The Approach to Salivary Gland Pathology
Michelle D. Williams, MD

Objectives:
1) to recognize the anatomic structures surrounding the major salivary glands and apply gross review for orientation and section submission
2) to delineate gross features in commonly encountered salivary tumors and tumors involving the parotid region.
3) To define how to approach, evaluate, and select tissue for submission in composite resections involving the parotid
4) To review staging of salivary gland tumors and updates in the 8th edition of AJCC.

Frequency of tumors encountered in the salivary glands:
Salivary glands are divided into major glands (parotid, submandibular and sublingual) and minor glands which are present throughout the upper aerodigestive tract including sinonasal region, oral cavity, and larynx. Primary salivary tumors account for ~5% of head and neck neoplasms.

- 80% of primary salivary tumors will arise in the parotid, where 80% are benign/20% malignant. ~25% of parotid masses may be non-neoplastic i.e. hemangiomas, branchial cleft cysts.
- 10-15% arising in the submandibular gland where 50% are benign and 50% are malignant.
- 5-10% are minor salivary gland where 80% are malignant.
- Remember - a metastasis to the parotid from cutaneous malignancies is the most common mass in the adult parotid (i.e. squamous carcinoma, melanoma, merkel cell carcinoma (a neuroendocrine tumor of skin origin), basal cell carcinoma and other rarer tumors such as sebaceous carcinoma).
- Thus a superficial parotidectomy specimen commonly accompanies the neck dissections for cutaneous tumors of the skin of the face, ear and scalp.
- Lymphomas may also involve intra/periparotid lymph nodes. Preoperative fine needle aspiration (FNA) evaluation can aid in this diagnosis and allow for triage of fresh material to flow cytometric analysis.
- Benign tumors are well circumscribed and range from solid and firm, common findings in pleomorphic adenoma, to cystic with dark thick secretions as seen in warthins tumor.
- Malignant tumors often have infiltrating borders, however may also be fairly defined and cystic as encountered in low-grade mucoepidermoid carcinoma. Thus cystic lesions in the parotid must be well sampled/to completely submitted for complete review and diagnosis.
- Similarly, some high-grade tumors arise as a transformation from a lower-grade tumor. Therefore when multiple nodules are encountered, or when there is variation within a mass, through sampling of both components and the interface is required.
<table>
<thead>
<tr>
<th>Benign (frequency)</th>
<th>Features</th>
<th>Other notes</th>
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<tbody>
<tr>
<td><strong>Solid</strong></td>
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| Pleomorphic adenoma (60%) | • Firm, grey, well demarcated  
• May be soft, friable on cutting | • Wide age range  
• Less circumscribed when arising from minor glands  
• May be multifocal in recurrent setting |
| Monomorphic adenoma | • Circumscribed  
• May mimic an enlarged lymph node when in the parotid tail | |
| Oncocytoma          | • Dark mahogany  
• May show central scar | |
| **Cystic**          |          |             |
| Warthins Tumor (7%) | Multiloculated  
May have variable solid component  
Thick 'motor-oil' secretions | May be bilateral  
More common males, 6-7th decades  
Associated with smoking |
| Lymphoepithelial cysts | Salivary epithelium expands into cystic spaces with lymphoid stroma/lymph node | Subset of patients with HIV |
| **Malignant**       |          |             |
| Mucoepidermoid carcinoma | Varied  
Low-grade cystic (mucin)  
High-grade invasive | Most common primary salivary malignancy in adults and children |
| Adenoid cystic carcinoma | Firm infiltrative mass  
May extend beyond visible lesion | *Common/extensive perineural invasion |
| Salivary duct carcinoma | Infiltrating, often extends extraglandular, often involves lymph nodes | Histologically perineural invasion is also common  
High-grade by definition |
| Carcinoma-expleomorphic adenoma | Look for hyalinize central nodule with tumor explosion around it.  
Sample well both components | The “carcinoma” component is often salivary duct carcinoma but may have varied morphology |
| “dedifferentiation” | Infiltrating tumor | High-grade tumor; histologically no longer shows the features of the original carcinoma |
Parotid orientation
A total parotid is composed of superficial and deep components.
Deep refers to the salivary tissue below the facial nerve. There is no true fascial plan between superficial and deep lobes.

Orienting the superficial parotid gland
1) identify the smooth superficial surface which corresponds to the subcutaneous region.
2) The deep aspect is composed of salivary lobules as there is no true compartmentalization of superficial versus deep parotid lobes (merely the plane formed by the facial nerve).

*Note: in general a parotid mass is frequently close at the deep surface secondary to preserving the facial nerve in all except aggressive tumors with nerve encasement/gross perineural invasion/fixation of tumor to nerve.*
3) The parotid is approximately triangular shaped with the posterior and inferior edges forming an “L” shape and are noticeably thicker. The 3rd side is anterior and slopes to a thin edge. Remember, “you have a smooth cheek”.
4) Along the thick posterior edge you may appreciated a slight indentation where the parotid was separated from it’s abutment at the ear canal.
   a. *Note: Thus parotid tumors may grow posteriorly into the ear canal requiring removal of the temporal bone to clear this margin.*

“Remember you want a smooth (thin) cheek”

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Composite resections for advanced parotid tumors may include: overlying skin, temporal bone (conical shaped), facial nerve (if grossly invaded by tumor), less commonly temporal mandibular joint, or zygoma (superior to parotid).
Note: periparotid and intraparotid lymph nodes are common and should be assessed in all submitted salivary gland specimens.

Submandibular
The submandibular gland is located in level Ib of a neck dissection and masses may represent primary or metastatic tumor. Although located adjacent to the mandible rarely are composite specimens from this site received.
Sublingual
Sublingual tumors are very rare and it may be unclear if the primary tumor is sublingual (below the tongue) or arising from the submandibular gland with is more lateral. Extension of sublingual tumors can extend to involve the floor of mouth, tongue, posteriorly the pharynx and rarely extend into the mandible.

Grossing
For all major salivary glands: assess specimen, size, location of mass with characteristics, (cystic, fluid content, necrosis, multifocal, etc) and denote closest margins. Relationship to periparotid soft tissue and if present skin, ear canal, and facial nerve should be described and sampled for staging. The background tissue should also be assessed for secondary masses and lymph nodes. Serially section tissue. General guidelines would be to entirely submit nodules up to 2 cm and then add additional sections for every additional cm. Sections should include interface of tumor to gland and importantly assessment and sampling of tumor to surrounding soft tissues or other included structures, which are required for staging (see below). Only removed lymph nodes separately if loosely attached on the surface of the gland, otherwise identify on serial sections and submit with surrounding parotid tissue. Submit all lymph nodes identified.

If bone is present, orient specimen and evaluate relationship to margins prior to removing bone from soft tissue. Then proceed with serially sectioning soft tissue. Temporal bone can be radially cut external to internal to look for bone and canal invasion. Assessment of mandible or zygoma should include closes sections of bone with tumor and margins.

Particularly for submandibular cancers, the primary nature of the nodule may not have been known leading to inadequate initial surgery. Therefore you may receive a resection of the tumor bed may occur with a neck dissection. Block in the prior surgical bed to assess for residual disease. (Know the history prior to grossing to avoid missing this critical component). The presence of residual disease and final margin status are important to determine the need for adjuvant radiation.

Correlative note:
The lacrimal gland is composed of ‘salivary like’ units and the same pathologic entities can occur particularly, pleomorphic adenoma, adenoid cystic carcinoma and lymphomas. For carcinomas in the lacrimal gland – look closely for thin orbital bone over the mass. If present document and sample as this is required for staging.

AJCC Staging for Major salivary glands
The 8th edition of AJCC will begin January 1st, 2018. The criteria for T classification is unchanged and requires knowing the size of the tumor, presence of extraglandular extension, and other structures involved. M categories also remains unchanged. The criteria for N classification has been updated to include the presence of extranodal extension which alters the N category. This revision applies to most of the staging chapters for head and neck tumors. Note that salivary tumors
that occur in the minor salivary glands are staged based on the tumor site (i.e. sinonasal, oral cavity, etc) and not chapter 8 “Major Salivary Glands”.

AJCC Cancer Staging Manual, Eighth Edition--Major Salivary Glands- Chapter 8

<table>
<thead>
<tr>
<th>T</th>
<th>T criteria</th>
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<tbody>
<tr>
<td>Tx</td>
<td>primary cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>no primary identified</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor ≤2cm greatest dimension without extraparenchymal extension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumors &gt;2 and ≤4 cm without extraparenchymal extension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumors &gt;4 cm or extraparenchymal extension PRESENT*</td>
</tr>
<tr>
<td>T4a</td>
<td>Moderately advanced -invasion of skin, mandible, ear canal +/—facial nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Very advanced – invades skull base +/—pterygoid plates +/—encases carotid artery</td>
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* gross extraparenchymal extension not just microscopic

### N Categorization (8th edition)

<table>
<thead>
<tr>
<th>Lymph node (LN) metastasis location, #</th>
<th>Extranodal extension ABSENT (ENE-)</th>
<th>Extranodal extension PRESENT (ENE+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LN size</td>
<td>≤3 cm, &gt;3-6 cm, &gt;6 cm</td>
<td>≤3 cm, &gt;3-6 cm, &gt;6 cm</td>
</tr>
</tbody>
</table>

|                  | pN1      | pN2a     | pN3a     | pN2a     | pN3b     | pN3b     |
| Contra-           |          |          |          |          |          |          |
| Single LN         | pN2b     | pN2b     | pN3b     | pN3b     | pN3b     | pN3b     |
| Multiple LNs      | pN2b     | pN2b     | pN3b     | pN3b     | pN3b     | pN3b     |

* includes errata clarifications

<table>
<thead>
<tr>
<th>M</th>
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</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No evidence of distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases present</td>
</tr>
</tbody>
</table>

References:
Cancer Protocol Templates (Updates in progress to align with 8th ed Staging)