

Lesions of Intralobular Stroma

Fibroadenoma and phyllodes tumor

Breast fibroepithelial pathology

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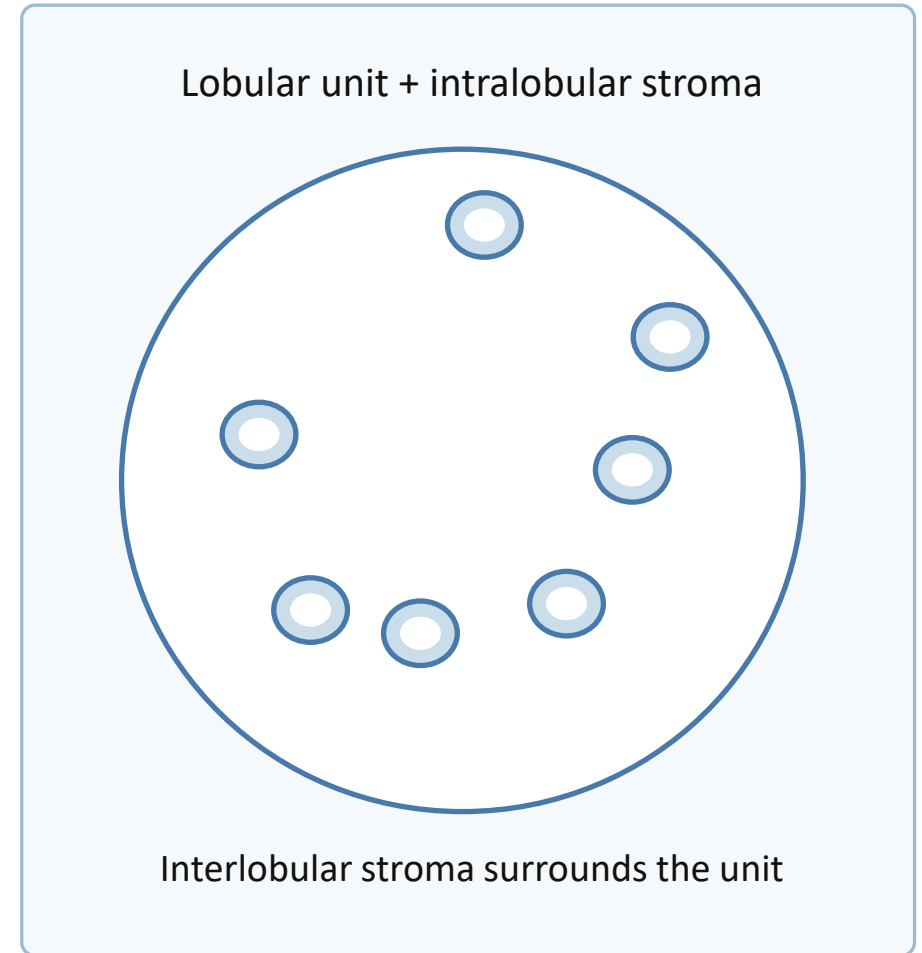
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Learning objectives

- Explain the biphasic composition and stromal origin of both tumors.
- Recognize the gross and microscopic patterns of fibroadenoma.
- Interpret MED12, RARA and related molecular findings cautiously.
- Distinguish fibroadenoma from the three grades of phyllodes tumor.
- Connect stromal grading and surgical margins to clinical behavior.

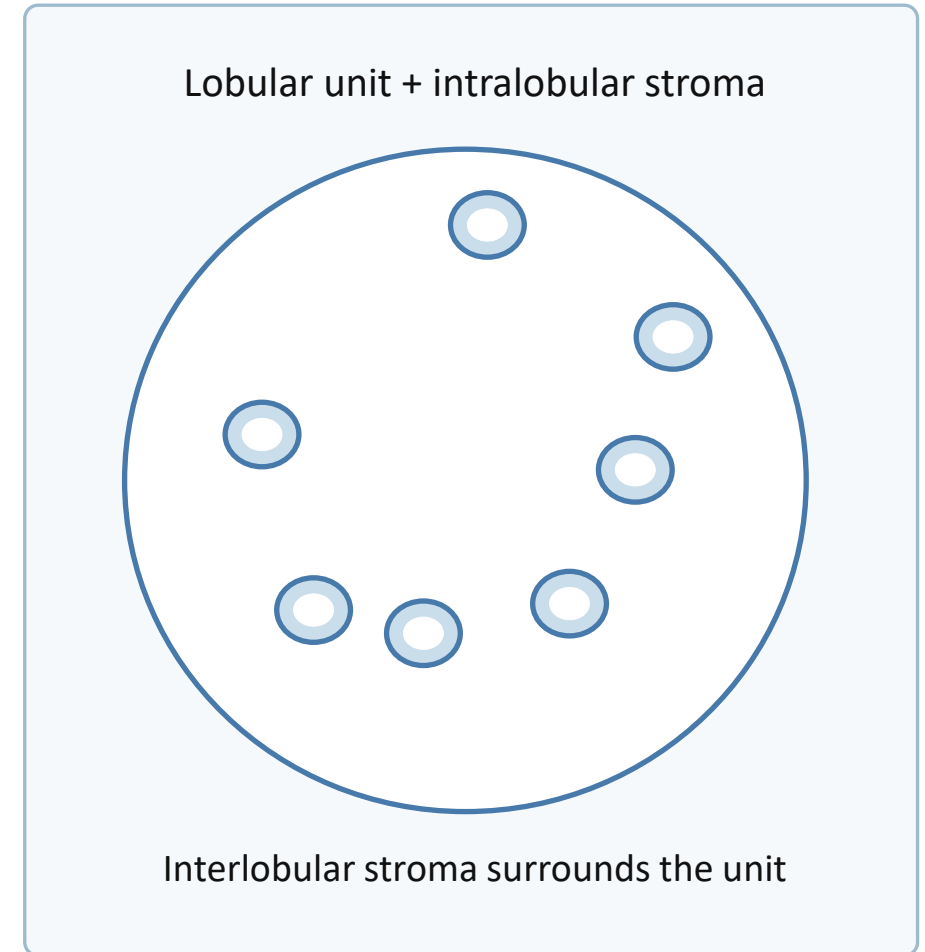
Two stromal compartments of the breast

- Intralobular stroma surrounds duct–lobular epithelial structures.
- Interlobular stroma lies between lobular units and supports connective tissue.
- The compartment of origin predicts the tumor's epithelial association.



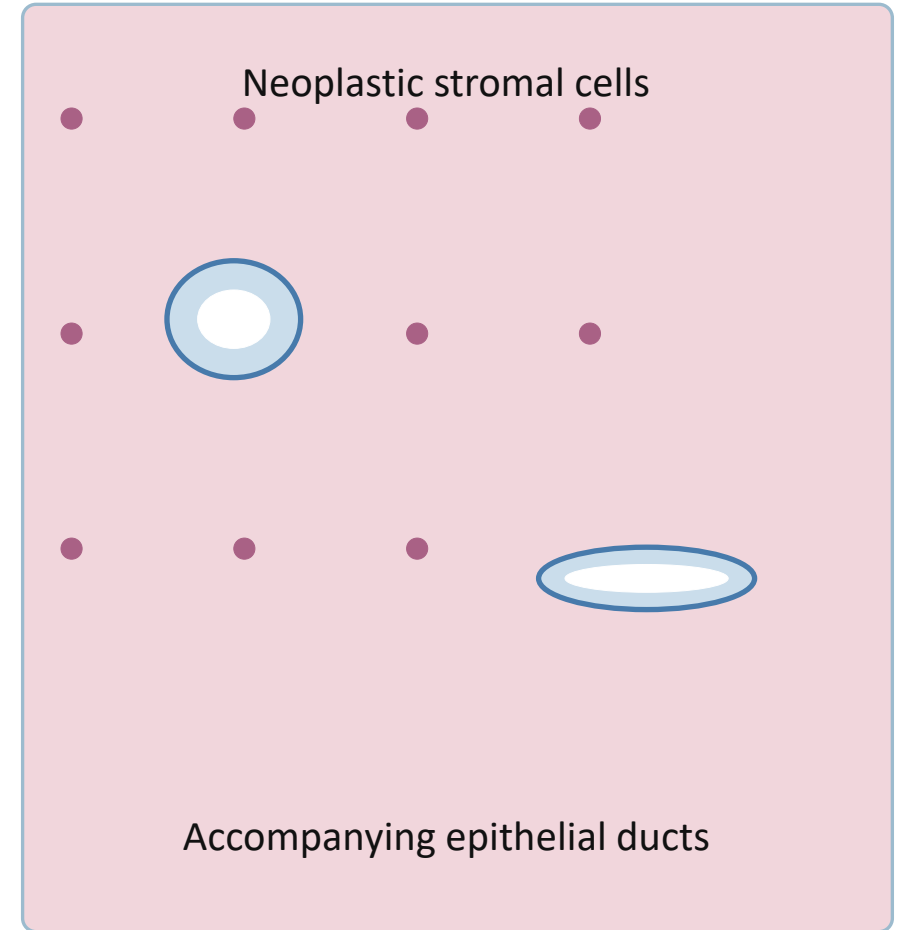
Stromal tumors: Two different families

- Intralobular origin: Fibroadenoma and phyllodes tumor.
- Interlobular origin: Mesenchymal tumors, including lipoma and angiosarcoma.
- The distinction is an origin-and-composition framework, not simply a location label.



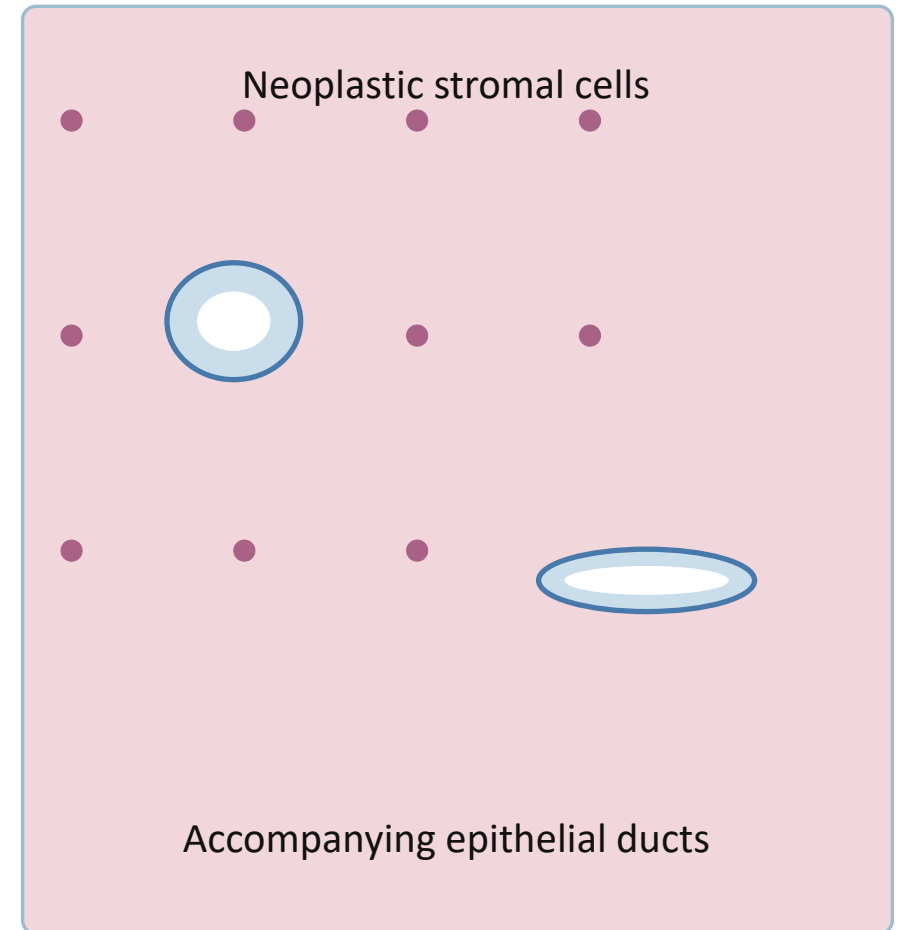
Fibroepithelial tumors are biphasic

- Fibroadenoma and phyllodes tumor contain neoplastic stroma.
- Both also contain epithelial elements that are nonneoplastic.
- Stromal-derived growth factors may stimulate the accompanying epithelium.



What “biphasic” does not mean

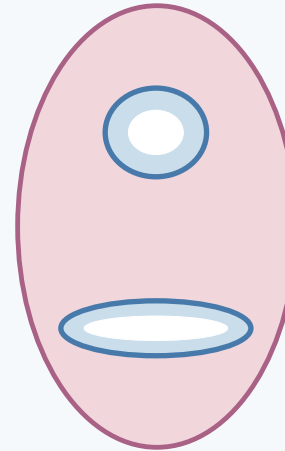
- Two visible components do not establish that both are neoplastic.
- In these tumors, stromal proliferation is the neoplastic driver.
- Epithelial lining can become compressed, stretched, or displaced by the stroma.



Histology separates the two major tumors

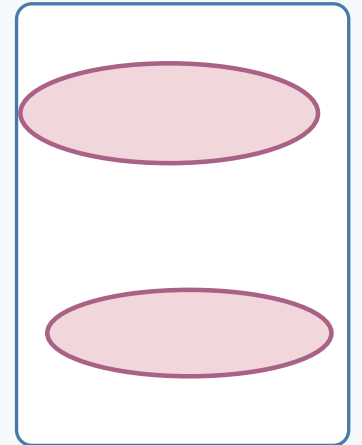
- Fibroadenoma usually has relatively delicate intralobular-type stroma.
- Phyllodes tumor tends toward greater stromal cellularity and mitotic activity.
- Architecture alone is insufficient: Stromal features must be considered.

Fibroadenoma



More delicate stroma

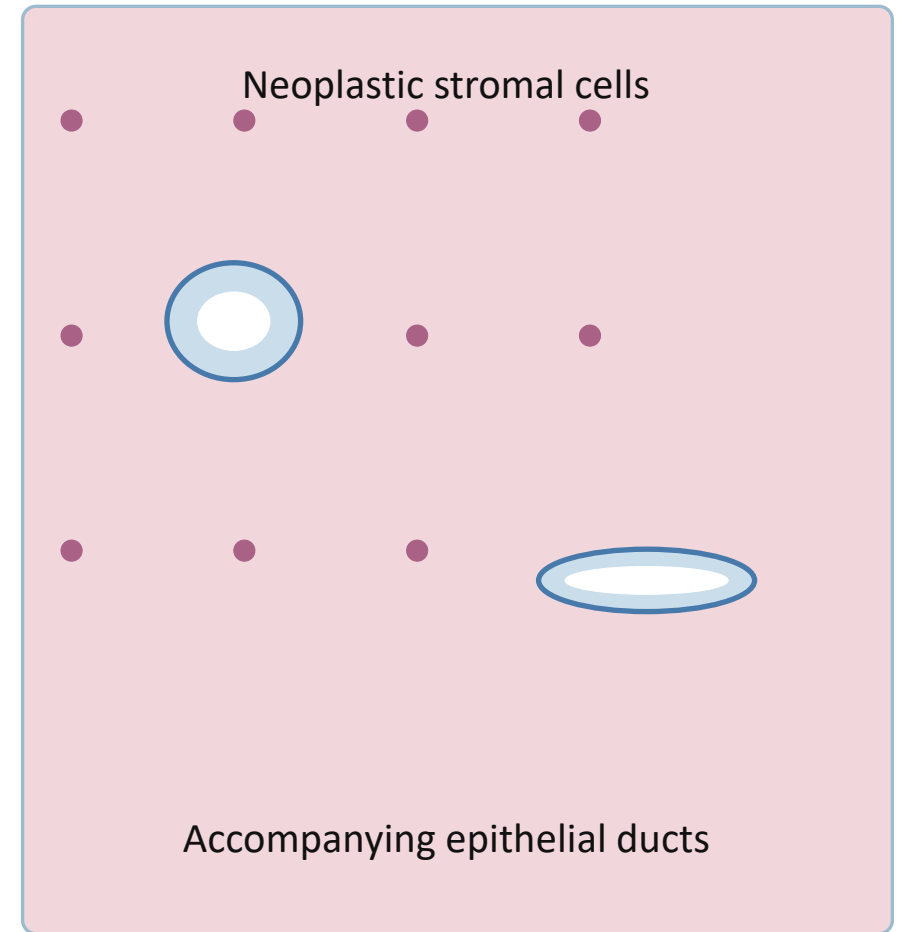
Phyllodes



Greater cellularity

Fibroadenoma: The defining concept

- Most common benign stromal tumor of the female breast.
- Benign fibroepithelial neoplasm derived from intralobular stroma.
- Produces a discrete lesion containing ducts embedded in proliferative stroma.



Typical age at presentation

- Most fibroadenomas occur in women in their 20s and 30s.
- Palpability is a common route to recognition in younger patients.
- The same tumor may instead be found incidentally by imaging.

Typical age at presentation

Fibroadenoma: 20s–30s

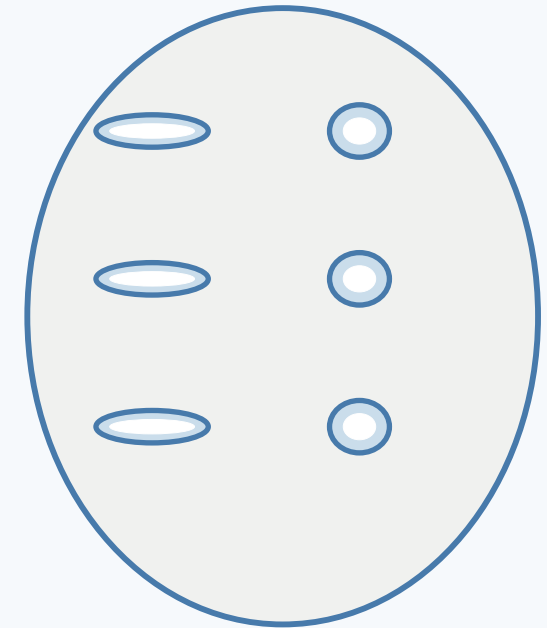
Phyllodes: Sixth decade

Overlap is possible

Morphology decides

Fibroadenomas may be multiple

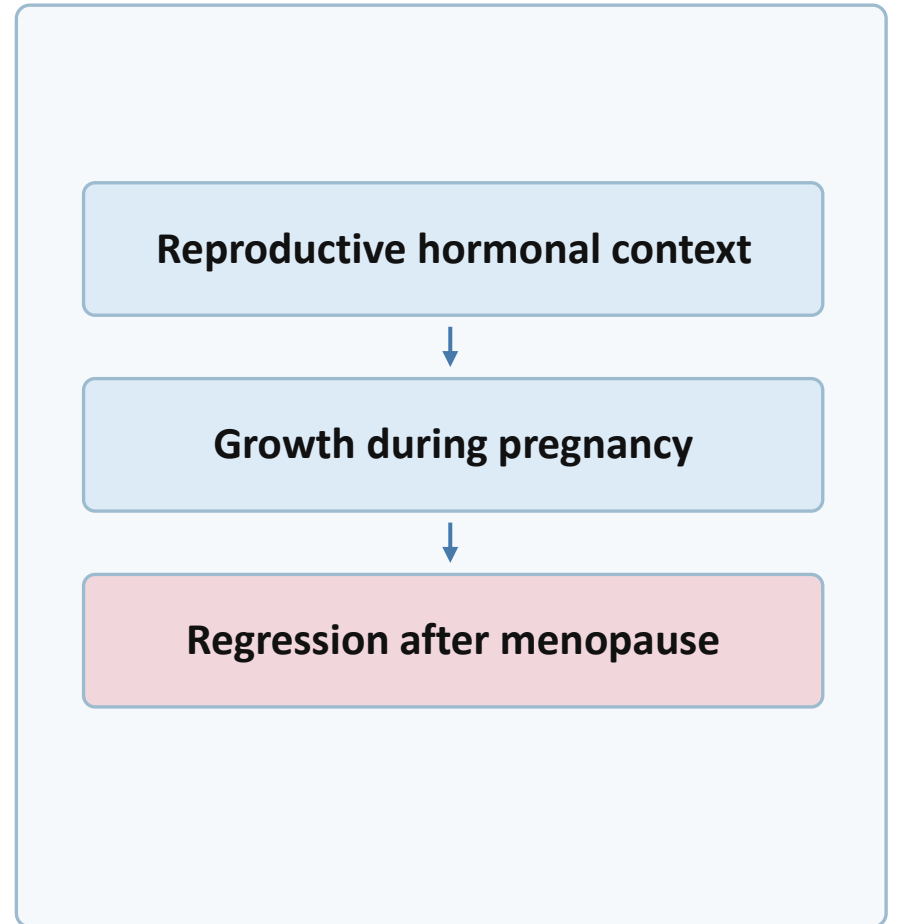
- Multiple lesions can occur within one breast.
- Bilateral fibroadenomas are also frequent.
- Multiplicity alone does not establish malignant disease.



Circumscribed stromal nodule

Hormone responsiveness is clinically visible

- Fibroadenomas respond to hormonal conditions.
- Growth may occur during pregnancy.
- Regression may occur after menopause.



Rapid growth in pregnancy: A diagnostic trap

- Accelerated enlargement may occur during pregnancy.
- Rapid expansion can sometimes lead to infarction.
- Rapid growth and infarction may falsely suggest carcinoma.

Reproductive hormonal context



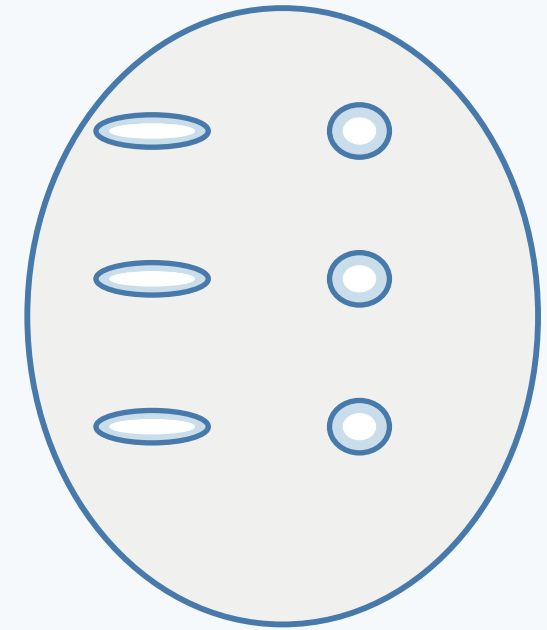
Growth during pregnancy



Regression after menopause

Fibroadenoma as an imaging abnormality

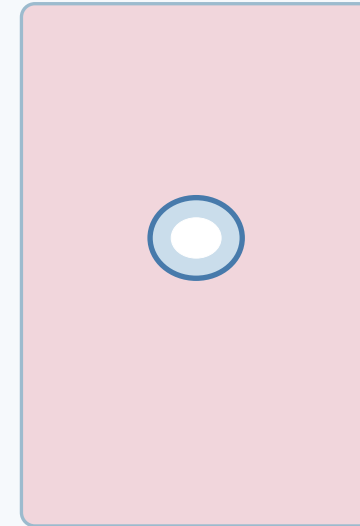
- In a young patient, a palpable mass is typical.
- Imaging may demonstrate a well-circumscribed mammographic density.
- Radiodensity relates to the absence of adipose tissue within the nodule.



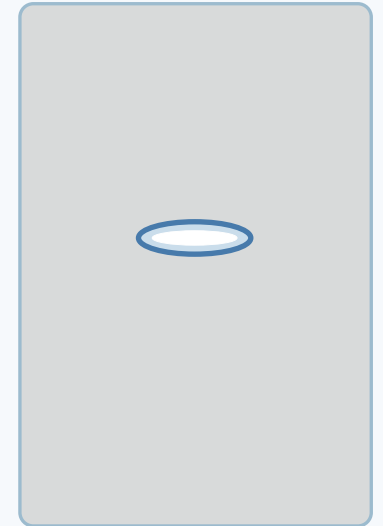
Circumscribed stromal nodule

Older patients: Calcification may dominate

- Some fibroadenomas are first detected by mammography in older women.
- Clustered calcifications may be the presenting imaging finding.
- Associated stromal hyalinization alters the lesion's appearance.



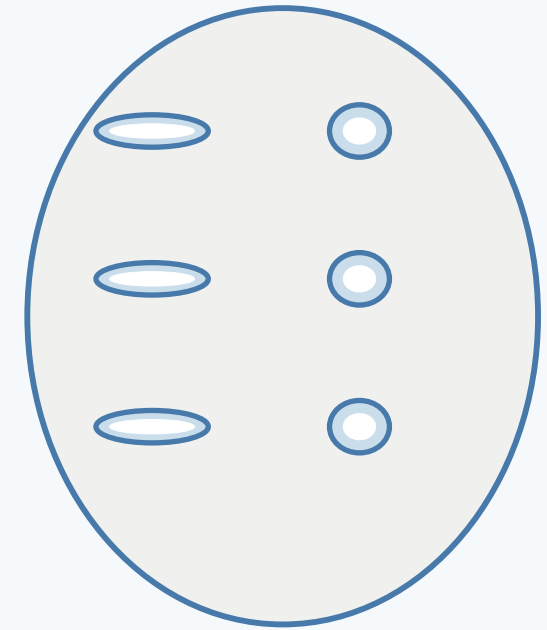
Delicate / myxoid



Hyalinized / atrophic

Gross pathology: The characteristic nodule

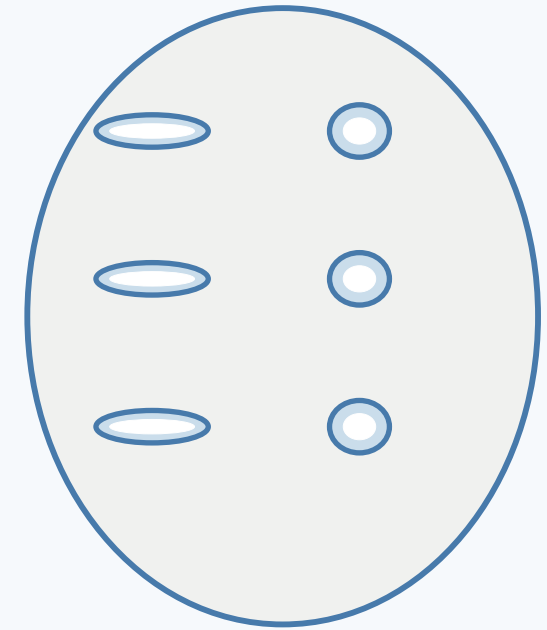
- Cut surface is gray-white and rubbery.
- Borders are well circumscribed; The mass bulges above the adjacent tissue.
- Slit-like epithelial-lined spaces may be seen on sectioning.



Circumscribed stromal nodule

Fibroadenoma spans a wide size range

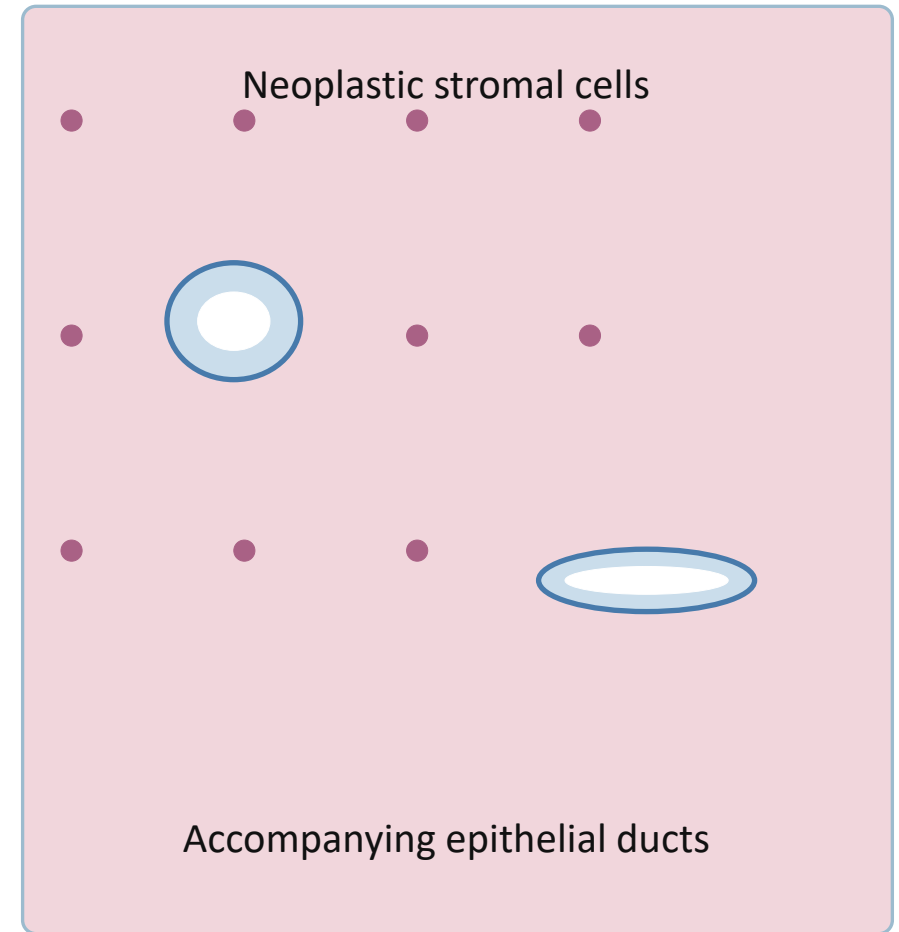
- Size may be less than 1 cm.
- Some lesions become sufficiently large to replace much of the breast.
- Size alone should not be used as a proxy for stromal malignancy.



Circumscribed stromal nodule

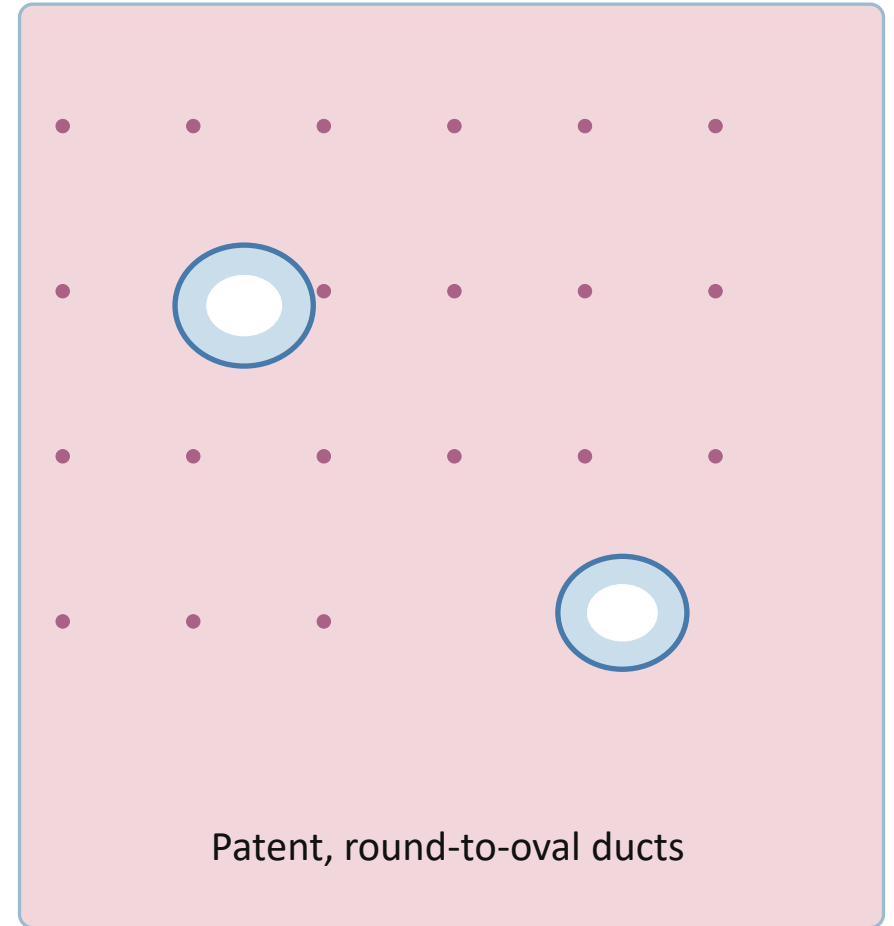
Microscopy: The core components

- Fibrous, often myxoid stroma resembles native intralobular stroma.
- Ductal epithelial structures are dispersed within the stroma.
- Stromal proliferation changes the contour of the epithelial profiles.



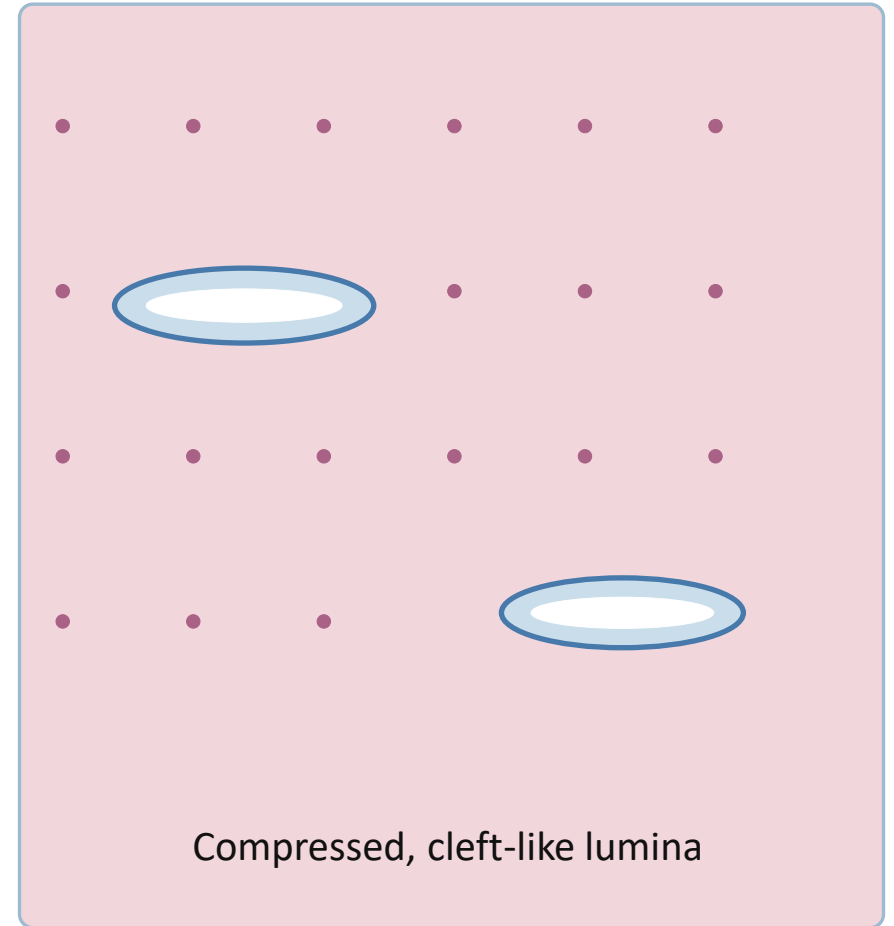
Pericanalicular growth pattern

- Stroma grows around ducts but leaves them patent.
- Ducts remain relatively rounded or oval.
- The named pattern refers to the spatial relationship between stroma and ducts.



Intracanalicular growth pattern

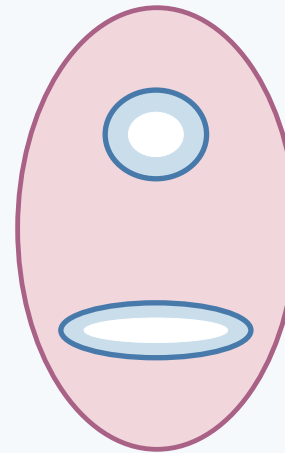
- Expanding stroma compresses and distorts epithelial ducts.
- Lumina become elongated and cleft-like.
- The distortion is produced by stromal growth rather than epithelial invasion.



Pericanalicular versus intracanalicular

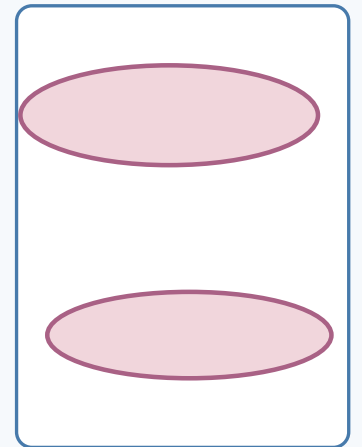
- Pericanalicular: Open epithelial lumina surrounded by stroma.
- Intracanalicular: Ducts are compressed into slits or clefts.
- Both patterns demonstrate the same benign biphasic tumor concept.

Fibroadenoma



Patent ducts

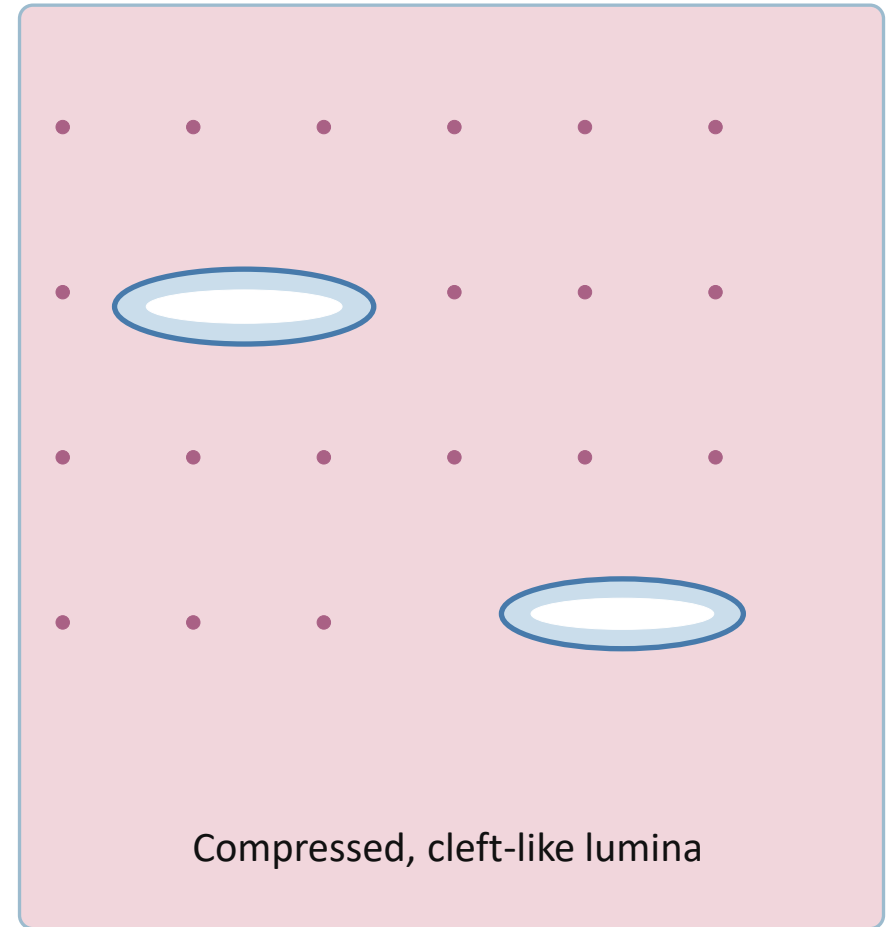
Phyllodes



Cleft-like ducts

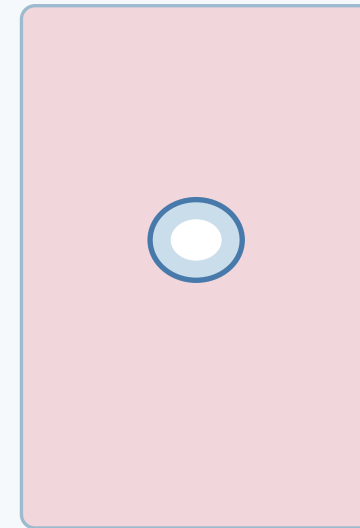
Architecture reflects stromal pressure

- The stromal component determines duct contour.
- Less-compressed ducts stay patent; Stronger compression creates clefts.
- Recognizing a cause–effect relationship is more useful than memorizing silhouettes.

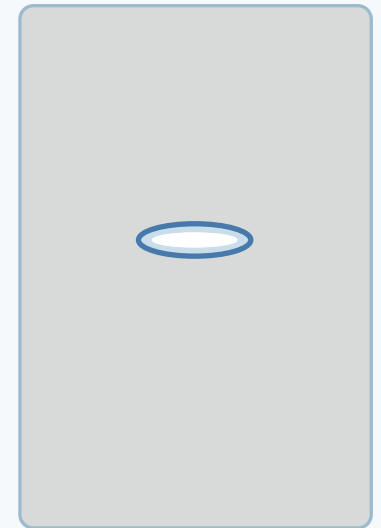


Aging fibroadenoma: Stromal change

- Stroma commonly becomes densely hyalinized in older patients.
- The initially delicate/myxoid component is replaced by more collagenized tissue.
- Appearance may therefore differ markedly from the textbook young-adult pattern.



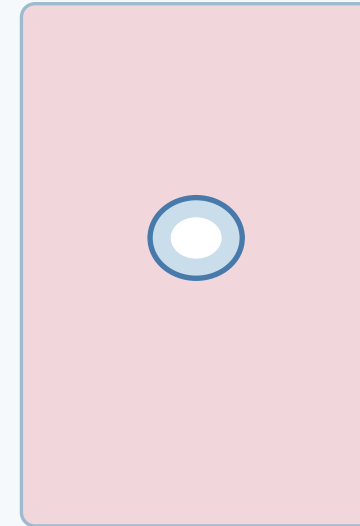
Delicate / myxoid



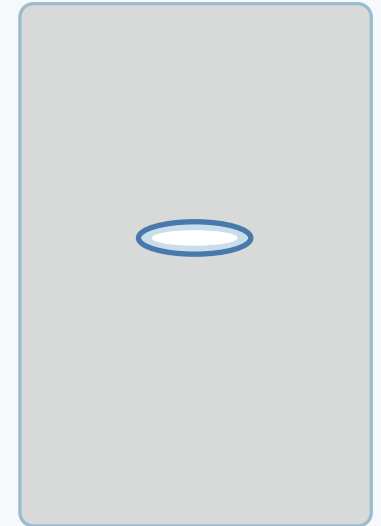
Hyalinized / atrophic

Aging fibroadenoma: Epithelial change

- Accompanying epithelium is often atrophic in older patients.
- Epithelial attenuation occurs alongside stromal hyalinization.
- Interpret the epithelial change within the otherwise benign fibroepithelial lesion.



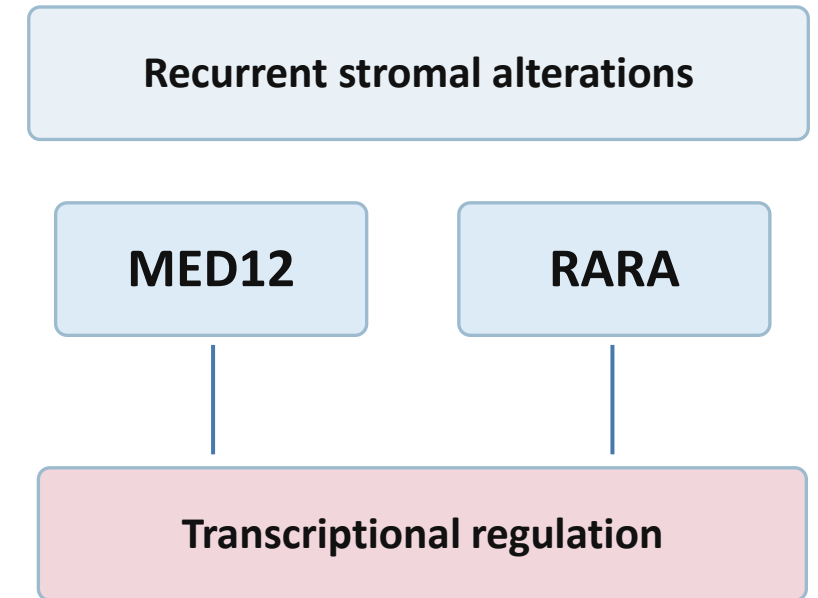
Delicate / myxoid



Hyalinized / atrophic

MED12 alterations: Common stromal drivers

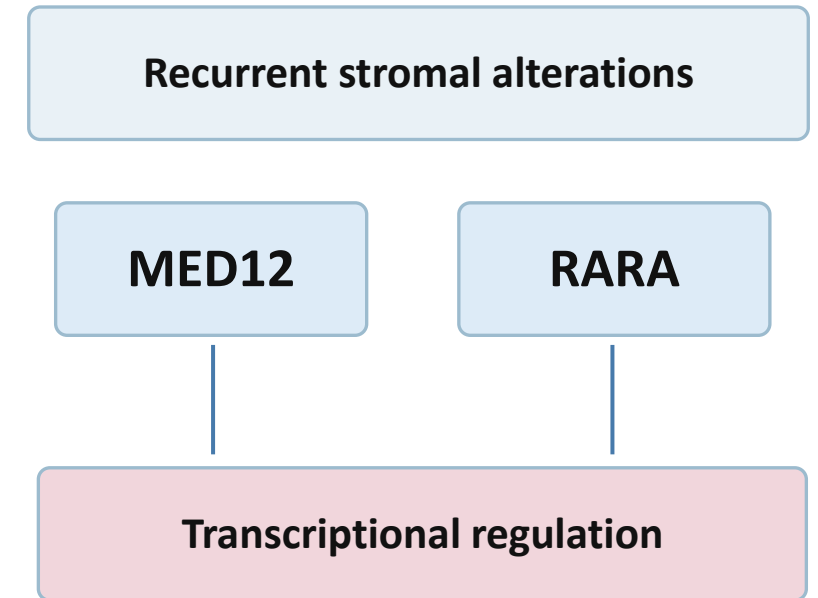
- Approximately two-thirds of fibroadenomas harbor driver mutations in MED12.
- MED12 encodes a mediator-complex subunit.
- The mediator complex participates in RNA polymerase II–dependent gene regulation.



Mechanism remains incompletely explained

Mediator biology links mutation to transcription

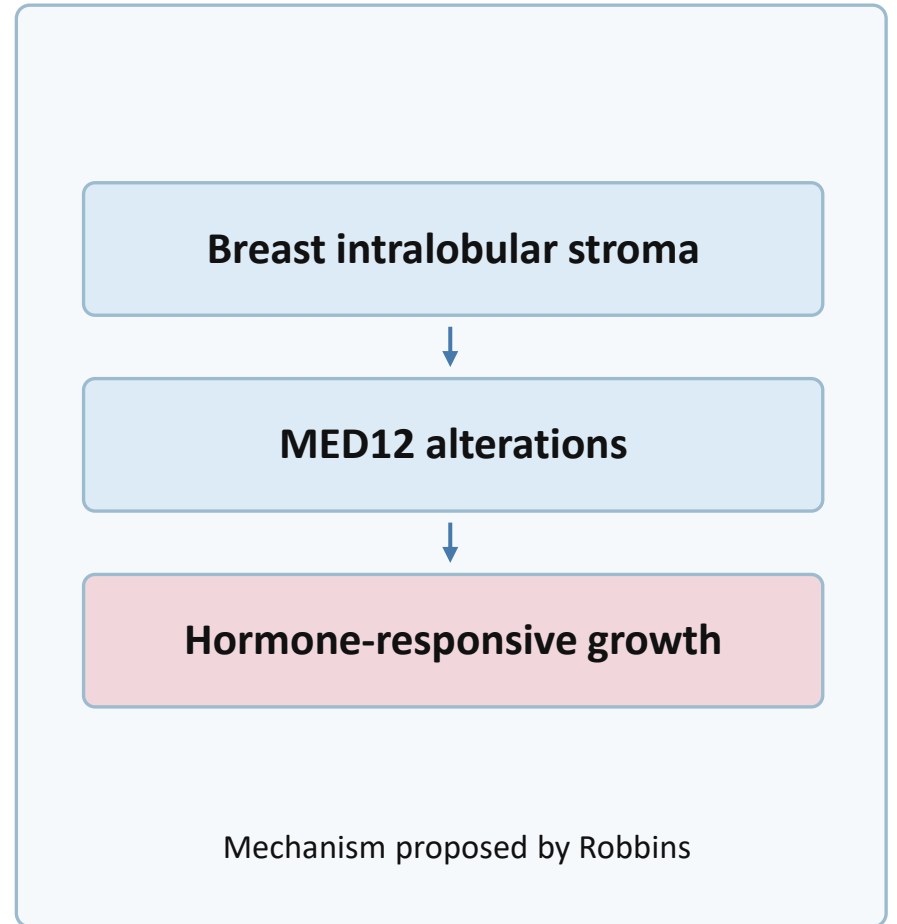
- Mediator helps regulate RNA polymerase II–dependent transcription.
- MED12 mutation may disrupt the expression of specific stromal growth/survival genes.
- This is a proposed mechanism, not a completely established causal pathway.



Mechanism remains incompletely explained

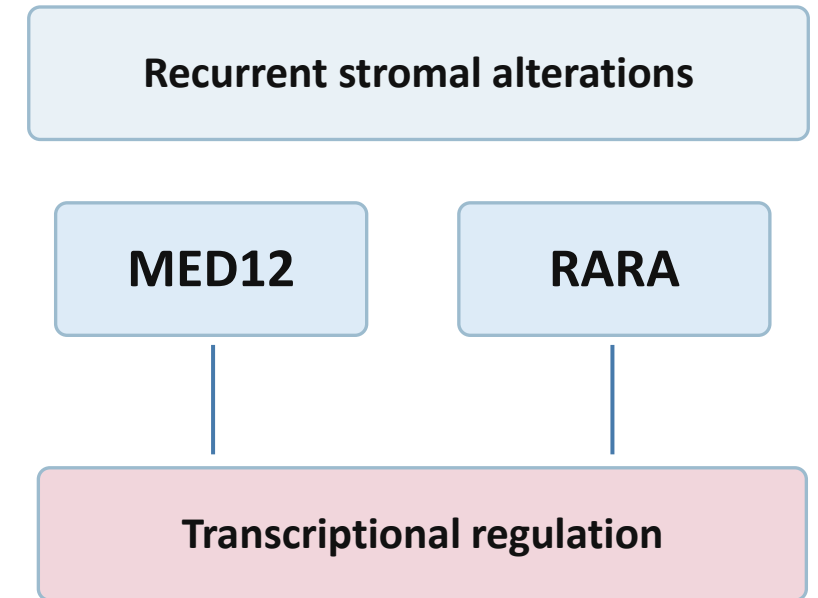
Hormone-sensitive stroma and MED12

- Both breast fibroadenoma and uterine leiomyoma are stromal tumors.
- Both arise in organs responsive to female sex hormones.
- Their shared MED12 association supports a possible hormone-regulated transcriptional mechanism.



RARA is a second recurrently altered gene

- Around one-third of fibroadenomas harbor RARA mutations.
- RARA encodes retinoic acid receptor alpha.
- The gene is an estrogen target and may cooperate with estrogen receptor in transcription.



Mechanism remains incompletely explained

MED12 and RARA: Interpret the evidence

- Mutation frequencies are reported independently in the source.
- They establish recurrent molecular associations, not a stand-alone histologic diagnosis.
- Do not assume all tumors carry both alterations or that their co-occurrence is obligatory.

Recurrent gene alterations

MED12: $\sim\frac{2}{3}$ of fibroadenomas

RARA: $\sim\frac{1}{3}$ of fibroadenomas

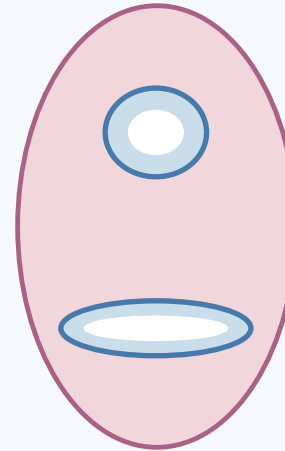
Shared with phyllodes

No stand-alone diagnostic test

Genes do not replace morphology

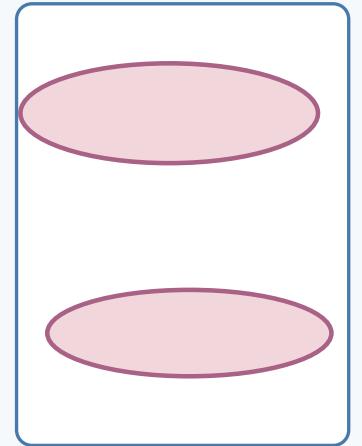
- MED12 and RARA are relevant to tumor pathogenesis.
- Routine distinction between fibroadenoma and phyllodes relies on morphology.
- Histologic stromal features as the basis for separation.

Fibroadenoma



More delicate stroma

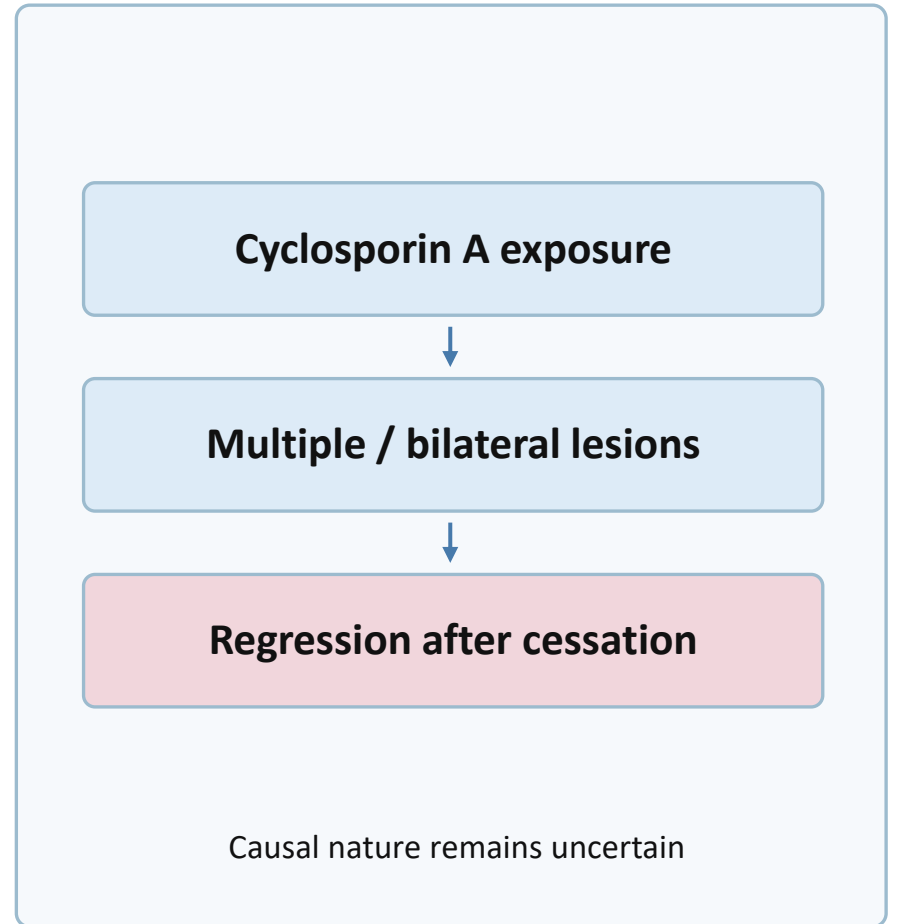
Phyllodes



Greater cellularity

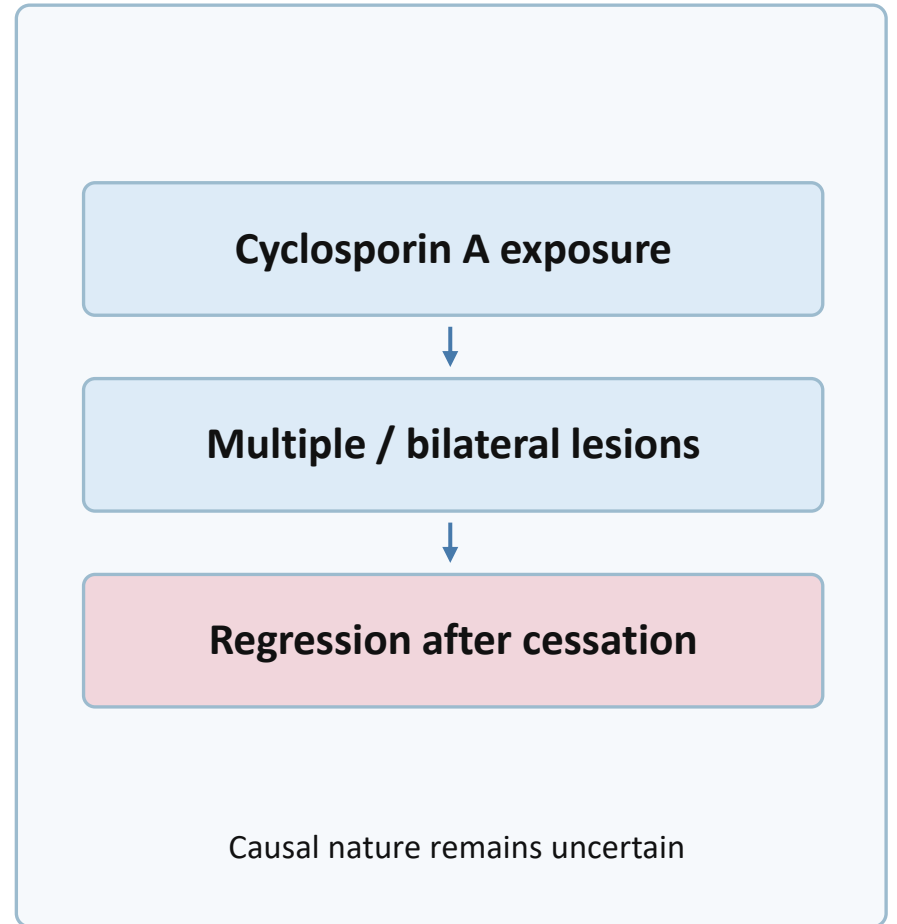
Cyclosporin A: A striking clinical association

- Multiple bilateral fibroadenomas in almost half of women receiving cyclosporin A after renal transplantation.
- Regression after cessation of treatment is described.
- This is an association; Causation and neoplastic status remain unsettled.



Cyclosporin-associated lesions: Uncertainty

- The lesions may be true neoplasms or reactive hyperplasia.
- Regression after discontinuation favors a potentially reversible proliferative process.
- Do not classify the mechanism as settled when the source identifies uncertainty.



Recognized fibroadenoma variants

- Myxoid fibroadenoma and complex fibroadenoma are named variants.
- A variant designation reflects a particular histologic constellation.
- These categories are not equivalent to malignant transformation.

Two named subtypes

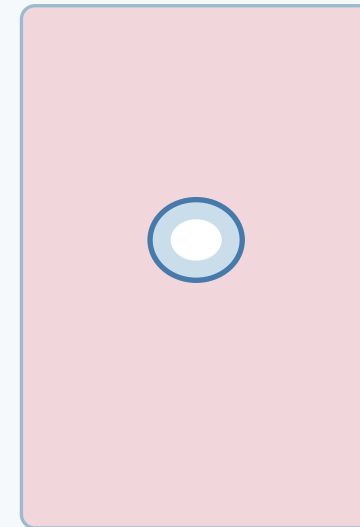
Myxoid fibroadenoma

Complex fibroadenoma

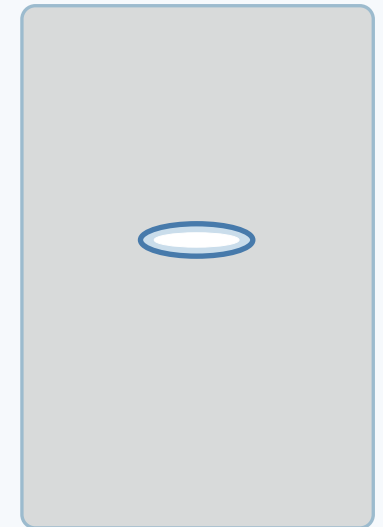
Sporadic or syndromic setting

Myxoid fibroadenoma: Stromal phenotype

- Myxoid fibroadenomas show a myxoid stromal character.
- Most cases are sporadic.
- A minority are associated with Carney complex.



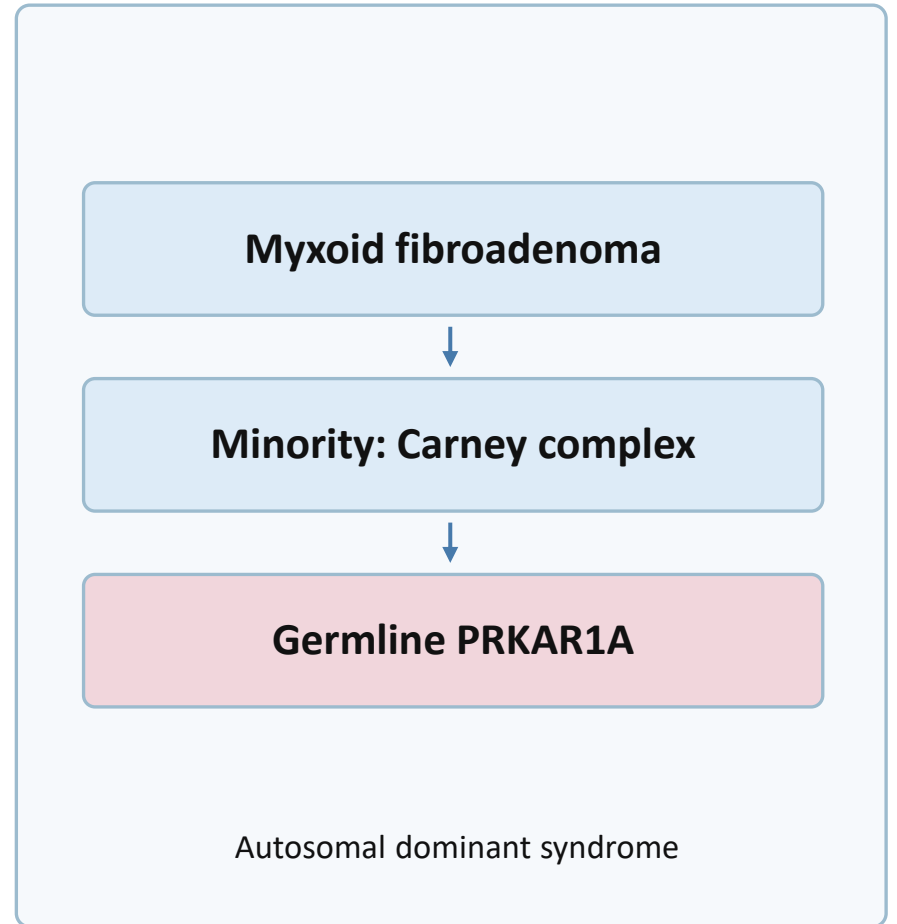
Delicate / myxoid



Hyalinized / atrophic

Carney complex: Inherited association

- A minority of myxoid fibroadenomas occur in Carney complex.
- Carney complex is an autosomal dominant condition.
- It is usually associated with inactivating germline PRKAR1A mutations.



Complex fibroadenoma: Operational definition

- Cysts larger than 0.3 cm are one defining change.
- Other qualifying findings: Sclerosing adenosis, epithelial calcifications, or papillary apocrine change.
- A complex fibroadenoma is defined by one or more of these tissue changes.

One or more qualifying changes

Cysts >0.3 cm

Sclerosing adenosis

Epithelial calcifications

Papillary apocrine change

Complex fibroadenoma: The four findings

- Cysts larger than 0.3 cm.
- Sclerosing adenosis.
- Epithelial calcifications or papillary apocrine change.

One or more qualifying changes

Cysts >0.3 cm

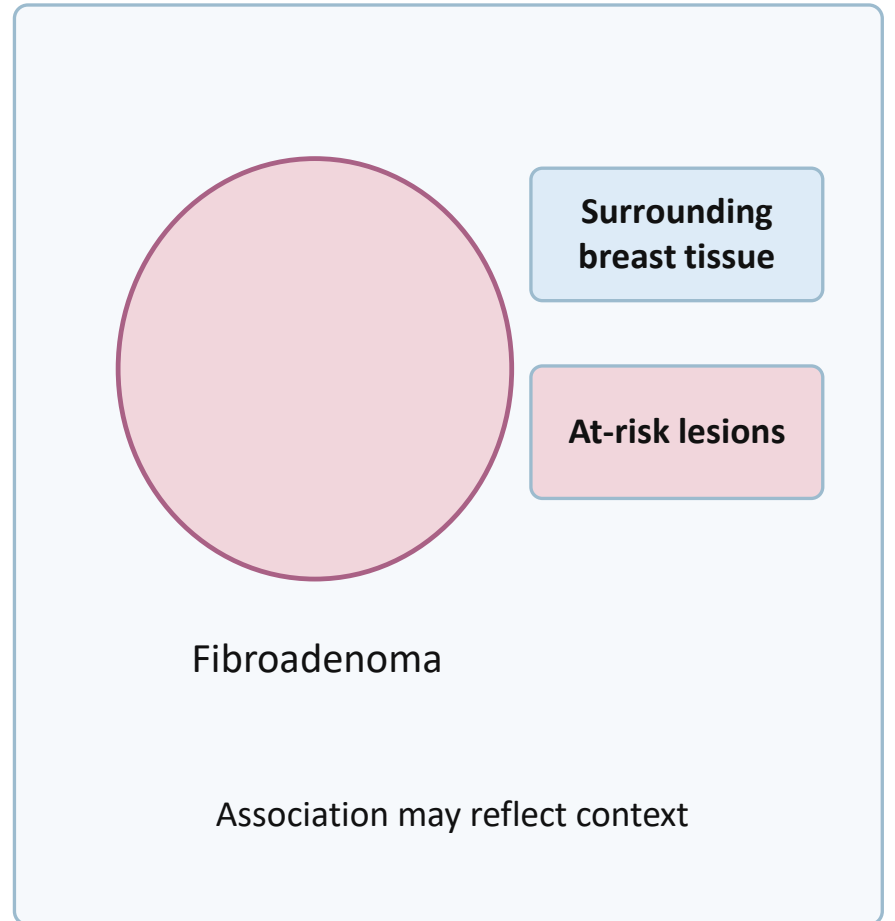
Sclerosing adenosis

Epithelial calcifications

Papillary apocrine change

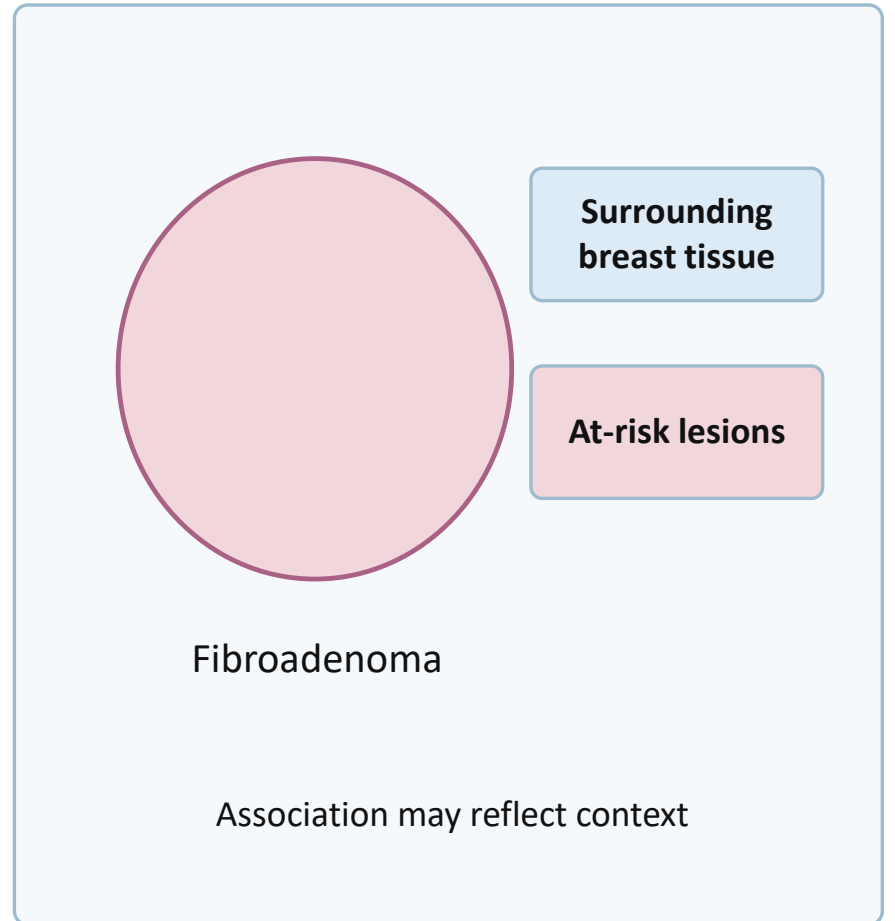
Complex fibroadenoma and later carcinoma risk

- A slightly increased subsequent breast carcinoma risk is described.
- The risk may partly reflect concurrent “at-risk” lesions in surrounding breast.
- Association should not be simplified into direct malignant progression of fibroadenoma.



Adjacent tissue can explain observed risk

- Atypical hyperplasia may occur in surrounding breast tissue.
- Such associated at-risk pathology could drive part of the observed risk association.
- Histologic context outside the nodule matters when interpreting risk.



Fibroadenoma: Integrating clinical and morphology

- Young patient, discrete mass, and benign biphasic histology are concordant.
- Patent ducts and compressed clefts are acceptable within fibroadenoma.
- Atypical presentation requires evaluation of the whole clinicopathologic picture.

Discrete mass in younger patient



Delicate stroma + ducts

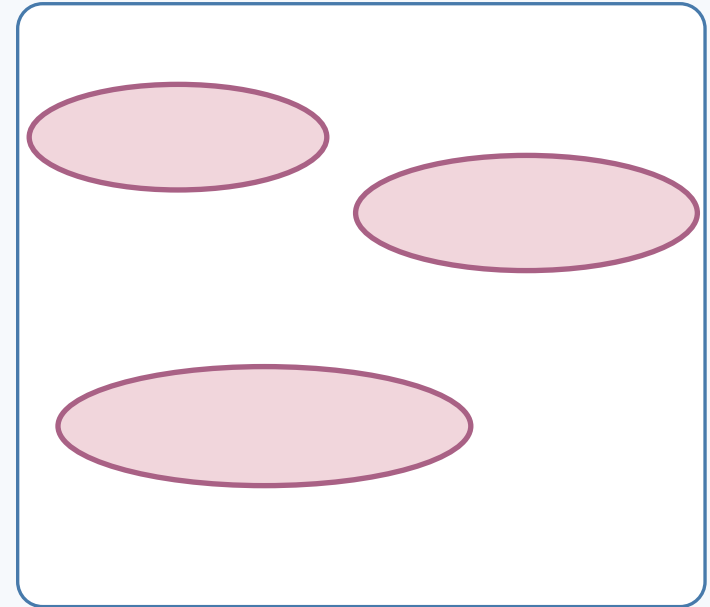


Fibroadenoma pattern

Interpret in clinical context

Phyllodes tumor: The related fibroepithelial neoplasm

- Phyllodes tumor also arises from intralobular breast stroma.
- It is much less common than fibroadenoma.
- It retains a biphasic tumor pattern but displays different stromal behavior.



Epithelial-lined stromal projections

How uncommon is phyllodes tumor?

- Phyllodes tumors account for approximately 2.5% of fibroepithelial lesions.
- The reported proportion refers to fibroepithelial lesions, not all breast masses.
- Fibroadenoma therefore dominates the everyday benign fibroepithelial differential.

How to read the proportion

Phyllodes: ~2.5%

Denominator: Fibroepithelial lesions

Much less common than FA

Age helps, but cannot establish the diagnosis

- Most phyllodes tumors present in the sixth decade.
- This is approximately 10–20 years later than the fibroadenoma peak.
- A patient's age is contextual evidence, not a histologic grading criterion.

Typical age at presentation

Fibroadenoma: 20s–30s

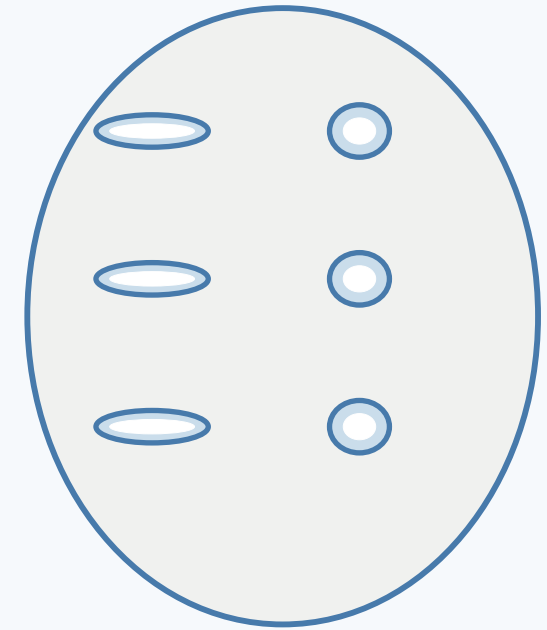
Phyllodes: Sixth decade

Overlap is possible

Morphology decides

Phyllodes tumor: How it presents

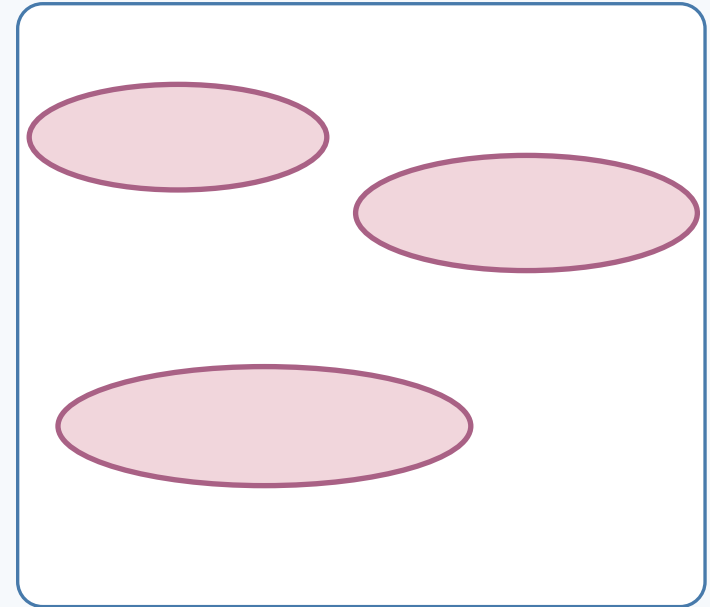
- Most are detected as palpable masses.
- Some are detected by mammography.
- Sizes extend from a few centimeters to massive tumors occupying the breast.



Circumscribed stromal nodule

Why the tumor is called “phyllodes”

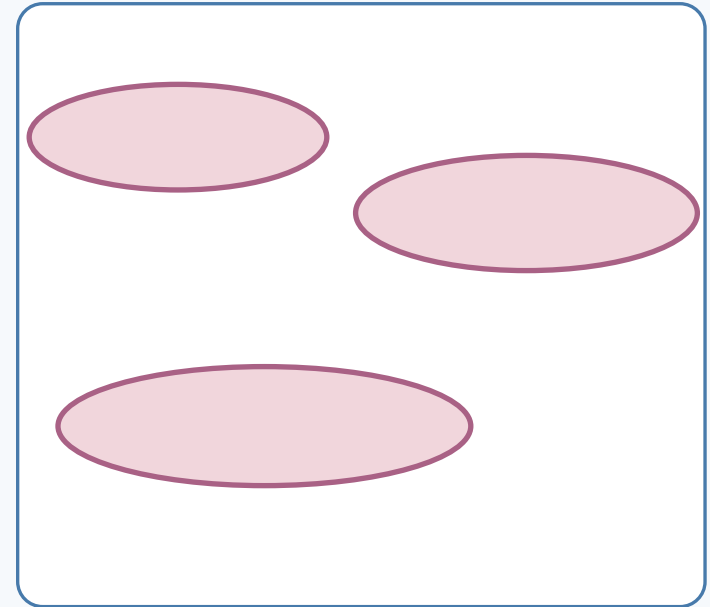
- Proliferating stromal nodules form bulbous projections.
- Each projection is covered by epithelial tissue.
- The resulting architecture resembles leaves (“phyllodes”).



Epithelial-lined stromal projections

Projections may extend into cystic spaces

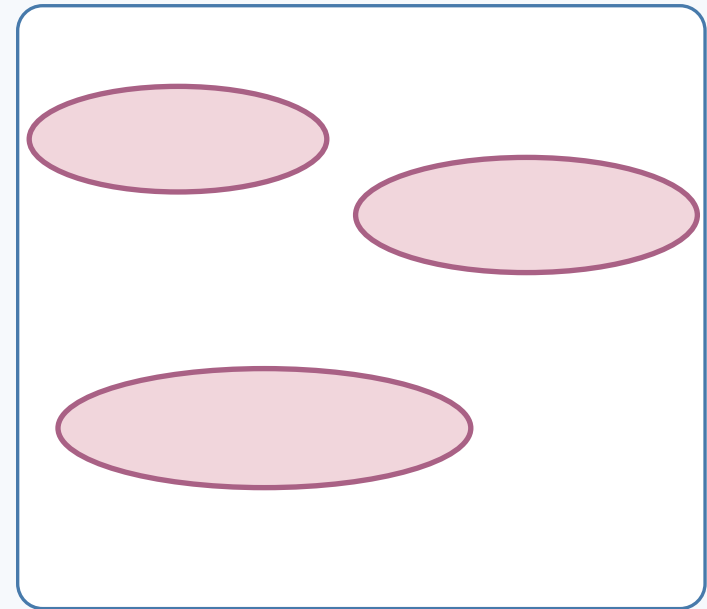
- Bulbous stromal fronds can project into a cystic cavity.
- The epithelial covering outlines the leaf-like spaces.
- This architecture is a growth pattern, not a stand-alone malignancy marker.



Epithelial-lined stromal projections

Leaf-like architecture is not synonymous with malignancy

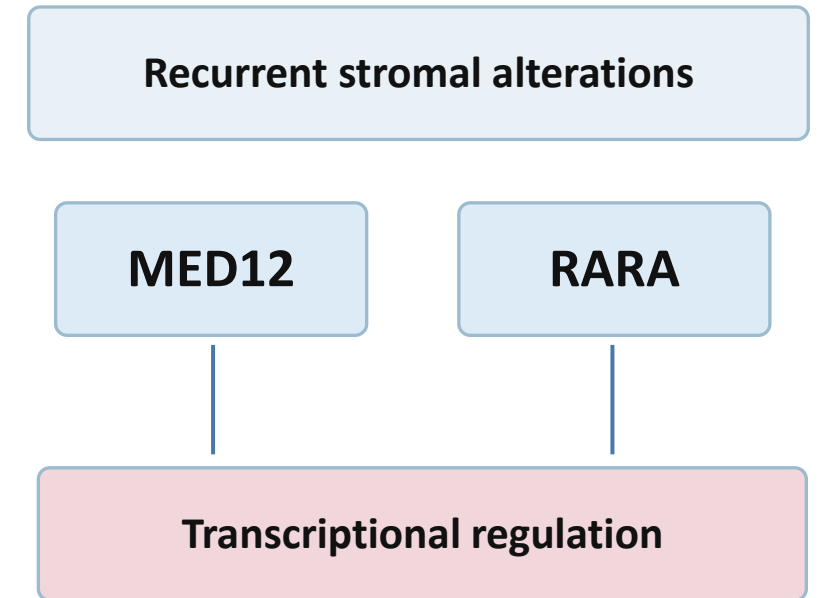
- Large fibroadenomas can occasionally show a phyllodes-like growth pattern.
- Phyllodes tumors themselves include benign, borderline, and malignant categories.
- Grade depends on stromal histologic characteristics rather than leaf shape alone.



Epithelial-lined stromal projections

Molecular overlap supports related pathogenesis

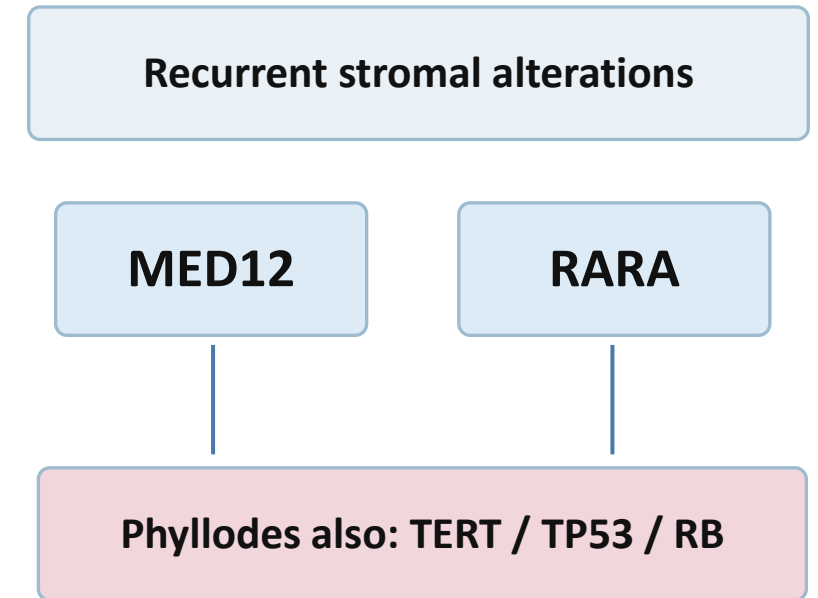
- Most phyllodes tumors harbor MED12 and RARA alterations.
- These are also common in fibroadenomas.
- The shared profile is consistent with related intralobular stromal biology.



Mechanism remains incompletely explained

Additional gene mutations in phyllodes tumor

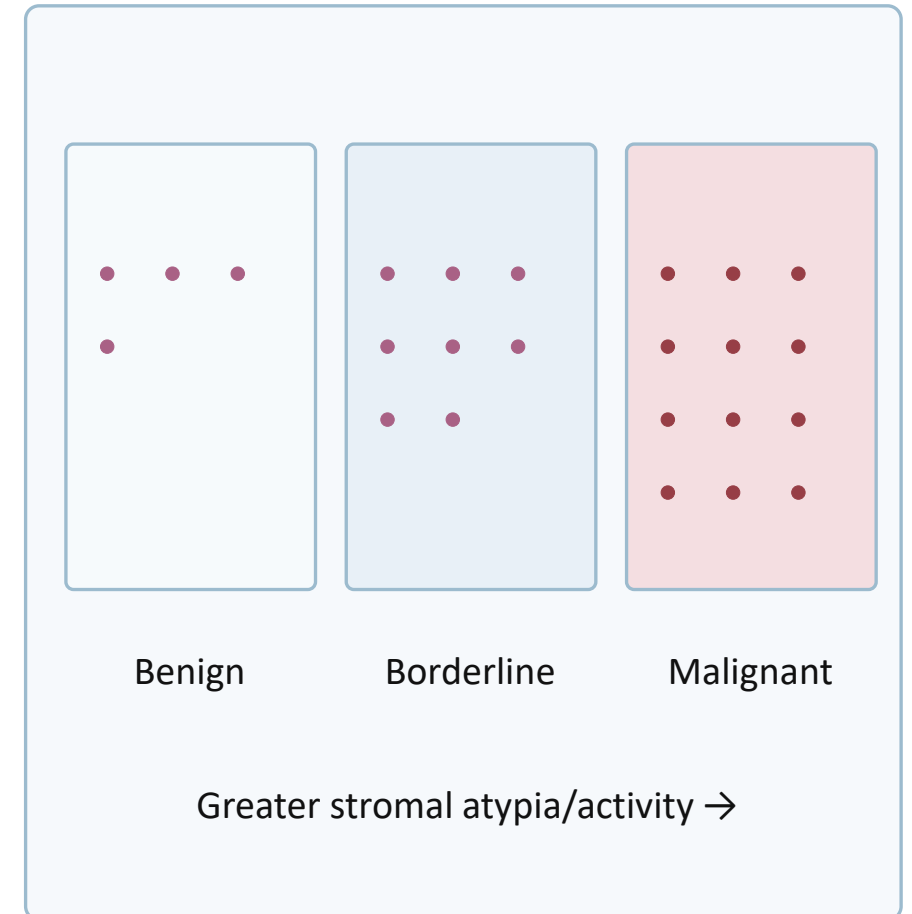
- Phyllodes tumors are more likely to harbor additional mutations.
- Examples reported by Robbins include TERT, TP53, and RB.
- The source presents these as comparative associations, not definitive grade-specific tests.



Associations; Not diagnostic cutoffs

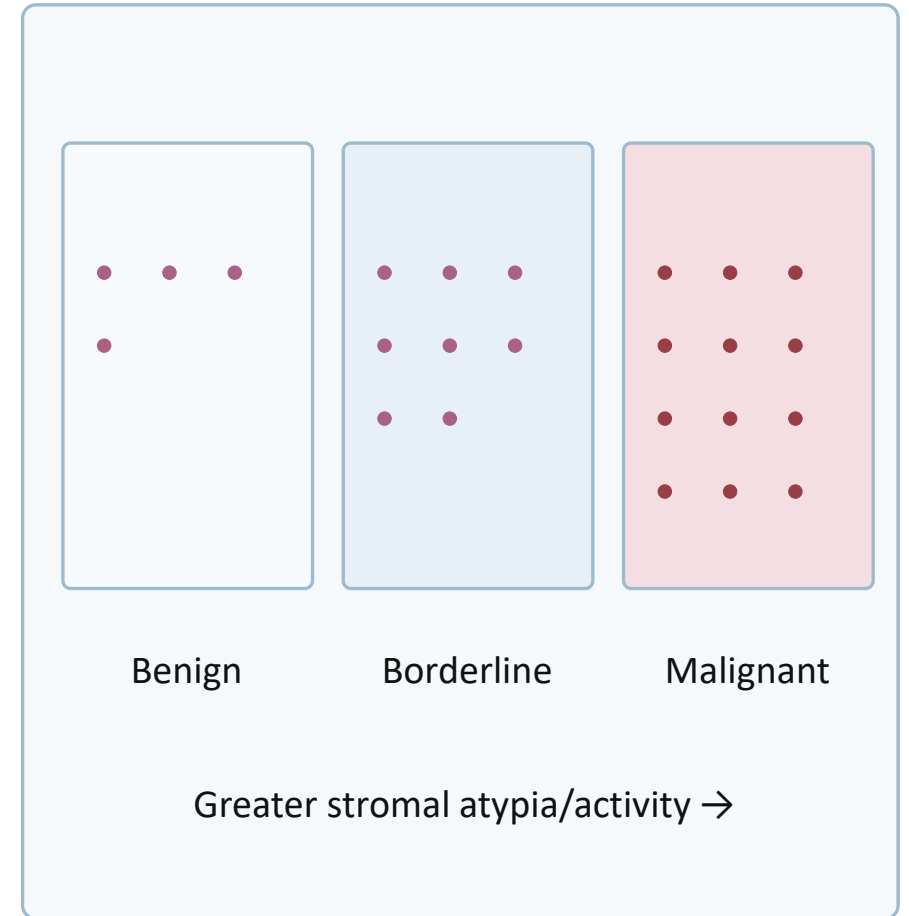
Phyllodes is graded in three categories

- Benign, borderline, and malignant are the recognized categories.
- Histologic evaluation focuses on stromal features.
- The grades describe different likelihoods of recurrence and metastatic behavior.



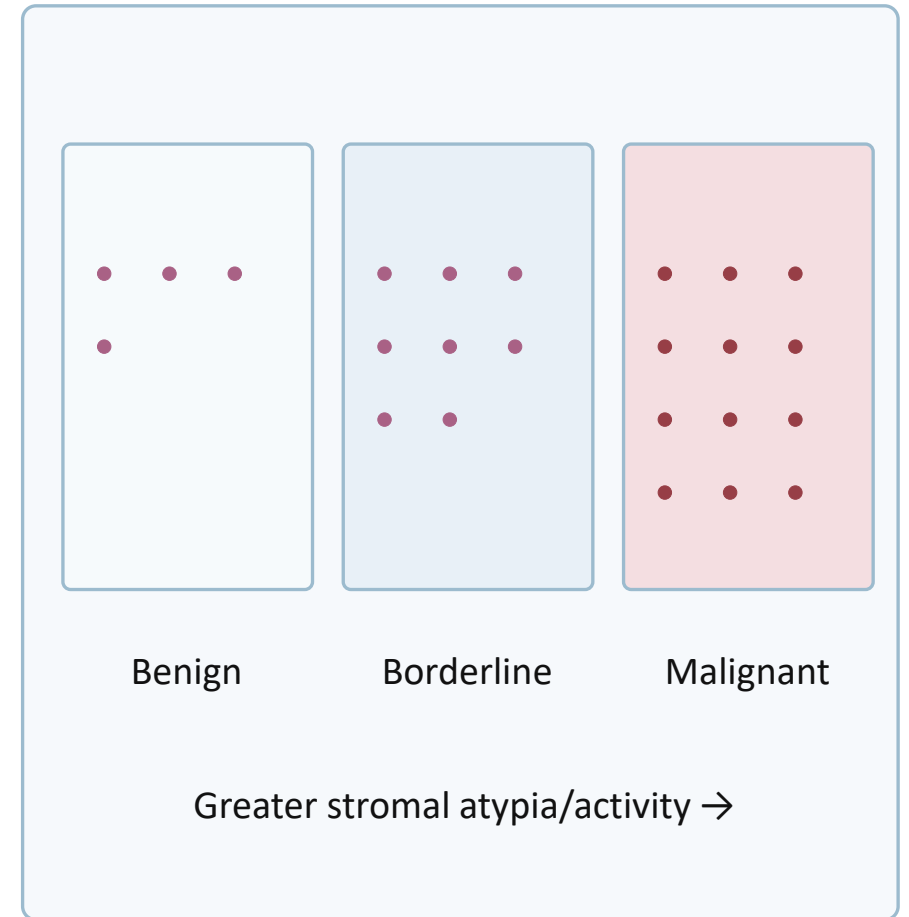
Benign phyllodes: Similarities to fibroadenoma

- Benign phyllodes resembles fibroadenoma.
- Relative stromal cellularity and mitotic activity are increased.
- Cytologically benign tumors can nonetheless recur locally.



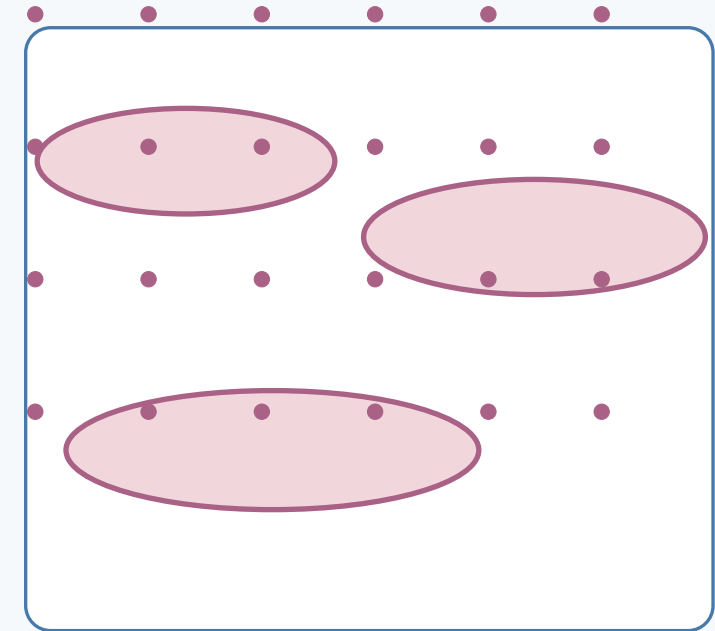
Borderline phyllodes: An intermediate phenotype

- Borderline tumors show more stromal atypia.
- Increased stromal cellularity and mitotic activity distinguish them from benign lesions.
- This category reflects a histologic assessment—not inevitable progression to malignancy.



Malignant phyllodes: Infiltrative stroma

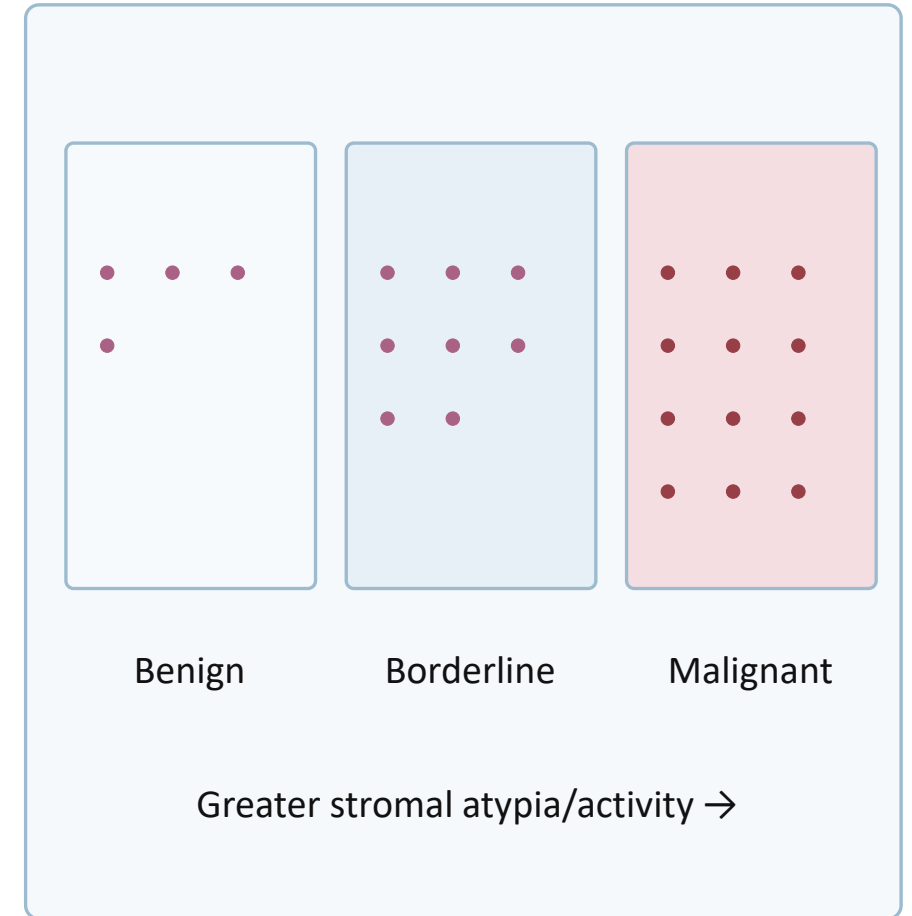
- Malignant tumors may be widely infiltrative.
- Marked stromal overgrowth may leave few residual epithelial elements.
- In advanced examples, separating the lesion from sarcoma can be difficult.



Epithelial-lined stromal projections

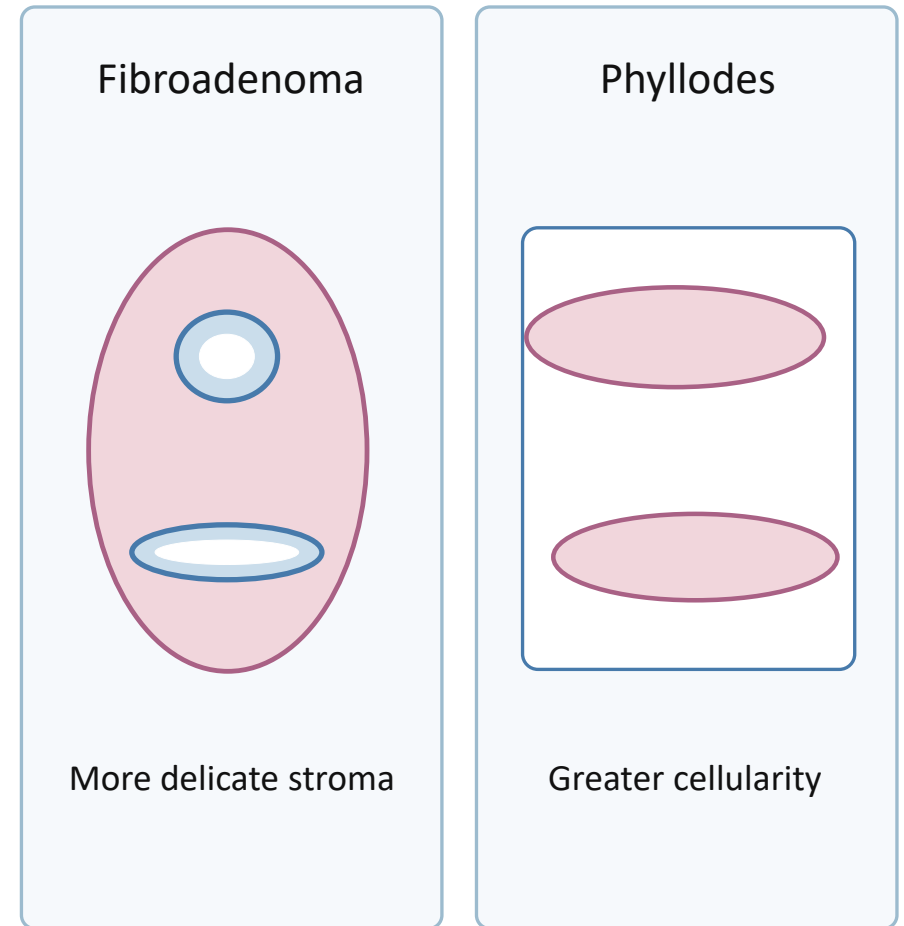
Stromal assessment determines category

- The features named include cellularity, atypia, mitotic activity, and infiltration.
- Stromal overgrowth is especially relevant in malignant tumors.
- The supplied excerpt does not specify numerical mitotic cutoffs or comprehensive modern grading criteria.



A practical fibroadenoma–phyllodes distinction

- Fibroadenoma: Delicate stroma; Usually lower cellularity.
- Phyllodes: Greater stromal cellularity and proliferative activity.
- Leaf-like architecture alone cannot resolve the differential.



Benign grade does not guarantee no recurrence

- Up to 75% of phyllodes tumors have benign cytologic features.
- These can occasionally recur locally.
- The source reports no metastases in the benign group.

Stromal phenotype / grade



Excision margin status



Local recurrence assessment

Margin predicts recurrence after excision

Margins influence local recurrence

- Borderline and malignant tumors show higher recurrence rates.
- Margin status is the most important predictor of local recurrence after excision.
- This connects the infiltrative stromal interface to surgical-pathology assessment.

Stromal phenotype / grade



Excision margin status

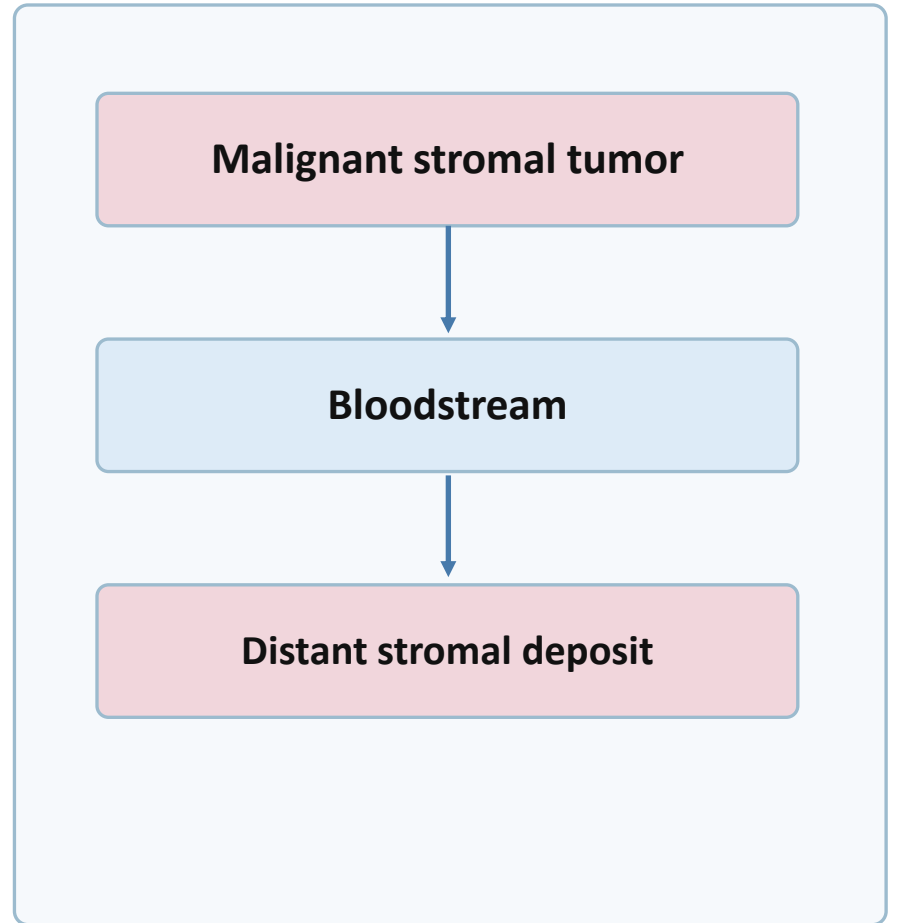


Local recurrence assessment

Margin predicts recurrence after excision

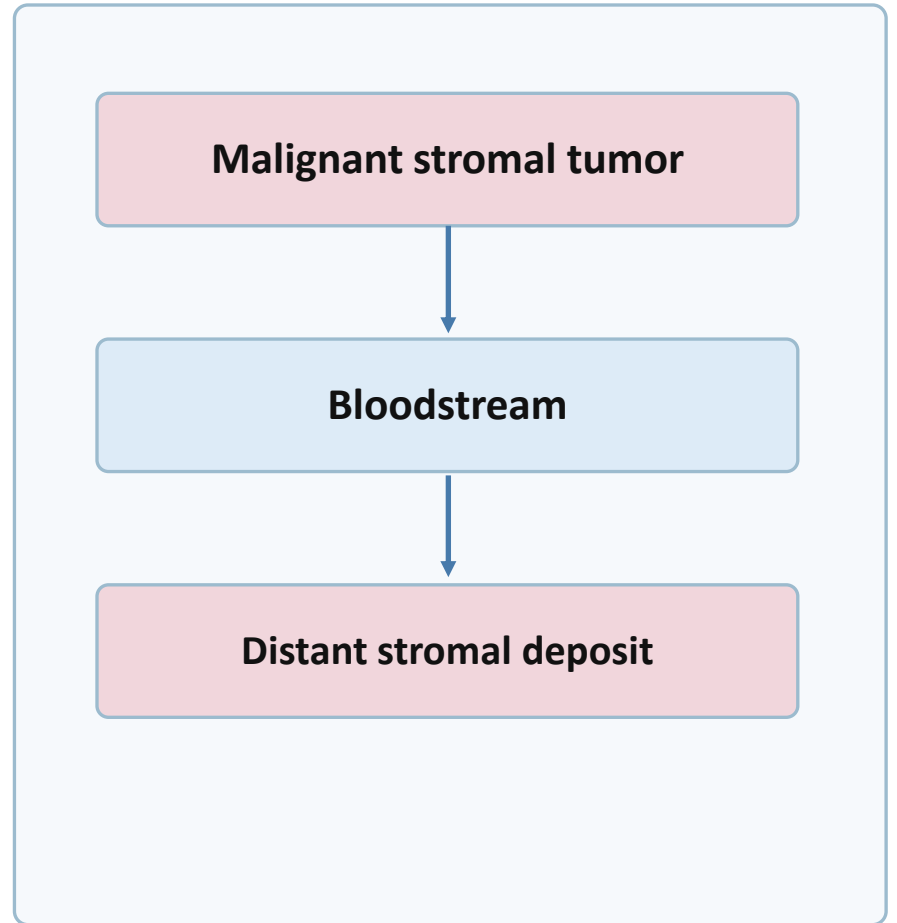
Lymphatic spread is uncommon

- Lymphatic spread is rare irrespective of grade.
- Axillary lymph node dissection is contraindicated.
- Nodal behavior differs from typical epithelial breast carcinoma.



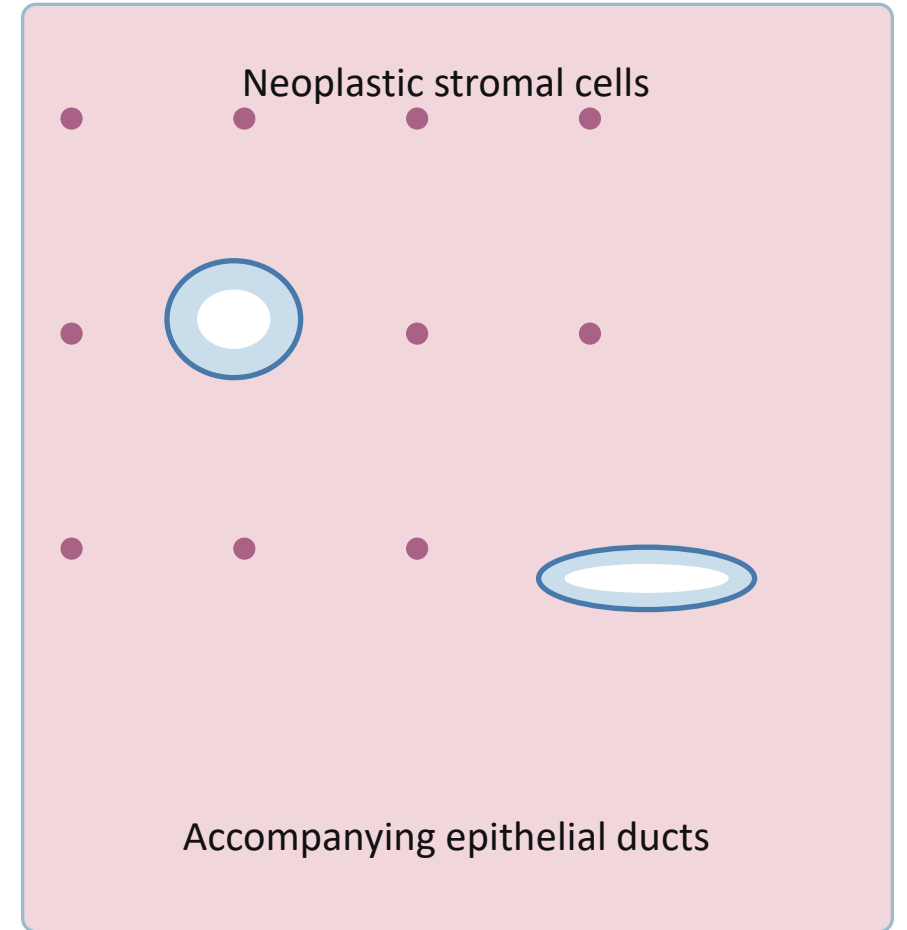
Malignant phyllodes can spread hematogenously

- Malignant phyllodes tumors are uncommon.
- About one-third of malignant lesions give rise to distant hematogenous metastases.
- The bloodstream—not the axillary lymphatic route—is the key metastatic pathway described.



Metastases contain only neoplastic stroma

- Epithelial elements accompany the primary biphasic tumor.
- Distant metastatic deposits contain the stromal neoplastic component alone.
- This observation reinforces which component is biologically malignant.



Integrating grade, margins, and spread

- Grade describes stromal histologic aggressiveness.
- Margin status predicts local recurrence after excision.
- Distant metastasis is associated with the uncommon malignant lesions.

Three clinical domains

Grade: Stromal aggressiveness

Margin: Local recurrence

Hematogenous metastasis

Nodal spread: Rare

Phyllodes tumor: Case reasoning

- Consider a large, fast-growing fibroepithelial mass in an older patient.
- Search histology for leaf-like stromal fronds and stromal hypercellularity.
- Then assess atypia, mitotic activity, infiltration, and stromal overgrowth.

Large mass in older patient



Stromal fronds + cellularity



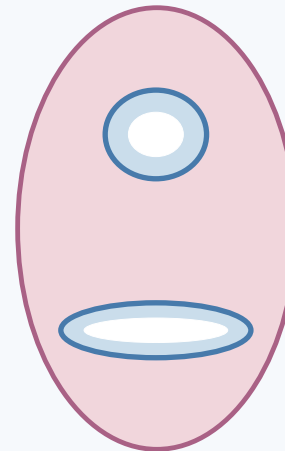
Phyllodes: Assess grade

Morphologic diagnosis

Fibroadenoma versus phyllodes: Synthesis

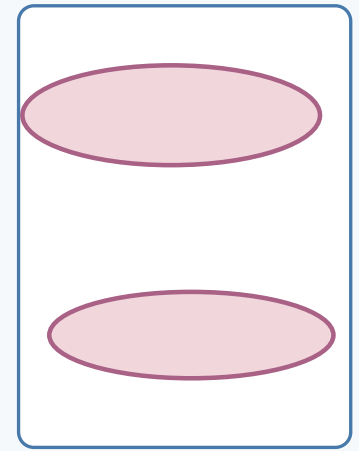
- Both are neoplastic-stromal, biphasic lesions of intralobular origin.
- Morphologic differences are most informative in the stromal compartment.
- Phyllodes grading predicts clinically important variation in behavior.

Fibroadenoma



More delicate stroma

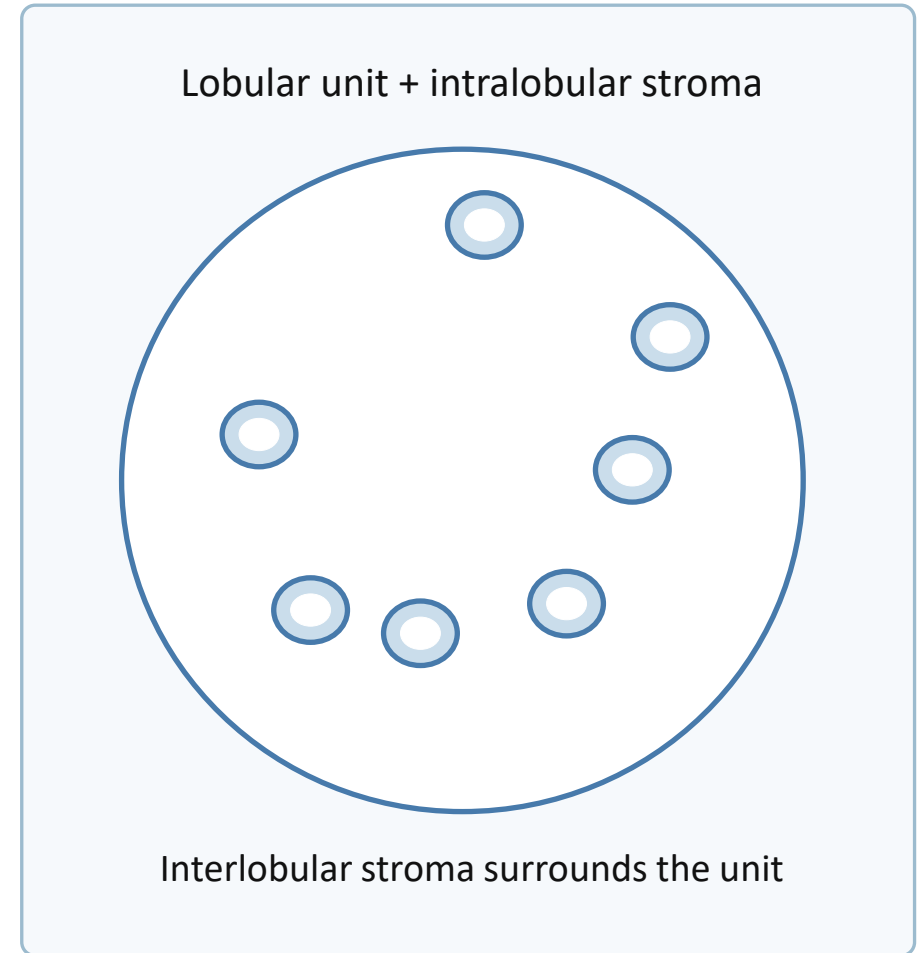
Phyllodes



Greater cellularity

An origin-based diagnostic summary

- Intralobular stromal tumors preserve epithelial association at the primary site.
- Interlobular tumors lack an accompanying epithelial component.
- Within intralobular tumors, stromal cytology and growth behavior separate entities.



Case 1: A young woman with a breast nodule

- A 25-year-old has a discrete, well-circumscribed breast mass.
- Histology shows bland myxoid stroma and compressed epithelial-lined clefts.
- Which biphasic stromal lesion is most consistent with these findings?

Clinical presentation



Architectural examination

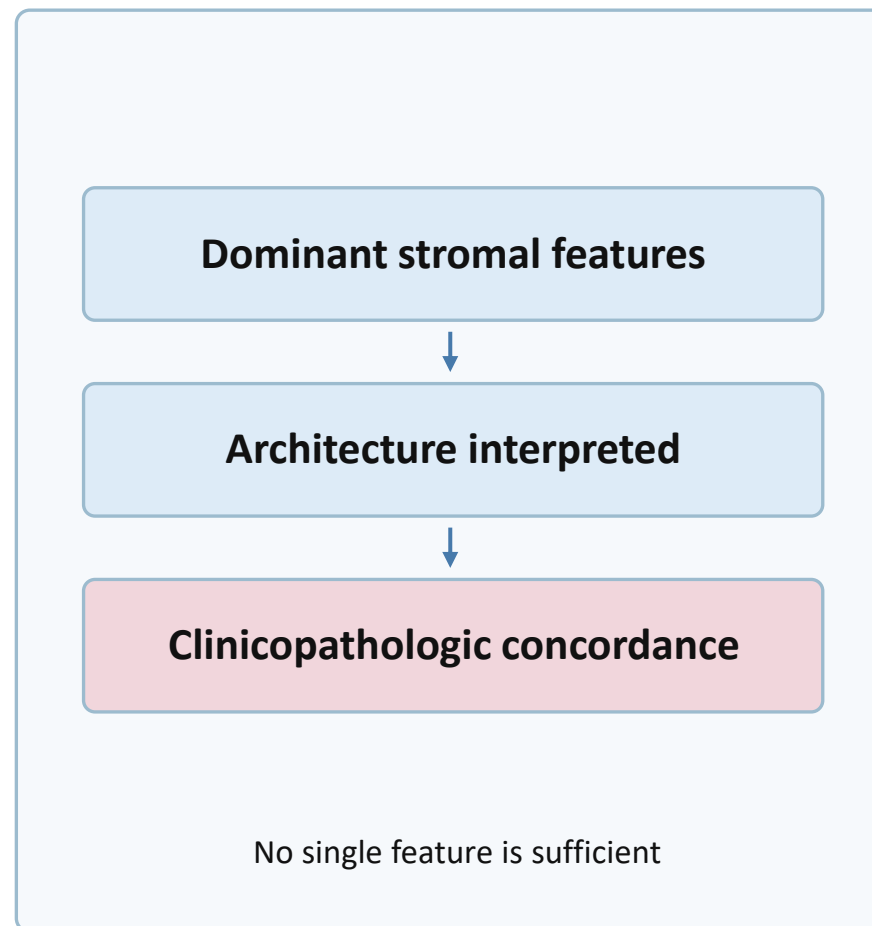


Stromal assessment

Use all levels of evidence

Case 1: Interpret the stromal architecture

- The pattern is consistent with fibroadenoma.
- Compressed, cleft-like ducts represent an intracanalicular pattern.
- Age, circumscription, and delicate stroma support the interpretation.



Case 2: An older patient with a large mass

- A woman in her sixth decade presents with a large breast mass.
- Sections show epithelial-covered leaf-like projections and cellular stroma.
- Which tumor family and histologic features should be assessed next?

Clinical presentation



Architectural examination

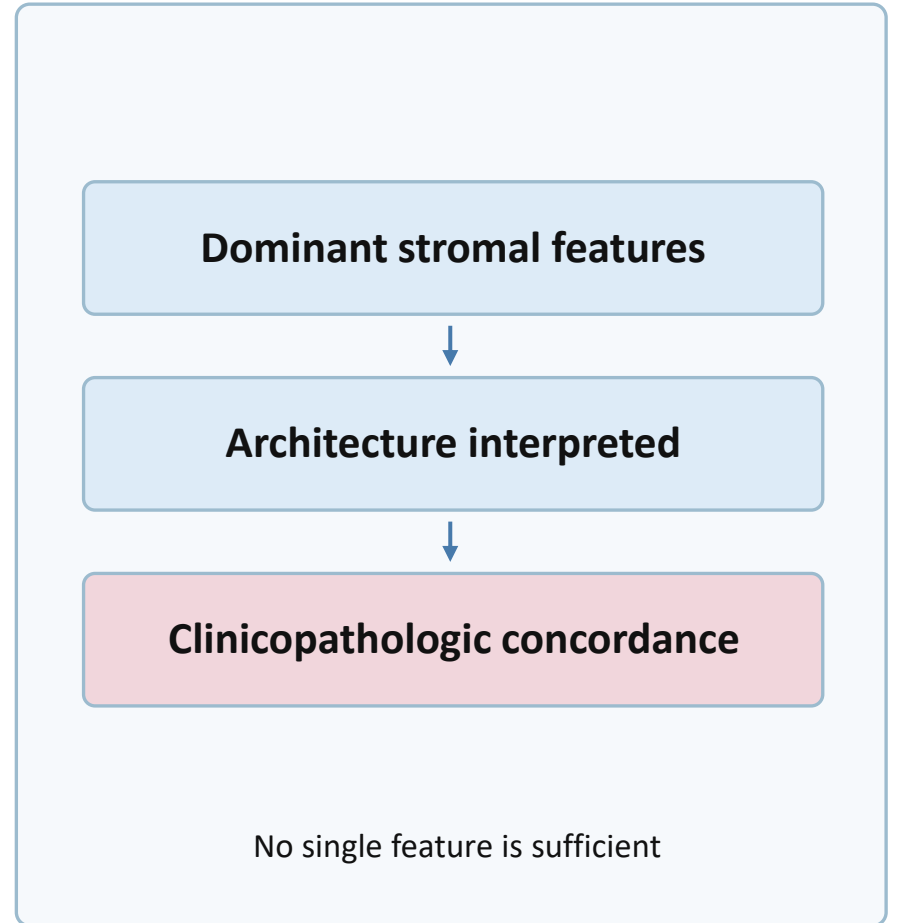


Stromal assessment

Use all levels of evidence

Case 2: Grade the stromal component

- The findings raise phyllodes tumor as the fibroepithelial lesion.
- Assess cellularity, atypia, mitotic activity, infiltration, and stromal overgrowth.
- Do not infer malignancy from leaf-like architecture or size alone.



Essential pathology distinctions

- Fibroadenoma is the dominant benign intralobular stromal tumor.
- Phyllodes tumor shares stromal origin and recurrent alterations but varies in grade.
- Local recurrence, lymphatic spread, and hematogenous metastasis are distinct outcomes.

Core facts

Origin: Intralobular

Tumor component: Stromal

Grading: Phyllodes

Metastasis: Malignant stromal cells

Reference and source limitations

- Primary source: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 23, pp. 967–969.
- The supplied Markdown extraction interleaves adjacent columns; relevant continuations were reconciled by section context.
- Original textbook figure images/chapter PDF were not supplied; microscopy is taught with editable schematics, not synthetic specimens.

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Breast chapter: pp. 967–969

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