

Salivary Gland Tumors, Histology, Molecular and beyond-Part II

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Adenoid cystic carcinoma

Polymorphous adenocarcinoma

Mucoepidermoid carcinoma

Acinic cell carcinoma

Secretory carcinoma

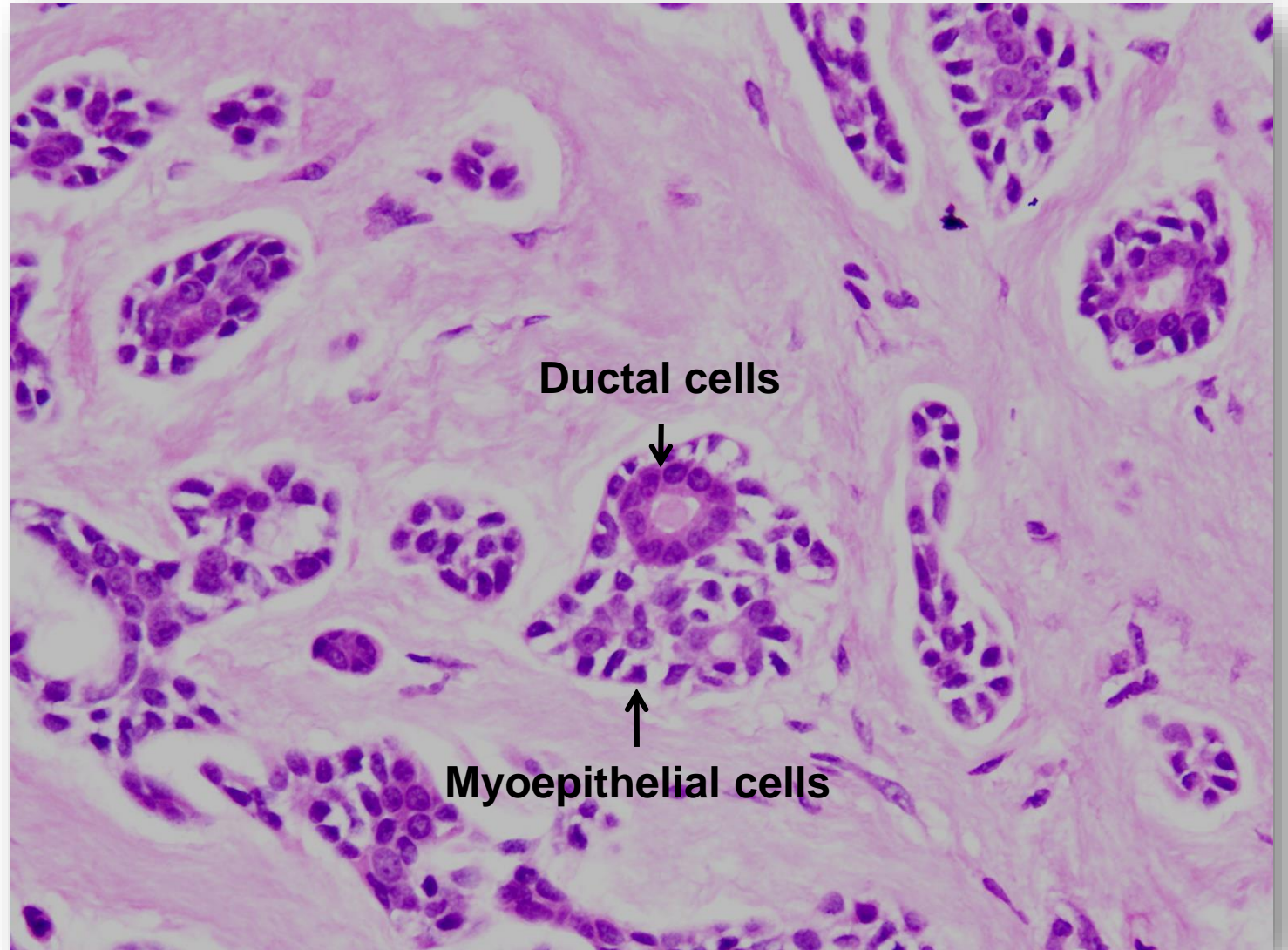
WHO 2022

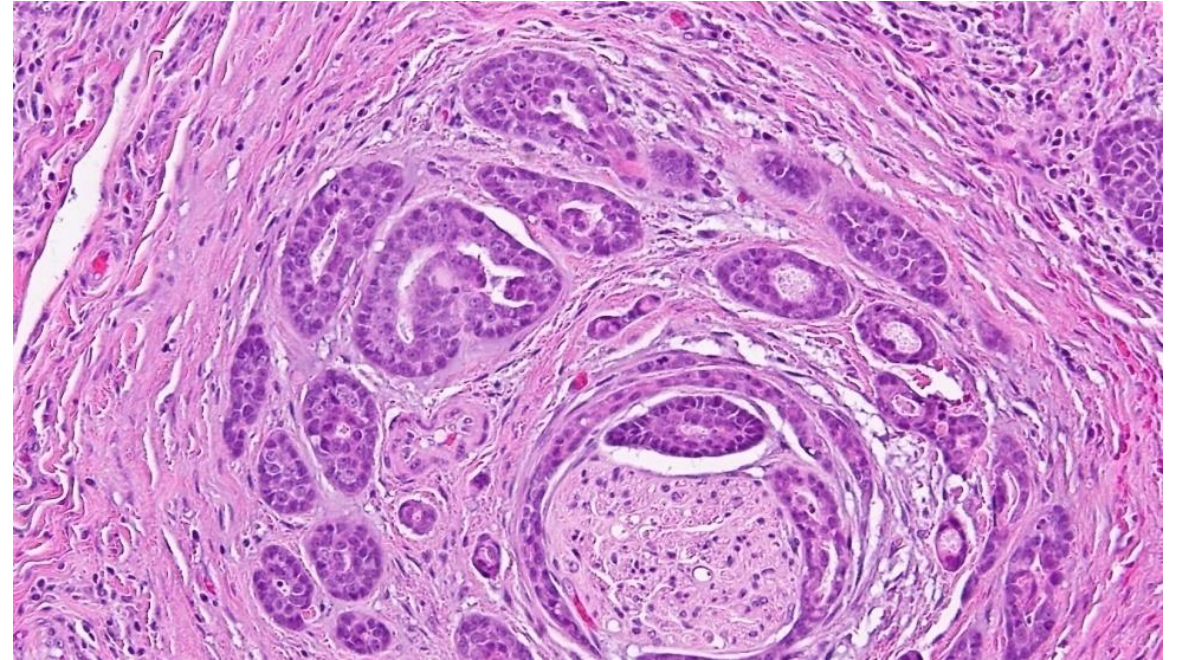
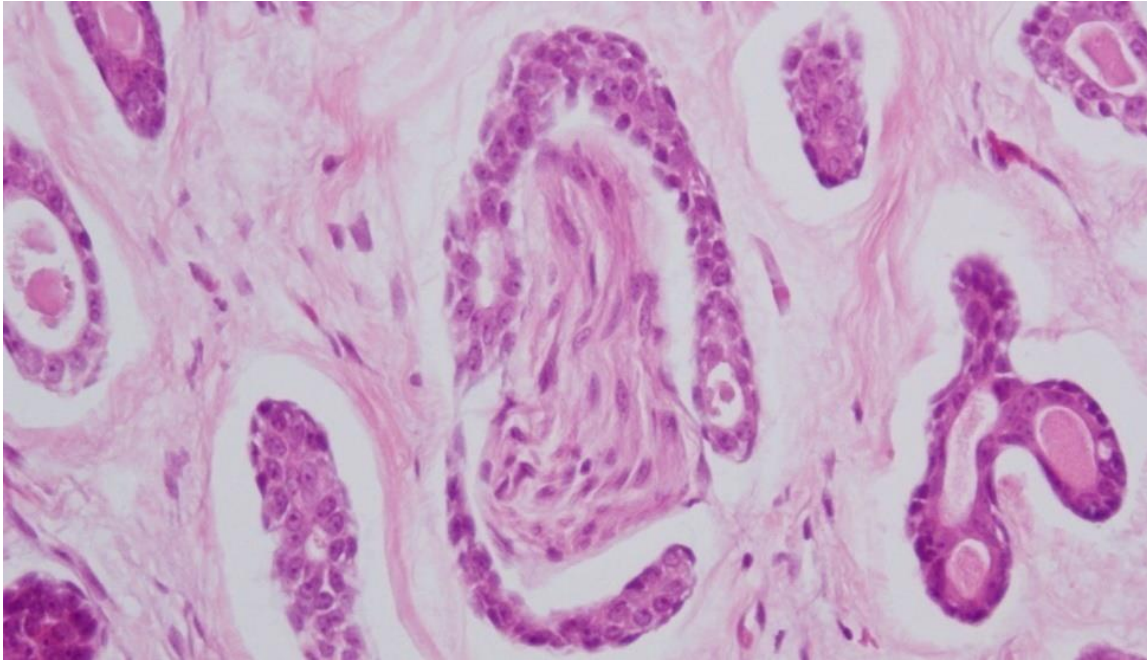
Adenoid cystic carcinoma (ACC)

- **Biphasic ductal and myoepithelial** differentiation
- 25% of salivary gland malignancies
- Most common=parotid
- 30% in minor salivary glands, highest frequency in palate
- All ages, high frequency in older patients

- **Good early survival:** 5-year survival is 75-80%
- **Poor long survival:** 15 years survival is 35%
- Morphologically bland but infiltrative
- **High rate of perineural invasion**
- **High risk category**
- Lymph nodes involvement is uncommon

ACC-
Histology
Biphasic
differentiation

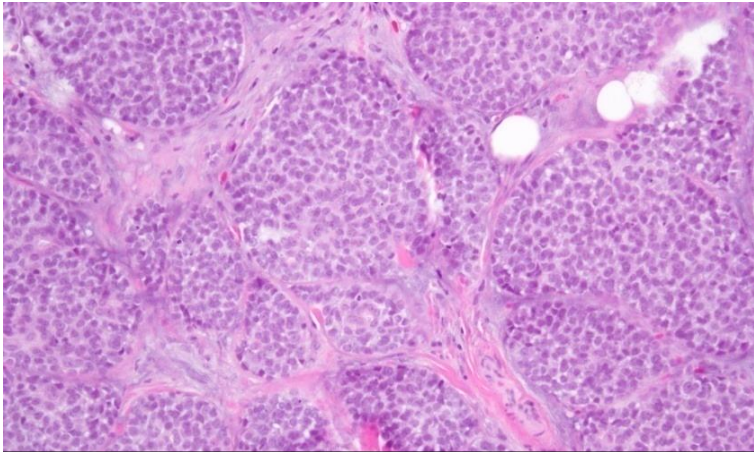




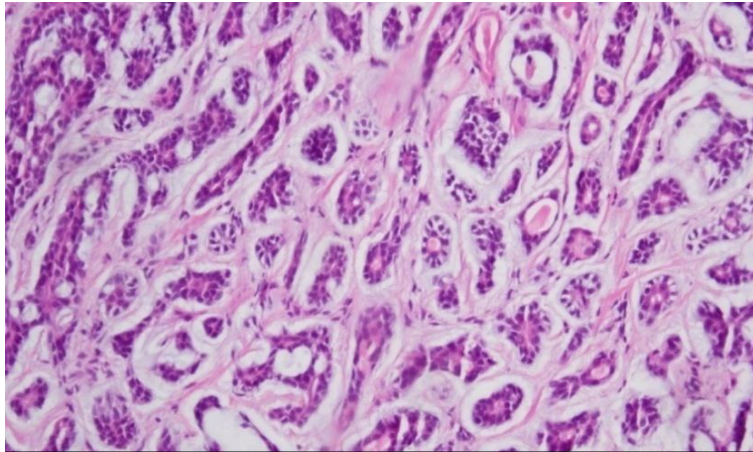
Perineural invasion

- PNI is common but not pathognomonic
- ACC has a propensity to infiltrate along nerve tract

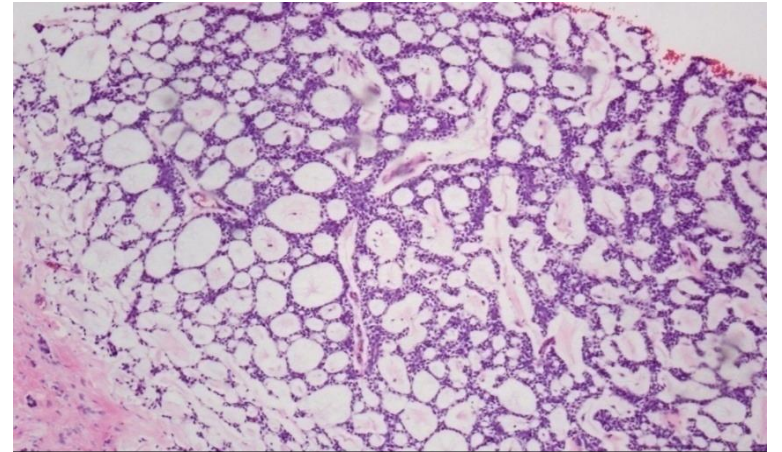
ACC-Growth patterns



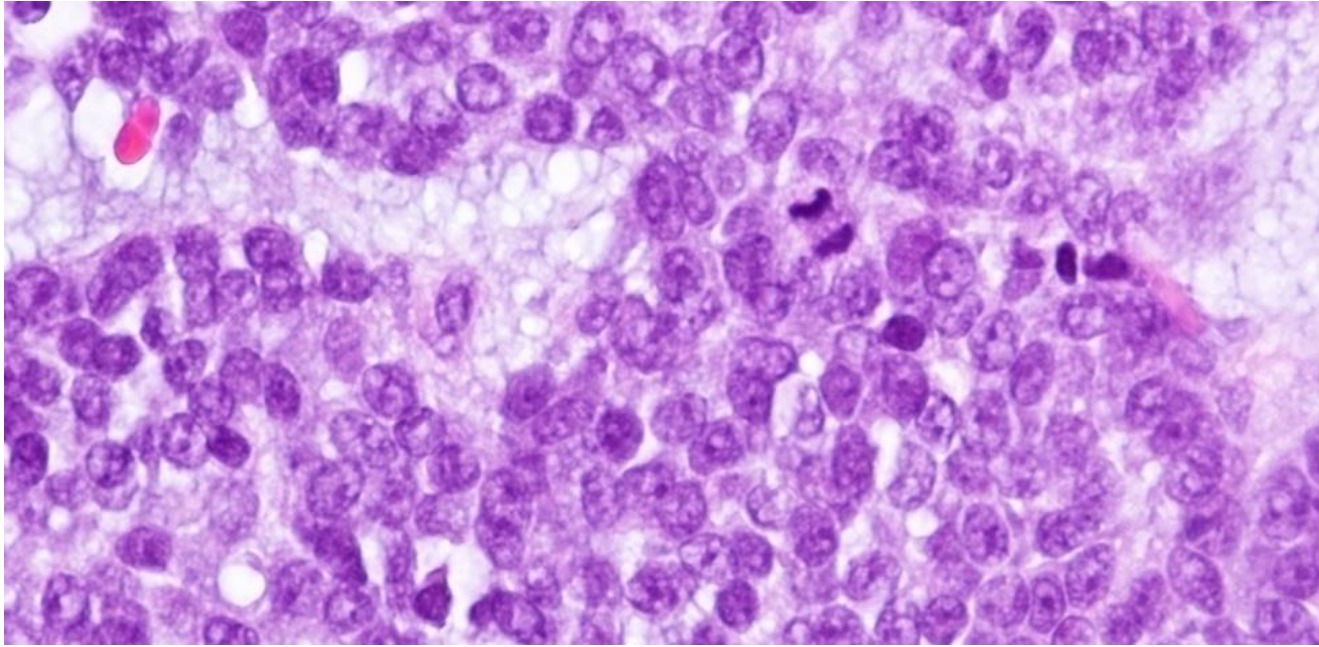
Solid



Tubular

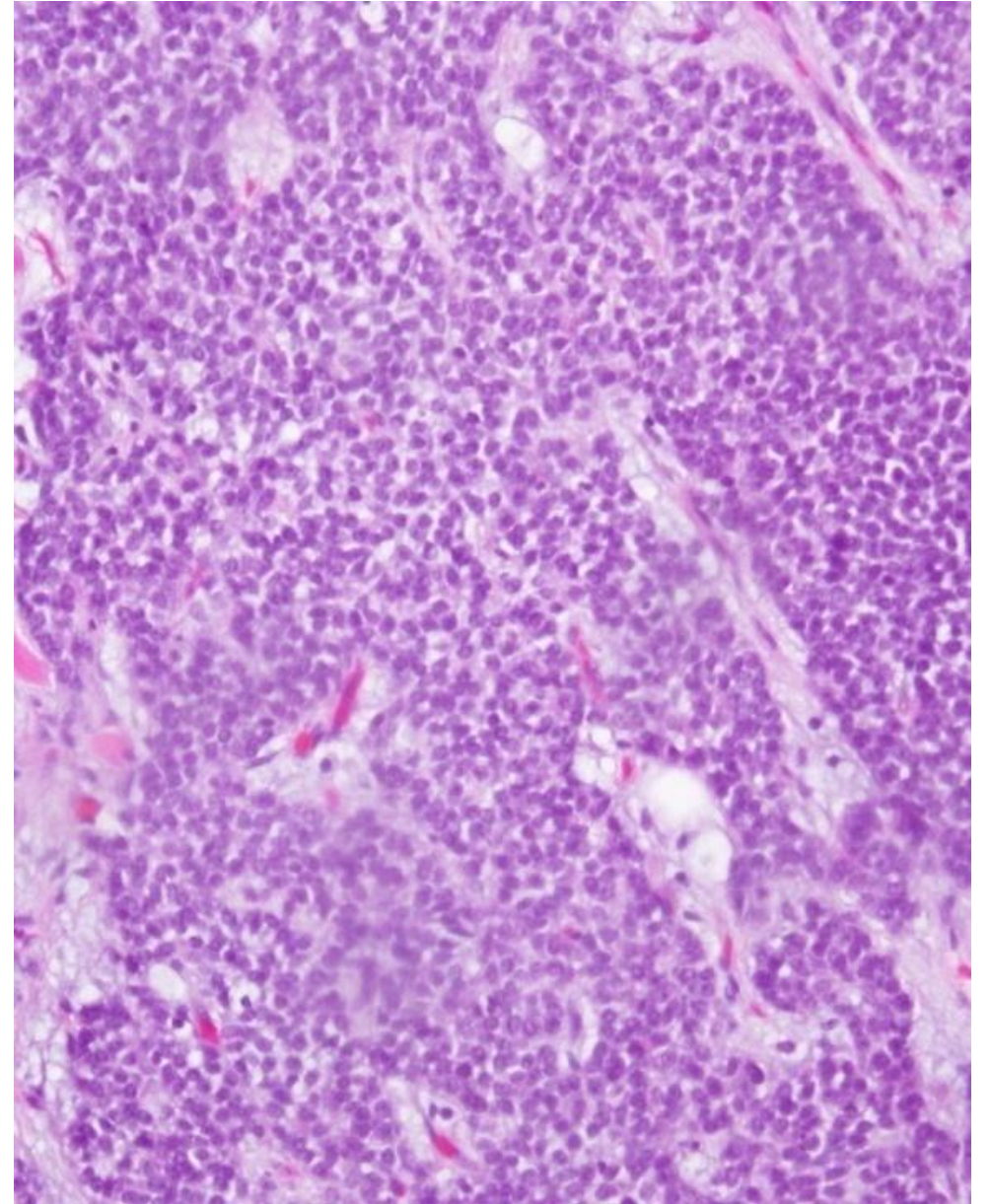


Cribriform



Solid pattern

- Biphasic differentiation is not obvious
- Cells are larger/more atypical
- Mitoses and focal tumor necrosis are common

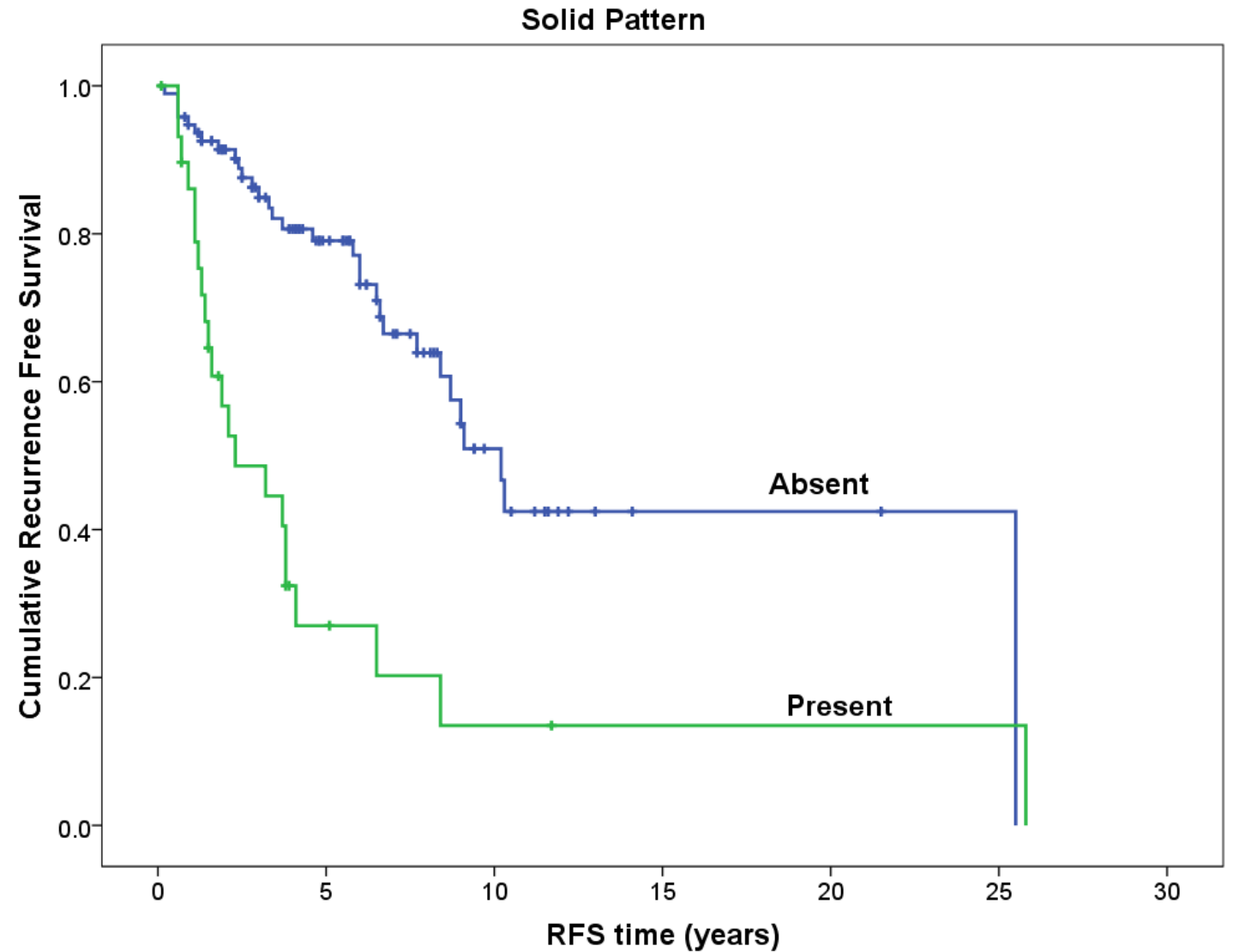


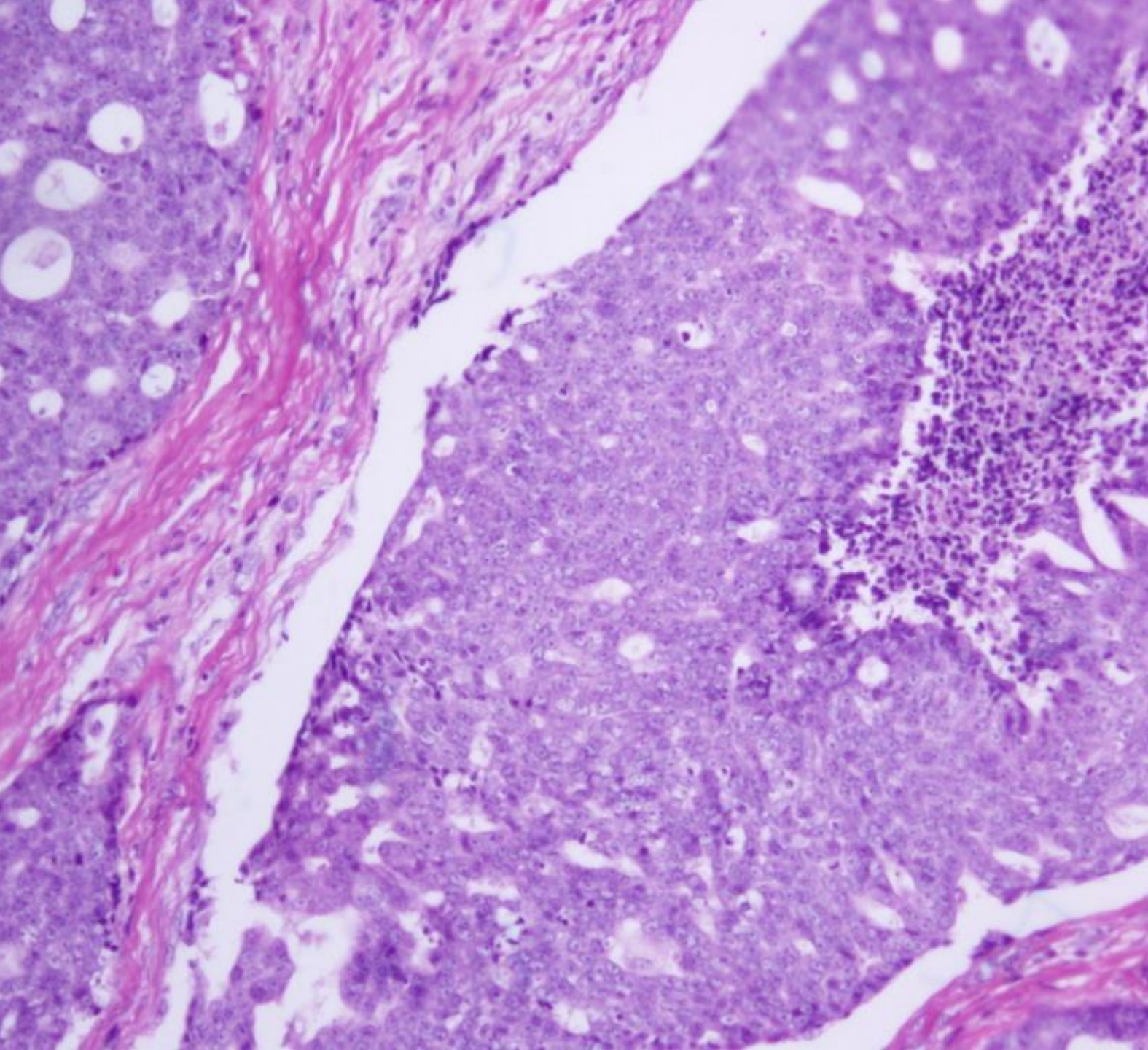
-
- **Solid component imparts poor prognosis**
 - Grading based on the amount of solid growth pattern
 - Grade 1: mostly tubular, no solid
 - Grade 2: mostly cribriform, $\leq 30\%$ solid
 - Grade 3: $>30\%$ solid
 - **At MSK: we report the presence and the amount of solid pattern**

Predictors of Outcome in Adenoid Cystic Carcinoma of Salivary Glands: A Clinicopathologic Study With Correlation Between MYB Fusion and Protein Expression

Bin Xu, Esther Drill, Allen Ho, Alan Ho, Lara Dunn, Carlos Nicolas Prieto-Granada, Timothy Chan, Ian Ganly Ronald Ghossein, and Nora Katabi
American Journal of Surgical Pathology 2017

Any solid pattern correlated with DFS





High Grade Transformation

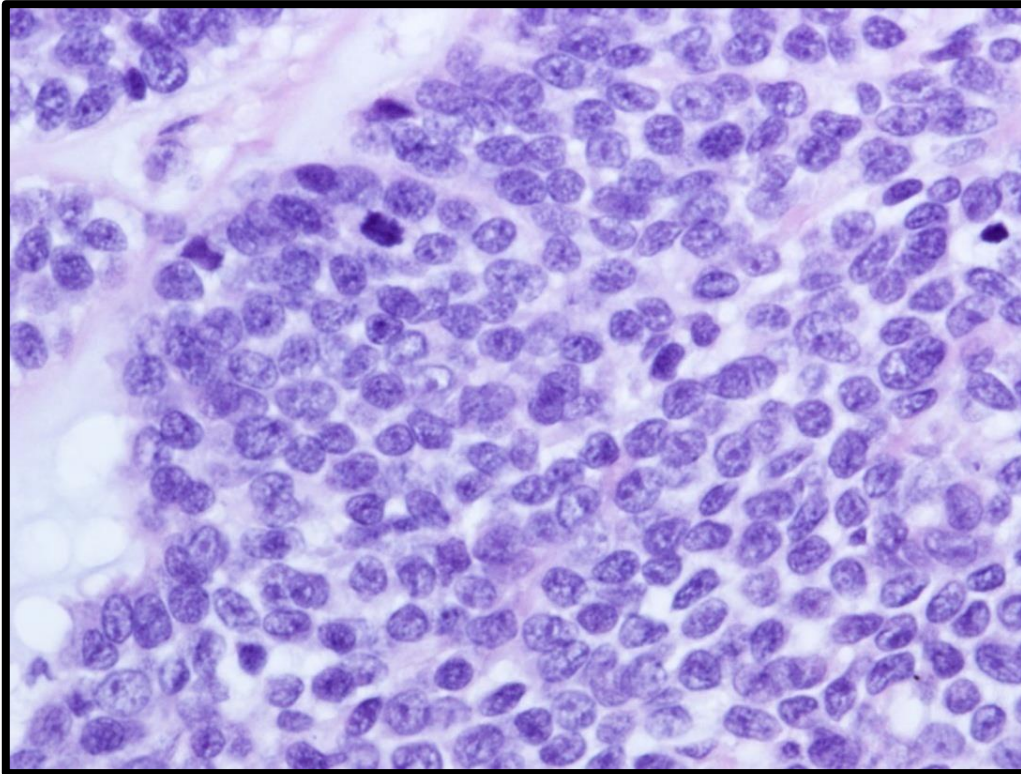
- Not unique for ACC
- HG pleomorphic, mitotically active carcinoma
- Morphologic overlapping with solid ACC
- High grade features in HGT are exaggerated

Seethala et al. 2009

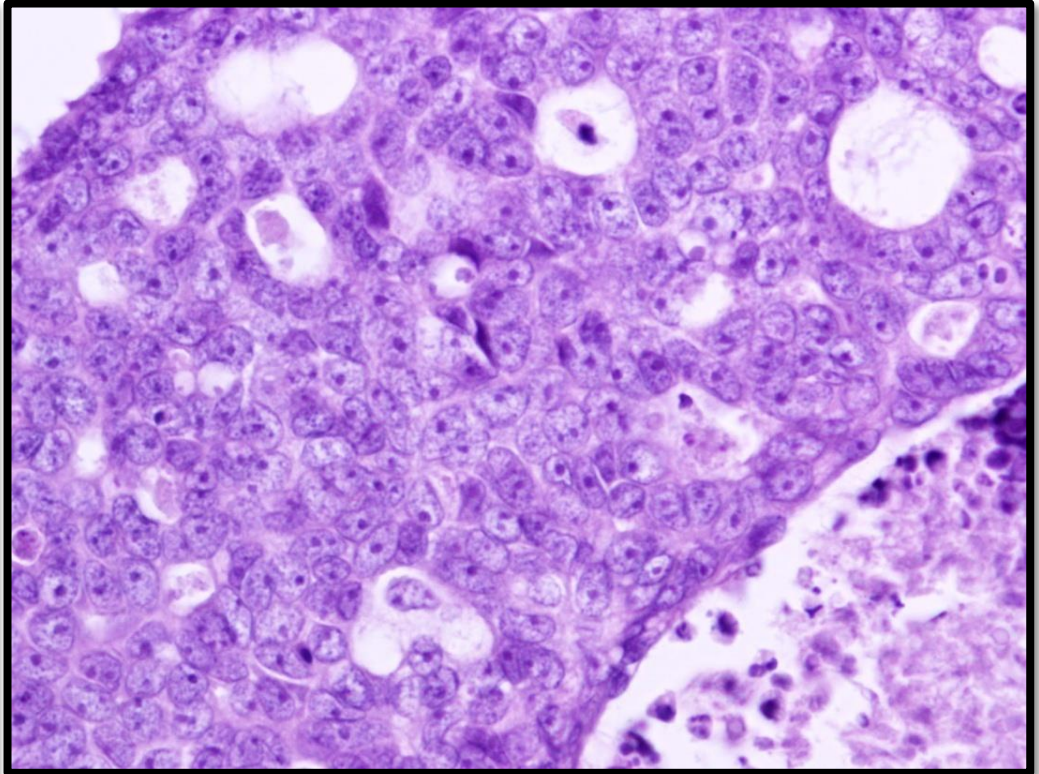
Features	Solid ACC	HGT-ACC
Growth	Solid nests	Solid confluent nests to sheet
Nuclei	<ul style="list-style-type: none">•Uniform in size•At most 2 X size of ACC of other patterns•Indistinct nucleoli	<ul style="list-style-type: none">•Variable in size•At least 2-3 X size of ACC of other patterns•Prominent central nucleoli
Stroma	Paucicellular myxoid or hyaline	Fibrocellular desmoplastic
Unique features		Squamoid areas, micropapillae
Mitoses	<10 HPF	>10 HPF
Ki-67	<50%	>50%
Comedonecrosis	Focal, punctuate	Often present, extensive
Microcalcifications	Rarely present	Often present
Abulimnal layer by immunohistochemistry	Present and complete	Incomplete and at least focally absent

ACC-High grade transformation

Solid ACC

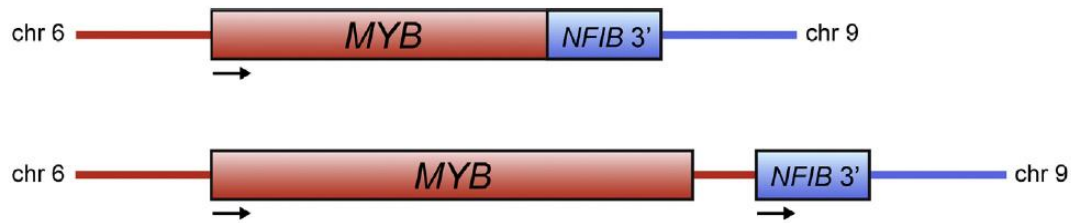


HGT-ACC



MYB-NFIB t(6;9)

MYBL1-NFIB t(8;9)



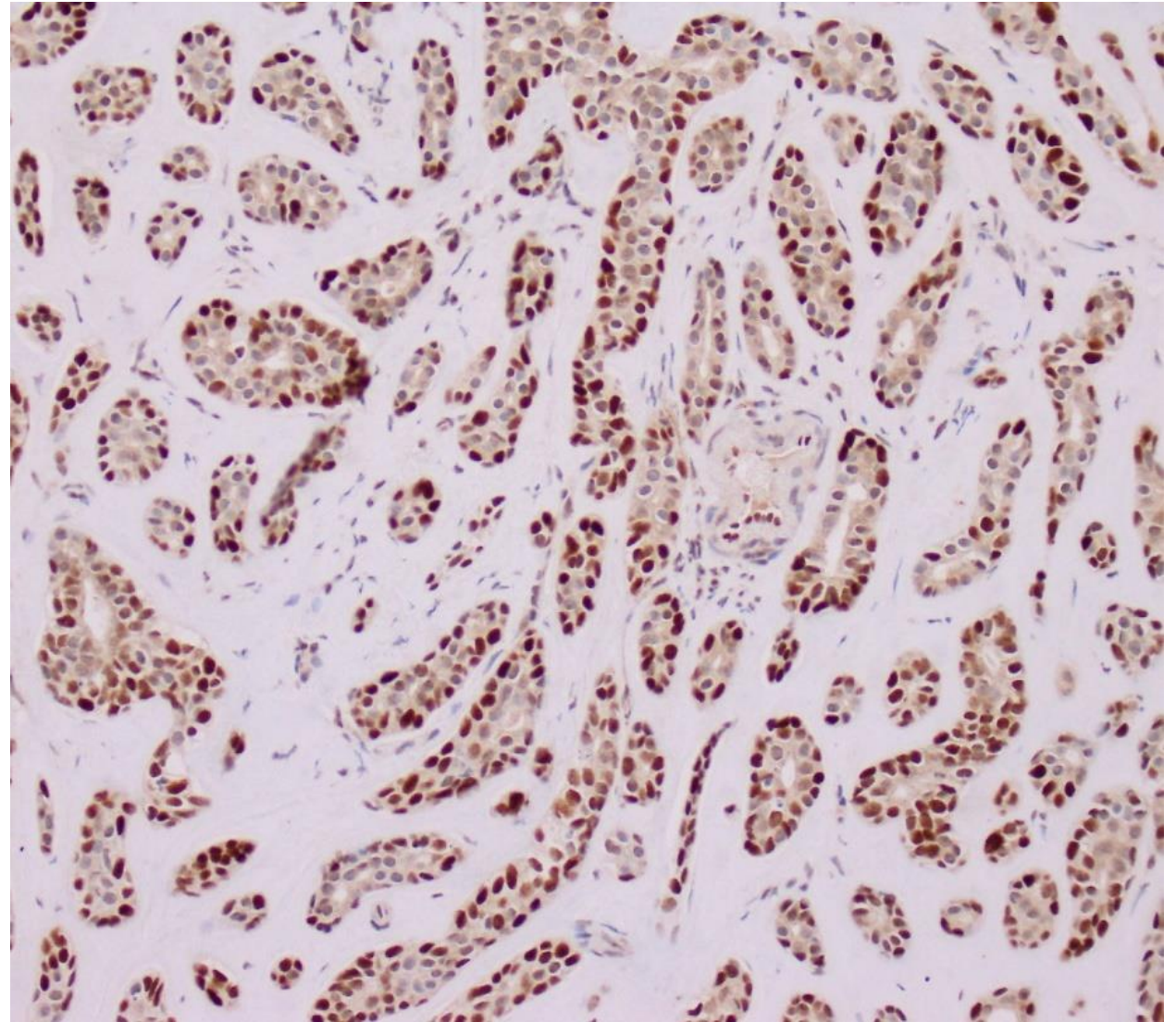
- t(6;9)(q22-23;p23-24) translocation resulting in the *MYB-NFIB* fusion gene
 - >50% of ACCs
 - Salivary and non-salivary gland sites
- *MYBL1* in 5% of ACCs
- NOTCH1 mutations

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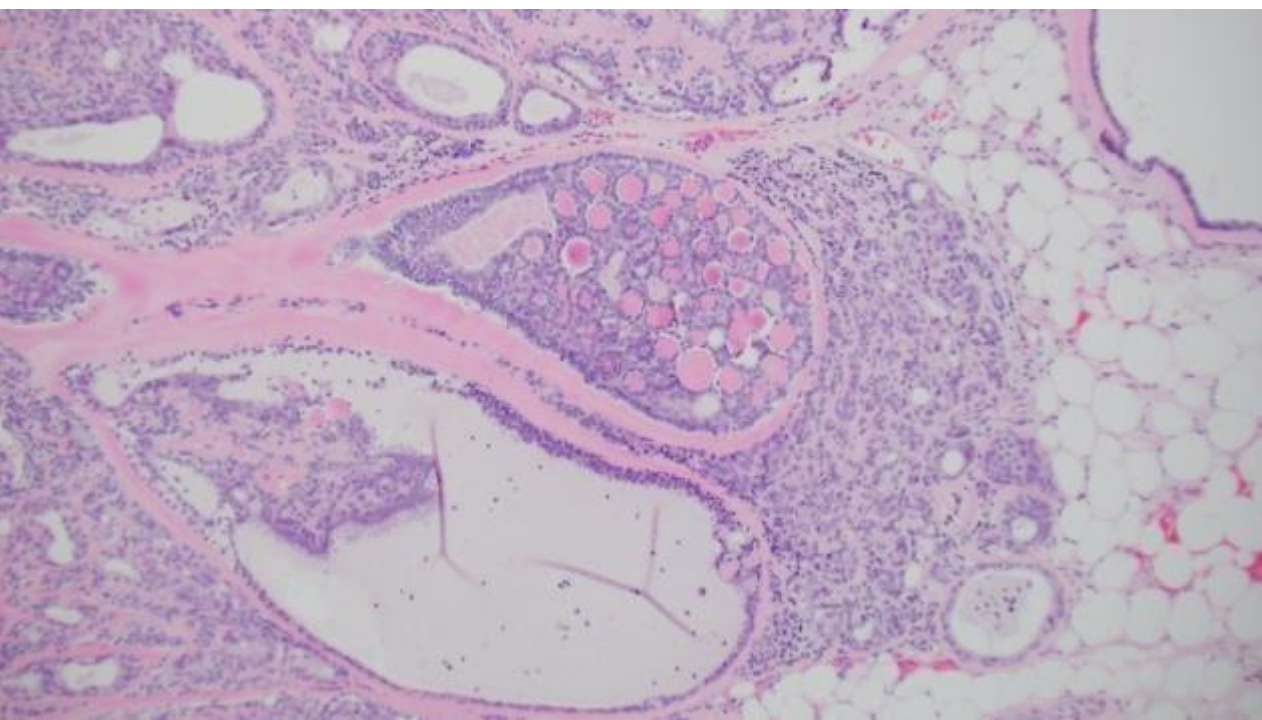
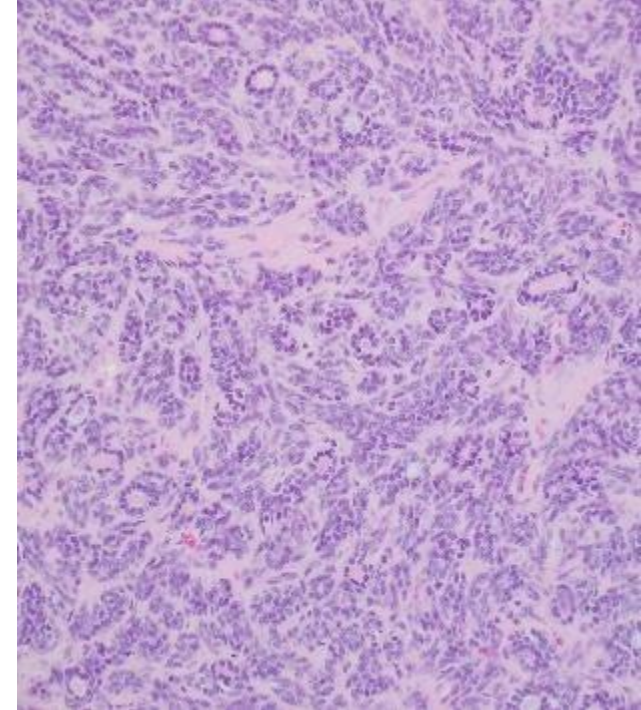
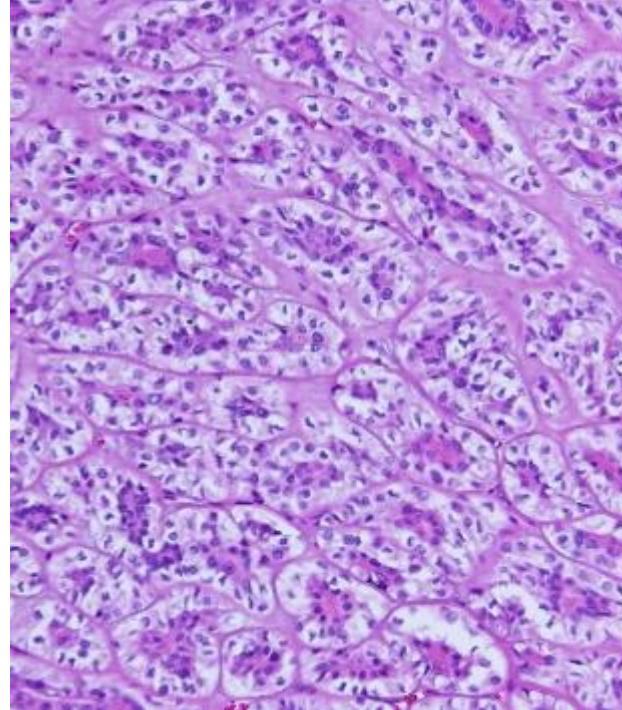
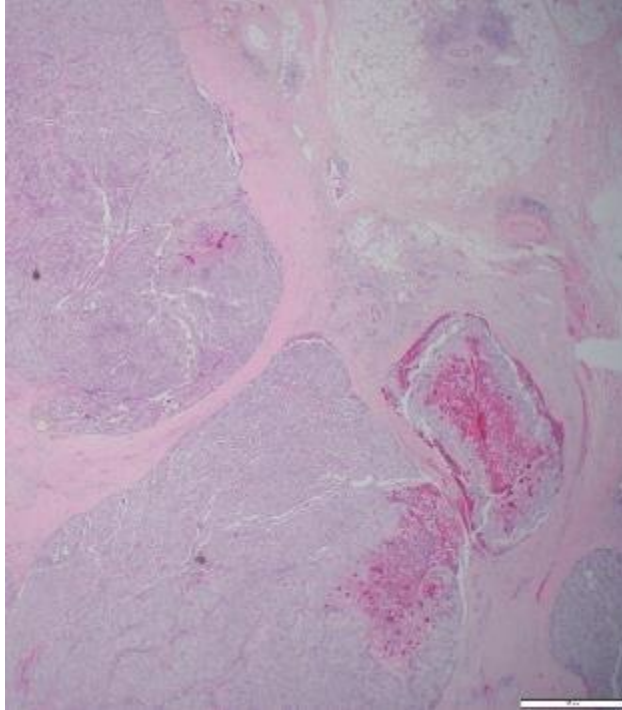
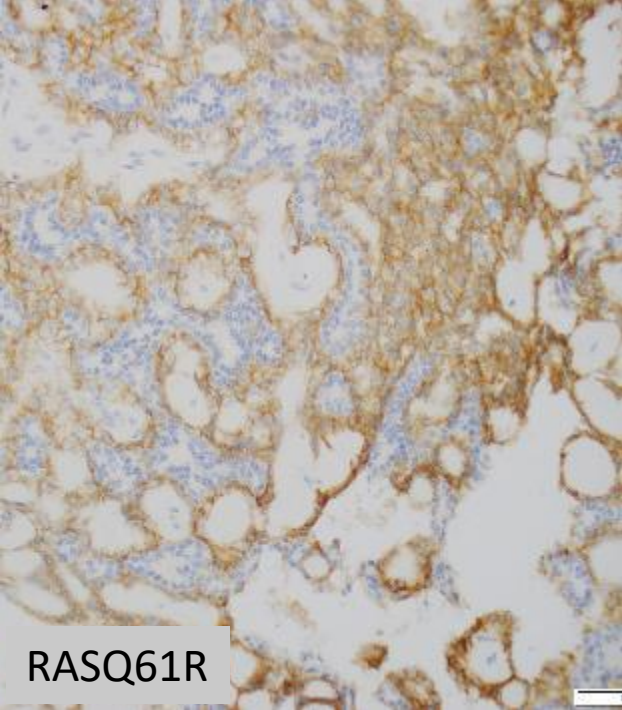
American Journal of Surgical Pathology 2017

- MYB IHC was positive 72%
- Specificity of MYB IHC in detecting MYB fusion 50%
- Can be positive in other tumors



ACC-Differential diagnosis

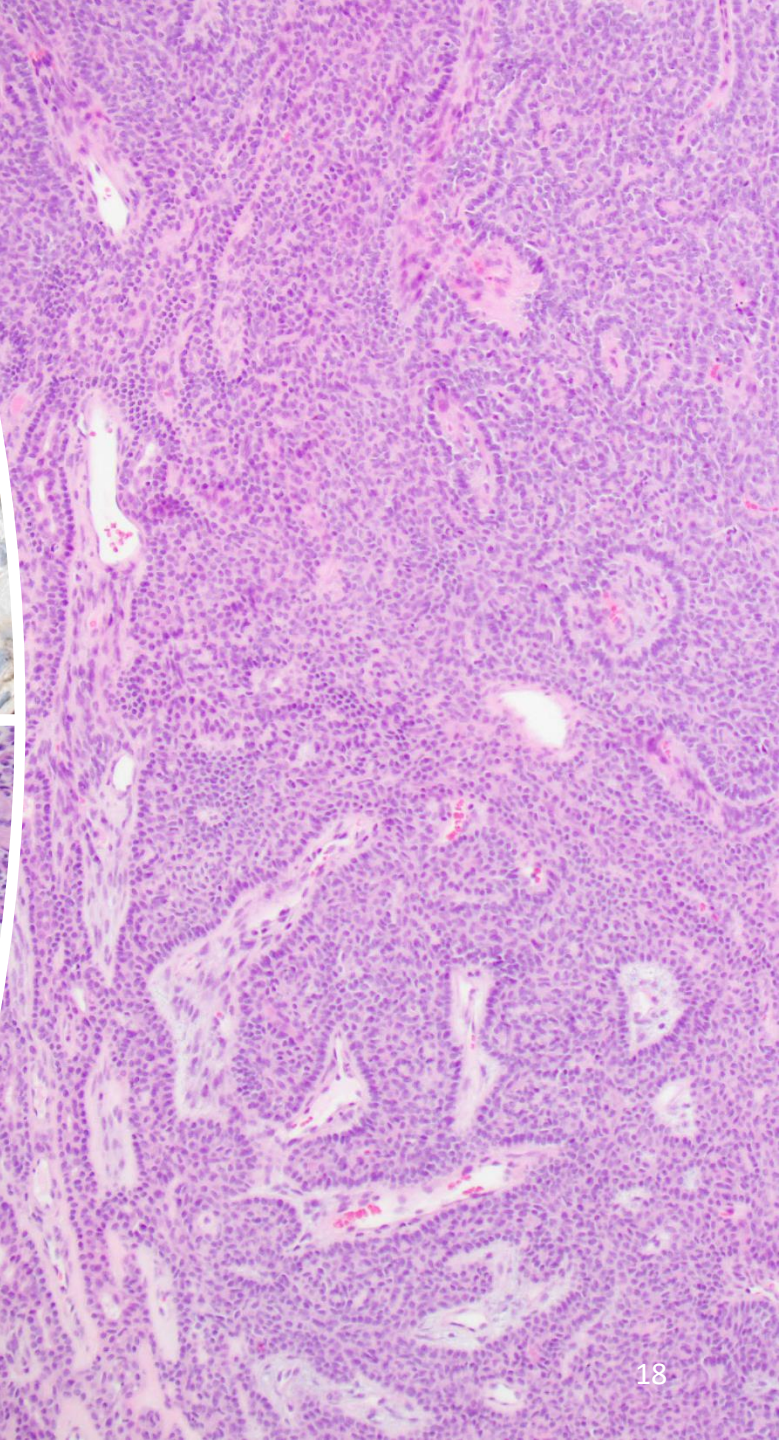
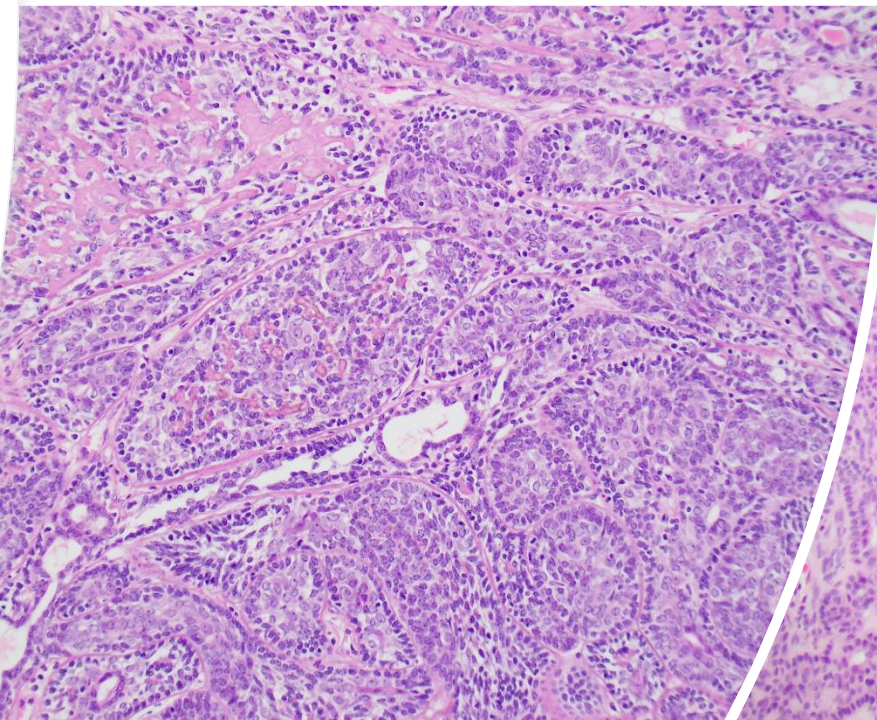
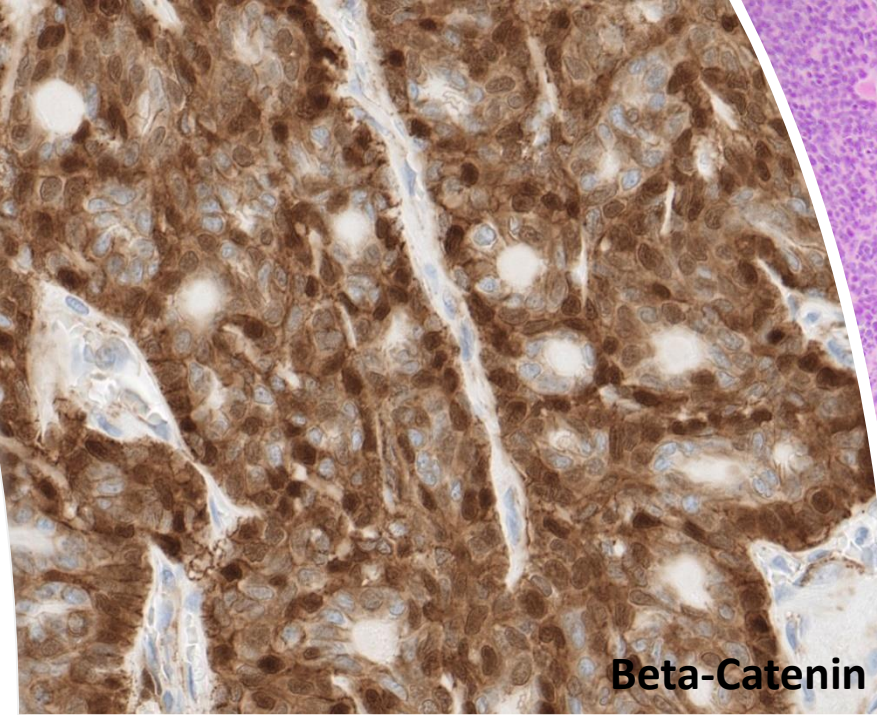
- Pleomorphic adenoma
- Epithelial myoepithelial carcinoma
- Basal cell adenoma/adenocarcinoma
- Nonkeratinizing/Basaloid squamous cell carcinoma
- NUT carcinoma
- HPV related polyphenotypic sinonasal carcinoma
- Polymorphous adenocarcinoma & cribriform adenocarcinoma



Epithelial myoepithelial carcinoma

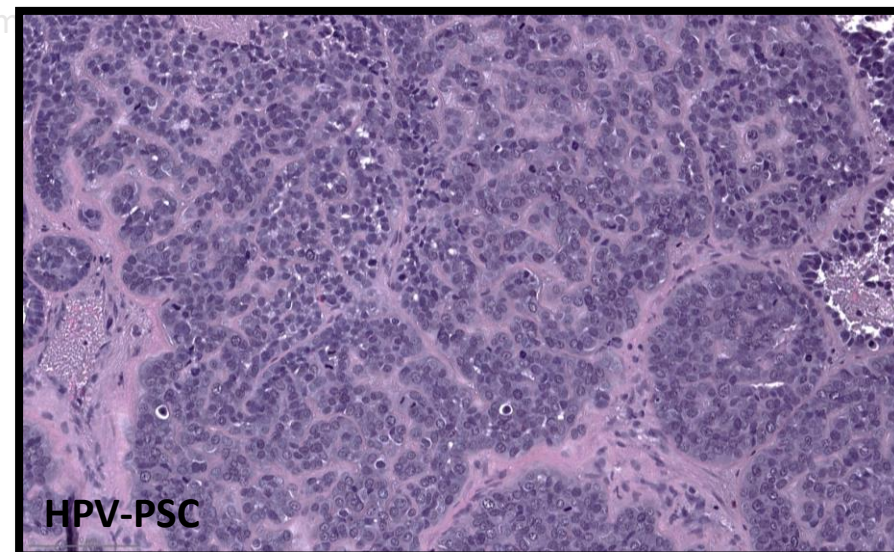
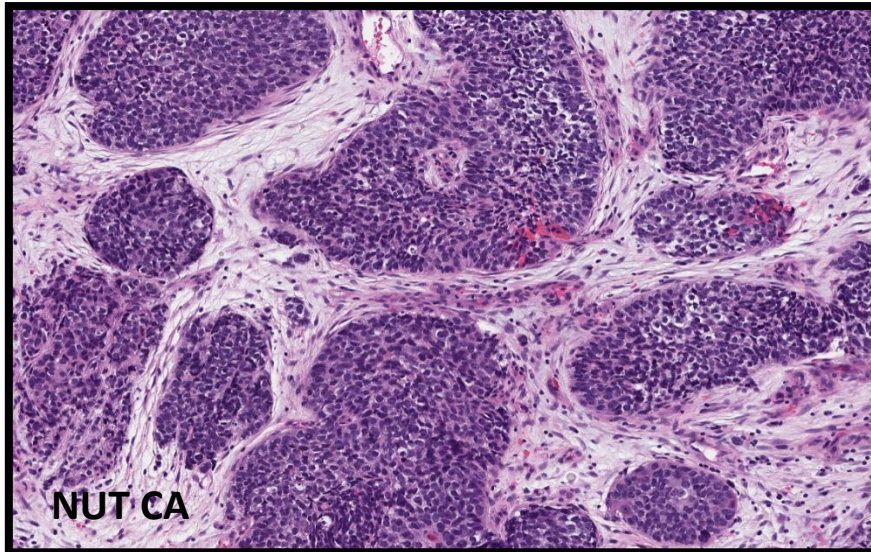
- **RAS Q61R IHC** cytoplasmic/membranous staining

**Basal cell
adenocarcinoma**



ACC-Differential diagnosis

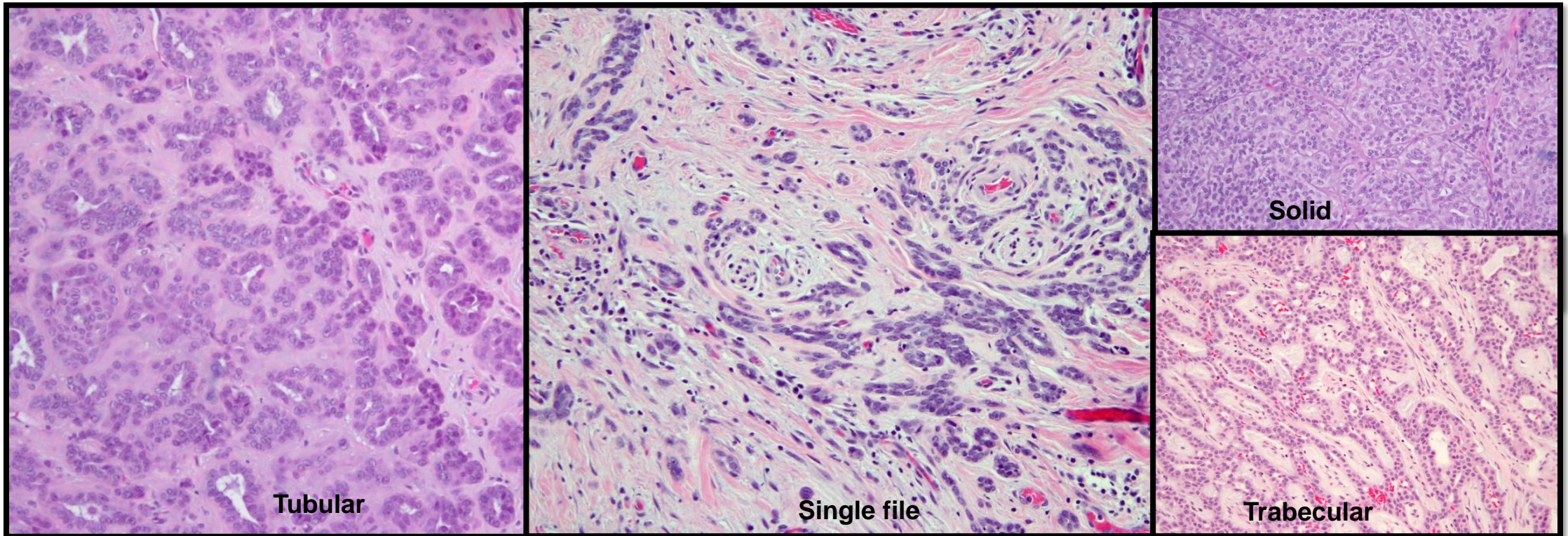
- Pleomorphic adenoma
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- HPV related polyphenotypic sinonasal carcinoma



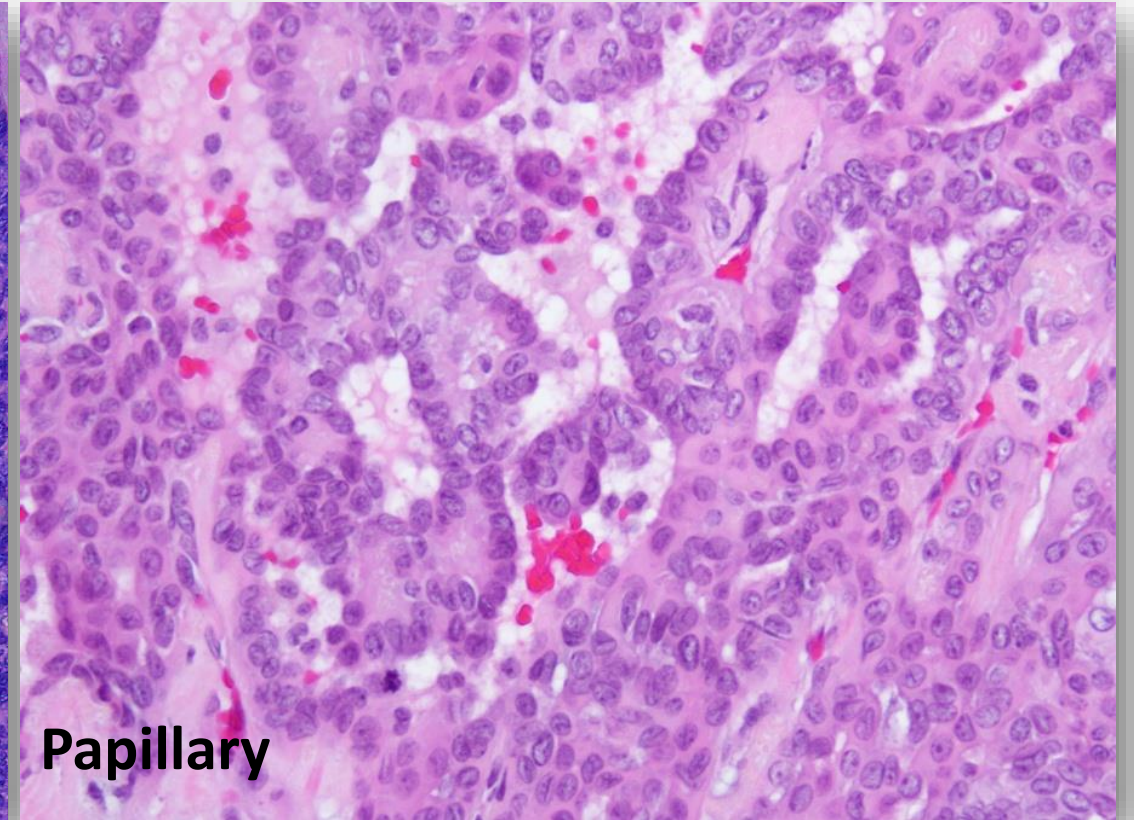
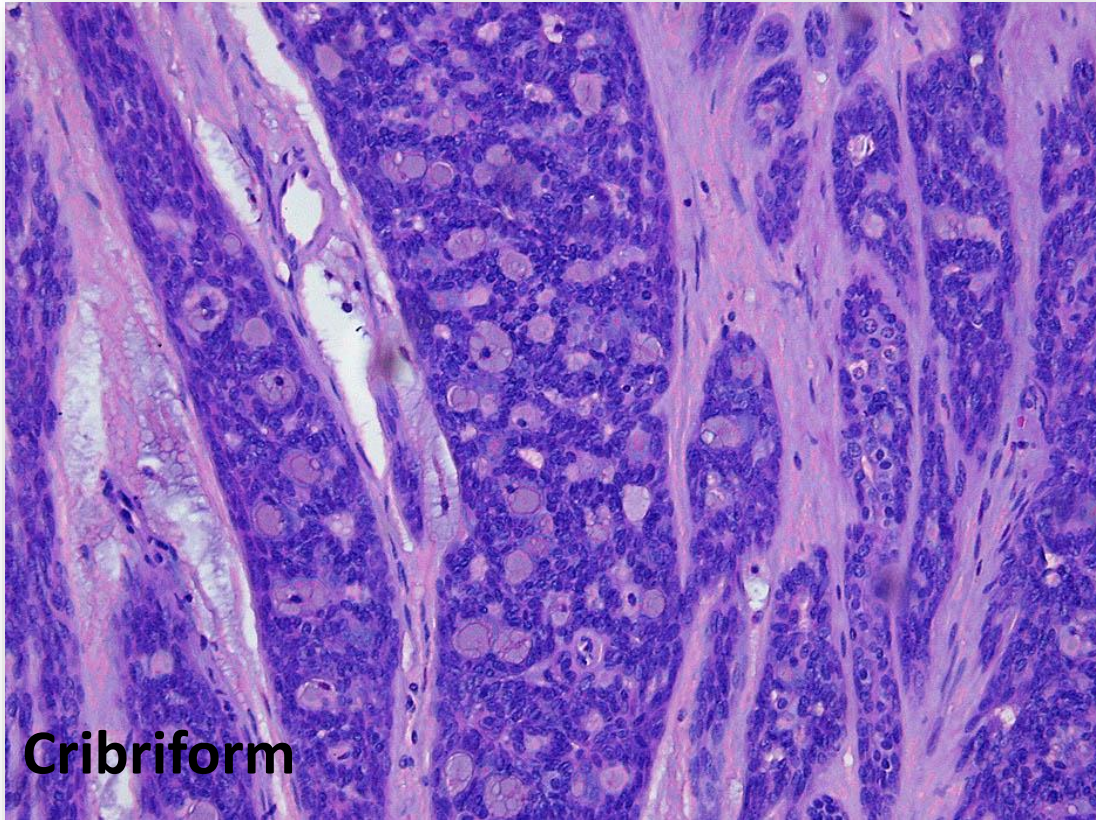
Polymorphous adenocarcinoma (PAC)

- Second most common intraoral SG malignancy
- **Over 95% in minor salivary gland** (palate-60%)
- Infiltrative growth pattern with swirled appearance
- PNI is common
- **Morphologic diversity and cytologic uniformity**
- **Good prognosis:** 5-33% local recurrence, 9-15% regional LN metastasis, rare distal metastases and deaths

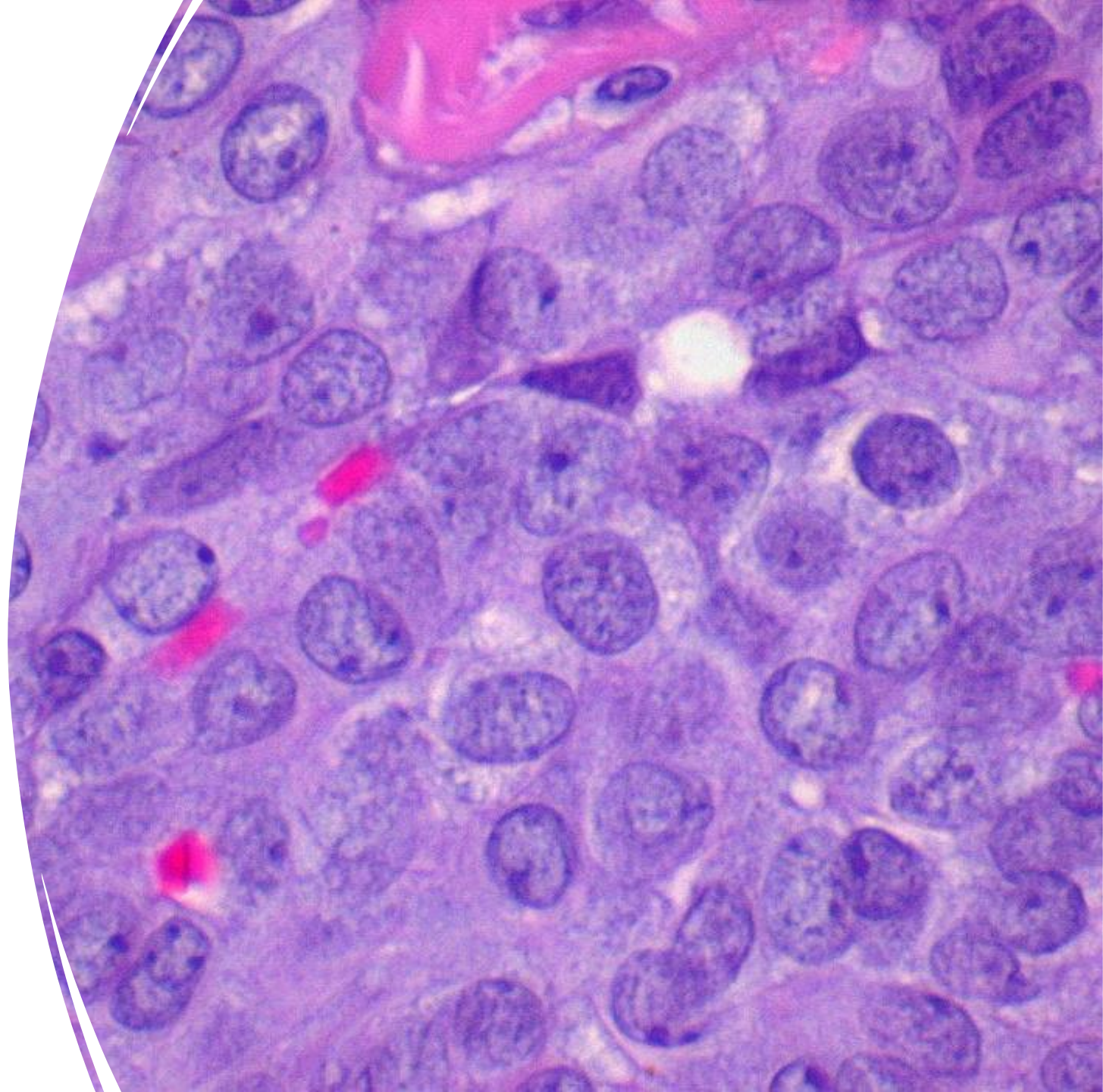
PAC-Multiple growth patterns



PAC-Multiple growth patterns

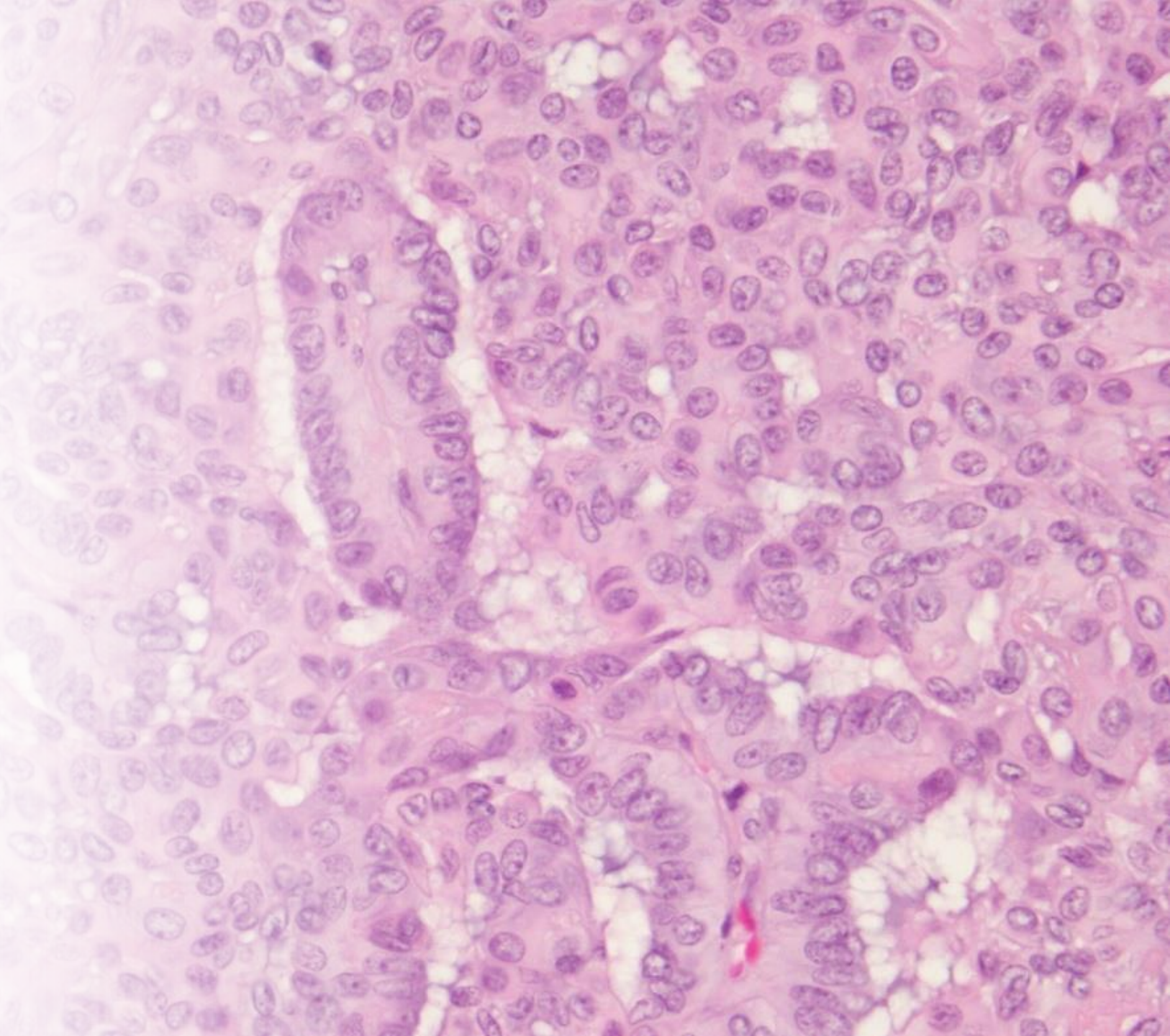


Uniform cytology



Papillary pattern in polymorphous adenocarcinoma??

Papillary patterned tumors
thought to behave more
aggressively and to have
greater capacity of
recurrences



Cribriform Adenocarcinoma

Cribriform adenocarcinoma of the tongue: a hitherto unrecognized type of adenocarcinoma of the tongue

*Michal¹, Skálová¹, Simpson¹,
Mukensnábl¹*

Histopathology. 1999 Dec

Cribriform Adenocarcinoma of Minor Salivary Gland
Origin Principally Affecting the Tongue:
Characterization of New Entity

Skalova, Alena MD, PhD; Sima, Radek PhD; Kaspirkova-Nemcova, Jana Mgr; Simpson, Roderick H.W. MD; Elmberger, Goran MD; Leivo, Ilmo MD, PhD; Di Palma, Silvana MD; Jirasek, Tomas MD, PhD; Gnepp, Douglas R. MD; Weinreb, Ilan MD; Perez-Ordoñez, Bayardo MD; Mukensnabl, Petr MD, PhD; Rychly, Boris MD; Hrabal, Petr MD; Michal, Michal MD

Am J Surg Pathol. 2011 Aug;35(8):1168-76

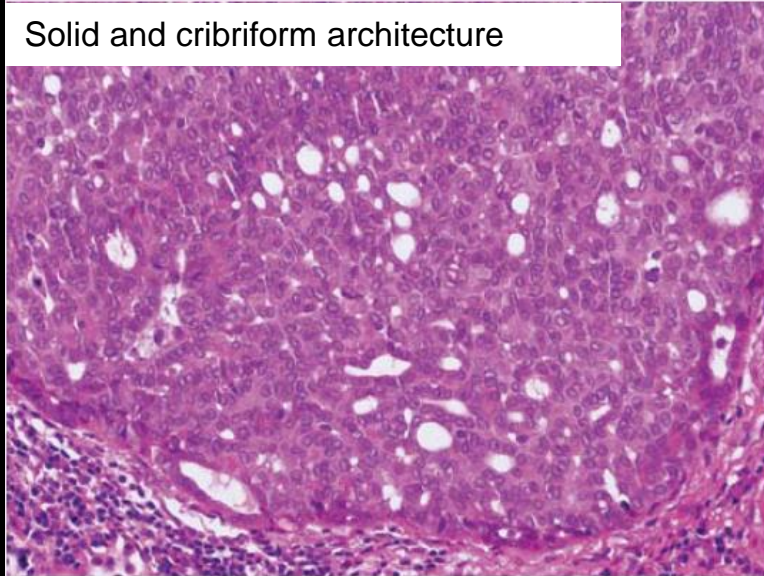


Cribriform Adenocarcinoma

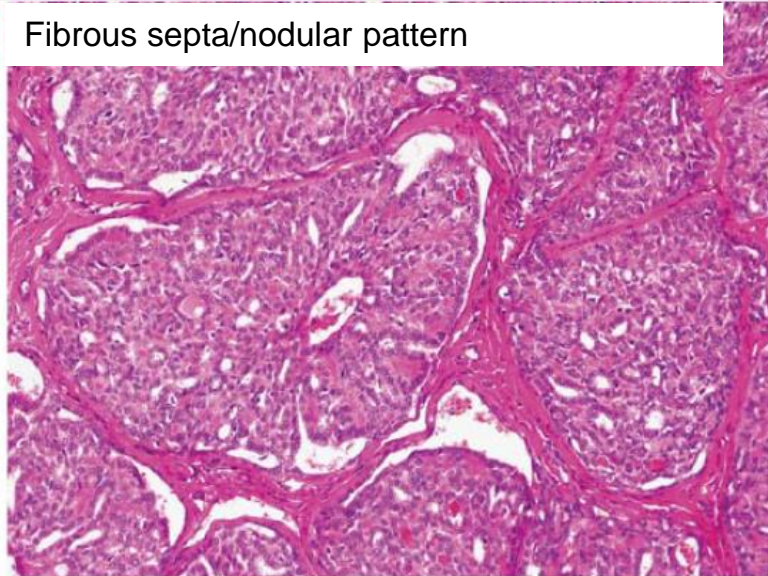
**A subtype of
polymorphous
adenocarcinoma?**

A separate entity??

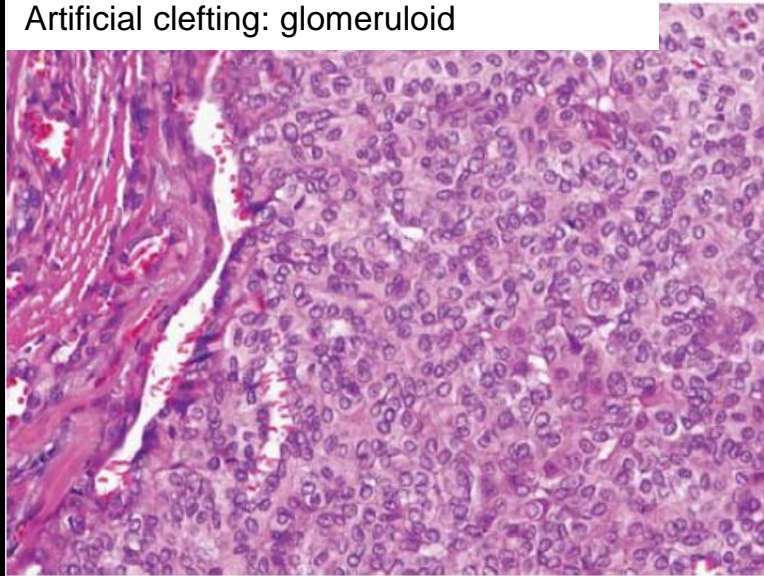
Solid and cribriform architecture



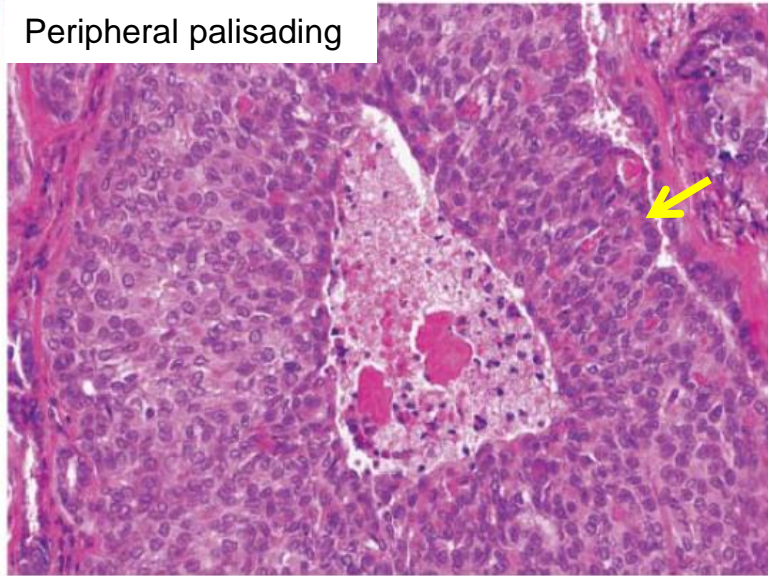
Fibrous septa/nodular pattern

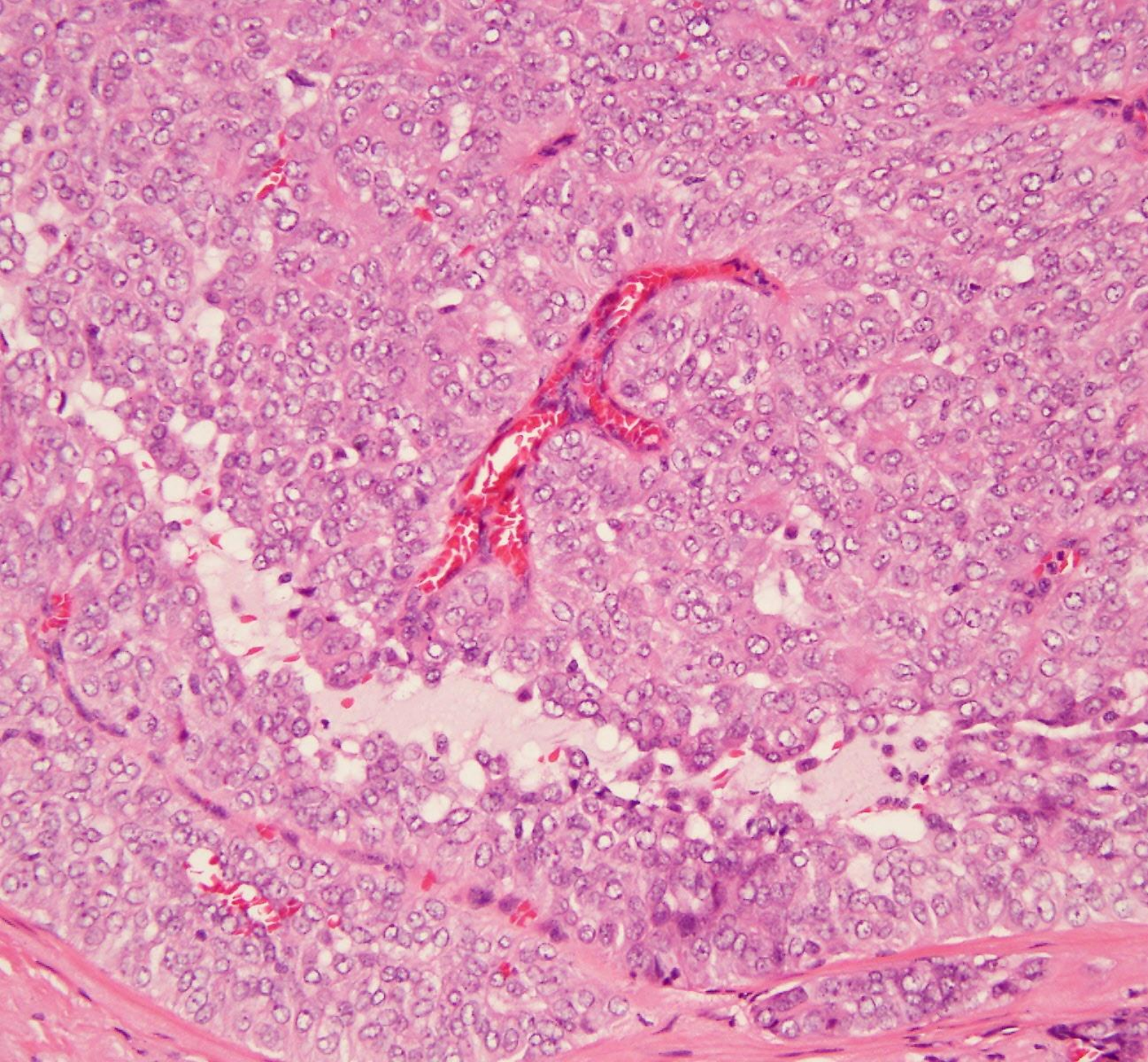


Artificial clefting: glomeruloid

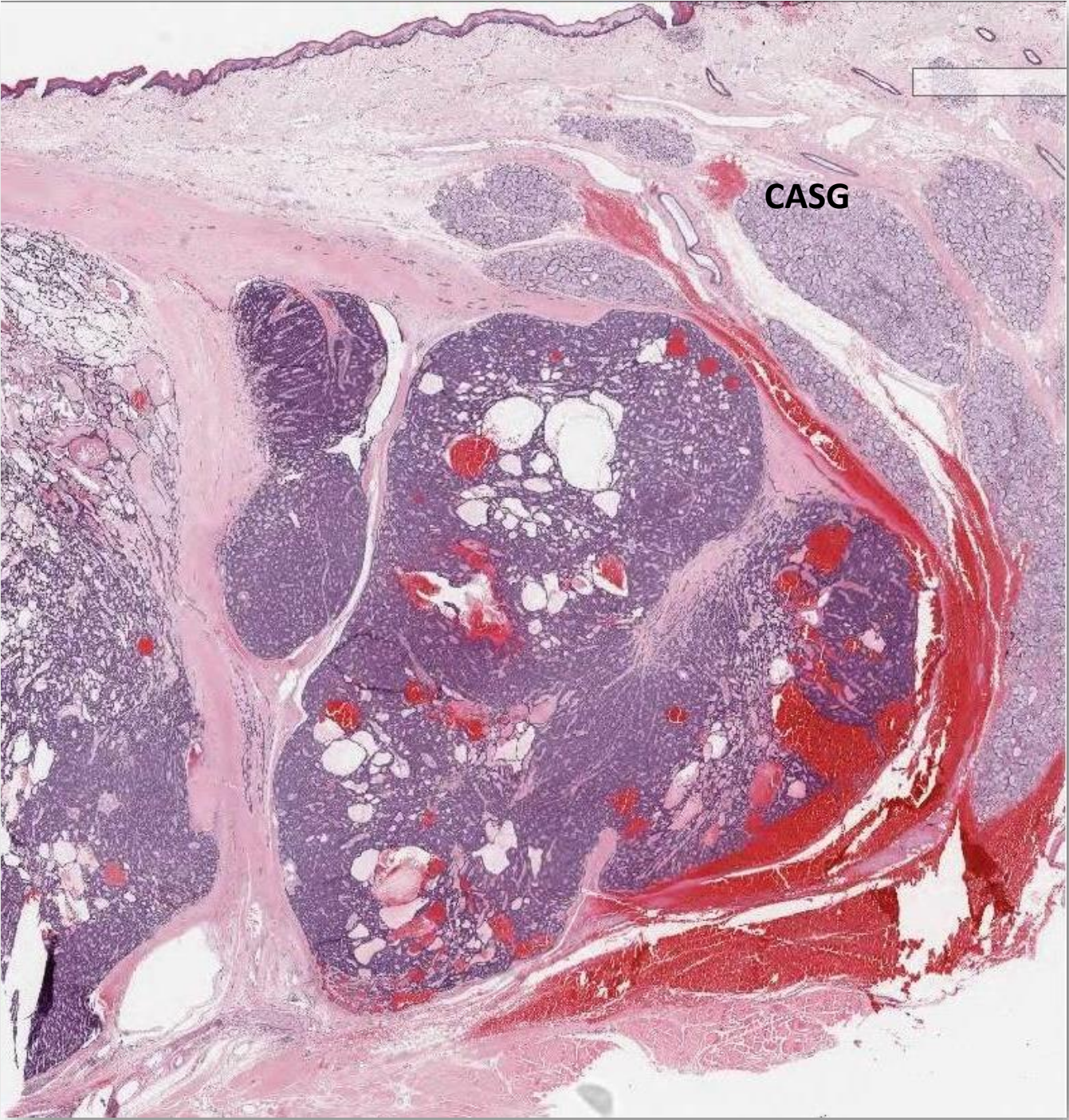


Peripheral palisading



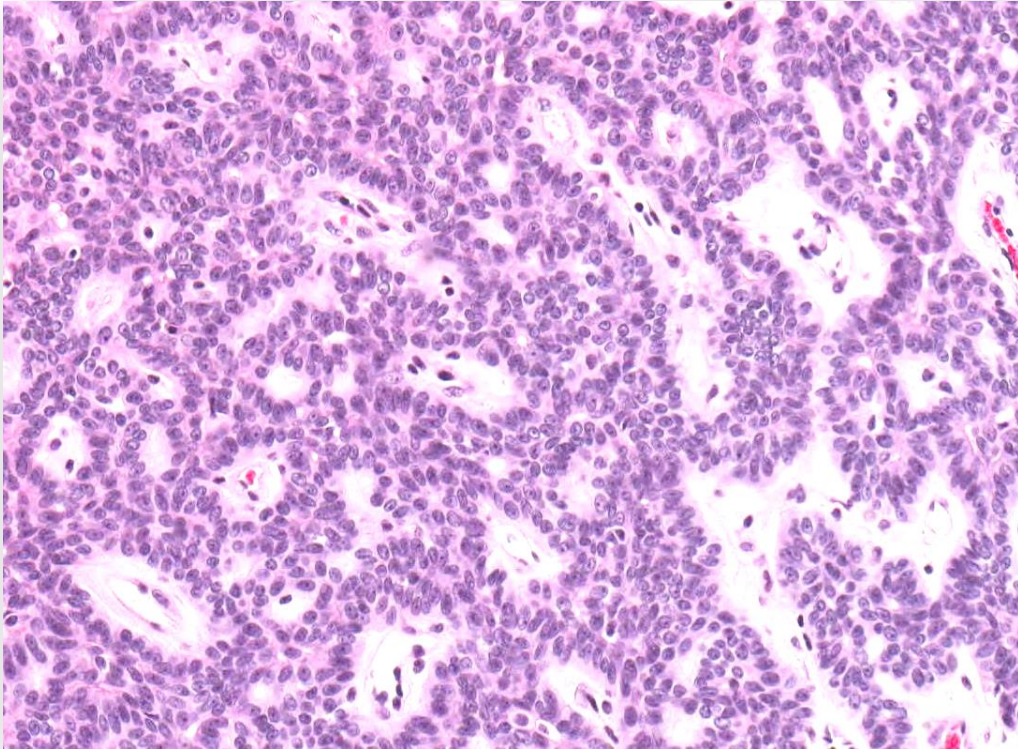


Optical clear
nuclear features



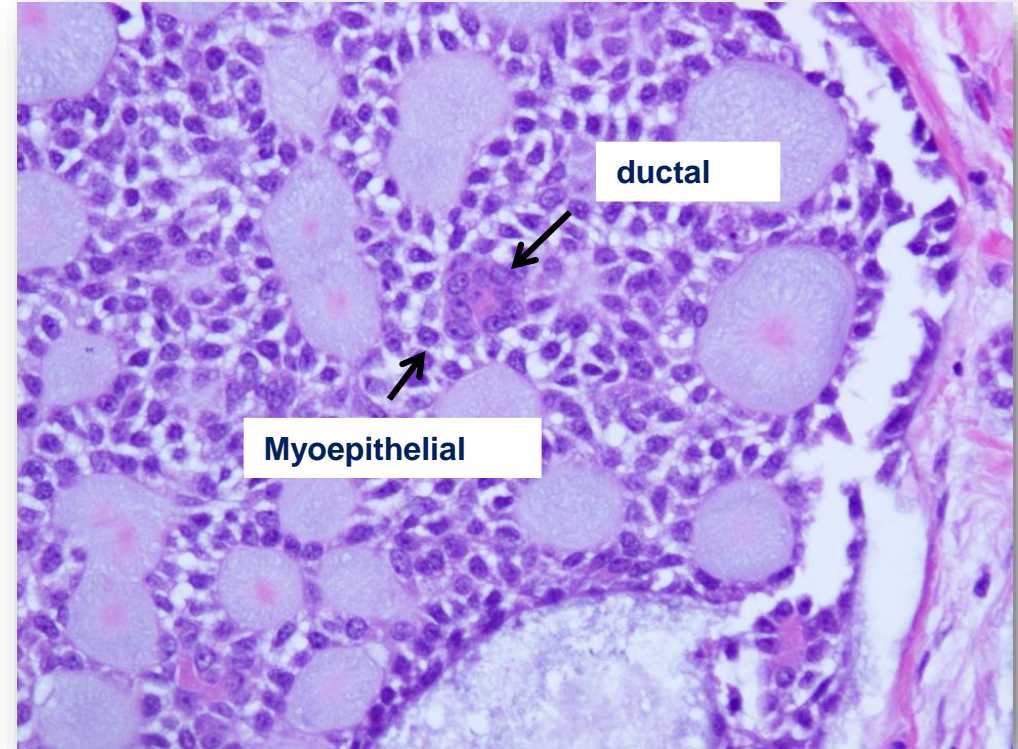
CASG

PAC/Cribriform adenocarcinoma



- One uniform cell type
- Ovoid open vesicular chromatin PTC like nuclei
- Low grade cytology
- Less infiltrative (CASG)

Adenoid cystic carcinoma



- Biphasic
- Hyperchromatic angulated nuclei (myoepithelial cells)
- Mitoses and apoptosis
- More infiltrative

Immunohistochemistry

CASG/PAC

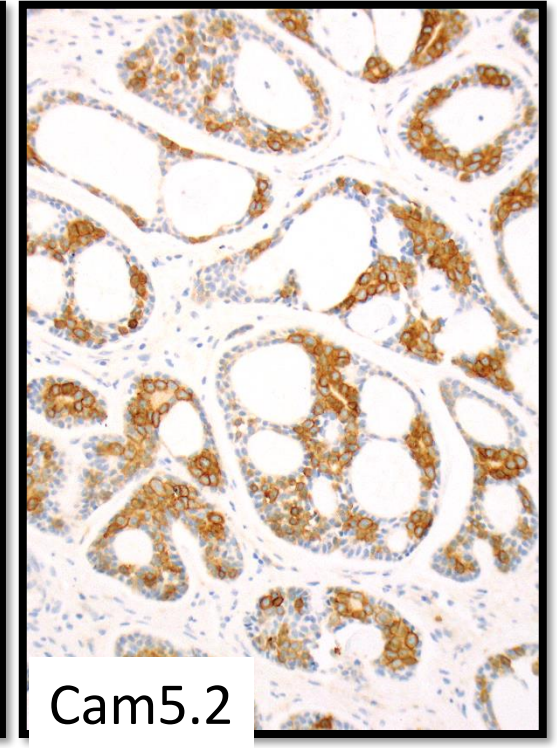
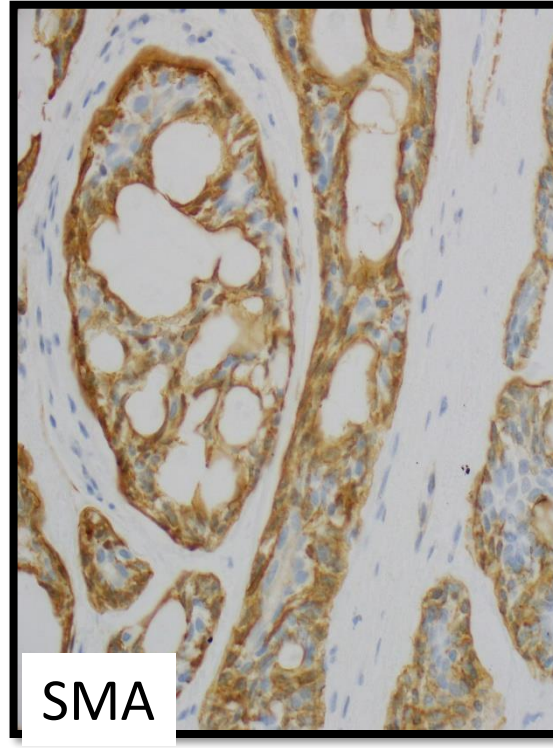
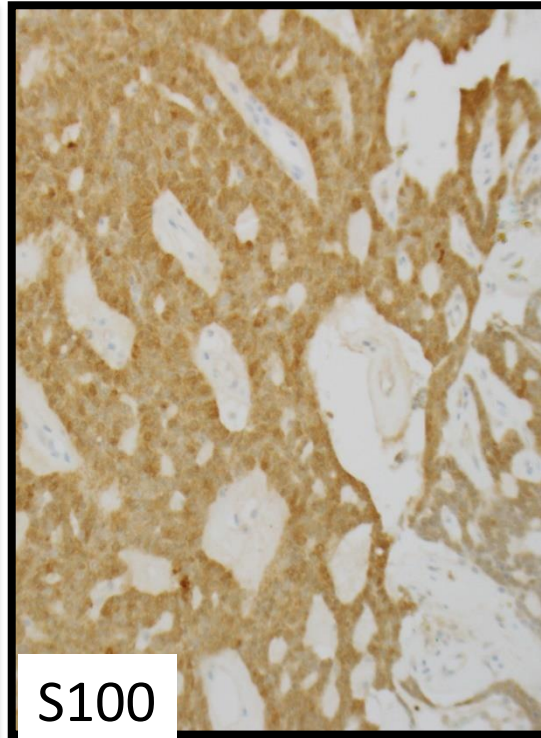
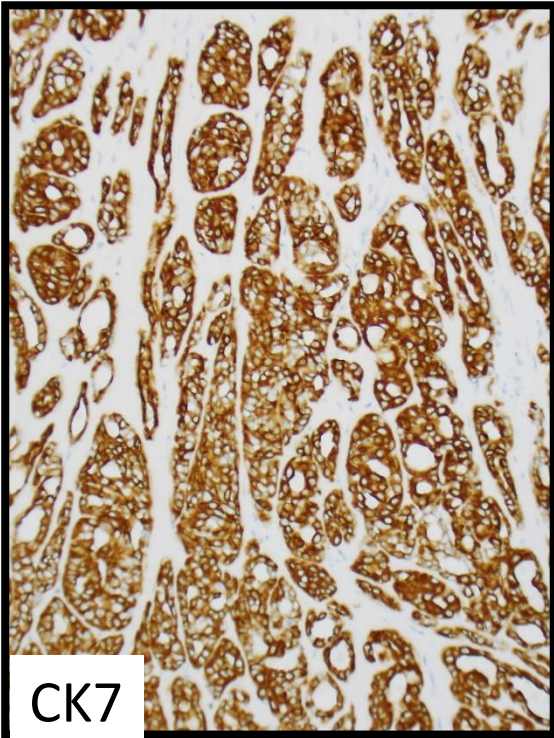
- Diffuse S100 and CK7
- CD117 (+/-)
- P63 usually + P40 –
- Calponin & SMA: + patchy

Adenoid cystic carcinoma

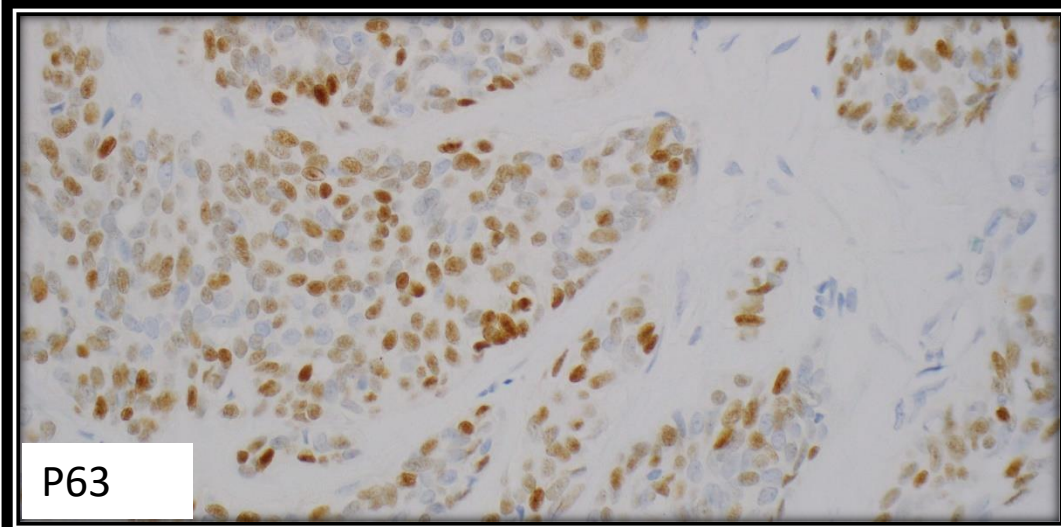
- S100 is variably +
- CD117 + (ductal cells)
- Similar staining for P63 and P40
- Myoepithelial (calponin, P63, P40, SMA) and ductal (cam5.2)

PAC/CASG

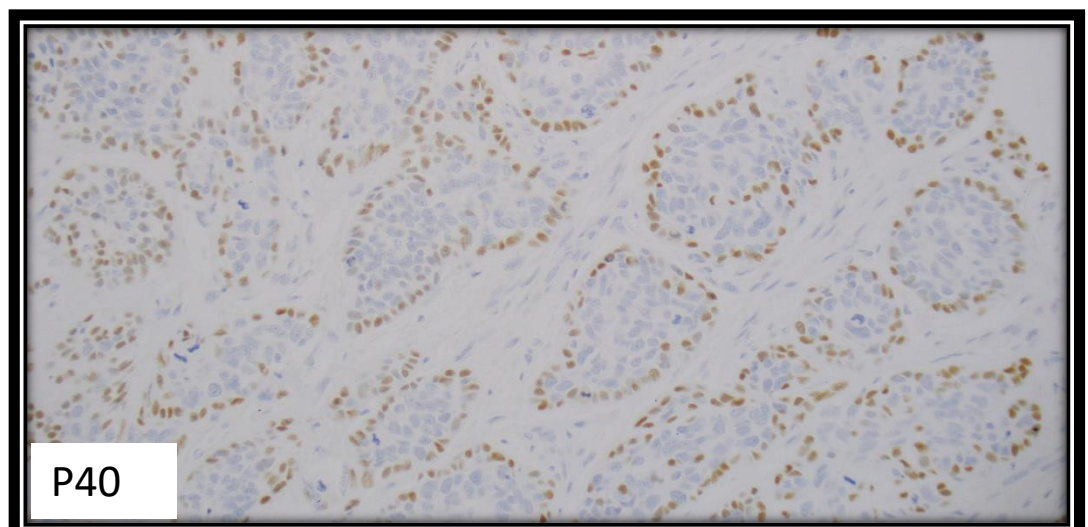
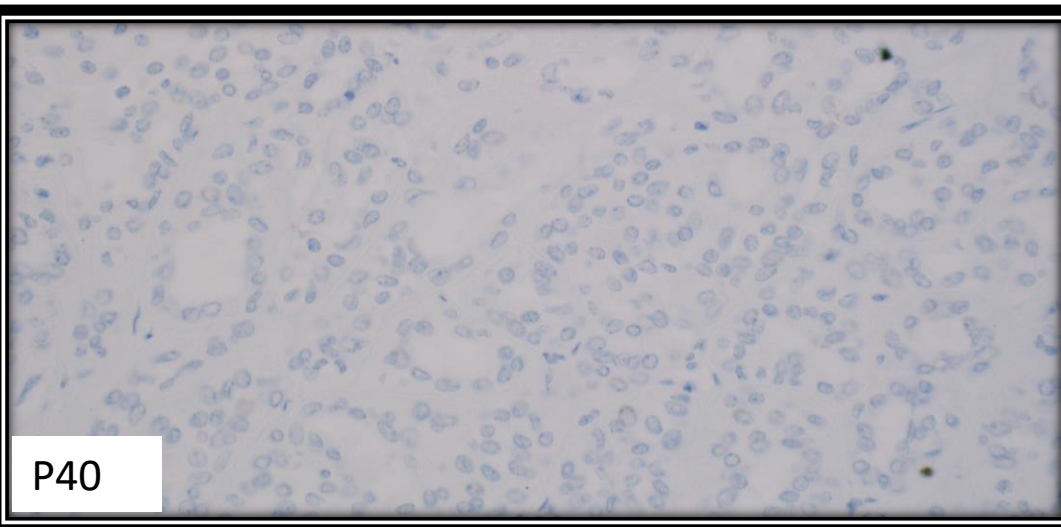
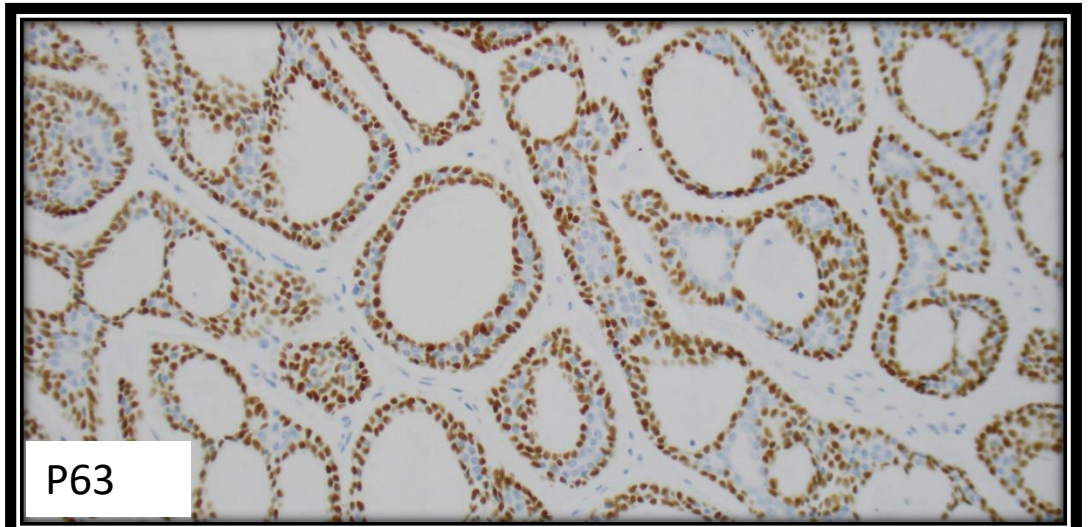
ACC



PAC/CASG



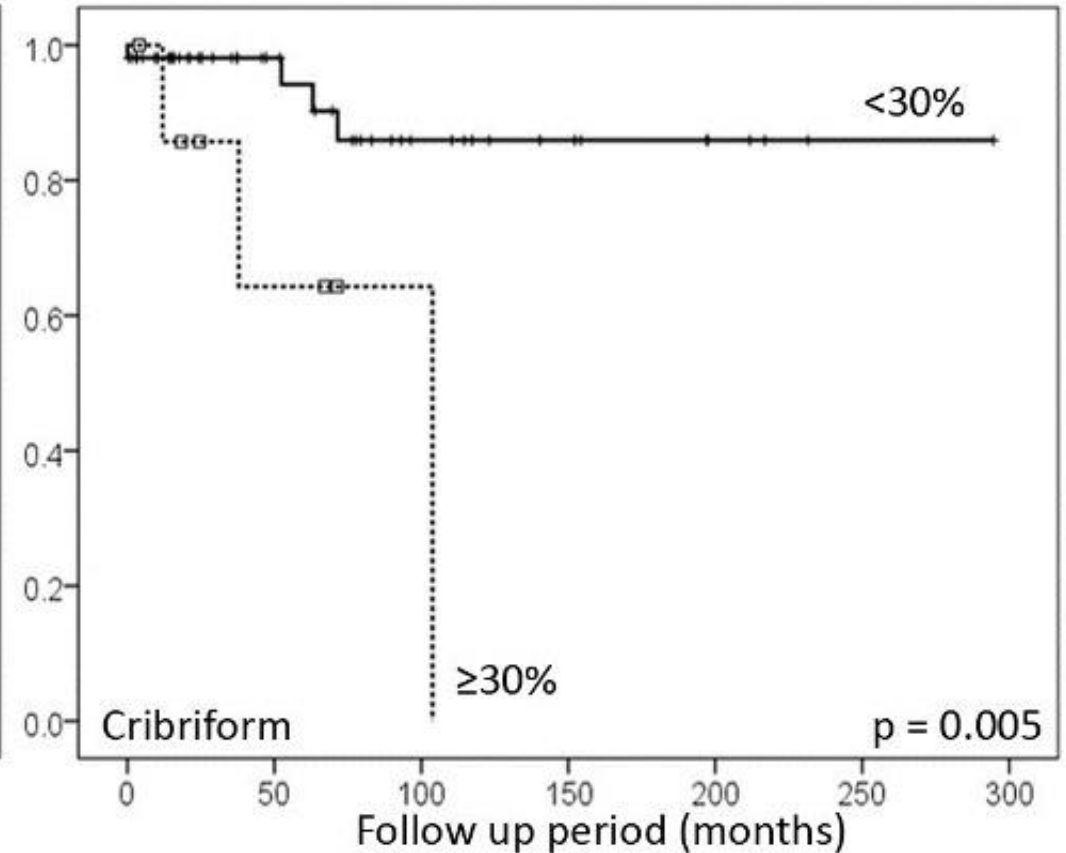
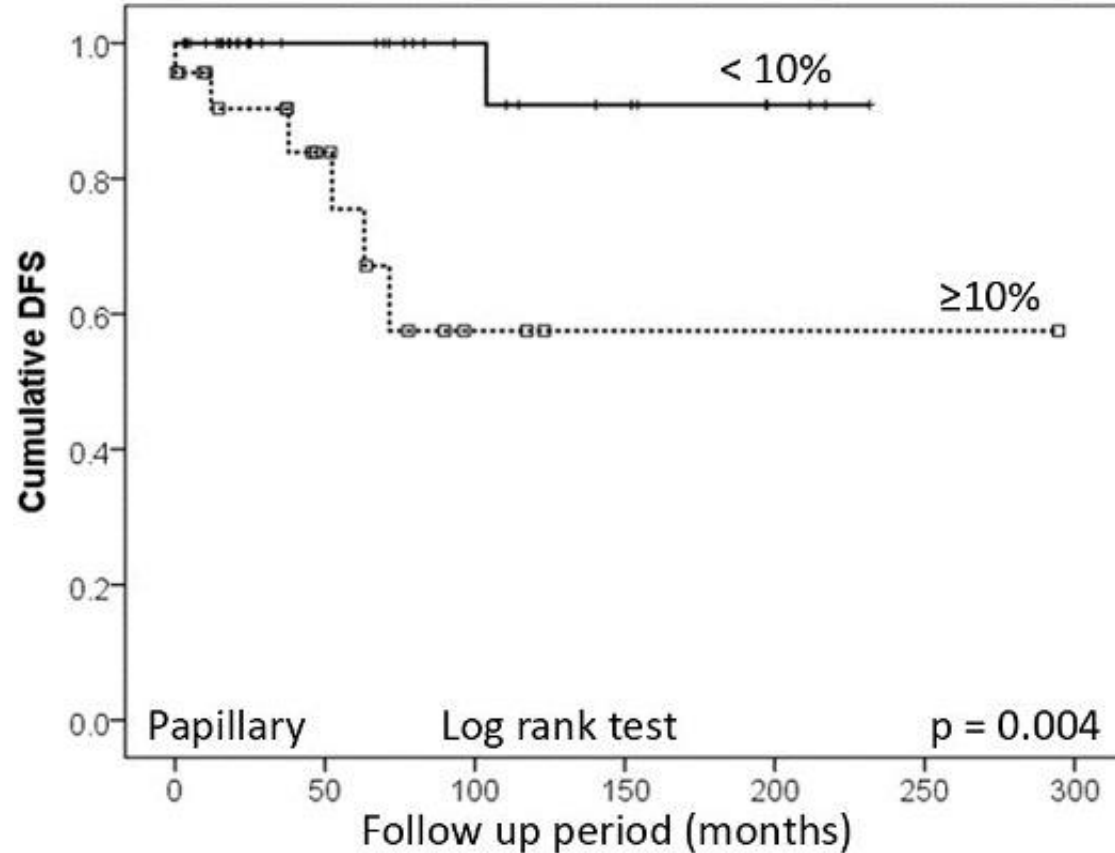
ACC



Predictors of Outcome in the Phenotypic Spectrum of PLGA/cribriform adenocarcinoma of salivary gland (CASG)

Xu B, Ghossein R, Aneja A, Katabi N.
American Journal of surgical Pathology 2017

- Multivariate analysis: **$\geq 10\%$ papillary and $\geq 30\%$ cribriform patterns** are independent predictors for DFS
- **The percentage of cribriform and papillary patterns should be documented**



Two cribriform adenocarcinomas in major SG

CASG

Histologic Spectrum of Polymorphous
Adenocarcinoma of the Salivary Gland Harbor
Genetic Alterations Affecting PRKD Genes

Sebastiao APM, Xu B, Lozada JR, Pareja F, Geyer FC, Da Cruz Paula A, da Silva EM,
Ghossein RA, Weinreb I, de Noronha L, Weigelt B, Reis-Filho JS, Katabi N.

Modern Pathology; Jan 2020; 33 (1): 65-73

Molecular findings

PRKD alterations

- *PRKD1* pGlu710ASP point mutation in 70-89% of PAC
- Fusion involving *PRKD1*, *PRKD2*, *PRKD3* in 70-94% CASG
- *PRKD* fusion-positive tumors
 - Have a high risk of nodal metastasis
- Molecular testing may provide prognostic information

Histologic Classification and Molecular Signature of Polymorphous Adenocarcinoma (PAC) and Cribriform Adenocarcinoma of Salivary Gland (CASG) An International Interobserver Study

Bin Xu, Andrea L. Barbieri, Justin A. Bishop, Simon I. Chiosea, Snjezana Dogan, Silvana Di Palma, William C. Faquin, Ronald Ghossein, Martin Hyrcza, Vickie Y. Jo, James S. Lewis Jr, John R. Lozada, Michal Michal, Fresia G. Pareja, Bayardo Perez-Ordóñez, Manju L. Prasad, Bibianna Purgina, Jorge S. Reis-Filho, Theresa Scognamiglio, Ana P.M. Sebastiao, Raja R. Seethala, Alena Skálová, Stephen M. Smith, Merva S. Tekkeşin, Lester D.R. Thompson, Jason K. Wasseman, Bruce M. Wenig, Ilan Weinreb, and Nora Katabi

American Journal of Surgical pathology

April 2020 44 (4) 545-552

- Interobserver agreements even among expert H&N pathologists are fair to moderate
 - 25 to 30% of cases showing indeterminate histologic features
 - Tumors with papillary architecture are part of the spectrum
 - Tumors with predominant papillary architecture have *PRKD* fusion
-
- **WHO 2022: CASG is a subtype of PAC**

**PAC/CASG
represent a
morphologic &
molecular spectrum**

**PAC/PRKD1 hotspot
mutation**

**IND/overlapping
morphologic &
molecular alteration**

**CASG/PRKD
fusion**

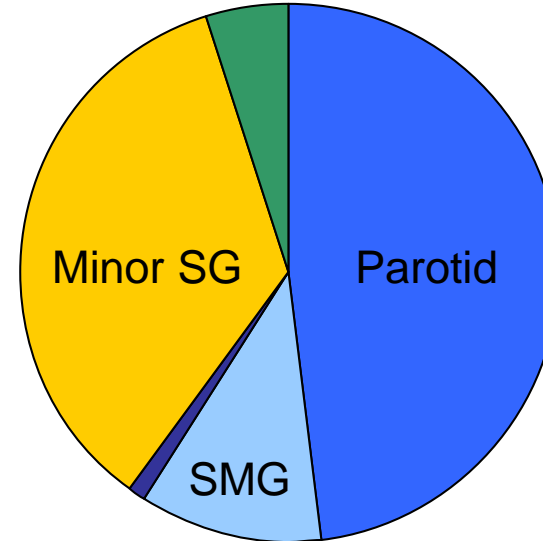


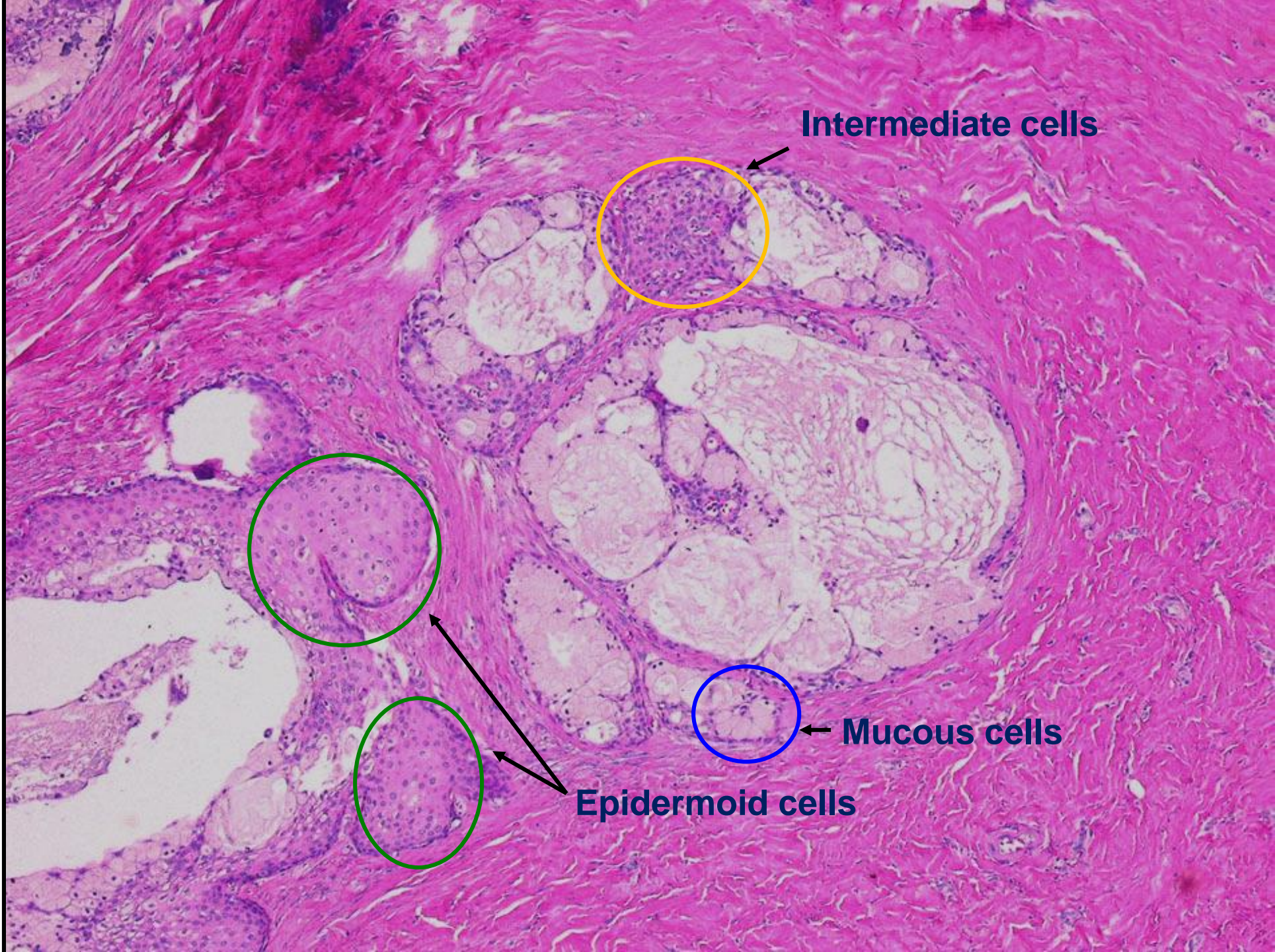
Mucoepidermoid Carcinoma(MEC)

- Most common malignancy (children and adults)
- Mean patient age is 45 years
- Female to male predilection 3:2
- Prior exposure to radiation

Mucoepidermoid carcinoma

- Major salivary glands 60%
 - 48% parotid
 - 11% submandibular
 - 1% sublingual
- Minor salivary glands 35%
(most frequent sites: palate & buccal mucosa)
- Reported in mandible and maxilla (central)



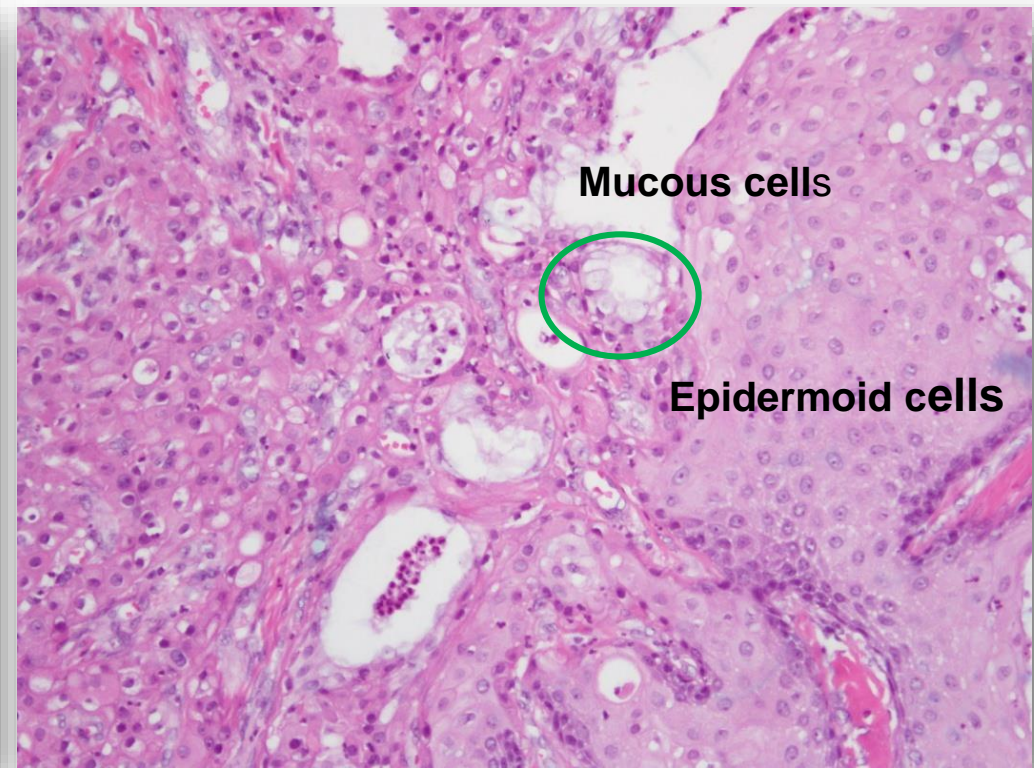
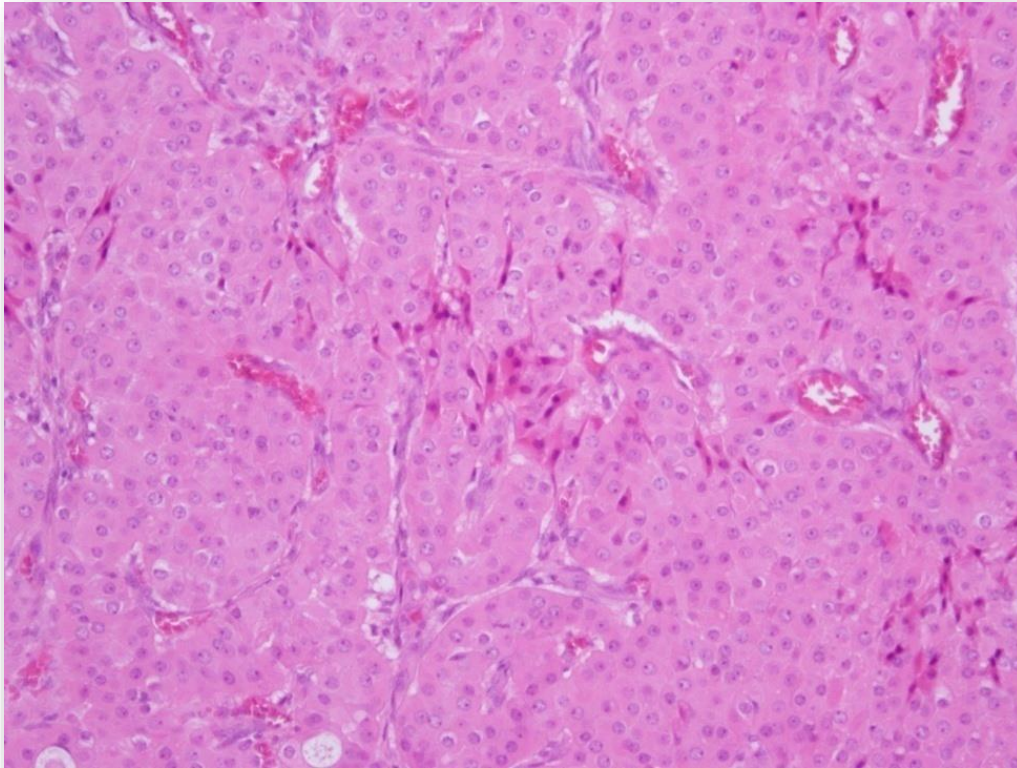


Intermediate cells

Mucous cells

Epidermoid cells

MEC variants: Oncocytic MEC

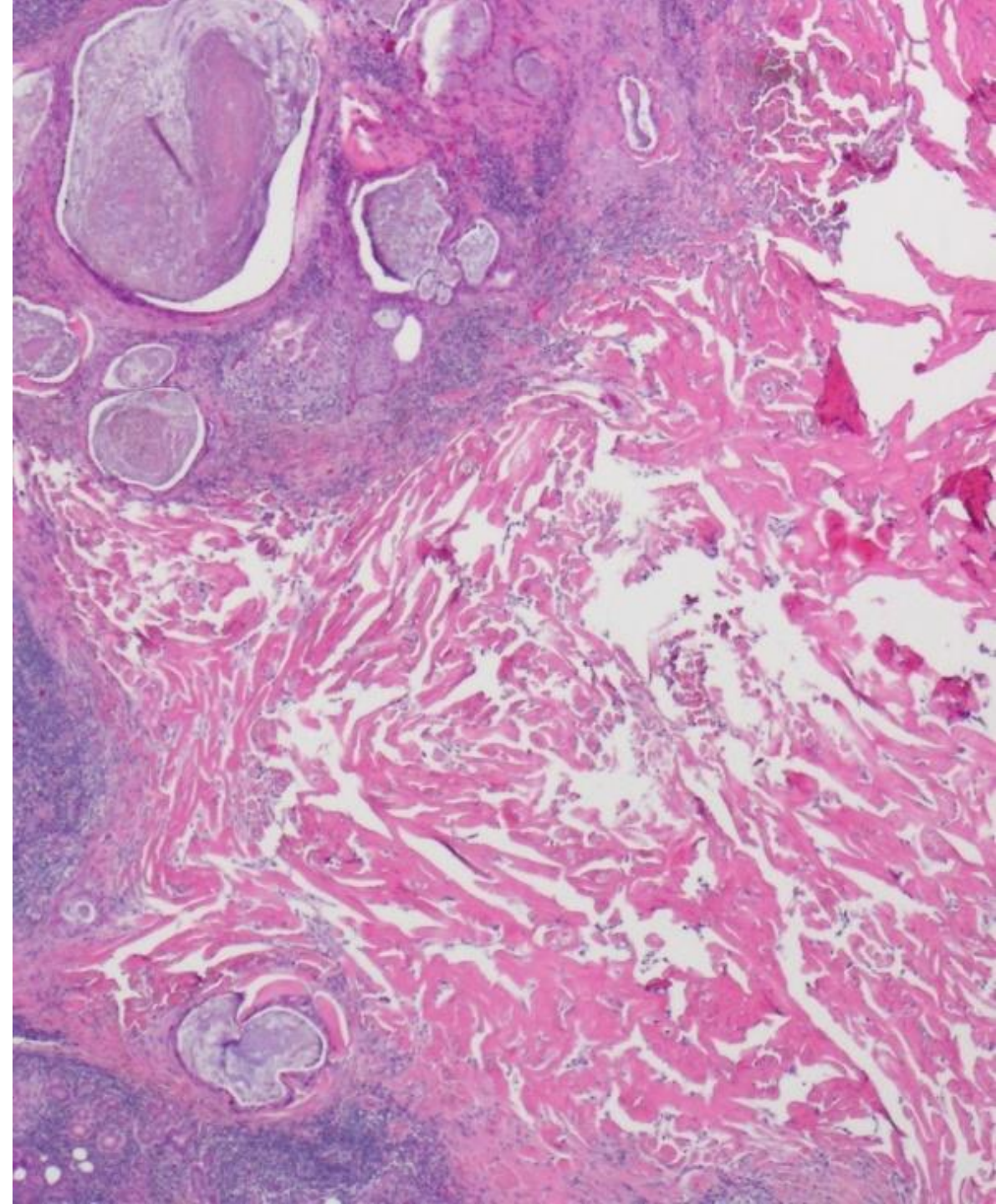
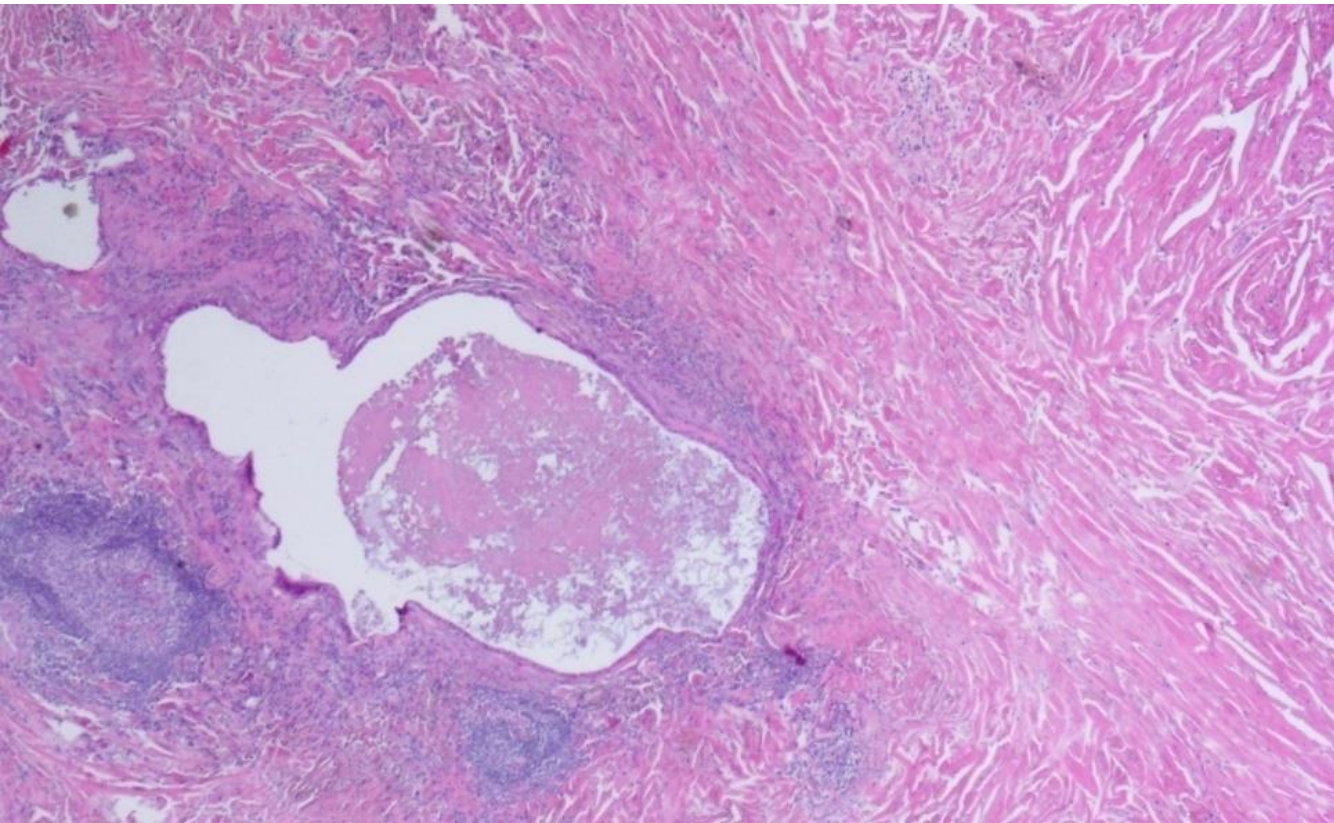


- Extensive oncocytic cells
- Presence of mucous cells and non-oncocytic tumor cells

MEC variants

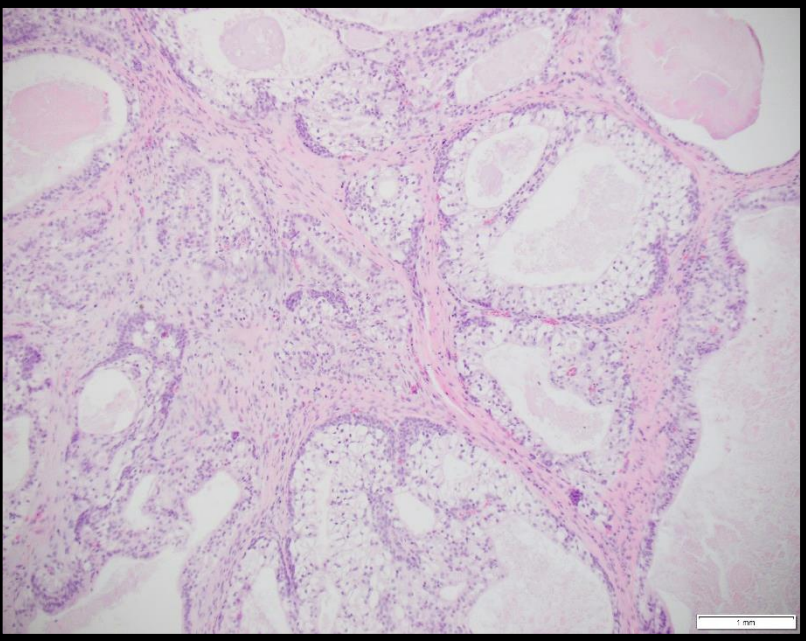
Sclerosing MEC

- Central sclerotic stroma
- Relatively circumscribed
- Peripheral lymphoid tissue

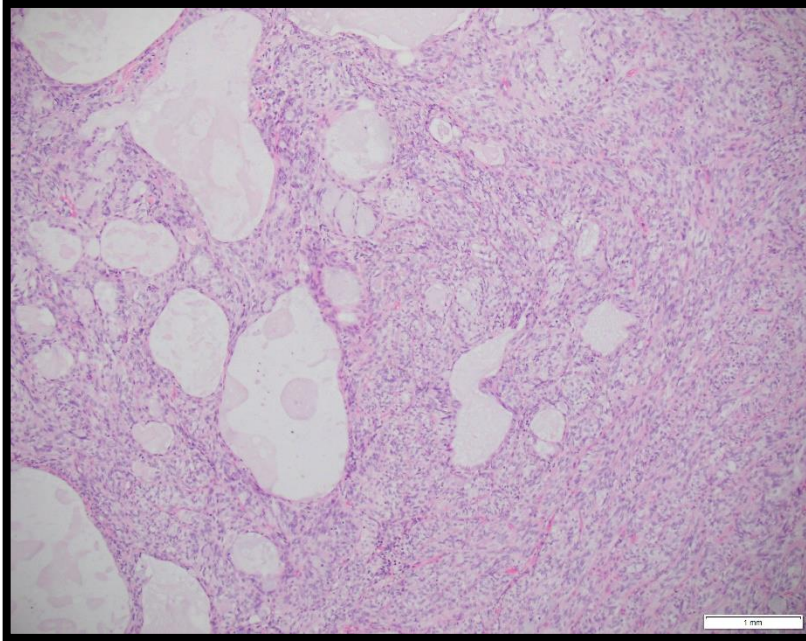


MEC variants

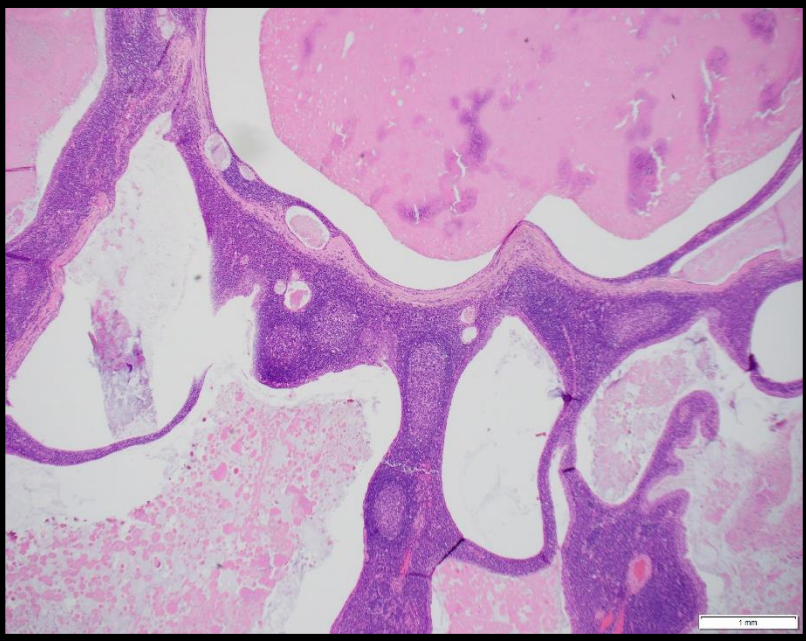
Clear cell MEC



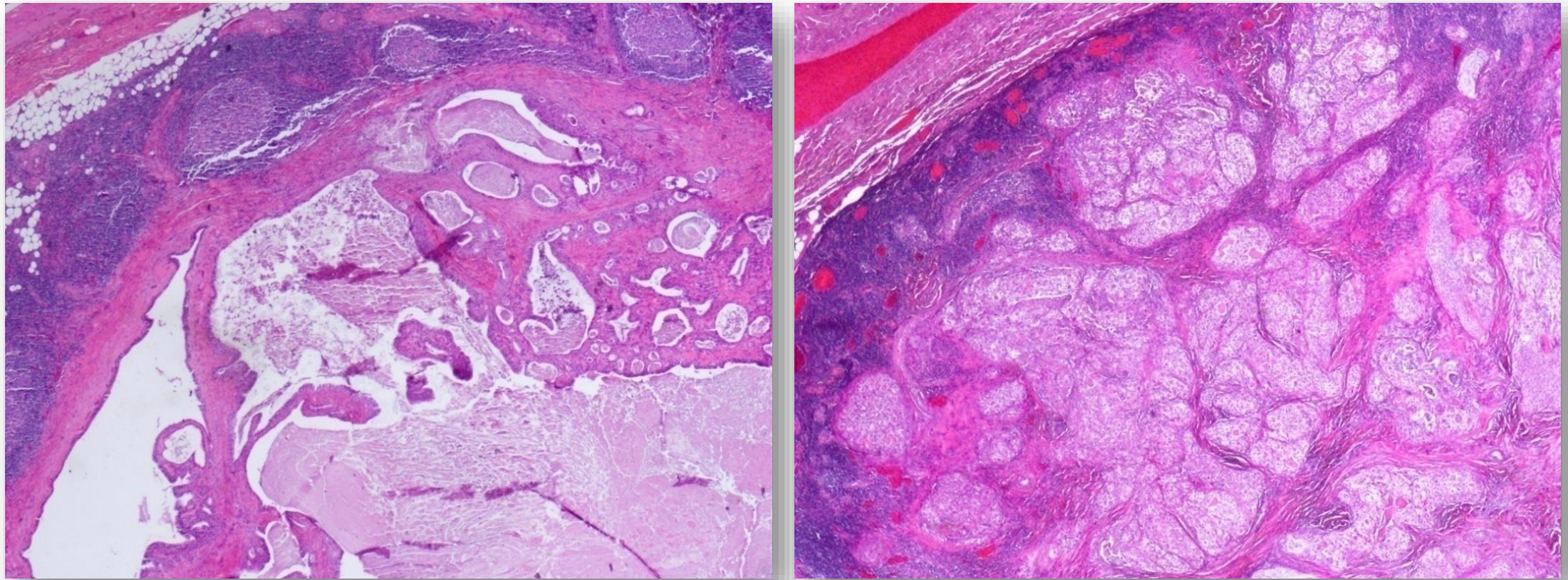
Spindle cell MEC



Warthin like MEC



Peripheral lymphoid stroma



**Lymphoid stroma should not be misinterpreted
as nodal metastases**

Grading MEC

3-tiered grading system

Low

Intermediate

High

MEC survival

5 years survival

Low Grade (LG): 92-100%

Intermediate Grade (IG): 62-92%

High Grade (HG): 0-43%



Low Grade: Surgical resection

High Grade: Surgical resection + adjuvant radiation

(↑ side effects) + neck dissection

Intermediate Grade???

MEC-Different grading systems

- **AFIP**
- **Brandwein**
- **Healy**
- **MSKCC**

AFIP grading system

Intracystic component <20%	+2
Neural invasion	+2
Mitoses ($\geq 4/10$ HPF)	+3
Necrosis	+3
Anaplasia	+4
Grade	Score
Low	0-4
Intermediate	5-6
High	7-14

*Goode &
Auclair 1997*

Brandwein grading system

- *Brandwein 2001*

Intracystic component <25%	+2
Neural invasion	+2
Tumor invades in small nests and islands	+2
Lymphatic/vascular invasion	+3
Pronounced nuclear atypia	+2
Bony invasion	+3
Mitoses ($\geq 4/10$ HPF)	+3
Necrosis	+3
Grade	Score
Low	0
Intermediate	2-3
High	4 or more

Modified Healy Qualitative

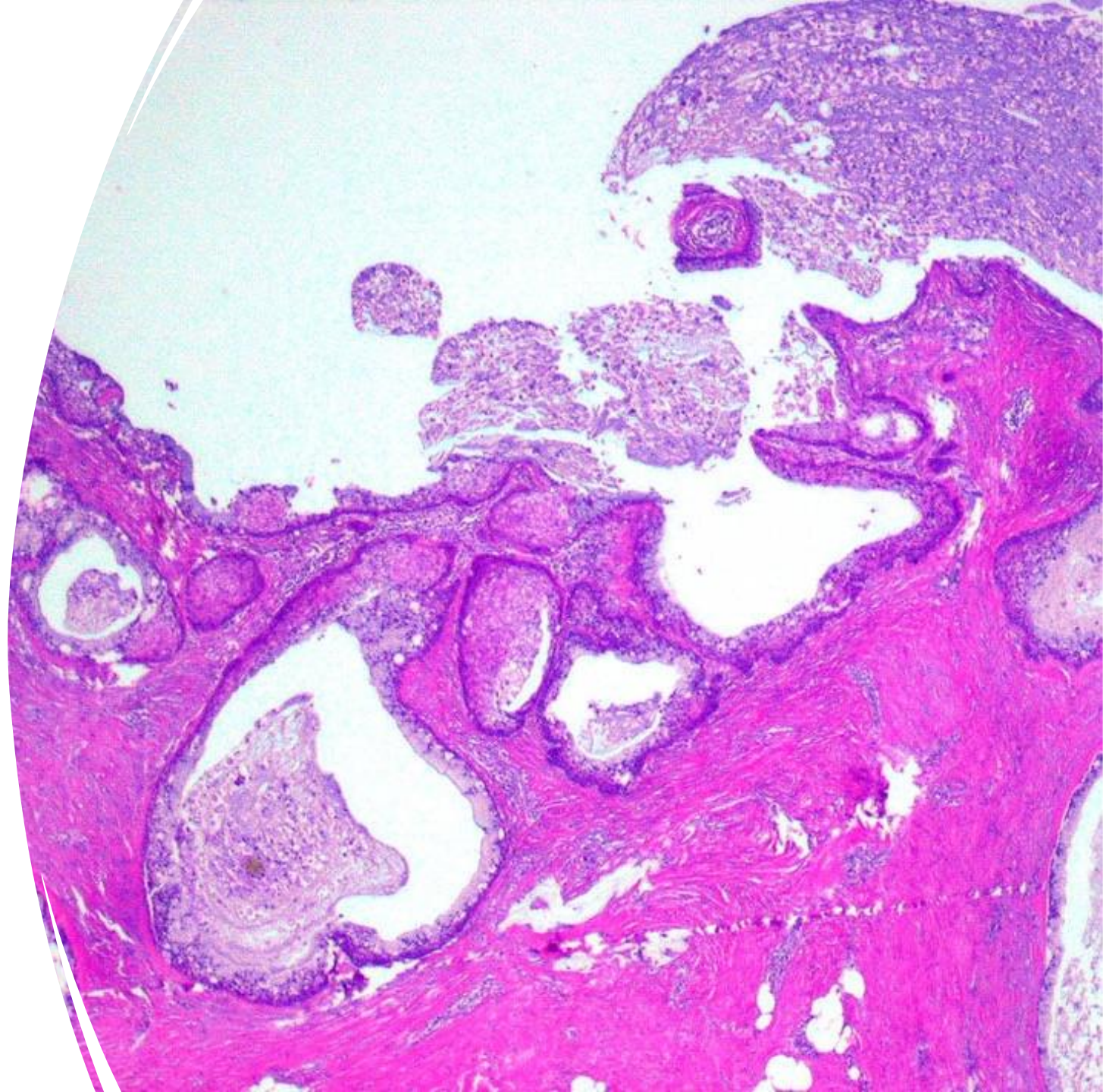
Low Grade	Intermediate Grade	High Grade
<u>Growth:</u> Macrocysts & microcysts	<u>Growth:</u> Solid nests	<u>Growth:</u> Predominately solid
1/1 mucin/epidermoid cells, minimal to moderate intermediate cells	Large duct are not obvious	Tumor cells range from poorly differentiated to epidermoid and intermediate
Transition to excretory duct		
<u>Cytology:</u> Absent to minimal pleomorphism and rare mitoses	<u>Cytology:</u> Mild to moderate pleomorphism, few mitoses, prominent nucleoli	<u>Cytology:</u> Marked pleomorphism, easily found mitoses
<u>Infiltration:</u> Circumscribed borders	<u>Infiltration:</u> Invasive, poorly circumscribed borders, fibrosis	<u>Infiltration:</u> PNI, VI, invasion into soft tissue, desmoplasia
Pools of extravasated mucin	Peripheral chronic inflammation	Less common peripheral chronic inflammation

Problems

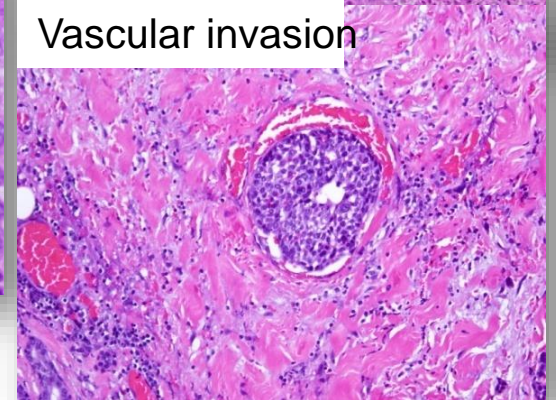
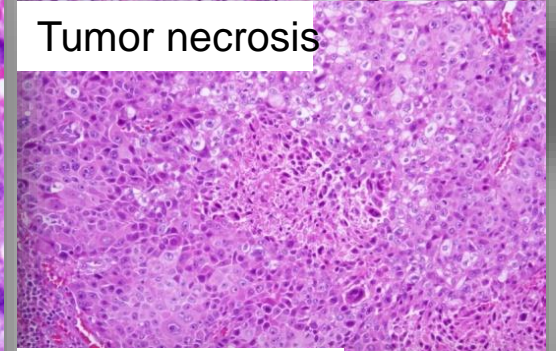
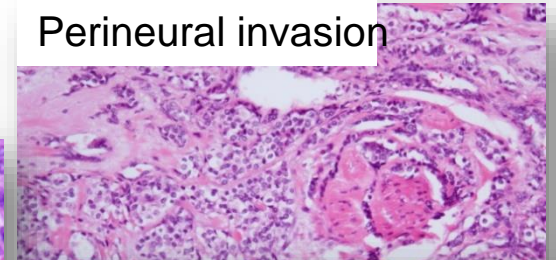
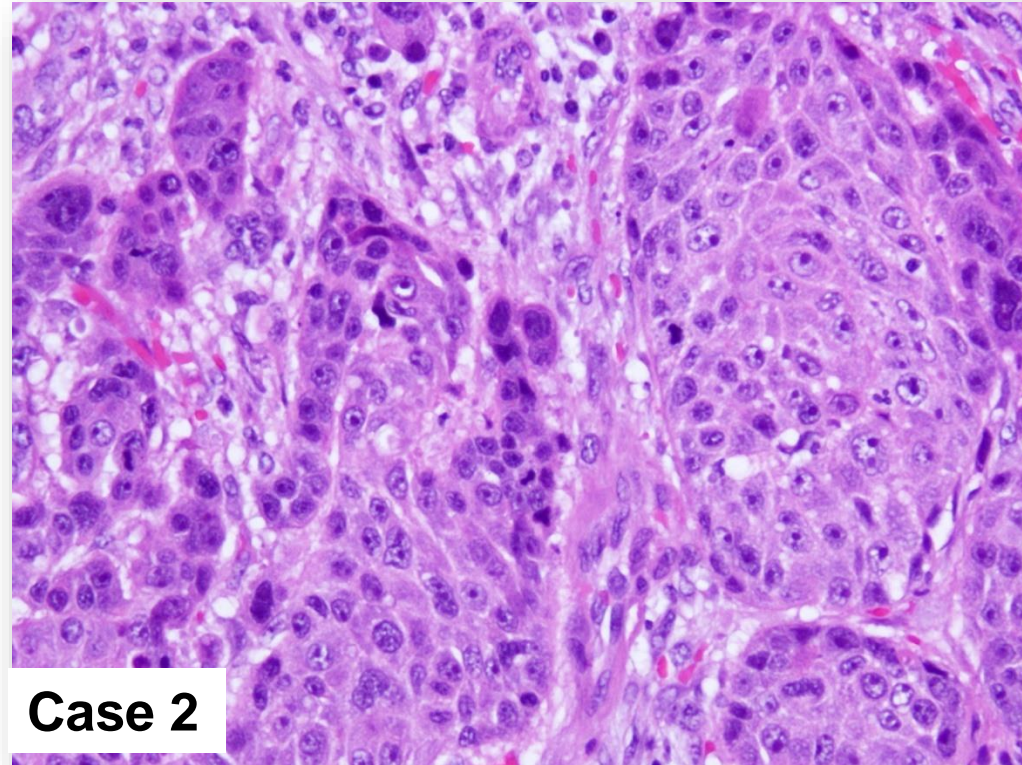
- **AFIP system**
 - Downgrades MEC
 - Fails to predict an indolent course for low grade
- **Brandwein system**
 - Upgrades MEC
 - Categorizes some indolent tumors as high grade
- **Healy system**
 - Ambiguous
 - Subjective

Case 1

All grading systems
Low grade MEC

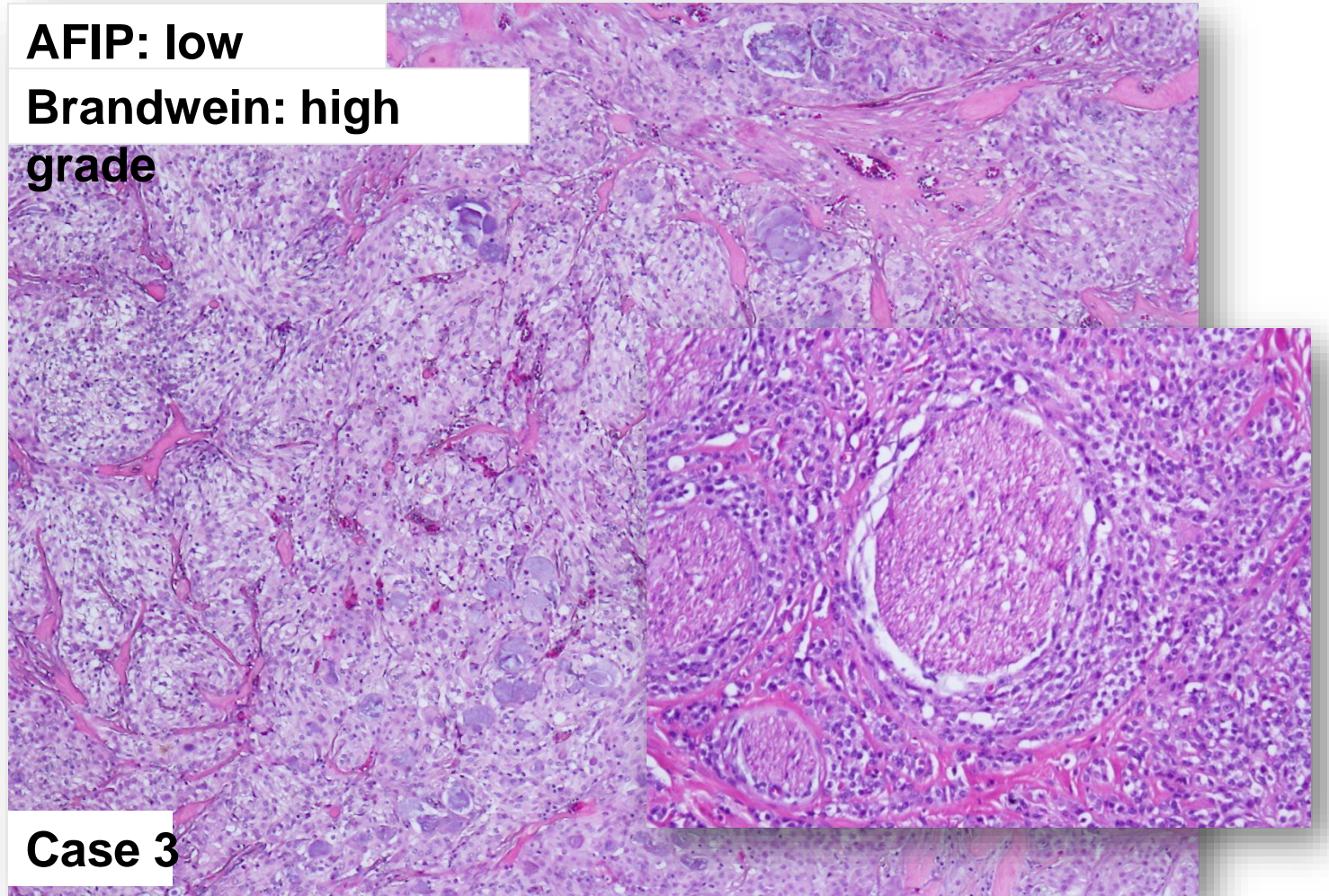


All grading systems
High grade MEC



AFIP: low

**Brandwein: high
grade**



Case 3

Prognostic Features in Mucoepidermoid Carcinoma of Major Salivary Glands with Emphasis on Tumour Histologic Grading

Katabi N, Ghossein R, Klimstra DS, Dogan S, Ganly I

Histopathology July 2014

- All grading systems (AFIP, Brandwein, Healy, MSKCC) correlated significantly with outcome
- **No consensus in 23/52 (44%)** and tumors called high-grade using Brandwein but low grade using AFIP
- **Mitosis, necrosis, pleomorphism, desmoplasia, and LN metastasis** were associated with adverse DFS and RFS ($p < 0.02$)



MSKCC Grading System

High grade MEC: ≥ 4 mitosis/10 HPFs and/or necrosis
Does not include PNI, VI, or bone invasion

	Low grade	Intermediate grade	High grade
Predominant growth pattern	Cystic	Predominantly solid	Any (usually solid)
Infiltration	Well circumscribed borders	Well circumscribed or infiltrative borders	Any (usually infiltrative borders)
Mitosis	0-1/10 HPFs	$< 4/10$ HPFs	$\geq 4/10$ HPFs
Necrosis	Absent	Absent	Present

WHO 2022 (5th edition)

Three grading systems:
AFIP, Brandwein and MSK
without endorsement

“**LG MECs** are usually circumscribed, partly cystic and contain groups of mucous cells.
IG MECs generally have more solid areas, while **HG neoplasms** are solid with fewer mucous cells, and may display nuclear pleomorphism, mitotic figures, necrosis, and perineural, lymphovascular or bony invasion.”

Critical Appraisal of Histologic Grading for Mucoepidermoid Carcinoma of Salivary Gland: is an Objective

Prognostic Two-Tiered Grading System Possible?

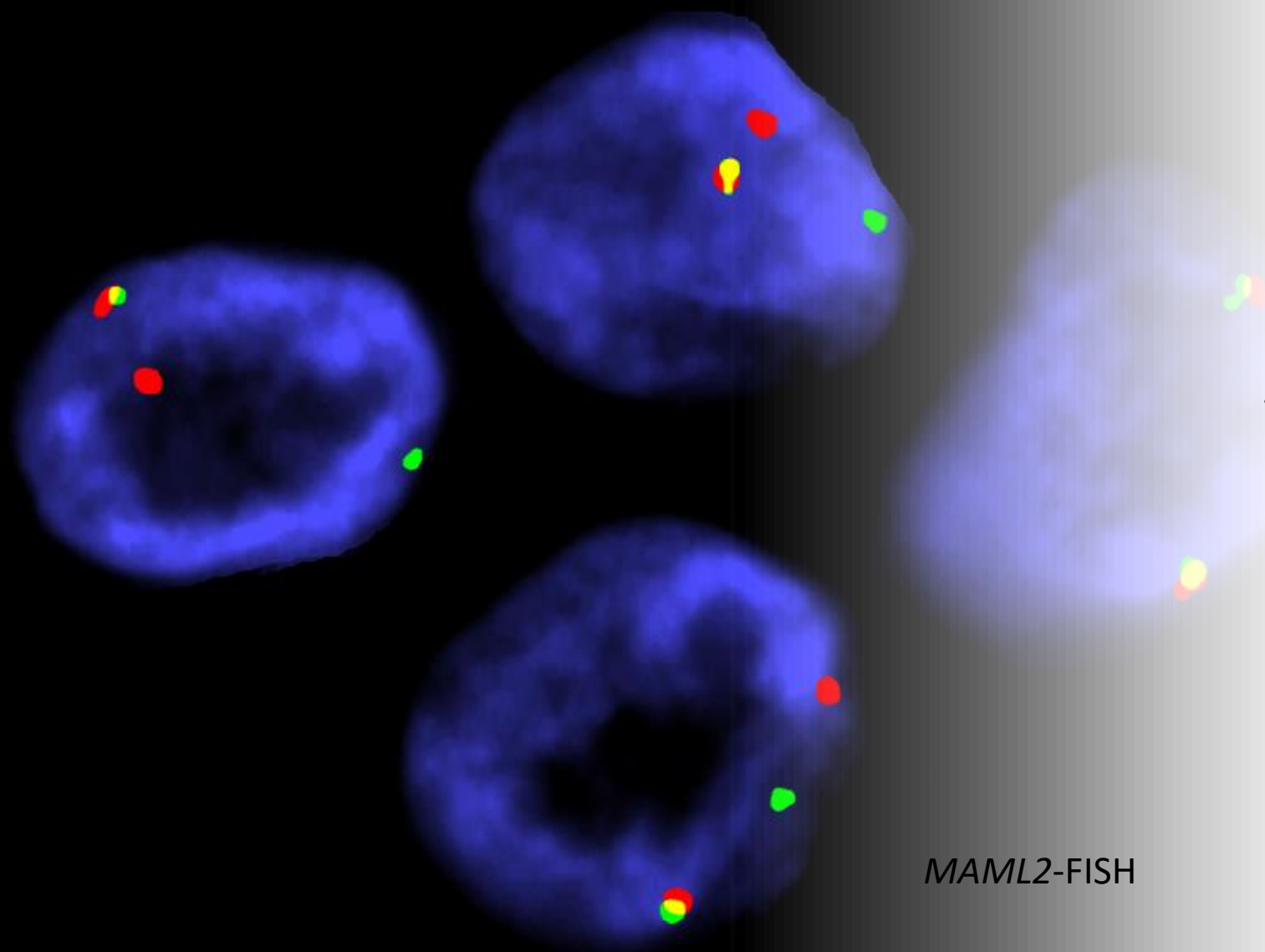
Bin Xu, Bayan Alzumaili, Karina C. Furlan, German H. Martinez, Marc Cohen, Ian Ganly, Ronald A. Ghossein, Nora Katabi

Am J Surg Pathol, September 2023

- **LG and IG MECs behave similarly** with comparable risk of nodal metastasis, recurrence, and distant metastasis
- **Modified MSKCC 2-tiered grading system (LG and HG)**

Low grade		High grade	
Mitotic count <4/10 HPFs	No tumor necrosis	Mitotic count ≥4/10 HPFs	Tumor necrosis

- Two-tiered grading system independently predicts RFS



MEC-Molecular
t(11,19) (q21;p13)
CRTC1::MAML2

MAML2-FISH

MEC-Differential Diagnosis

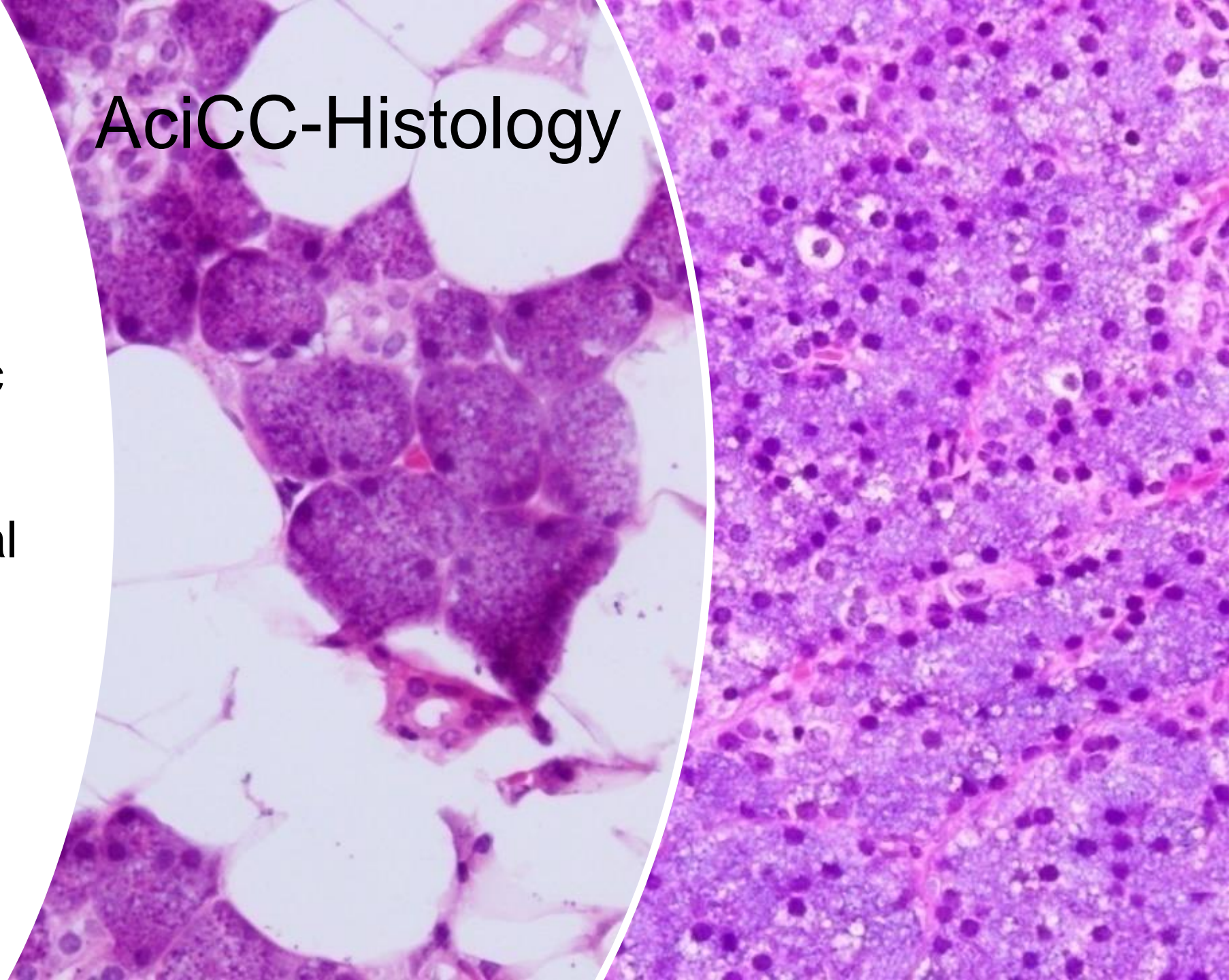
- Benign cyst
- Warthin's Tumor
- Hyalinizing clear cell carcinoma
- Salivary duct carcinoma
- Squamous cell/Adenosquamous carcinoma

Acinic cell carcinoma (AciCC)

- Serous acinar differentiation
- Wide range of age
- Slightly more common in females
- Most common site parotid (90-95%)

AciCC-Histology

Spectrum of acinic cell carcinoma is broad and not limited to the typical acinar cells



AciCC-Histology

Cell types

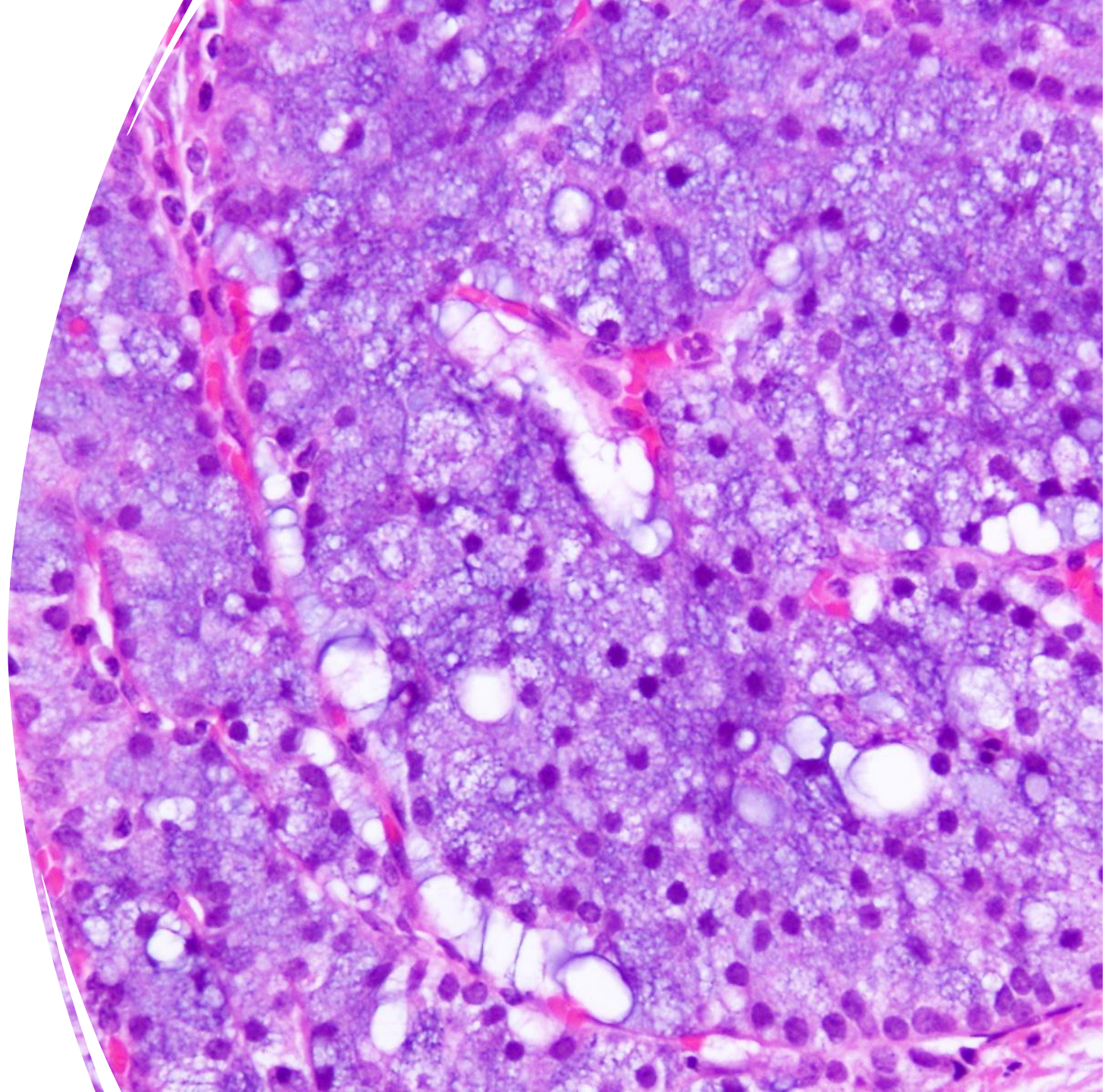
- Acinar
- Intercalated duct
- Vacuolated
- Non-specific glandular

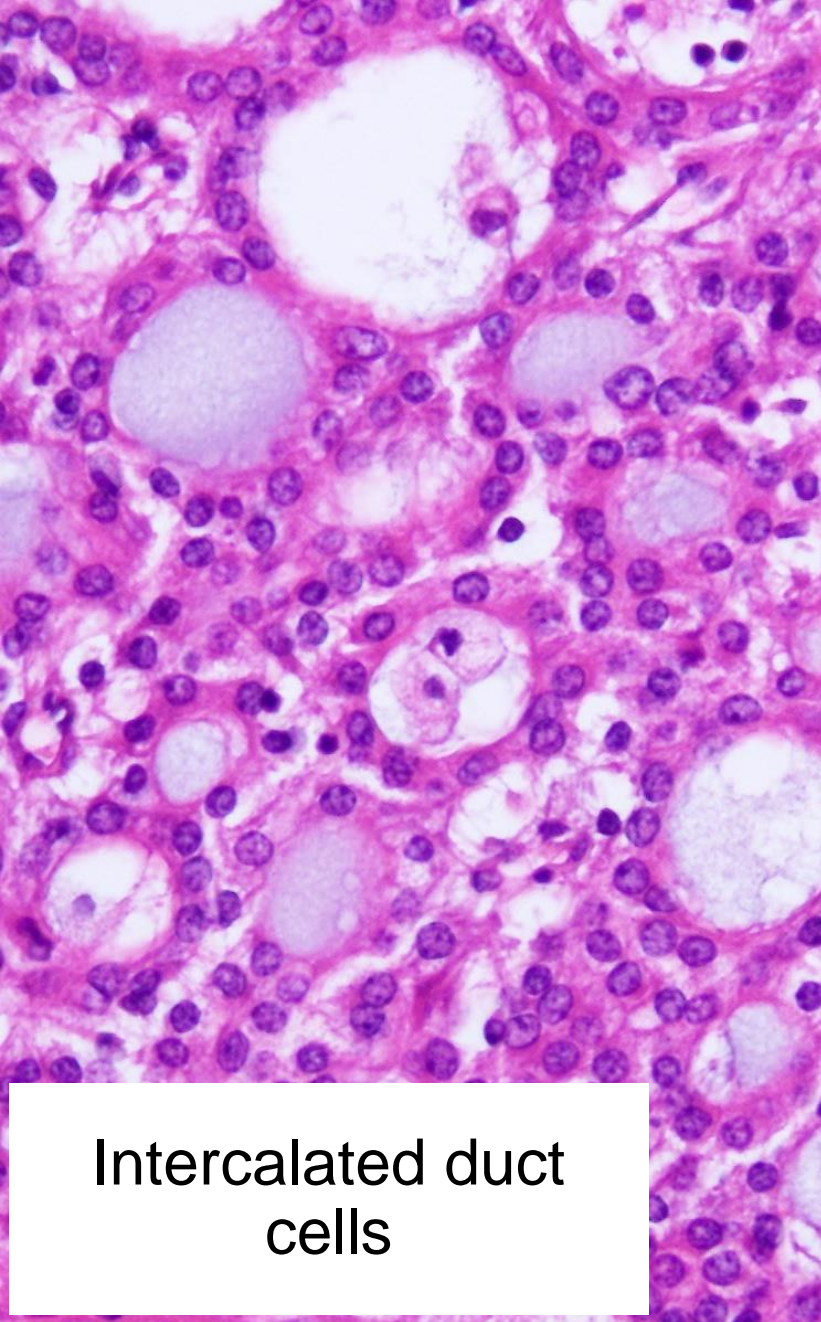
Growth patterns

- Solid/lobular
- Microcystic
- Follicular

Acinar cells

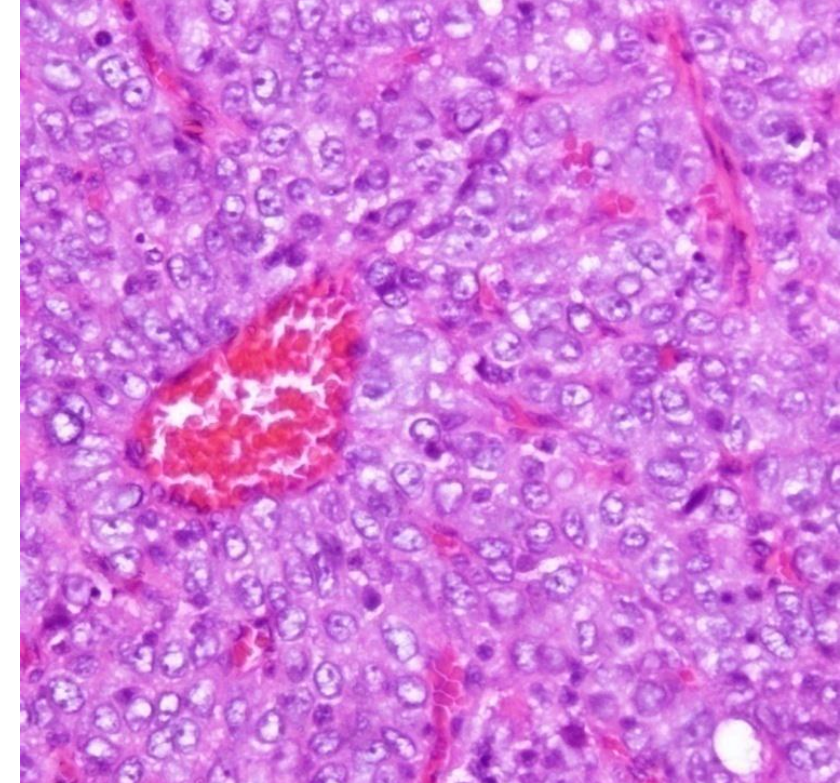
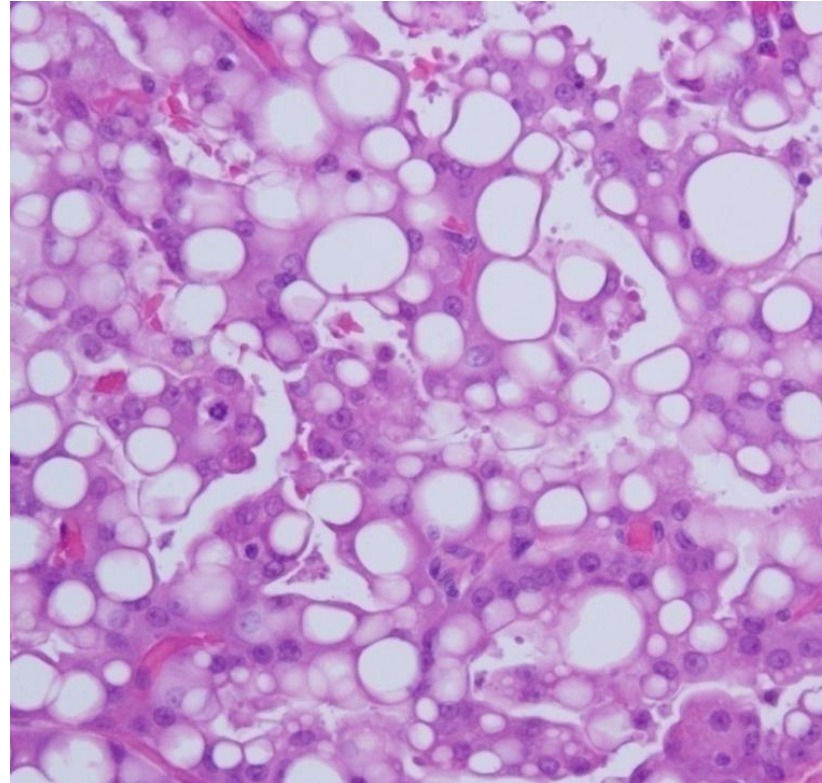
Eccentric uniform nuclei with abundant basophilic cytoplasm

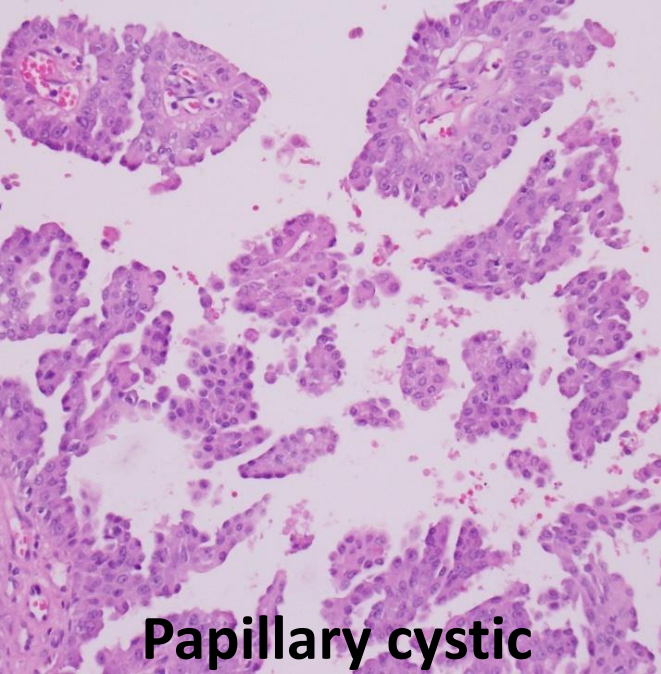




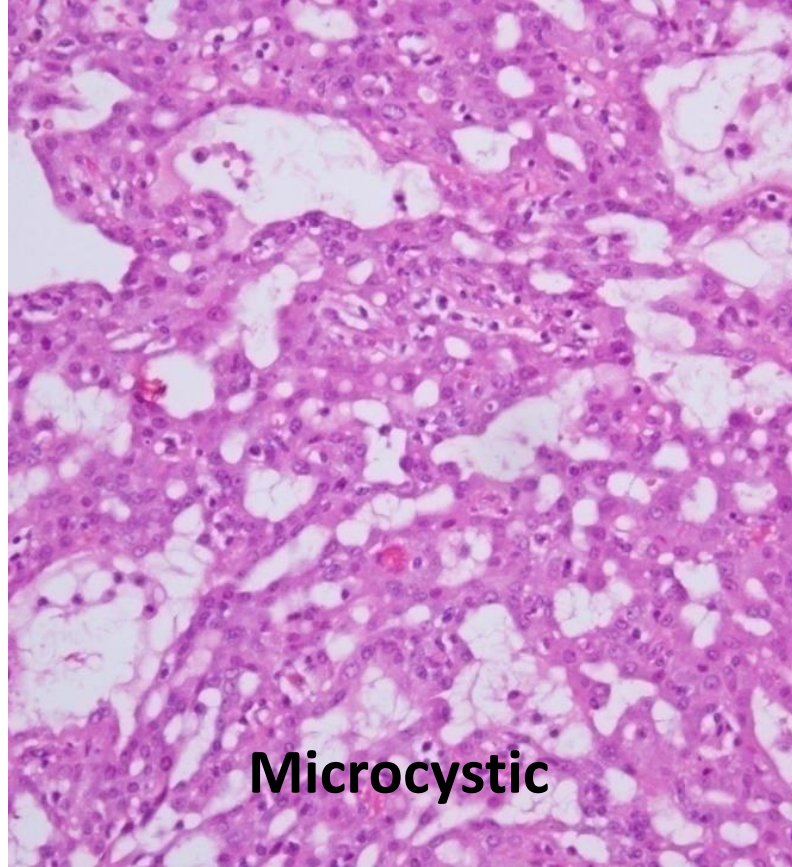
Vacuolated cells

Non-specific glandular cells





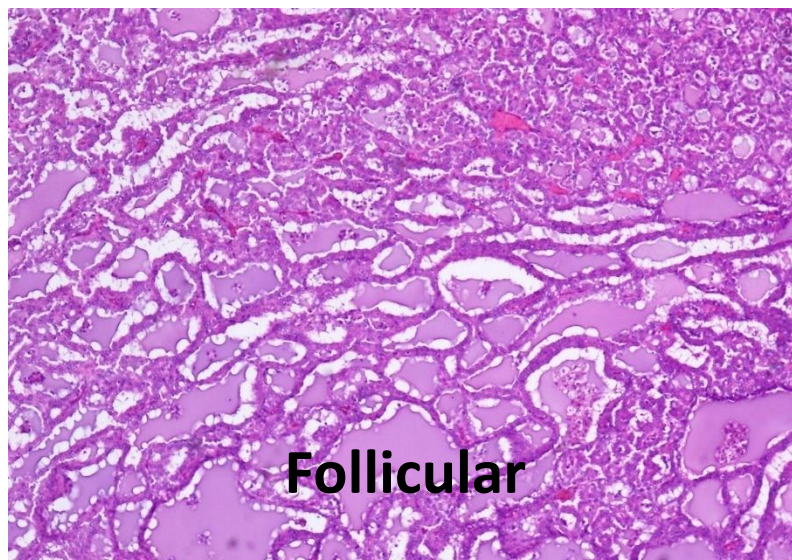
Papillary cystic



Microcystic



Papillary cystic



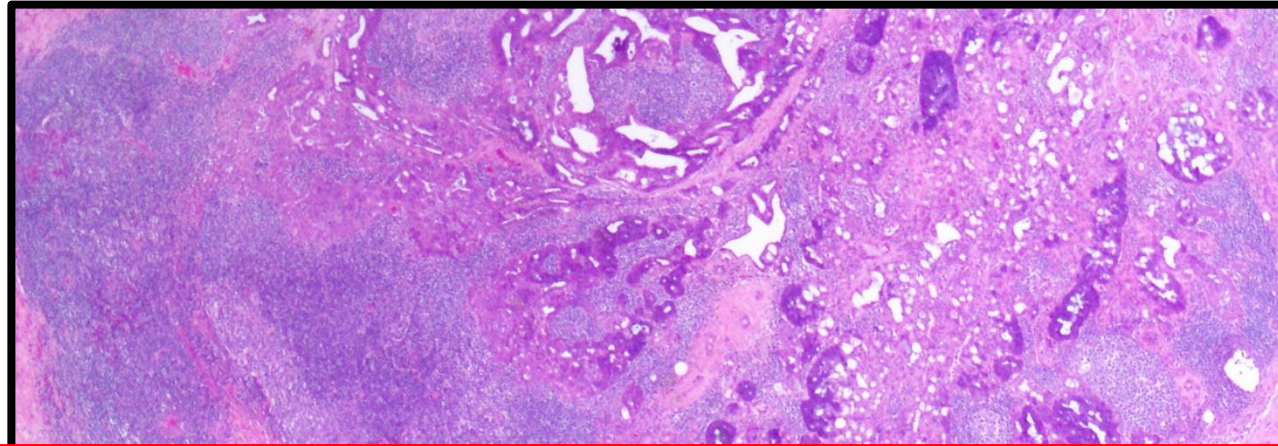
Follicular

AciCC Growth patterns

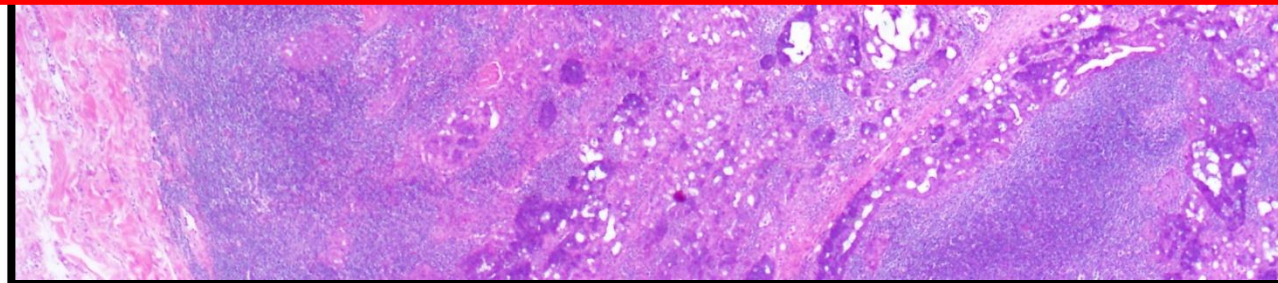


Solid

Associated lymphoid stroma



**Lymphoid stroma should not be misinterpreted
as nodal metastases**



AciCC-Prognosis

Low grade indolent tumor

High grade and
aggressive behavior may
occur

AciCC

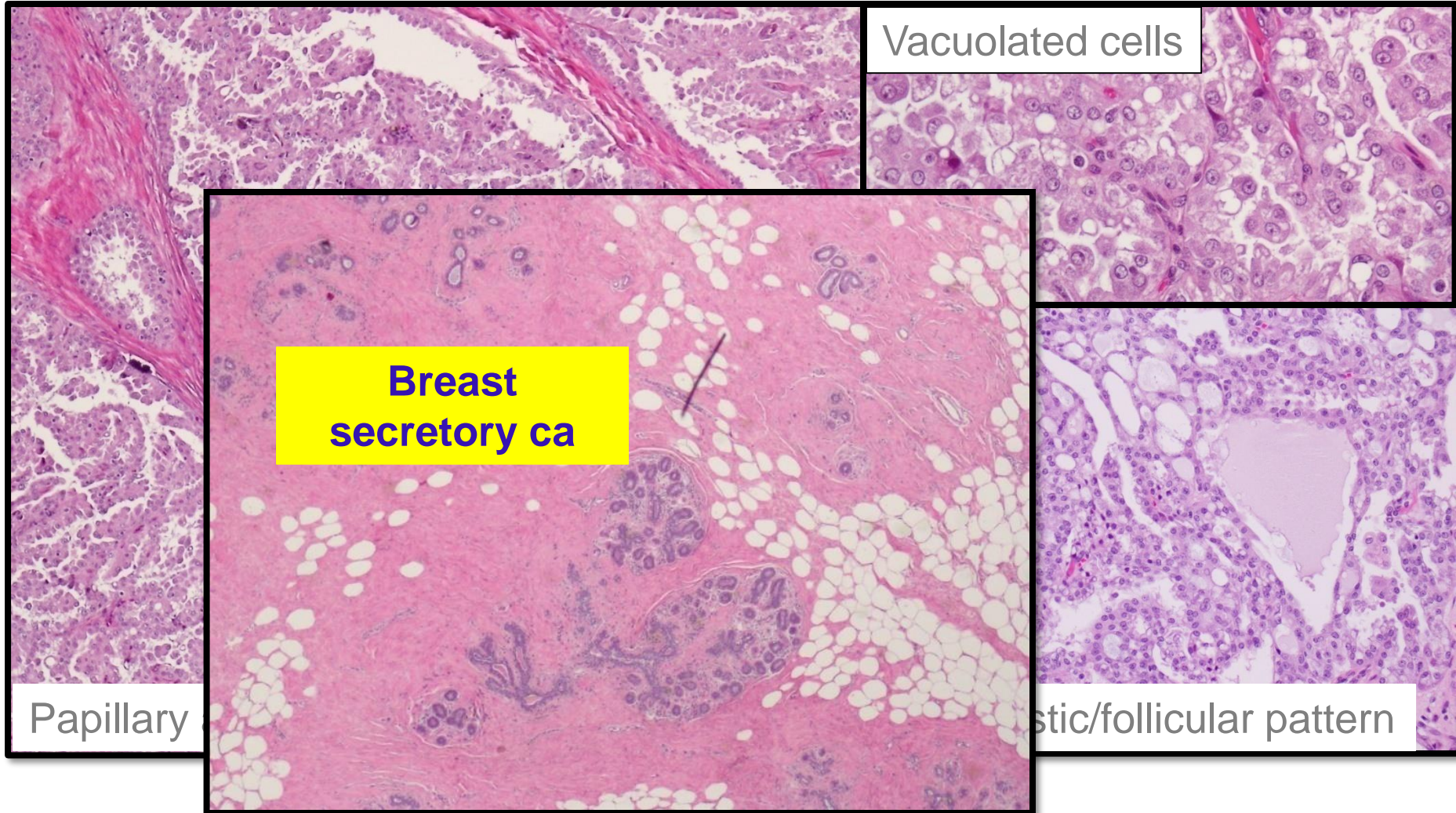
Molecular/IHC

- Molecular: t(4;9)(q13;q31) involving the upstream region of transcription factor **NR4A3** (Nuclear Receptor Subfamily 4 Group A Member3)
- IHC: **Positive for DOG1, SOX10 and NOR1 (highly specific and sensitive marker)**



NOR1

What is your diagnosis?



Papillary

Vacuolated cells

**Breast
secretory ca**

Follicular/follicular pattern

Mammary Analogue Secretory Carcinoma of Salivary Glands, Containing the ETV6-NTRK3 Fusion Gene: A Hitherto Undescribed Salivary Gland Tumor Entity

Skálová Alena, Vanecek Tomas, Sima Radek, Lace Jan, Weinreb Ilan, Perez-Ordones Bayardo, Starek Ivo, Geierova Marie, Simpson Roderrick HW, Passador-Santos Fabricio, Ryska Ales, Leivo Ilmo, Kinkor Zdenek, Michal Micha

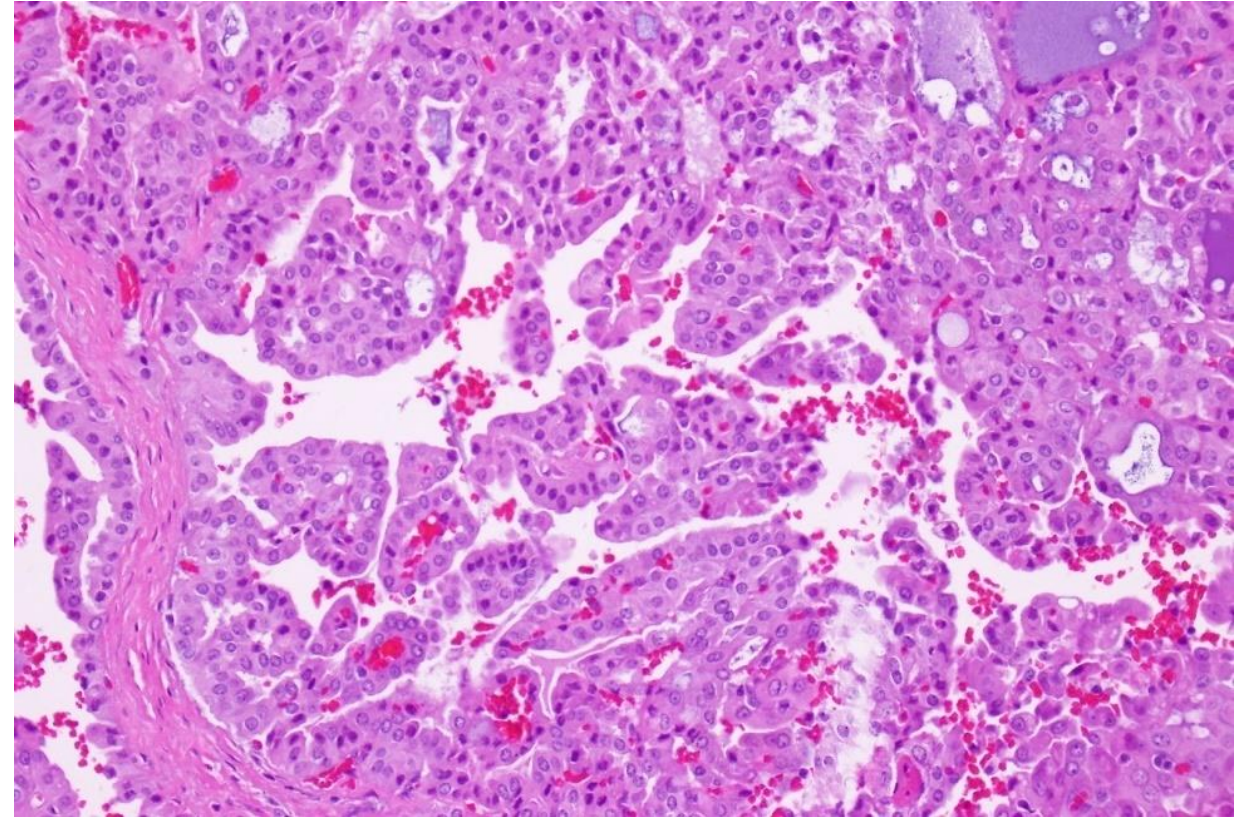
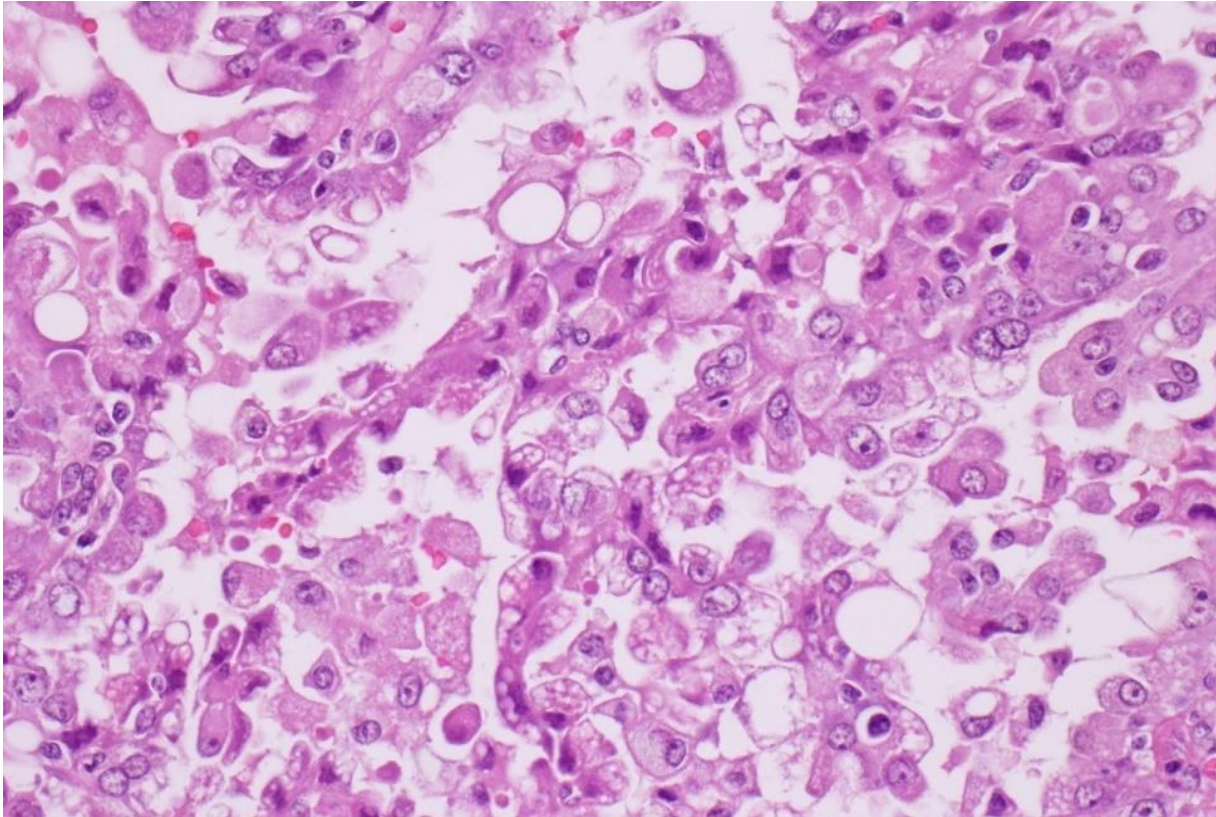
Am J surg pathol. 2010 May;34(5):599-608

Secretory carcinoma

- Morphologic and genetic similarities to secretory carcinoma of breast
- t(12,15) resulting in *ETV6-NTRK3*
- Parotid is the most common site
- Previously diagnosed as AciCC
- Zymogen granules are absent

Secretory carcinoma-Histology

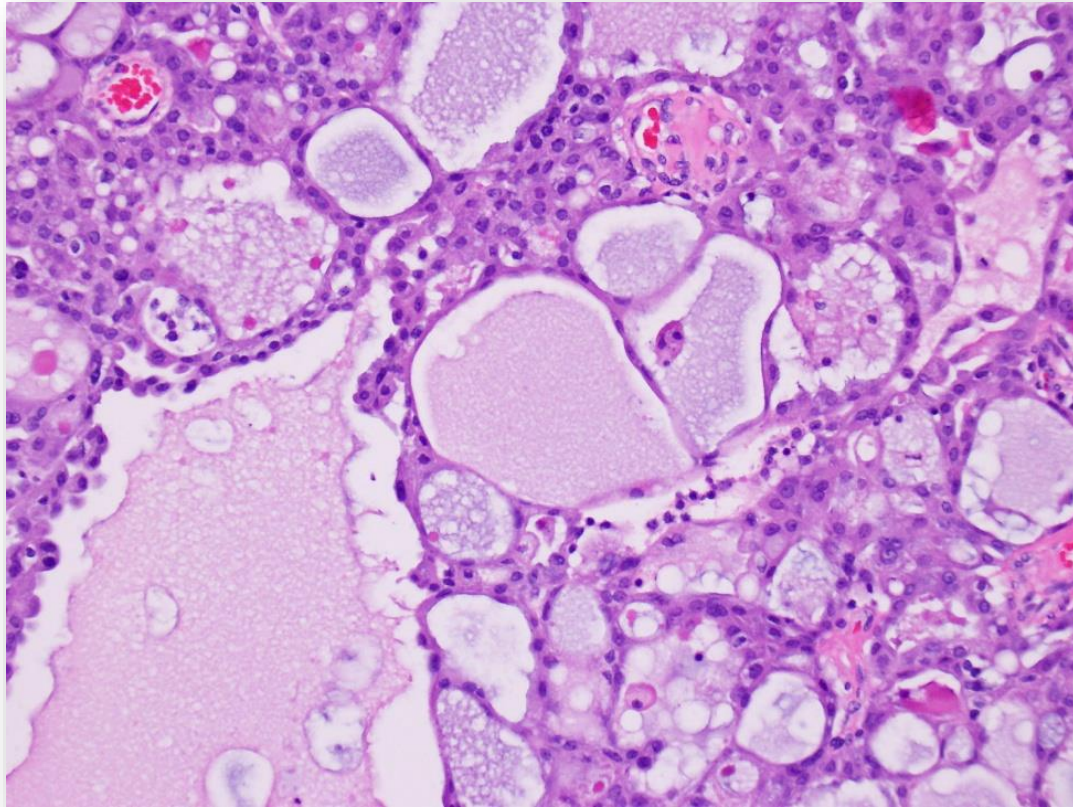
Eosinophilic cells with vacuolation



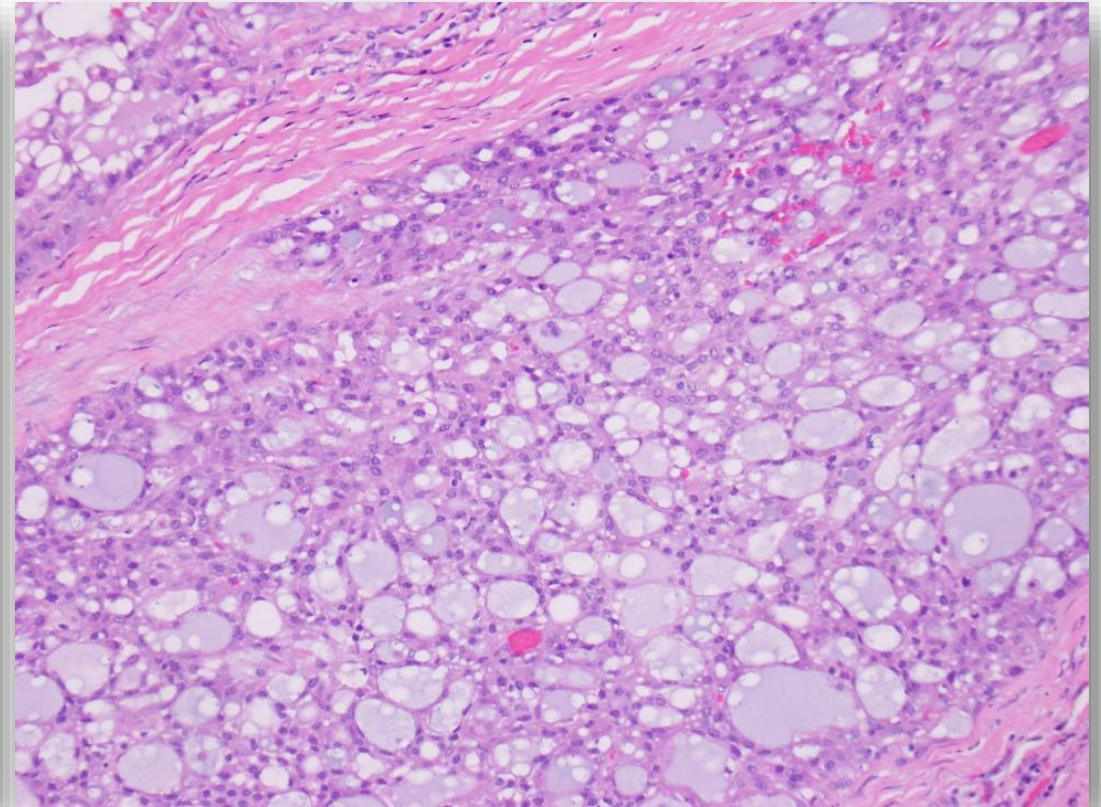
Secretory carcinoma-Histology

Microcysts, macrocysts, tubules with intraluminal secretions

Macrocystic

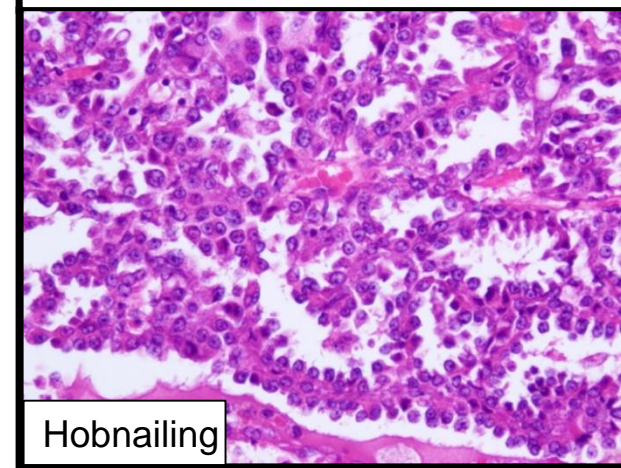
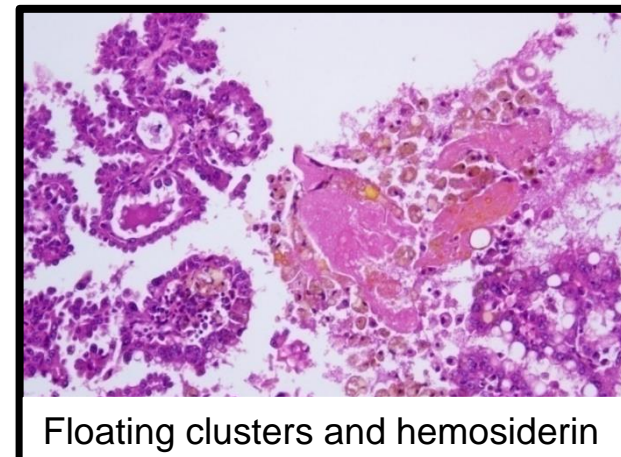
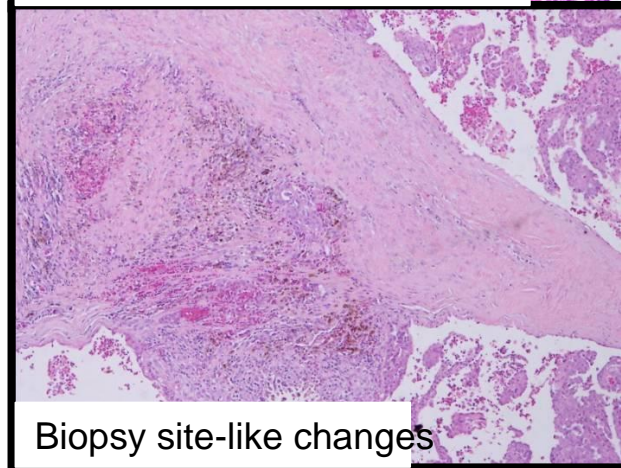
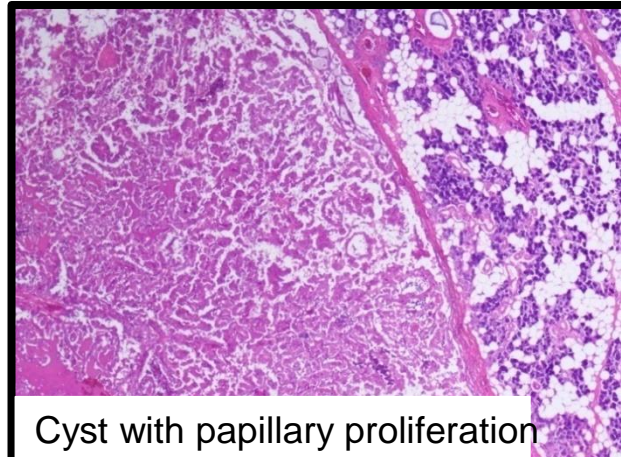


Microcystic

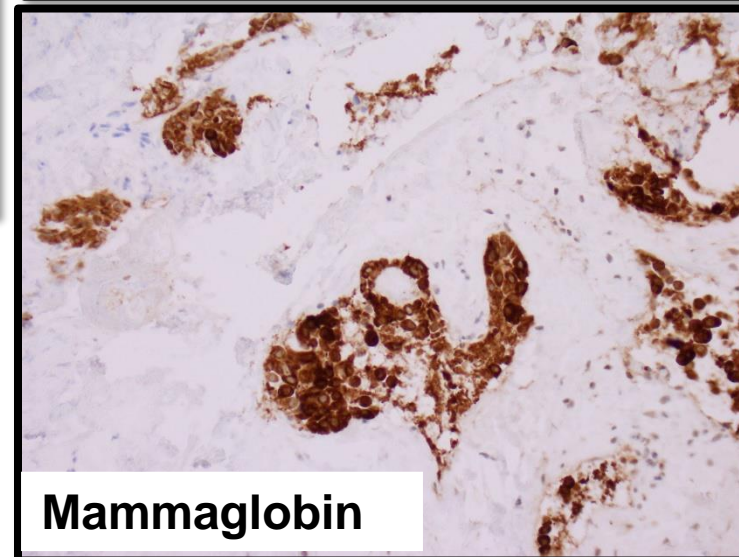
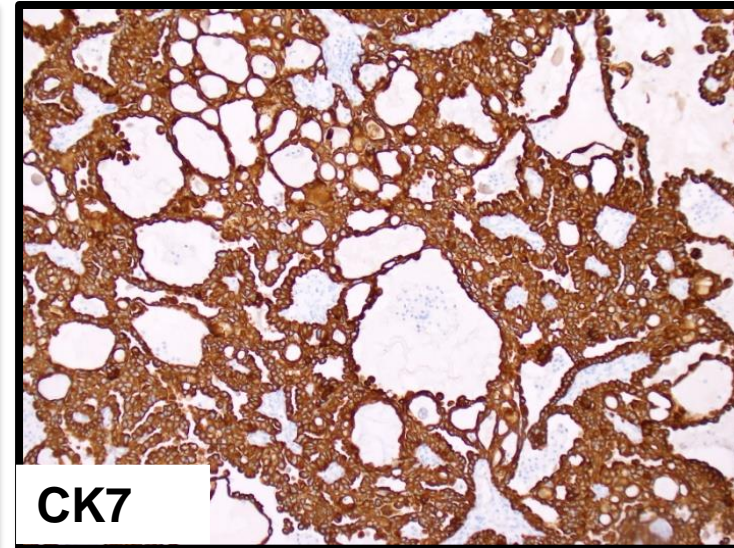
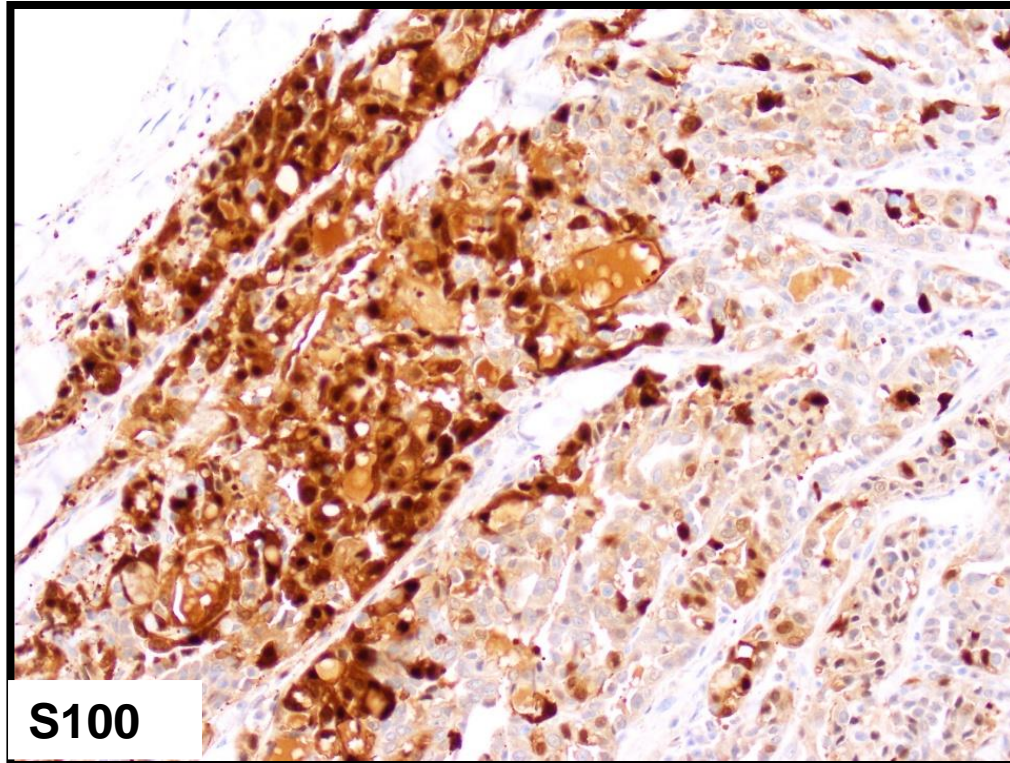


Secretory carcinoma-Histology

Papillary cystic growth pattern



Secretory carcinoma-IHC



Positive: CK7, **S100**, SOX10
mammaglobin, GCDFP, GATA3
Negative: AR, DOG1, NOR1, p63/p40

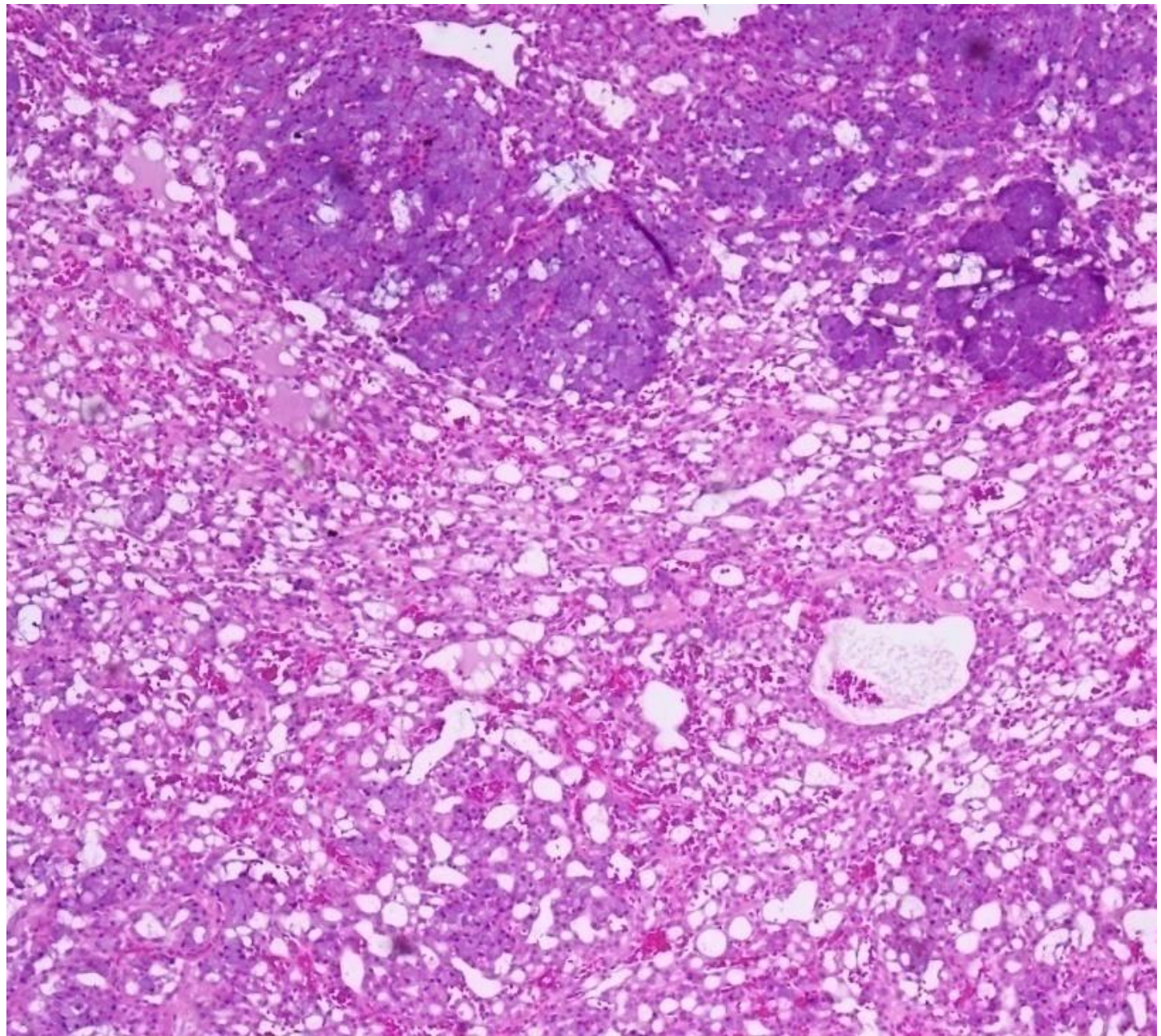
Secretory carcinoma Prognosis

- Indolent with the capacity of HG behavior
- Lymph node metastases up to 25%
- Rare distant metastases
- Potential therapeutic options with Trk inhibition in an NTRK3-rearranged tumors

Secretory carcinoma-Differential Diagnosis

- **Mucoepidermoid carcinoma**
 - Squamoid/epidermoid cells and abundant mucocytes
 - IHC: positive for p63 and negative for S100
- **Intraductal carcinoma**
 - Ductal proliferations surrounded by myoepithelial cells
 - Intact myoepithelial rim around tumor cells-IHC
- **Salivary carcinoma NOS**
 - Diagnosis of exclusion

Acinic cell carcinoma



Secretory carcinoma vs AciCC

Secretory carcinoma

- Growth patterns: papillary-cystic, microcystic/tubular, follicular
- Zymogen-rich acinar cells absent
- Vacuolated cells more common

- Positive for S100, CK7
Mammaglobin, GCDFP-15, GATA3
- Negative or focal DOG1, NOR1

ETV6 rearrangements

AciCC

- Growth patterns: solid, microcystic
- Zymogen-rich acinar cells present (diagnostic)
- Vacuolated cells less common

- Negative for S100, CK7, Mammaglobin, GCDFP-15
- GATA3 (-/focal)
- Positive for DOG1, NOR1, SOX10

NR4A3 fusion

WHO 2022

5th edition

WHO 2022

Benign tumors

- Keratocystoma
- Intercalated duct adenoma
- Striated duct adenoma
- Sclerosing polycystic adenoma

Malignant tumors

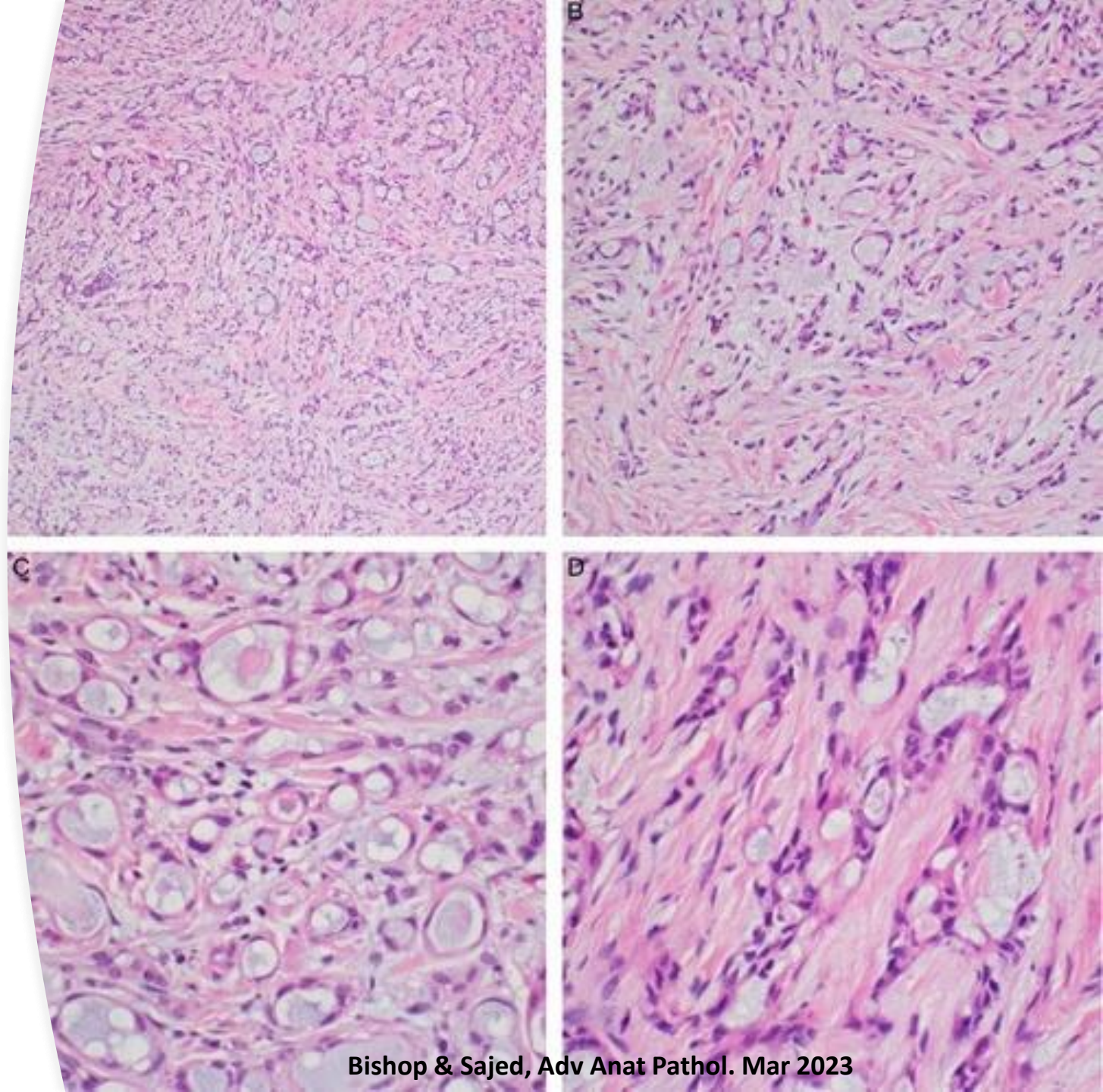
- CASG is now a subtype of PAC
- Intraductal carcinoma
- Sclerosing microcystic adenocarcinoma
- Microsecretory adenocarcinoma
- Mucinous adenocarcinoma
- Salivary carcinoma NOS & emerging entities
 - Poorly differentiated carcinoma
 - Oncocytic carcinoma

Microsecretory adenocarcinoma(MSA)

- **Oral cavity**: palate and buccal mucosa
- Perineural invasion is rare
- Necrosis is absent and mitotic rates are low
- No reported recurrence or metastasis

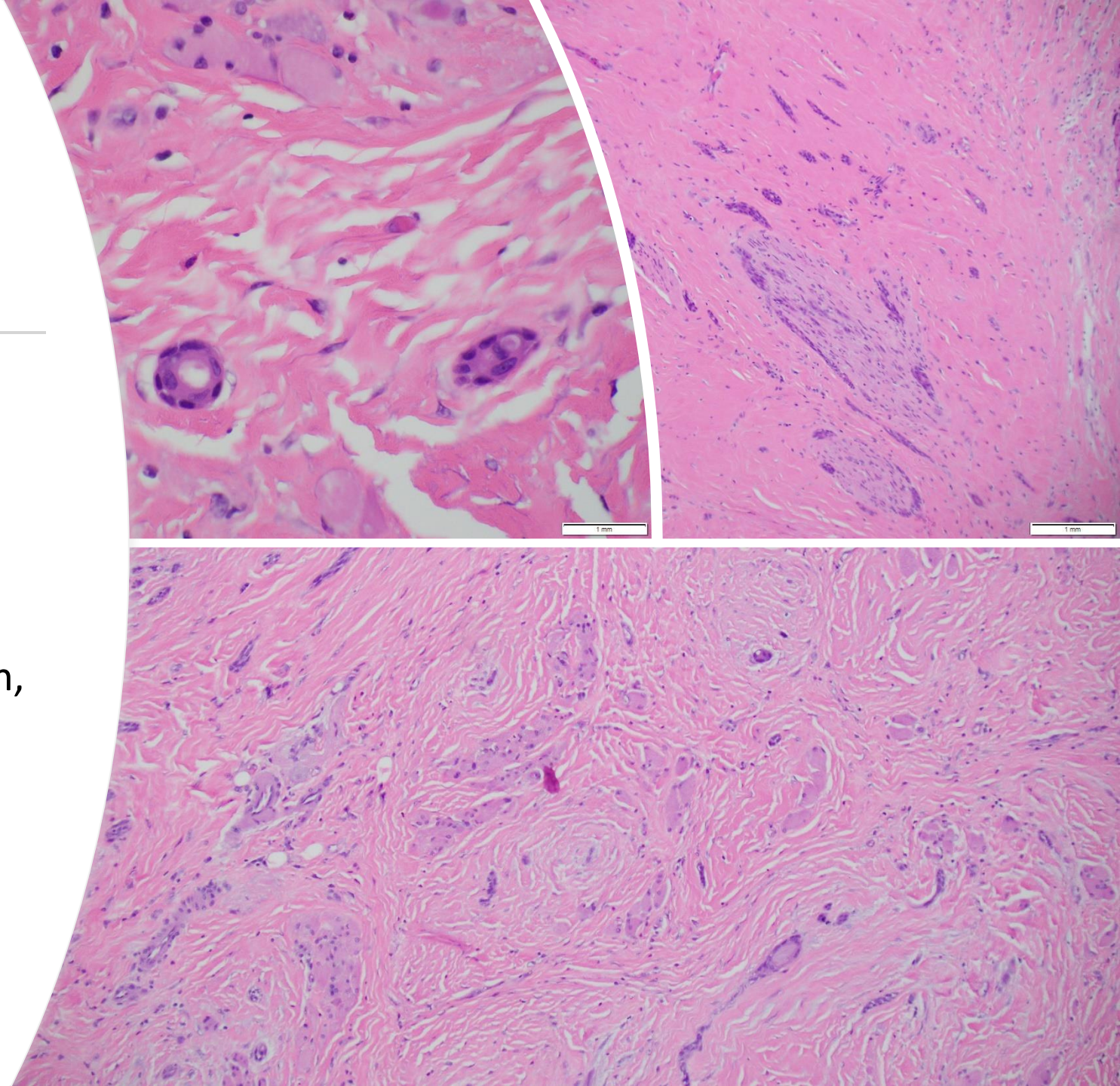
Microsecretory adenocarcinoma (MSA)

- Rounded borders
- Microcystic growth pattern
- Intercalated duct-like cells, eosinophilic/clear cytoplasm, hyperchromatic nuclei
- Basophilic luminal secretions
- Cellular fibromyxoid stroma
- *MEF2C::SS18 fusion*
- IHC: Positive for S100, SOX10, and p63, and negative for p40, mammaglobin, and calponin. SMA (+/-)



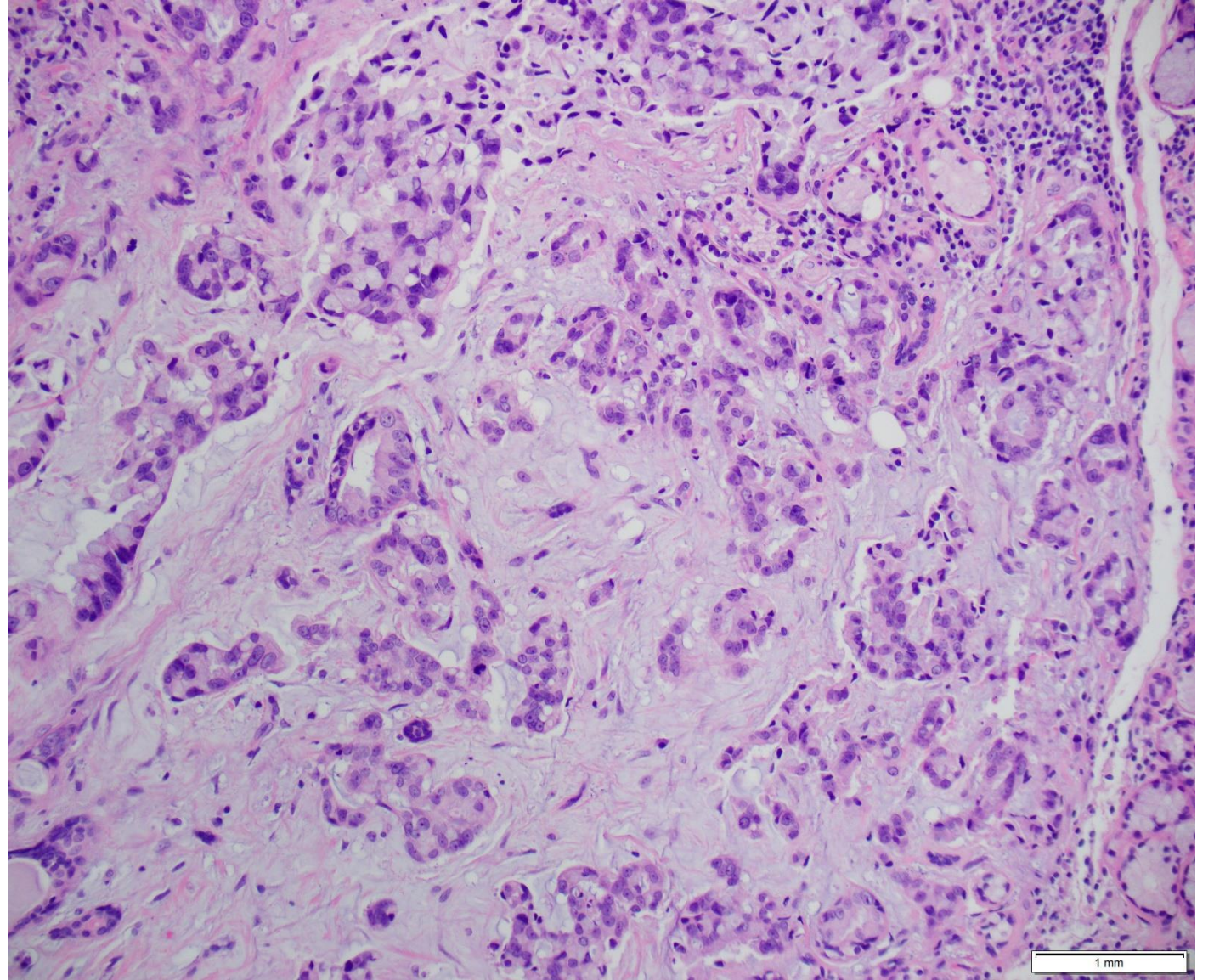
Sclerosing microcystic adenocarcinoma (SMA)

- Intraoral sites: tongue, lip, Buccal mucosa, FOM
- Infiltrative tubules, cords, nests, embedded in **collagenous stroma**
- **Biphasic** ductal (CK7, pan-CK) and myoepithelial (p63/p40, S100, calponin, SMA)
- **Perineural invasion is common**
- Low proliferative rate
- Good outcome



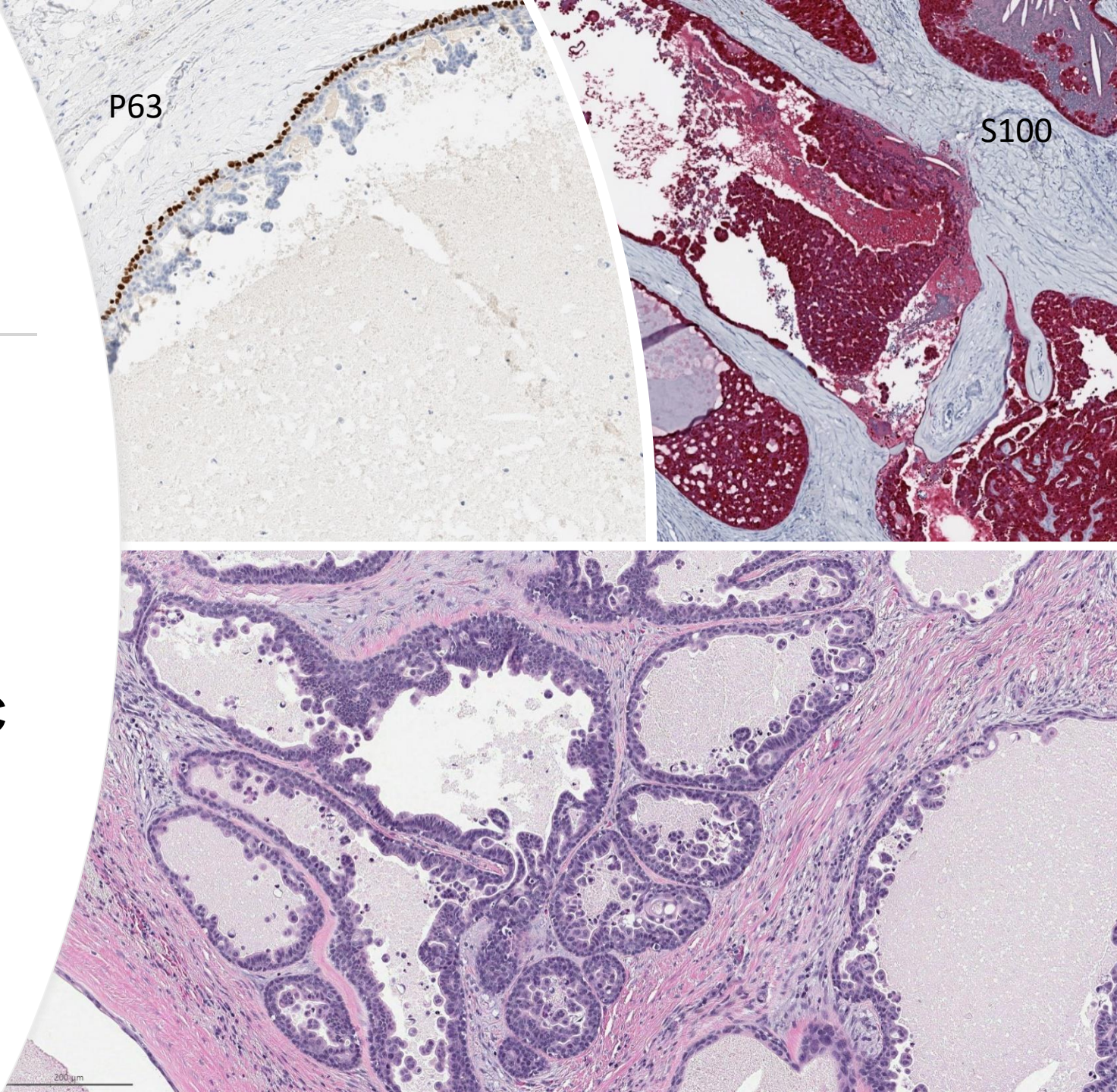
Mucinous adenocarcinoma

- Intraoral sites
- Intracellular/extracellular mucin
- Variable architecture
- Papillary, colloid and signet ring, mixed
- Cytologic atypia varies
- IHC: (+) for CK7 and (-) for CK20, CDX2, p63/p40, TTF1, S100, calponin, SMA, and AR
- AKT1 p.E17K mutation
- IPMN?



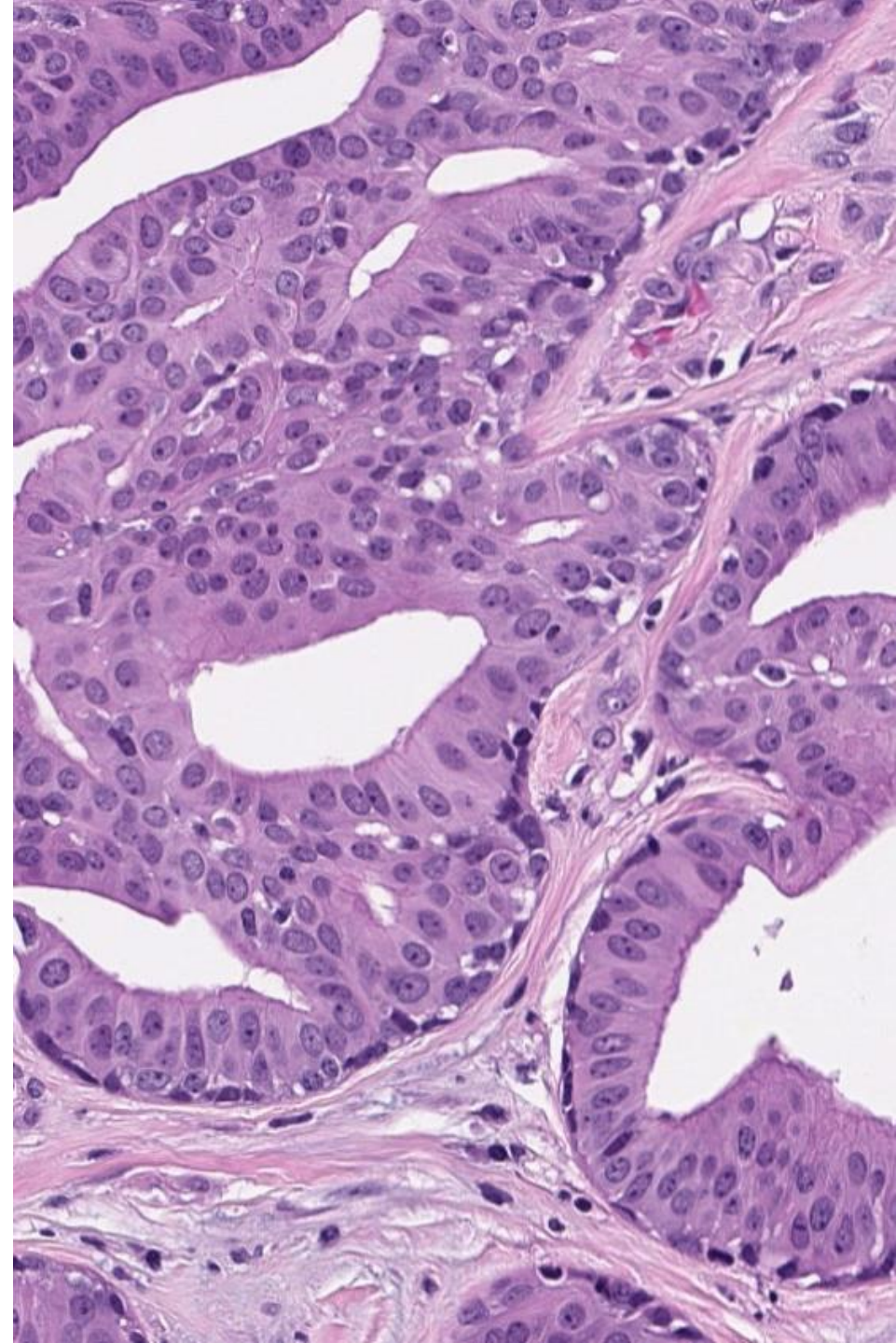
Intraductal carcinoma (IDC)

- Ductal proliferations in cysts and lobules, with variable architecture, surrounded by myoepithelial cells (p40, p63 calponin, SMA)
- **Intercalated and oncocytic IDC**
 - Positive for S100/SOX10 and negative for AR and GCDFP-15
 - *RET* fusion, BRAF V600E
 - Low grade

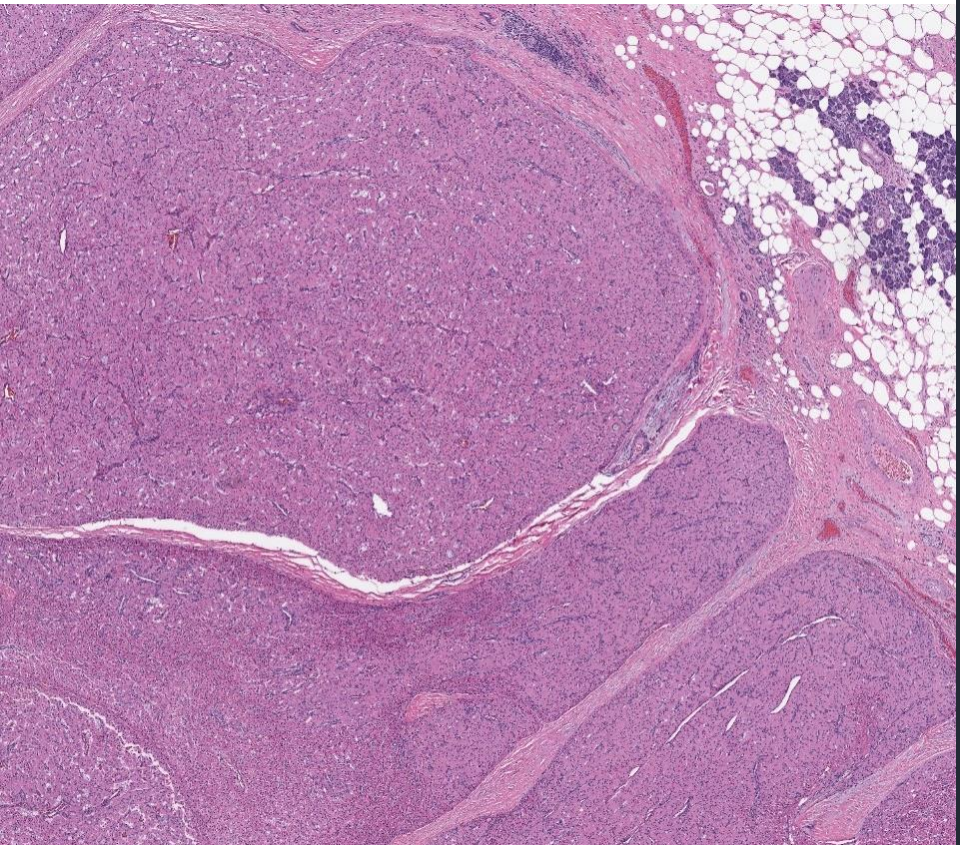
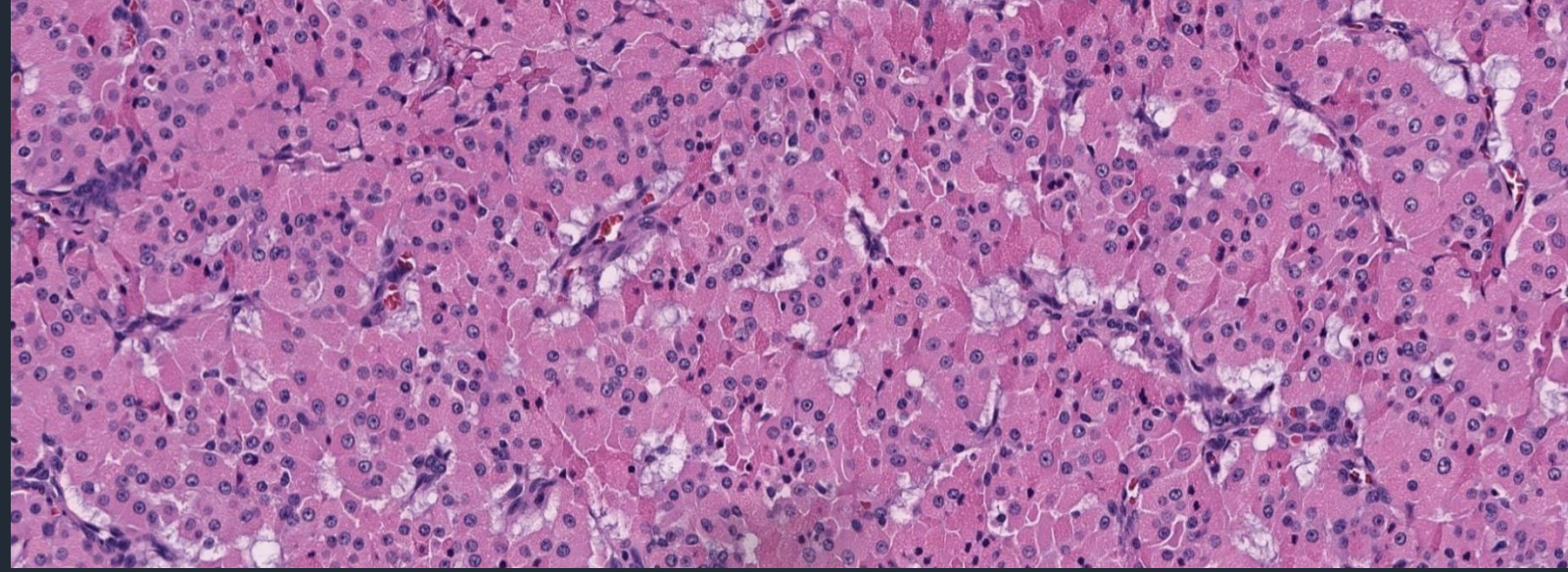


Intraductal Carcinoma (IDC)

- **Apocrine IDC**
 - **Positive for AR** and GCDFP-15, negative for S100/SOX10)
 - HRAS, PIK3CA, TP53
 - Low grade or high grade
- **Mixed type**
 - **Biphasic rather than intraductal or in situ**



Oncocytic Carcinoma



- Carcinomas consisting entirely of oncocytes
- **No consensus about the existence of oncocytic carcinoma**
- Most are salivary duct carcinomas
- It has been included in as an emerging entity

Thanks!

