MUCOEPIDERMOID CARCINOMA OF SALIVARY GLANDS

Edited by:

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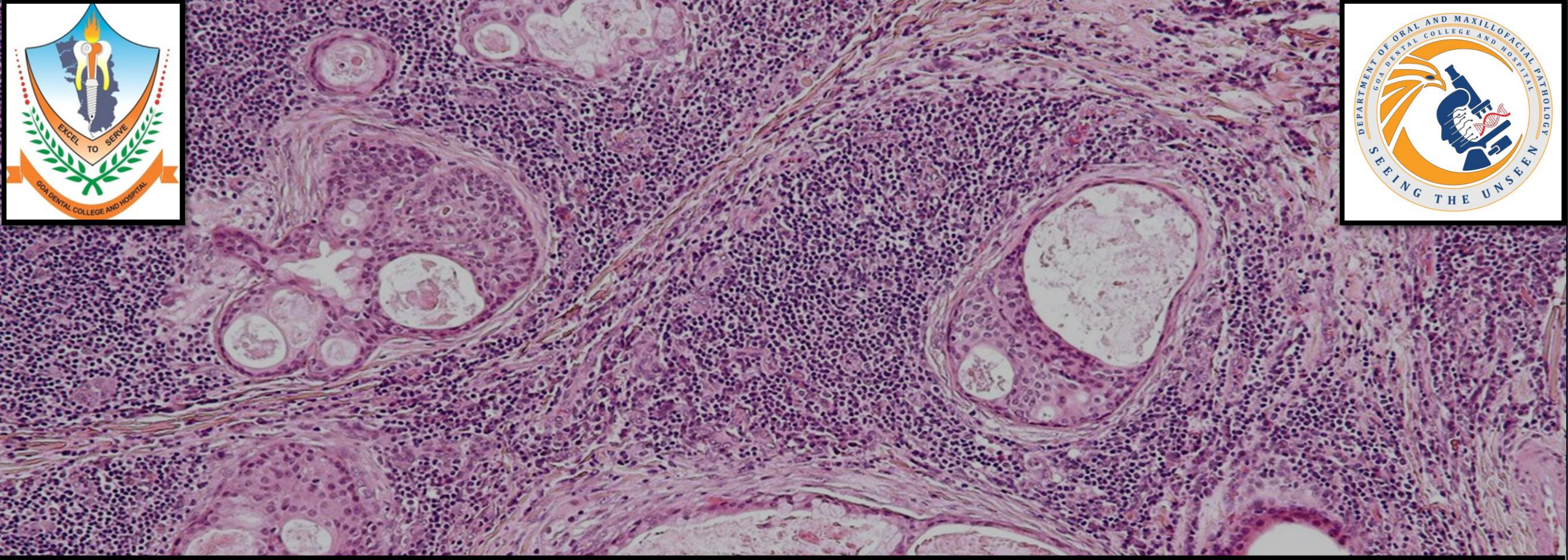
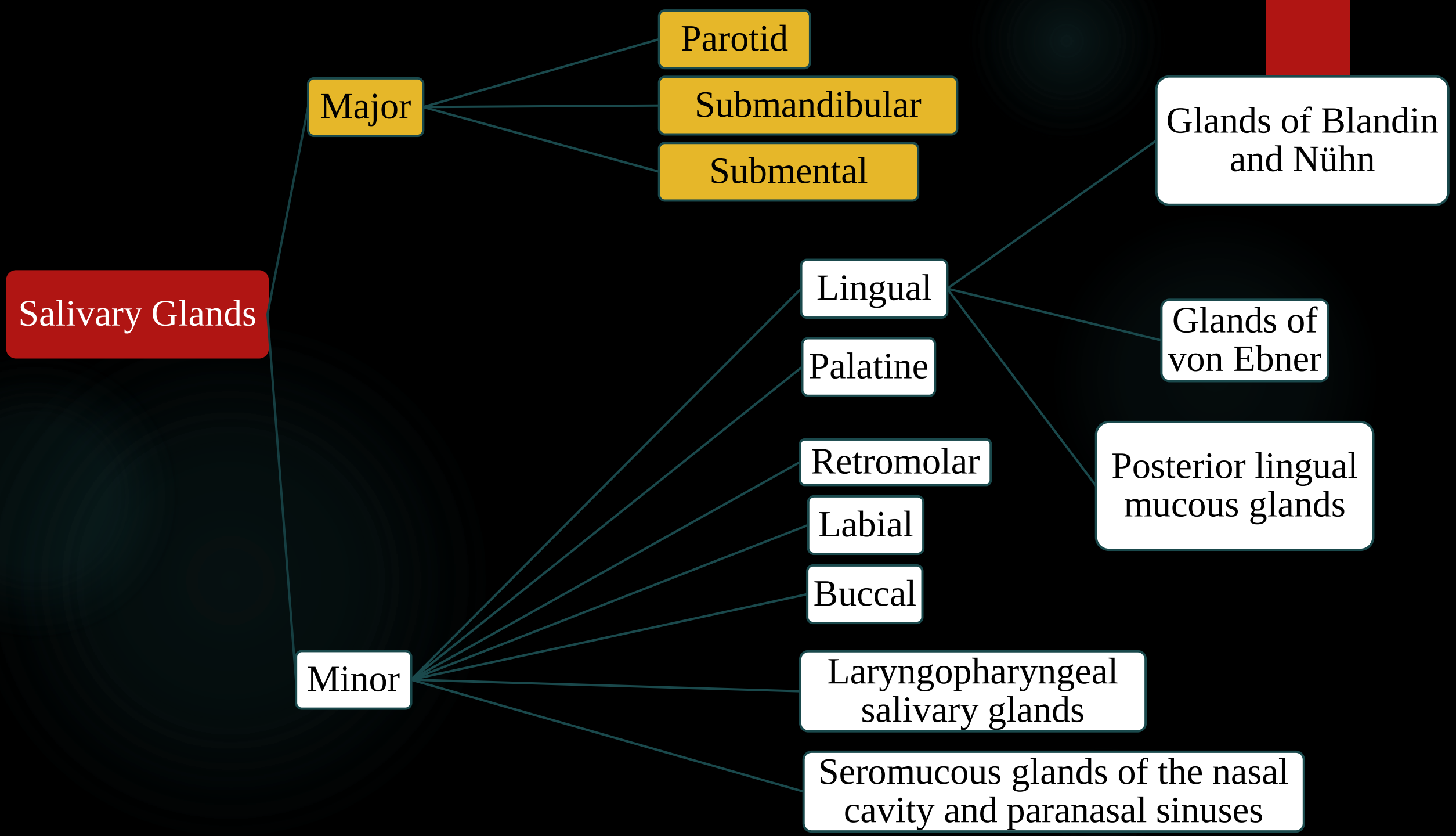
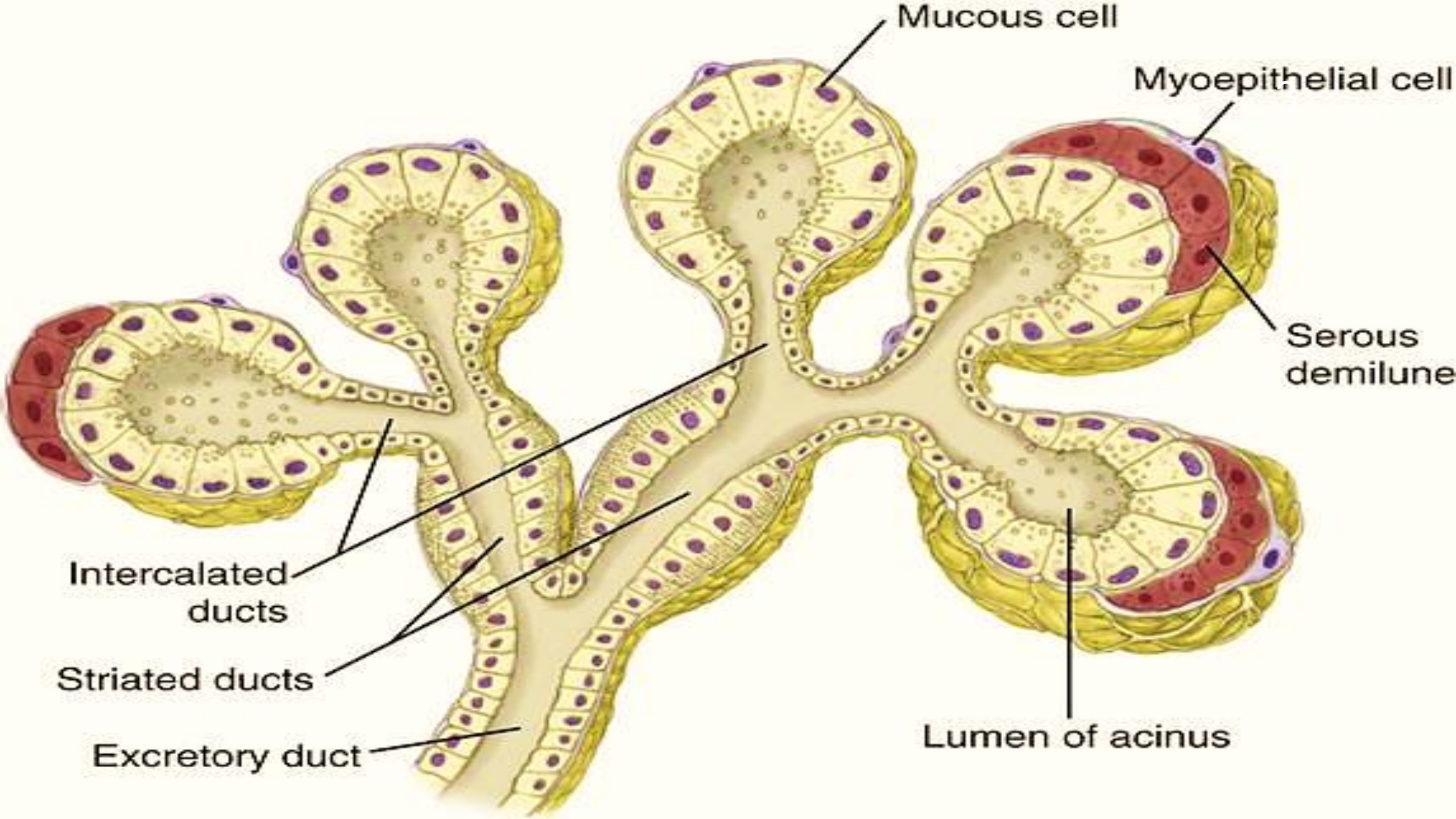
August 2024

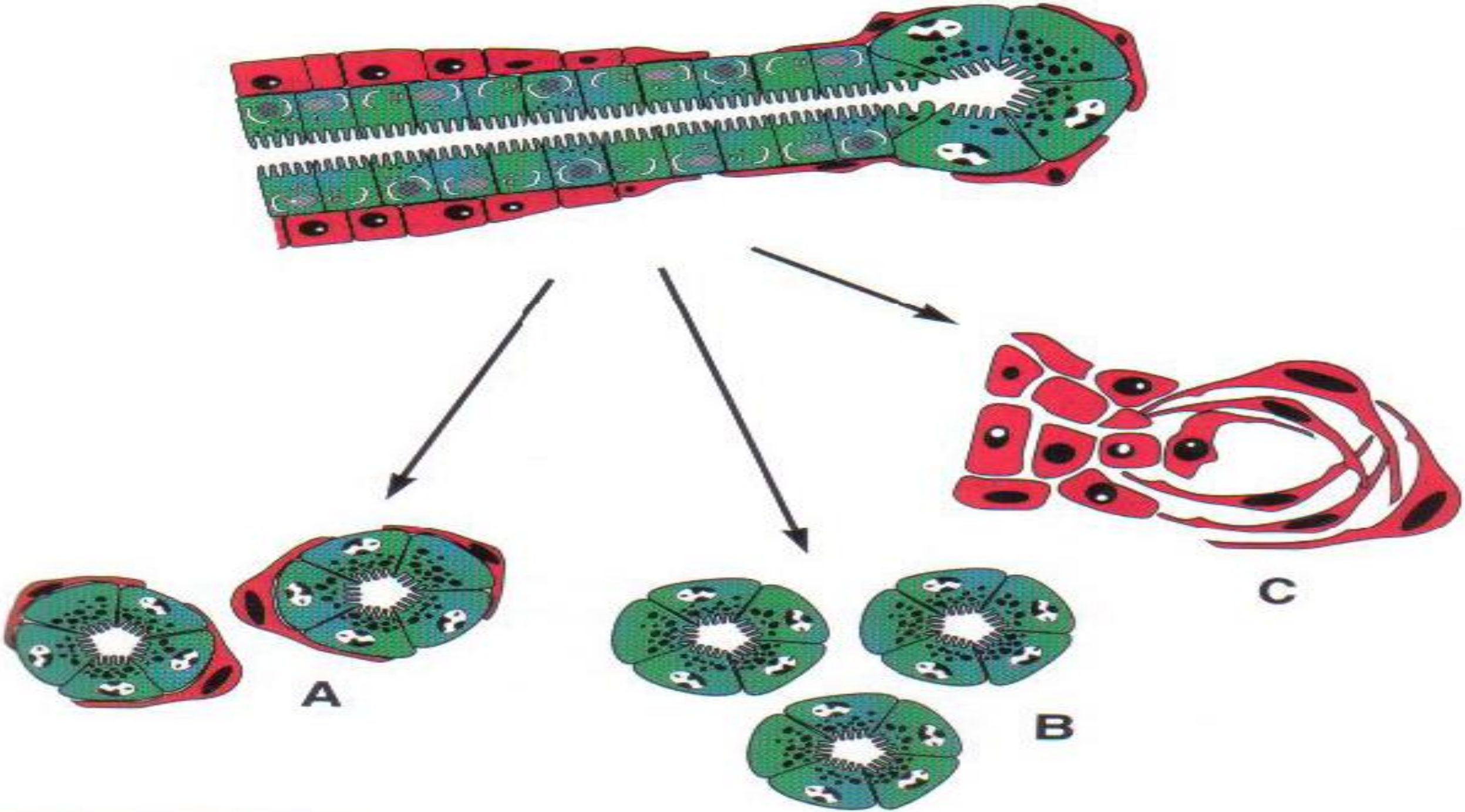


Mucoepidermoid carcinoma of the minor salivary glands

Dr. Nairica Rebello, Lecturer, Department of Oral and Maxillofacial Pathology, Goa Dental College and Hospital


Salivary Glands
Major
Parotid
Submandibular
Submental
Minor
Lingual
Palatine
Retromolar
Labial
Buccal
Glands of Blandin and Nühn
Glands of von Ebner
Posterior lingual mucous glands
Laryngopharyngeal salivary glands
Seromucous glands of the nasal cavity and paranasal sinuses


Mucous cell
Myoepithelial cell
Serous demilune
Intercalated ducts
Striated ducts
Excretory duct
Lumen of acinus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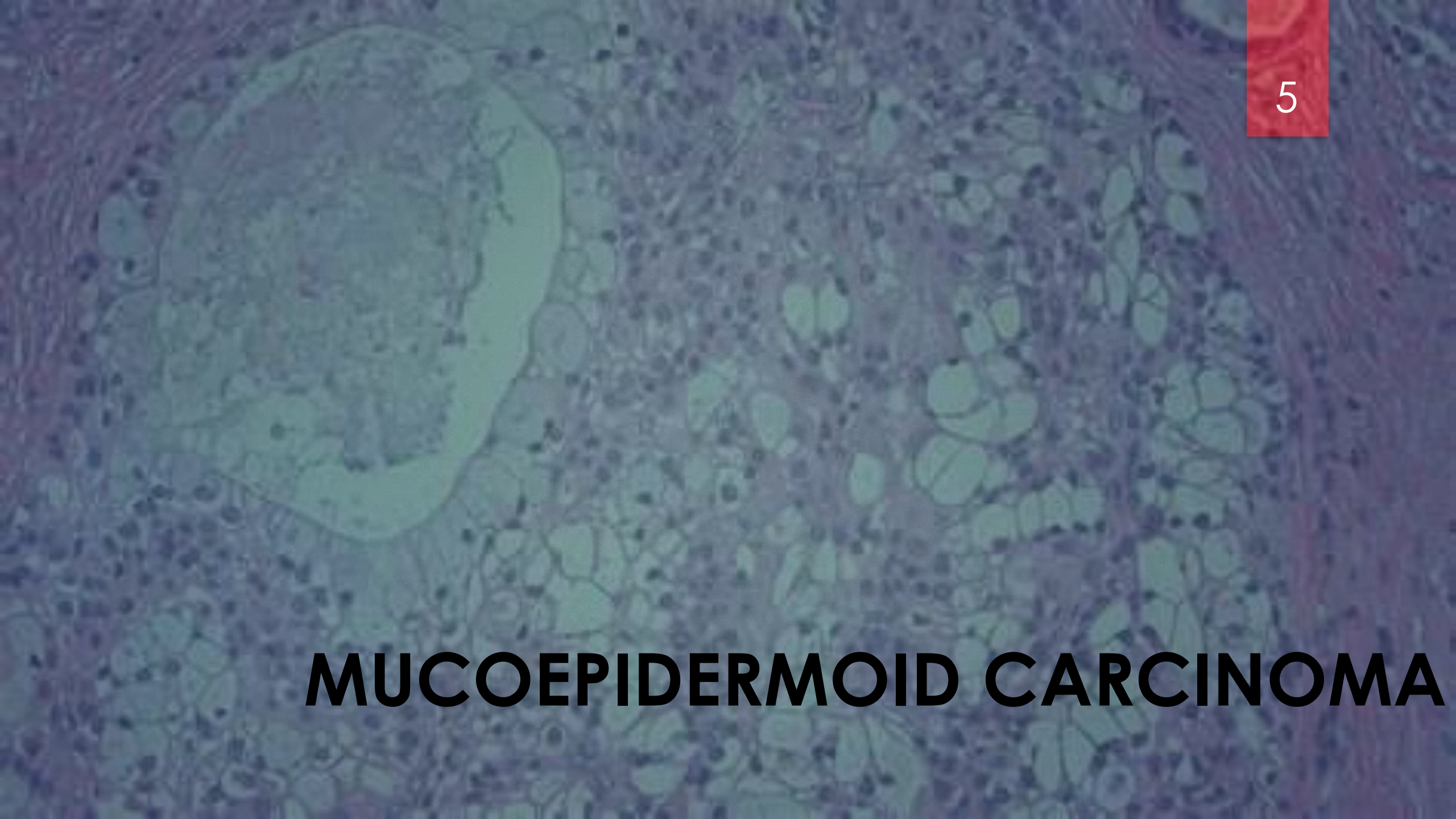


MUCOEPIDERMOID CARCINOMA

First described by Masso and Berger in 1924

Considered a benign tumor and termed “mucoepidermoid tumor”

Reclassified as a malignant neoplasm by WHO in 1990 and termed mucoepidermoid carcinoma

Ellis GL et al, 1991; Saldanha C et al, 2018

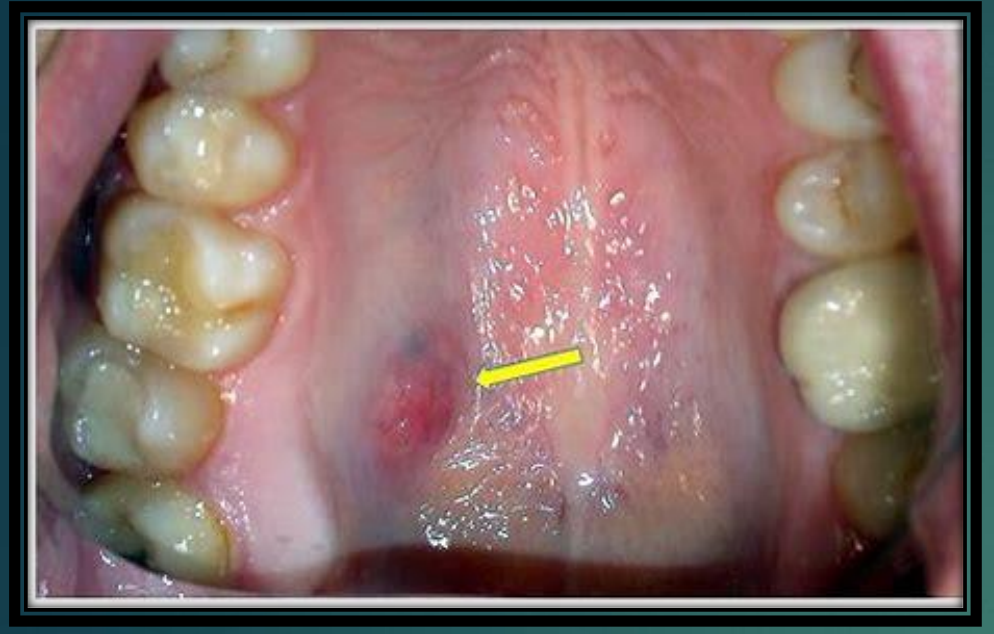
Malignant Tumours	
Mucoepidermoid carcinoma	8430/3
Adenoid cystic carcinoma	8200/3
Acinic cell carcinoma	8550/3
Polymorphous adenocarcinoma	8525/3
Clear cellcarcinoma	8310/3
Basal cell adeno carcinoma	8147/3
Intraductal carcinoma	8500/2
Adenocarcinoma NOS	8140/3
Salivary duct carcinoma	8500/3
Myoepithelial carcinoma	8982/3
Epithelial-myoepithelial caronoma	8562/3
Carcinoma ex pleomorphic adenoma	8941/3
Secretory carcinoma	8502/3
Oncocytic carcinoma	8290/3
Uncertain malignant potential	
Sialoblastoma	8974/1

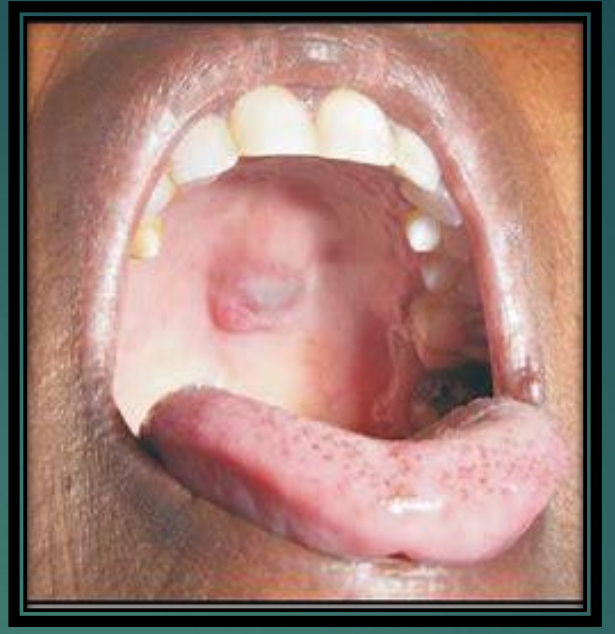
Benign tumours	
Pleomorphic adenoma	8940/0
Myoepithelioma	8982/0
Basal cell adenoma	8147/0
Warthin tumour	8561/0
Oncocytoma	8290/0
Lymphadenoma	8563/0
Cystadenoma	8440/0
Sialadenoma papilliferum	8406/0
Ductal papillomas	8503/0
Sebaceous adenoma	8410/0
Canalicular adenoma and other ducatal adenomas	8149/0

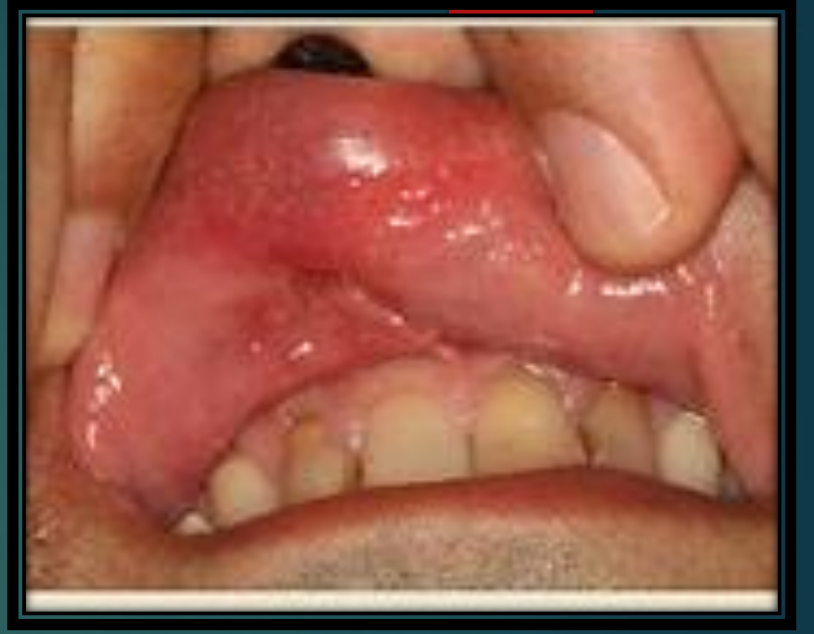
Non-neoplastic epithelial lesions
Sclerosing polycystic adenosis
Nodular oncolytic hyperplasia
Lymphoepithelial sialadenitis
Intercalated duct hyoerplasia

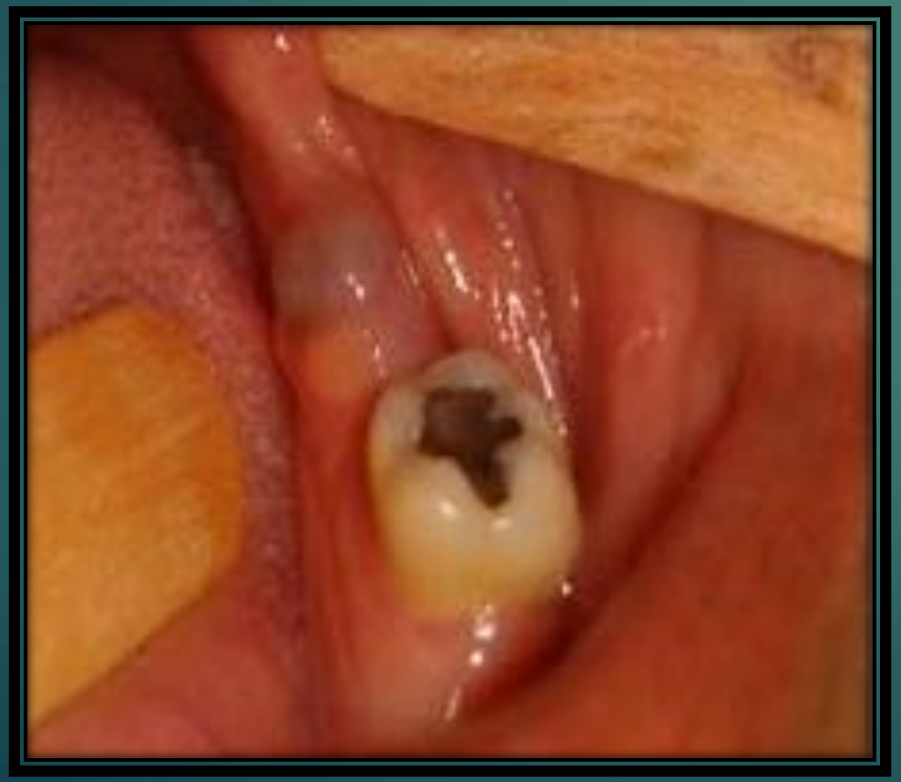
Unchanged in the WHO 2022 Classification

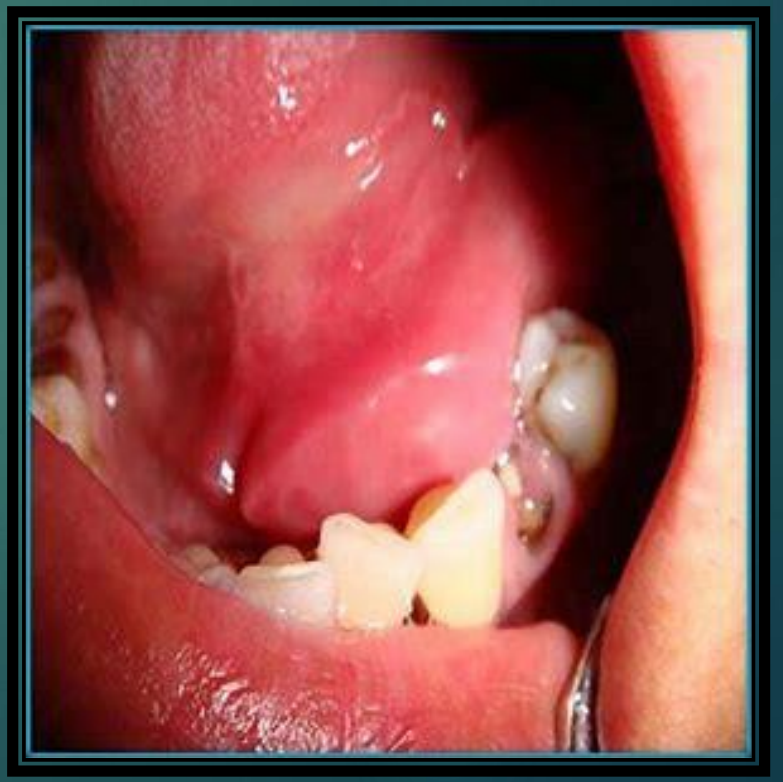
Behaviour coding for tumours	
/0	Benign tumours
/1	Unspecified borderline or uncertain behaviour
/2	Carcinoma insitu and Gr III intraepithelial Neoplasia
/3	Malignant tumours









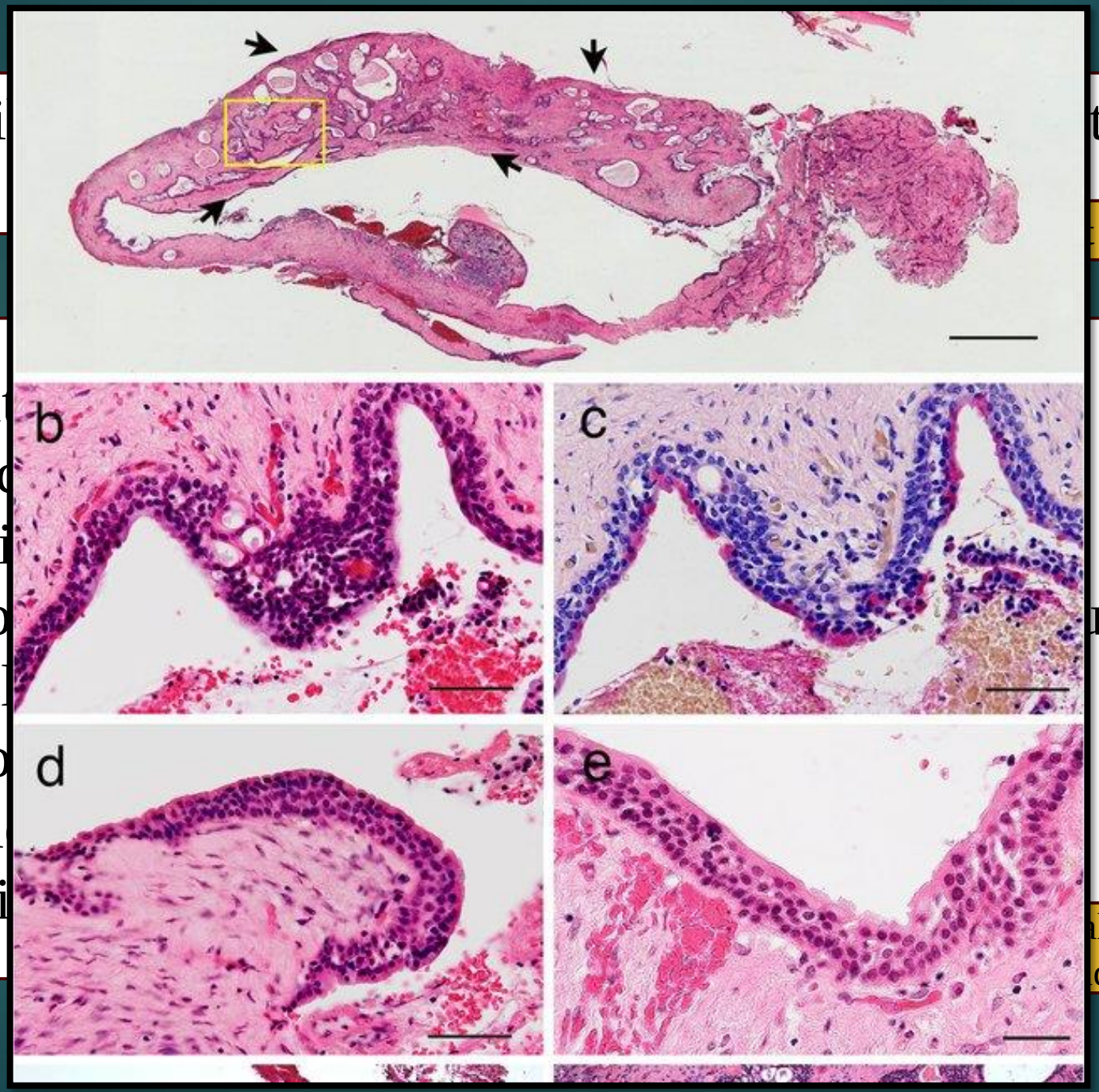


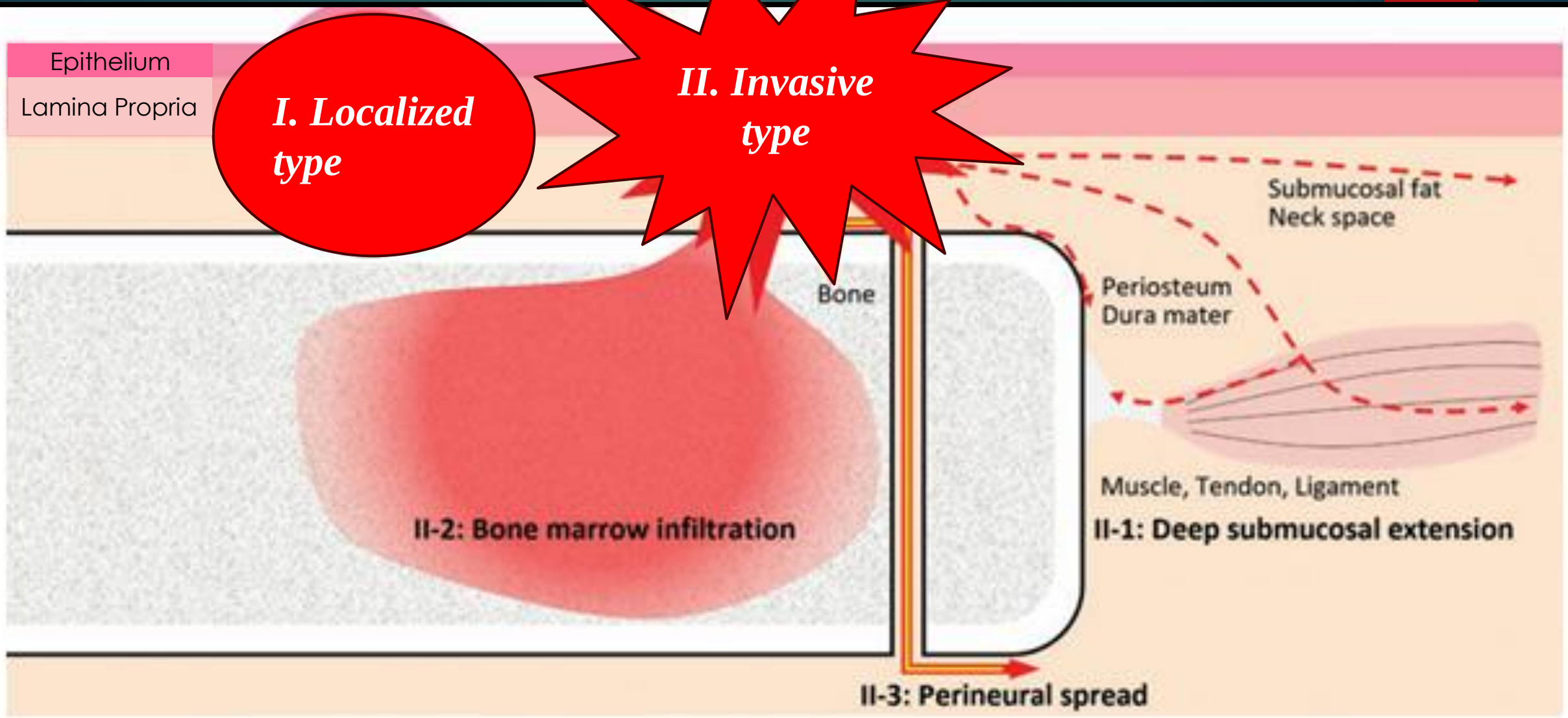
Posterior mandi … t of MEC

… al, 2018

Diagnostic Crit…
(a) intact cortic…
(b) radiographi…
(c) exclusion o… …uld histological…
(d) exclusion o…
(e) histopathol…
(f) detectable i…

… l, 1974
… dron, 1990




Epithelium
Lamina Propria
I. Localized type
II. Invasive type
Submucosal fat
Neck space
Periosteum
Dura mater
Bone
Muscle, Tendon, Ligament
II-1: Deep submucosal extension
II-2: Bone marrow infiltration
II-3: Perineural spread

Compared to major salivary gland tumors, *a higher frequency of malignant neoplasms* are reported within minor salivary gland tumors

da Silva LP et al, 2018

Mucoepidermoid carcinoma may represent *up to 45%* of all minor salivary gland tumors

Morais ML et al, 2011 Sarmento DJ et al, 2016;

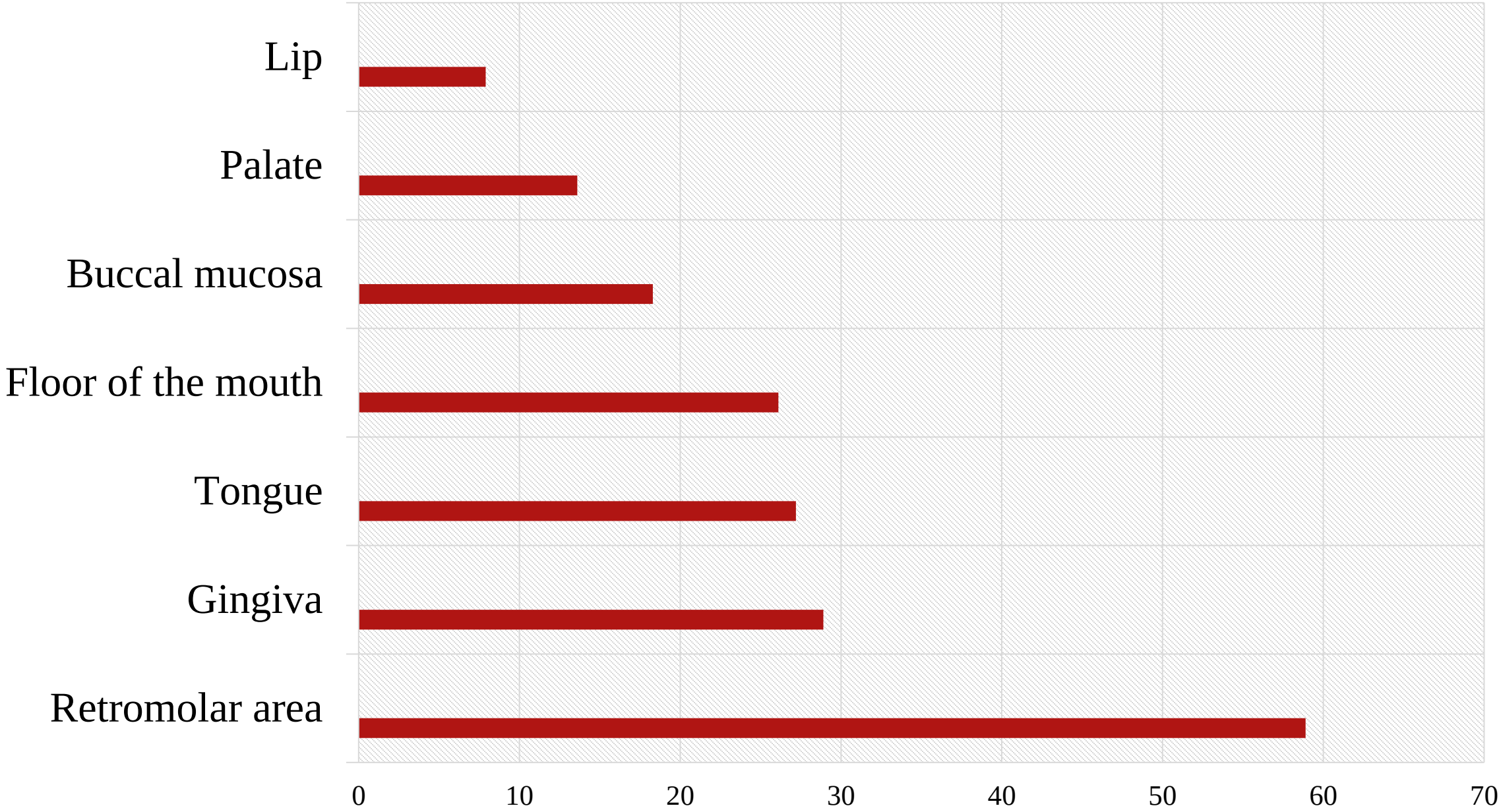
Prevalence of MEC among intraoral minor salivary gland tumors is 16.5%

Poletto AG et al, 2020

Malignant tumors in children under 10 years old tend to be of a higher grade with poorer prognosis

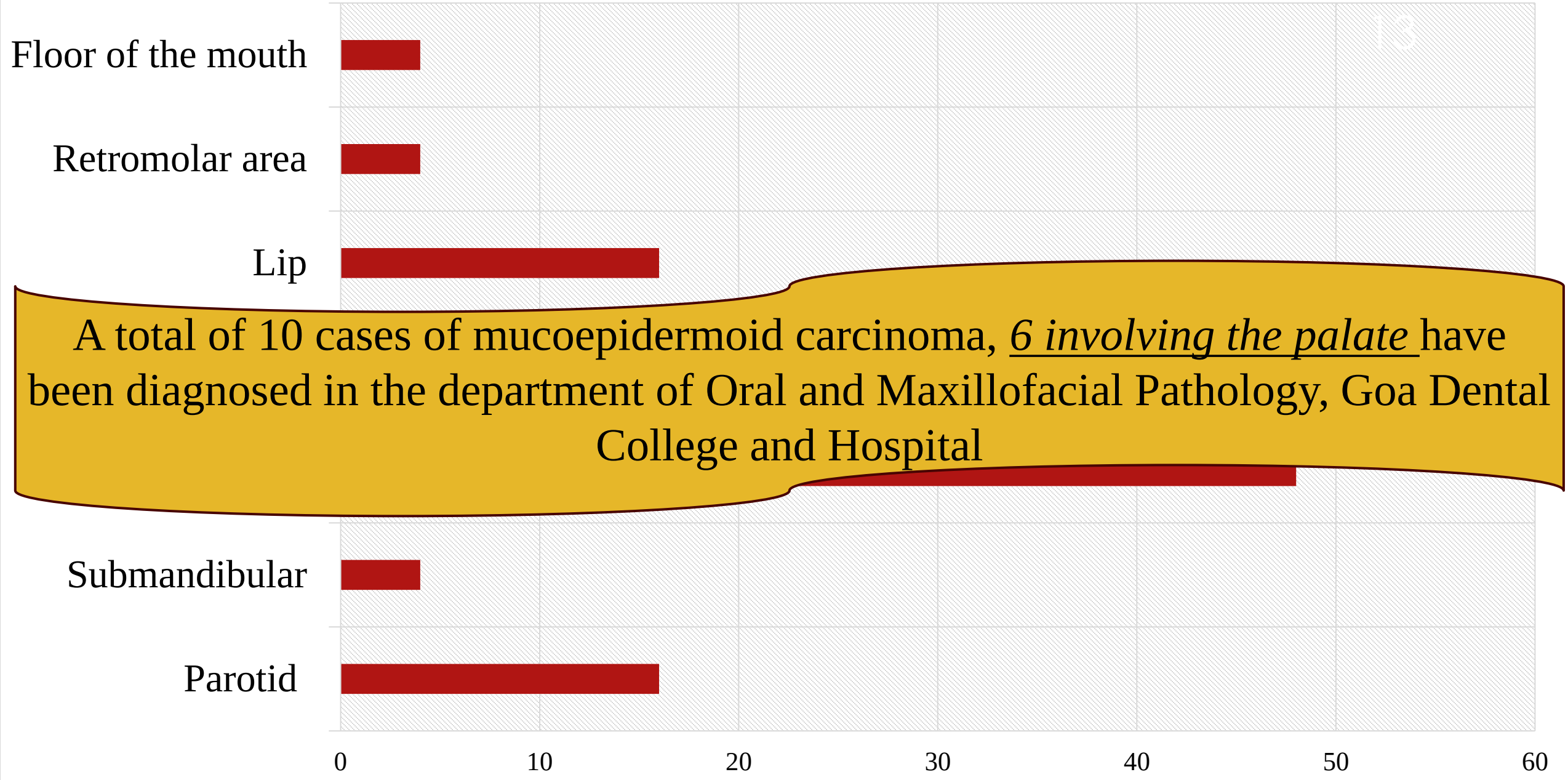
Bradley PJ et al, 2016

Site-wise Distribution of MEC of the Minor Salivary Glands



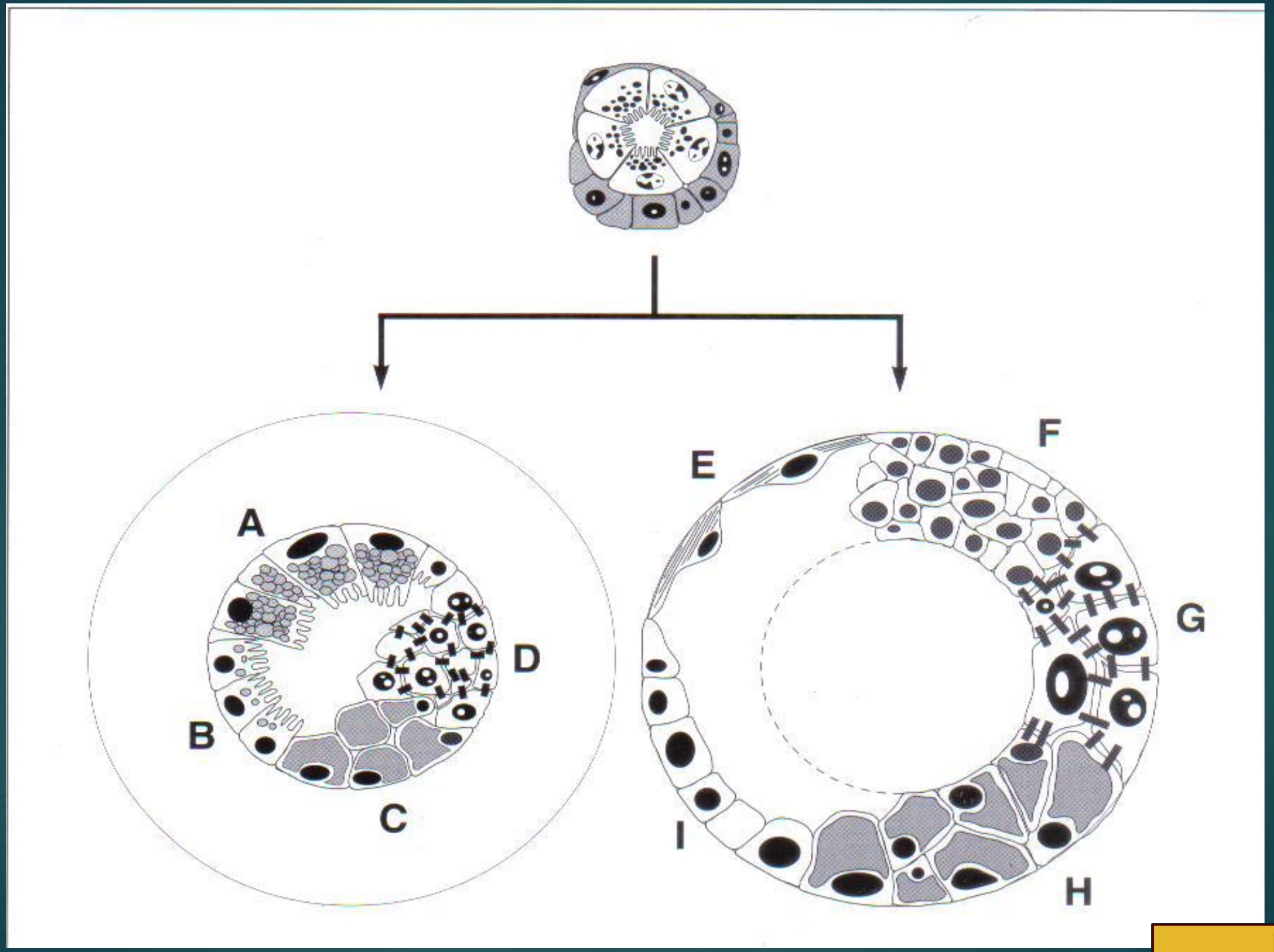
Poletto AG et al, 2020

Site wise Distribution of MEC in the Indian subcontinent



A total of 10 cases of mucoepidermoid carcinoma, *6 involving the palate* have been diagnosed in the department of Oral and Maxillofacial Pathology, Goa Dental College and Hospital

Jeergal P et al, 2021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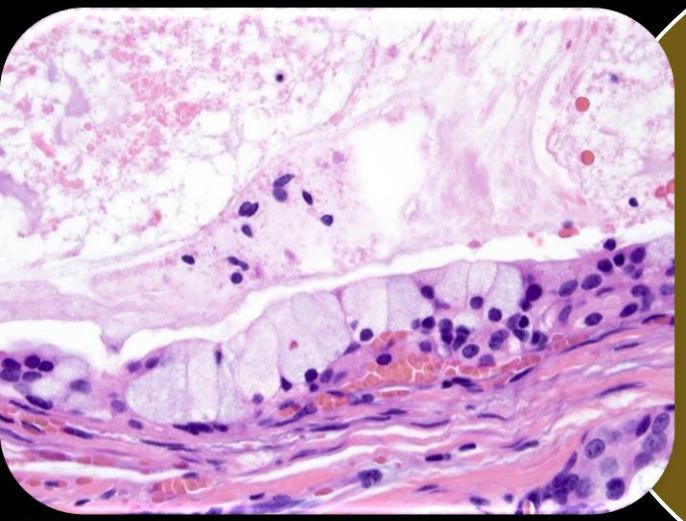
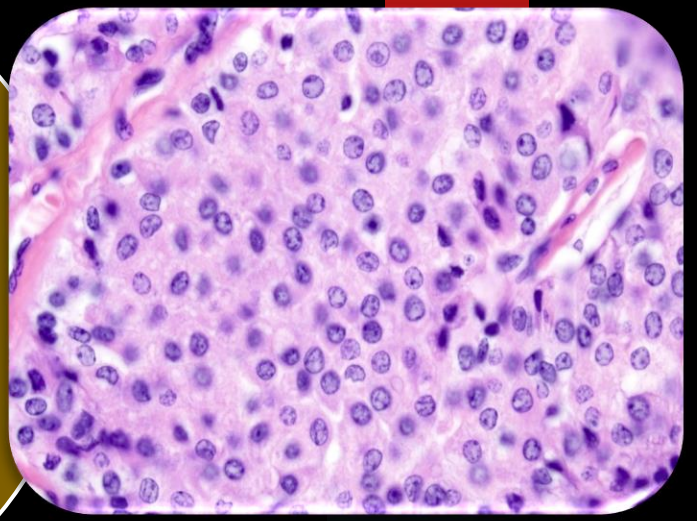
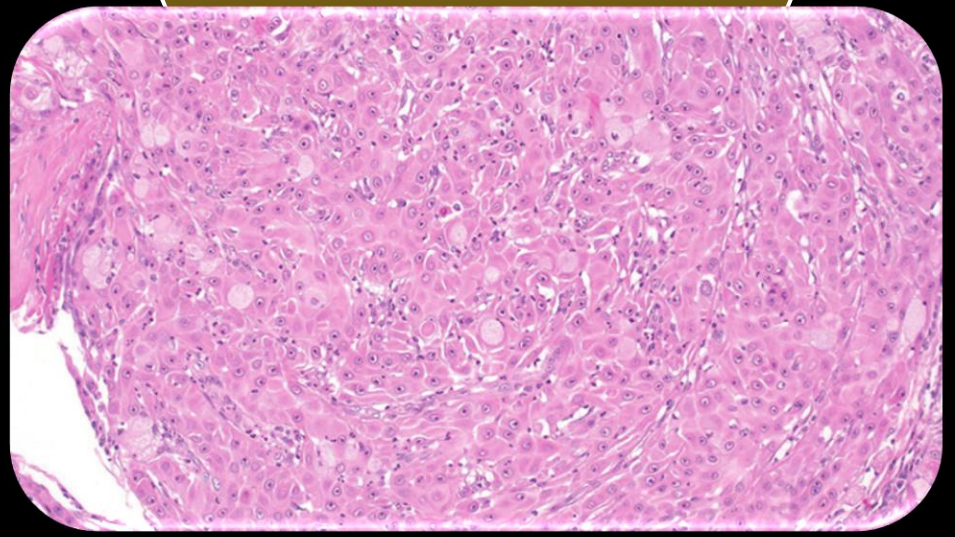


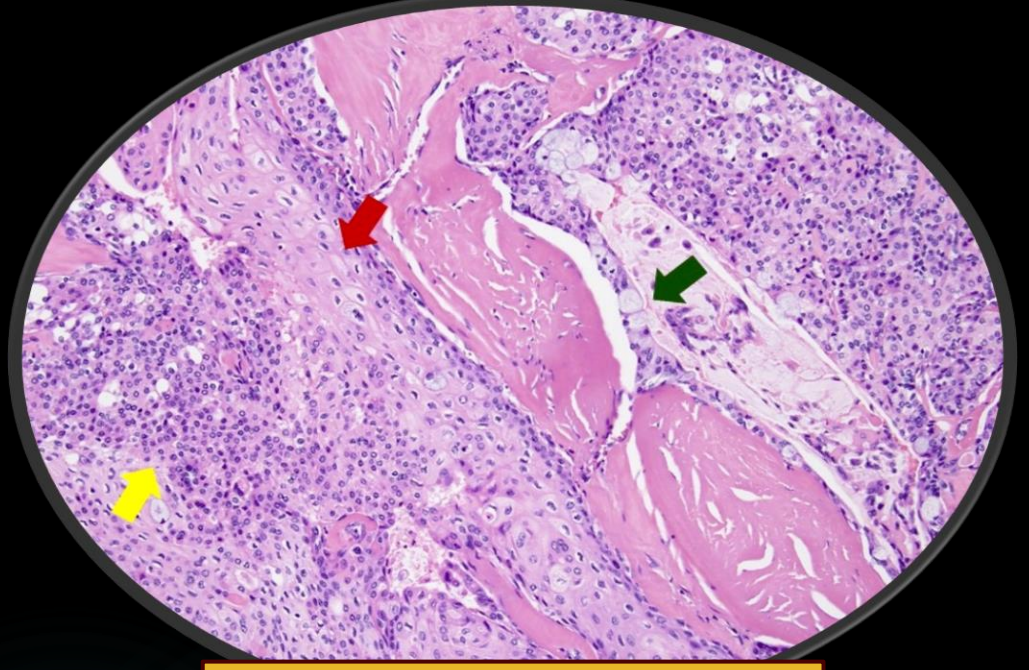
Mucous cells

Intermediate cells

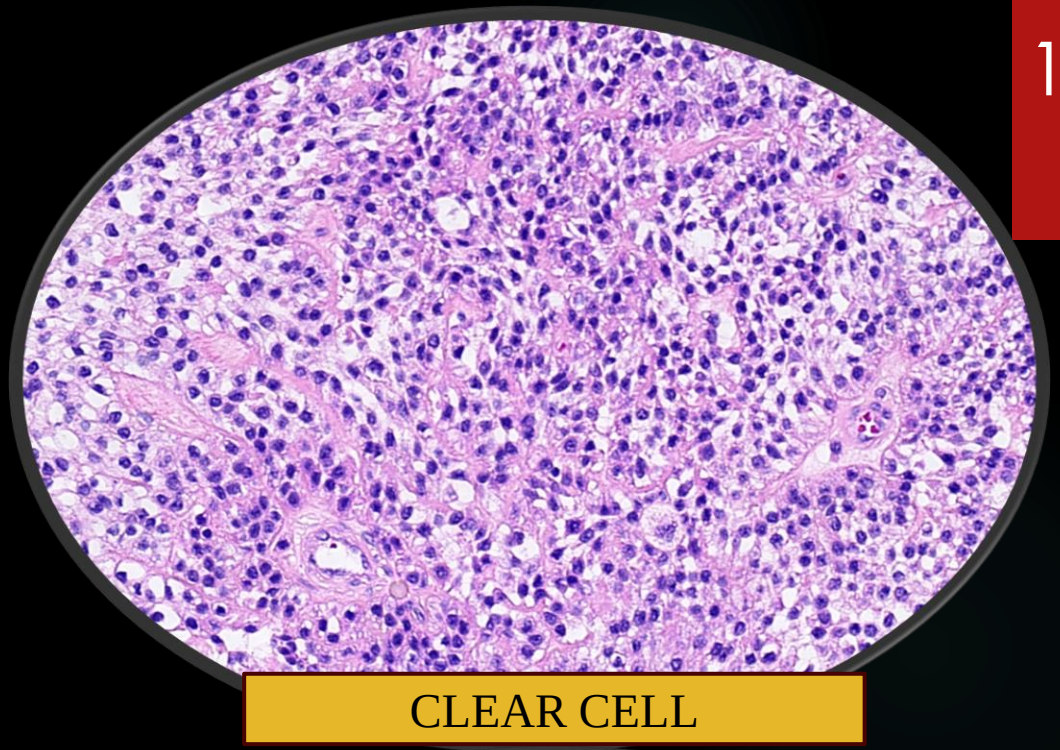


Epidermoid cells

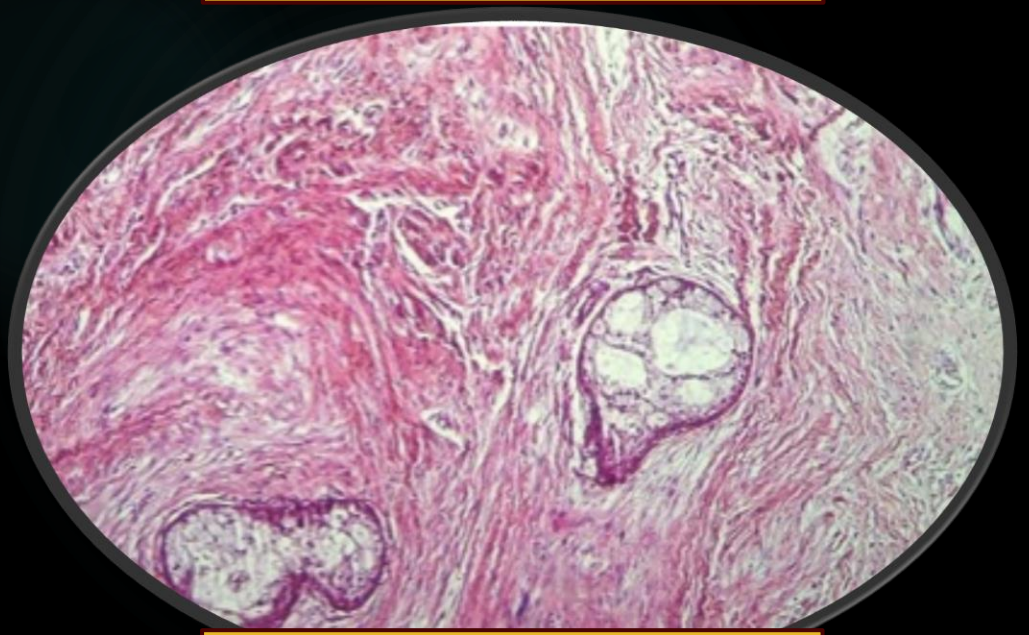




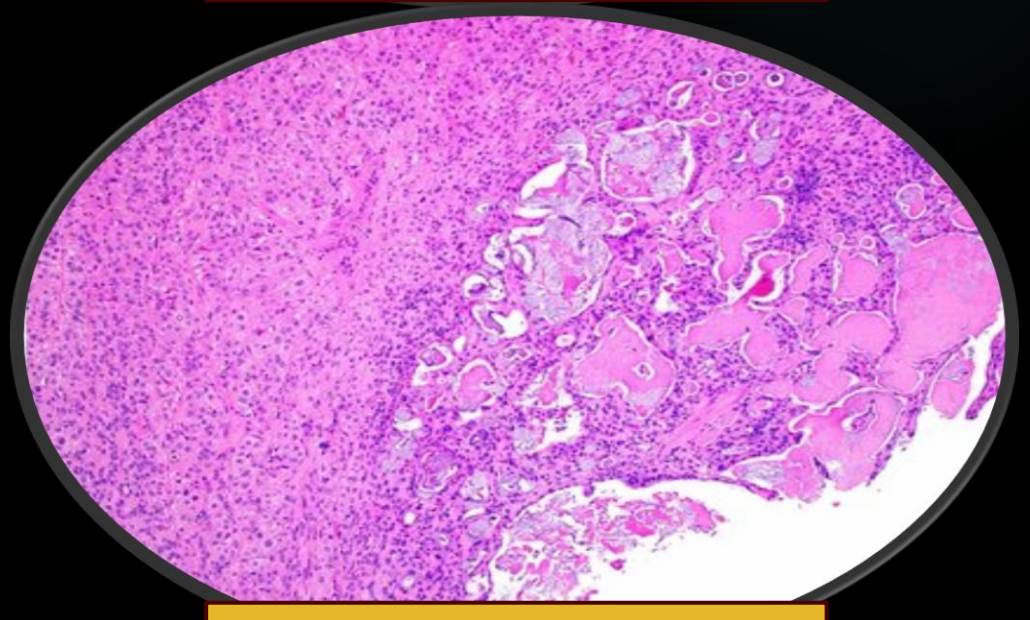
CONVENTIONAL



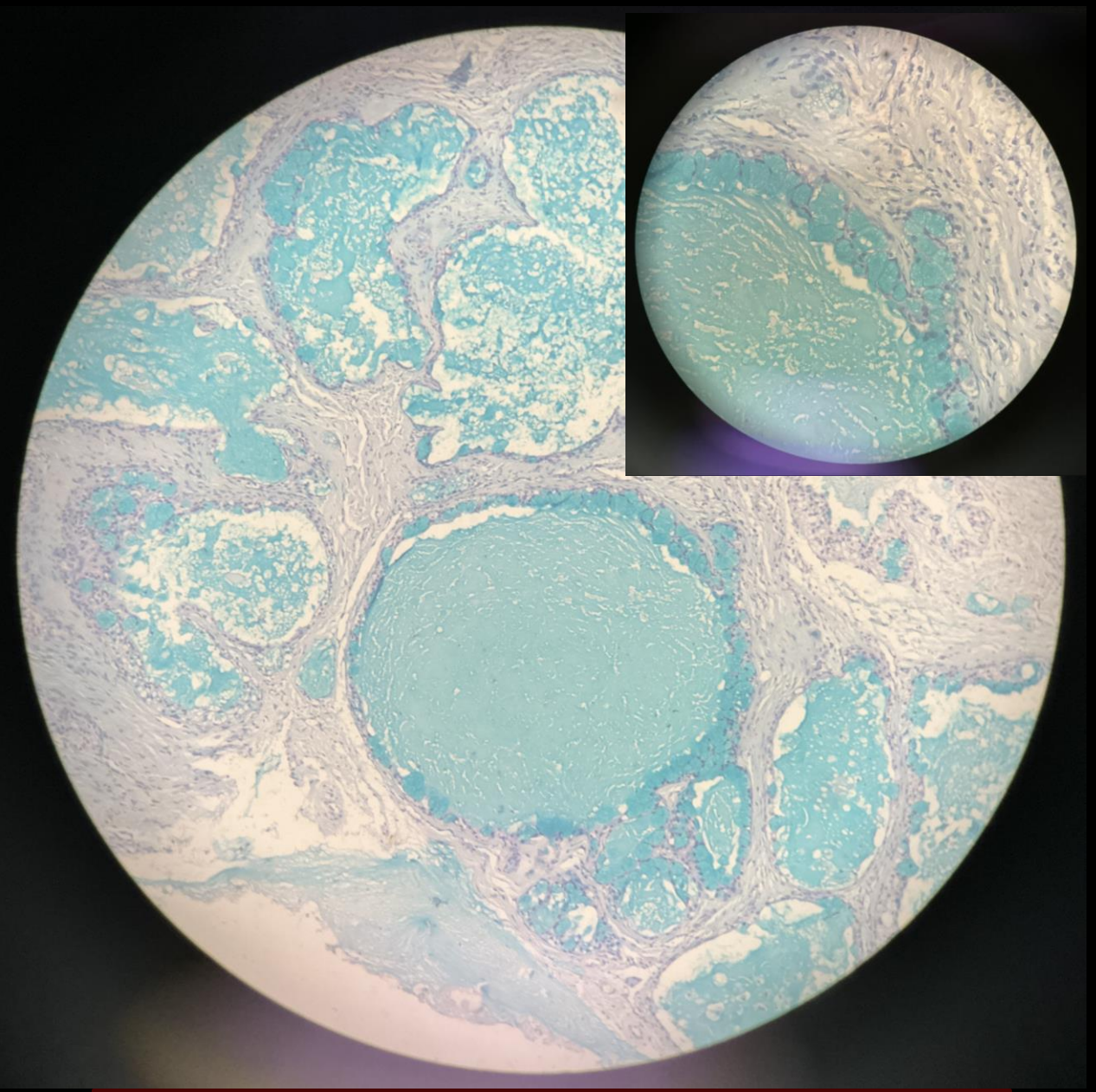
CLEAR CELL



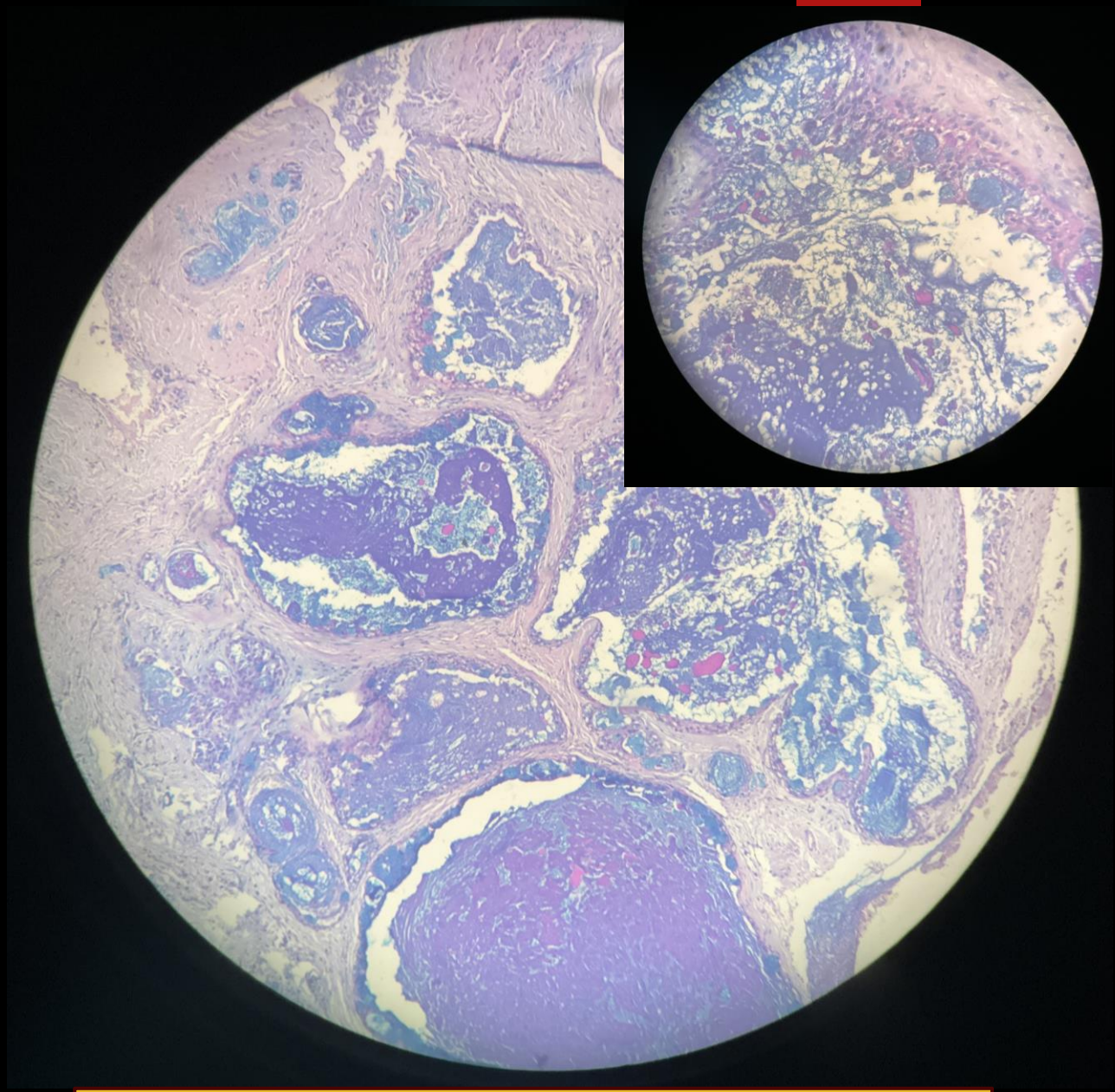
SCLEROSING



ONCOCYTIC



Alcian Blue



Alcian Blue-Periodic acid Schiff

Pan cytokeratin

CK 5/6

CK7

CK14

p63

p40

Epithelial membrane antigen

MUC1, MUC2, MUC4, MUC5AC, MUC5B

S100

GFAP

Calponin

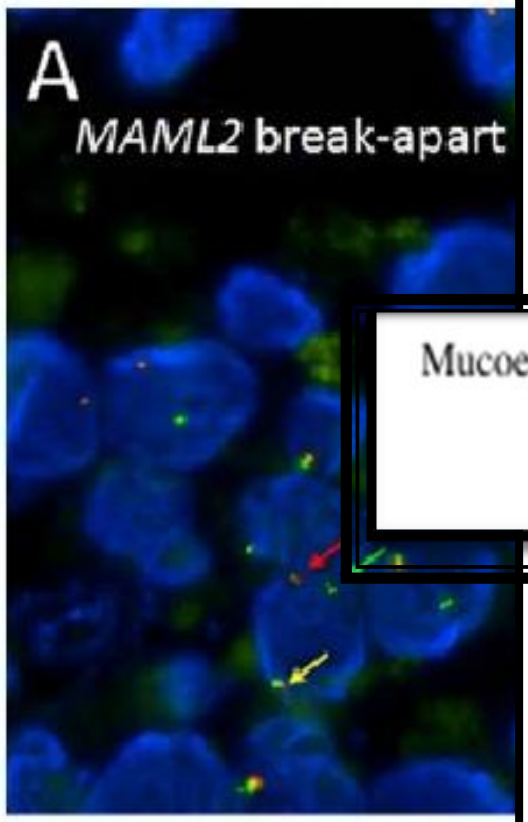
Muscle specific actin

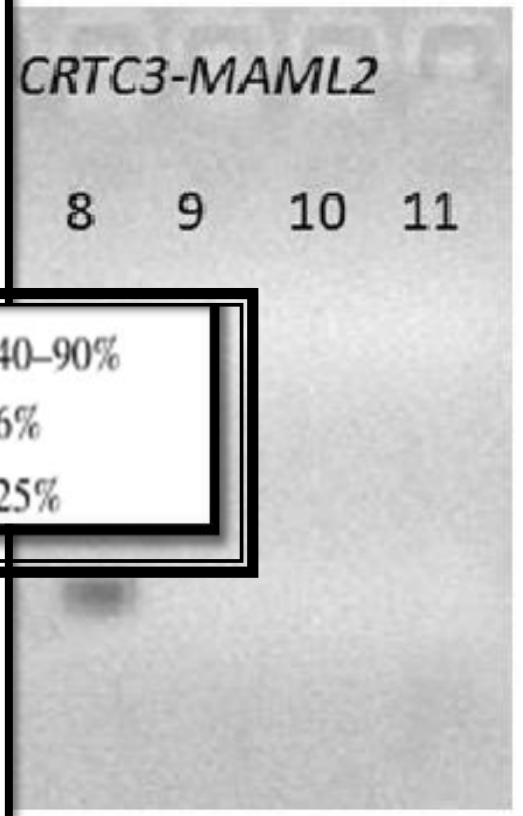
HER2

CK20

SOX10

DOG1





Tumour type	Gene	Mechanism	Prevalence
Acinic cell carcinoma	NR4A3	Fusion/activation	86%
Adenoid cystic carcinoma	MYB	Fusion/activation/amplification	80%
	MYBL1	Fusion/activation/amplification	10%
	NOTCH	Mutation	14%
Basal cell adenocarcinoma	CYLD	Mutation	29%
Carcinoma ex pleomorphic adenoma	PLAG1	Fusion/amplification	73%
	HMGA2	Fusion/amplification	14%
	TP53	Mutation	60%
Epithelial-myoepithelial carcinoma	HRAS	Mutation	78%
[illegible]	EWSR1-ATF1	Fusion	92%
Mucoepidermoid carcinoma	CRTC1-MAML2	Fusion	40–90%
	CRTC3-MAML2	Fusion	6%
	CDKN2A	Deletion	25%
[illegible]	FGFR1	Amplification	10%
	TP53	Mutation	56%
	PIK3CA	Mutation	33%
	HRAS	Mutation	33%
	AR	Copy gain	35%
	PTEN	Loss	38%
	CDKN2A	Loss	10%
Microsecretory adenocarcinoma	MEF2C-SS18	Fusion	>90%
Mucinous adenocarcinoma	AKT1 E17K	Mutation	100%
	TP53	Mutation	88%
Mucoepidermoid carcinoma	CRTC1-MAML2	Fusion	40–90%
	CRTC3-MAML2	Fusion	6%
	CDKN2A	Deletion	25%

Histological feature	Score	
	AFIP (Goode et al, 1998)	Brandwein et al (2001)
Cystic component <25%	2	2
Neural invasion	3	3
Necrosis	3	3
Mitoses >4/10 hpf	3	3
Anaplasia (nuclear atypia)	4	2
Invasion in small nests and islands	NI	2
Lymphatic or vascular invasion	NI	3
Bone invasion	NI	3
Grade I (low grade)	0–4	0
Grade II (intermediate grade)	5–6	2–3
Grade III (high grade)	7–14	4 or more

NI – features not included in the AFIP scheme.

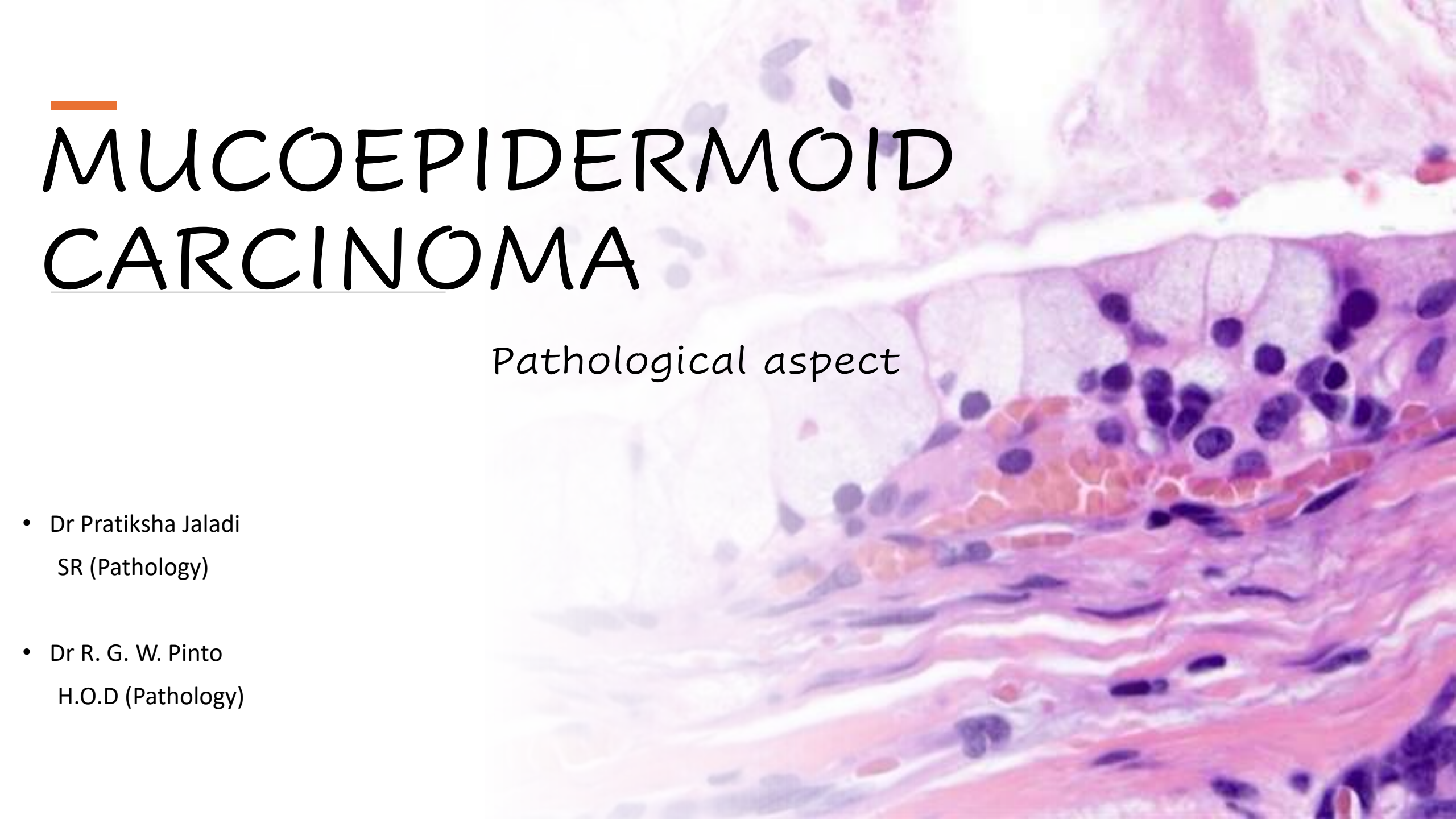
The unencapsulated structure of minor salivary glands could potentially explain the aggressive nature of malignant neoplasms involving these glands.

Current literature has conclusively established the presence of salivary gland tissue in sites other than the oral cavity.

The absence of a unified grading and prognostication system for mucoepidermoid carcinoma highlights the importance of a multidisciplinary approach aimed at early diagnosis and effective management.

MUCOEPIDERMOID CARCINOMA

Pathological aspect

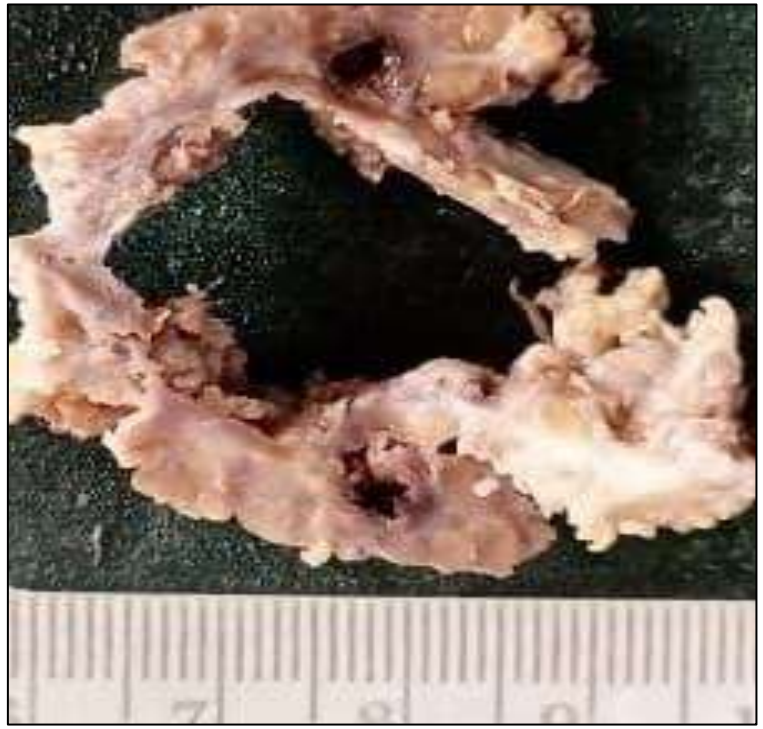


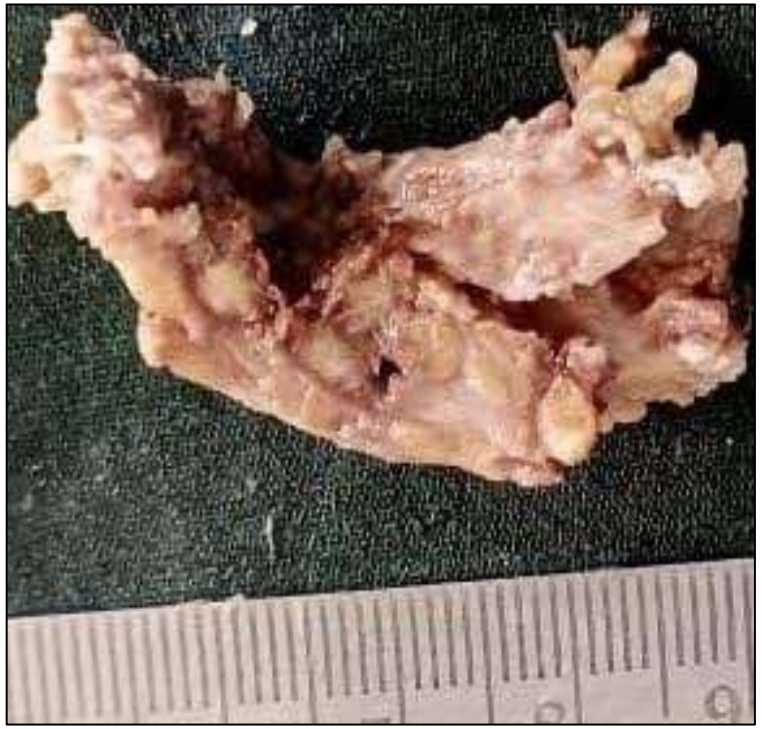
- Dr Pratiksha Jaladi
  SR (Pathology)
- Dr R. G. W. Pinto
  H.O.D (Pathology)

Gross

2 Brownish white tissue bits measuring 3.5*2*2cm and 4*2.5*1.5cm.

C/s –multiple whitish nodules measuring 0.2 to 0.8 cm in diameter.





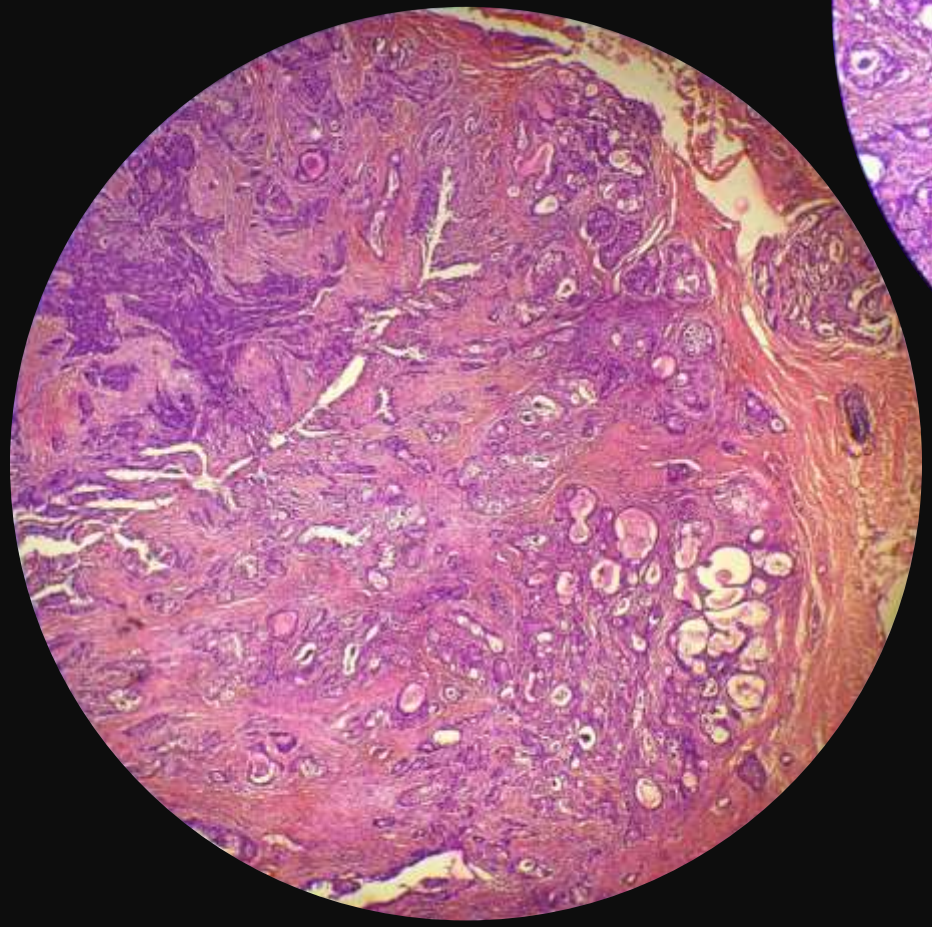
Microscopy

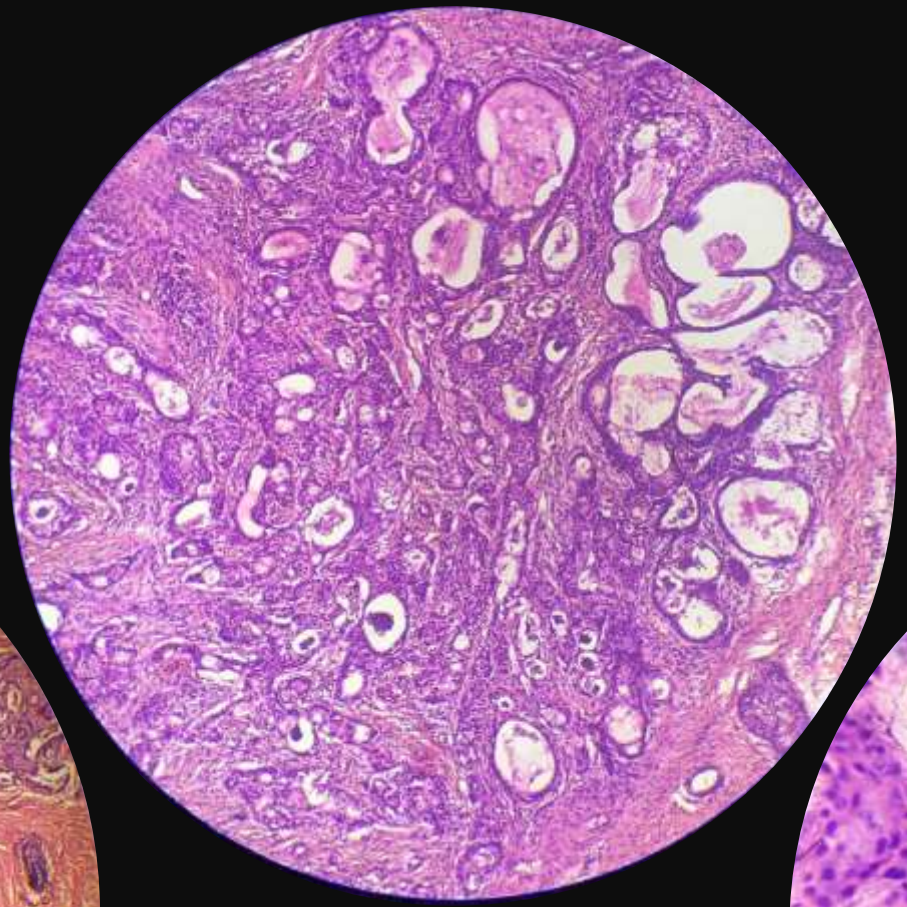
- Sections from the nodules showed cystic spaces lined by mucus secreting cells surrounded by intermediate cells having scanty cytoplasm resembling basal cells and squamoid cells with abundant eosinophilic cytoplasm and distinct cell membrane.
- Invasion into surrounding soft tissue and skin.
- Surrounding parotid gland showed chronic nonspecific sialadenitis.

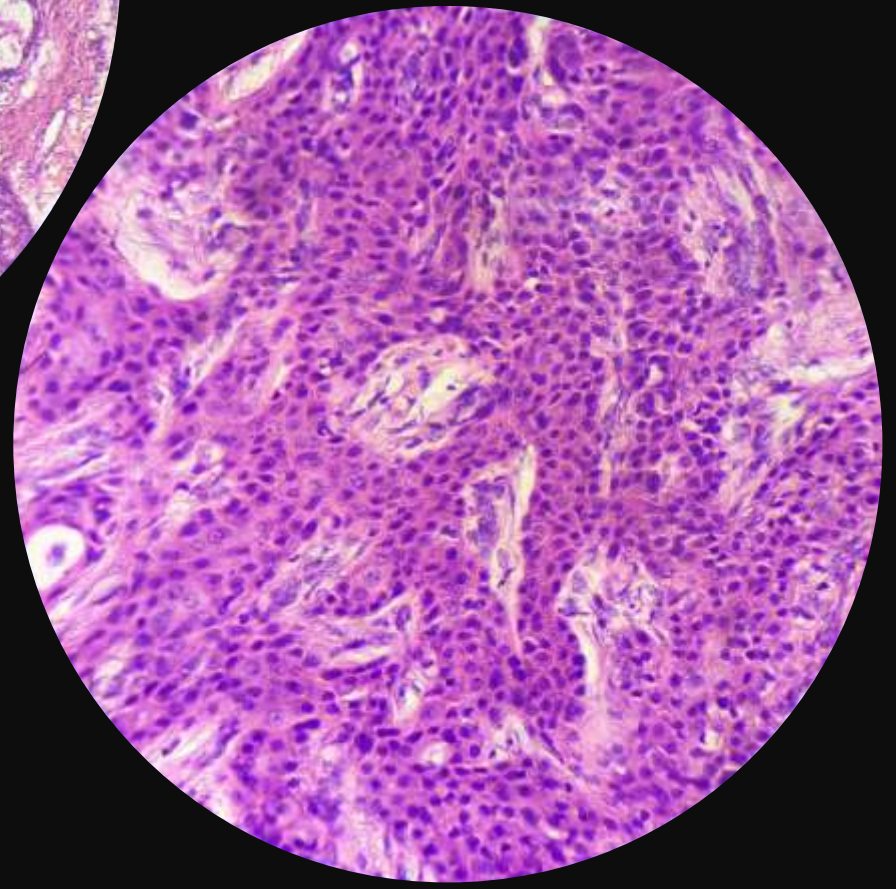
Diagnosis

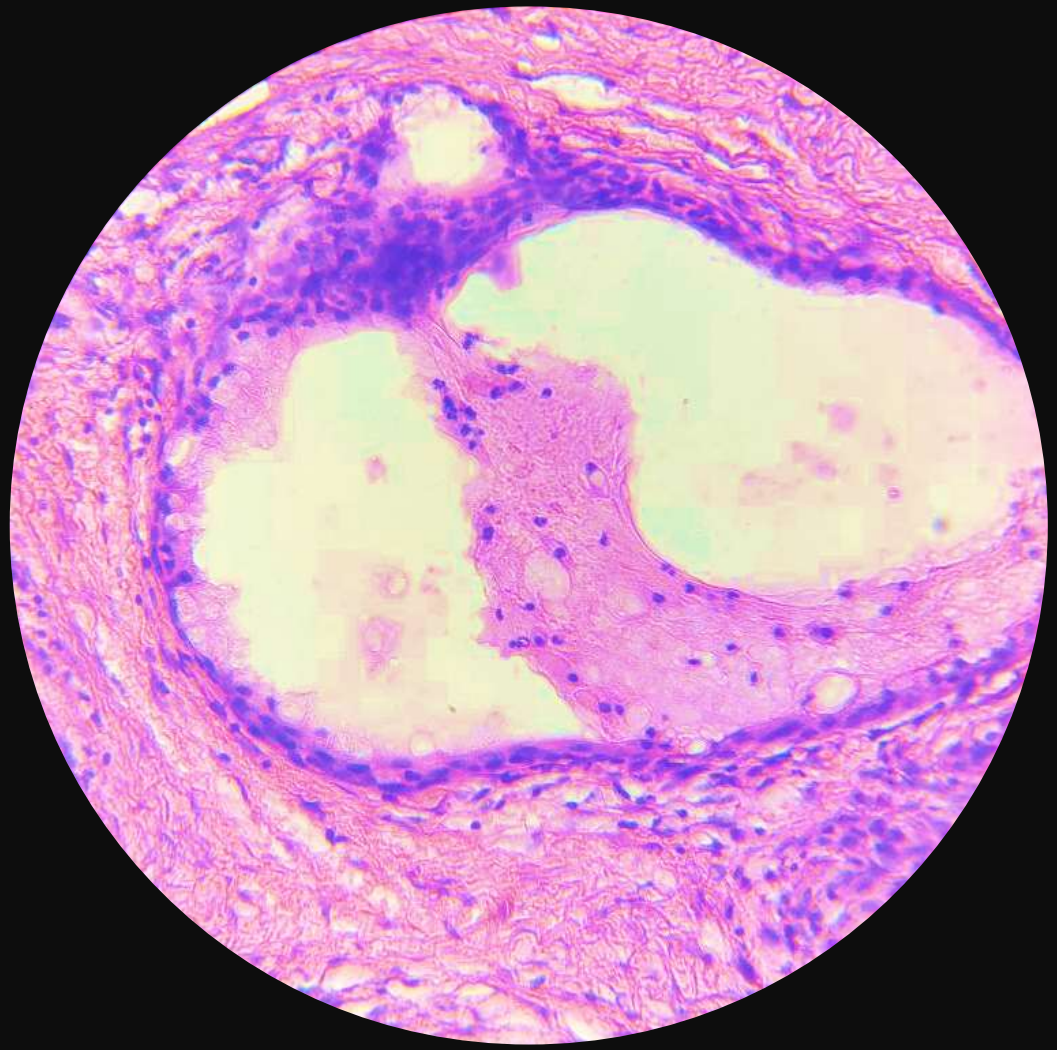
Invasive, moderately differentiated
Mucoepidermoid carcinoma – Grade 2
with surrounding showing chronic nonspecific sialadenitis.

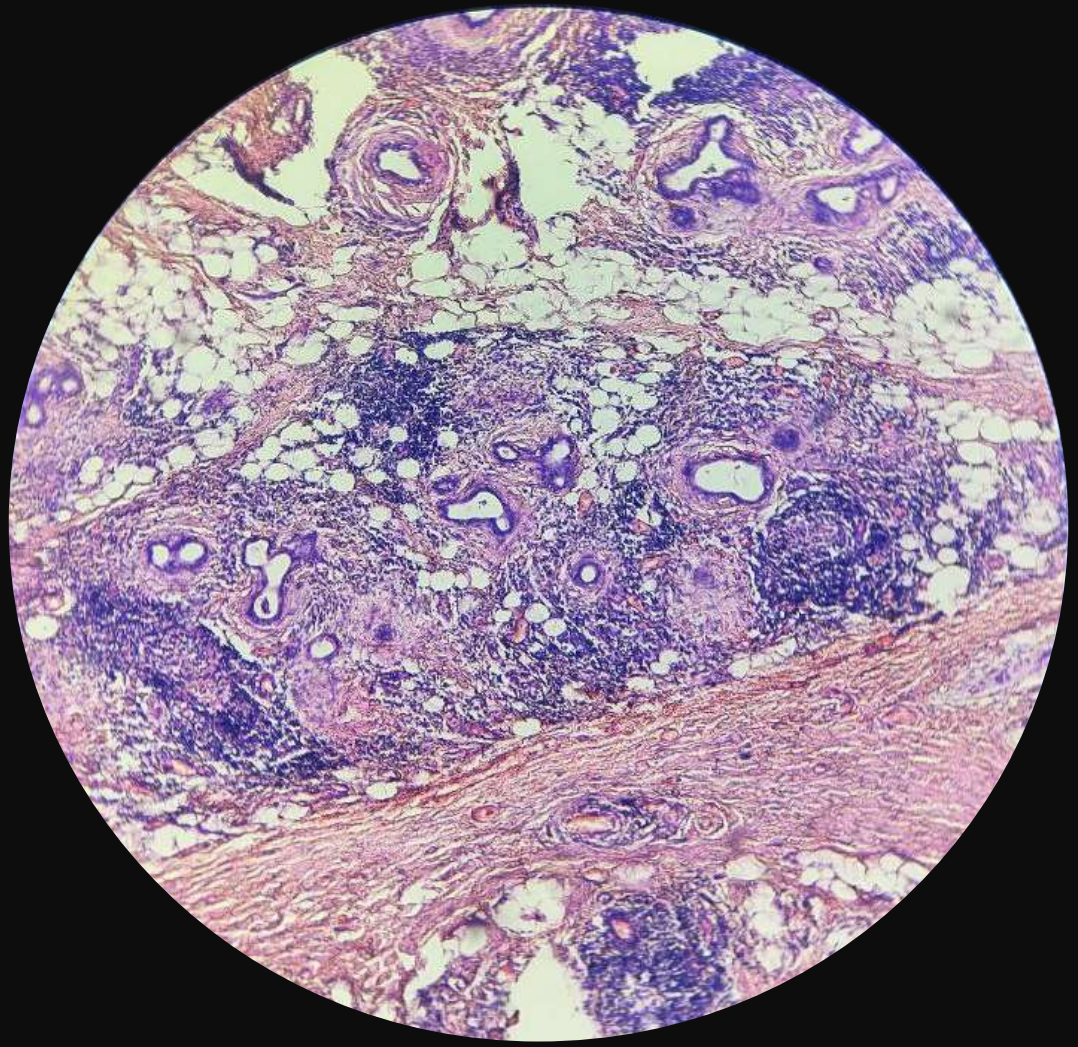
microscopy

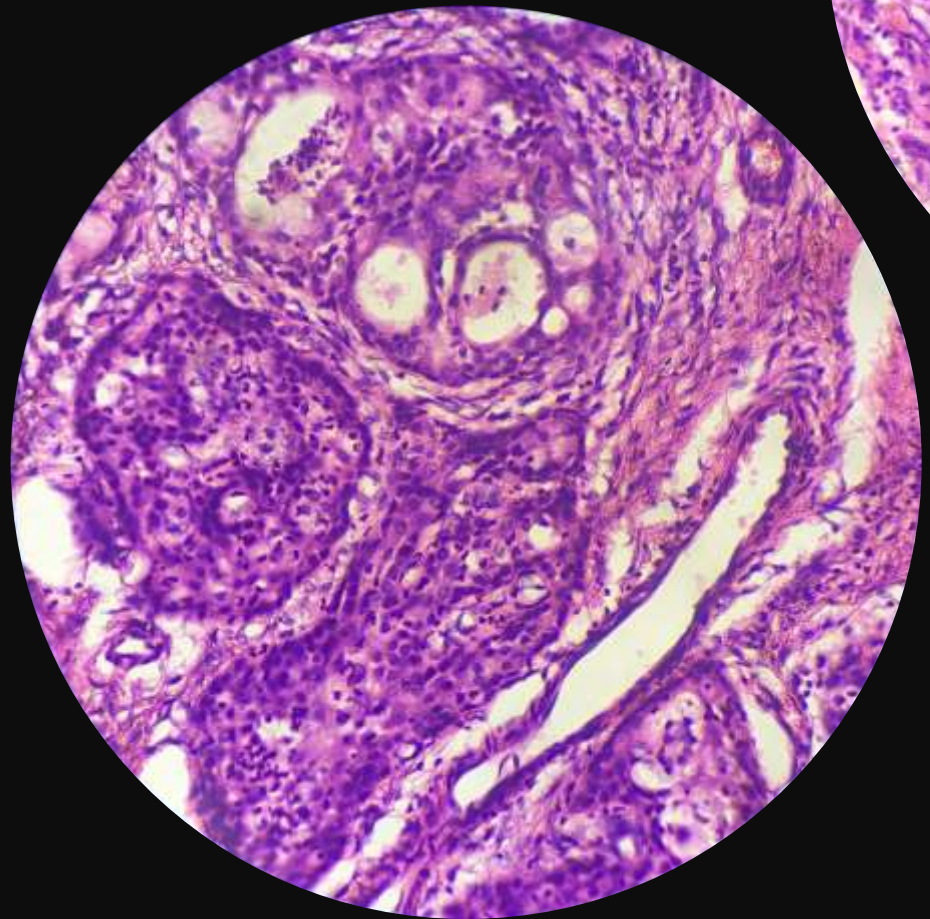


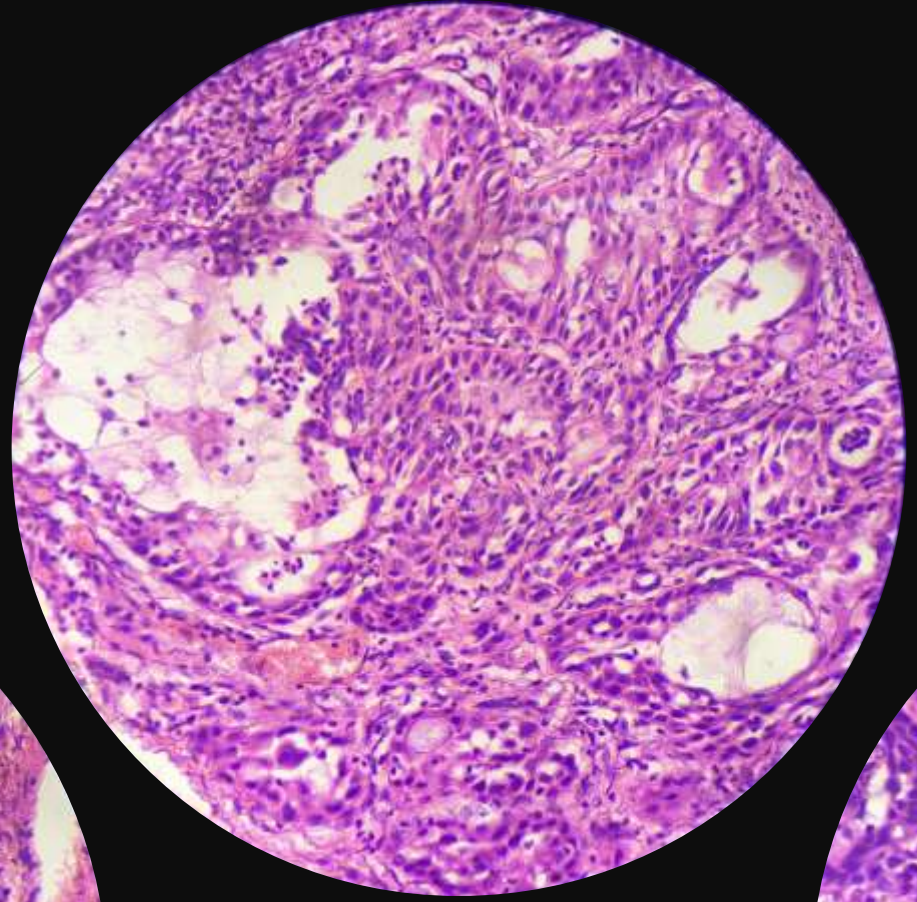


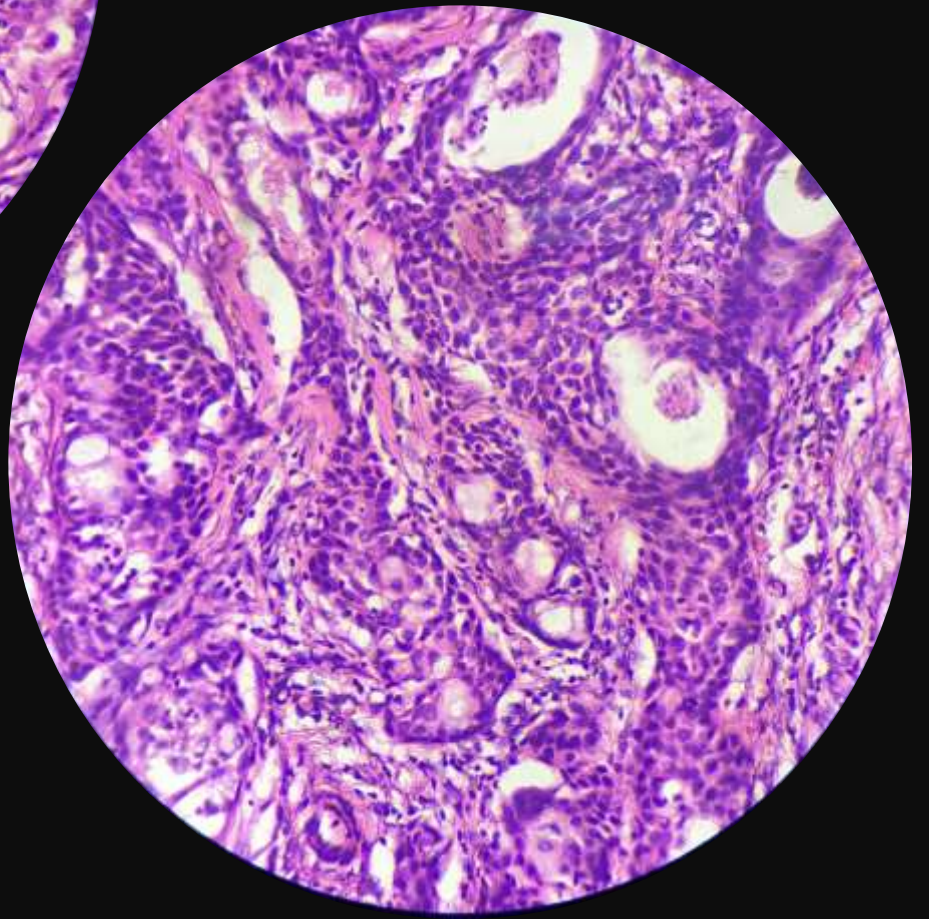




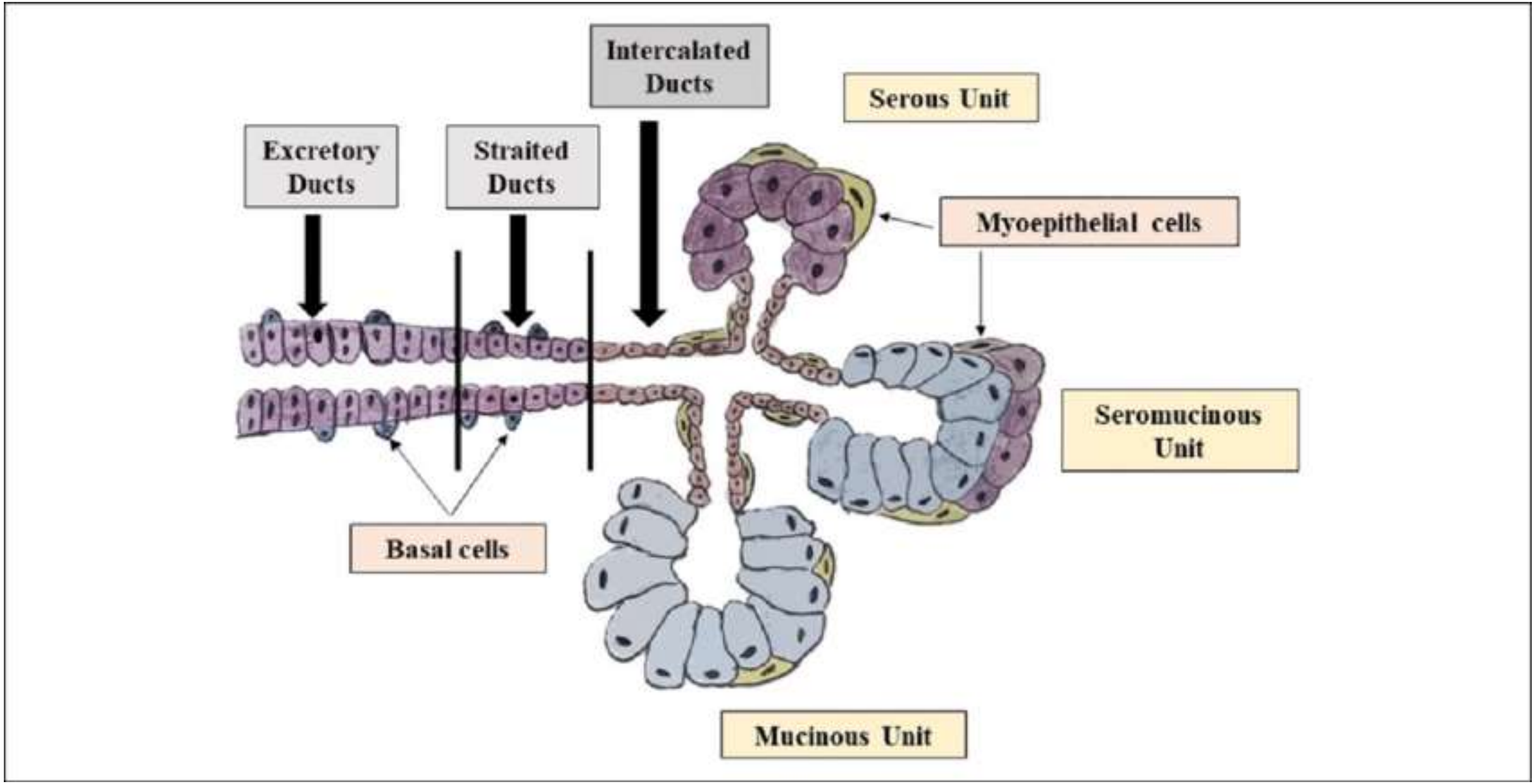


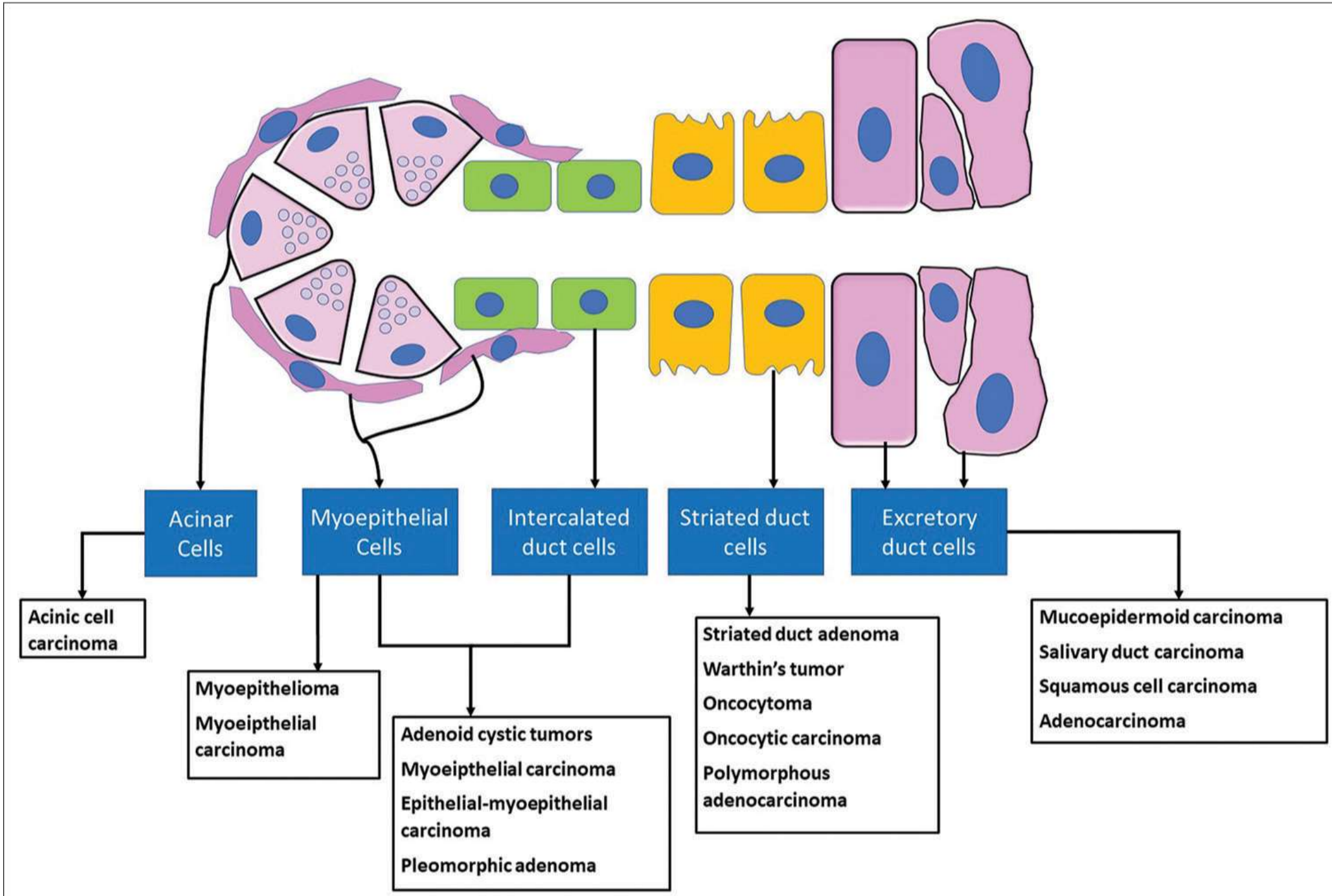






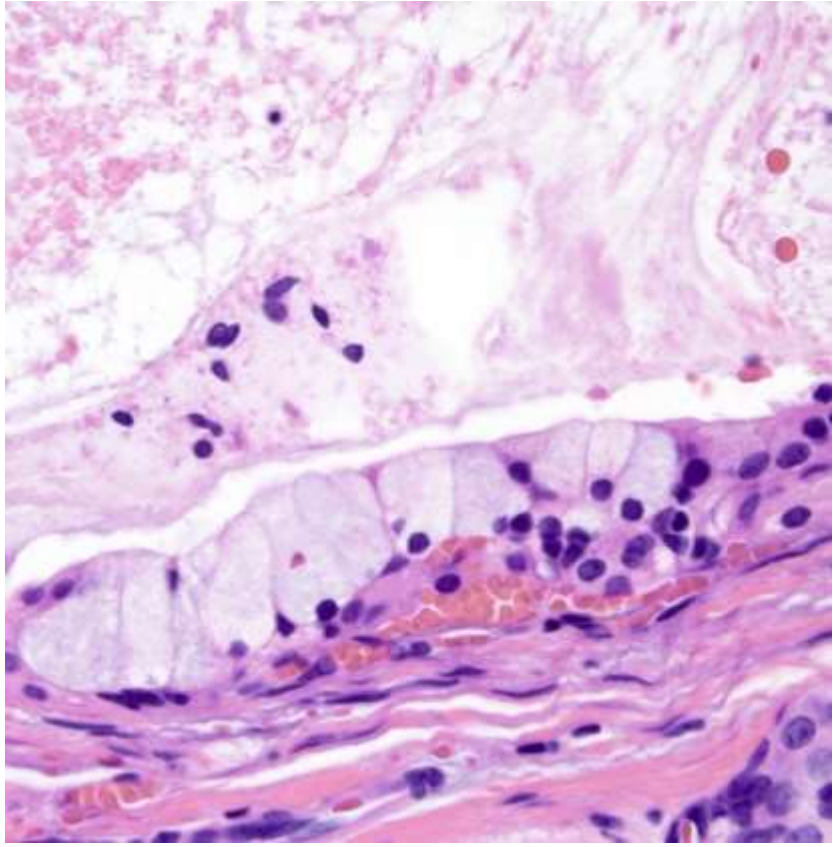
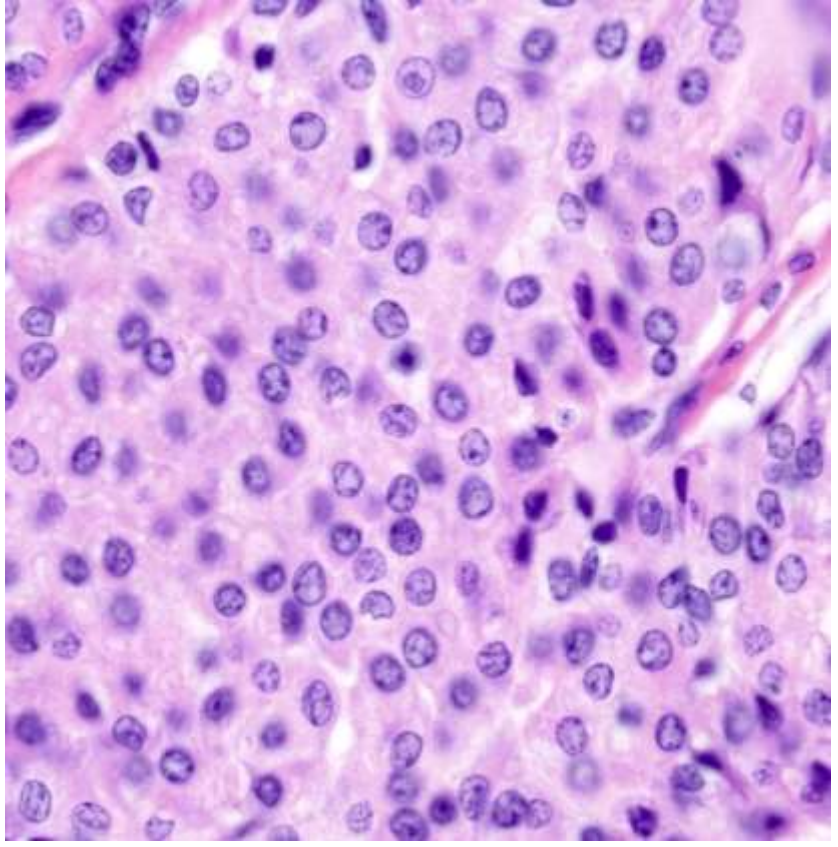
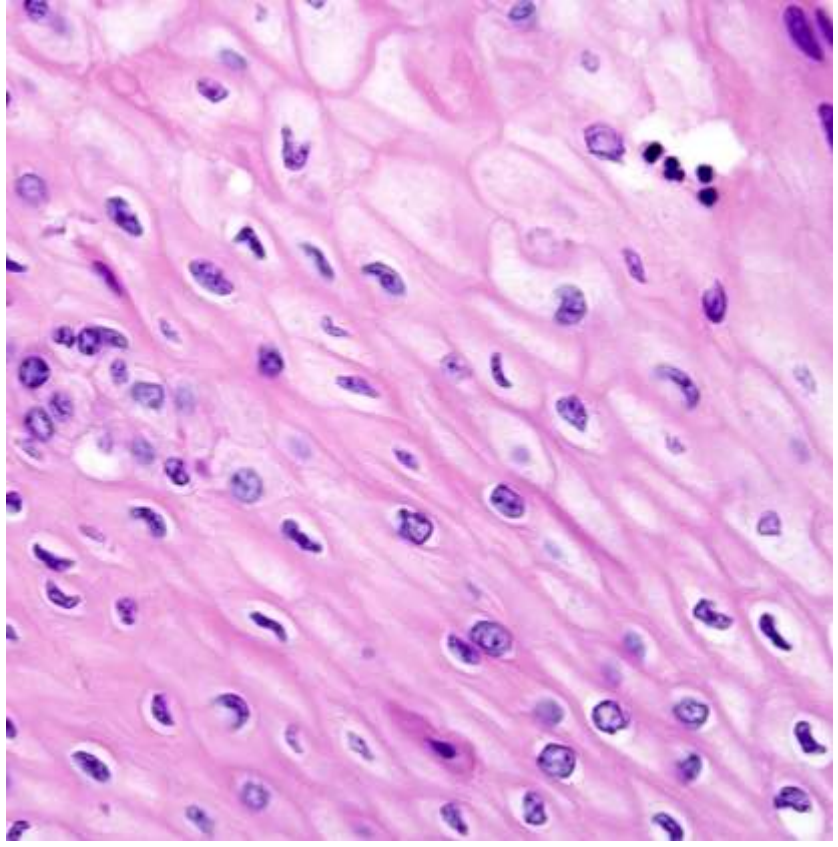
Discussion


Intercalated Ducts
Serous Unit
Excretory Ducts
Straited Ducts
Myoepithelial cells
Seromucinous Unit
Basal cells
Mucinous Unit


Acinar Cells
Myoepithelial Cells
Intercalated duct cells
Striated duct cells
Excretory duct cells
Acinic cell carcinoma
Myoepithelioma
Myoeipthelial carcinoma
Adenoid cystic tumors
Myoeipthelial carcinoma
Epithelial-myoepithelial carcinoma
Pleomorphic adenoma
Striated duct adenoma
Warthin's tumor
Oncocytoma
Oncocytic carcinoma
Polymorphous adenocarcinoma
Mucoepidermoid carcinoma
Salivary duct carcinoma
Squamous cell carcinoma
Adenocarcinoma

WHO Classification(5th edition 2022)

- **Non-neoplastic epithelial lesions**
- Nodular oncocytic hyperplasia
- Lymphoepithelial sialadenitis
- **Benign epithelial tumours**
- Pleomorphic adenoma
- Basal cell adenoma
- Warthin tumour
- Oncocytoma
- Salivary gland myoepithelioma
- Canalicular adenoma
- Cystadenoma of salivary gland
- Ductal papillomas
- Sialadenoma papilliferum
- Lymphadenoma
- Sebaceous adenoma
- Intercalated duct adenoma and hyperplasia
- Striated duct adenoma
- Sclerosing polycystic adenoma
- Keratocystoma
- **Malignant epithelial tumours**
- **Mucoepidermoid carcinoma**
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Secretory carcinoma
- Microsecretory adenocarcinoma
- Polymorphous adenocarcinoma
- Hyalinizing clear cell carcinoma
- Basal cell adenocarcinoma
- Intraductal carcinoma
- Salivary duct carcinoma
- Myoepithelial carcinoma
- Epithelial-myoepithelial carcinoma
- Mucinous adenocarcinoma
- Sclerosing microcystic adenocarcinoma
- Carcinoma ex pleomorphic adenoma
- Carcinosarcoma of the salivary glands
- Sebaceous adenocarcinoma
- Lymphoepithelial carcinoma
- Squamous cell carcinoma
- Sialoblastoma
- Salivary carcinoma, NOS and emerging entities
- **Mesenchymal tumours specific to the salivary glands**
- Sialolipoma

MUCOEPIDERMOID CARCINOMA

- Malignant epithelial neoplasm characterized by mucin secreating cells, intermediate cells and squamoid cells(epidermoid).
- Associated with a specific translocation t(11;19)(q14-21;p12-13) with *CRTC1(MECT1)-MAML2* fusion

- Most common malignant salivary gland tumor.
- Represents 10 - 15% of all salivary gland tumors.
- Age: wide age range.

- SITES :- Major and minor salivary glands (major > minor)

  Major: parotid > submandibular > sublingual

  Minor: palate, buccal mucosa, tongue.

  Rarely occurs in sinonasal tract, nasopharynx, lungs,

  skin, breast and cervix.

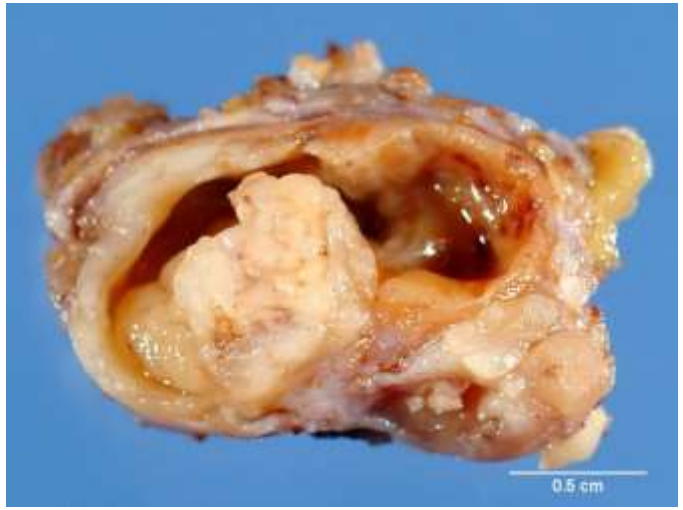
GROSS

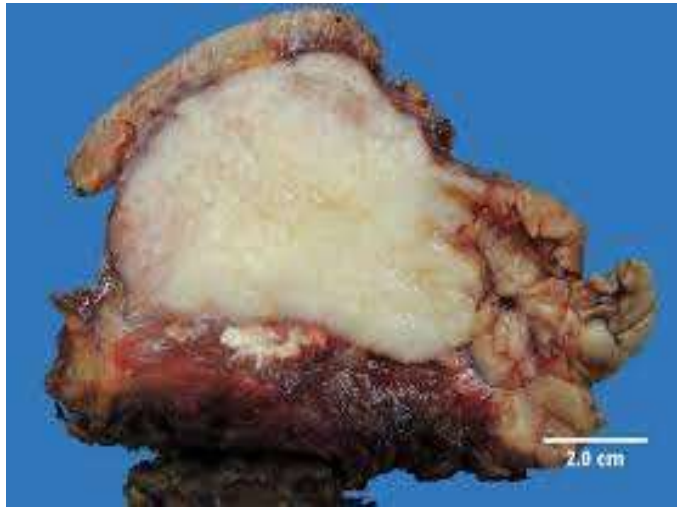
- **LOW GRADE**

  soft, cystic, circumscribed.

- **HIGH GRADE**

  firm, solid, infiltrative.

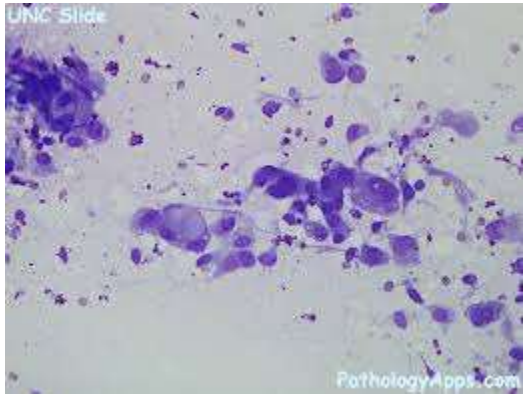




CYTOLOGY

- **LOW GRADE**

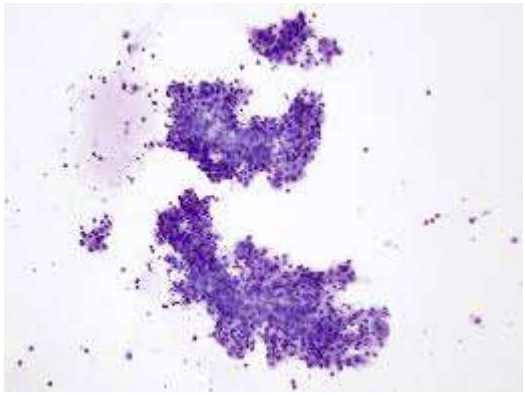
Predominantly mucus and macrophages with occasional bland epithelial cells.



- **HIGH GRADE**

Cellular smears with admixture of mucus cells, intermediate cells and squamoid cells.

Pleomorphism, necrosis, mitotic activity.



HISTOPATHOLOGY

- Solid, cystic or mixed growth patterns with Varying proportions of epidermoid cells, intermediate cells and mucocytes.
- Extravasation of mucin and keratin may result in dense inflammation and sclerosis.

X Marked nuclear atypia.

X Frequent mitosis

X Extensive keratinization

X Extensive necrosis

Poorly differentiated adenocarcinoma and Adenosquamous carcinoma to be considered.

VARIANTS

- Clear cell.
- Oncocytic
- Sclerosing with eosinophilia.
- Warthin-like.
- With sebaceous cells.
- Dedifferentiated
- Pleomorphic adenoma with squamous metaplasia.

Warthin Tumor

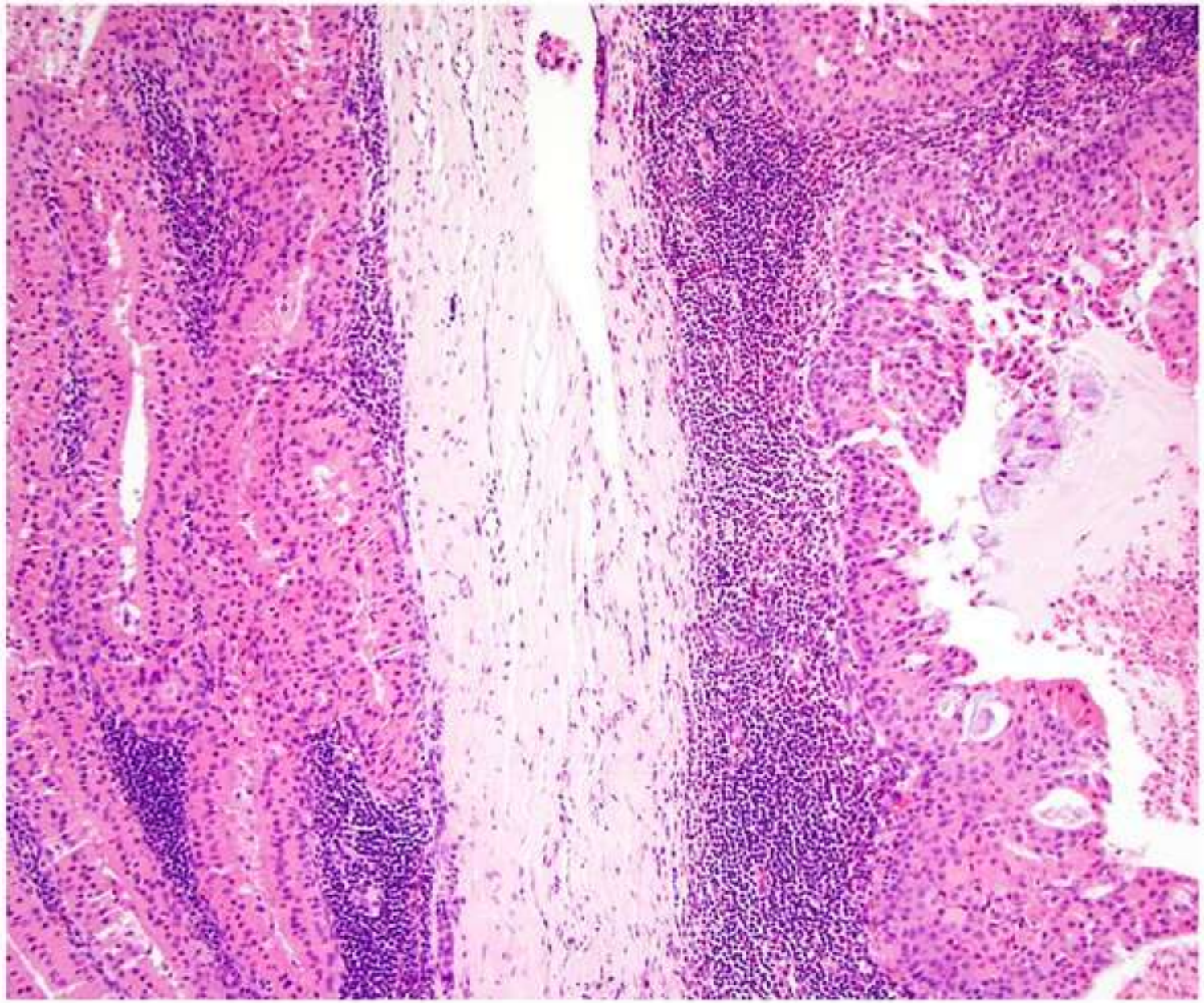
Second most common benign salivary gland tumor

Classic well-organized bilayered oncocytic epithelium and dense lymphoid stroma

Can have squamous and mucinous metaplasia but lacks architectural complexity

p63/p40 expression restricted to basal layer

No MAML2 rearrangement



Warthin-Like MEC

Rare variant of mucoepidermoid carcinoma

Oncocytic epithelium, cystic change, and dense lymphoid stroma can mimic Warthin tumor

Can have bilayered areas, but generally more complex and stratified epithelium

p63/p40 tends to have more diffuse positivity

MAML2 rearrangement

@LisaRooperMD

Histopathologic grading

4 histologic grading systems (2 quantitative and 2 qualitative)

- Armed Forces Institute of Pathology (AFIP) grading scheme (quantitative)
- Brandwein et al. grading scheme (quantitative).
- Modified Healy grading system (qualitative).
- Memorial Sloan Kettering Cancer Center (MSKCC) grading system (qualitative)

Modified Healey system

Low Grade

- Macrocysts, microcysts, transition with excretory ducts
- Differentiated Mucin producing Epidermoid Cells, often in a 1:1 ratio; minimal to moderate intermediate cell population
- Daughter cyst proliferation from large cysts
- Minimal to absent pleomorphism, rare mitoses
- Broad-front, often circumscribed invasion
- Pools of extravasated mucin with stromal reaction

Intermediate Grade

- No macrocysts, few microcysts, solid nests of cells
- Large duct not conspicuous
- Slight to moderate pleomorphism, few mitoses, prominent nuclei and nucleoli
- Invasive quality, usually well defined and uncircumscribed
- Chronic inflammation at periphery, fibrosis separates nests of cells and groups of nests

High Grade

- No macrocysts, predominantly solid but may be nearly all glandular
- Cell constituents range from poorly differentiated to recognizable epidermoid and intermediate to ductal type adenocarcinoma
- Considerable pleomorphism, easily found mitoses
- Unquestionable soft tissue, perineural and intravascular invasion
- Chronic inflammation less prominent, desmoplasia of stroma may outline invasive clusters

AFIP grading system

Parameter	Point value
Intracystic component < 20%	2
Neural invasion	2
Necrosis	3
Mitoses (4 or more/10 HPF)	3
Anaplasia	4

Grade	Total point score
Low	0-4
Intermediate	5-6
High	7 or more

MSKCC grading system

Low Grade

- Predominantly cystic
- Well circumscribed borders
- Mitosis: 0–1/10 HPF
- Necrosis: Absent

Intermediate Grade

- Predominantly solid
- Well circumscribed or infiltrative borders
- Mitosis: <4/10 HPFs
- Necrosis: Absent

High Grade

- Predominant growth pattern: Any (usually solid)
- Infiltration: Any (usually infiltrative borders)
- ≥4/10 HPFs
- Present

Brandwein grading system

Feature	Points
Intracystic component < 25%	2
Tumor front invades in small nests islands	2
Pronounced nuclear atypia	2
Bony invasion	3
> 4 mitoses/10 HPF	3
Perineural spread	3
Necrosis	3

Grade	Points
I	0
II	2-3
III	4 or more

	AFIP	Brandwein
Cystic component	(<20%) 2	(<25%) 2
Perineural invasion	2	3
Necrosis	3	3
≥4 Mitoses per 10 hpf	3	3
Anaplasia/Nuclear atypia	4	2
Pattern of infiltration (nests/islands)		2
Angiolymphatic invasion		3
Bone Invasion		3
Grade	0-4 LG 5-6 IG ≥ 7 HG	0-1 LG 2-3 IG ≥4 HG

- Armed Forces Institute of Pathology (AFIP) scoring system is widely accepted.
- This scoring system is only applicable to parotid and minor salivary gland tumors and does not predict the outcome of submandibular gland neoplasms which have significant metastatic potential irrespective of histologic grade.
- Brandwein et al. noted that there is considerable grading disparity among skilled pathologists and the scoring criteria proposed by AFIP tend to downgrade mucoepidermoid carcinomas. Therefore, a modified grading schema to include additional criteria such as lymphovascular and bony invasion, as well as, the pattern of tumor invasion in the form of small nests/islands which enhances both predictability and reproducibility.

SPECIAL STAINS

- P.A.S
- Mucicarmin.

IMMUNOHISTOCHEMISTRY

- MUC1,MUC2, MUC4, MUC5AC, MUC5B – positive
- MUC 3 – negative (positive in adenoid cystic carcinoma).
- MUC1 – High grade
- MUC4 – Low grade
- CK7+
- CK14+
- CK20-
- P63 + In epidermoid and intermediate cell

DIFFERENTIAL DIAGNOSIS

- Necrotizing sialometaplasia.
- Pleomorphic adenoma.
- Cystadenoma.
- Squamous cell carcinoma.
- Clear cell tumors.
- Adenosquamous carcinoma.

MUCOEPIDERMOID CARCINOMA OF PAROTID GLAND

DR JOEL BARBOSA NORONHA
SENIOR RESIDENT
DEPARTMENT OF OTORHINOLARYNGOLOGY
GOA MEDICAL COLLEGE AND HOSPITAL

General points

Salivary neoplasms are uncommon- 2.3-3/100000/year
5 percent of all head and neck cancers
Rule of 80
Diverse/variable and overlapping histological appearances
Indolent/recurrences
Source of confusion

Parotid- benign- pleomorphic adenoma>Warthin’s tumor
Malignant- mucoepidermoid carcinoma>carcinoma ex pleomorphic adenoma>acinic cell carcinoma
Common site for metastasis

Submandibular- benign- pleomorphic adenoma
Malignant- adenoid cystic carcinoma

Sublingual- most are malignant- adenoid cystic

Minor salivary glands- benign- pleomorphic adenoma
Malignant- mucoepidermoid carcinoma

Pathogenesis

Theories - Bicellular reserve cell (stem cell) theory and Multicellular theory.
Genetics
Radiation
Environmental factors

Clinical features

Face/cheek/upper neck swelling
Slowly growing
Asymptomatic/medial displacement of tonsil

Features s/o malignancy- pain/paresthesis/sudden increase in size/fixity to skin/ulceration/facial nerve involvement/cervical lymphadenopathy

Investigations

USG
MRI
FNAC

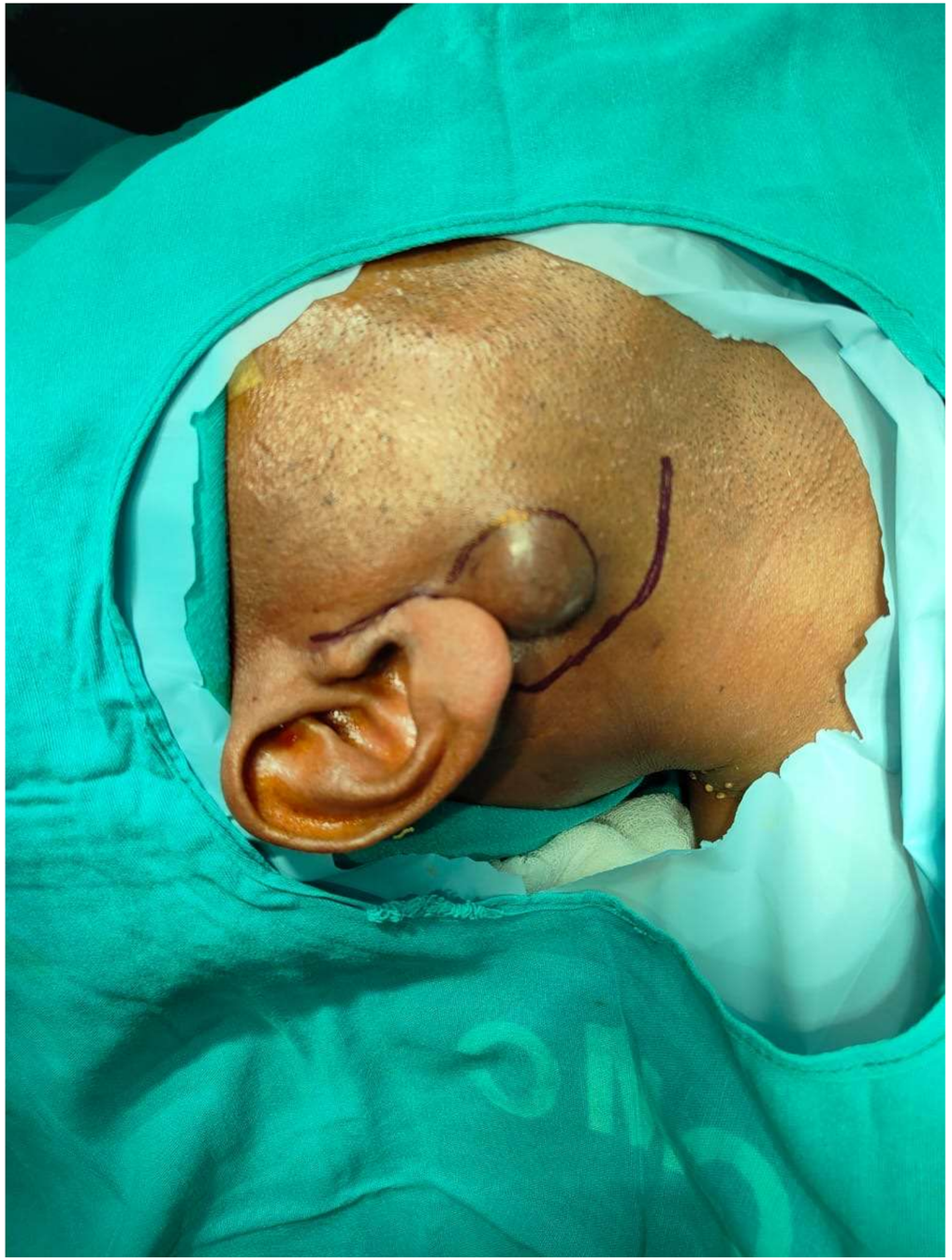
CASE

Rohidas Kalangutkar
54/M
K/c/o HTN
CC- Right cheek swelling * 7months
Underwent superficial parotidectomy under GA in January 2024 in Asilo, Mapusa
HPE- chronic sialadenitis

Had recurrence of cystic swelling at surgical site 1week post op
Was aspirated (straw coloured fluid) multiple times
Treated as recurrent sialocele
Referred to GMC for further management

O/E- Right Blair incision scar +
Infra auricular 2*2cm swelling +
Cystic, mobile, nontender, overlying skin normal, facial nerve normal

MRI- Multiloculated cystic lesion 2.3*1.9cm in residual parotid gland, another cystic lesion 8.2*5.3mm adjacent to it



Patient was taken up for revision parotidectomy under GA on 04/07/2024
O/E- cyst +, aspirated and fluid sent for cytology
Adjacent parotid tissue indurated, extending to deep lobe and distorting anatomy
Extensive fibrosis +
Branches of facial nerve could not be identified because of fibrosis
Accidentally transected and later reanastomosed

GOA MEDICAL COLLEGE AND HOSPITAL

Medico - 128

BAMBOLIM - GOA
DEPARTMENT OF PATHOLOGY
HISTOPATHOLOGY REPORT

ent's Name: Rohidas Kalangutkar IND/OPD Reg. No.: 24/64690
e: 54yr Sex: F Ward No.: Cot:
epartment: ENT Doctor:
Slide No.: HP-4093/24 Previous Slide No.:

Date: 12/07/24

Right Parotid gland

Gross :- Two brownish white bits,
One skin covered specimen measuring 3.5 x 2 x 2 cm, other measuring 4 x 2.5 x 1.5 cm. Cut section shows a whitish nodule measuring 0.8 cm, located 6 cm from skin in subdermal region. Cut section of nodule is whitish.
Cut section of other bit shows multiple whitish nodules ranging in size 0.2 cm to 0.5 cm.

Microscopy: Sections show Mucoepidermoid carcinoma of the parotid, invading into the surrounding soft tissue and skin.
The surrounding adjacent parotid shows chronic nonspecific sialadenitis.

Conclusion: Mucoepidermoid carcinoma, invasive, moderately differentiated (medium grade, grade 2)
Surrounding shows chronic nonspecific sialadenitis.

Pathologist

Govt. Ptg. Press, Panaji-Goa—1312/15,000—12/2013.

...GE AND HOSPITAL
BAMBOLIM-GOA.
DEPARTMENT OF PATHOLOGY
CYTOPATHOLOGY REPORT

Patient's Name Rohidas Kalangutkar Reg.No. _____

Age: 54yr Sex: M Wd. No. 102 Bed No. _____ Hosp. No.: 64690

Department ENT Doctor: _____

Slide No: CP-2947/24 Previous Slide No: _____

Date: 8/7/24 Parotid Gland Fluid Cytology

- Smears show, amorphous material, abundant neutrophils, lymphocytes and Macrophages.
No malignant cells seen in the material

Sent.

Pathologist

Department Of Radiation Oncology
Goa Medical Collage & Hospital
Bambolim- Goa

Mr. Rohidas Kalangutkar 54yrs/M
24/64690

Right Parotid Ca. sialadenitis
Underwent right superficial parotidectomy
on Dec 24.

Remnant swelling in Max.
Underwent Rt total parotidectomy GMC
GMC HPR 4093/24 : Mucoepidermoid
Carcinoma invasive, Moderately differentiated
grade II.

Presently no complaints
Op site Portop scan healing healing
WHD

Adv To come on 31.I.2024 for portop x-ray

Consultant Radiation Oncology,
Goa Medical Collage & Hospital
Bambolim- Goa.

Mucoepidermoid Carcinoma

Most common salivary malignancy, 45 percent

50-70 percent from parotid

All ages and both sexes, F>M, mean 45 years

Most common pediatric salivary malignancy

Histologically, composed of 3 cell types: epidermoid, mucous and intermediate cells.

On the basis of histological features, divided into high, intermediate and low grade

They have a propensity to metastasize to regional lymph nodes; occurs in 30–50 percent of patients with high-grade tumours

Treatment- WLE with 1cm cuff around

Management of the facial nerve

Neck dissection

Post operative external beam radiotheraphy

Facial rehabilitation

THANK YOU