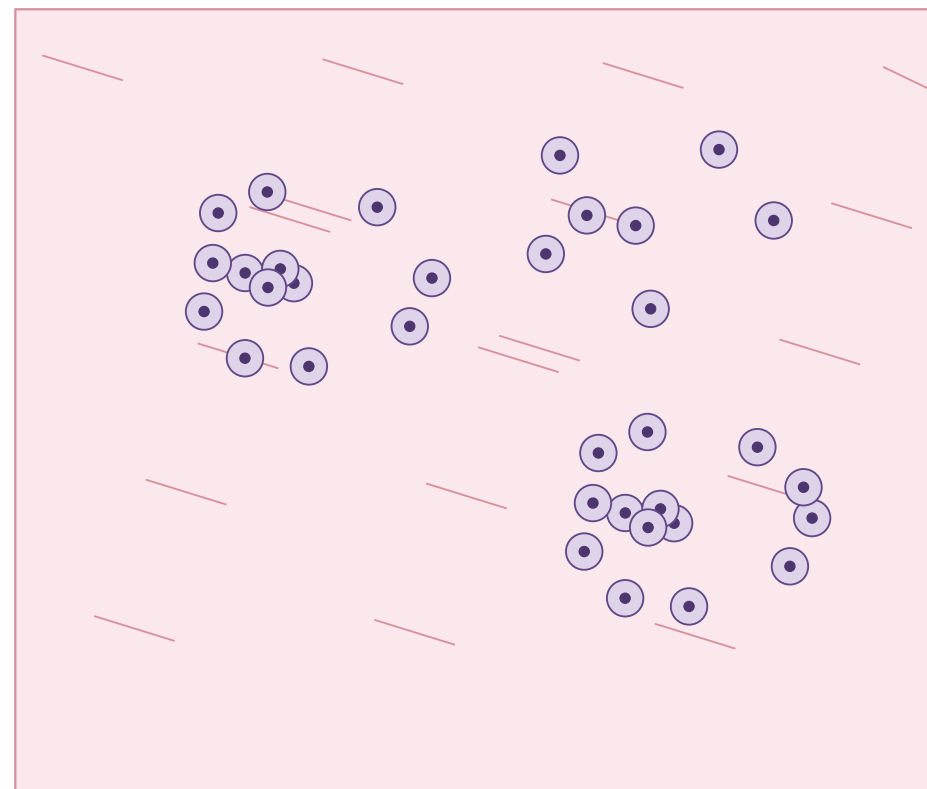
NST: An irregular infiltrative architecture

- Tumor cells infiltrate fibrofatty tissue in haphazard glands, nests, cords, or single cells.
- The extent of associated stromal reaction is highly variable.
- Irregular invasion can produce an ill-defined gross and radiologic margin.
- Architectural variability helps explain the breadth of NST appearances.



Desmoplasia drives the classic hard mass

- An exuberant fibrous stromal reaction commonly surrounds infiltrating NST glands or nests.
- Stromal fibrosis contributes to firmness and irregular radiodense margins.
- Cut sections may be chalky-white; Focal calcifications can produce a grating sensation.
- This classical appearance is common, not universal.



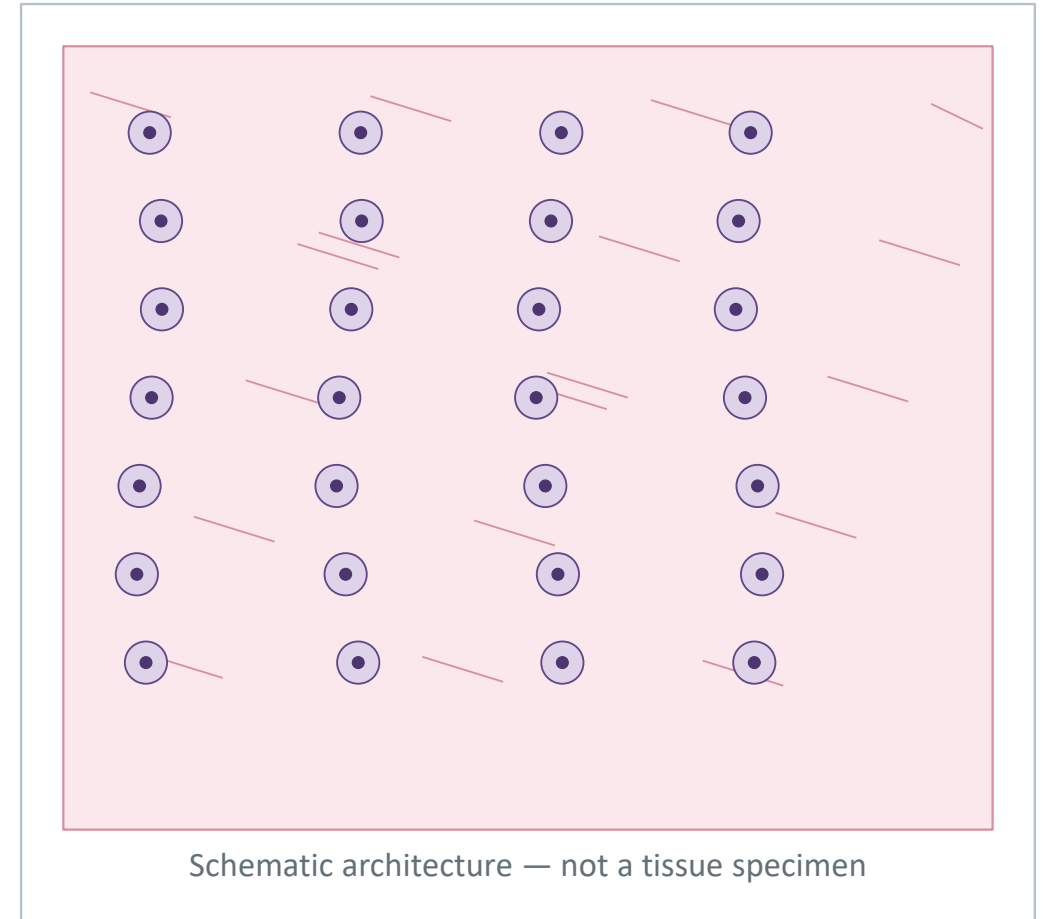
Schematic architecture — not a tissue specimen

NST can be deceptively well circumscribed

- If tumor grows as sheets with little stromal reaction, the mass may appear circumscribed.
- Circumscription does not demonstrate benignity or exclude invasive carcinoma.
- Architectural assessment must consider the lesional periphery and surrounding tissue.
- The source contrasts this pattern with strongly desmoplastic NST.

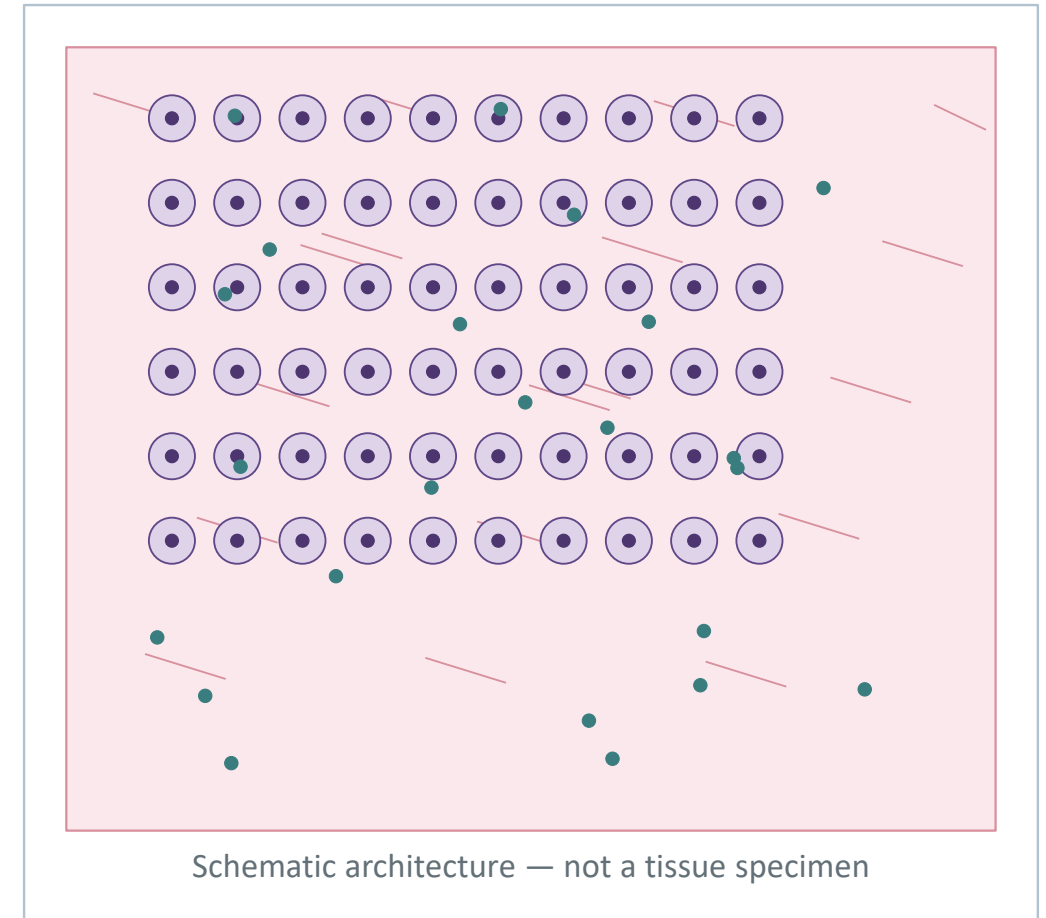
NST may be almost invisible macroscopically

- Scattered neoplastic glands or single cells can infiltrate otherwise unremarkable fat.
- Weak desmoplastic response may make a primary tumor hard to palpate or image.
- This mechanism helps explain some clinically occult invasive carcinomas.
- An inconspicuous mass does not imply an in situ process.



Medullary pattern belongs within NST

- Some high-grade NSTs form relatively cohesive sheets with prominent tumor-infiltrating lymphocytes.
- These were previously designated “medullary carcinoma.”
- The separate entity proved insufficiently reproducible diagnostically.
- Robbins calls this NST with medullary pattern.



Tumor-infiltrating lymphocytes: Contextual feature

- Prominent lymphocytes may accompany high-grade tumors showing a medullary pattern.
- The inflammatory infiltrate is a tumor-associated microscopic observation.
- It does not, by itself, establish a special histologic type.
- Do not confuse this finding with the clinical entity inflammatory breast carcinoma.

Nottingham grade measures differentiation

Tubule formation

How much of the tumor develops recognizable glandular lumina?



Nuclear pleomorphism

How variable and atypical are tumor nuclei?



Mitotic activity

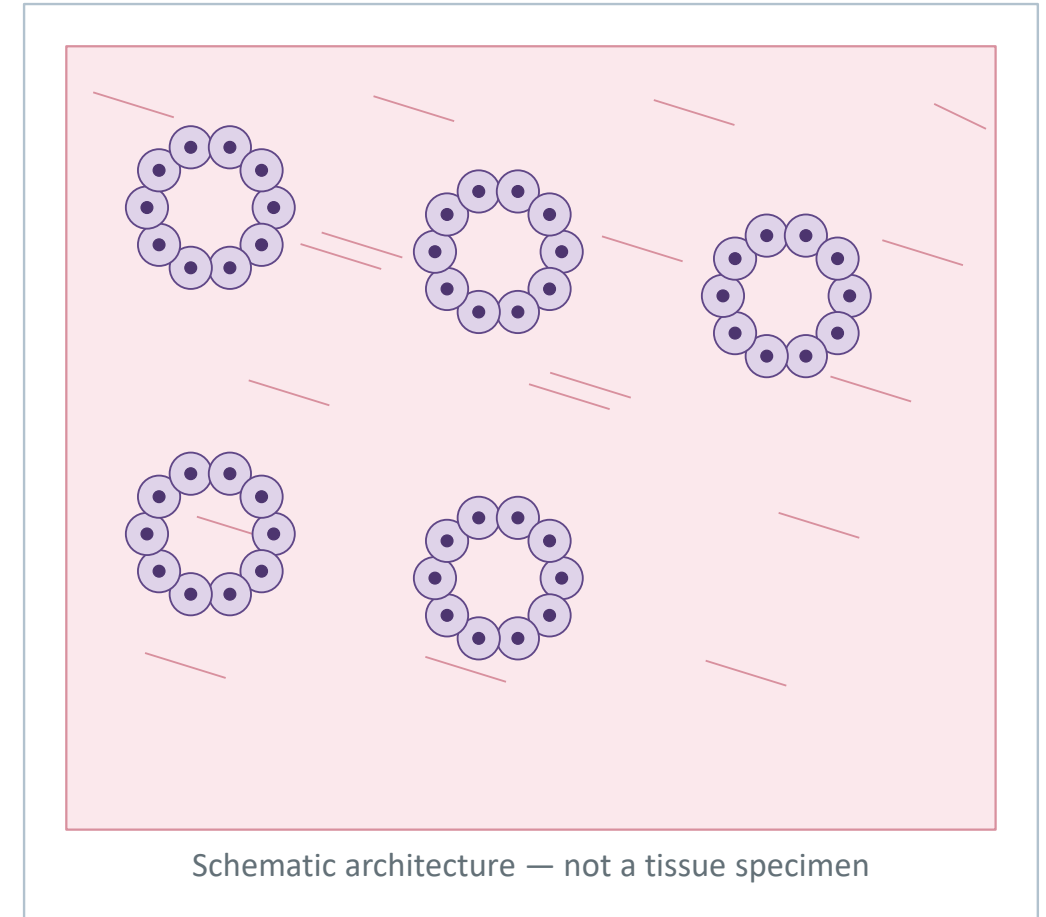
How actively are cells dividing on histologic assessment?

Grading and typing answer different questions

Descriptor	What it measures	Examples
Histologic type	Predominant architectural / cellular pattern	NST, lobular, tubular
Histologic grade	Differentiation and proliferation	Nottingham grades 1–3
Receptor phenotype	ER, PR, HER2 expression	Luminal-associated, HER2-positive, TNBC

Tubule formation indicates glandular differentiation

- Well-formed lumina reflect retention of glandular epithelial architecture.
- Grade 1 carcinomas frequently grow in tubules or cribriform formations.
- Poorly differentiated tumors tend to form solid nests or sheets.
- Tubule formation is one component of the composite Nottingham assessment.



Nuclear pleomorphism indicates cytologic atypia

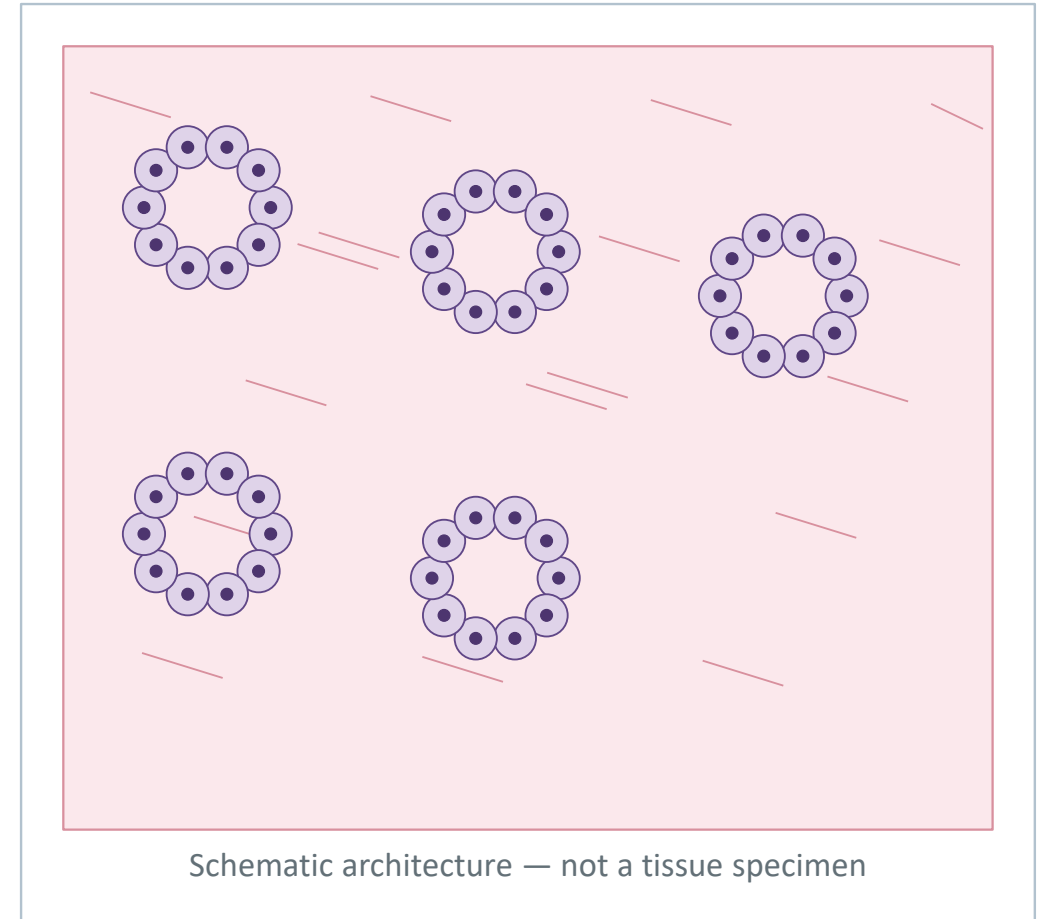
- Grade 1 cells show relatively small, uniform nuclei.
- With loss of differentiation, nuclei become enlarged and irregular.
- Grade 3 carcinomas typically show striking nuclear atypia.
- Nuclear morphology is interpreted together with architecture and mitoses.

Mitotic activity estimates proliferative behavior

- Grade 1 tumors show a low proliferative rate and scarce mitoses.
- Grade 2 tumors have more mitotic figures than well-differentiated examples.
- High mitotic activity commonly accompanies grade 3 morphology.
- Counts require a standardized laboratory method; No unsupported numeric thresholds are given here.

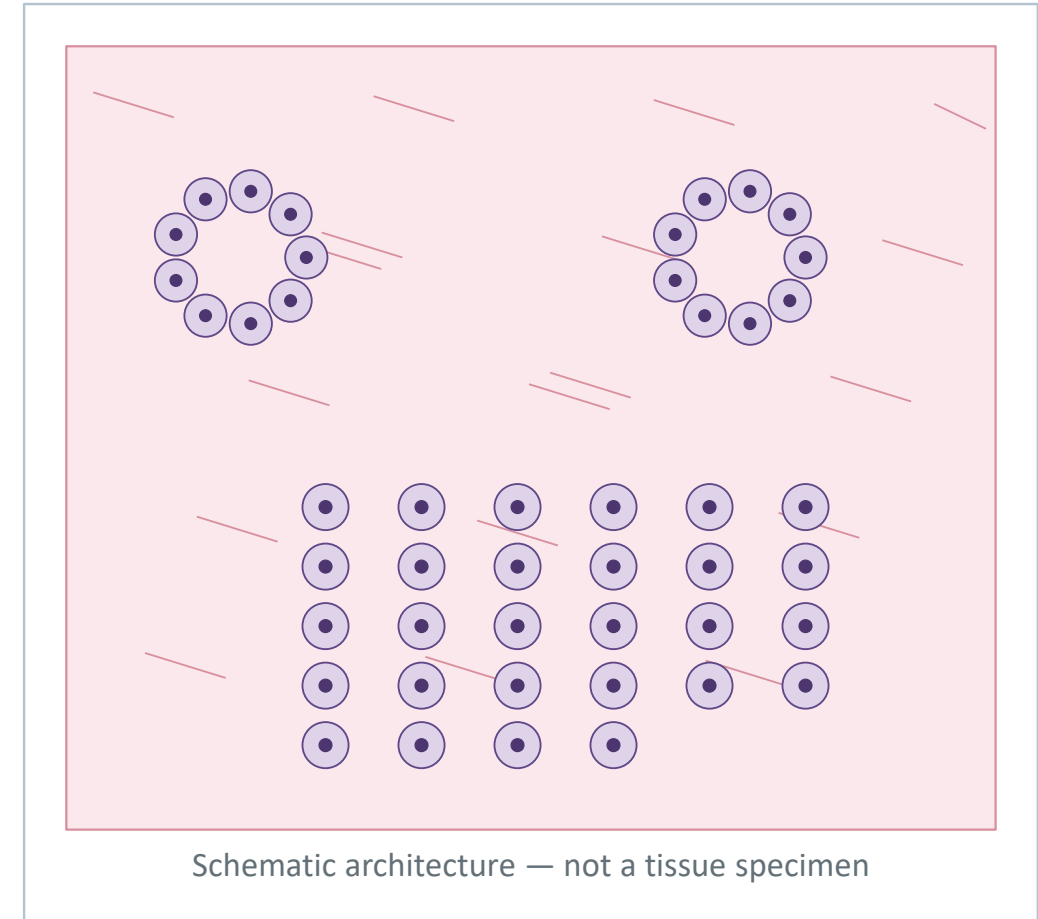
Grade 1: Structured glands and uniform nuclei

- Tubular or cribriform glandular architecture predominates.
- Nuclei are small and relatively monomorphic.
- Mitotic figures are uncommon examples.
- This combination represents well-differentiated morphology.



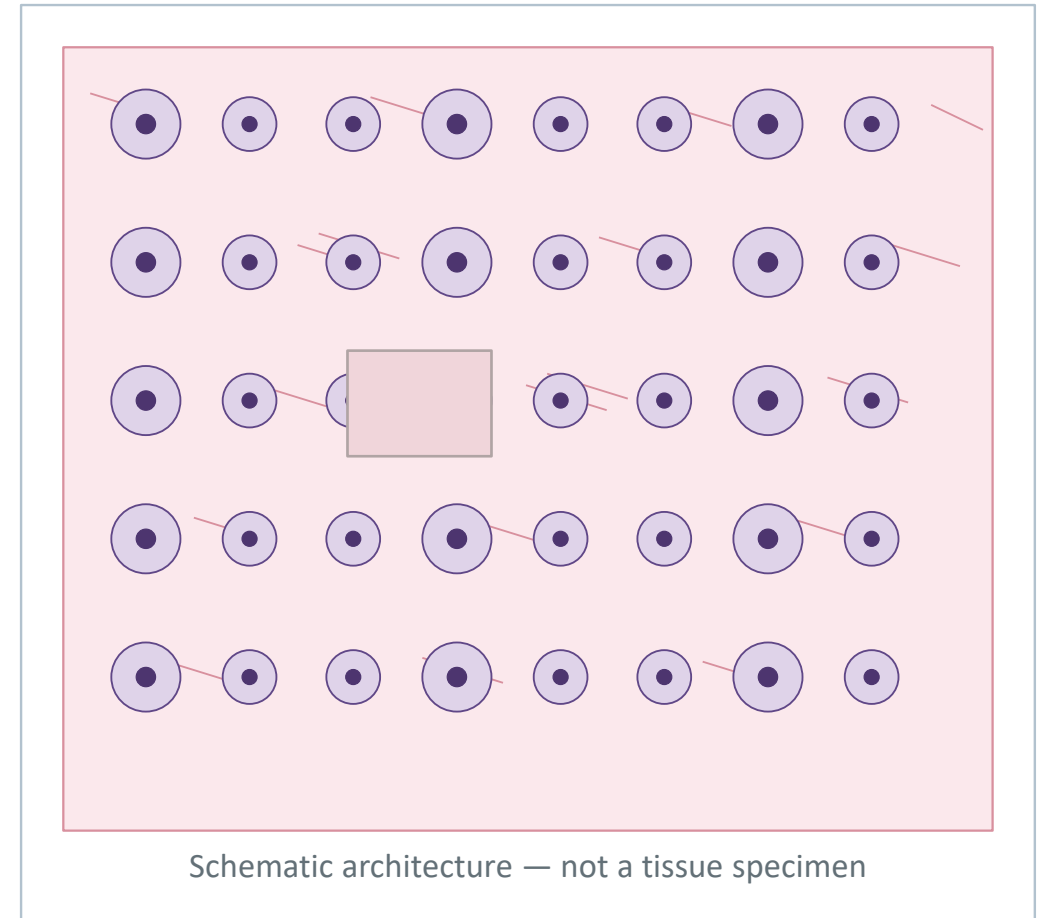
Grade 2: Mixed glandular and solid growth

- Tumor may show glandular structures beside solid cell clusters.
- Single infiltrating cells can be present.
- Nuclear atypia and mitoses are intermediate relative to grades 1 and 3.
- This represents moderately differentiated morphology.



Grade 3: Ragged nests and sheets

- Infiltrating irregular sheets or nests replace organized gland formation.
- Nuclei are enlarged and pleomorphic.
- Proliferation is high and tumor necrosis may be present.
- This combination signifies poorly differentiated morphology.



Morphologic differences across grades

Feature	Grade 1	Grade 2	Grade 3
Architecture	Tubular / cribriform	Mixed glands and solid clusters	Ragged nests / solid sheets
Nuclei	Small, uniform	More atypical	Large, irregular
Mitoses	Few	Intermediate	Many
Necrosis	Not characteristic	Variable	May be prominent

Histologic grade is relevant across invasive types

- All invasive carcinomas are graded using the Nottingham system.
- The composite score incorporates tubule formation, pleomorphism, and mitotic rate.
- Grade is not synonymous with invasive tumor size or anatomical stage.
- Specific histologic types may differ substantially in their usual differentiation.

Special histologic types form biologic clusters

Usually luminal

Lobular, mucinous, tubular,
cribriform, papillary.

Often HER2-positive

Apocrine and invasive
micropapillary.

Often triple-negative

Metaplastic and certain
salivary gland-like types.

“Usually” is not “always” for receptor groups

- The subtype-to-receptor associations are probabilistic.
- Histomorphology does not replace ER, PR, or HER2 testing.
- Exceptions must remain possible even when a pattern is classical.
- Receptor and histologic classifications supply complementary information.

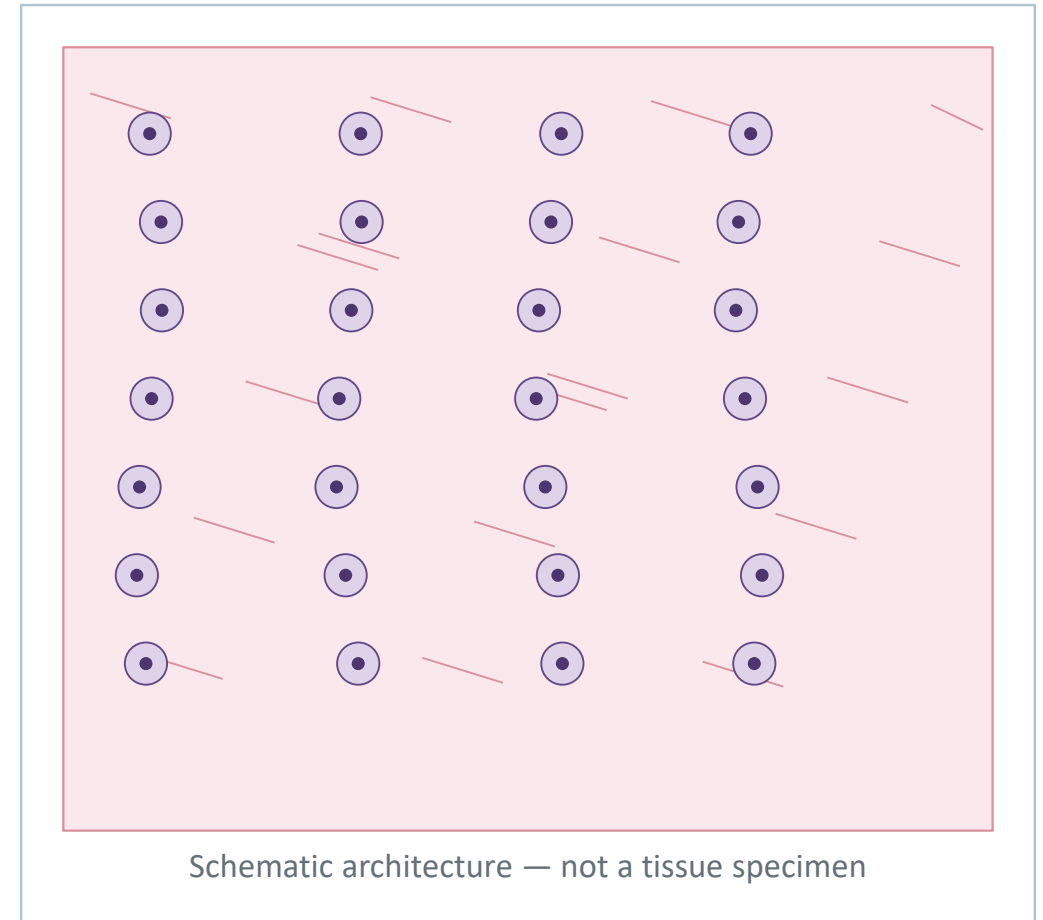
Invasive lobular carcinoma is the main special type

Invasive lobular carcinoma is second most common and accounts for up to 15% of invasive cases.

Defining feature: Loss of cellular cohesion • Often luminal ER-positive/HER2-negative

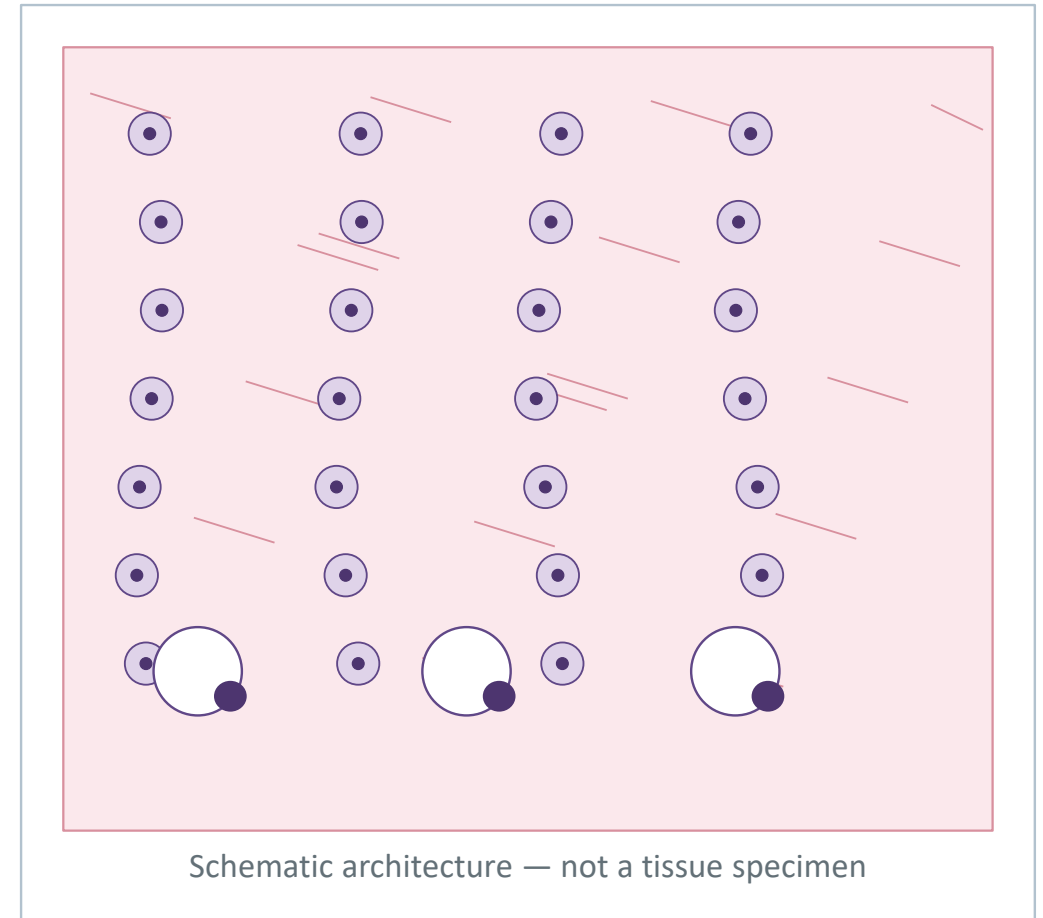
Lobular carcinoma: A single-file invasion pattern

- Dyscohesive neoplastic cells infiltrate as linear cords or individual cells.
- The single-file architecture is a diagnostic morphologic hallmark.
- Minimal mass-forming stromal reaction may conceal disease on imaging.
- Assessment requires inspection of tumor distribution in the stroma.



Signet-ring change in lobular carcinoma

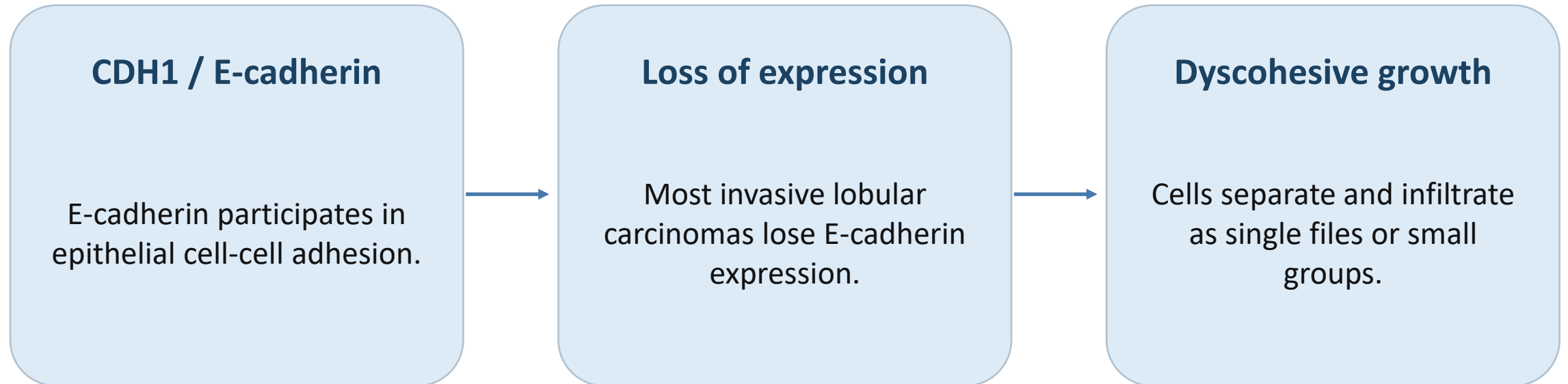
- Intracytoplasmic mucin can displace the nucleus to the cellular periphery.
- Signet-ring cells may be found amid dyscohesive tumor cells.
- Distinguish intracellular mucin from large extracellular mucin lakes.
- A signet-ring phenotype alone is not equivalent to mucinous carcinoma.



Lobular carcinoma often causes little desmoplasia

- Rather than a conspicuous firm nodule, the lesion may diffusely infiltrate breast tissue.
- Minimal stromal response contributes to subtle imaging findings.
- Detection difficulties derive partly from how cells occupy the existing tissue.
- Clinical and radiologic findings must be integrated with histology.

E-cadherin links genotype to cell cohesion



The CDH1 germline association

- Heterozygous germline CDH1 mutations in affected families.
- Such carriers have increased risk for lobular breast carcinoma.
- The same association encompasses gastric signet-ring carcinoma.
- This is a susceptibility association, not evidence that every lobular carcinoma is hereditary.

Lobular carcinoma has distinctive metastatic sites

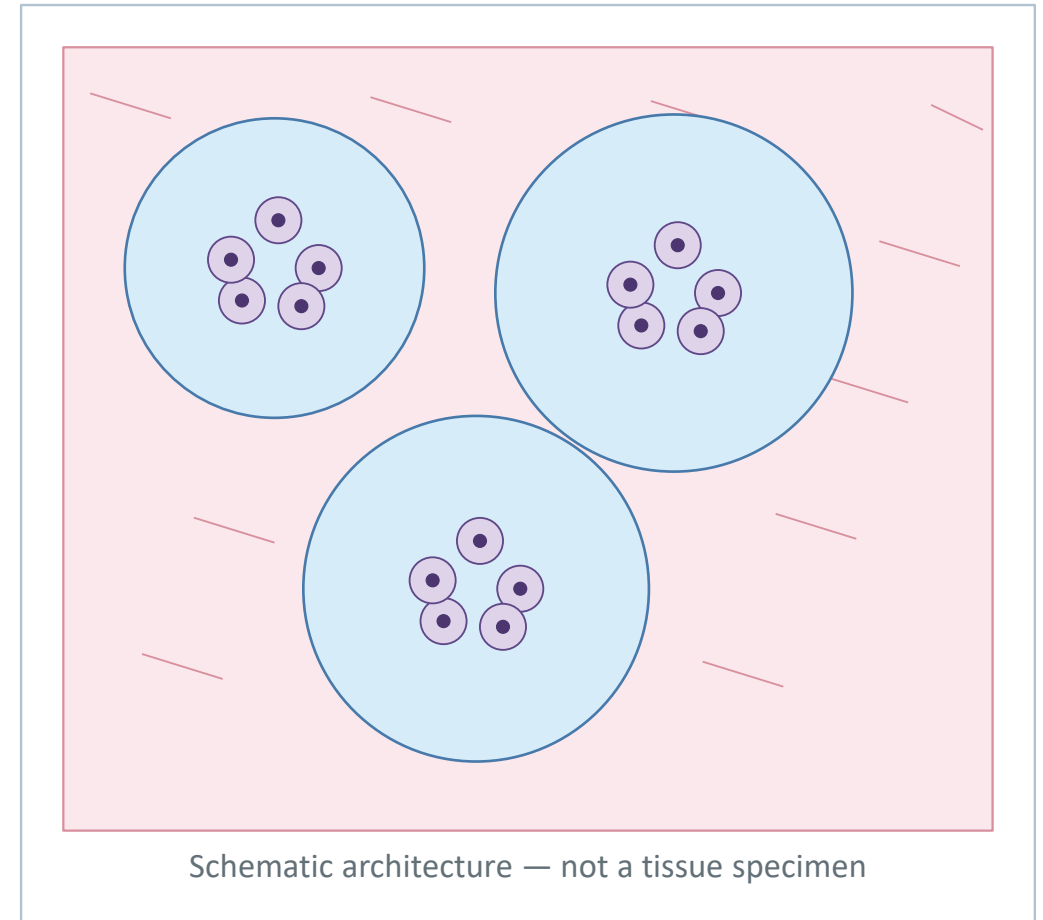
- Peritoneum and retroperitoneum are recognized sites.
- Gastrointestinal tract, ovaries, and uterus can be involved.
- Leptomeningeal spread may produce carcinomatous meningitis.
- The unusual distribution broadens the differential diagnosis of secondary lesions.

Lobular carcinoma versus NST

Feature	Invasive lobular	Invasive NST
Invasion	Dyscohesive, single-file cords	Variable glands, nests, sheets
Stromal reaction	Often scant	Often desmoplastic
E-cadherin	Usually lost	Not defined by loss
Detection	May be subtle / diffuse	Often irregular mass
Distinctive spread	Peritoneal and GI sites	No subtype-specific pattern stated here

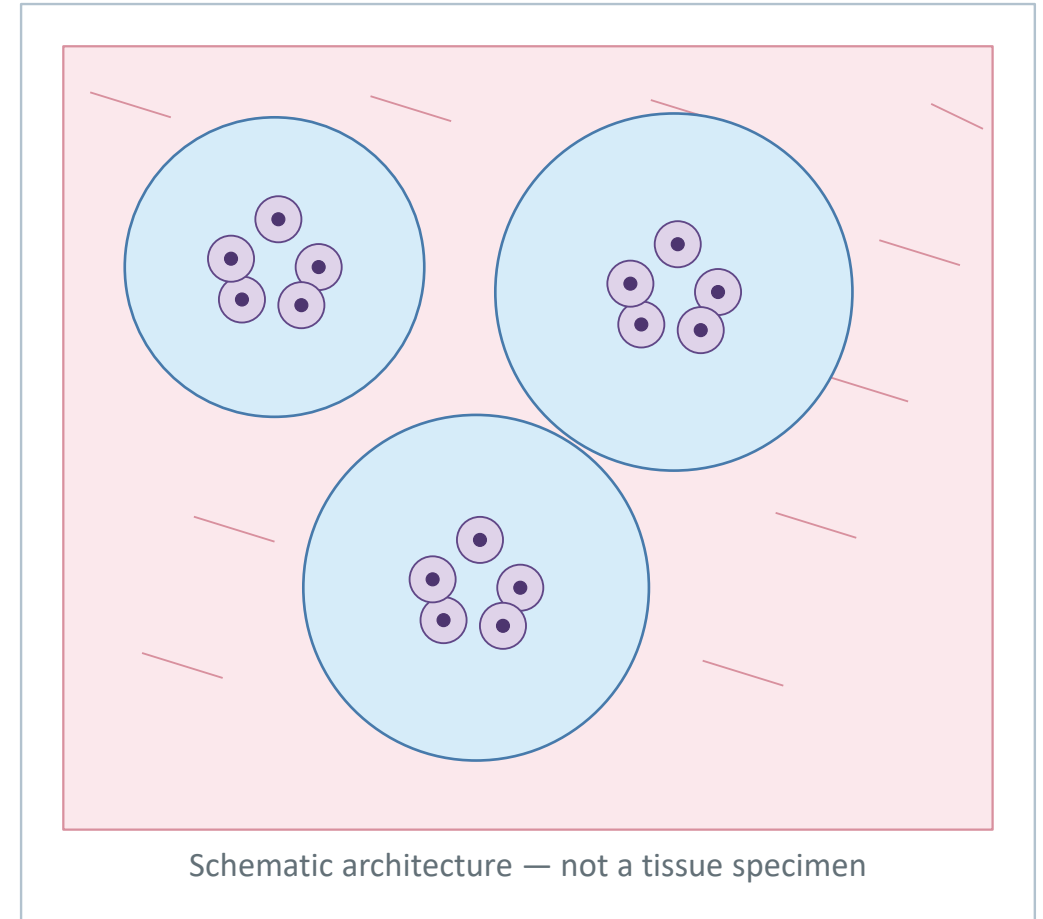
Mucinous carcinoma: Gelatinous gross appearance

- The mass may be soft, rubbery, and gelatinous.
- Gross borders can be pushing or relatively circumscribed.
- Extracellular mucin accounts for its characteristic consistency.
- Mucinous carcinoma belongs among the subtypes usually in the luminal group.



Mucinous carcinoma: Tumor islands in mucin

- Neoplastic epithelial clusters float in abundant extracellular mucin lakes.
- Cell clusters vary in size and arrangement.
- The extracellular location of mucin is diagnostically essential.
- This architecture explains the gelatinous cut-surface appearance.

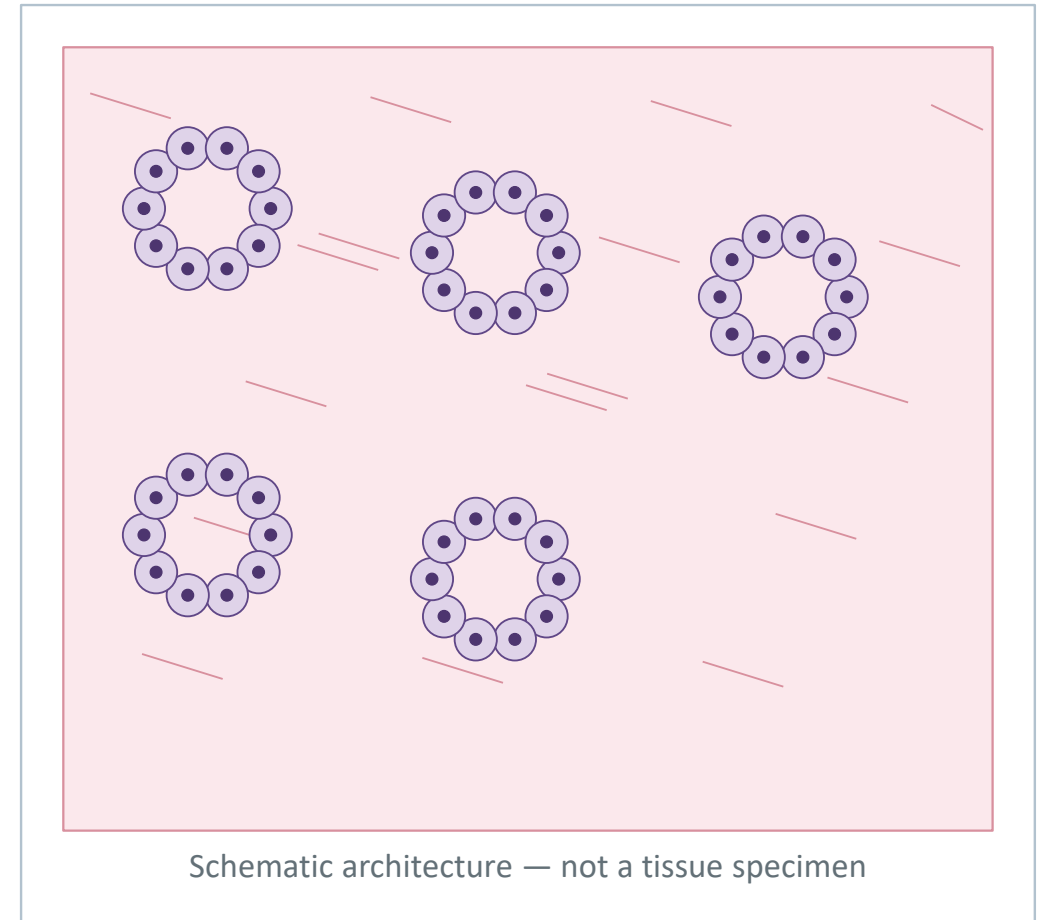


Extracellular versus intracellular mucin

Feature	Mucinous carcinoma	Lobular carcinoma with signet-ring cells
Mucin location	Extensive extracellular mucin pools	Inside individual tumor cells
Tumor architecture	Clusters floating in mucin	Dyscohesive single files
Diagnostic emphasis	Mucin lakes and cell groups	Discohesion and epithelial phenotype

Tubular carcinoma: Infiltrating well-formed glands

- Invasive architecture consists of well-formed tubular structures.
- The cells show a striking degree of glandular differentiation.
- Tubular carcinoma is usually within the luminal receptor group.
- Architecture can appear bland despite genuine stromal invasion.

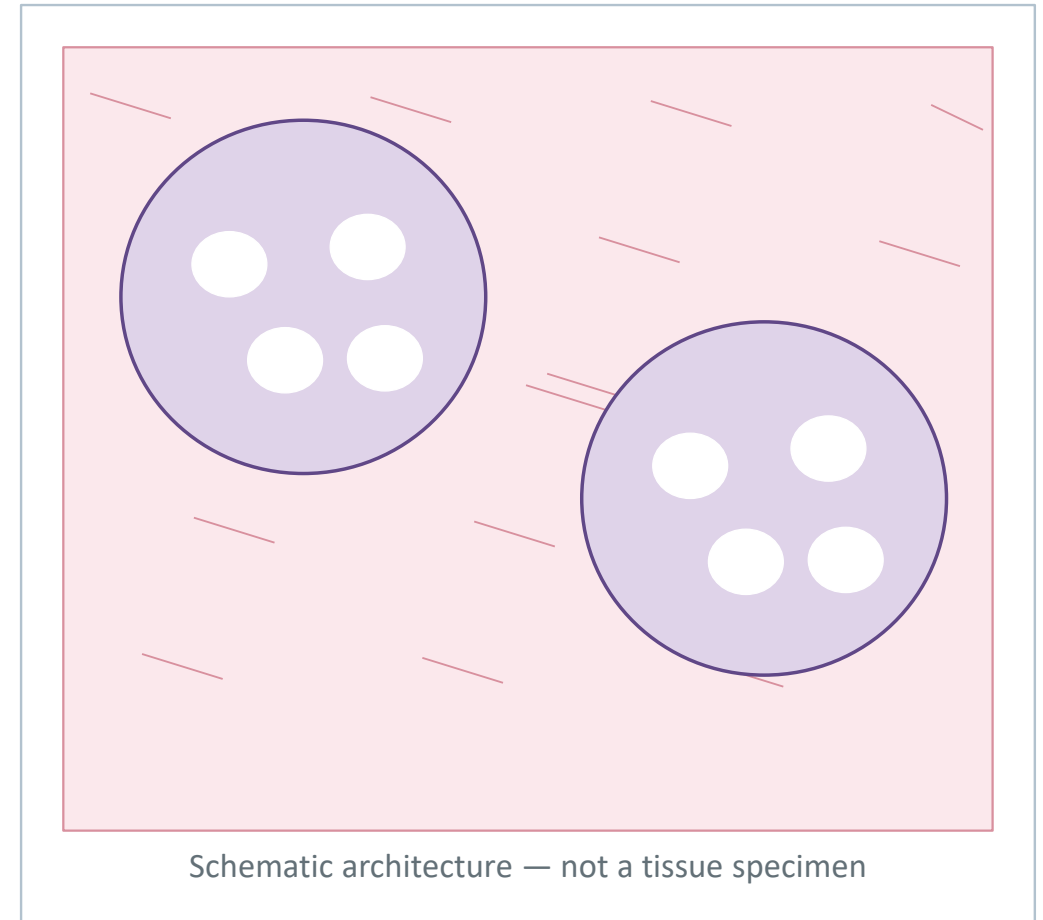


Tubular carcinoma may mimic a benign lesion

- Small, well-organized glands may be mistaken for a sclerosing benign process.
- The central diagnostic question is the invasive arrangement of atypical tubules.
- Apparent blandness does not eliminate the need to establish invasion.
- This sclerosing-lesion diagnostic pitfall.

Cribriform carcinoma: Perforated tumor nests

- Invasive tumor nests contain multiple rounded punched-out spaces.
- This creates a sieve-like or cribriform architecture.
- Cribriform carcinoma usually belongs to the luminal group.
- The key recognition feature is invasive cribriform growth.

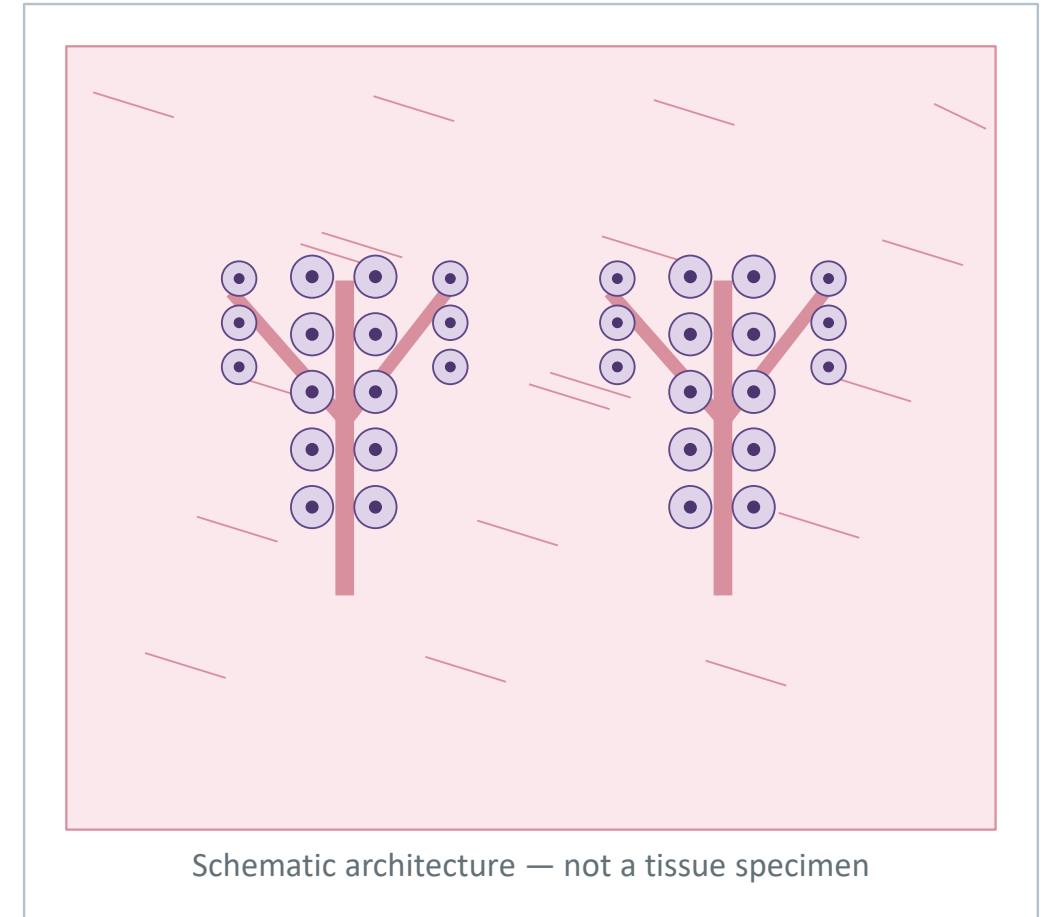


Tubular versus cribriform architecture

Feature	Tubular carcinoma	Cribriform carcinoma
Principal structure	Separate small glandular tubules	Invasive nests with multiple lumina
Visual impression	Discrete open-lumen glands	Sieve-like nests
Shared association	Often ER-positive/HER2-negative	Often ER-positive/HER2-negative
Teaching pitfall	Can resemble sclerosing lesions	Do not identify type from a single lumen

Papillary carcinoma contains true fibrovascular cores

- The papillae are real fronds lined by neoplastic epithelial cells.
- Each true papilla has a fibrovascular central axis.
- Papillary carcinoma is included among usually luminal special types.
- The presence of true cores distinguishes it from micropapillary pattern.



Papillary is an architectural, not receptor-only diagnosis

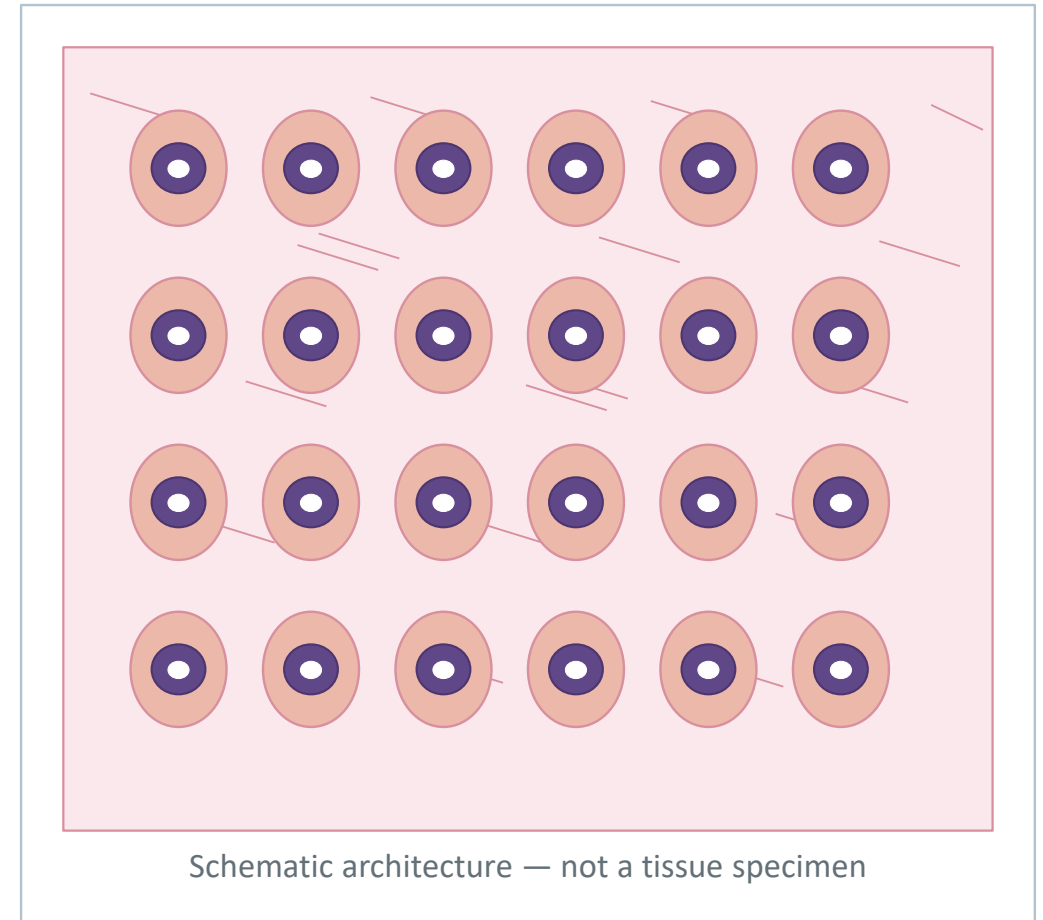
- Observe cellular lining and supporting fibrovascular fronds.
- Papillary histology must be assessed in the context of invasion.
- An ER-positive result cannot independently identify papillary carcinoma.
- Micropapillary carcinoma uses the name “papillary” despite lacking these cores.

Luminal-associated special types: Comparison

Subtype	Signature morphology	Selected clinical/biologic note
Lobular	Single-file, discohesive cells	E-cadherin loss; unusual metastases
Mucinous	Clusters in mucin lakes	Soft gelatinous gross lesion
Tubular	Well-formed small glands	Can mimic benign sclerosis
Cribriform	Perforated invasive nests	Sieve-like architectural growth
Papillary	True epithelial-lined fibrovascular cores	Distinguish from micropapillary

Apocrine carcinoma: Eosinophilic cytoplasm

- Tumor cells resemble glandular cells lining sweat glands.
- Cytoplasm is abundant, eosinophilic, and may be granular.
- Nuclei are enlarged with conspicuous nucleoli.
- Apocrine carcinoma among types more likely to overexpress HER2.

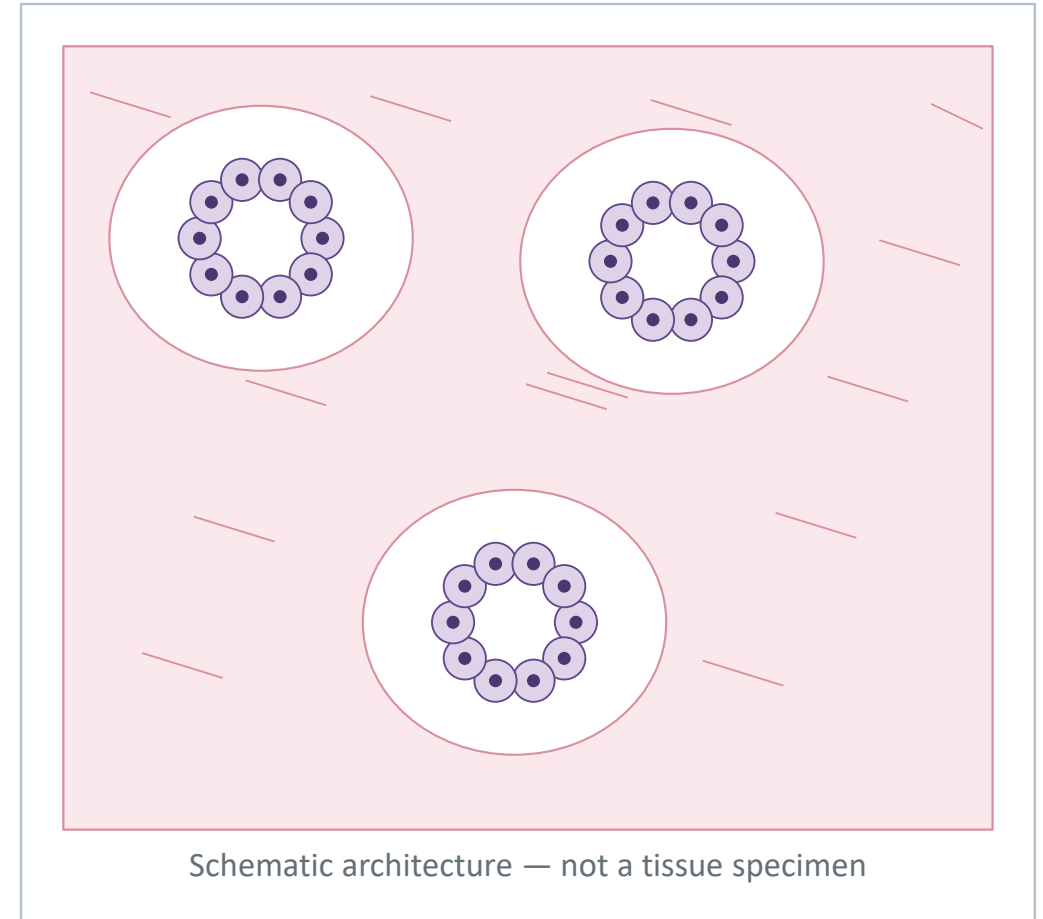


Apocrine morphology is not a HER2 test

- The apparent apocrine phenotype is cytologic: Large nuclei, nucleoli, abundant cytoplasm.
- HER2 overexpression is an association rather than a defining histologic criterion.
- Direct receptor assessment remains necessary.
- The source does not assert uniform HER2 positivity in apocrine carcinoma.

Invasive micropapillary carcinoma forms hollow balls

- Aggregates of neoplastic cells form hollow ball-like structures.
- They lie in intercellular fluid spaces, giving an illusion of papillary formations.
- The apparent papillae lack genuine fibrovascular cores.
- Robbins groups this type among carcinomas more likely to overexpress HER2.



Micropapillary is a morphologic misnomer

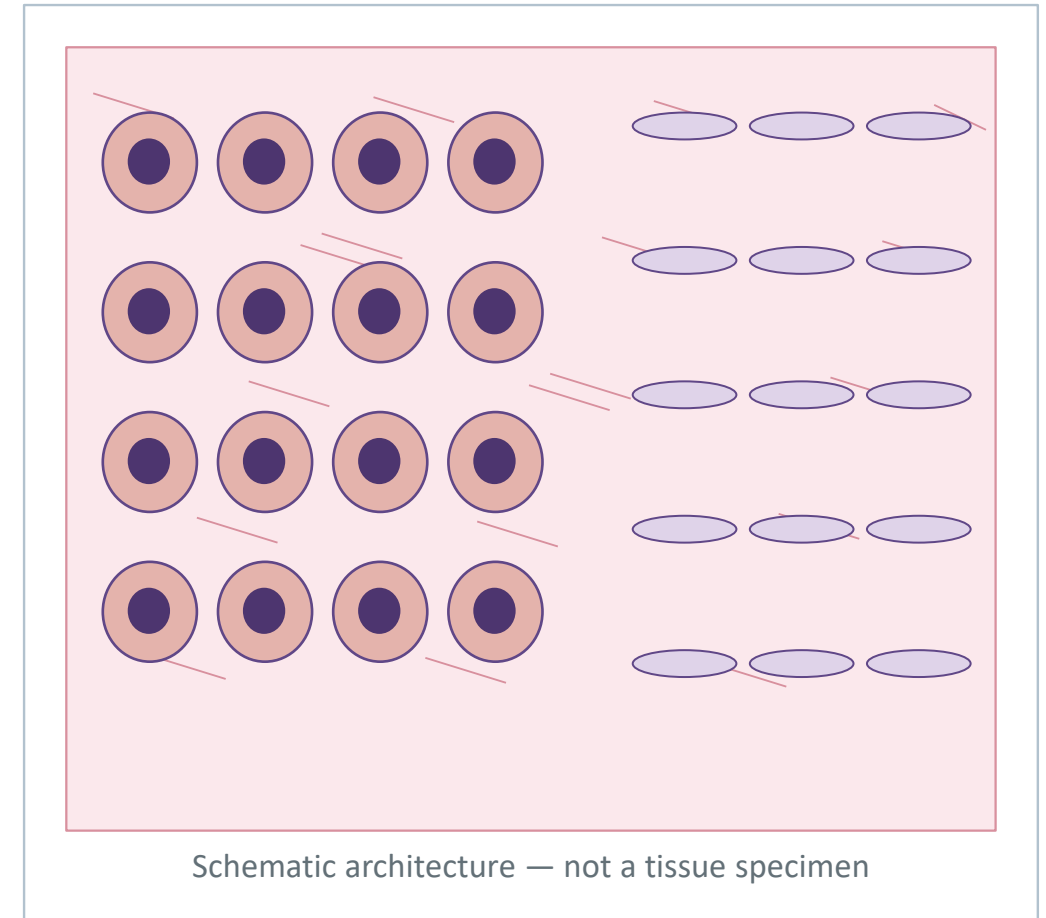
Feature	True papillary carcinoma	Invasive micropapillary carcinoma
Core	Fibrovascular core present	No true fibrovascular core
Growth	Epithelial-lined fronds	Hollow balls in fluid spaces
Receptor association	Usually luminal	More likely HER2-overexpressing
Classification lesson	True papillary architecture	Papillary-like illusion

HER2-associated morphologies are not interchangeable

- Apocrine and micropapillary carcinomas are architecturally dissimilar.
- Apocrine refers mainly to eosinophilic granular cytoplasm and nucleoli.
- Micropapillary refers to hollow cell clusters lacking true vascular cores.
- Their shared HER2 association must not obscure these structural differences.

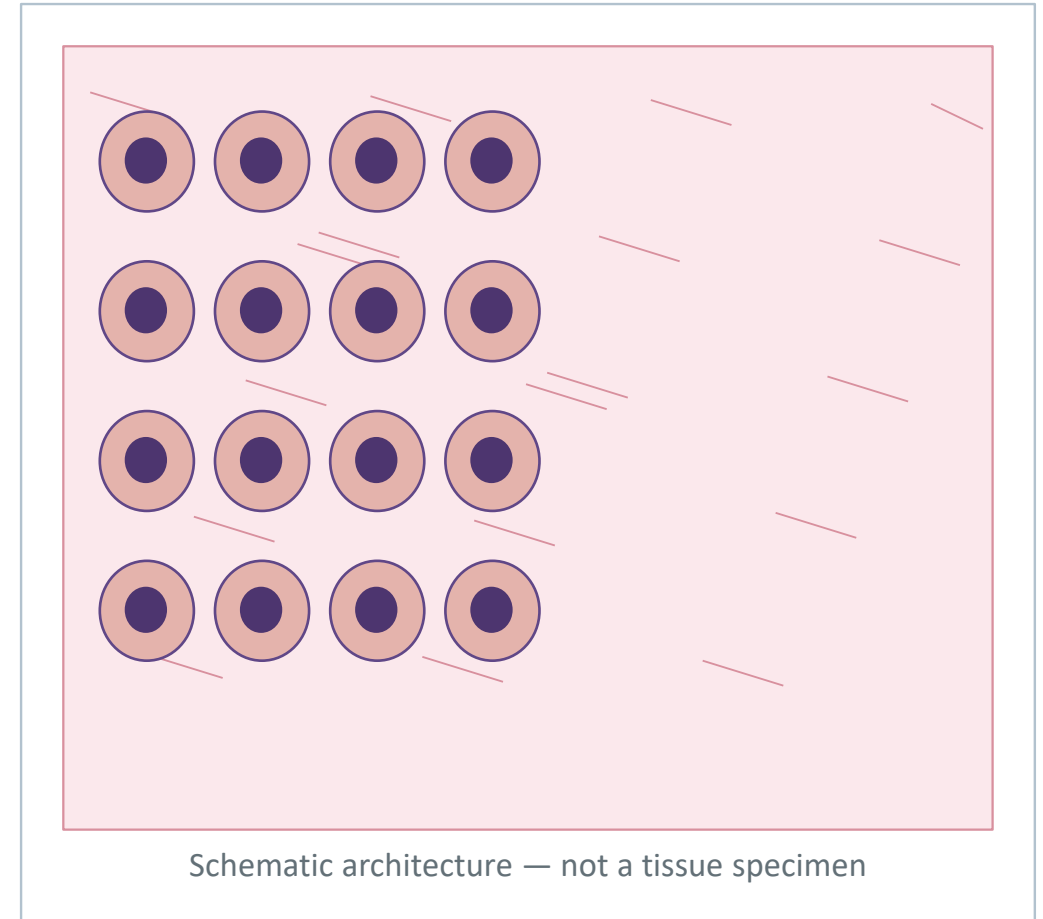
Metaplastic carcinoma shows divergent differentiation

- Carcinoma develops overt squamous or mesenchymal-like differentiation.
- Mesenchymal-like elements may be spindle-shaped, cartilaginous, or osseous.
- Many metaplastic tumors are triple-negative.
- The category is biologically and prognostically heterogeneous.



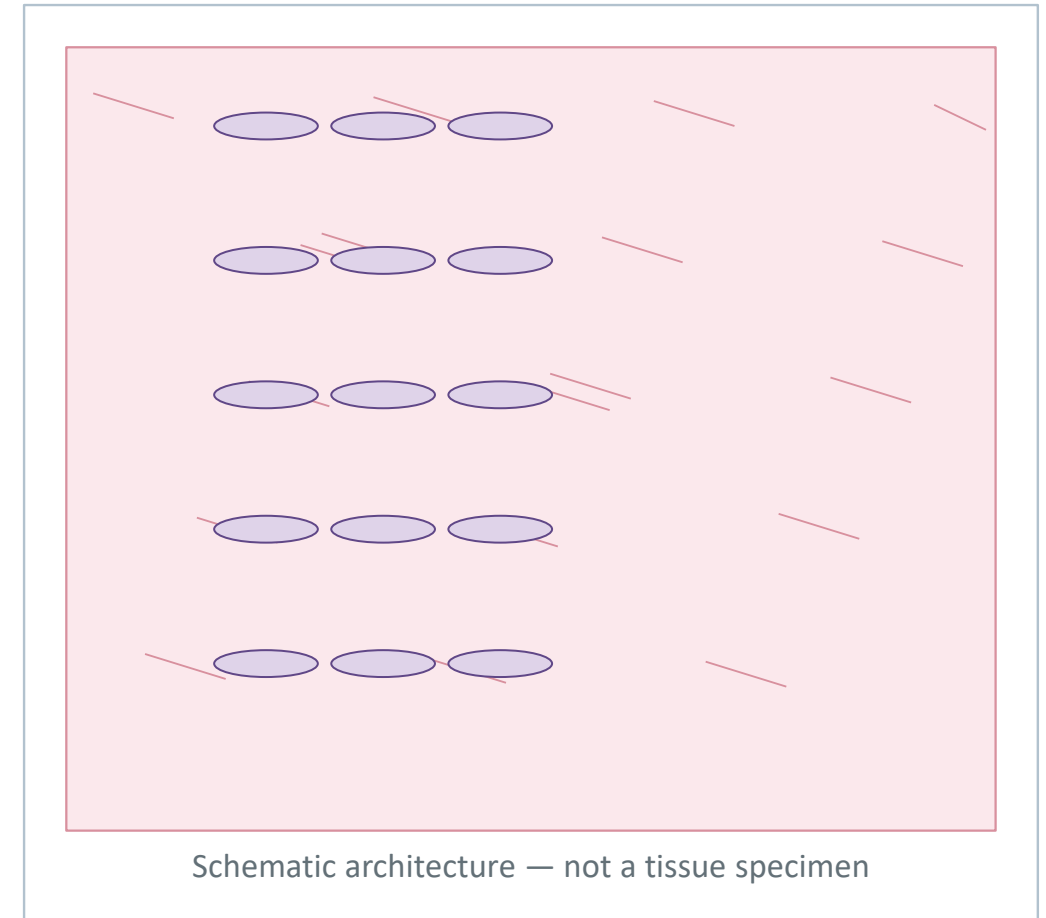
Squamous differentiation in metaplastic carcinoma

- Neoplastic epithelium acquires a squamous phenotype.
- This is evidence of divergent tumor differentiation.
- The epithelial lineage must be reconciled with the unusual histology.
- Not all metaplastic carcinomas are predominantly squamous.



Spindle and mesenchymal morphology

- Spindle-cell architecture can resemble a primary stromal lesion.
- Other metaplastic forms may display chondroid or osseous differentiation.
- The broad phenotype explains important morphologic differential diagnoses.
- The subtype is not defined by a single uniform cell shape.



Metaplastic tumors may express myoepithelial-like profiles

- Many metaplastic carcinomas with myoepithelial-like gene expression.
- These tumors are frequently triple-negative by ER, PR, and HER2 criteria.
- The molecular resemblance is a group-level observation.
- Do not infer a specific marker positivity rate or diagnostic panel from this excerpt.

Metaplastic carcinoma: Prognosis is not uniform

- Metaplastic breast carcinoma is often associated with poor clinical outcome.
- Robbins recognizes unusual indolent metaplastic subtypes.
- Low-grade adenosquamous carcinoma is one example.
- Fibromatosis-like metaplastic carcinoma is another exception.
- Broad categorization must preserve these prognostic distinctions.

Low-grade adenosquamous carcinoma

- An uncommon, relatively indolent metaplastic subtype.
- The name reflects the combination of glandular and squamous differentiation.
- It should not be presumed to share the outcome of aggressive metaplastic forms.
- Exact diagnostic criteria are not detailed in the supplied section.

Fibromatosis-like metaplastic carcinoma

- An uncommon, relatively indolent metaplastic subtype.
- Its fibromatosis-like growth broadens the differential of spindle-cell breast lesions.
- Its clinical behavior differs from the generally aggressive metaplastic group.
- Detailed immunohistochemical criteria are beyond the provided Robbins excerpt.

Triple-negative carcinomas are histologically diverse

- TNBC means absence of ER, PR, and HER2 expression, not one morphology.
- Metaplastic carcinomas are commonly triple-negative and often aggressive.
- Some triple-negative salivary gland–like carcinomas have a comparatively favorable course.
- Receptor status alone cannot determine prognosis without tumor type and extent.

Salivary gland–like breast carcinomas

Adenoid cystic

Rare breast counterpart of salivary gland morphology.

Mucoepidermoid

Rare tumor with the salivary-type designation.

Secretory

Rare subtype with distinctive histologic morphology.



Salivary gland–like types: A prognostic exception

- Robbins groups adenoid cystic, mucoepidermoid, and secretory breast carcinomas.
- They closely resemble corresponding salivary gland tumors.
- These rare forms are usually triple-negative yet are relatively favorable compared with usual aggressive TNBC patterns.
- This demonstrates why histologic type can qualify receptor-based expectations.

Adenoid cystic carcinoma

- An uncommon salivary gland–like subtype of invasive breast carcinoma.
- It among rare triple-negative tumors with relatively favorable prognosis.
- Its designation reflects similarity to its salivary gland counterpart.
- The supplied section does not provide detailed architecture or molecular criteria.

Mucoepidermoid carcinoma

- An uncommon breast carcinoma analogous to the salivary gland entity.
- It belongs to a small favorable-outcome group of triple-negative special types.
- The given textbook excerpt lists the type without detailed morphology.
- Avoid adding unverified diagnostic thresholds or translocation claims.

Secretory carcinoma: A distinct special type

- Secretory carcinoma is a rare salivary gland–like breast carcinoma.
- It among special types and groups it with relatively favorable TNBC subtypes.
- The label denotes a distinct histologic type, not nonspecific glandular secretion.
- Exact molecular alterations are not provided in the supplied source excerpt.

Subtype, receptor phenotype, and outcome

Group	Selected types	Robbins emphasis
Usually luminal	Lobular, mucinous, tubular, cribriform, papillary	Distinct architectures; usually ER+/HER2–
More likely HER2+	Apocrine, micropapillary	Distinct cytology vs structure
Often TNBC, aggressive	Many metaplastic forms	Squamous / mesenchymal differentiation
Rare TNBC, favorable	Adenoid cystic, mucoepidermoid, secretory	Salivary gland–like counterparts

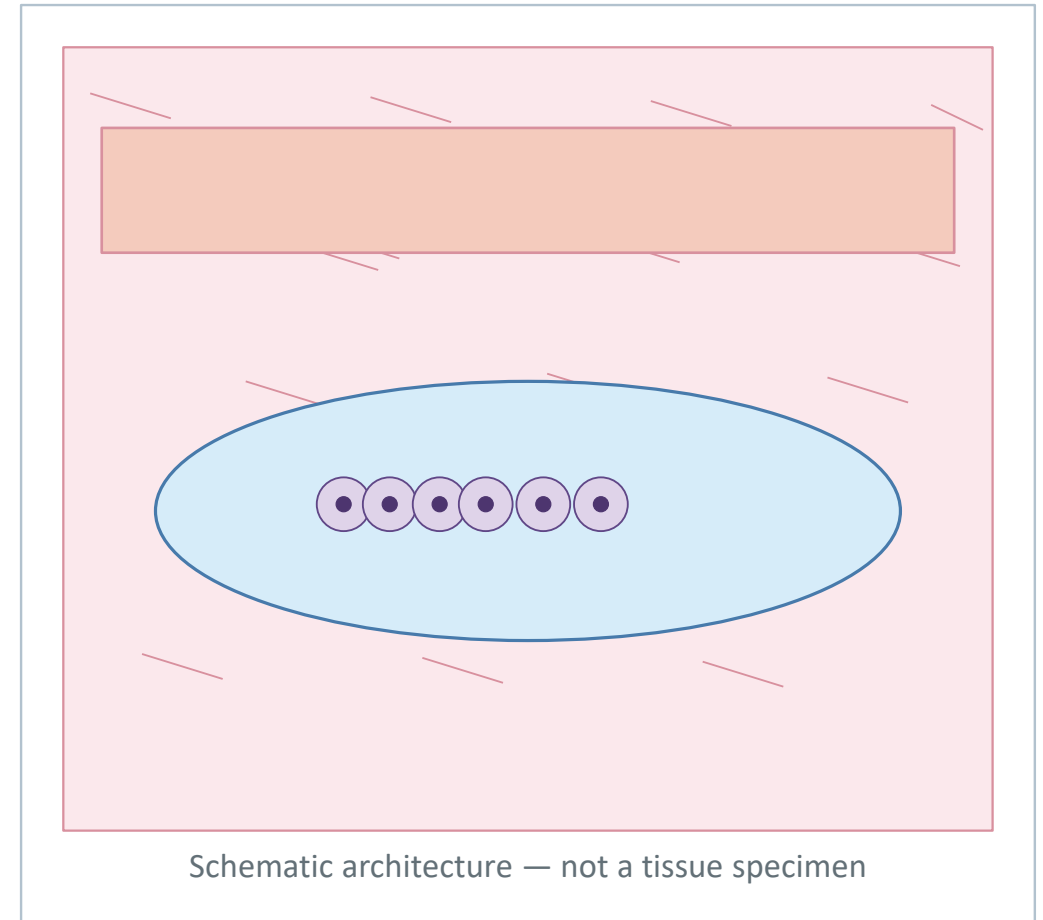
Inflammatory breast carcinoma is not a histologic type

“Inflammatory” breast carcinoma describes a clinical presentation caused by dermal lymphovascular tumor emboli.

Clinical syndrome, not a distinctive epithelial architecture • The term does not imply primary infection

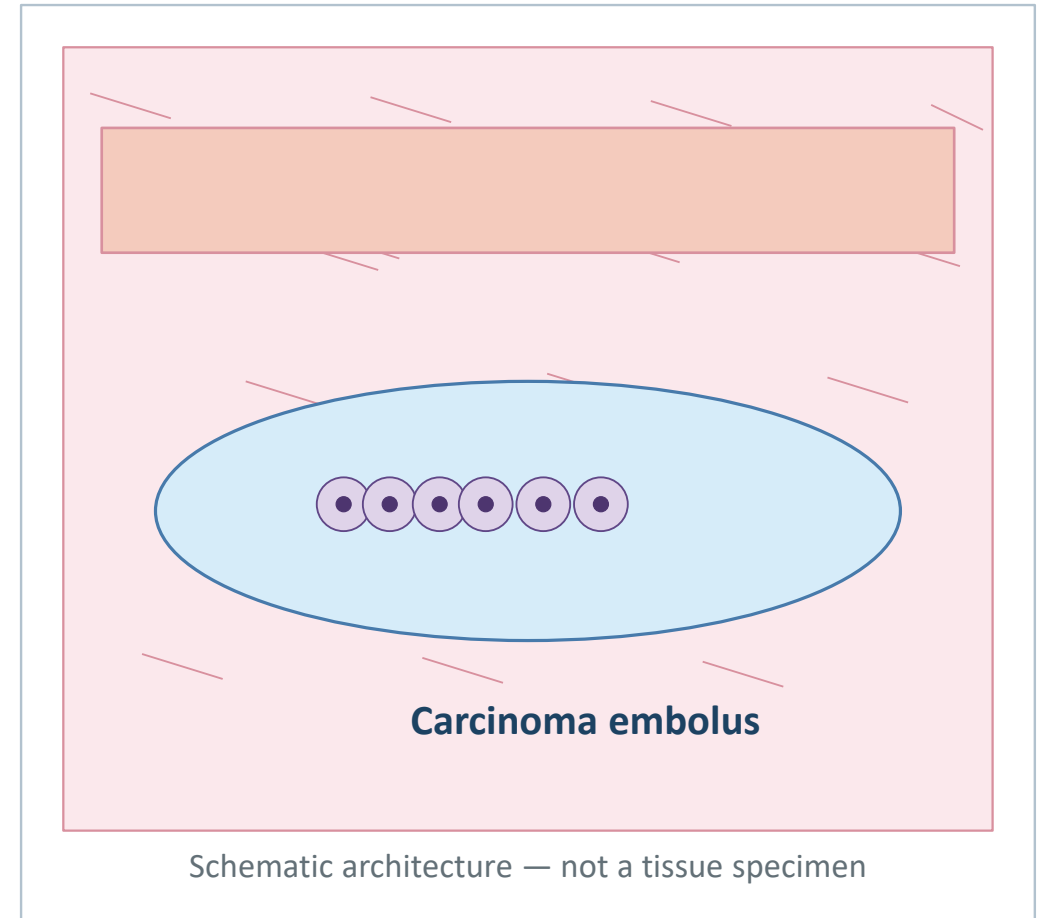
Dermal lymphovascular obstruction causes edema

- Extensive carcinoma cell plugs occupy dermal lymphovascular spaces.
- Lymphatic outflow obstruction produces diffuse swelling and skin thickening.
- Clinical erythema accompanies the edematous presentation.
- The defining mechanism is tumor embolization, not inflammatory-cell infiltrates.



Peau d'orange is a mechanical consequence

- Edematous skin remains tethered to deep breast structures by Cooper ligaments.
- Localized tethering against diffuse swelling produces an orange-peel texture.
- The skin changes reflect dermal lymphatic blockage and fixation.
- This finding can occur without a palpable discrete mass.



Inflammatory carcinoma: Why clinical confusion occurs

- Erythema and swelling may resemble an infectious process.
- The designation is a misnomer because inflammatory infiltrates are typically not the explanation.
- Delay can occur if the appearance is attributed solely to infection.
- Underlying carcinoma is commonly high grade and diffusely infiltrative.

Most invasive cancers present as a palpable or screened mass

- Primary cancers are identified by palpation or imaging-based screening.
- Screen-detected cancers are often smaller luminal tumors confined to the breast.
- Clinically apparent masses are more common with aggressive HER2-positive and triple-negative disease.
- The detection pattern is an association, not a substitute for receptor testing.

Advanced local growth alters the breast examination

- Pectoralis invasion can produce fixation to the chest wall.
- Dermal involvement can result in retraction or dimpling.
- Central tumors may retract the nipple.
- These clinical findings reflect anatomic extent rather than a specific histologic subtype.

Occult primary carcinoma may first appear as metastasis

- An axillary node or distant metastasis may occasionally precede identification of the breast primary.
- The primary can be small, obscured by dense tissue, or minimally desmoplastic.
- Ultrasound or MRI may reveal lesions missed by examination or mammography.
- Insidious invasive patterns should remain in the differential.

Illustrative case: Subtle invasive lobular carcinoma

Illustrative teaching vignette

Breast imaging shows only ill-defined subtle distortion. Histology reveals individual tumor cells aligned in linear cords with limited stromal response.

Interpretation

- Pattern favors invasive lobular carcinoma rather than a desmoplastic NST mass.
- E-cadherin loss is an expected biologic association, not a replacement for morphology.
- A weakly palpable lesion is consistent with insidious infiltration.

Illustrative case: Grading a high-grade NST

Illustrative teaching vignette

An invasive lesion grows as irregular sheets. Tumor cells have enlarged pleomorphic nuclei, conspicuous mitotic activity, and a focus of necrosis.

Interpretation

- Morphology is compatible with poorly differentiated (grade 3) carcinoma.
- Grading rests on gland formation, nuclear atypia, and mitotic rate together.
- The histologic grade alone does not establish HER2 or triple-negative status.

Illustrative case: Papillary or micropapillary?

Illustrative teaching vignette

An invasive tumor forms round cellular aggregates apparently floating in tissue spaces. No central fibrovascular core is seen in the aggregates.

Interpretation

- The absence of true cores favors invasive micropapillary architecture.
- True papillary carcinoma instead contains epithelial-lined fibrovascular fronds.
- Assess HER2 directly; A receptor association is not proof of type.

Illustrative case: A triple-negative spindle lesion

Illustrative teaching vignette

An invasive breast malignancy shows a substantial spindle-cell component. ER, PR, and HER2 are negative.

Interpretation

- Metaplastic carcinoma belongs in the differential because mesenchymal-like growth is recognized.
- Triple-negative status supports a group association but does not independently establish type.
- Clinical behavior differs among metaplastic subtypes.

Pattern-based differential: Five recognition pivots

Look for	Consider	Exclude confusion with
Single-file discohesive cells	Invasive lobular	NST with scattered glands
Large extracellular mucin lakes	Mucinous	Signet-ring intracellular mucin
Infiltrating well-formed small glands	Tubular	Benign sclerosis
True fibrovascular cores	Papillary	Micropapillary
Hollow clusters without true cores	Micropapillary	Papillary
Spindle / squamous elements	Metaplastic	Purely stromal lesion

Histologic pattern is a map, not the whole diagnosis

- Histologic type captures reproducible growth pattern and tumor cytology.
- Nottingham grade captures degree of differentiation and cell division.
- ER, PR, and HER2 provide biologic and therapeutic context.
- Clinical extent and metastatic spread remain separate dimensions.
- Subtype assessment should preserve uncertainty when architecture is incomplete.

Five distinctions that prevent classification errors

- NST with medullary pattern is not a separate medullary histologic type.
- Papillary carcinoma has real fibrovascular cores; Micropapillary carcinoma does not.
- Lobular signet-ring change is not equivalent to extracellular mucinous growth.
- Triple-negative receptor status does not imply a single prognosis.
- Inflammatory carcinoma is a clinical syndrome, not a special microscopic carcinoma subtype.

Primary reference and source limits

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026), Chapter 23, The Breast.
- Core source: “Types of Invasive Breast Carcinoma,” printed pp. 961–964.
- Adjacent source context: “Clinical Presentation” (p. 964) and prognostic factors (p. 964).
- Figures 23.20–23.22 were described in source text but not reproduced; native figures here are explanatory schematics.
- Original chapter PDF was not available for direct page/figure verification.