

Adenoid Cystic Carcinoma

Salivary gland pathology

Morphology · molecular profile · clinical behavior

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning outcomes

- Locate the tumor within the salivary neoplasm spectrum.
- Explain the molecular–morphologic association.
- Recognize cribriform, tubular, solid, and perineural patterns.
- Interpret recurrence, metastatic tropism, and long-term outcome.

Salivary neoplasms: A diverse diagnostic group

- Salivary glands give rise to more than 30 histologically distinct tumors.
- A small number of entities account for more than 90% of cases.
- Adenoid cystic carcinoma belongs among the malignant epithelial tumors.

Benign tumors

Pleomorphic adenoma · Warthin

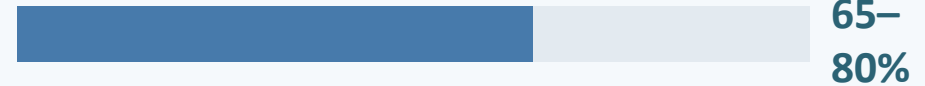
Malignant tumors

ACC · mucoepidermoid · acinic

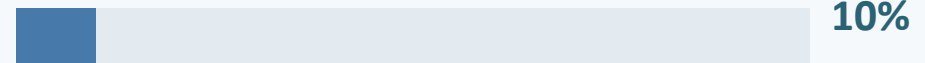
Most salivary tumors arise in the parotid gland

- About 65%–80% of salivary neoplasms involve the parotid.
- Approximately 10% arise in the submandibular gland.
- The remainder occur in minor salivary glands, including sublingual glands.

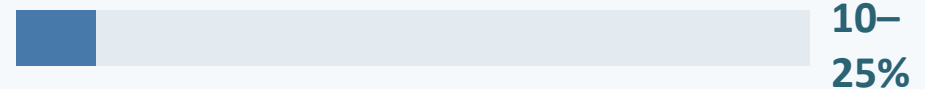
Parotid



Submandibular



Remainder

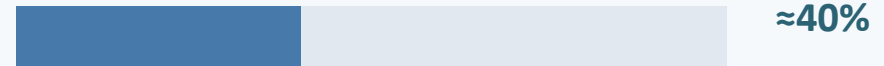


Ranges displayed at minimum reported fraction

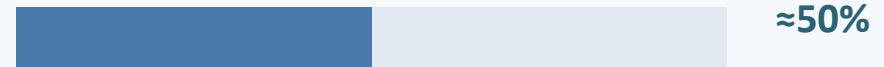
Risk of malignancy varies by salivary site

- Most parotid neoplasms are benign.
- Approximately 40% of submandibular and 50% of minor-gland tumors are malignant.
- About 70%–90% of sublingual neoplasms are malignant.

Submandibular



Minor glands



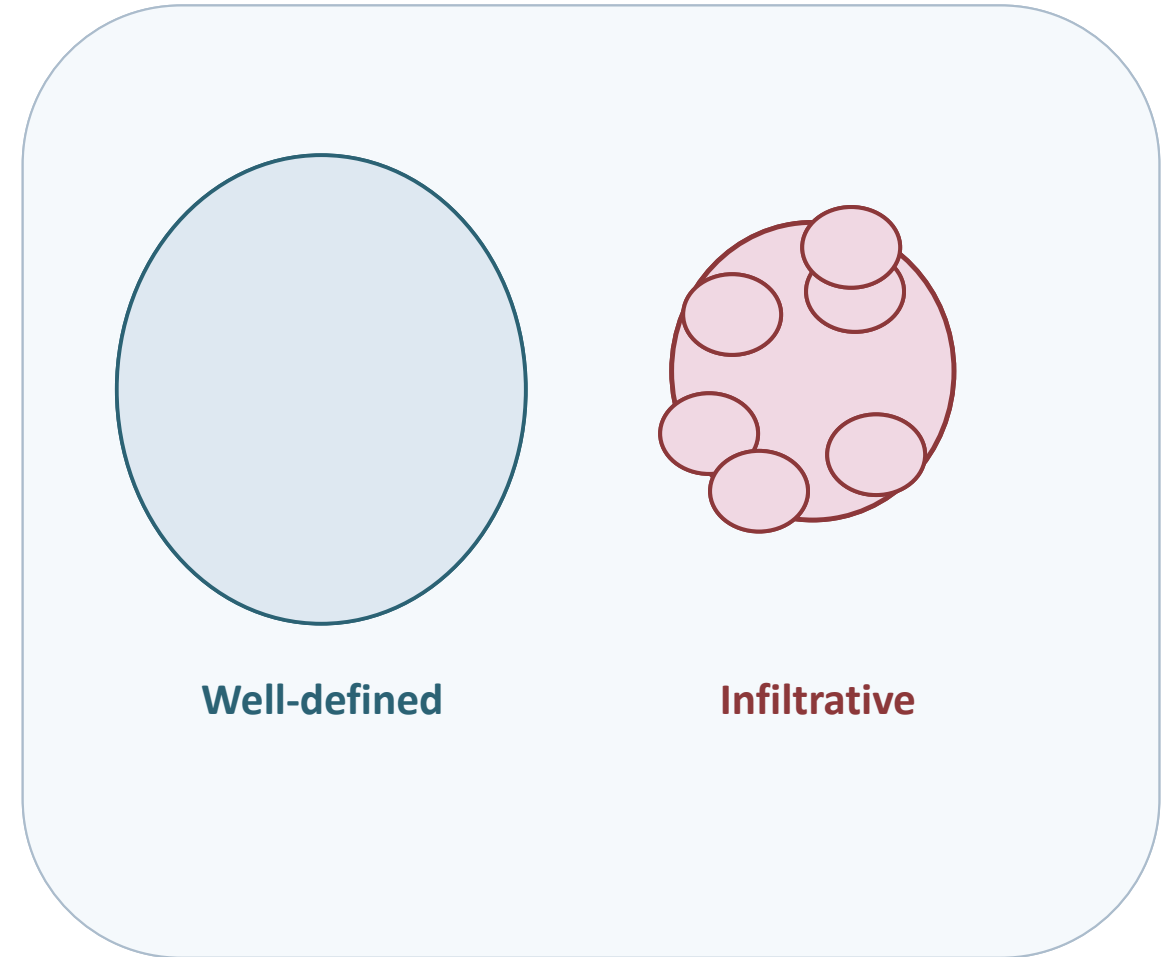
Sublingual



Sublingual bar uses 70% lower bound

The definition is a behavior–morphology combination

- Adenoid cystic carcinoma is a malignant epithelial neoplasm of salivary-type glands.
- The source emphasizes characteristic architecture, infiltration, and prolonged clinical risk.
- Indolent growth does not imply biologic innocence.



Schematic — comparison of border geometry

Minor salivary glands are a major ACC site

- Around one half of ACCs arise in minor salivary glands.
- Palatine glands are particularly affected.
- This contrasts with the parotid predominance of salivary tumors overall.

Minor glands

≈50% of ACC; Palate prominent

Parotid

Major-gland origin

Submandibular

Major-gland origin

The major salivary-gland sites

- Among major glands, the parotid and submandibular glands are most often involved.
- Site should be recorded because the source identifies prognostic differences.
- The gland of origin cannot be inferred from cribriform morphology alone.

Minor glands

≈50% of ACC; Palate prominent

Parotid

Major-gland origin

Submandibular

Major-gland origin

Adenoid cystic carcinoma is not confined to saliva

- The same tumor designation is used in the nose and paranasal sinuses.
- Upper airways and lung are additional sites.
- Breast and other sites may also harbor this tumor type.

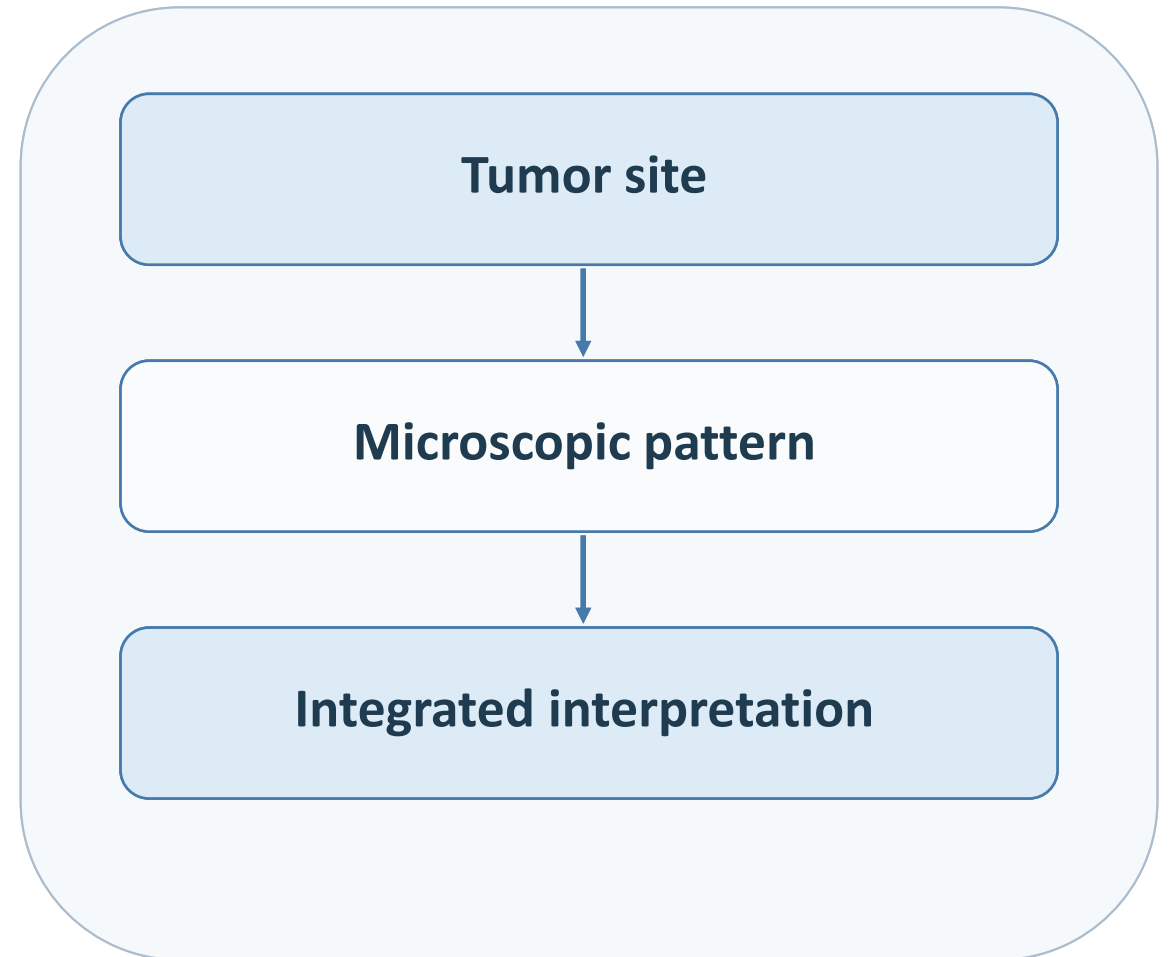
Minor glands / major glands

Nose · sinuses · upper airways

Lung · breast · other sites

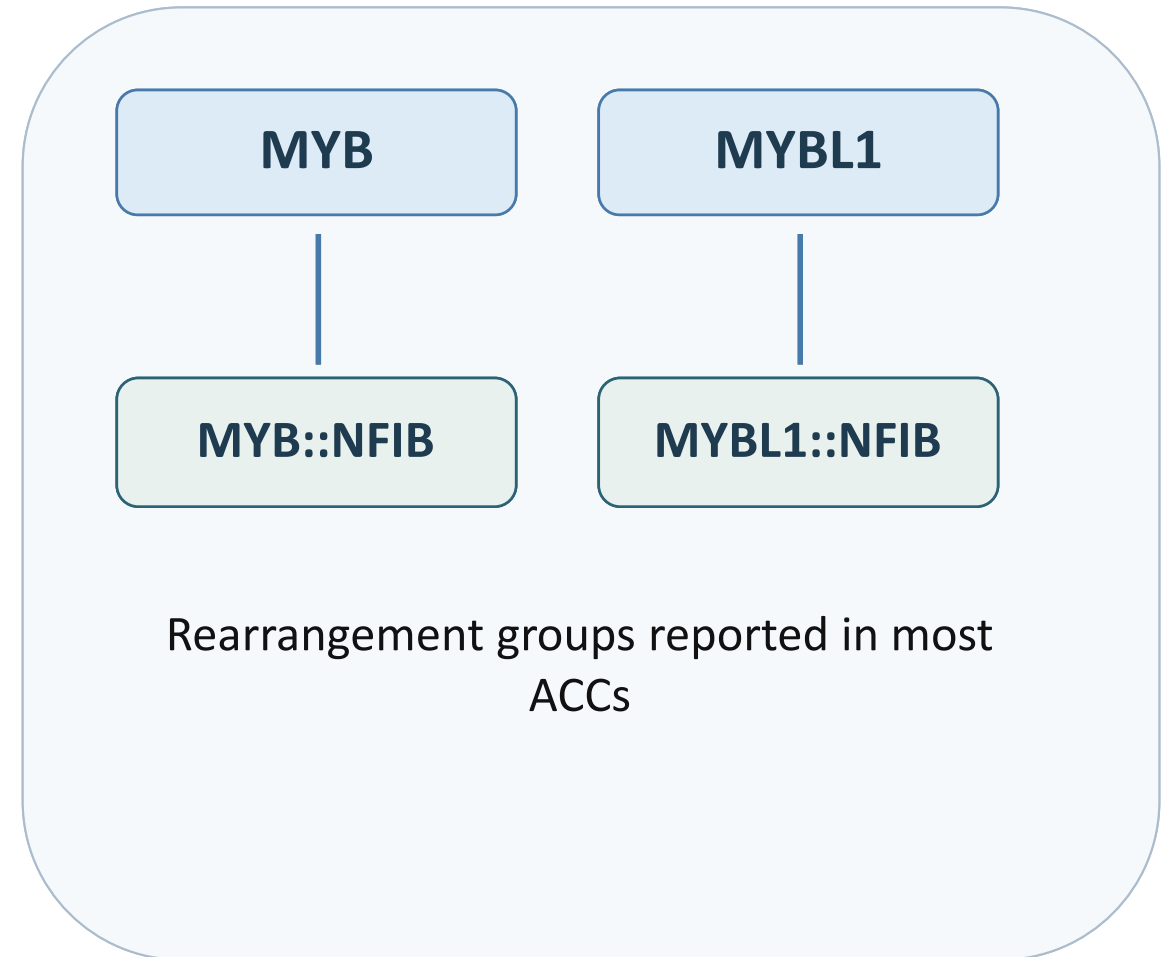
Anatomic site and tumor identity are separate

- The presenting compartment identifies the primary site.
- Histomorphology determines whether ACC is a plausible tumor type.
- Site and morphology must be integrated rather than used as substitutes for each other.



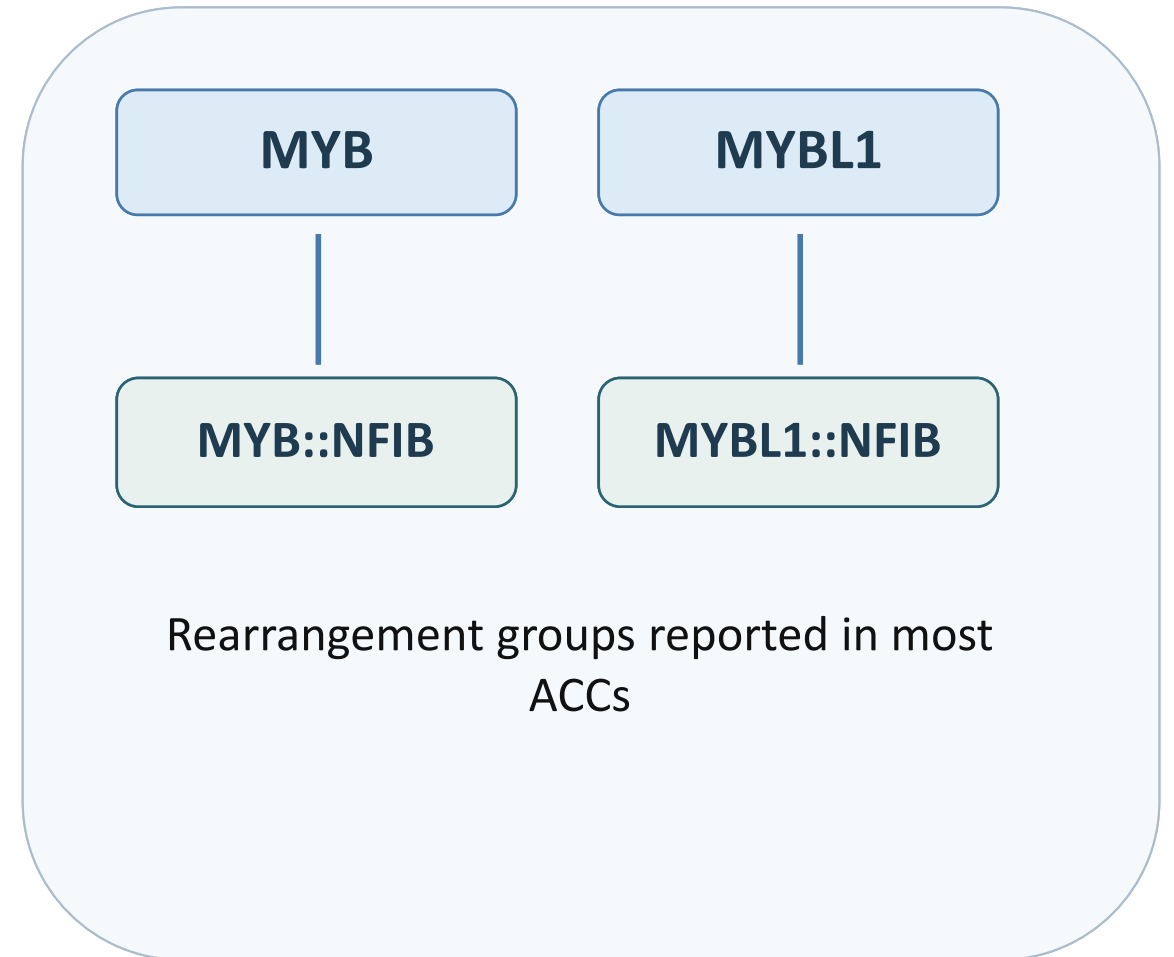
Two recurrent gene-rearrangement groups

- MYB::NFIB rearrangements are found in ACC.
- MYBL1::NFIB rearrangements are an alternative recurrent group.
- Together these rearrangements occur in the majority of tumors.



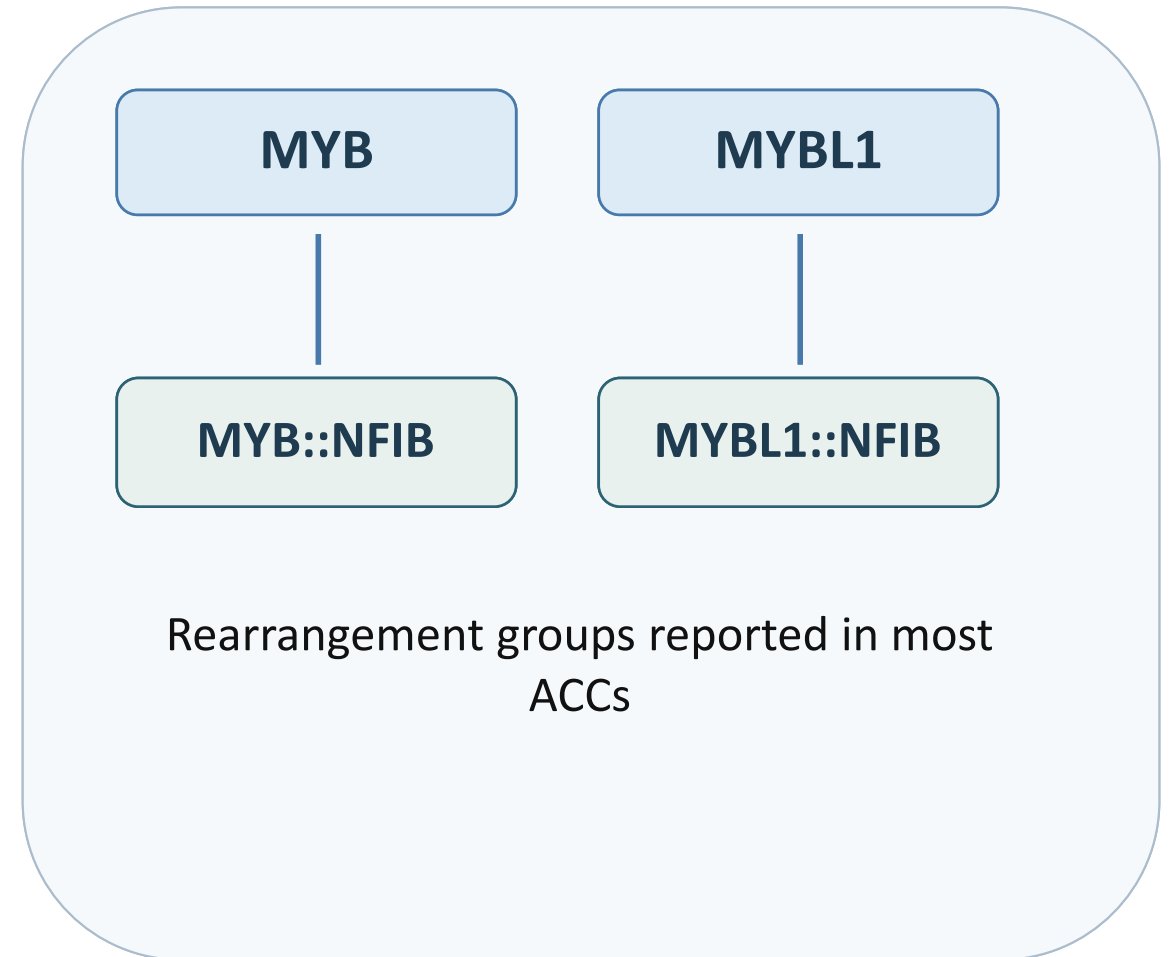
How to read a fusion designation

- “MYB::NFIB” denotes a rearrangement involving the named genes.
- “MYBL1::NFIB” denotes a different upstream gene with the same listed partner.
- The text establishes frequency, not a complete signaling mechanism.



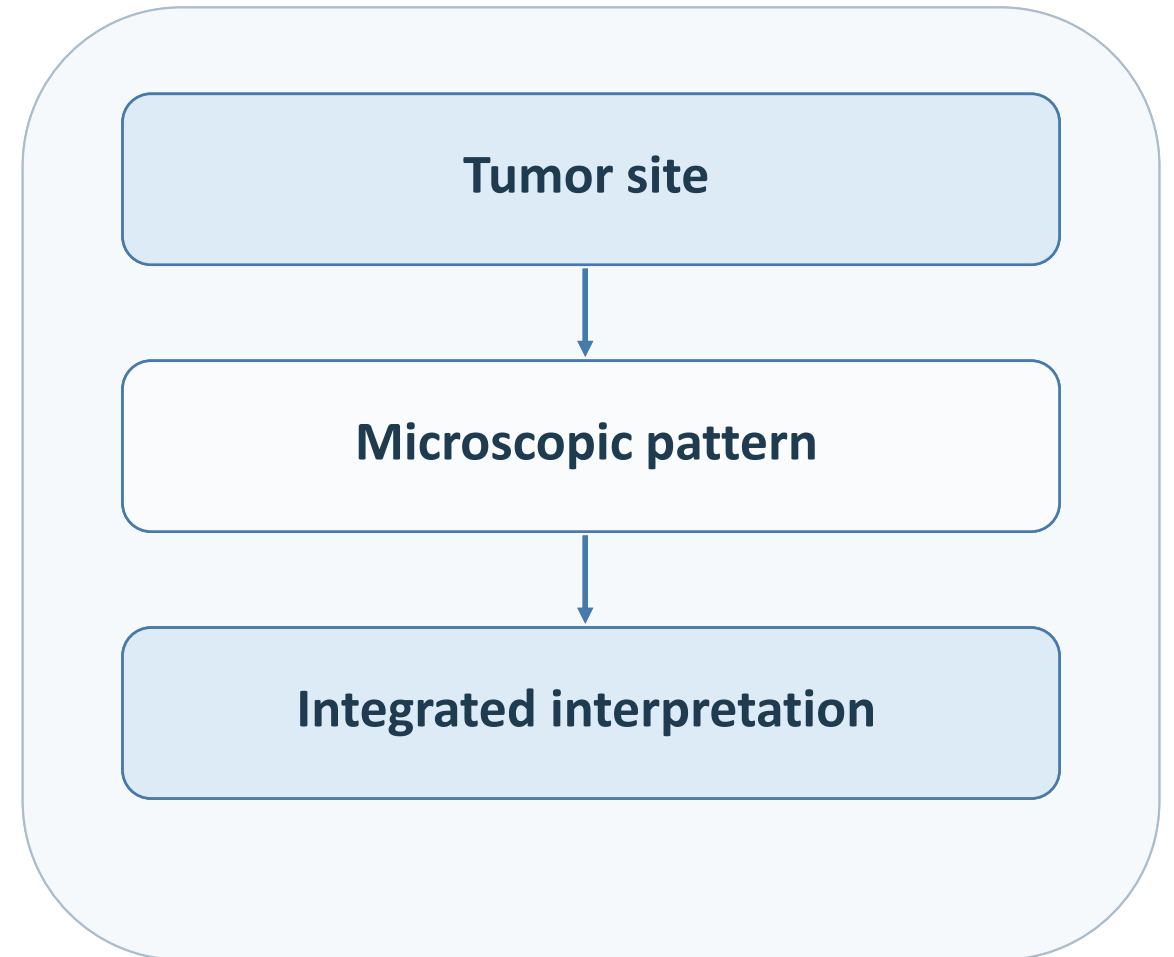
MYB and MYBL1 are not interchangeable spellings

- MYB and MYBL1 are distinct gene names.
- Both appear in rearrangements partnered with NFIB.
- A report should retain the exact gene and double-colon notation.



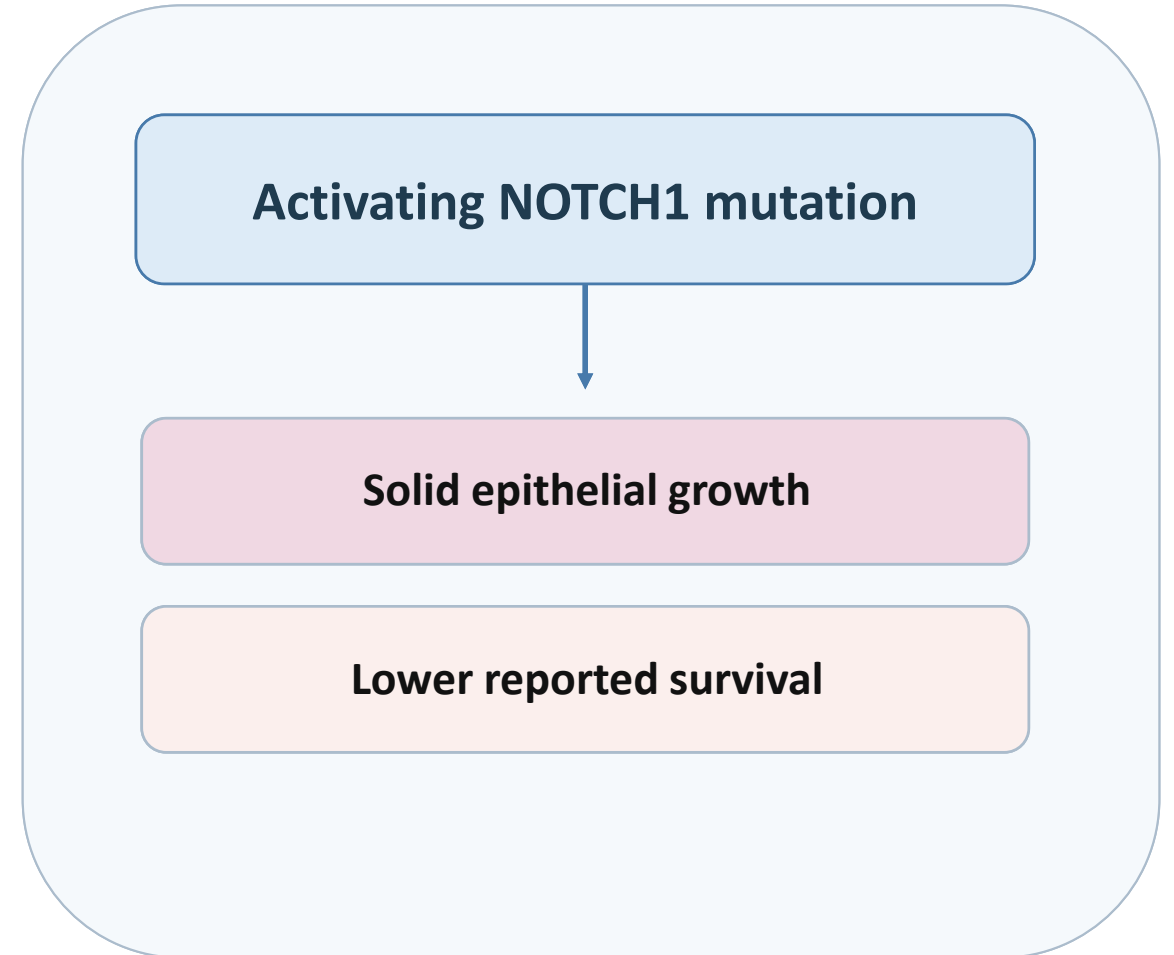
A rearrangement does not specify one microscopic pattern

- ACC with common rearrangements.
- The source separately describes NOTCH1-associated tumor morphology.
- Do not equate the presence of an MYB-family rearrangement with an automatic histologic subtype.



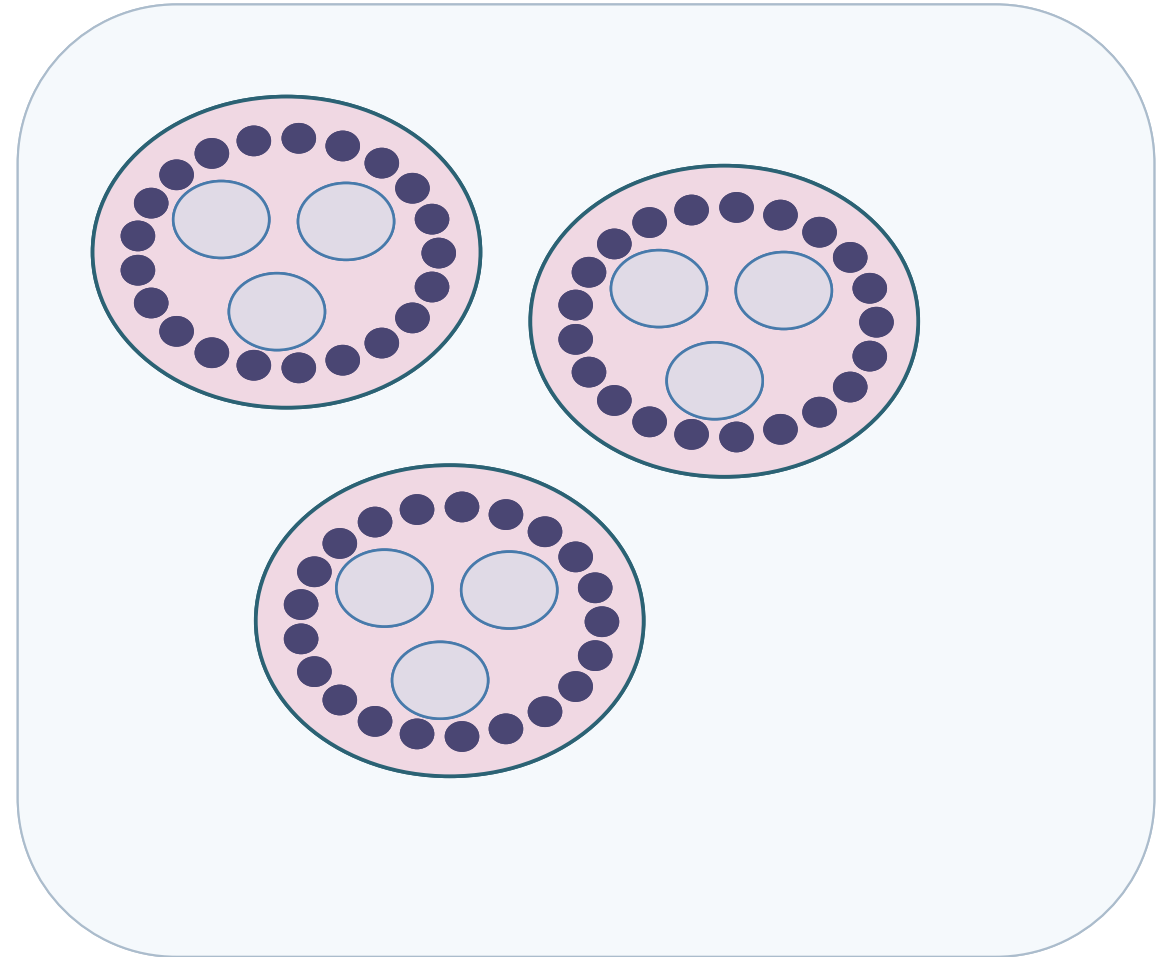
NOTCH1 mutation identifies a clinically relevant subset

- Activating NOTCH1 mutations occur in a subset of ACC.
- This subset has a distinctive histologic phenotype.
- The source also associates it with different metastatic behavior and poorer survival.



NOTCH1 wild type: A mixed cellular population

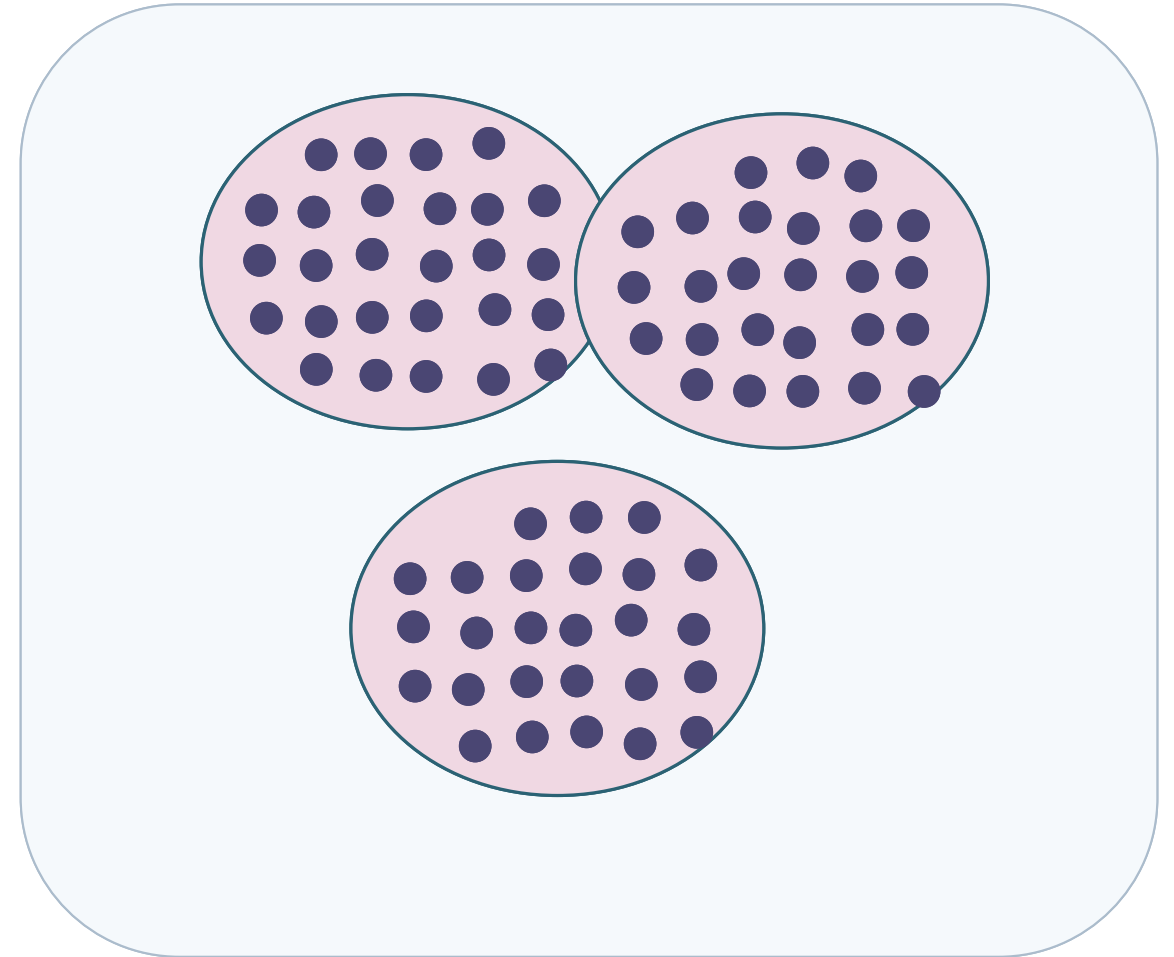
- The described wild-type group contains basal myoepithelial and epithelial cells.
- Cribriform architecture is usual in this group.
- The characteristic spaces may contain hyaline basement-membrane-like material.



Original explanatory schematic — not H&E

NOTCH1 mutant: Epithelial-predominant growth

- Mutant tumors are described as predominantly epithelial.
- They characteristically form solid nests or sheets.
- Their outcome is poorer than the wild-type group in the source.



Schematic — epithelial-predominant solid nests

Molecular and morphological phenotype should be read together

- Wild type: Mixed basal myoepithelial and epithelial composition; Often cribriform.
- Mutant: Predominantly epithelial; Often solid.
- These are associations, not a claim that appearance alone establishes genotype.

NOTCH1 wild-type

Cribriform · mixed cell populations

NOTCH1 mutant

Solid · epithelial predominant

Genotype is not determinable from a cartoon

- Cribriform growth supports the classic morphologic pattern.
- Solid growth raises the source-described mutant phenotype.
- Definitive molecular status requires actual molecular testing; Morphology is not a surrogate result.

NOTCH1 wild-type

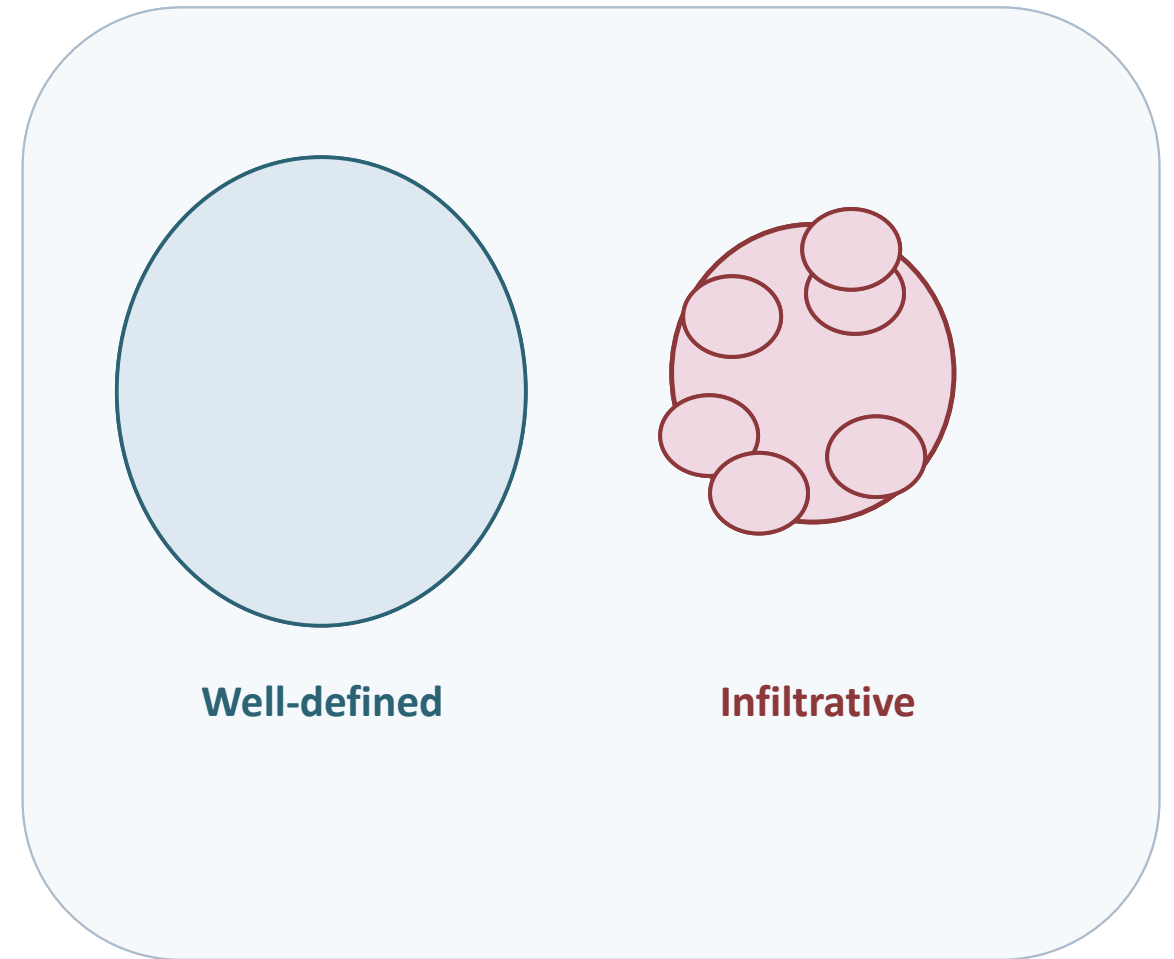
Cribriform · mixed cell populations

NOTCH1 mutant

Solid · epithelial predominant

Grossly, the tumor is poorly circumscribed

- ACC typically forms an infiltrative gray-pink lesion.
- The border is not described as a well-defined capsule.
- Macroscopic size alone does not capture microscopic spread.



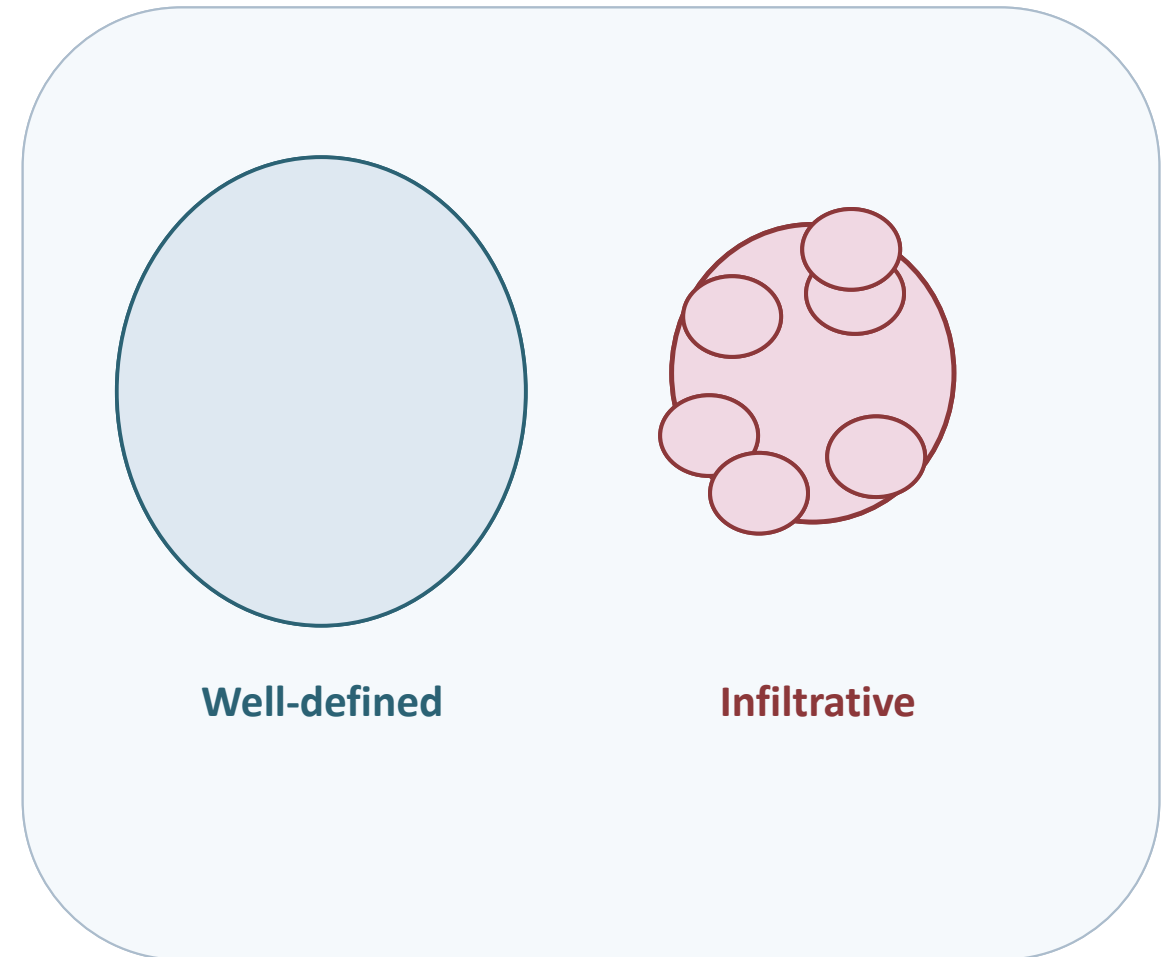
Well-defined

Infiltrative

Schematic — comparison of border geometry

Infiltration is different from simple expansion

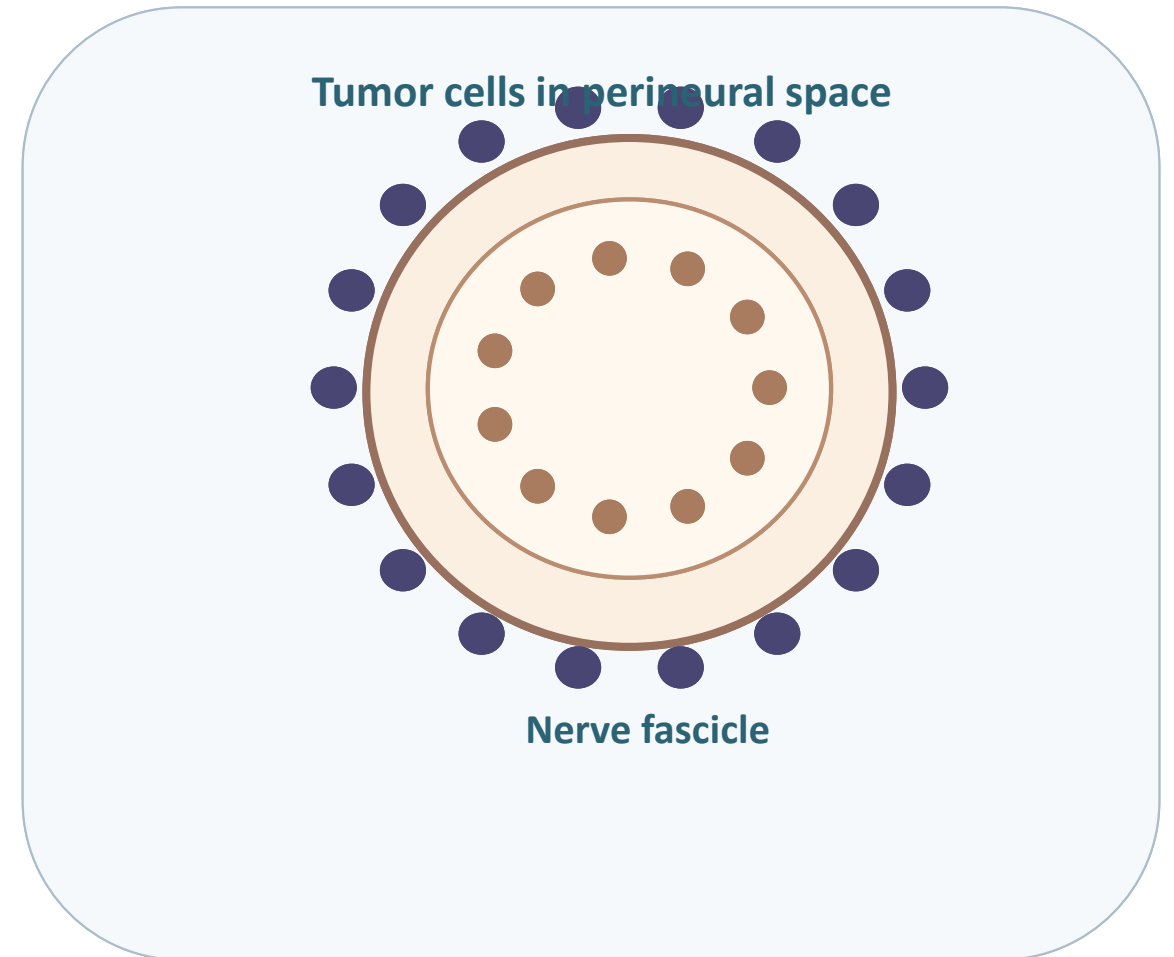
- An infiltrative edge extends irregularly into adjacent tissue.
- A well-demarcated appearance is not synonymous with biological benignity.
- True microscopic extent may exceed the visually obvious mass.



Schematic — comparison of border geometry

Gross borders and neural spread can disagree

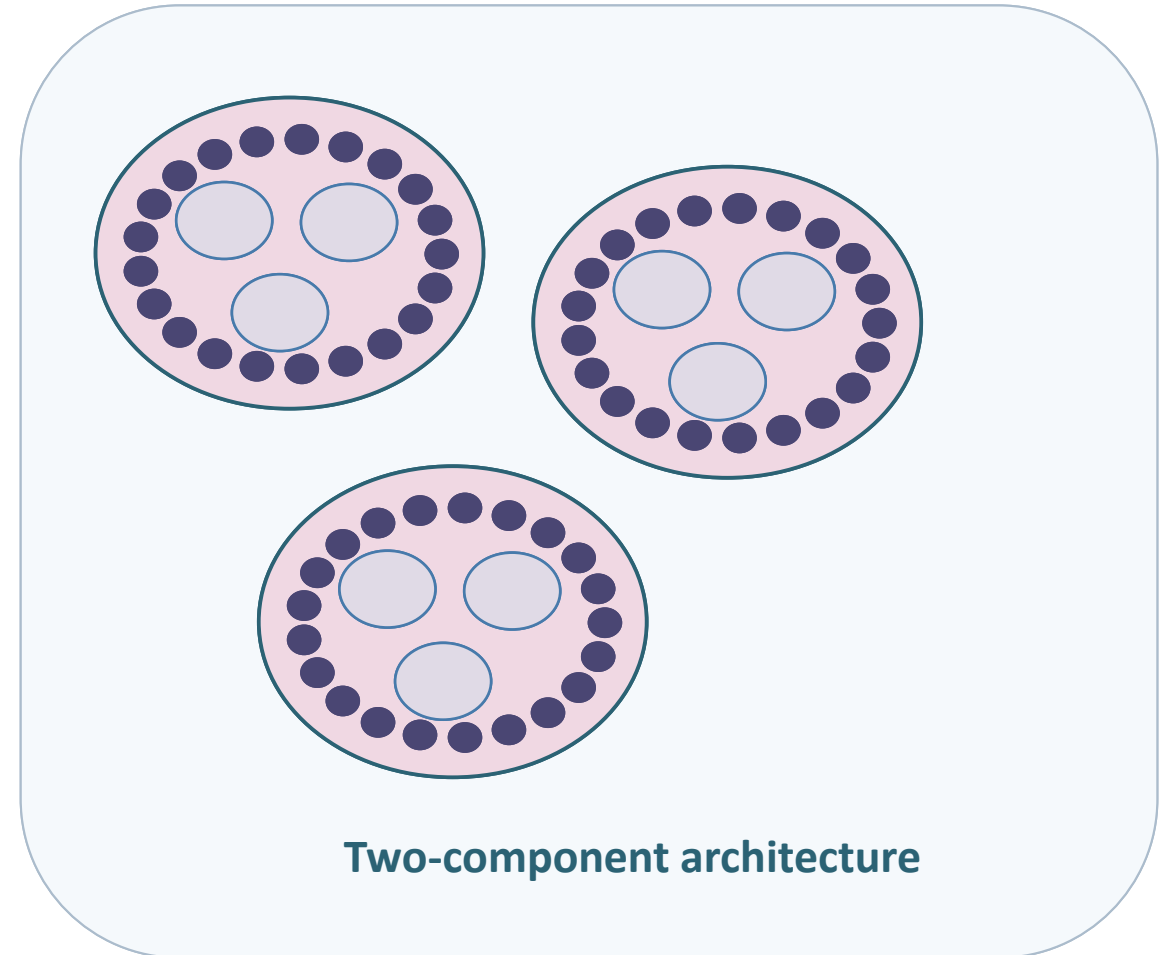
- The gross tumor may appear localized despite infiltrative behavior.
- ACC has a marked tendency to grow in perineural spaces.
- Margins must therefore be considered as a microscopic issue, not only a gross one.



Schematic — not a histologic specimen

Two cell populations characterize the classic pattern

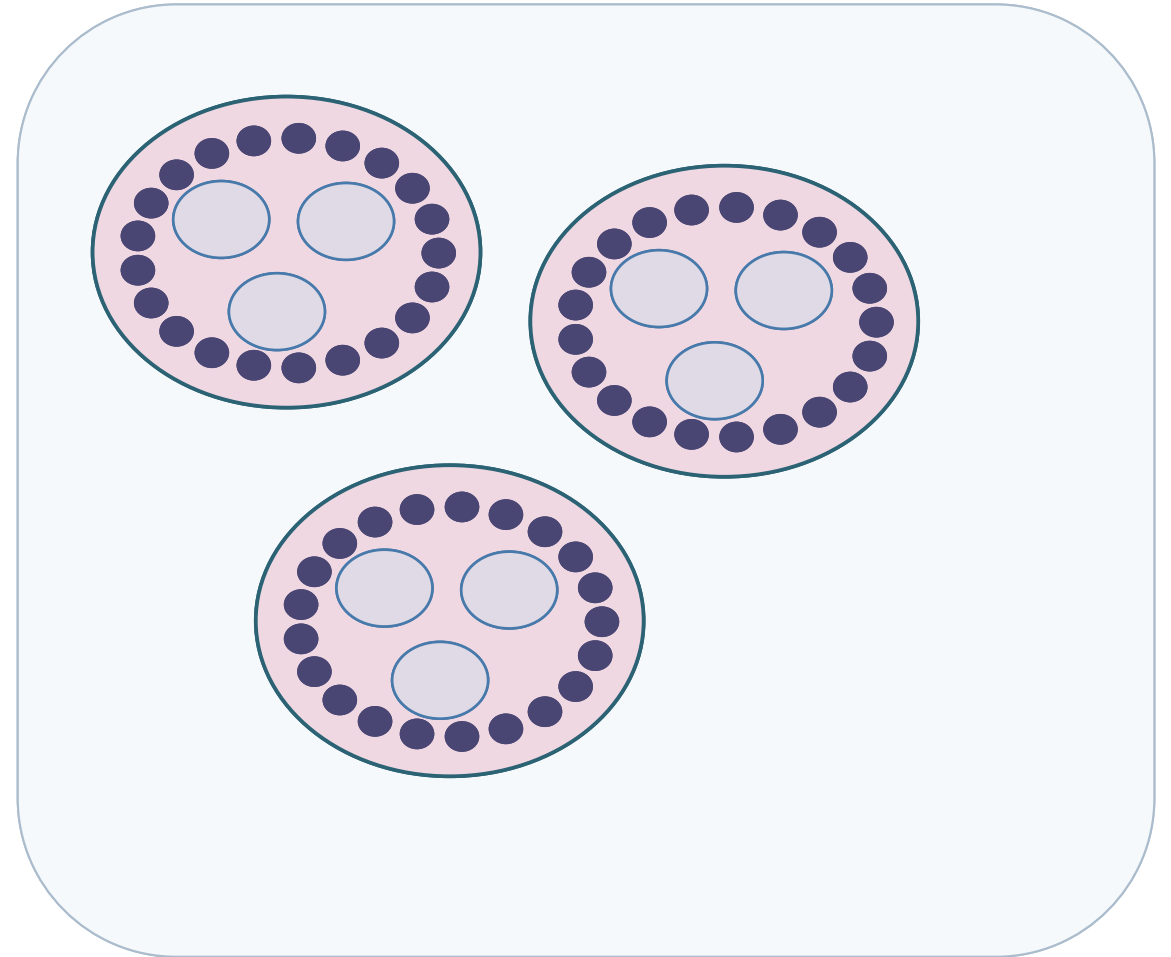
- Basal myoepithelial cells are one component of NOTCH1 wild-type tumors.
- Epithelial cells are the second component.
- The spatial organization of these cells contributes to the cribriform appearance.



Original explanatory schematic — not H&E

Cribriform means a sieve-like arrangement

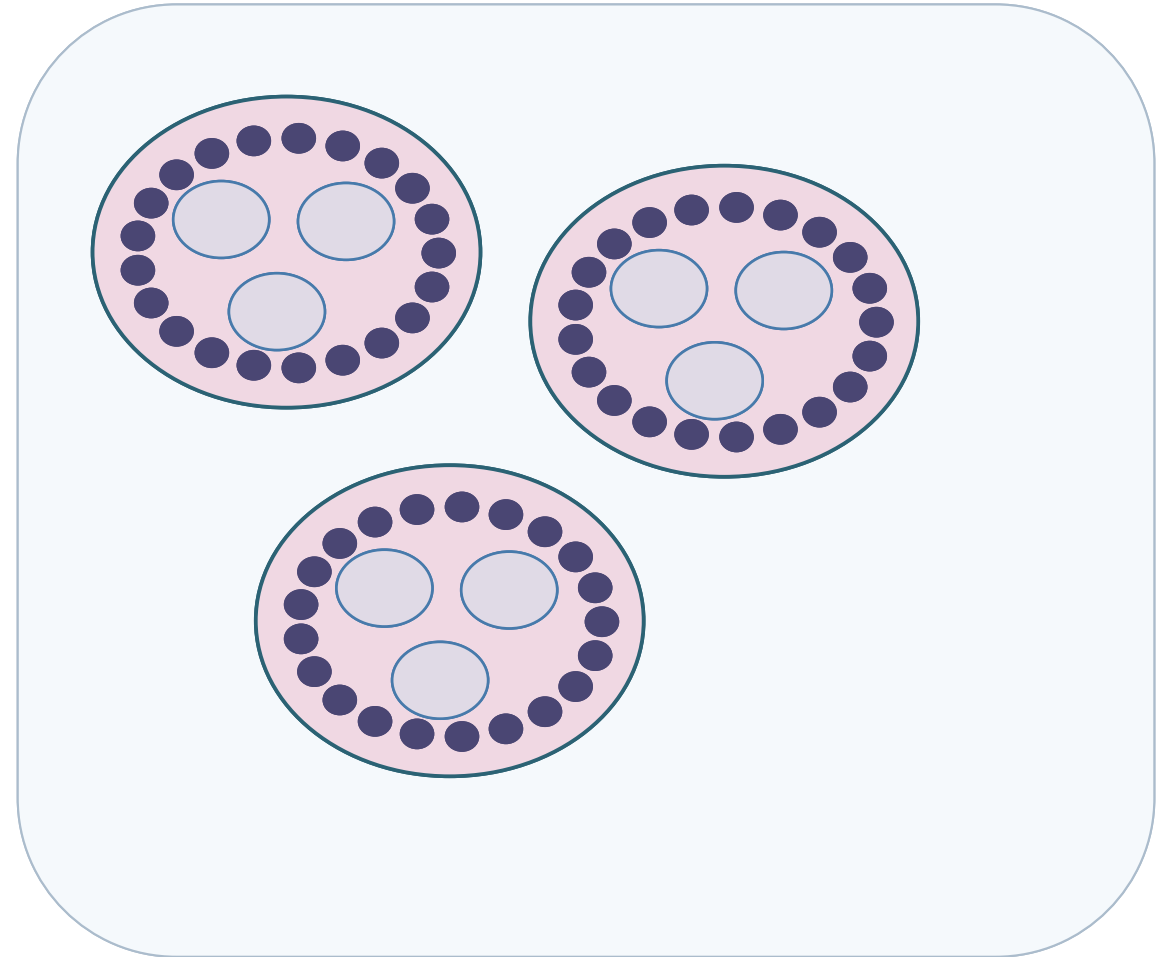
- Cribriform nests contain multiple punched-out spaces.
- Robbins likens this architecture to a sieve or Swiss cheese.
- This is an architectural description—not evidence that the spaces are true cysts.



Original explanatory schematic — not H&E

Reading a cribriform nest from outside inward

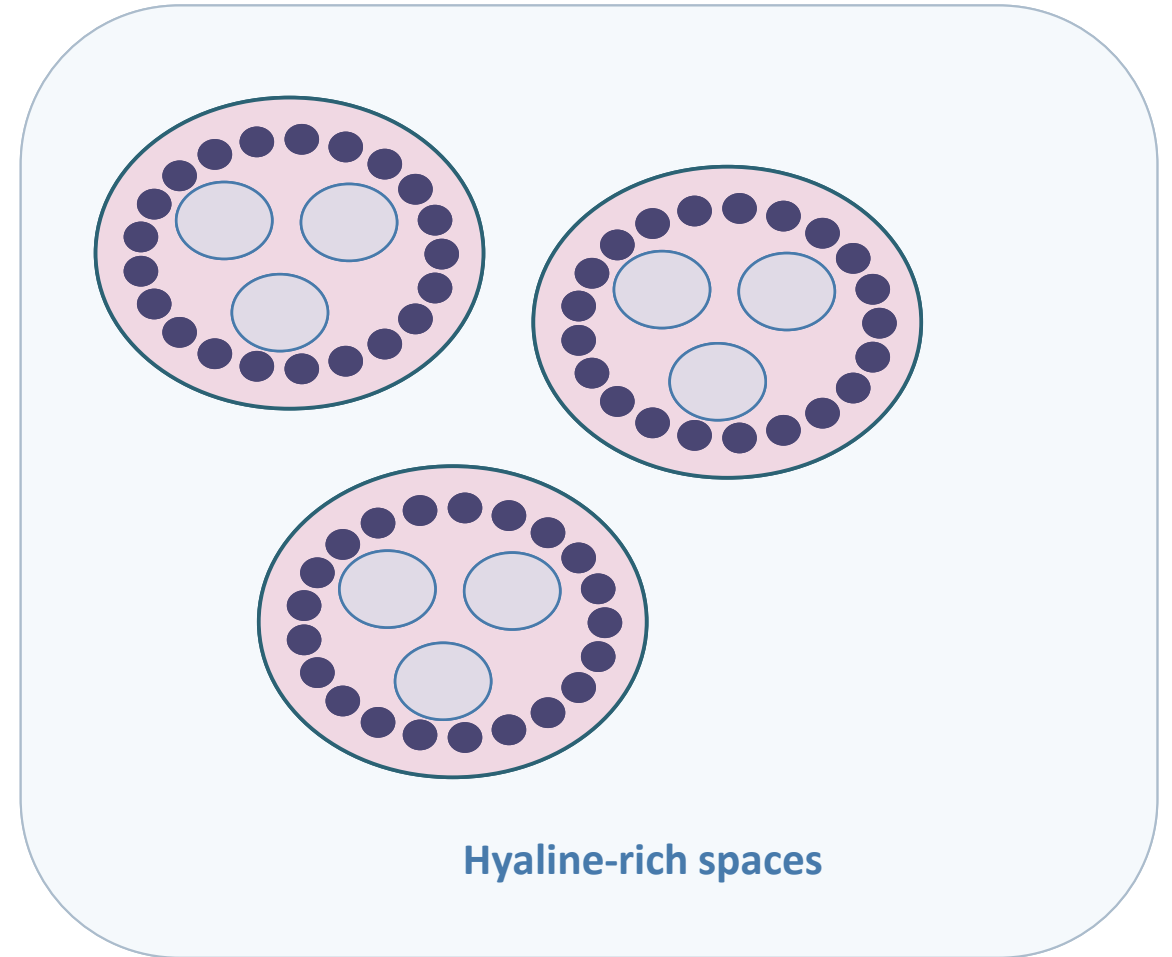
- Identify the cellular tumor nest first.
- Then identify the multiple rounded intranest spaces.
- Finally examine the contents of these spaces and the adjacent stroma.



Original explanatory schematic — not H&E

The luminal-looking spaces often hold hyaline material

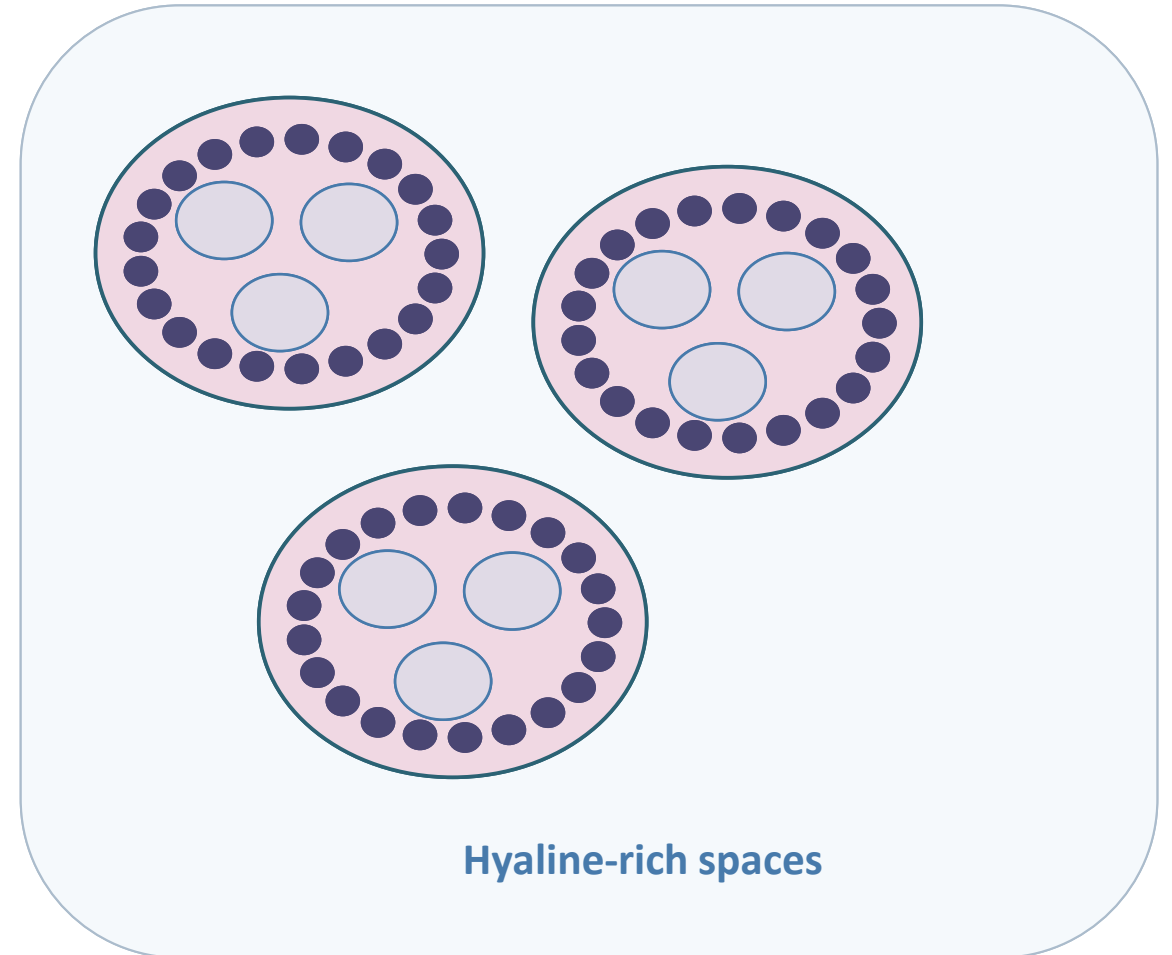
- The spaces between tumor cells are frequently filled with hyaline material.
- This material likely to represent excess basement membrane.
- The material helps explain the characteristic “punched-out” microscopic appearance.



Original explanatory schematic — not H&E

Basement-membrane material explains the texture

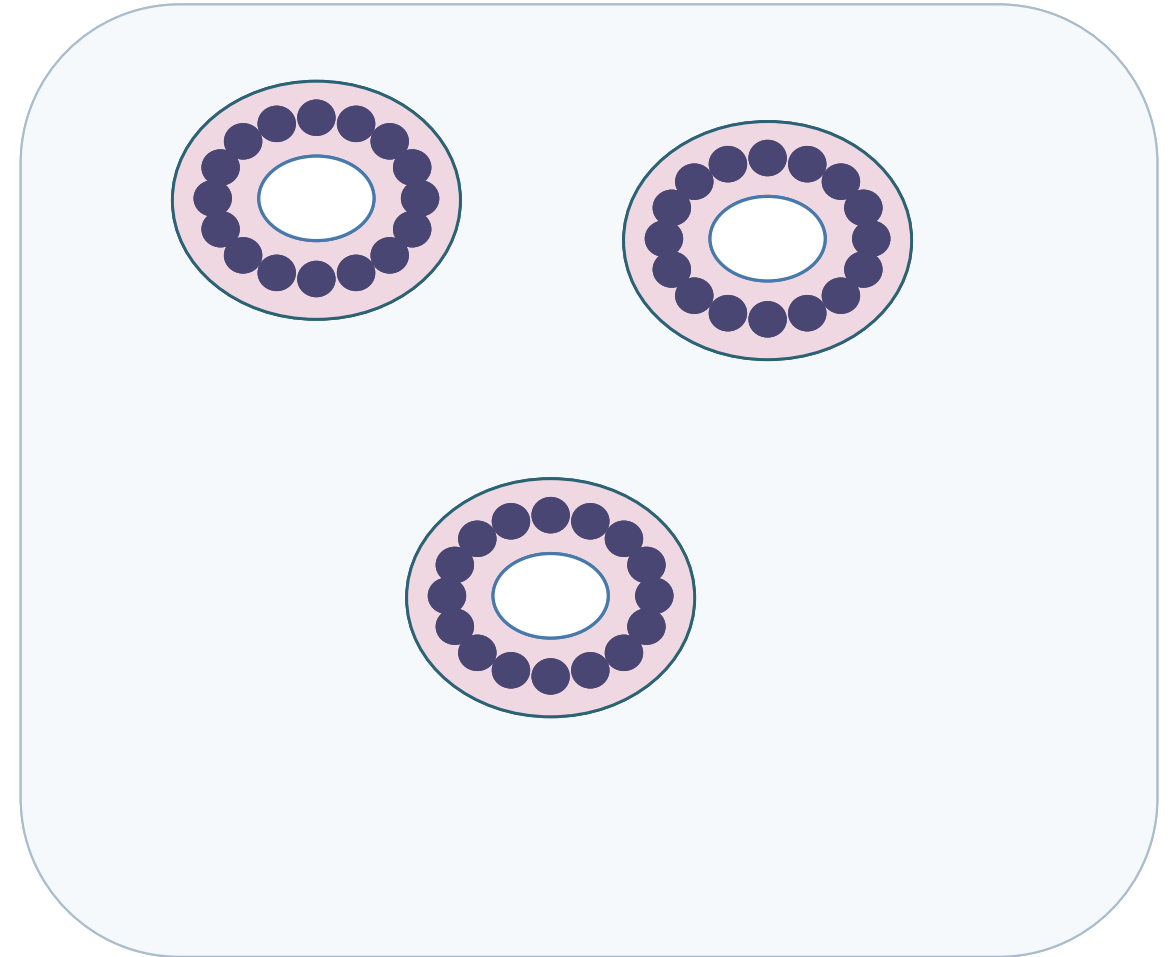
- Excess extracellular material can accumulate among tumor cells.
- In a two-dimensional section, this creates conspicuous pale spaces.
- The proposed origin of the material is stated as “thought to represent,” not proven in every case.



Original explanatory schematic — not H&E

Tubular growth is part of the documented spectrum

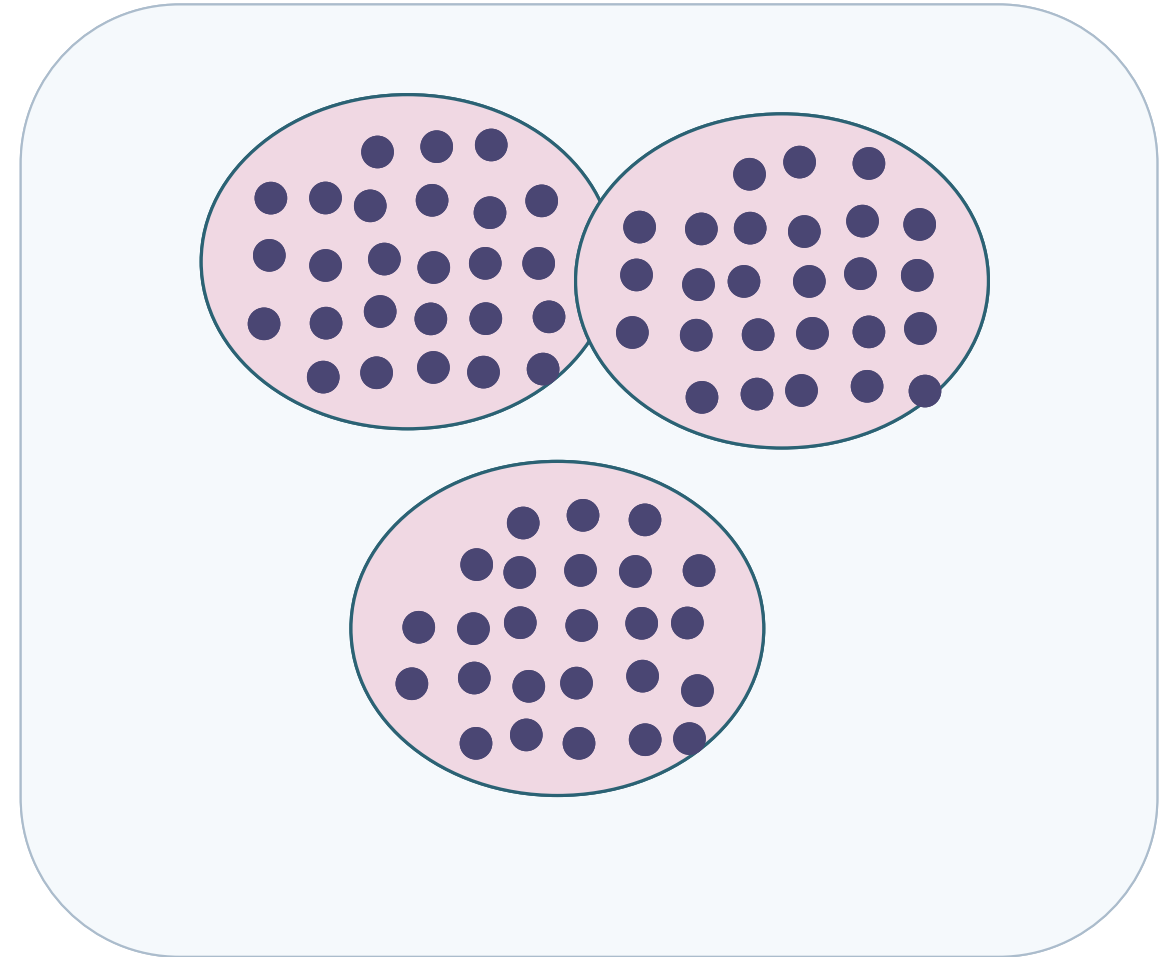
- The Robbins figure caption identifies tubular architecture in ACC.
- Tubular structures are an alternative to cribriform and solid areas.
- A single section may not represent all architecture in a tumor.



Original schematic — tubular architecture

Solid growth removes the sieve-like visual pattern

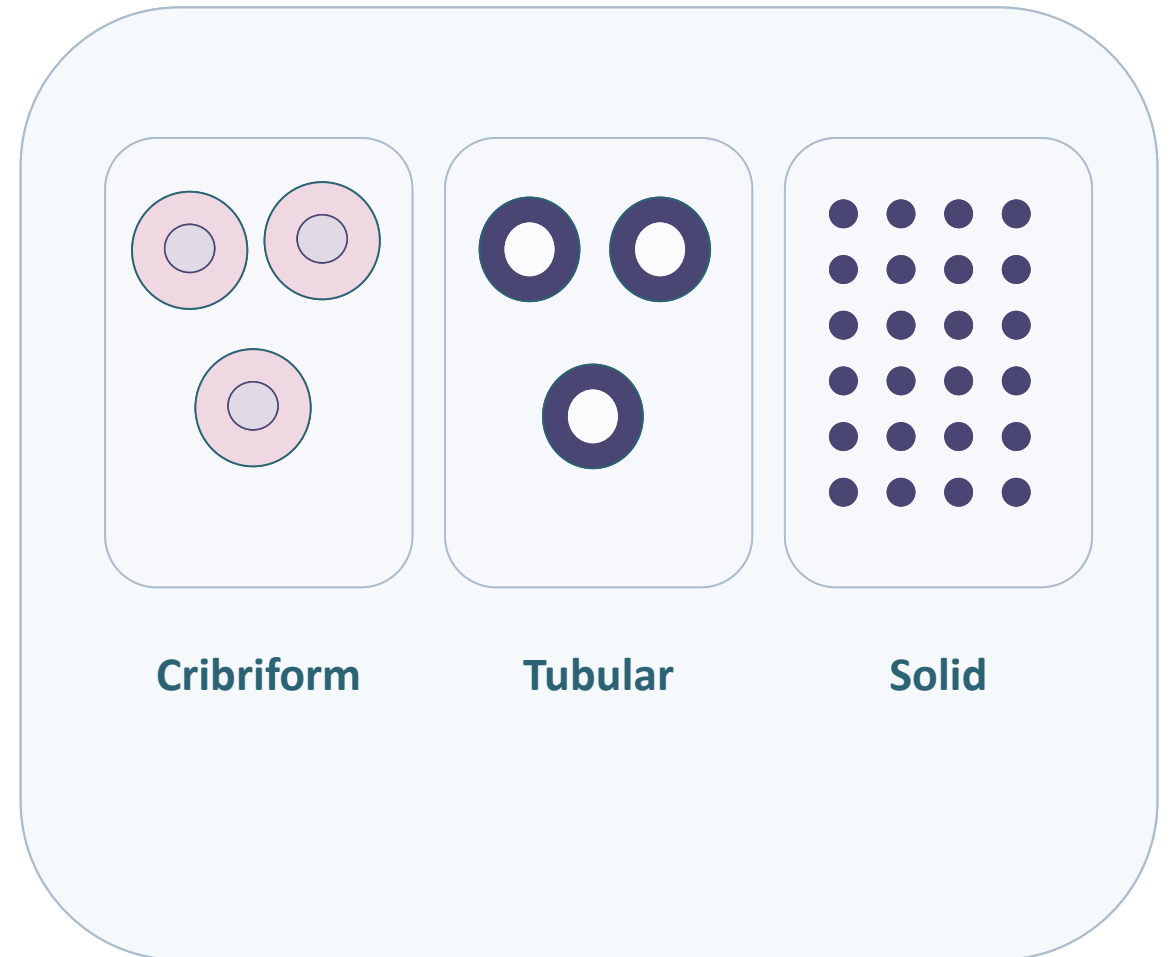
- Solid nests or sheets lack the prominent multitude of spaces seen in cribriform areas.
- This pattern with NOTCH1-mutant ACC.
- A solid area warrants interpretation in its complete tumor context.



Schematic — epithelial-predominant solid nests

Three architectural patterns in one view

- Cribriform: Nests with multiple spaces.
- Tubular: Gland-like formations with a central lumen.
- Solid: Cohesive cell nests or sheets.



Simplified schematic — none of these are micrographs

Architecture and cellular composition are related

- Classic NOTCH1 wild-type tumors contain two named cellular compartments.
- The source describes epithelial predominance in NOTCH1-mutated tumors.
- The growth pattern summarizes organizational differences, not every cell's identity.

NOTCH1 wild-type

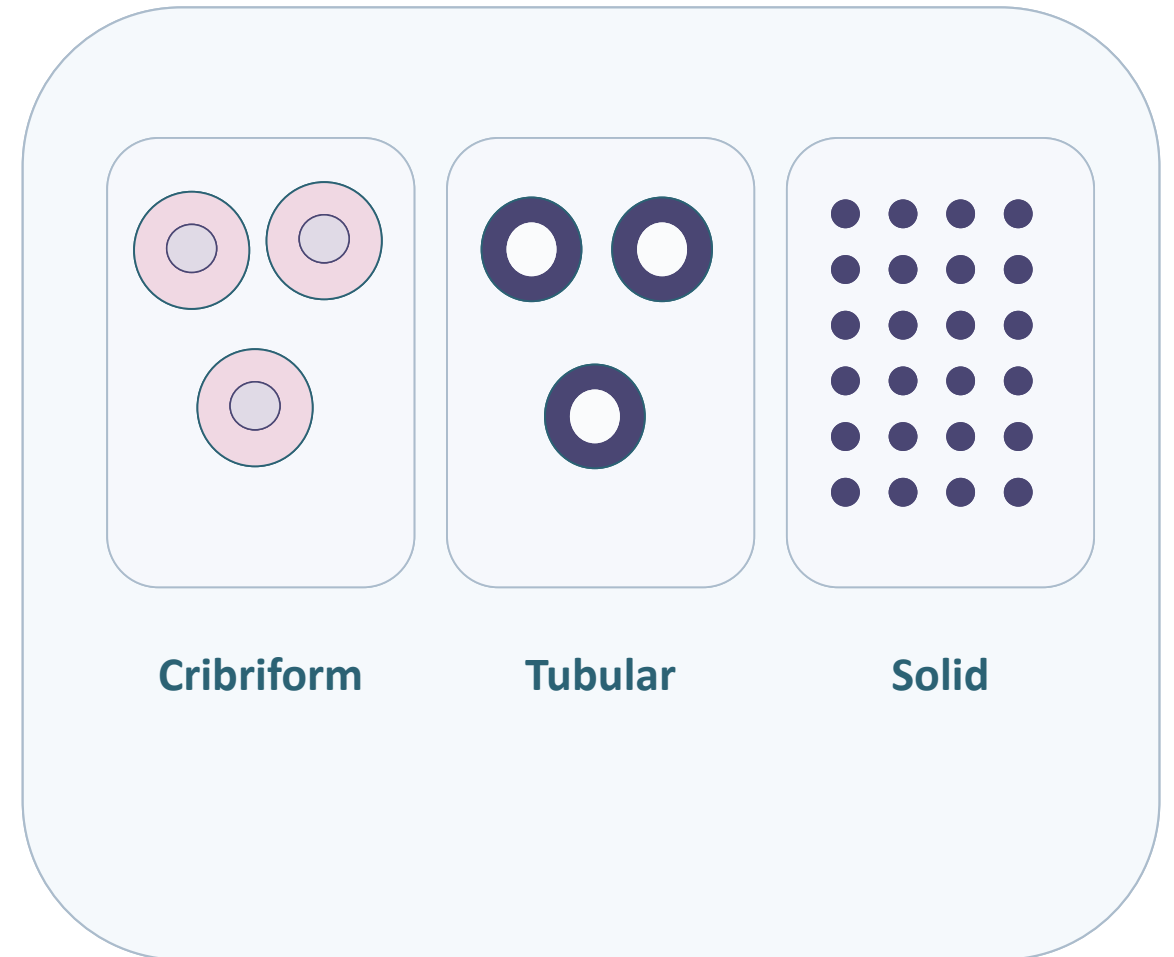
Cribriform · mixed cell populations

NOTCH1 mutant

Solid · epithelial predominant

Pattern recognition is not a substitute for tissue context

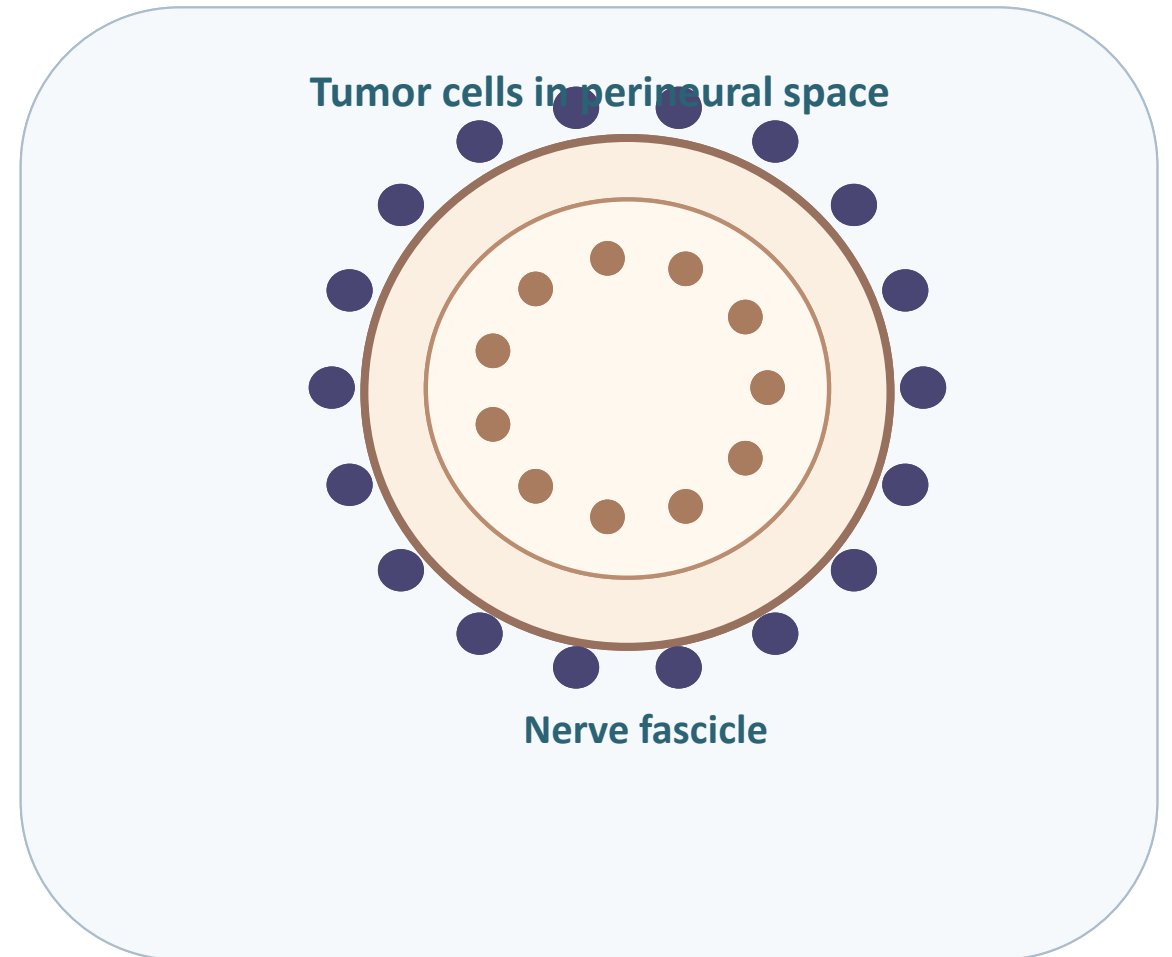
- Assess architecture alongside gland of origin and invasive edge.
- A single cribriform field cannot establish all behavior of the lesion.
- The source's major clinical warning is prolonged recurrence risk.



Simplified schematic — none of these are micrographs

Perineural invasion is a signature behavior

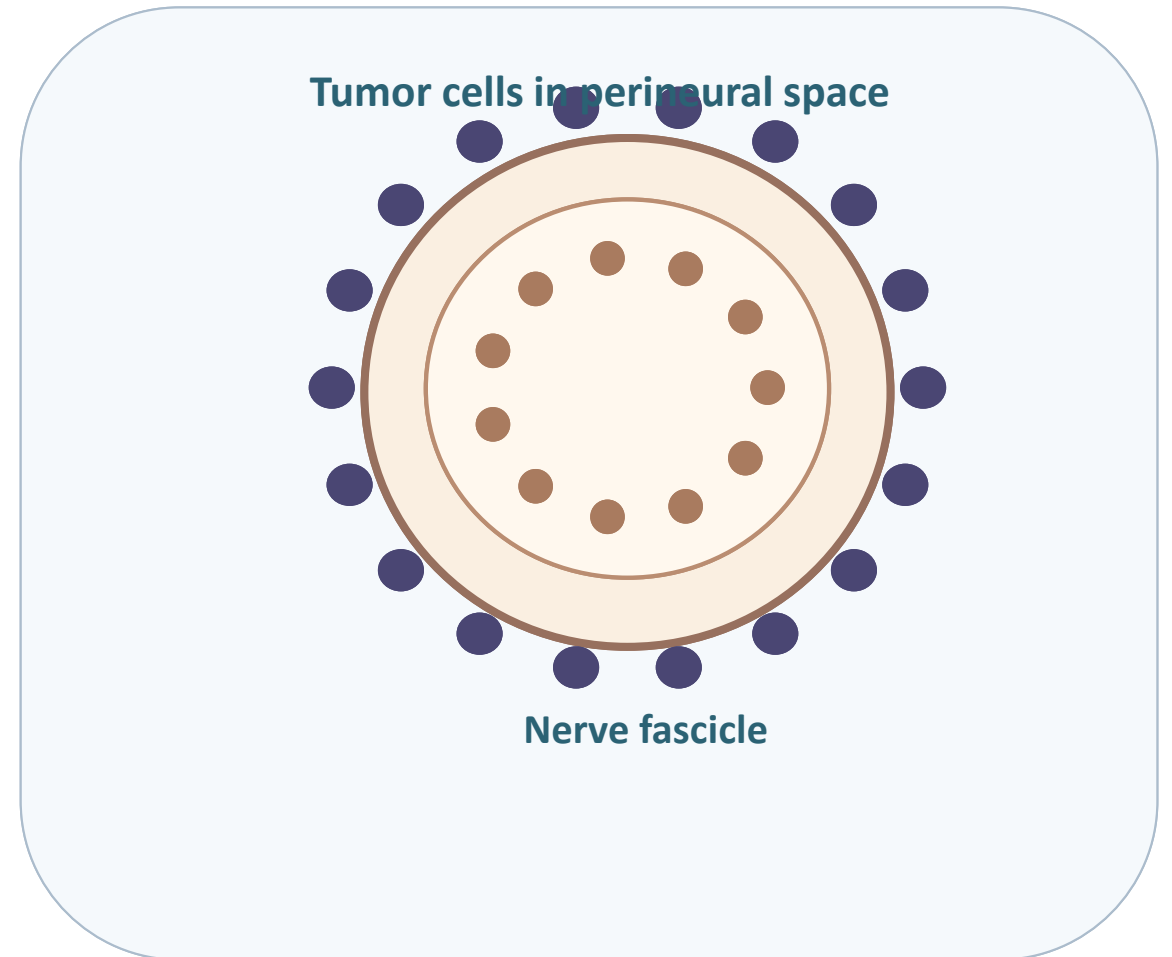
- ACC tends to invade perineural spaces.
- This is specifically illustrated Fig. 16.23B.
- Neural involvement is part of the infiltrative phenotype.



Schematic — not a histologic specimen

What perineural invasion means spatially

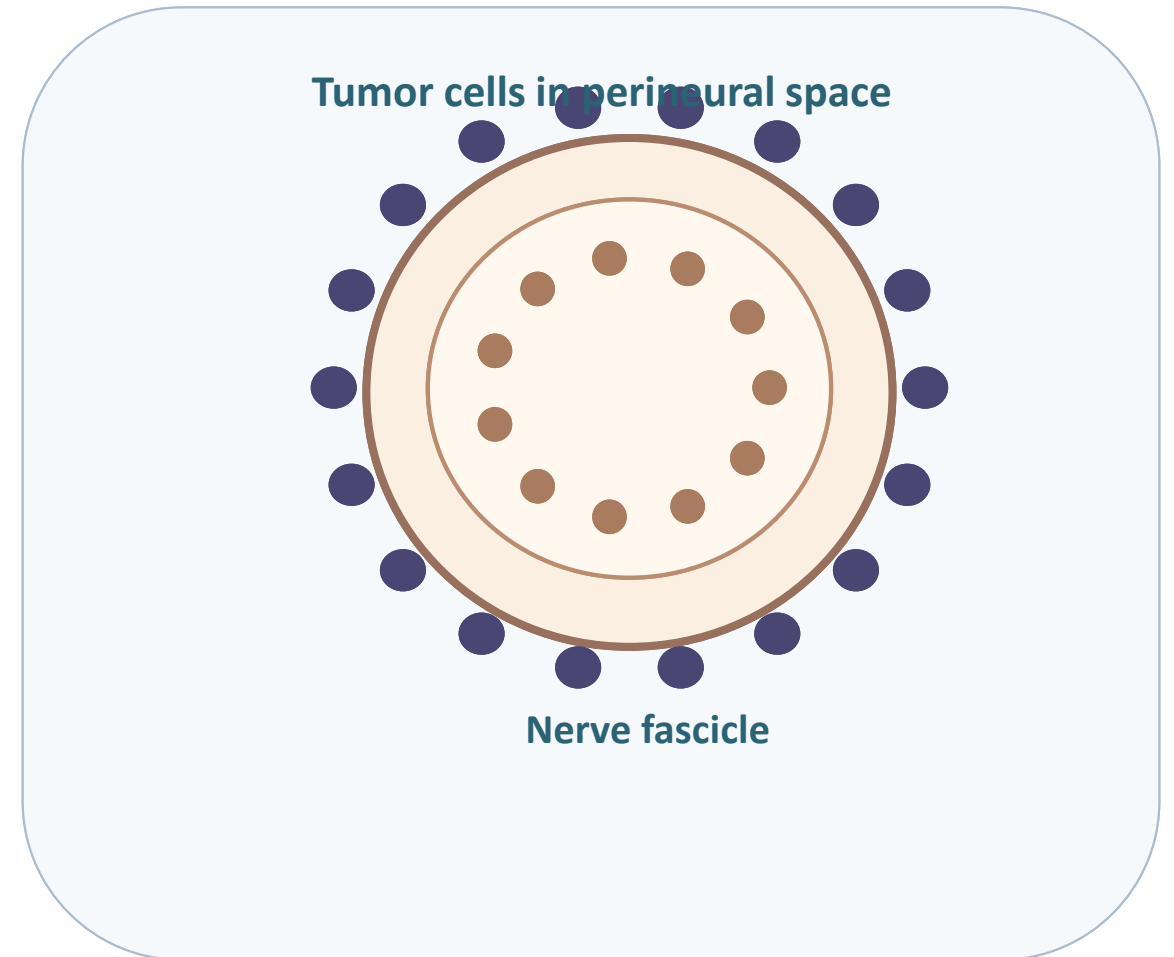
- The relevant tumor cells occupy tissue immediately around a nerve.
- A nerve and adjacent tumor must be distinguished anatomically.
- This schematic shows an invasion route, not a real microscopic field.



Schematic — not a histologic specimen

Perineural involvement matters for local extent

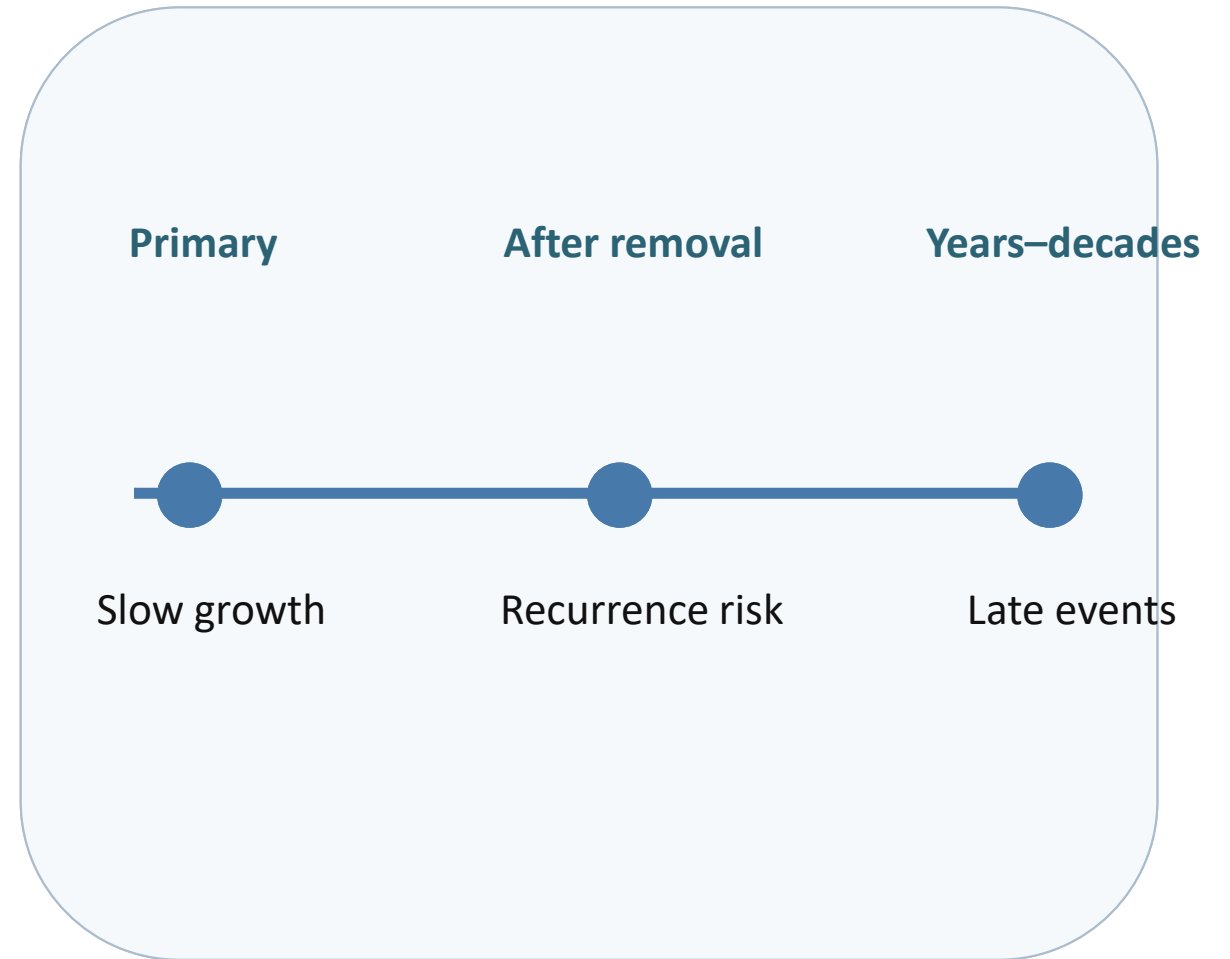
- Perineural spaces can extend away from the obvious bulk of a tumor.
- Thus a small gross mass does not guarantee limited microscopic distribution.
- The original source emphasizes invasion; Clinical consequences here are interpretation.



Schematic — not a histologic specimen

Slow growth and clinical hazard can coexist

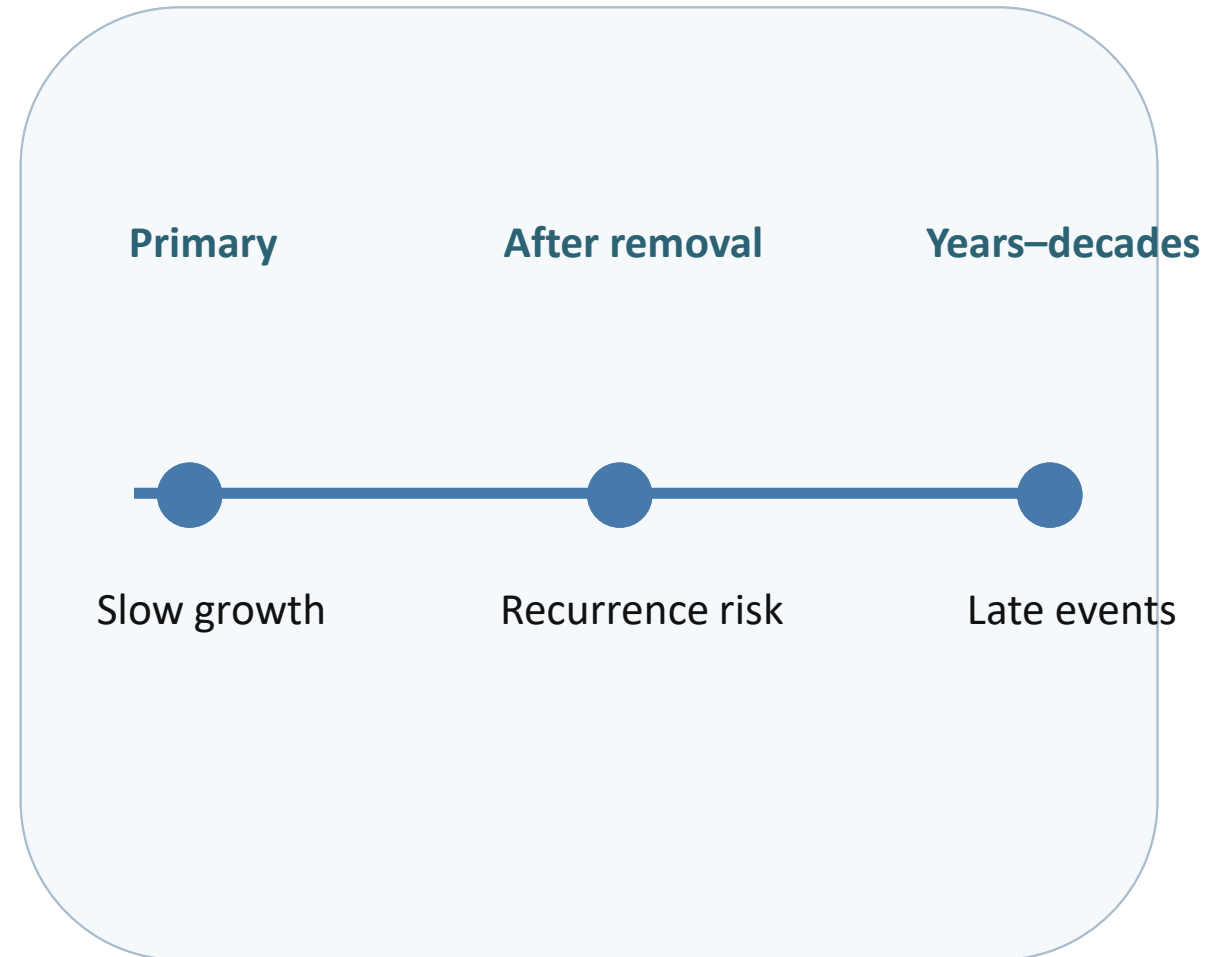
- ACC is described as slow-growing.
- Yet it is also infiltrative and capable of repeated recurrence.
- Growth speed alone is therefore an inadequate measure of risk.



Conceptual trajectory — no individual patient data

Local recurrence belongs to the natural history

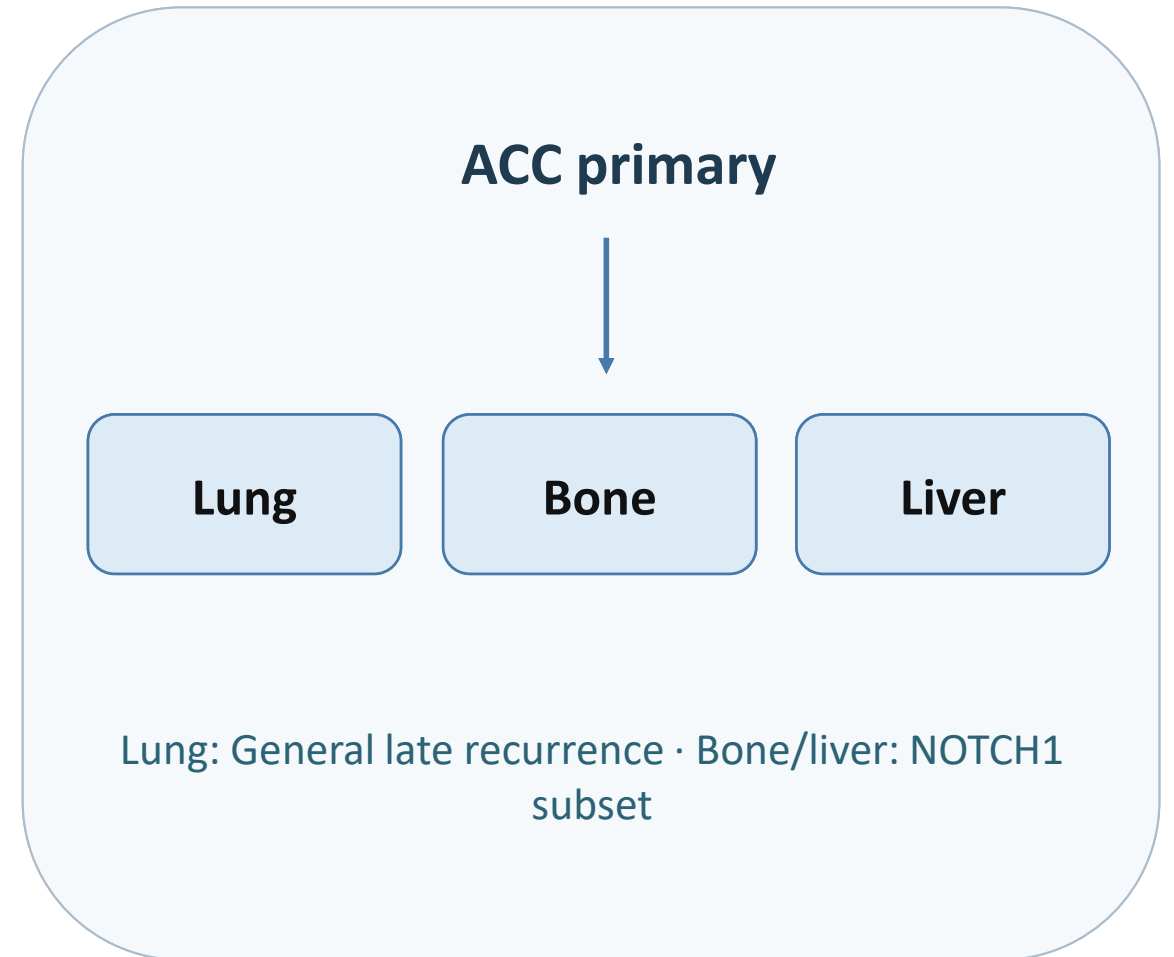
- ACC regularly recurs after attempted removal.
- This is consistent with its described infiltrative and perineural growth.
- A local recurrence history should not be mistaken for a newly benign lesion.



Conceptual trajectory — no individual patient data

Distant recurrence is a major cause of late failure

- At least half of cases eventually recur at distant sites in the cited account.
- Distant events may occur long after the original treatment.
- The primary site must remain part of the pathologic history.



Conceptual trajectory — no individual patient data

Lung is the named distant site to remember

- The lung is explicitly identified as a site of distant recurrence.
- A distant lung lesion years later requires attention to prior ACC history.
- The source does not provide a lung-specific incidence breakdown.

Minor glands / major glands

Nose · sinuses · upper airways

Lung · breast · other sites

NOTCH1-mutated tumors have a different metastatic bias

- An increased tendency to metastasize to bone and liver.
- This is in addition to the general possibility of distant relapse.
- Metastatic tropism is an association, not a rule for every mutant tumor.

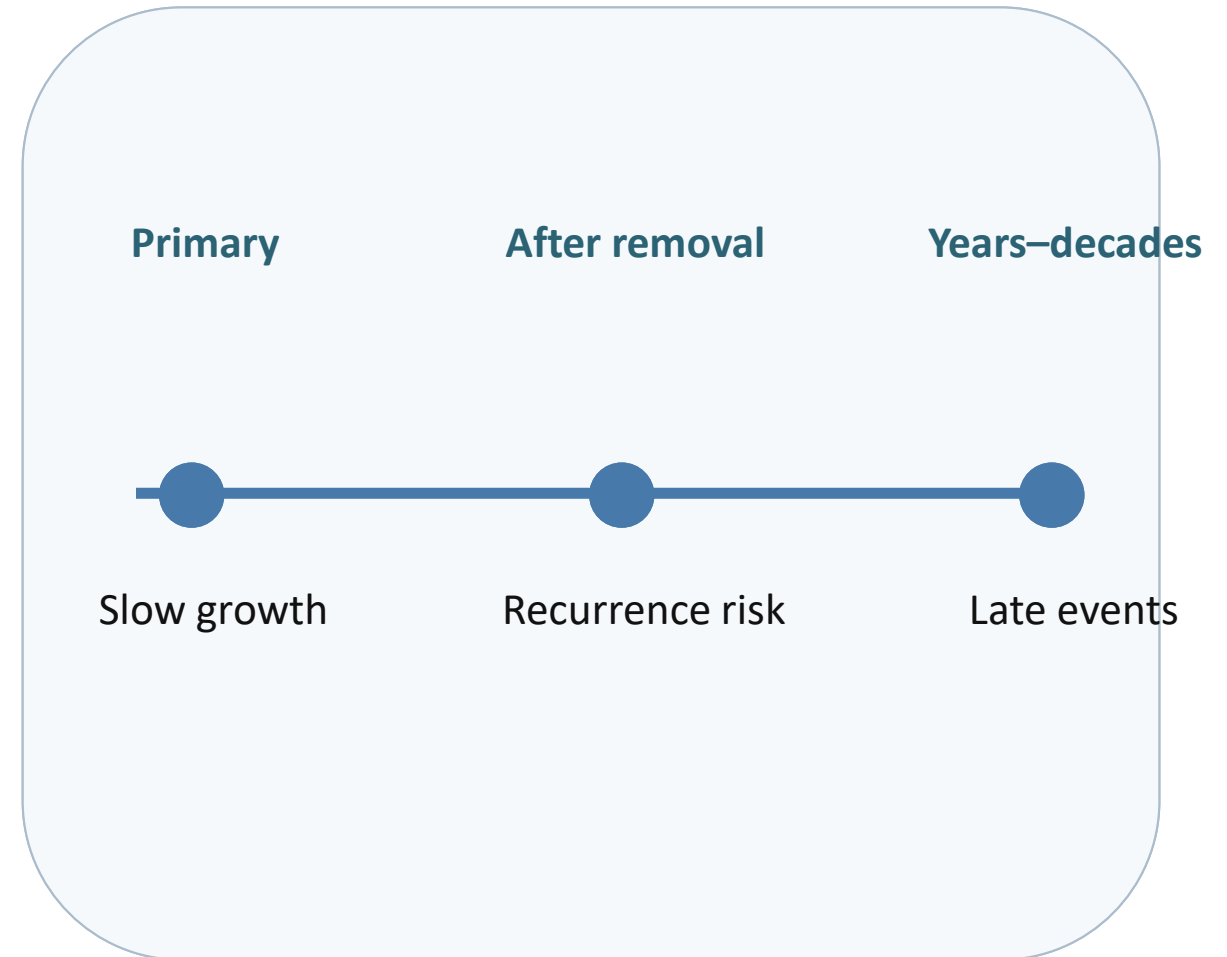
Minor glands / major glands

Nose · sinuses · upper airways

Lung · breast · other sites

Recurrence can emerge decades later

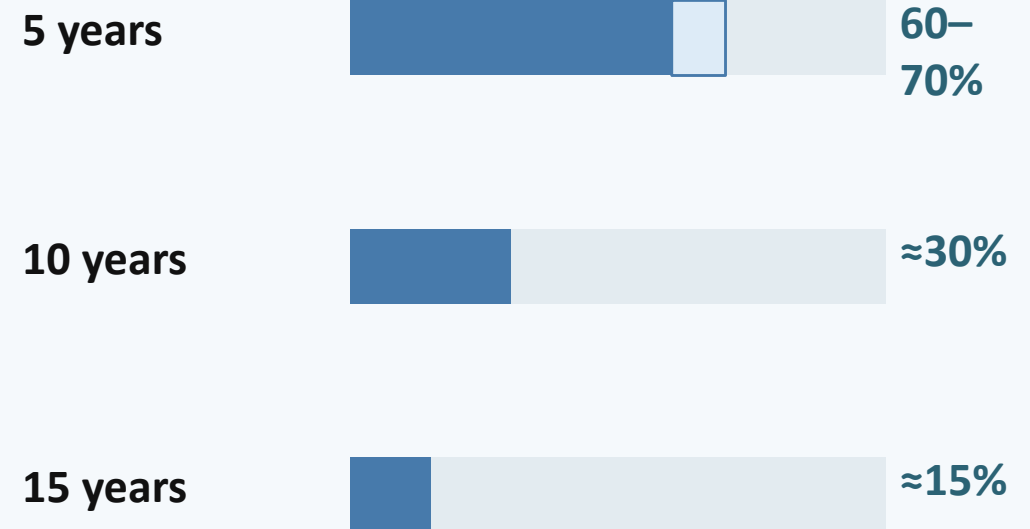
- The source explicitly allows distant relapse decades after attempted removal.
- A disease-free interval measured in years does not extinguish future risk.
- Short follow-up can therefore mischaracterize the full natural history.



Conceptual trajectory — no individual patient data

Five-year survival is only the early part of the story

- The quoted 5-year survival is about 60%–70%.
- This figure is not a long-term cure fraction.
- The distinction matters because very late events are described.

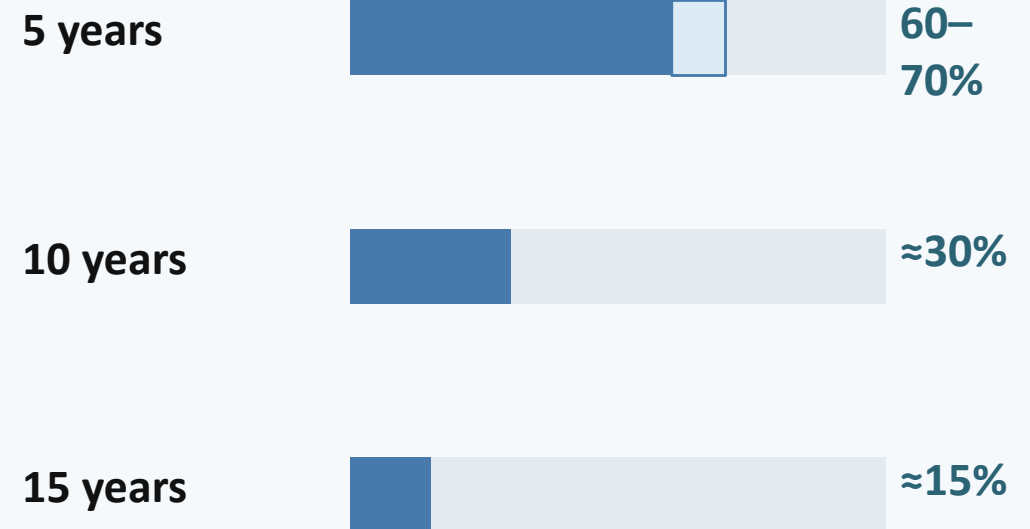


Five-year value shown as a 60%–70% range

Reported survival at specified follow-up years

Outcomes decline at later follow-up points

- Robbins quotes approximately 30% survival at 10 years.
- At 15 years, the quoted survival is about 15%.
- These are reported time-specific values; No intervening survival curve was reconstructed.

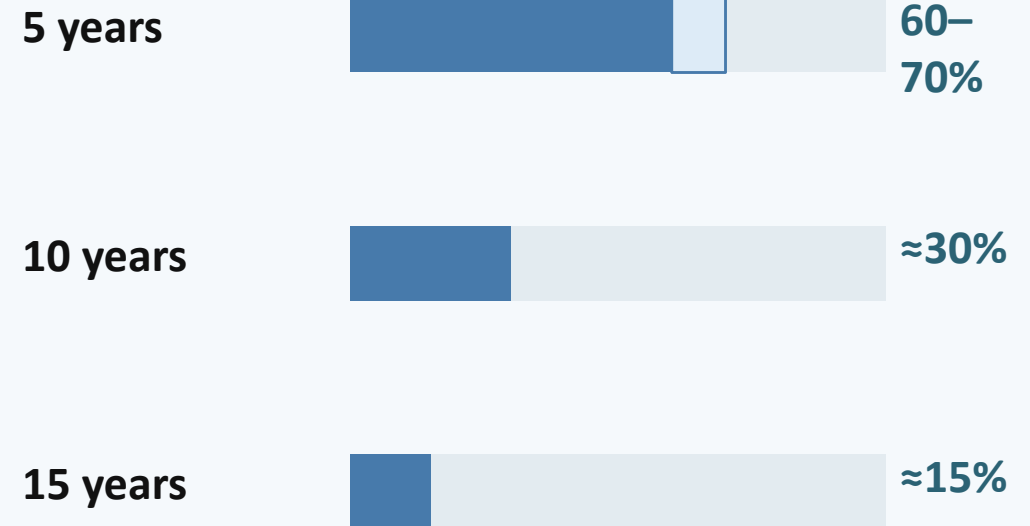


Five-year value shown as a 60%–70% range

Reported survival at specified follow-up years

Read survival values as discrete observations

- A plot of three reported intervals shows substantial long-term decline.
- The source does not provide a cohort, confidence intervals, or survival-function shape.
- Do not extrapolate these points to an invented continuous curve.

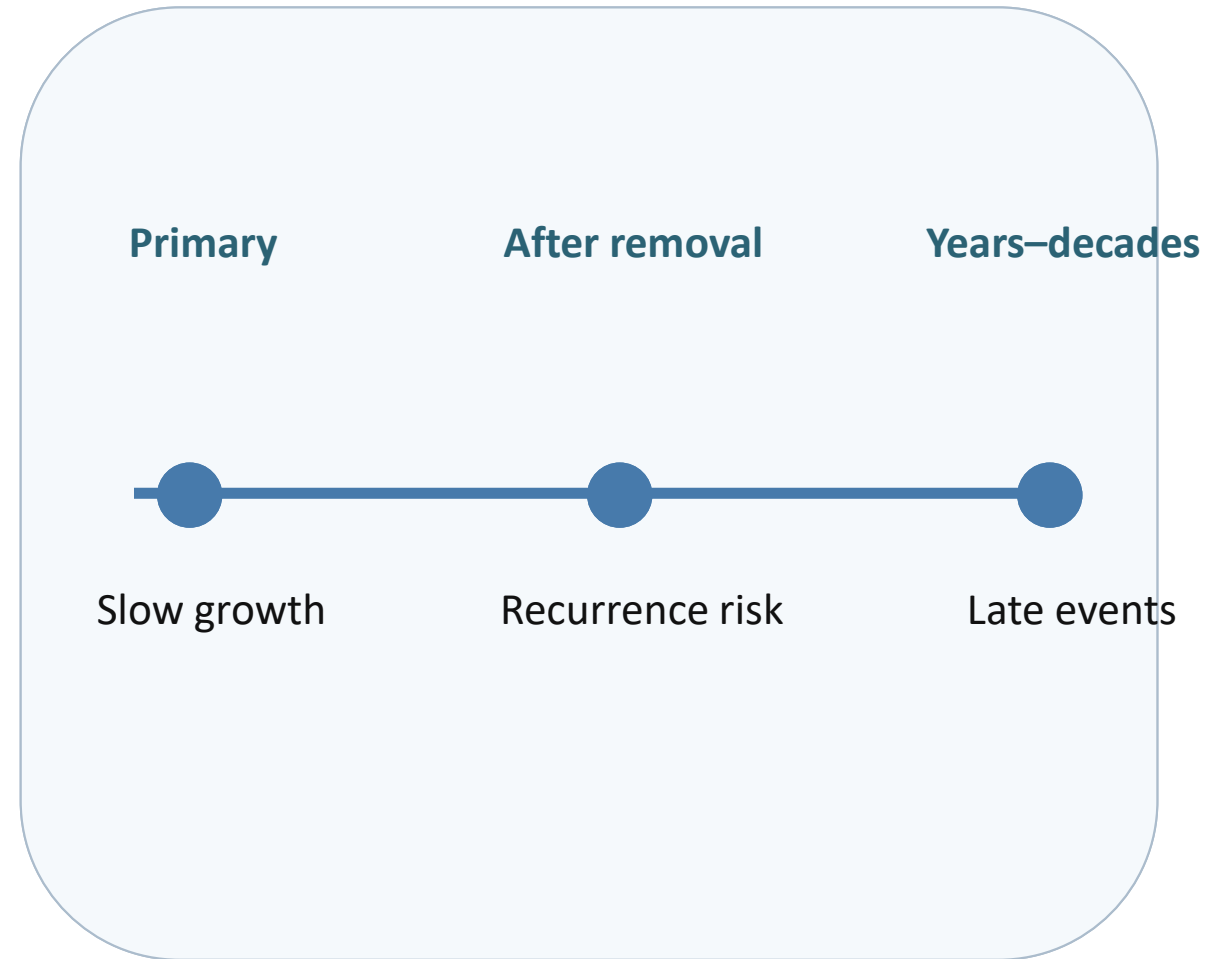


Five-year value shown as a 60%–70% range

Reported survival at specified follow-up years

Why five-year reporting can be misleading

- The tumor may recur after a prolonged clinically quiet period.
- Therefore, five-year survival alone understates the duration of the hazard.
- The clinical narrative and the 10–15-year outcomes must be considered together.



Conceptual trajectory — no individual patient data

Minor-gland ACC has worse reported prognosis

- Poorer outcome for tumors of minor salivary glands than for parotid primaries.
- This is a between-site tendency, not a numerical risk model.
- Palatine primaries deserve attention because they are a frequent minor-gland site.

Minor glands

≈50% of ACC; Palate prominent

Parotid

Major-gland origin

Submandibular

Major-gland origin

NOTCH1 status separates prognostic groups

- Survival is lower in the NOTCH1-mutated subset.
- The subset also tends toward solid architecture.
- Association does not provide a patient-specific survival probability.

NOTCH1 wild-type

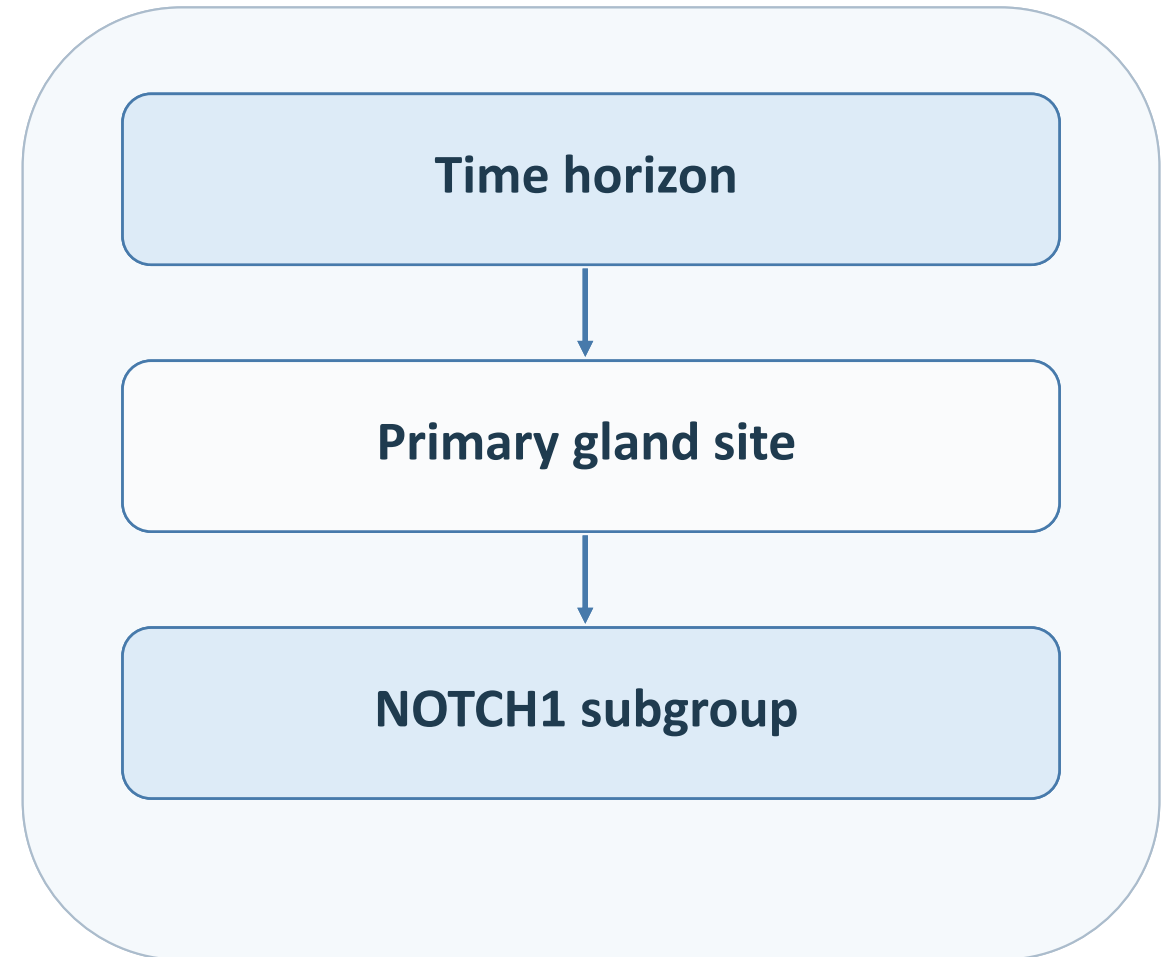
Cribriform · mixed cell populations

NOTCH1 mutant

Solid · epithelial predominant

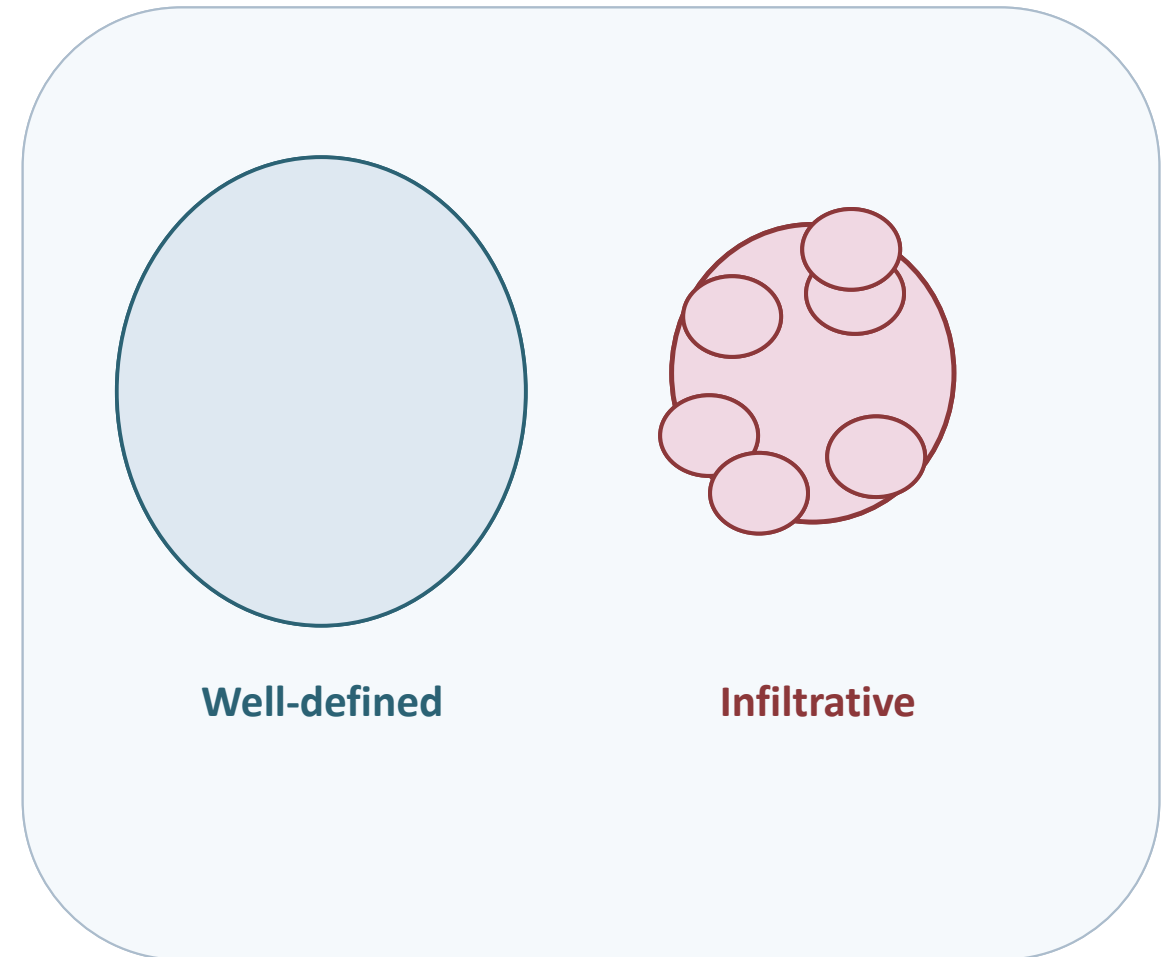
Three axes organize the prognostic narrative

- Time: Relapses can occur decades later.
- Anatomic origin: Minor-gland primaries fare worse than parotid in the source.
- Biology: NOTCH1-mutated tumors have worse outcome and different tropism.



Why a slowly enlarging salivary mass is not reassuring

- Many benign salivary tumors have a long presenting history.
- ACC may also grow slowly despite malignant potential.
- The parent chapter states there are no reliable clinical criteria for benign versus malignant separation.



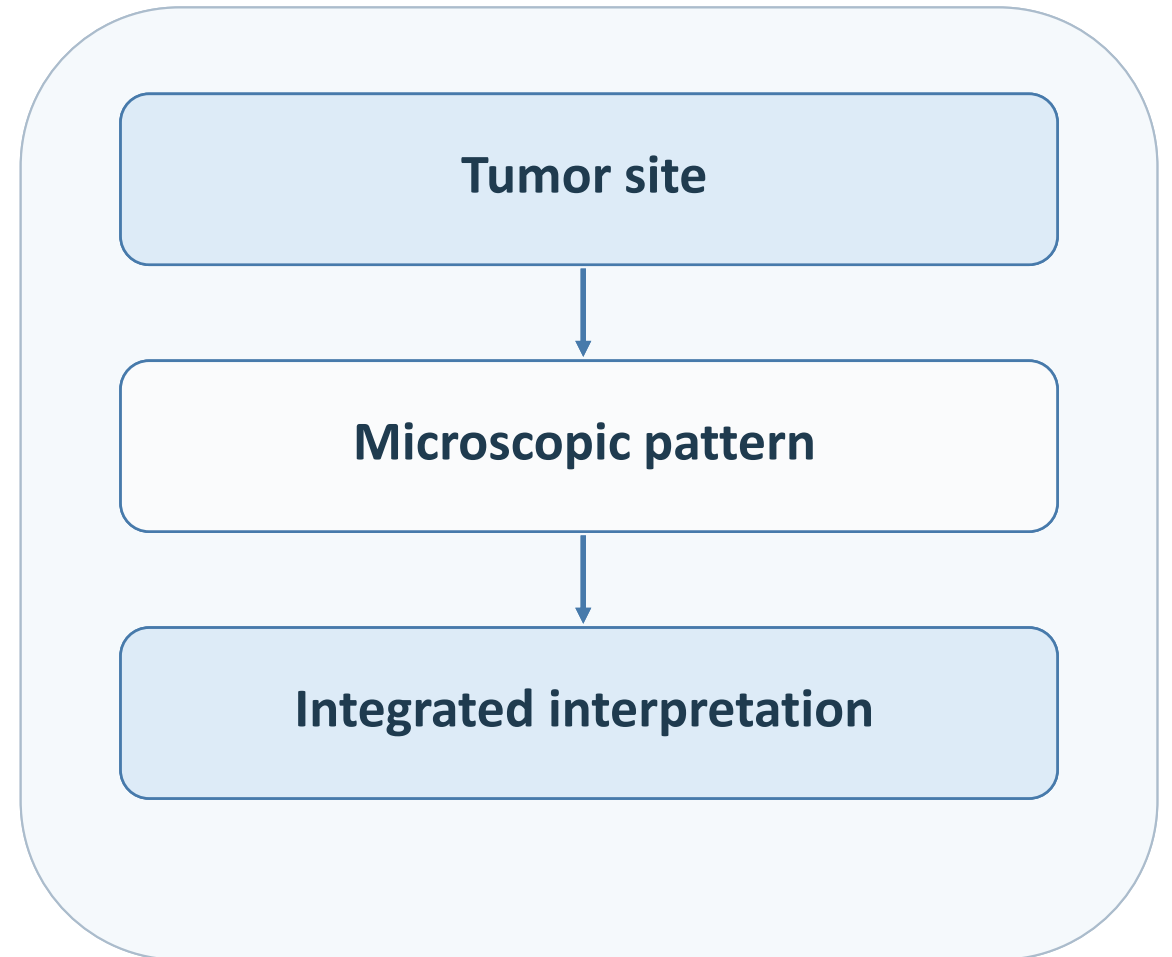
Well-defined

Infiltrative

Schematic — comparison of border geometry

The diagnostic problem is tissue-based

- Clinical examination alone cannot reliably classify salivary masses.
- Biopsy and/or surgical resection is needed for definitive diagnosis.
- Histology establishes tumor architecture and its invasive features.



Mucoepidermoid carcinoma: A different cell mixture

- Mucoepidermoid carcinoma contains mucous, squamous, and intermediate cells.
- It often contains small mucin-filled cysts.
- ACC is distinguished in the source by basaloid/epithelial architecture and hyaline spaces.

ACC

Cribriform / hyaline spaces

Mucoepidermoid

Mucous + squamous cells

**Pleomorphic
adenoma**

Chondromyxoid stroma

Morphologic discriminators — simplified comparison

Pleomorphic adenoma: Mixed tumor, usually benign

- Pleomorphic adenoma is a benign ductal/myoepithelial mixed tumor.
- Its stroma may be chondromyxoid, unlike the described ACC hyaline spaces.
- Its usual circumscription contrasts with the ACC infiltrative edge.

ACC

Cribriform / hyaline spaces

Mucoepidermoid

Mucous + squamous cells

**Pleomorphic
adenoma**

Chondromyxoid stroma

Morphologic discriminators — simplified comparison

Warthin tumor: An epithelial–lymphoid lesion

- Warthin tumor nearly always arises in the parotid gland.
- It comprises bilayer oncocytic epithelium and a lymphoid stroma.
- This constellation is different from cribriform ACC and perineural invasion.

ACC

Cribriform / hyaline spaces

Mucoepidermoid

Mucous + squamous cells

**Pleomorphic
adenoma**

Chondromyxoid stroma

Morphologic discriminators — simplified comparison

Acinic cell carcinoma: Serous-acinar differentiation

- Acinic cell carcinoma is usually a parotid tumor.
- Cells can resemble serous acini with zymogen-like cytoplasmic granules.
- The distinct cellular differentiation contrasts with classic ACC architecture.

ACC

Cribriform / hyaline spaces

Mucoepidermoid

Mucous + squamous cells

**Pleomorphic
adenoma**

Chondromyxoid stroma

Morphologic discriminators — simplified comparison

Salivary differential: The discriminating feature

- Cribriform nest with hyaline spaces: Favor an ACC pattern.
- Mucous + squamous + intermediate cells: Favor mucoepidermoid carcinoma.
- Chondromyxoid stroma, lymphoid stroma, or serous-acinar features point elsewhere.

ACC

Cribriform / hyaline spaces

Mucoepidermoid

Mucous + squamous cells

**Pleomorphic
adenoma**

Chondromyxoid stroma

Warthin tumor

Oncocytic + lymphoid

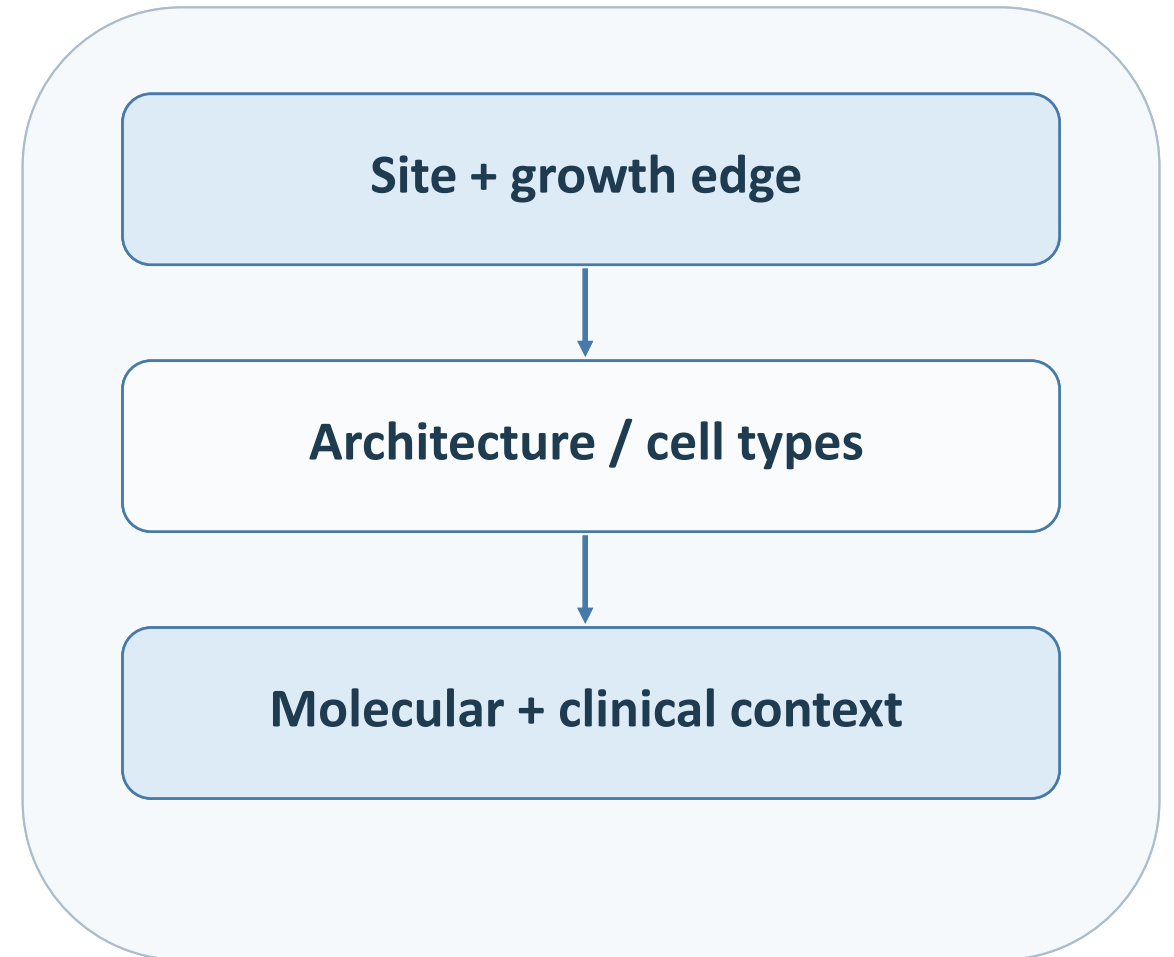
Acinic cell

Serous acinar granules

Morphologic discriminators — simplified comparison

Interpret morphology within a diagnostic sequence

- First identify tumor site and overall growth margin.
- Next determine whether cribriform/tubular/solid or another lineage pattern predominates.
- Finally integrate perineural invasion and available molecular findings.



Application: A palatine-gland mass

- A palatal lesion is sampled after a slowly progressive history.
- The tissue shows infiltrative cribriform nests with hyaline spaces.
- Question: Which source-described findings support ACC despite slow growth?

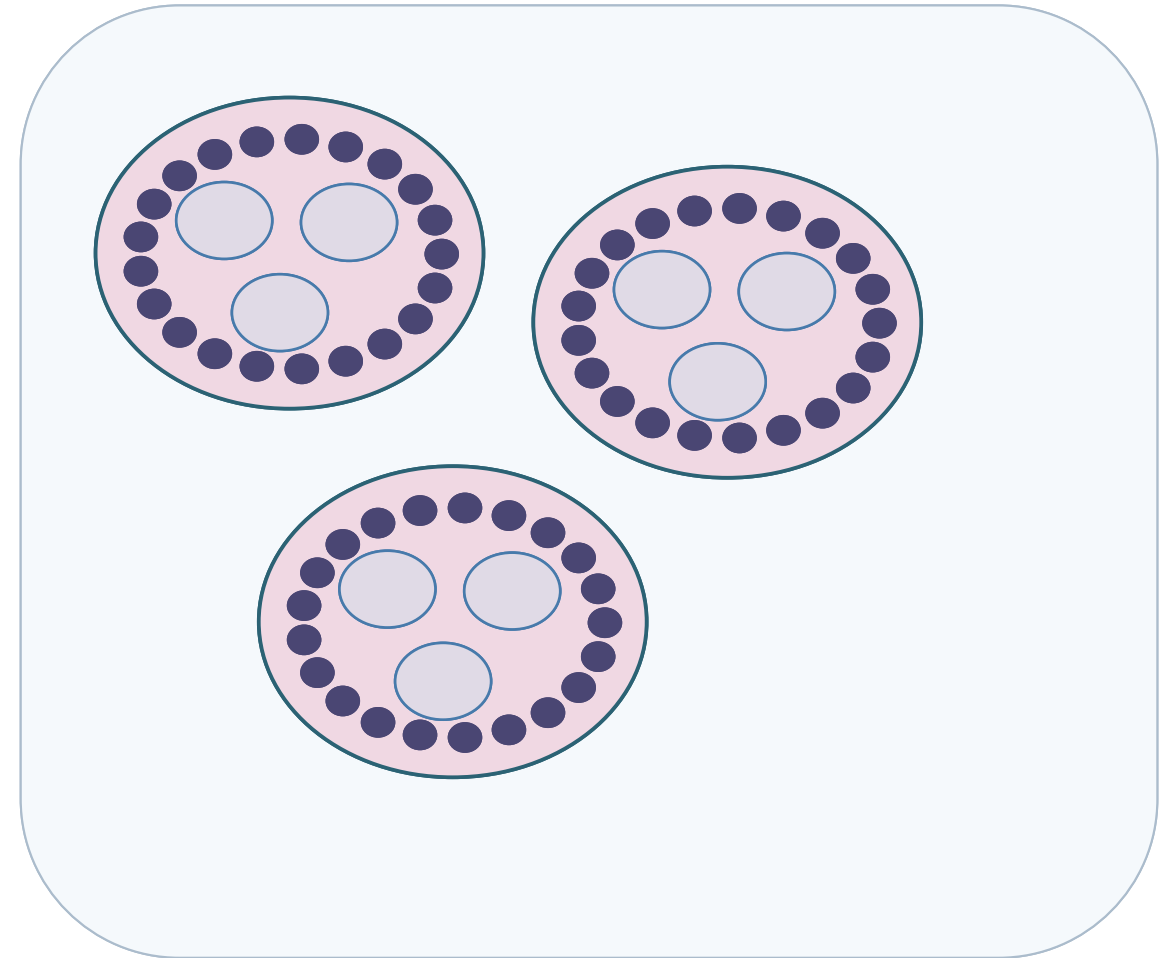
Which tissue finding carries the decisive implication?

1. Site and growth pattern
2. Invasive or neural involvement
3. Timing and molecular context

Hypothetical case for teaching; No patient data

Palatine-gland case: Interpretation

- The palatine gland is a favored minor-gland ACC location.
- Cribriform spaces and hyaline material match classic morphology.
- Infiltration overrides reassurance from slow growth.



Original explanatory schematic — not H&E

Application: A predominantly solid tumor

- A malignant salivary tumor consists largely of epithelial solid nests.
- Molecular testing detects an activating NOTCH1 mutation.
- Question: What clinical behavior would the Robbins subgroup predict qualitatively?

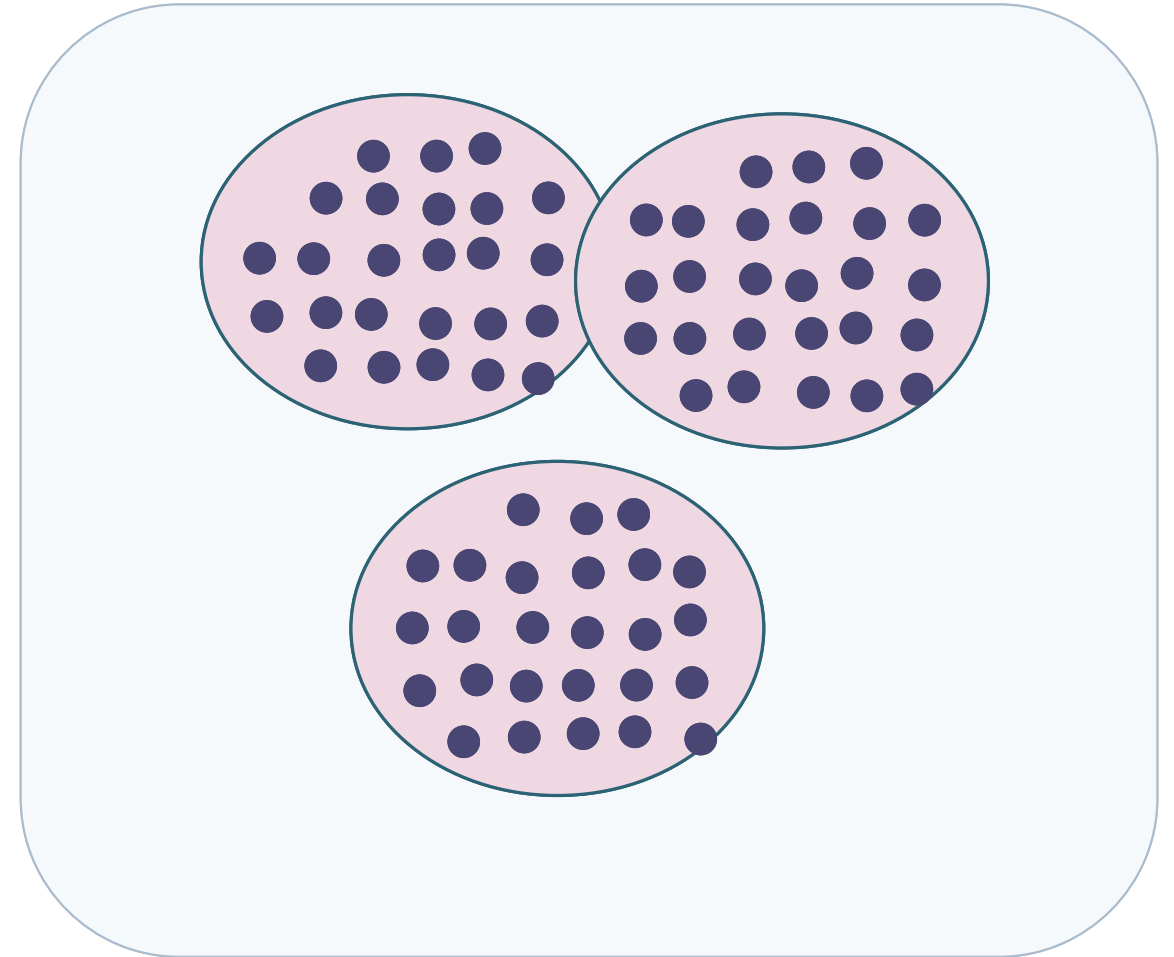
Which tissue finding carries the decisive implication?

1. Site and growth pattern
2. Invasive or neural involvement
3. Timing and molecular context

Hypothetical case for teaching; No patient data

Solid-tumor case: The subgroup implication

- The solid epithelial-predominant pattern aligns with the described mutant group.
- The source associates this group with lower survival.
- Bone and liver are particularly noted metastatic destinations.



Schematic — epithelial-predominant solid nests

Application: New lung lesion years later

- A patient with previously removed ACC develops a pulmonary lesion after a long interval.
- Question: Is the elapsed time sufficient to rule out late recurrence?
- What element of prior clinical history is necessary for interpretation?

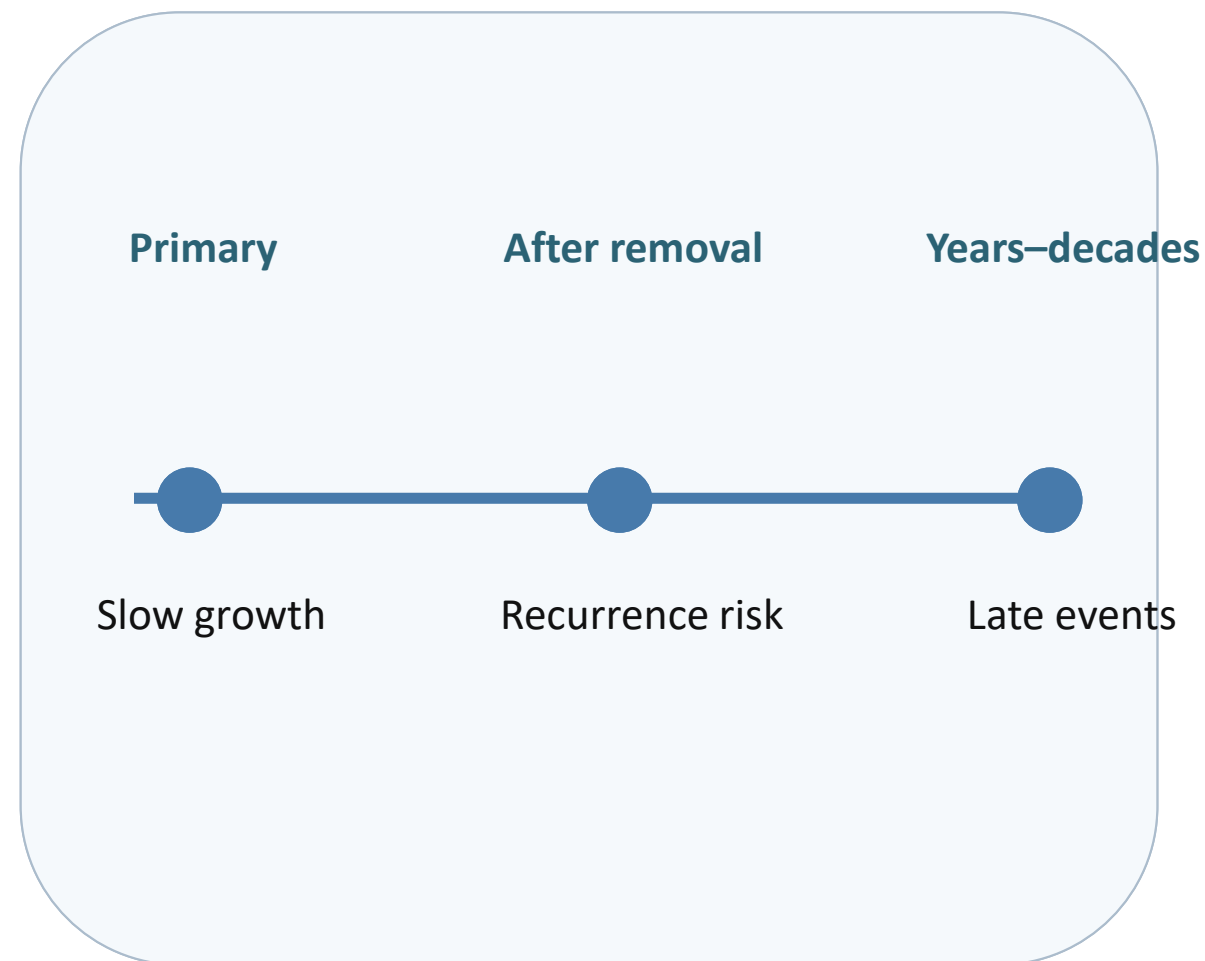
Which tissue finding carries the decisive implication?

1. Site and growth pattern
2. Invasive or neural involvement
3. Timing and molecular context

Hypothetical case for teaching; No patient data

Late-lung case: Time does not exclude disease

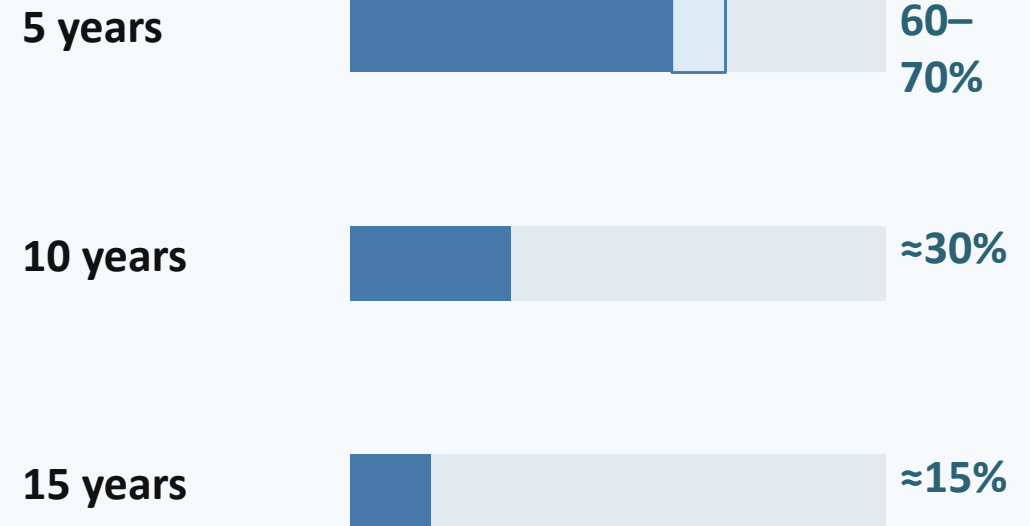
- ACC can recur distantly even decades after removal.
- Lung is a specifically reported site.
- A long interval is therefore compatible with the textbook natural history.



Conceptual trajectory — no individual patient data

Application: Reading the survival data

- The textbook gives roughly 60%–70%, 30%, and 15% at years 5, 10, and 15.
- Question: Which number best characterizes lifetime risk?
- Answer: No single reported interval captures all late recurrences.

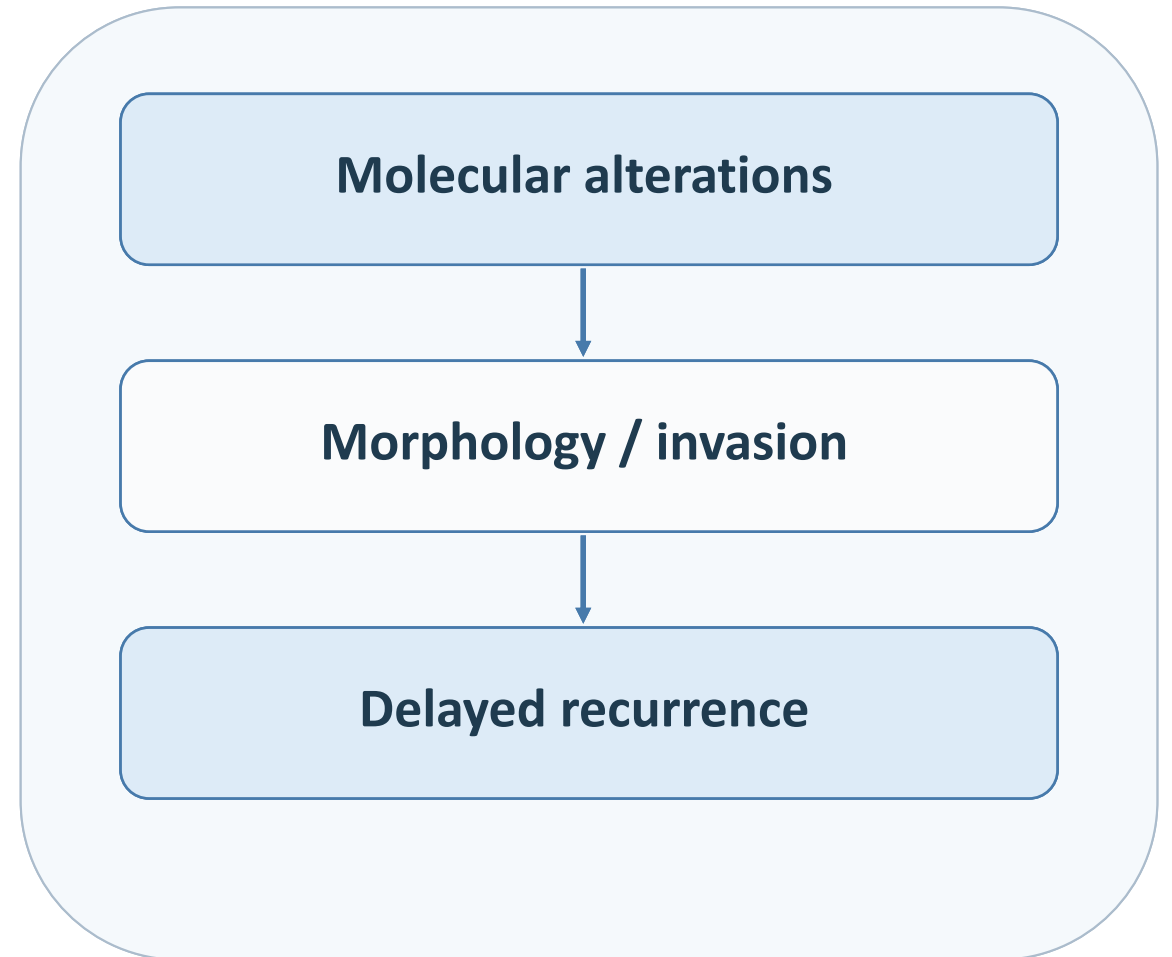


Five-year value shown as a 60%–70% range

Reported survival at specified follow-up years

Synthesis: Morphology, behavior, biology

- Cribriform/tubular/solid architecture supplies a diagnostic entry point.
- Infiltrative and perineural spread explain why growth speed is misleading.
- MYB-family rearrangements and NOTCH1 status contextualize molecular biology.
- Long follow-up is needed to understand the late recurrence burden.



Primary sources and visual provenance

- Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 16, pp. 679–683.
- ACC section: p. 682; morphology and clinical text; Fig. 16.23 described in source conversion.
- Original editable schematics constructed for teaching; none are clinical specimens.
- Original book chapter PDF and copyrighted histology panels were not supplied.