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HELEN DILLER FAMILY COMPREHENSIVE CANCER CENTER
HEAD AND NECK ONCOLOGY

Overview of parotid neoplasms

Patrick Ha, MD FACS

Irwin Mark Jacobs and Joan Klein Jacobs Distinguished Professor
Chief, Division of Head and Neck Surgical Oncology
Medical Director, Mission Bay Adult Services
University of California San Francisco
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Disclosures

- Educational Grant Funding: Axogen, Stryker, J&J, Medtronic
- Advisory board: Atos Medical, Rakuten Medical

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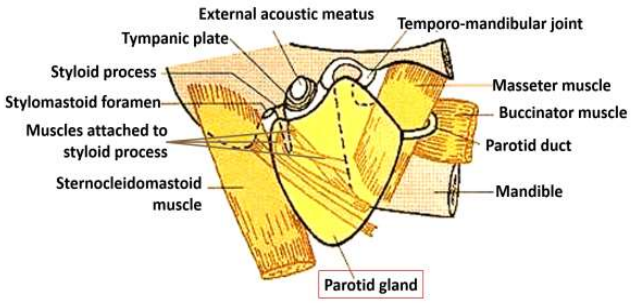
Parotid basics

- Derived from ectodermal bud, gland itself contains mesenchymal and neural crest cells
- Capsule of the investing layer of the deep cervical fascia
- Serous, watery secretions



www.anatomyqa.com

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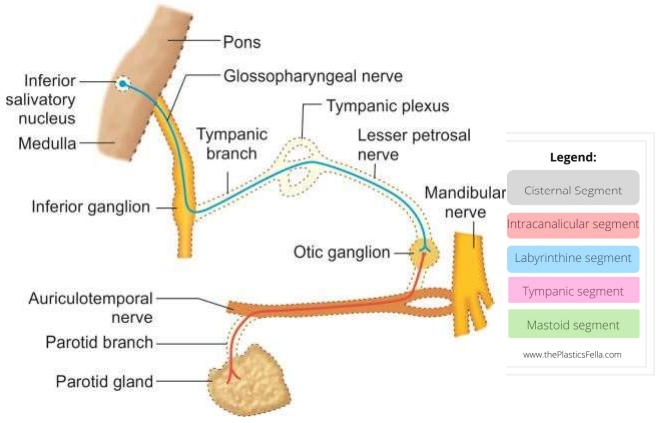
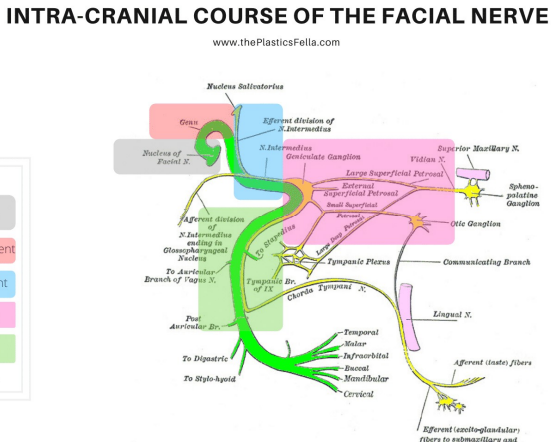
Innervation





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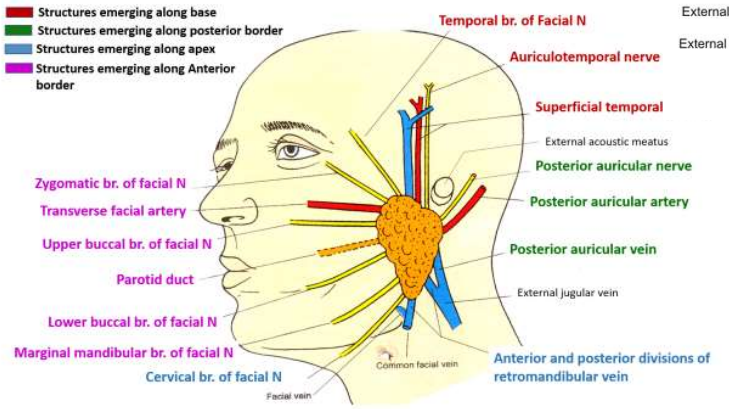
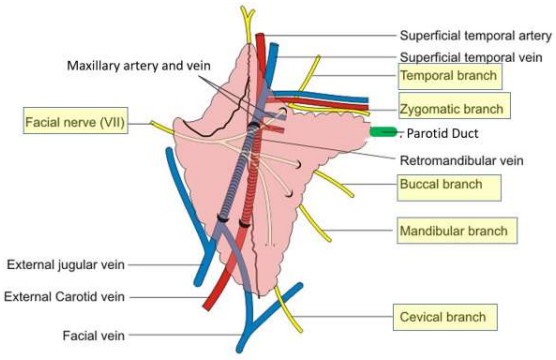
Anatomy





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So many tumors!

- 2017 World Health Organization
- Tumors behave differently, so worth knowing the highlights

Benign epithelial tumors	Malignant epithelial tumors
Pleomorphic adenoma 8940/0	Acinic cell carcinoma 8550/3
Myoepithelioma 8982/0	Mucoepidermoid carcinoma 8430/3
Basal cell adenoma 8147/0	Adenoid cystic carcinoma 8200/3
Warthin tumor 8561/0	Polymorphous adenocarcinoma 8525/3
Oncocytoma 8290/0	Epithelial-myoepithelial carcinoma 8562/3
Canalicular adenoma and other ductal adenomas 8149/0	Clear cell carcinoma 8310/3
Sebaceous adenoma 8410/0	Basal cell adenocarcinoma 8147/3
Lymphadenoma	Sebaceous adenocarcinoma 8410/3
Sebaceous 8410/0	Secretory carcinoma 8502/3
Non-sebaceous 8410/0	
Ductal papillomas 8503/0	Intraductal carcinoma
	Oncocytic carcinoma 8290/3
Sialadenoma papilliferum 8406/0	Salivary duct carcinoma 8500/3
Cystadenoma 8440/0	Adenocarcinoma, NOS 8140/3
	Myoepithelial carcinoma 8982/3
Soft tissue tumors	Carcinoma ex pleomorphic adenoma 8941/3
Hemangioma 9120/0	Poorly differentiated carcinoma 8020/3
	Carcinosarcoma 8980/3
Hematolymphoid tumors	Squamous cell carcinoma 8070/3
Hodgkin lymphoma	
Diffuse large B-cell lymphoma 9680/3	
Extranodal marginal zone	Lymphoepithelial carcinoma 8082/3
B-cell lymphoma 9699/3	
Hodgkin lymphoma	Sialoblastoma 8974/1
	Secondary tumors

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Diagnostics

- Fine needle aspiration
  - Risks: infection, hematoma, pain, facial nerve weakness, tumor seeding
  - Benefits: know your enemy, preoperative planning/discussion, set expectations, can sample nodes, maybe nonoperative (lymphoma, lymphoepithelial cyst?)
- Core biopsy
  - Difference between anatomic path vs cytopath in training
  - Up to experience of the pathologist – not for us to decide

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FNA – sensitivity/specificity/accuracy

Benign vs malignant

- Stewart et al (2000): 92%, 100%, 98%
- Postema et al (2004): 88%, 99%, 96%
- Seethala et al (2005): 86%, 92%, 90%
- Zbaren et al (2008): 79%, 74%, 88%
- Jafari et al (2009): 67%, 96%, 91%

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Milan Classification

Diagnostic Category	ROM	Management
1: **Non-Diagnostic**	25% (0-67%)	Clinical and radiologic correlation or repeat FNA
2: **Non-Neoplastic**	10% (0-20%)	Clinical follow-up and radiologic correlation
3: **Atypia of Undetermined Significance (AUS)**	10-35%	Repeat FNA or surgery
4: **Neoplasm**		Surgery or clinical follow-up
i) **Benign**	<5% (0-13%)	
ii) Salivary Gland Neoplasm of Uncertain Malignant Potential (**SUMP**)	35% (0-100%)	
5: **Suspicious for Malignancy**	60% (0-100%)	Surgery
6: **Malignant**	90% (57-100%)	Surgery

9 Presenta /MilanSystem alth

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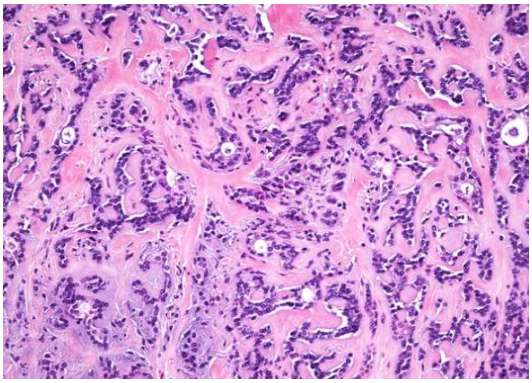
Pleomorphic Adenoma

- Most common neoplasm – 80% of parotid tumors
- Almost always in parotid (85%)
- Progressive growth, risk of malignant transformation (3-8%)
- T1 low, T2 high, homogeneous contrast enhancement
- Surgery



- Recurrence rate of 3-15%
- Radiation may be useful in those cases

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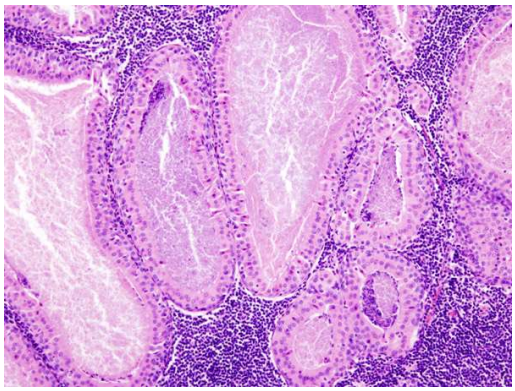
Papillary Cystadenoma Lymphomatosum (Cystadenolymphoma, Warthin tumor)

- 2-15% of tumors
- Only tumor smoking related
- Can be multifocal/bilateral
- Often cystic
- Malignant transformation low (0.3%)
- Observation an option



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Other benign tumors

- Basal cell adenoma, myoepithelioma, oncocytoma
- Less common, but you will see them
- Favor resection, as FNA diagnosis is challenging or part of a larger differential

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Salivary gland cancers

- ~5% of all head and neck cancers
- Various histologies depending on cell or origin
- Behavior dependent on type
- Surgery +/- radiation is typical
- Extent of surgery, neck dissection, adjuvant therapy up for debate

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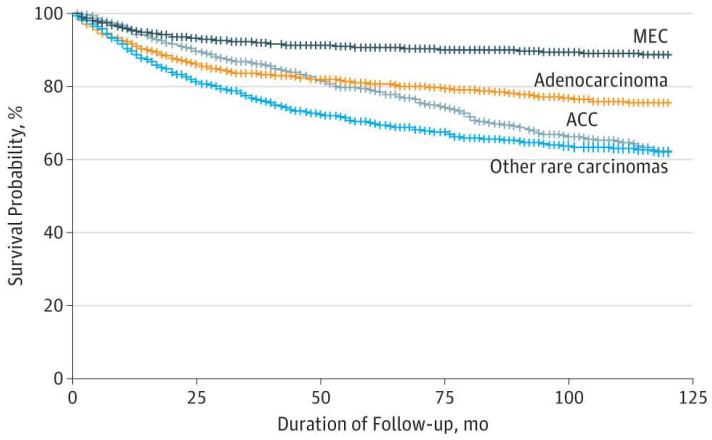
Salivary gland cancer survival



No. at risk						
MEC	1568	1225	980	780	572	386
Adenocarcinoma	1313	923	689	527	363	246
ACC	1228	912	681	492	319	228
Other rare carcinomas	1225	871	626	446	288	201

Baddour HM et al, JAMA OHNS 2016

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Histologic risk

Low Risk	Intermediate Risk	High Risk
Low grade mucoepidermoid carcinoma	Intermediate grade mucoepidermoid carcinoma	High grade mucoepidermoid carcinoma
Acinic cell carcinoma	Sebaceous adenocarcinoma	Adenocarcinoma
Basal cell adenocarcinoma	Myoepithelial carcinoma	Salivary duct carcinoma
Polymorphous adenocarcinoma	Adenoid cystic carcinoma (cribriform/tubular)	Adenoid cystic carcinoma (solid variant)
Clear cell carcinoma		Small cell carcinoma
Cystadenocarcinoma		Large cell undifferentiated carcinoma
Secretory carcinoma		Carcinoma ex-pleomorphic

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Fusions define salivary cancer

Tumor Type	Translocation	Gene	Comments
Mucoepidermoid	t(11;19) t(11;15)	CRTC1-MAML2 CRTC3-MAML2	Mostly low-intermediate grade
Adenoid Cystic	t(6;9) t(8;9)	MYB-NFIB MYBL1-NFIB	MYB also upregulated without translocation
Clear Cell Carcinoma	t(12;22)	EWSR1-ATF1	
Secretory Carcinoma	t(12;15)	ETV6-NTRK3	Druggable
Carcinoma-ex pleomorphic	t(8q12) t(12q14-15)	PLAG1 HMGA2	Similar to pleomorphic adenoma

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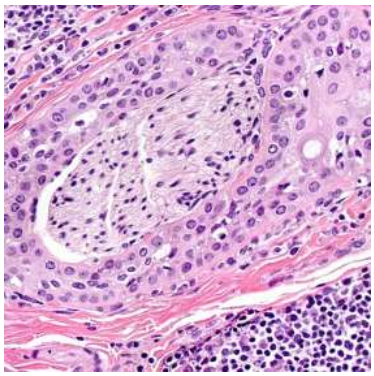
Mucoepidermoid carcinoma



- 1st or 2nd most common
- Most common in children
- Grade means something
  - Low, intermediate, high
- Characterized by MECT1-MAML2 fusion
- Can be cystic
- Usually excision only needed unless intermediate/high grade

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Salivary duct carcinoma

- Aggressive, but rare
- High likelihood of nodal spread
- Should check mammogram to make sure not metastasis
- ERBB2 (Her2) positive in ~60%
- Androgen receptor positivity in ~66%
- Raises the possibility of androgen deprivation therapy, or anti Her2 therapies (think breast or prostate cancer)

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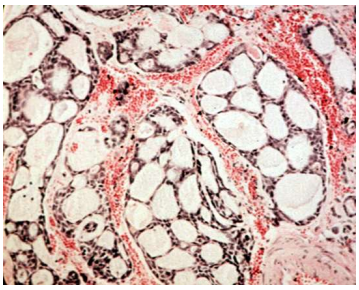
Adenoid cystic carcinoma

- 10% of salivary tumors, 1-2% of head and neck malignancies
- Slow but aggressive growth.
  - 80% 5yr, 45% 15yr survival
- Perineural invasion (up to 100%)
- Distant metastasis (35-50%)
  - Average onset ~30 months
  - 3yr survival ~40%, 5 yr survival 10-15%
- Regional disease relatively uncommon (5-15%)
- Marked by gene fusion, Myb-NFIB



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Radiotherapy

- No prospective randomized controlled study
- Doses >60Gy more effective
- Not effective as primary treatment (may have palliative role)
- Appears to be good for local control in adjuvant setting
- ?effect on survival
- Retrospective bias

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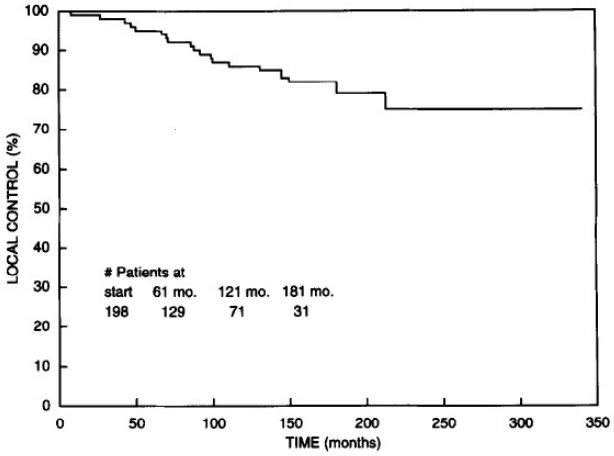

Fig. 1. Actuarial local control in 198 patients with adenoid cystic carcinoma treated with surgery and postoperative radiotherapy.

Garden AS et al, Int J Radiation Oncol Biol Phys 1995

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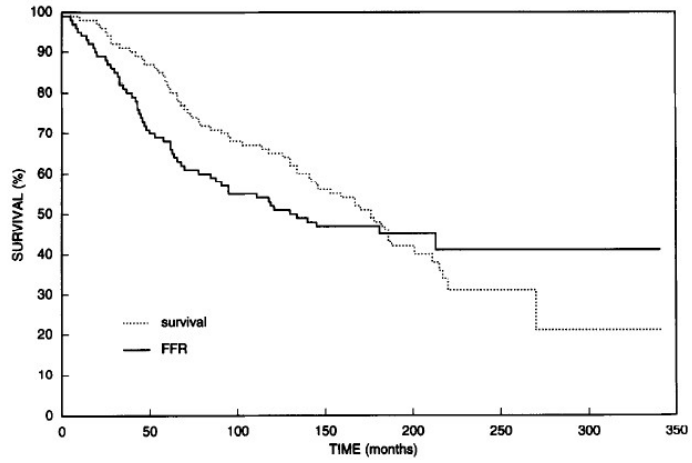

Fig. 5. Actuarial survival and freedom from relapse in 198 patients with adenoid cystic carcinoma treated with surgery and postoperative radiotherapy.

Garden AS et al, Int J Radiation Oncol Biol Phys 1995

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Indications for postop radiation therapy

- Advanced stage tumors (T3/4)
- Invasion into adjacent structures
- Nodal involvement
- High grade histology:
  - High grade MEC, salivary duct, adenoid cystic, squamous, adenocarcinoma
- Perineural invasion
- Recurrent disease
- Positive margin*, tumor spillage

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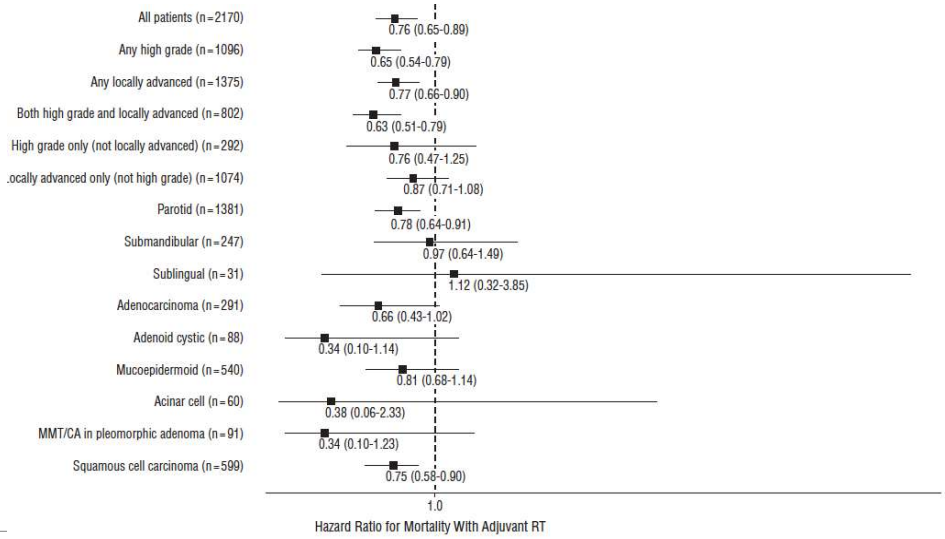
SEER analysis of postop radiation therapy



Mahmood U et al, Arch Otolaryngol HN Surg 2011

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Fun facts

- Acinic cell carcinoma – bilateral 10% of the time
- Clear cell carcinoma – can be mistaken for renal cell CA mets
- Polymorphous adenocarcinoma – (low grade), characterized by perineural invasion, often on the palate
- Secretory carcinoma – Loxo drug available for NTRK fusion
- Squamous cell carcinoma – probably metastasis 100%

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Primary Tumor (T)

T Category	T Criteria
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or smaller without extraparenchymal extension*
T2	Tumor >2 but <4cm without extraparenchymal extension
T3	Tumor >4cm and/or tumor with extraparenchymal extension
T4	Moderately advanced or very advanced disease
T4a	Tumor invades skin, mandible, ear canal, and/or facial nerve
T4b	Tumor invades skull base and/or pterygoid plates and/or encases carotid

*clinically evident or macroscopic extension

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Clinical Regional Lymph Node (cN)

N Category	N Criteria
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral node, <3cm and no ENE
N2a	Metastasis in a single ipsilateral node >3cm but <6cm, no ENE
N2b	Metastases in multiple ipsilateral nodes, <6cm, no ENE
N2c	Metastases in bilateral or contralateral nodes, <6cm, no ENE
N3a	Metastasis in node >6cm, no ENE
N3b	Metastasis in any node(s) with **clinically overt ENE**

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Pathologic Regional Lymph Node (pN)

N Category	N Criteria
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral node, <3cm and no ENE
N2a	Metastasis in a single ipsilateral node >3cm but <6cm, no ENE ***Or* single ipsilateral node <3cm with ENE**
N2b	Metastases in multiple ipsilateral nodes, <6cm, no ENE
N2c	Metastases in bilateral or contralateral nodes, <6cm, no ENE
N3a	Metastasis in node >6cm, no ENE
N3b	**Metastasis in single ipsilateral node >3cm with ENE** ***Or* multiple ipsi-, contra-, or bilateral nodes, with ENE** ***Or* single contralateral node or any size with ENE**

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AJCC Prognostic Stage Groups

T	N	M	Stage Group
Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	III
T0,T1,T2,T3	N1	M0	III
T4a	N0, N1	M0	IVa
T0, T1, T2, T3, T4a	N2	M0	IVa
Any T	N3	M0	IVb
T4b	Any N	M0	IVb
Any T	Any N	M1	IVc

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Decisions

- Work-up
  - To image or not (CT vs MRI)
  - Fine needle aspiration biopsy
- Surgery
  - Incision
  - Extent of surgery/parotidectomy
  - Intraoperative nerve monitoring
  - Nerve sacrifice/preservation
  - Neck dissection
  - Reconstruction
- Adjuvant therapy
  - Radiotherapy (proton, neutron, carbon)
  - Chemotherapy

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What to tell patients to expect about parotidectomy

- Numbness around ear/incision
- Soft tissue 'divot'
- Frey's syndrome
- First bite syndrome
- Possibility of facial nerve weakness (esp. marginal mandibular branch)
- Salivary fistula requiring serial drainage

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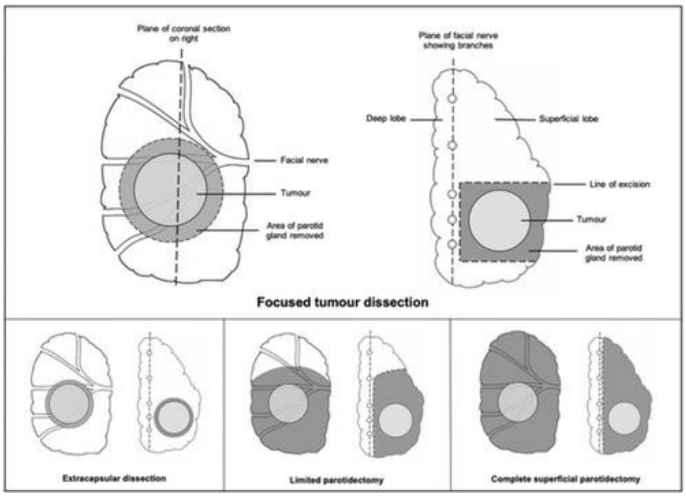
Extent of parotidectomy

- Total parotidectomy
- Superficial parotidectomy
- Partial (limited) superficial parotidectomy
- Extracapsular parotidectomy



Petrides GA et al, ANZ Journal of Surgery 2020

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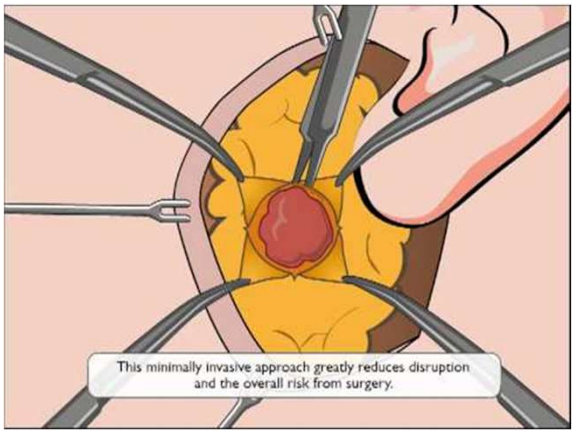
Extracapsular parotidectomy

- Gaining in favor for benign tumors
- Studies suggest lower incidence of Frey, nerve weakness, sialocele
- No apparent increase in recurrence
- Selection bias exists



Auger SR et al, Am J Otrolaryngol 2021
Psychogios G et al, Eur Arch Otorhinnolaryngol 2020
Schapher M et al, Laryngoscope 2020
Bar B et al, Laryngoscope 2020

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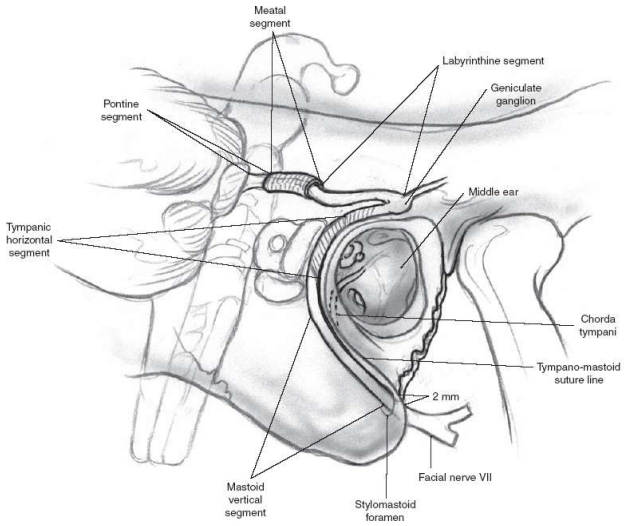
Mastoidectomy

- May be useful to identify uninvolved area of facial nerve
- Easier to identify nerve
- Can help clear nerve involved with tumor
- Can be helpful for proximal nerve grafting



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Facial Nerve Monitoring

- 2 vs 4 lead monitoring
- Which product to choose?
- Auditory vs visual feedback

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Operative Discussion: Facial Nerve Management

- General consensus: if you can save the nerve, then preserve
  - Radiation is our backup plan
- Poorly studied – difficult to normalize/ randomize
- Iyer et al (2008) – cutaneous SCC to parotid. Preservation might lead to increased local recurrence, but not survival

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Operative Discussion: Facial Nerve Management

- Iseli et al, 2008
- Adenoid cystic carcinoma
- Improved local control
- 10-yr improved survival

Local Control and Observed Survival by Facial Nerve Preservation Status for Patients With Adenoid Cystic Carcinoma of the Parotid Gland.

Outcome/Treatment Group	5 Yr	10 Yr	15 Yr
Rate of local control (n = 44)			
Facial nerve preserved (%)	78.9	70.0	40.0
Facial nerve resected (%)	100	100.0	100.0
P	.259	.420	.286
Observed survival rate (*P* = .569) (n = 47)			
Facial nerve preserved (%)	78.1	46.8	41.3
Facial nerve resected (%)	83.8	58.8	44.1

Iseli TA et al, Laryngoscope, 2008

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Neck dissection in salivary gland cancer

- Overall incidence of ~15% in salivary gland cancer
- Occult nodal disease
  - Important to identify for proper staging
  - Helps determine adjuvant treatment
- In the setting of N+ disease
  - Improved locoregional control
  - May improve survival

Medina JE, Otolaryngol Clin North Am; 1998

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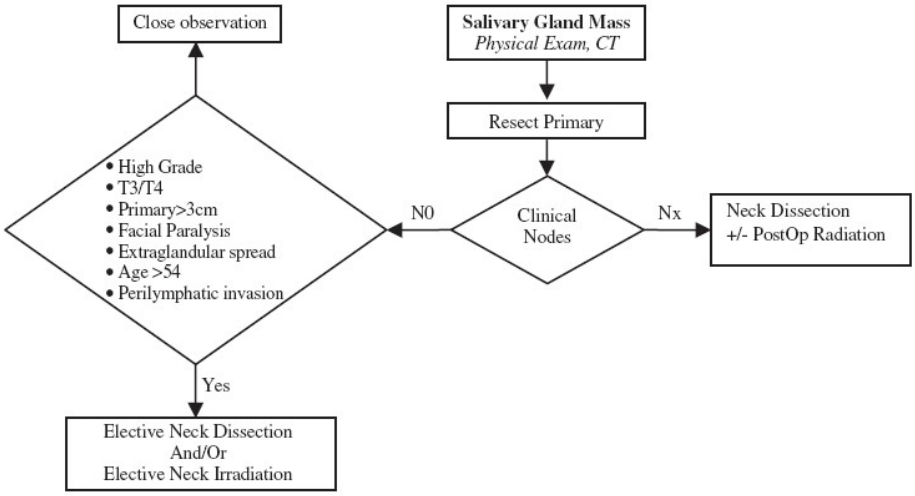

Fig. 1. Summary of treatment of neck in major salivary gland malignancy.

Gold DR et al, Otolaryngol Clin N Am;2005;38(1);99-105

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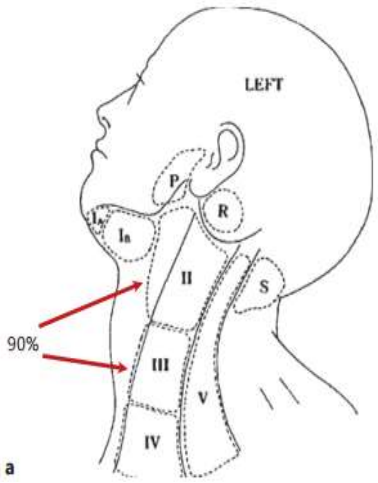
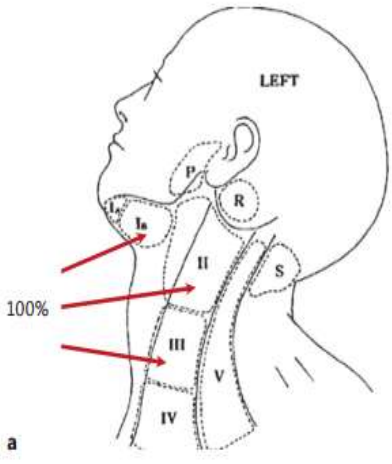
What levels of the neck?





Medina JE et al, Adv Otorhinolaryngol, 2016

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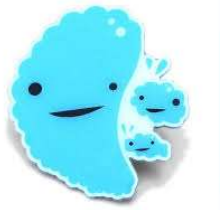
Conclusions



- Parotid tumors are diverse
- The anatomy is contained, but complex
- Diagnostics are important, use when meaningful
- Surgery involves shared decision making and sometimes intraoperative nuance
- Adjuvant therapy important, evolving slowly
- Histology drives therapy

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