

Cystic Neoplasms

Pancreatic pathology

Morphology · molecular profiles · malignant potential

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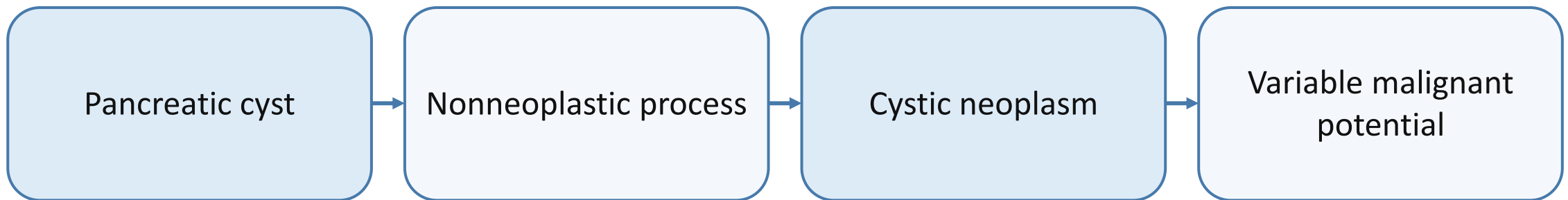
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Learning objectives

- Discriminate nonneoplastic cysts from pancreatic cystic neoplasms.
- Recognize defining morphology and anatomical patterns of four major neoplastic groups.
- Relate recurrent mutations to diagnostic differentiation and malignant potential.
- Explain when a noninvasive mucinous lesion becomes clinically important.

Pancreatic cysts form a biologically mixed group



Conceptual pathway; Arrows denote stated biological or clinical relationships.

Only a minority of pancreatic cysts are neoplastic

5%–15%

Of pancreatic cysts are neoplastic

<5%

Of pancreatic neoplasms are cystic

Four major pancreatic cystic neoplasms

Serous cystic neoplasm

Microcysts · clear fluid · VHL

Mucinous cystic neoplasm

Mucin + ovarian stroma · KRAS / RNF43

Intraductal papillary mucinous neoplasm

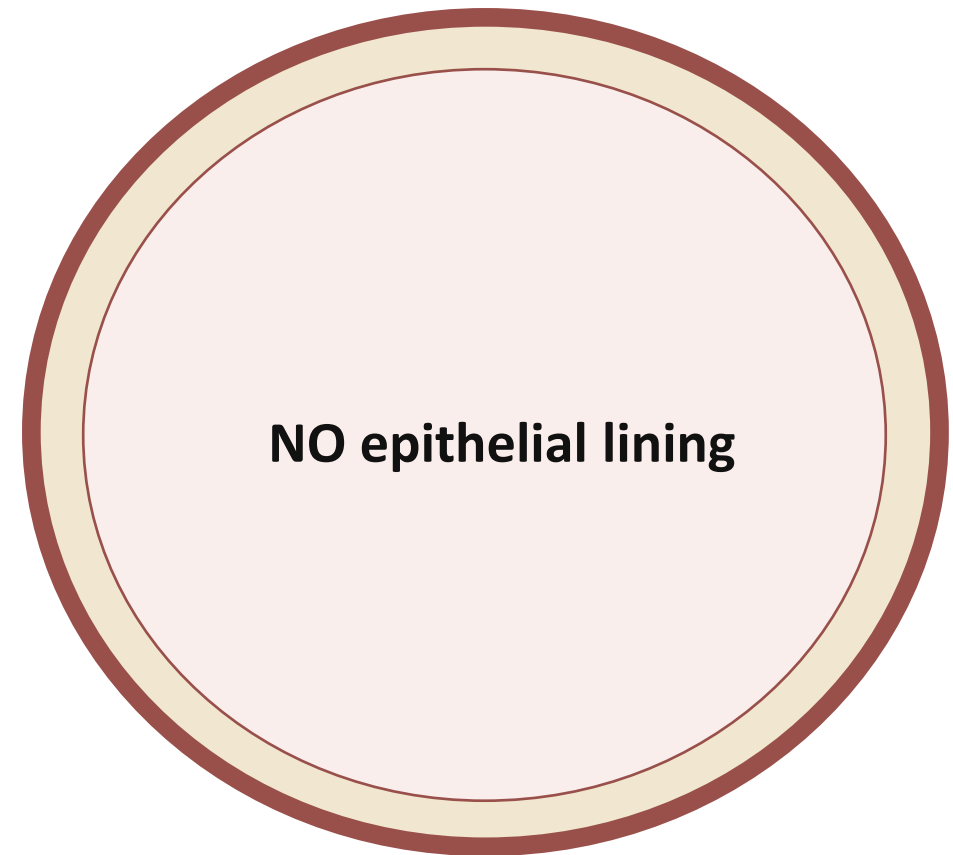
Duct-centered mucin · GNAS

Solid pseudopapillary neoplasm

Solid–cystic · hemorrhage · CTNNB1

A pancreatic pseudocyst is not a cystic neoplasm

- Pseudocysts result from walled-off hemorrhagic fat necrosis.
- The wall contains fibrosis and granulation tissue, not a true epithelial lining.
- An epithelial-lined neoplasm must not be confused with a pseudocyst.

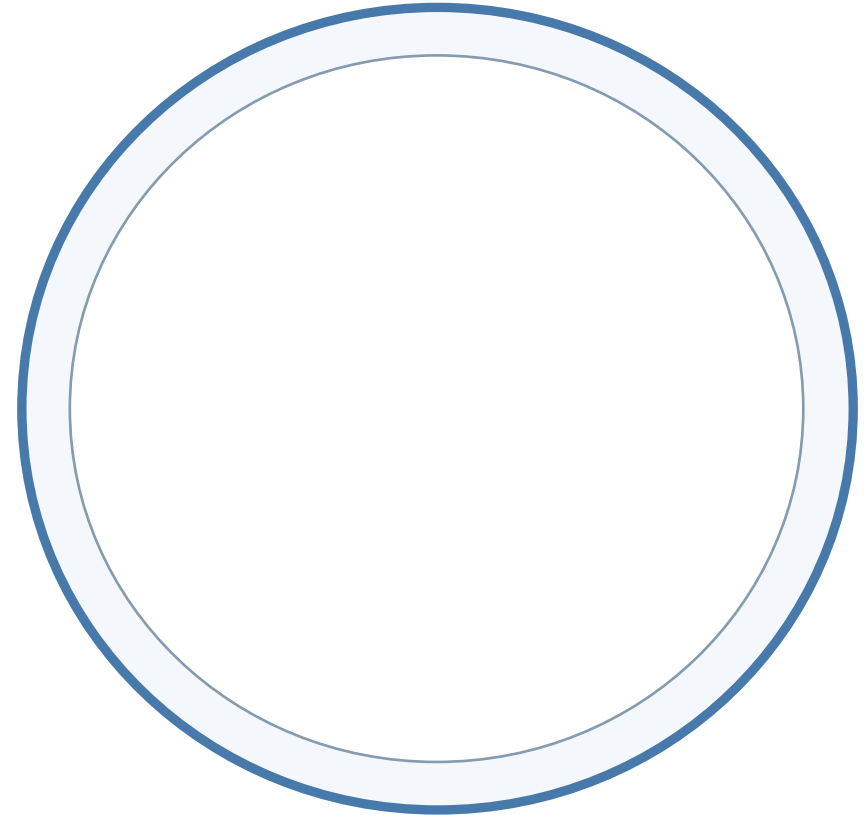


Granulation / fibrous wall

Schematic · not a clinical or histologic specimen

Congenital cysts provide a second comparator

- Congenital pancreatic cysts can be lined by cuboidal or attenuated epithelium.
- They are typically thin-walled and contain clear serous fluid.
- A true epithelial lining does not by itself imply a neoplasm.



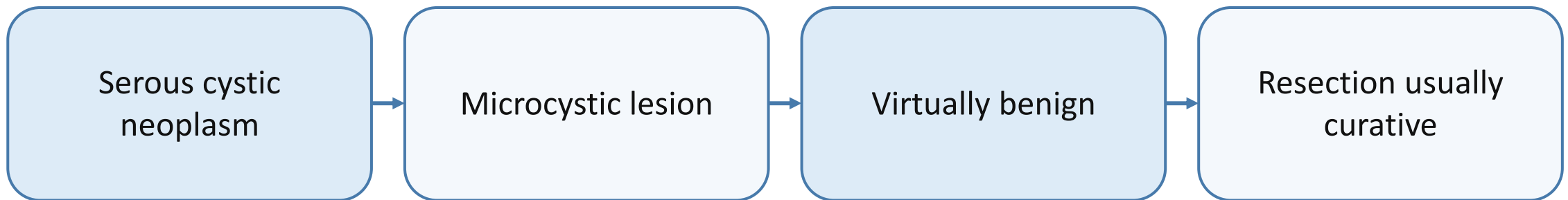
Thin epithelial lining

Schematic · not a clinical or histologic specimen

Four observations guide morphological classification

Entity	Architecture	Cyst contents	Key tissue clue
SCN	Microcysts	Clear fluid	Glycogen-rich cells
MCN	Large cysts	Thick mucin	Ovarian-type stroma
IPMN	Dilated ducts	Mucin	Main / branch ducts
SPN	Solid + cystic	Hemorrhagic	Pseudopapillae

Serous cystic neoplasms are nearly always benign



Conceptual pathway; Arrows denote stated biological or clinical relationships.

SCN: Demographic distribution

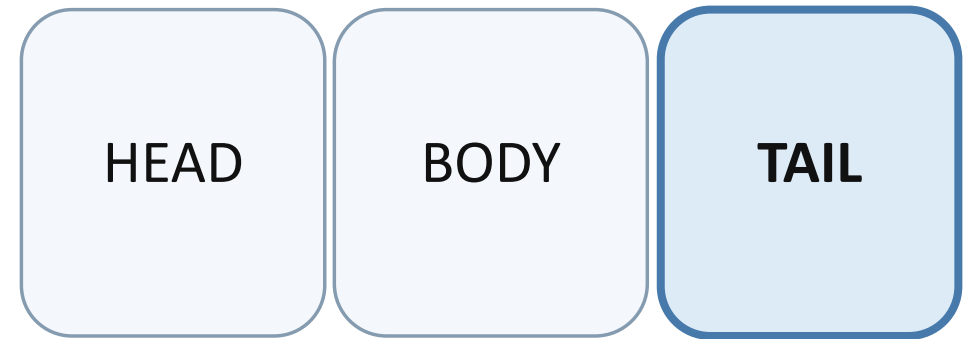
- Serous lesions represent 15%–25% of all pancreatic cystic neoplasms.
- They occur about twice as often in females as in males.
- Typical clinical presentation is in the sixth to seventh decades.

15%–25%

Of pancreatic cystic neoplasms

SCN: Characteristic pancreatic location

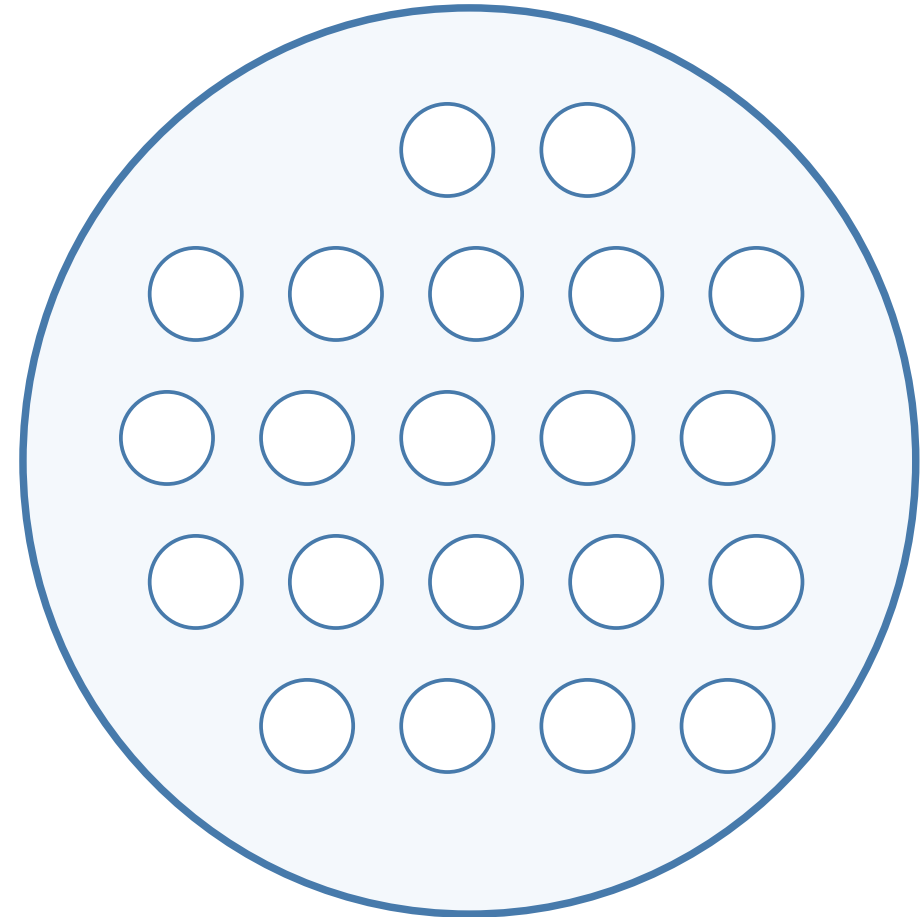
- SCNs usually occur in the pancreatic tail.
- Location is supportive rather than independently diagnostic.
- Demographics, imaging architecture and epithelial phenotype must be integrated.



Conceptual head–body–tail orientation (not anatomical scale)

SCN: Microcystic honeycomb architecture

- Individual cysts are usually small: Approximately 1–3 mm.
- Cysts may be solitary, multiple or arranged as a honeycomb of microcysts.
- The small-cyst pattern contrasts with the larger cavities of MCN.

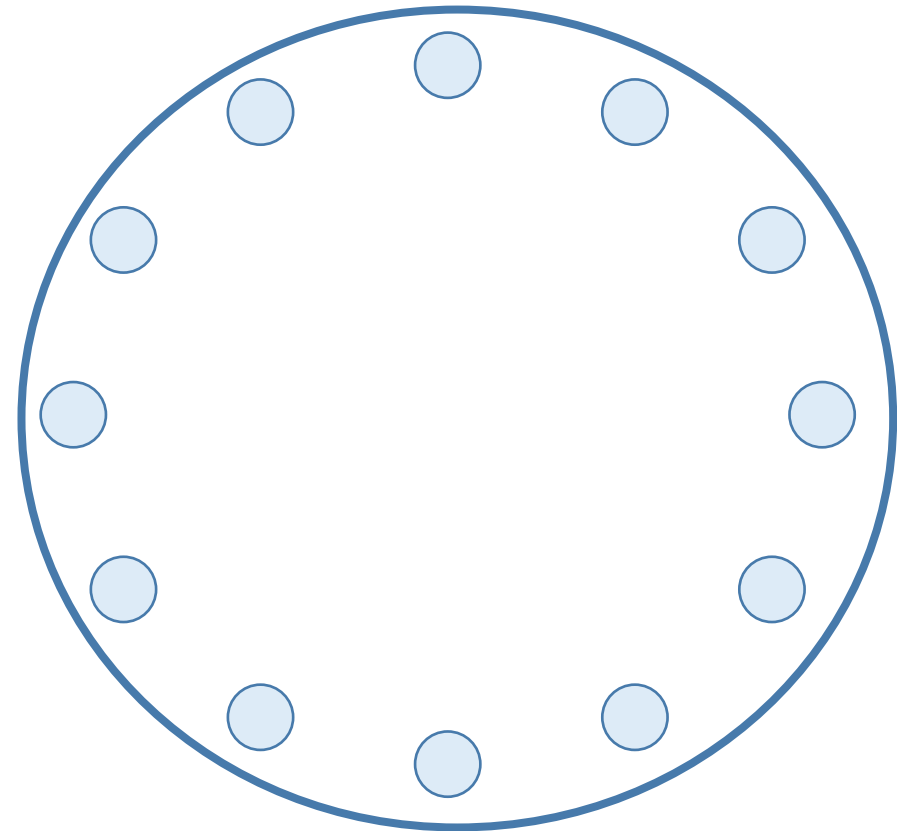


Small, crowded cavities

Schematic · not a clinical or histologic specimen

SCN: Glycogen-rich epithelial cells

- Serous cavities are lined by cuboidal epithelium.
- The neoplastic lining cells contain abundant glycogen.
- The cited illustration describes bland cuboidal cells without atypia.



Cuboidal, glycogen-rich cells

Schematic · not a clinical or histologic specimen

SCN: Clear, watery cyst contents

- Serous cysts contain thin, clear, straw-colored

SCN

Clear, thin, straw-colored fluid

MCN

Thick, tenacious mucin

mucin

SCN: VHL inactivation is the characteristic alteration

- Inactivation of the VHL tumor suppressor gene is most common.
- The VHL locus is on chromosome 3p.
- This profile contrasts with KRAS-, RNF43- and GNAS-associated mucinous lesions.

VHL

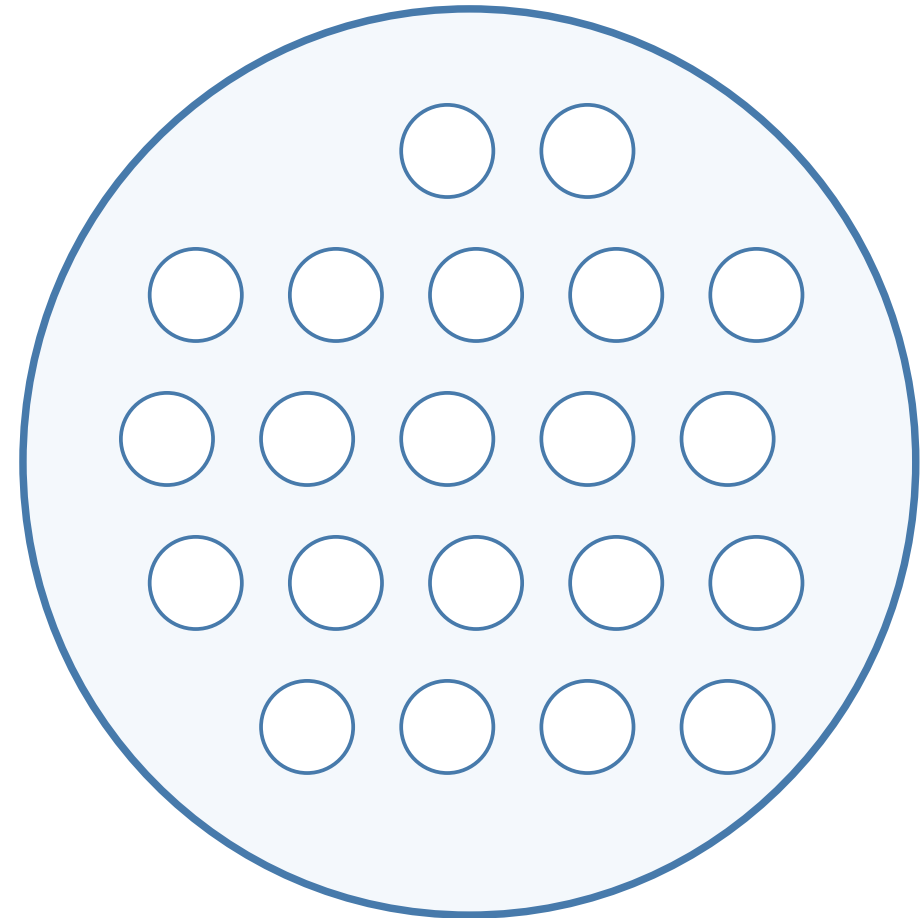
Most common SCN genetic abnormality

SCN: Incidental discovery is common

- Many serous lesions are found on imaging performed for another reason.
- Others cause nonspecific abdominal pain.
- Symptoms alone do not differentiate benign SCN from a precursor lesion.

SCN: Clinicopathologic synthesis

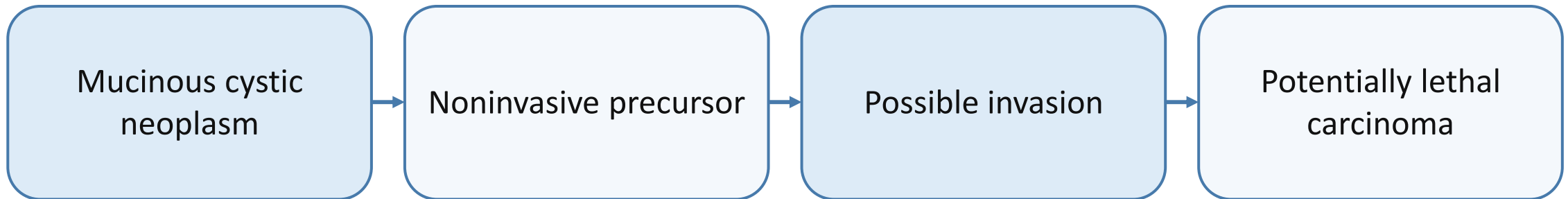
- Typical pattern: Older patient, tail-based microcystic lesion and clear fluid.
- Bland glycogen-rich cuboidal lining reinforces the diagnosis.
- A VHL-centered molecular profile is distinct from the mucinous neoplasms.



Small, crowded cavities

Schematic · not a clinical or histologic specimen

MCN is a genuine precursor to invasive carcinoma



Conceptual pathway; Arrows denote stated biological or clinical relationships.

MCN has a marked female predominance

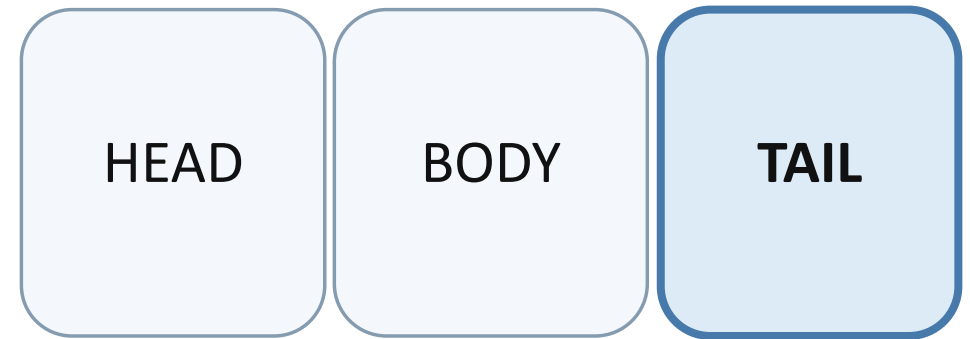
- Nearly 95% of MCNs arise in females.
- This striking distribution contrasts with IPMN, which is more frequent in males.
- Sex is supportive clinical evidence, not a histologic diagnostic criterion.

≈95%

Of MCNs arise in females

MCN commonly arises in the pancreatic tail

- Most MCNs arise in the tail of the pancreas.
- The same broad location is common for SCN: Additional features must distinguish them.
- IPMN, by contrast, tends to involve the pancreatic head.



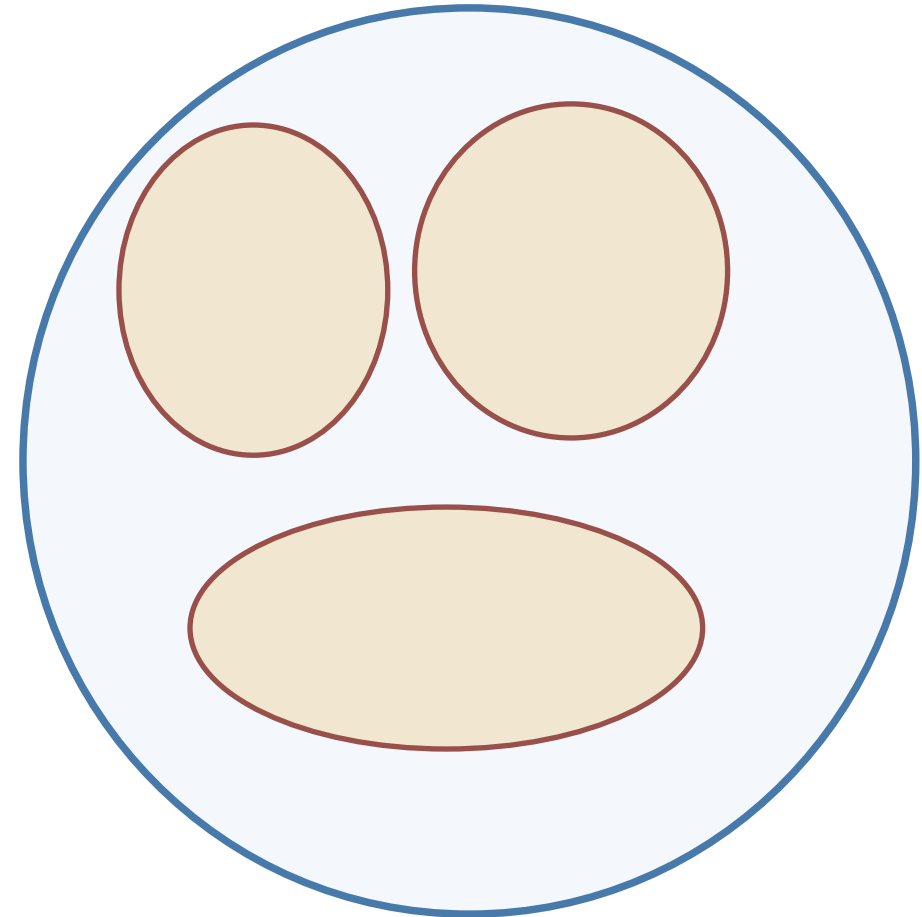
Conceptual head–body–tail orientation (not anatomical scale)

MCN commonly presents as a slow-growing mass

- Mucinous lesions may present as painless, slow-growing pancreatic masses.
- Absence of pain does not establish innocuous biology.
- Gross and microscopic architecture determine the distinctive diagnosis.

MCN: Larger cystic cavities

- MCN cavities are generally larger than serous microcysts.
- The lesion may be multiloculated and arises commonly in the pancreatic tail.
- A large-cyst appearance supports, but does not independently prove, MCN.



Large mucin-filled cavities

Schematic · not a clinical or histologic specimen

MCN: Viscous luminal mucin

- The cavities are filled with thick, tenacious

Serous contents

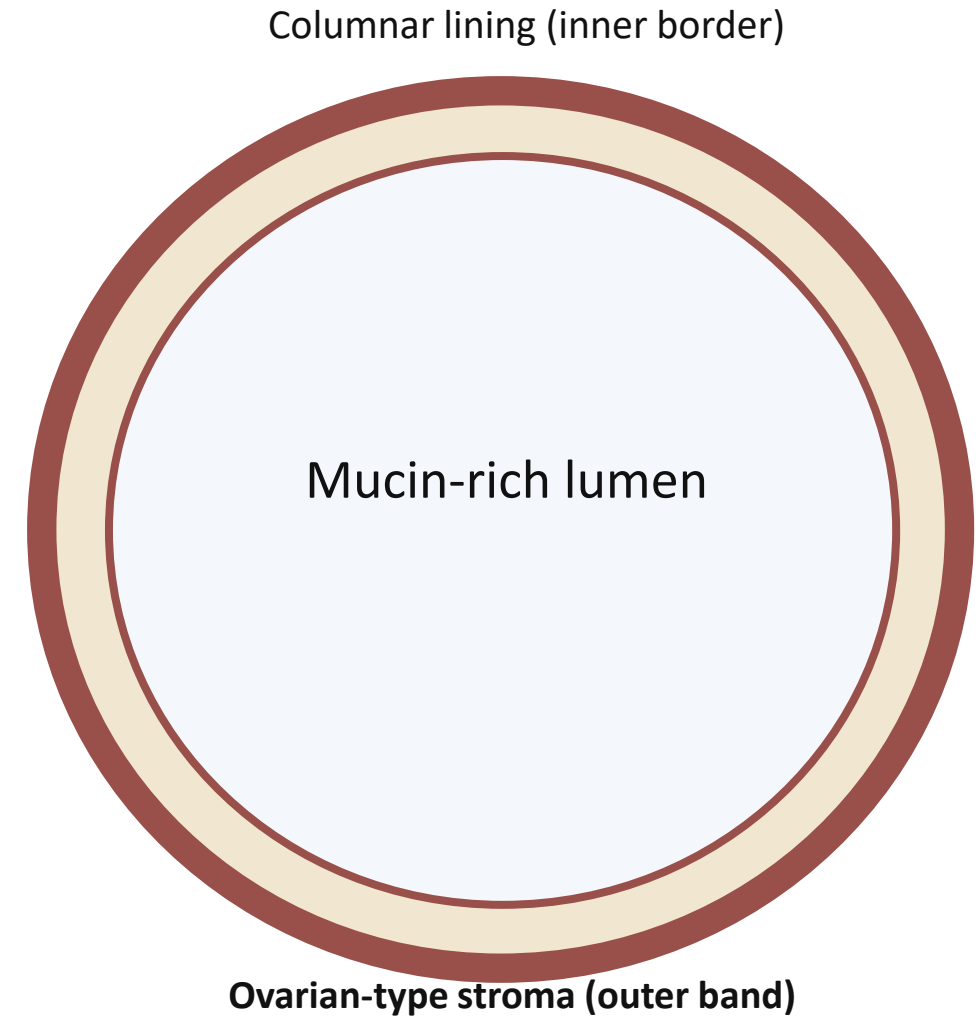
Watery / straw-colored

Mucinous contents

Viscous / tenacious

MCN: Columnar mucin-producing epithelium

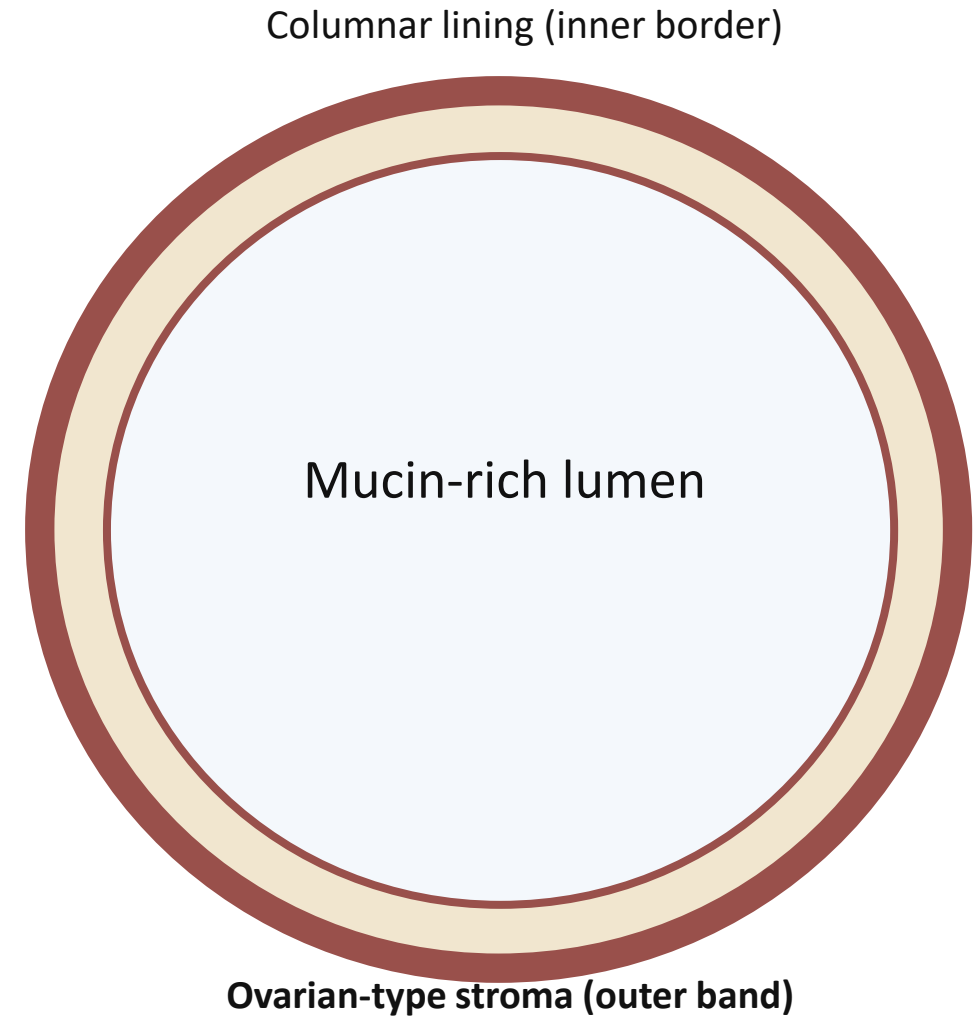
- A columnar mucinous epithelial lining is a defining morphological component.
- The lining must be interpreted with the underlying stromal phenotype.
- Invasive carcinoma, if present, changes biological classification and prognosis.



Schematic · not a clinical or histologic specimen

MCN: Ovarian-type stroma is a decisive feature

- Dense stroma resembling ovarian stroma supports MCN.
- The combination of mucinous lining and ovarian-type stroma distinguishes MCN from IPMN.
- IPMN lacks the dense ovarian-type stroma of MCN.



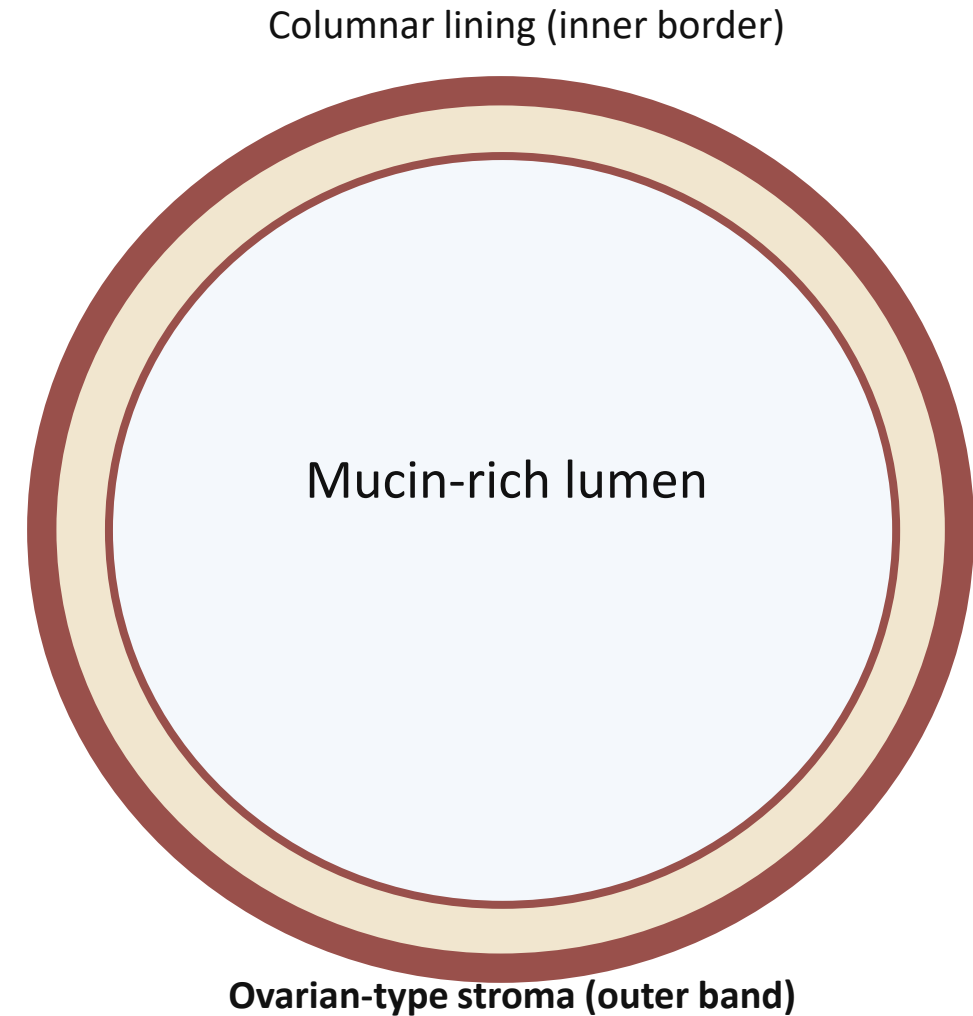
Schematic · not a clinical or histologic specimen

MCN: Stromal immunophenotype

Marker	Compartment	Interpretive role
Estrogen receptor	Ovarian-type stroma	Supports stromal phenotype
Progesterone receptor	Ovarian-type stroma	Supports stromal phenotype
Inhibin	Ovarian-type stroma	Supports stromal phenotype

MCN: Integrate two essential tissue components

- Mucin-producing columnar epithelium forms the cyst lining.
- Dense ovarian-type stroma forms the characteristic supporting tissue.
- Neither pancreatic tail location nor mucin alone substitutes for the composite morphology.



Schematic · not a clinical or histologic specimen

MCN: Invasion can already be present at detection

- Up to one-third of MCNs harbor an invasive adenocarcinoma.
- A neoplasm containing invasion is distinct from a noninvasive precursor.
- This is why assessment for invasive growth is central to specimen evaluation.

Up to $\frac{1}{3}$

May harbor invasive
adenocarcinoma

MCN: Prognosis changes with invasive carcinoma

Noninvasive

Resection is curative

Up to 50%

5-year mortality with invasive cancer

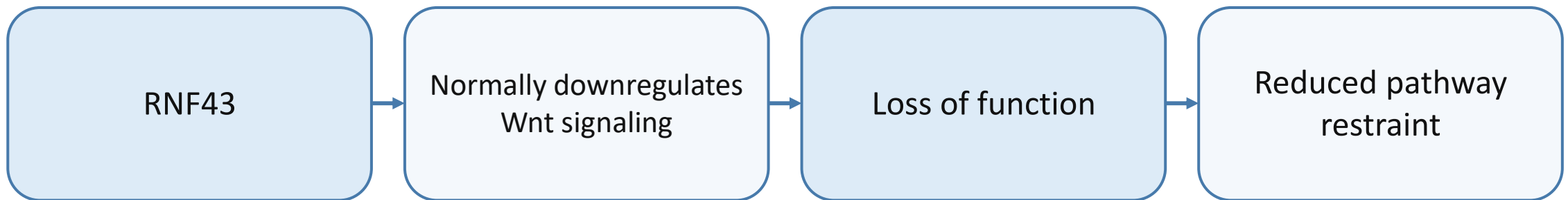
MCN: KRAS is a common early-profile alteration

- Oncogenic KRAS mutations occur in approximately half of MCNs.
- KRAS is part of the MCN-associated molecular profile.
- KRAS alteration alone is not specific enough to replace morphology.

KRAS

Mutated in approximately half of
MCNs

MCN: RNF43 loss is another recurrent alteration



Conceptual pathway; Arrows denote stated biological or clinical relationships.

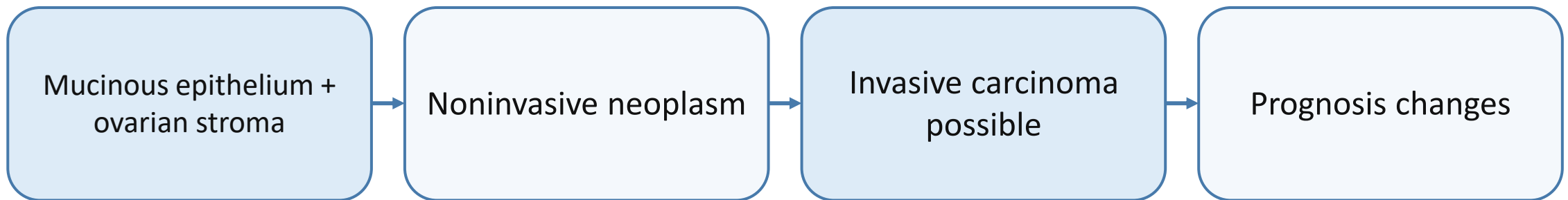
MCN: TP53 and SMAD4 accompany invasive disease

- TP53 and SMAD4 mutations are typically seen in invasive neoplasms arising from MCN.
- Their association with invasion differs from frequent KRAS mutations in MCNs.
- The source supports this association; It does not provide a deterministic gene sequence.

TP53 · SMAD4

Typically associated with invasive
MCN-derived carcinoma

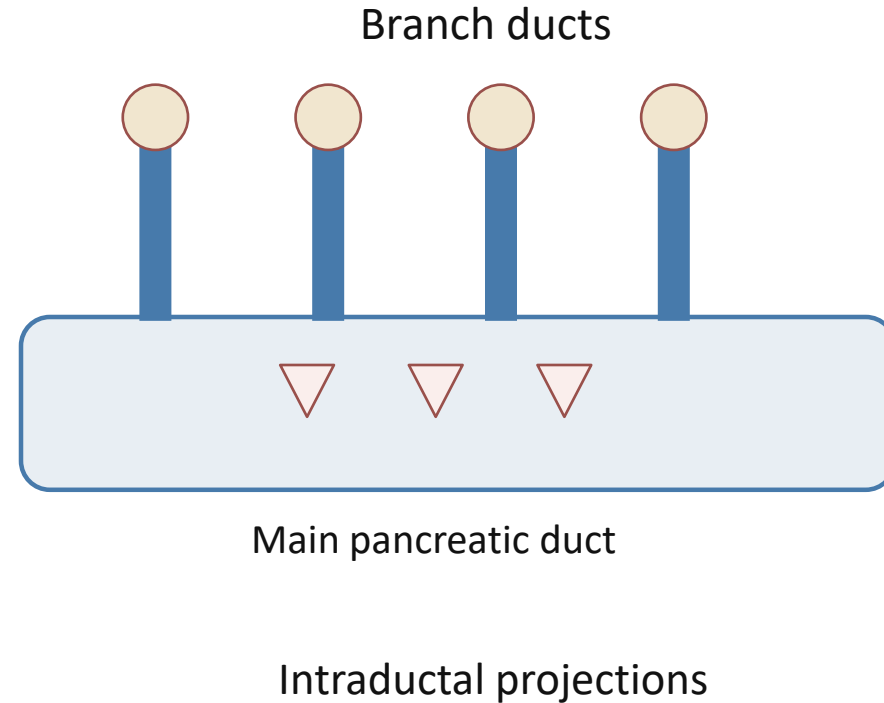
MCN: The clinical turning point is invasion



Conceptual pathway; Arrows denote stated biological or clinical relationships.

IPMN is an intraductal mucin-producing neoplasm

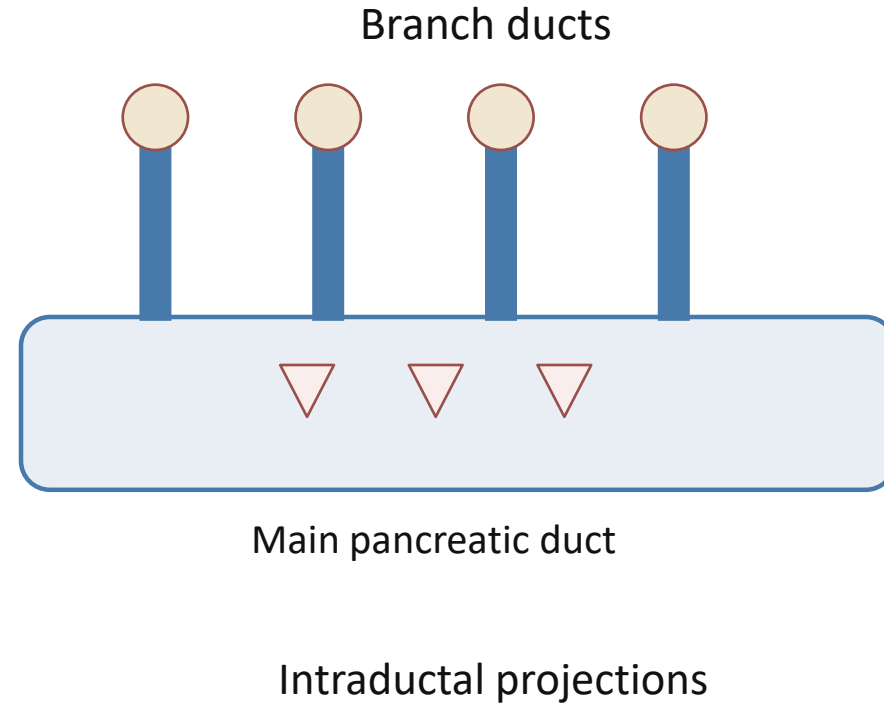
- Intraductal papillary mucinous neoplasms involve the larger pancreatic ducts.
- Their relationship to main or branch ducts is a defining anatomical feature.
- This duct-centered pattern distinguishes them from MCN.



Schematic · not a clinical or histologic specimen

IPMN can involve main or branch pancreatic ducts

- IPMN arises in the main pancreatic duct or one of its branch ducts.
- Duct dilatation and intraductal epithelial growth form the conceptual architecture.
- Mucinous character alone cannot distinguish IPMN from MCN.



Schematic · not a clinical or histologic specimen

IPMN differs from MCN in sex and regional bias

- IPMNs arise more frequently in males

IPMN

More common in males · head preference

MCN

~95% female · tail preference

IPMN can be multifocal

- Up to 20% of IPMNs are multifocal.
- The possibility of multiple lesions reflects their intraductal disease pattern.
- The source does not specify a required imaging or surgical surveillance protocol.

Up to 20%

IPMNs may be multifocal

IPMN lacks MCN-type ovarian stroma

- The absence of dense ovarian-type stroma is

MCN

Mucinous lining + ovarian-type
stroma

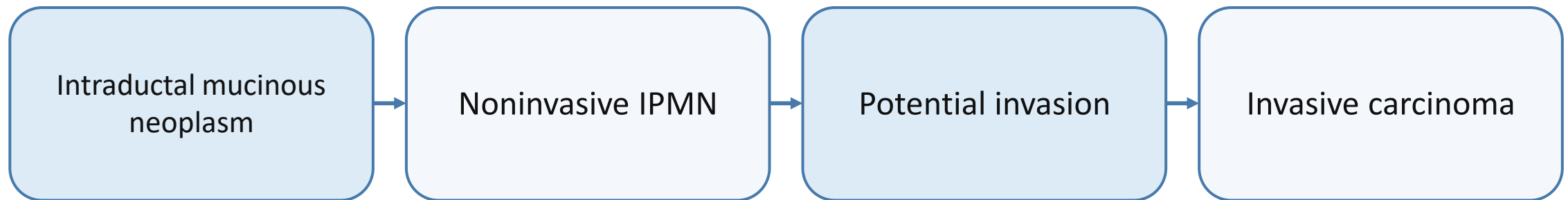
nt of

IPMN

Mucinous epithelium + duct
involvement

;

IPMN: Progression to invasion is the main hazard



Conceptual pathway; Arrows denote stated biological or clinical relationships.

IPMN: KRAS alterations are frequent

- Oncogenic KRAS mutations occur in approximately 80% of IPMNs.
- This is more frequent than the approximately half of MCNs cited in the text.
- Shared KRAS mutations do not erase distinctive tissue architecture.

KRAS

Mutated in approximately 80% of
IPMNs

IPMN: RNF43 loss recurs

- Loss-of-function RNF43 mutations occur in up to 50% of IPMNs.
- These alterations also occur in MCNs.
- RNF43 is therefore shared across mucinous neoplasms, not specific to IPMN.

RNF43

Loss-of-function in up to 50% of
IPMNs

IPMN: BRAF alterations form an additional subset

- BRAF alterations occur in approximately 10% of IPMNs.
- Their reported presence broadens the IPMN molecular spectrum.
- This figure is a source-reported frequency, not a diagnostic threshold.

BRAF

Altered in approximately 10% of
IPMNs

IPMN: GNAS is a major discriminating signature

- Oncogenic GNAS mutations occur in approximately two-thirds of IPMNs.
- GNAS encodes the α subunit of the stimulatory G protein (G α s).
- The Robbins excerpt states these mutations are not found in other pancreatic cysts.

GNAS

Approximately two-thirds of IPMNs;
Distinguished in source

IPMN: TP53 and SMAD4 are invasion-associated

- TP53 and SMAD4 mutations typically occur with transition to invasive cancer.
- This is analogous to the invasion-associated pattern described for MCN.
- The mutation association should not be presented as a complete staging system.

TP53 · SMAD4

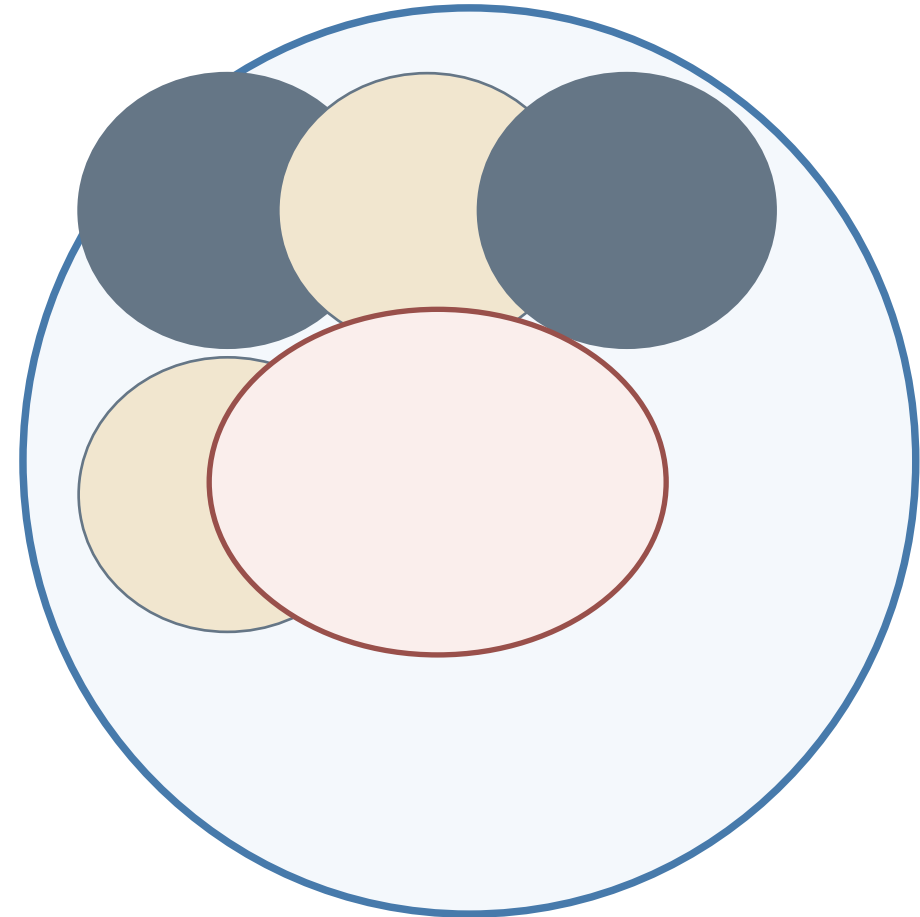
Typically associated with invasive
transition

IPMN: Shared versus distinguishing alterations

Alteration	MCN	IPMN
KRAS	≈50%	≈80%
RNF43	Up to ⅓	Up to 50%
GNAS	Not reported as typical	≈⅔; Highlighted as distinctive
TP53 / SMAD4	Usually with invasion	Usually with invasion

SPN is a distinctive, uncommon pancreatic tumor

- Solid pseudopapillary neoplasms are uncommon.
- They differ from secretory cystic neoplasms because both solid and cystic components are typical.
- The diagnosis integrates characteristic architecture and a distinct CTNNB1 profile.



Solid areas + hemorrhagic cyst

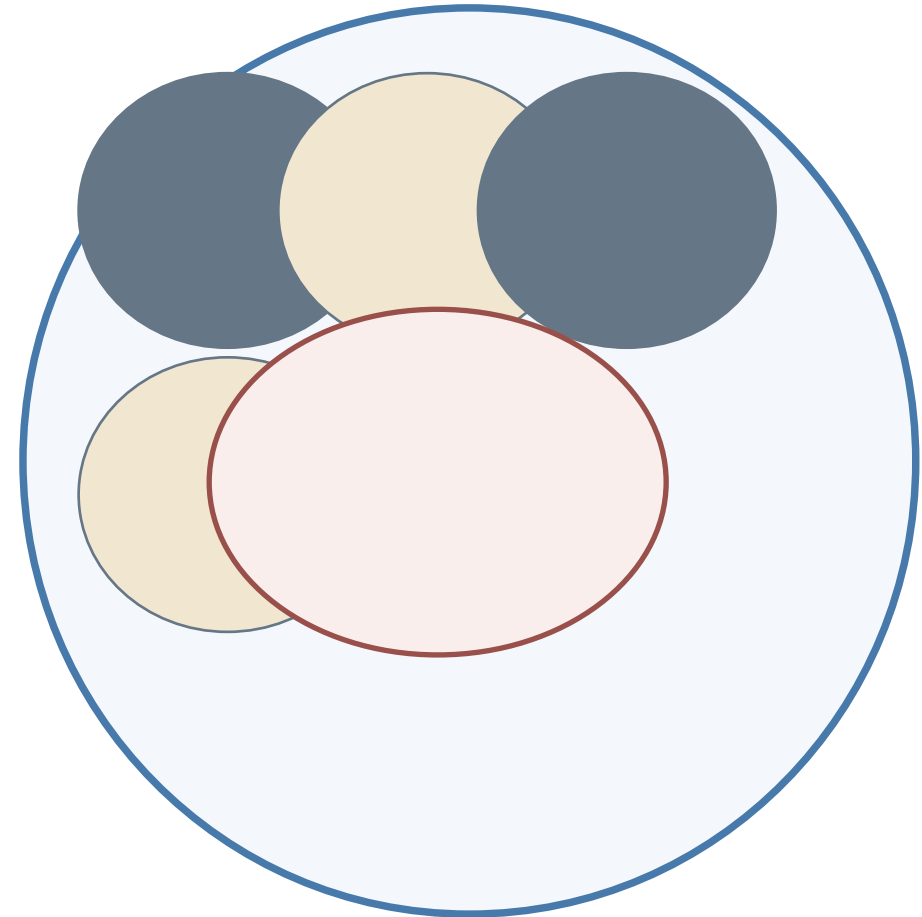
Schematic · not a clinical or histologic specimen

SPN mainly affects young females

- Solid pseudopapillary neoplasms occur primarily in young females.
- Lesions often become large before presentation.
- Abdominal discomfort may reflect their size.

SPN: Mixed solid and cystic cut surface

- The tumor is usually well circumscribed.
- Solid components coexist with cystic spaces.
- The cystic portions contain hemorrhagic debris, not characteristic serous fluid or mucin.

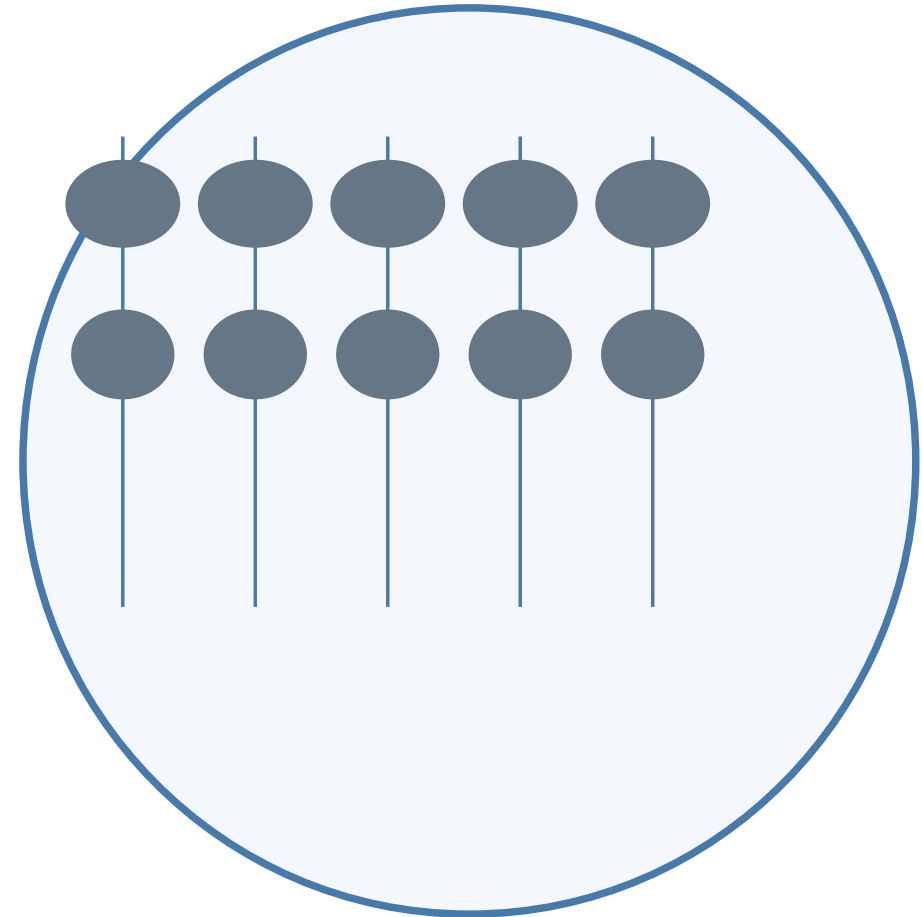


Solid areas + hemorrhagic cyst

Schematic · not a clinical or histologic specimen

SPN: Pseudopapillary growth pattern

- Tumor cells may form solid sheets or pseudopapillary projections.
- The neoplastic cells often appear poorly cohesive.
- These architectural features explain the term “solid pseudopapillary.”



Solid sheets / pseudopapillae

Schematic · not a clinical or histologic specimen

SPN: Nearly universal CTNNB1 activation

- Activating CTNNB1 (β -catenin) mutations occur in nearly all SPNs.
- The predominance of CTNNB1 is a key molecular contrast with SCN, MCN and IPMN.
- The excerpt does not prescribe a separate molecular testing algorithm.

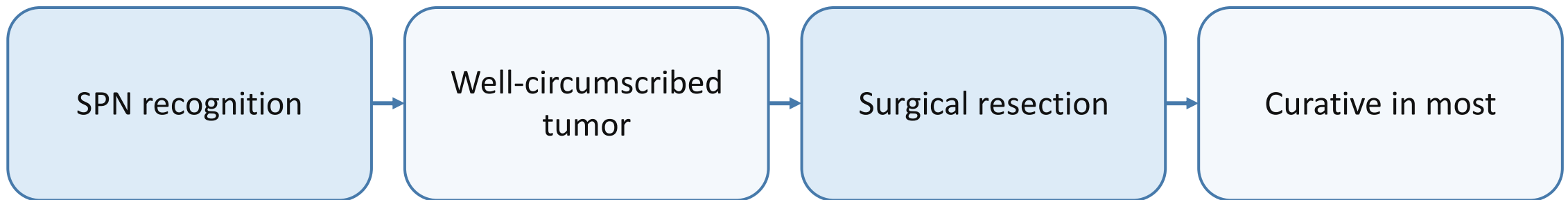
CTNNB1

Activating mutations in nearly all
SPNs

SPN: Other cystic-tumor driver profiles are absent

SPN profile	Mutation pattern
CTNNB1 (β -catenin)	Activating mutations: Nearly all
KRAS / RNF43	Not observed in source description
GNAS / VHL	Not observed in source description

SPN: Resection is usually curative



Conceptual pathway; Arrows denote stated biological or clinical relationships.

Four entities: Structural signatures

Serous cystic neoplasm

Microcysts · clear fluid · VHL

Mucinous cystic neoplasm

Mucin + ovarian stroma · KRAS / RNF43

Intraductal papillary mucinous neoplasm

Duct-centered mucin · GNAS

Solid pseudopapillary neoplasm

Solid–cystic · hemorrhage · CTNNB1

Morphology is the anchor of differentiation

Neoplasm	Architecture	Contents / cell clue
SCN	Microcystic	Clear fluid; Glycogen-rich cuboidal lining
MCN	Large cysts	Mucin; Ovarian-type stroma
IPMN	Duct-centered	Mucin-producing papillary neoplasm
SPN	Solid + cystic	Hemorrhage; Poorly cohesive cells

Anatomic and demographic clues are supportive

Entity	Typical anatomical / demographic pattern
SCN	Tail; Older adults; Female > male
MCN	Tail; Approximately 95% female
IPMN	Head; More frequent in males
SPN	Young females; Large mass

The mutational profiles are not interchangeable

Entity	Characteristic changes	Invasion-associated changes
SCN	VHL inactivation	Not detailed
MCN	KRAS; RNF43 loss	TP53; SMAD4
IPMN	KRAS; RNF43; GNAS; BRAF	TP53; SMAD4
SPN	CTNNB1 activation	Not detailed

Behavior determines why classification matters

SCN	MCN / IPMN	SPN
Virtually benign	Potentially invasive	Curative after resection in most
Serous, microcystic	Mucinous, distinct compartments	Solid and cystic

Teaching case: Incidental microcystic tail lesion

- An older patient undergoes abdominal imaging for an unrelated reason.
- A pancreatic-tail lesion shows a honeycomb of tiny cysts containing clear fluid.
- Question: Which neoplasm is most consistent with this profile?

Educational case

Choose the lesion using morphology, anatomical setting and molecular pattern.

Clinical vignette • not real patient data

Teaching case: Mucin-filled tail mass

- A woman has a painless, slowly growing cystic mass in the pancreatic tail.
- Large mucin-filled cavities are lined by columnar epithelium over ovarian-type stroma.
- Question: What is the diagnosis and what critical adverse event must be excluded?

Educational case

Choose the lesion using morphology, anatomical setting and molecular pattern.

Clinical vignette • not real patient data

Teaching case: Mucin-producing duct lesion

- A pancreatic-head tumor grows within the main pancreatic duct and produces mucin.
- No dense ovarian-type stromal component is identified.
- Question: Which entity is favored, and which mutation is especially characteristic?

Educational case

Choose the lesion using morphology, anatomical setting and molecular pattern.

Clinical vignette • not real patient data

Teaching case: Circumscribed hemorrhagic mass

- A young woman presents with discomfort from a large well-circumscribed pancreatic mass.
- Solid sheets coexist with hemorrhagic cysts and pseudopapillary projections.
- Question: Which entity and dominant molecular alteration fit best?

Educational case

Choose the lesion using morphology, anatomical setting and molecular pattern.

Clinical vignette • not real patient data

Avoid overcalling a mucinous lesion from sex or site

- SCN and MCN both often arise in the tail, but

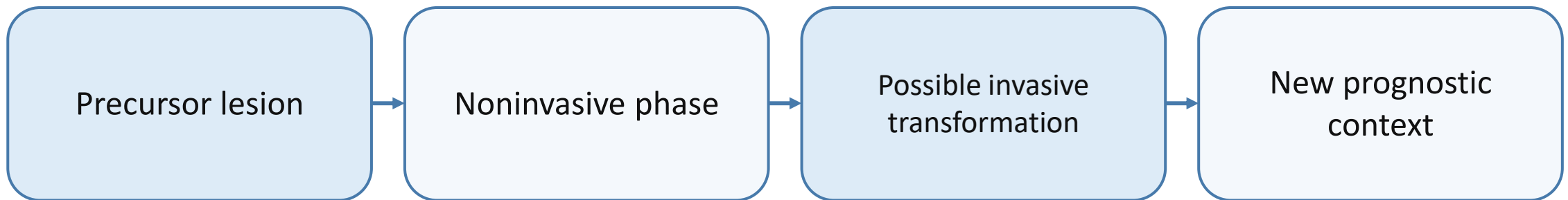
SCN

Microcystic · clear · glycogen-rich

MCN

Large cysts · mucin · ovarian
stroma

Avoid equating precursor status with invasive cancer



Conceptual pathway; Arrows denote stated biological or clinical relationships.

Summary: The four high-yield distinctions

Serous cystic neoplasm

Microcysts · clear fluid · VHL

Mucinous cystic neoplasm

Mucin + ovarian stroma · KRAS / RNF43

Intraductal papillary mucinous neoplasm

Duct-centered mucin · GNAS

Solid pseudopapillary neoplasm

Solid–cystic · hemorrhage · CTNNB1

Primary reference and interpretation limits

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026).
- Chapter: The Pancreas; section: Cystic Neoplasms.
- Diagrammatic depictions are original editable schematics—not histologic or radiologic evidence.
- No external guidelines, contemporary management algorithms or staging systems were introduced.