

Acinic Cell Carcinoma

Salivary gland pathology: morphology, diagnostic reasoning,
and clinical behavior

Undergraduate foundations → postgraduate diagnostic interpretation

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Learning outcomes

Define acinic cell carcinoma within salivary gland neoplasia.

Recognize serous acinar cytology and variable architectural patterns.

Identify features of high-grade transformation and their significance.

Integrate morphology, diagnostic adjuncts, and long-term outcome.

A malignancy with serous acinar differentiation

Acinic cell carcinoma is a malignant epithelial salivary gland neoplasm.

The neoplastic cells resemble normal serous acinar cells.

A bland nuclear appearance can coexist with malignant behavior.

Cell differentiation and clinical behavior must be assessed separately.

Distinctive principle: Acinar-like cytology does not imply a benign tumor.

Place among common salivary gland tumors

Benign examples	Malignant examples
Pleomorphic adenoma	Mucoepidermoid carcinoma
Warthin tumor	Acinic cell carcinoma
Oncocytoma	Adenoid cystic carcinoma
Canalicular / basal cell adenoma	Salivary duct carcinoma

Selected entities Table 16.5; Not an exhaustive classification.

Acinic cell carcinoma is uncommon

2–3%

Salivary gland tumors

Proportion attributed to acinic
cell carcinoma

>30

Histologic tumor types

Breadth of the salivary
neoplasm classification

Use source-specific denominators; Estimates vary among published series.

Most salivary gland tumors arise in major glands

65–80%

Parotid gland

All salivary gland tumors

~10%

Submandibular

All salivary gland tumors

Remainder

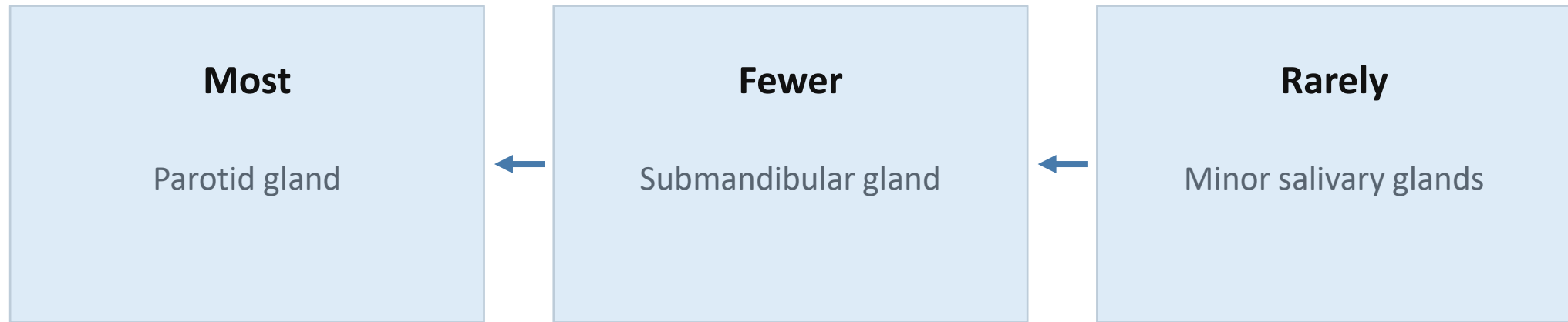
Other glands

Includes minor and sublingual
glands

Parent-section population data; Not the distribution specific to acinic cell carcinoma.

Where acinic cell carcinoma occurs

Acinic cell carcinoma favors glands containing normal serous acinar cells.



Why minor salivary glands are uncommon sites

Minor salivary glands contain relatively few normal serous acinar cells.

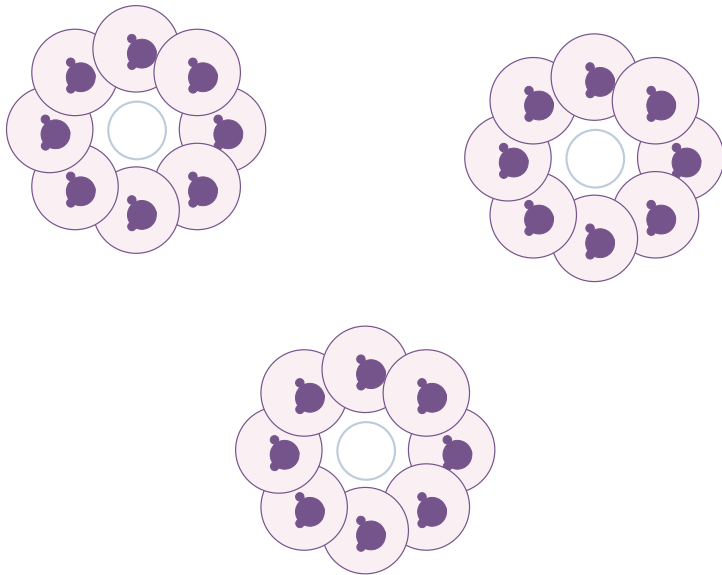
Acinic cell carcinoma recapitulates serous acinar differentiation.

Its site distribution therefore correlates with a normal cell phenotype.

This is a morphologic–anatomic association, not proof of cell of origin.

Normal serous acini: The reference phenotype

SCHEMATIC — not a histologic specimen



Normal gland architecture

Clusters of differentiated secretory acinar cells.

Round nuclei and cytoplasmic secretory granules.

Serous acinar phenotype supplies the comparison for tumor cells.

Secretory granules explain cytoplasmic basophilia

Conceptual relationship between cell differentiation and the morphologic clue.



Normal acinar cell versus neoplastic counterpart

Normal serous acinus

Cells organized into functional secretory units.

Small round nuclei; Granular cytoplasm.

Ducts, fat, and normal lobular architecture remain.

Acinic cell carcinoma

Acinar-type cells form a neoplastic proliferation.

Nuclei may remain small and monotonous.

Architectural growth patterns replace normal organization.

The decisive change is a tumor-forming proliferation—not necessarily striking nuclear atypia.

Macroscopic appearance: Typically circumscribed

Acinic cell carcinomas are generally small.

Many lesions appear well-circumscribed grossly.

A circumscribed border is not a histologic declaration of benignity.

Clinical and histologic assessment remain necessary.

Why a smooth contour can mislead

Salivary gland neoplasms may be mobile or appear clinically benign.

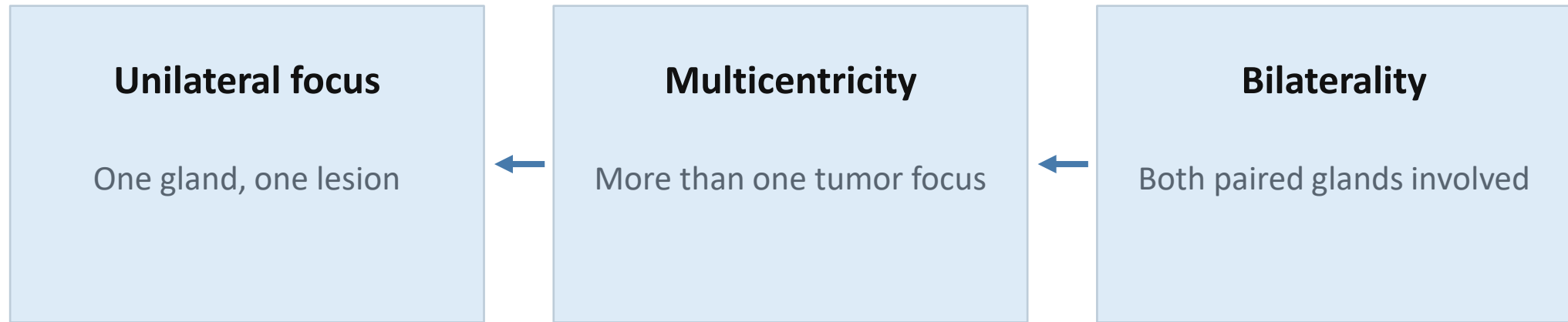
Robbins cautions that clinical criteria cannot reliably separate benign and malignant lesions.

Well-circumscribed acinic cell carcinoma illustrates this limitation.

Tissue diagnosis is required to classify the lesion.

Bilateral and multicentric presentations

Acinic cell carcinomas may be bilateral or multicentric.



Multicentricity is not the same as metastasis

Multicentricity

More than one intraglandular tumor focus.

An anatomic descriptor.

Does not itself establish nodal spread.

Metastasis

Tumor deposits at sites beyond the primary neoplasm.

Regional lymph nodes are a recognized site.

Implies dissemination rather than multiple primary foci.

Low-power architecture: Solid sheet

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Solid / sheet-like growth

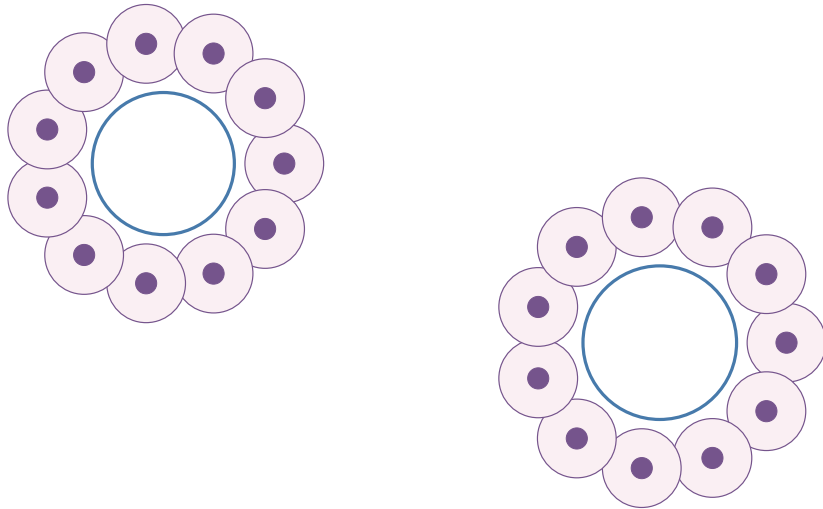
Confluent aggregates of serous-like tumor cells.

Architecture is less acinar and more sheet-like.

A solid pattern alone should not be equated with high-grade change.

Microcystic architecture: Small lumina

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Microcystic pattern

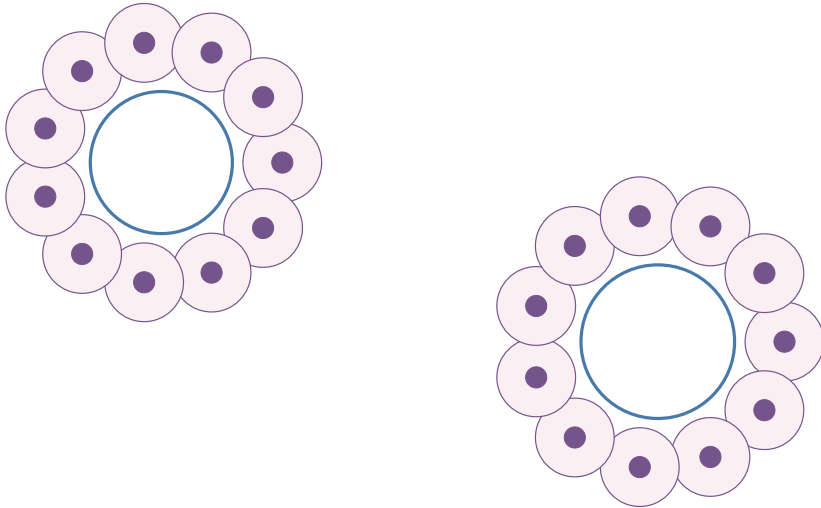
Numerous small cystlike spaces within tumor.

Acinar-type cells surround variably sized lumina.

Look for associated granules and nuclear morphology.

Glandular architecture: Formed lumina

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Glandular pattern

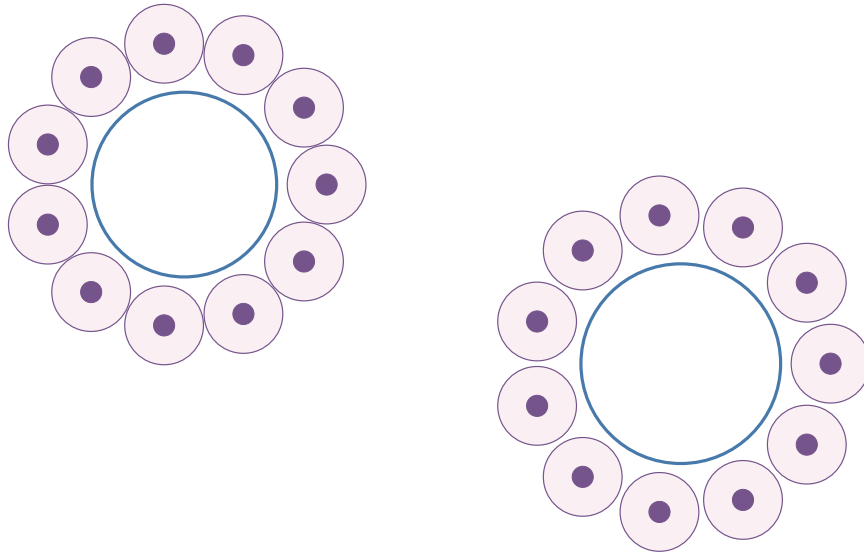
Tumor nests organize around true-looking lumina.

Gland formation is one accepted acinic carcinoma pattern.

Interpret architecture together with cytology.

Follicular architecture: Expanded spaces

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Follicular pattern

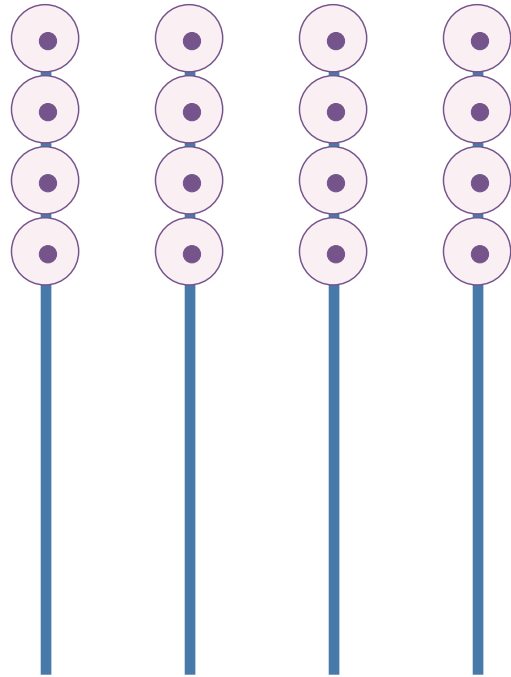
Follicle-like or cystlike profiles may occur.

Architecture is variable even within one diagnostic entity.

Compare epithelial morphology instead of relying on pattern alone.

Papillary architecture: Projecting fronds

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Papillary pattern

Epithelial projections extend into luminal spaces.

Papillary change is among the patterns listed by Robbins.

A single architectural pattern does not establish identity.

Architectural spectrum on one diagnostic map

Acinic cell carcinoma may grow as sheets, microcysts, glands, follicles, or papillae.

Architectural diversity is a defining diagnostic challenge.

Cellular evidence of serous acinar differentiation unites these patterns.

The entire lesion must be interpreted, not a single attractive field.

Five patterns: What the observer recognizes

Pattern	Primary architecture	Question to ask
Sheets	Confluent cell groups	What is the nuclear grade?
Microcysts	Multiple small spaces	Do the cells look acinar?
Glands	Epithelial lumina	What is the cytoplasm?
Follicles	Rounded spaces	Could another tumor mimic this?
Papillae	Luminal projections	Is there acinar differentiation?

Conventional tumor cytology: Acinar-like

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Low-grade cytologic profile

Small, round nuclei are common.

Cells may appear cytologically uniform.

Purple granular cytoplasm supports serous differentiation.

Nuclear findings in conventional tumors

Monotonous small round nuclei may dominate.

Nuclear uniformity must not override tumor architecture.

High-grade transformation introduces a different cytologic profile.

Examine atypia in context with mitoses and necrosis.

Granular cytoplasm: The pivotal clue

Purple cytoplasmic granules are typical in acinic cell carcinoma.

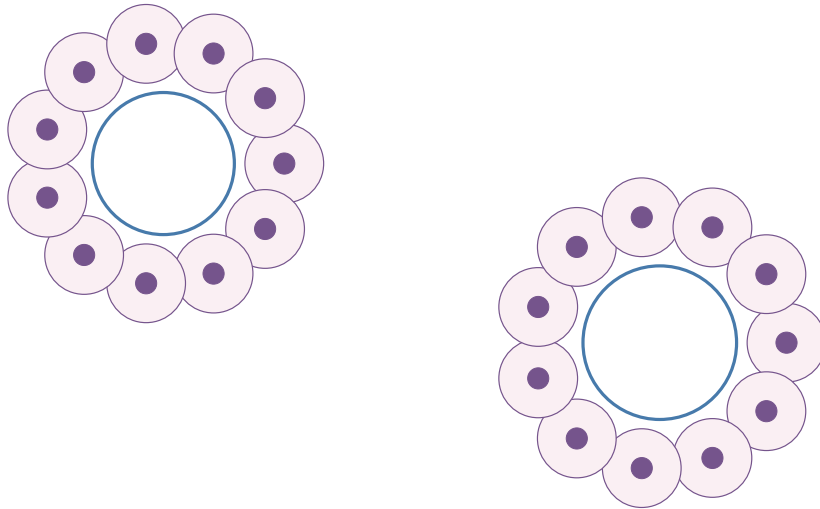
These correspond to serous zymogen granules.

Granules help connect tumor cells to a normal secretory phenotype.

Granularity can vary between tumor cells and sampled regions.

Not every tumor cell is overtly granular

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Clear / vacuolated forms

Some neoplastic cells are clear or vacuolated.

Cytoplasmic variability can coexist with acinar-like cells.

Use the architectural and nuclear context across the specimen.

Cytoplasmic alternatives within one tumor

Granular cell phenotype

Basophilic to purple intracytoplasmic granules.

Closest resemblance to normal serous acinar cells.

Provides an immediate morphologic diagnostic clue.

Clear or vacuolated phenotype

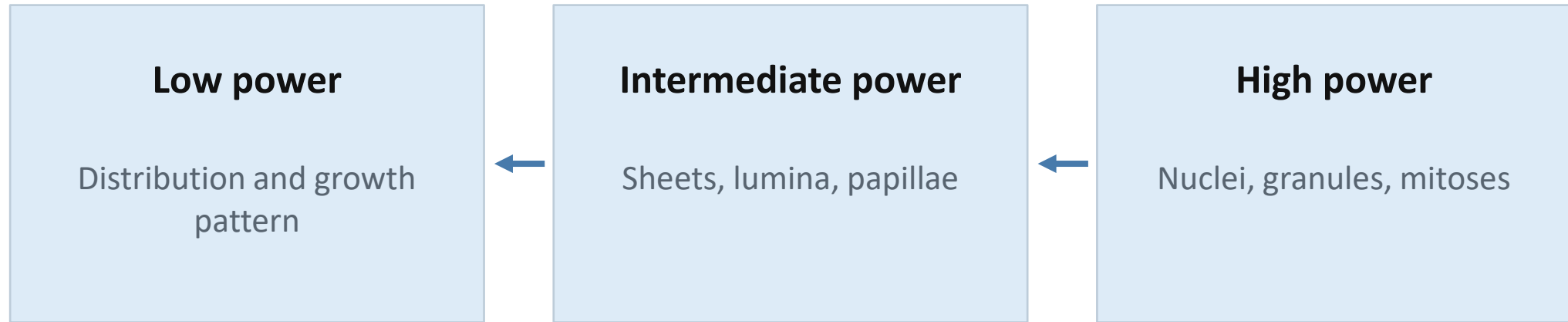
Cytoplasm appears empty or optically pale.

May be less recognizably serous at first glance.

Demands integration with remaining tumor areas.

A practical microscopic reading sequence

Integrating scale reduces overreliance on a single striking feature.



Why cytologic blandness does not exclude carcinoma

Cancer classification is not synonymous with overt anaplasia.

Acinic cell carcinoma may retain pronounced normal-cell resemblance.

Neoplastic proliferation and clinical behavior define the entity.

Diagnostic confidence comes from convergent architectural and cellular evidence.

High-grade transformation: Definition

Some tumors acquire a distinctly more aggressive microscopic phenotype.

Sheet-like growth with pleomorphism, mitoses, and necrosis.

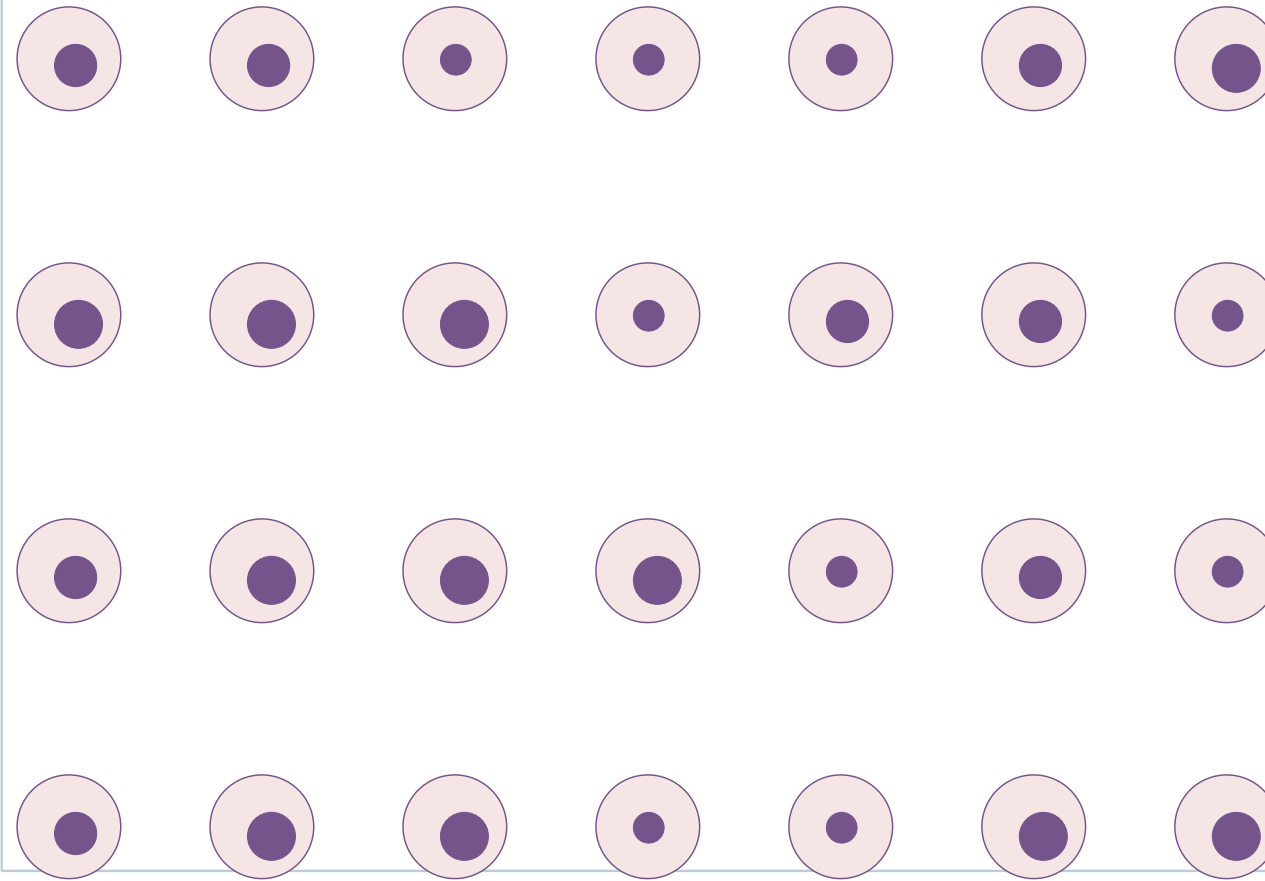
The older term “dedifferentiation” is also used.

The transformed component must be distinguished from ordinary architectural variation.

Do not equate sheet-like growth alone with high-grade transformation.

High-grade change: Altered nuclear phenotype

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High-grade appearance

Nuclear pleomorphism contrasts with the conventional monotonous nuclei.

Mitotic activity becomes an important feature.

Necrosis adds evidence of biologically aggressive growth.

Nuclear pleomorphism: Why it matters

Pleomorphism indicates variation in nuclear size and shape.

In acinic cell carcinoma it is a grade-associated feature.

Interpret heterogeneity alongside mitoses and necrosis.

This is distinct from the small, monotonous nuclei typical of conventional tumor.

Mitotic activity: A proliferative signal

Mitoses are included in the histologic grade assessment.

Increased mitotic activity contributes to concern for aggressive tumor biology.

Assess in representative areas, especially cytologically atypical regions.

Robbins does not provide a numeric mitotic cutoff for this entity.

Tumor necrosis: A significant warning feature

Necrosis is part of the Robbins high-grade morphologic profile.

It should be interpreted with nuclear pleomorphism and mitotic activity.

Necrosis is not described as a universal feature of acinic cell carcinoma.

When present, it changes the biologic interpretation of the lesion.

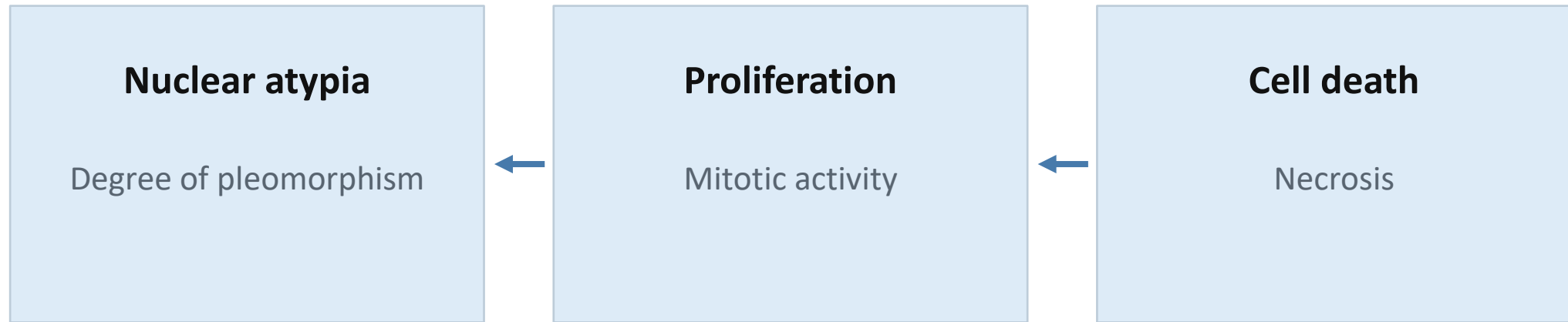
Conventional versus high-grade morphology

Feature	Conventional pattern	High-grade transformation
Nuclei	Small and round	Pleomorphic
Cytology	Often monotonous	More atypical
Growth	Several patterns	May be sheet-like
Mitoses	Not defining	Increased activity
Necrosis	Not characteristic	Can be conspicuous

Qualitative Robbins description; Not a formal numeric grading rubric.

Histologic grade integrates three warning domains

Robbins explicitly connects these features to the clinical course.



Heterogeneity creates a sampling problem

Conventional and high-grade areas may differ markedly in appearance.

Small samples may not represent the highest-grade component.

Architectural diversity can obscure a focal aggressive population.

This is a diagnostic sampling principle—not a claim about a fixed transformation frequency.

Pathology report: Essential morphologic content

Establish the definitive salivary gland tumor type.

Describe predominant architectural and cytologic differentiation.

Document nuclear atypia, mitotic activity, and necrosis.

Explicitly identify high-grade transformation if recognized.

Reporting framework shown is instructional, not a formal synoptic checklist.

Regional nodal metastatic potential

10–15%

Lymph-node metastasis

Range reported by Robbins

Uncommon

Recurrence

Following resection description

A generally favorable course does not make this tumor incapable of metastasis.

Survival: Early versus long-term follow-up

~90%

Five-year survival

Reported

~60%

Twenty-year survival

Reported

These are source-specific summary estimates, not individualized patient predictions.

What long-term survival figures teach

An excellent five-year figure does not capture the full time horizon.

The difference between five- and twenty-year estimates emphasizes prolonged follow-up.

Survival depends on patient and disease factors not quantified in this excerpt.

Do not extrapolate these rates to an individual case without staging/context.

Histology connects directly with prognosis

The clinical course reflects degree of pleomorphism, mitoses, and necrosis.

High-grade transformation changes the risk interpretation.

Metastases can occur even though postoperative recurrence is uncommon overall.

Clinical assessment must remain linked to microscopic grade.

Acinic carcinoma versus mucoepidermoid carcinoma

Acinic cell carcinoma

Serous acinar resemblance; Purple granules.

Sheets, microcysts, glands, follicles, papillae.

Parotid predominance.

Mucoepidermoid carcinoma

Mucous, squamous, and intermediate tumor cells.

Cords, sheets, cysts; Variable histologic grades.

Most common primary malignant salivary tumor.

Acinic carcinoma versus adenoid cystic carcinoma

Acinic cell carcinoma

Acinar-like granular tumor cytoplasm.

Diverse epithelial growth patterns.

Regional nodal metastasis in a subset.

Adenoid cystic carcinoma

Cribriform or solid patterns; Hyaline material.

Predilection for perineural invasion.

Distant relapse can arise many years later.

Acinic carcinoma versus Warthin tumor

Acinic cell carcinoma

Malignant salivary epithelial neoplasm.

Serous acinar cytology.

Can be bilateral or multicentric.

Warthin tumor

Benign tumor usually found in the parotid.

Double oncocytic epithelium on lymphoid stroma.

Can also be bilateral or multifocal.

Bilateral or multifocal presentation alone is not a diagnostic discriminator.

Differential diagnosis: Choose the discriminating clue

Entity	Architectural / cytologic clue	Clinical-pathologic emphasis
Acinic cell carcinoma	Serous-type granules; Round nuclei	May be well-circumscribed
Mucoepidermoid carcinoma	Mucous + squamous + intermediate cells	Histologically graded
Adenoid cystic carcinoma	Cribriform spaces / hyaline material	Perineural invasion
Warthin tumor	Oncocytic bilayer + lymphoid stroma	Benign; Multifocal possible

Differential diagnosis: Common reasoning traps

A bland tumor cannot automatically be labeled benign.

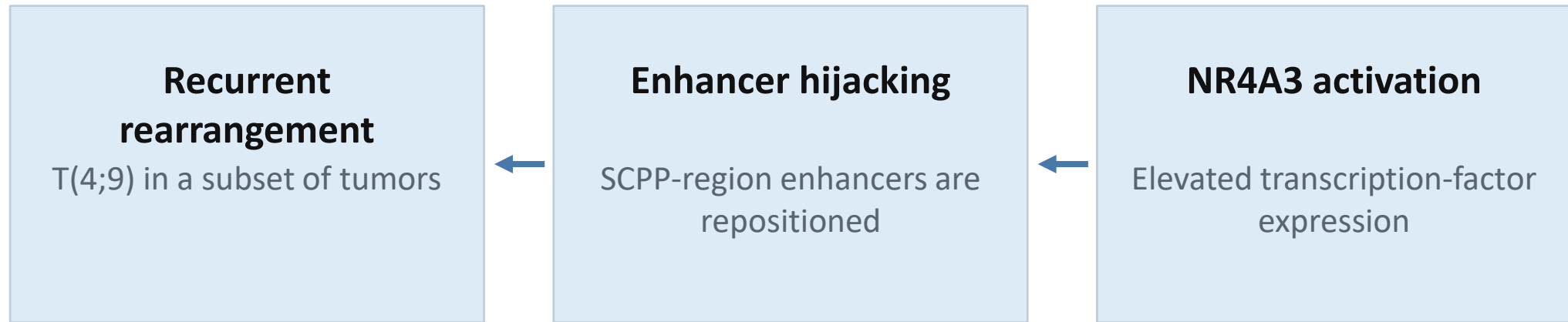
Microcysts or solid sheets are not exclusive to acinic cell carcinoma.

Multifocality overlaps with Warthin tumor.

The decisive evidence is an integrated pattern of differentiation.

Molecular mechanism: NR4A3 upregulation

Chromosomal rearrangement can reposition a regulatory enhancer near NR4A3.



NR4A3 immunostaining: Diagnostic support

Nuclear NR4A3 expression supports acinic cell carcinoma.

An immunohistochemistry study reported positivity in 34 of 37 tumors.

Moderate-to-strong/diffuse nuclear staining was especially informative.

Interpret the stain with morphology and laboratory-specific validation.

NR4A3 performance: One published cohort

92%

Sensitivity

34 of 37 AciCC cases in one
study

97%

Specificity

Among 120 non-AciCC salivary
tumors

Study-specific diagnostic accuracy; Not a universal laboratory cutoff.

A negative NR4A3 stain does not exclude AciCC

Three acinic cell carcinomas were IHC-negative in the Wong et al. Cohort.

Morphology and other corroborating findings remained important.

Interpret weak or focal positivity cautiously.

Antibody performance and positivity criteria vary by study.

DOG1 and PAS-D: Interpret as adjuncts

DOG1 may show a canalicular or membranous pattern, but lacks absolute specificity.

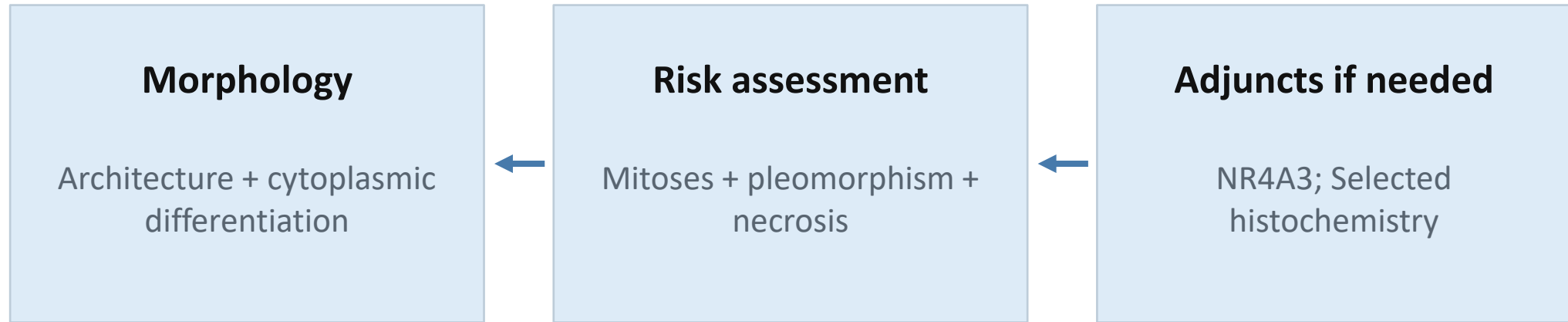
PAS-positive, diastase-resistant cytoplasmic granules can support serous differentiation.

Neither test replaces the architectural and cytologic diagnosis.

On limited cytology specimens, normal acini may mimic the tumor.

Diagnostic integration: Avoid the single-test trap

Slide combines textbook morphology with separately published immunodiagnostic evidence.



Exercise: Well-circumscribed parotid lesion

A parotid mass is well-defined. Histology reveals serous acinar-like tumor cells with monotonous round nuclei and purple granules.

Reason through the findings

Can gross circumscription exclude carcinoma?

Which microscopic feature anchors the provisional diagnosis?

Interpretation: Acinic cell carcinoma remains likely; Acinar-type granularity matters more than a smooth edge.

Exercise: A deceptively bland microscopic field

A small biopsy shows numerous uniform round nuclei and granular cytoplasm. In a second region, the same lesion forms solid sheets.

Reason through the findings

Which observations are compatible with acinic cell carcinoma?

What must be checked before calling high-grade transformation?

Interpretation: Seek pleomorphism, mitotic activity, and necrosis; Sheets alone are insufficient.

Exercise: Tumor with clear/vacuolated cells

A salivary gland neoplasm shows microcysts and many pale, vacuolated cells; Scattered areas resemble granular serous acini.

Reason through the findings

Which phenotype supports the diagnosis?

Why is evaluation of multiple areas useful?

Interpretation: The granular acinar-like areas support AciCC; Cytoplasm varies across the tumor.

Exercise: Interpreting an adverse focus

Most of a tumor has small, monotonous nuclei; A distinct area displays marked pleomorphism, mitoses, and necrosis.

Reason through the findings

How should the component be interpreted?

Why is it important for risk assessment?

Interpretation: This profile supports high-grade transformation, linked to a different clinical course.

Exercise: Bilateral parotid masses

Two lesions are found in paired parotid glands. A histologic section shows serous acinar-type tumor cells.

Reason through the findings

Does bilaterality rule out malignancy?

Which benign tumor also can be bilateral?

Interpretation: Bilaterality occurs in AciCC and Warthin tumor; Cytology separates the entities.

Exercise: Long-term counseling logic

A lecture reports approximately 90% five-year survival, but approximately 60% twenty-year survival for acinic cell carcinoma.

Reason through the findings

Why is five-year survival an incomplete description?

What caveat applies to population rates?

Interpretation: Late outcomes matter; Source-level rates are not individualized prognostic estimates.

Exercise: Choosing a molecular adjunct

A salivary gland lesion has suggestive acinar cytology, but the diagnosis remains uncertain on limited material.

Reason through the findings

Which nuclear immunostain may support acinic cell carcinoma?

Does a negative result conclusively exclude the entity?

Interpretation: NR4A3 is a useful adjunct; Negative staining cannot conclusively exclude AciCC.

Diagnostic summary: Three decisive domains

Identity: Malignant tumor with serous acinar cell differentiation.

Morphology: Variable architecture plus small round nuclei and often granular cytoplasm.

Behavior: High-grade change includes pleomorphism, mitoses, and necrosis.

Risk: Regional lymph-node spread occurs; Long-term outcome remains relevant.

What should be retained for practice

Do not diagnose benignity from gross circumscription or bland nuclei.

Examine multiple architectural patterns and cytoplasmic phenotypes.

Explicitly assess for high-grade transformation.

Use NR4A3 as a supported adjunct, not a substitute for morphology.

References and further reading

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 16, pp. 679–683.

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