Management of Salivary Gland Tumors

Ashok R. Shaha
Salivary Glands

Major:
Parotid
Submandibular
Sublingual

Minor salivary glands:
600 - 800 all over the upper aerodigestive tract

Majority on the palate
# Salivary Literature

## 1990 to 2011

<table>
<thead>
<tr>
<th>Subject</th>
<th># Papers</th>
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<tbody>
<tr>
<td>Salivary gland diseases</td>
<td>19,754</td>
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<tr>
<td>Salivary neoplasms</td>
<td>7,914</td>
</tr>
<tr>
<td>Needle biopsies</td>
<td>14,713</td>
</tr>
<tr>
<td>Salivary – needle biopsies</td>
<td>397</td>
</tr>
</tbody>
</table>
Salivary Gland Neoplasms

Management Issues

Evaluation (FNAB, CT, MRI)
Stage v. Grade
Imaging
Facial nerve
Adjunctive radiotherapy
Definitive radiotherapy
## Salivary Tumors

### Sites of Origin

<table>
<thead>
<tr>
<th>Sites</th>
<th># Pts</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>Parotid</td>
<td>1,965</td>
<td>70.0</td>
</tr>
<tr>
<td>Submandibular</td>
<td>235</td>
<td>8.4</td>
</tr>
<tr>
<td>Palate</td>
<td>228</td>
<td>8.0</td>
</tr>
<tr>
<td>Lips/Cheek</td>
<td>73</td>
<td>2.6</td>
</tr>
<tr>
<td>Antrum</td>
<td>72</td>
<td>2.6</td>
</tr>
<tr>
<td>Tongue</td>
<td>63</td>
<td>2.2</td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>60</td>
<td>2.1</td>
</tr>
<tr>
<td>Gingiva</td>
<td>34</td>
<td>1.2</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>22</td>
<td>0.8</td>
</tr>
<tr>
<td>Larynx</td>
<td>21</td>
<td>0.8</td>
</tr>
<tr>
<td>Tonsil</td>
<td>13</td>
<td>0.5</td>
</tr>
<tr>
<td>Ethmoid</td>
<td>9</td>
<td>0.3</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>9</td>
<td>0.3</td>
</tr>
<tr>
<td>Pharyngeal wall</td>
<td>3</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**TOTAL** | **2,807** | **100.0**
Salivary Gland Neoplasms*

PROPORTION MALIGNANT

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid</td>
<td>25%</td>
<td>75%</td>
</tr>
<tr>
<td>Submandibular</td>
<td>57%</td>
<td>43%</td>
</tr>
<tr>
<td>Minor</td>
<td>82%</td>
<td>18%</td>
</tr>
</tbody>
</table>

# Pts
- Parotid: n=1965
- Submandibular: n=235
- Minor: n=607

*MSKCC 1939-73 (Head Neck Surg 1986)
Salivary Tumors - Histologic Distribution

- **Parotid**
  - Mucoepidermoid
  - Adenoid cystic
  - Adenocarcinoma
  - Malignant mixed
  - Acinic cell
  - Squamous
  - Other

- **Sub-Max**
  - Mucoepidermoid
  - Adenoid cystic
  - Adenocarcinoma
  - Malignant mixed
  - Acinic cell
  - Squamous
  - Other

- **Minor**
  - Mucoepidermoid
  - Adenoid cystic
  - Adenocarcinoma
  - Malignant mixed
  - Acinic cell
  - Squamous
  - Other
Tumors of Minor Salivary Glands. Site Distribution

- Palate
- Tongue
- Cheek/Lip
- Antrum
- Nasal Cavity
- Gum
- Larynx
- FOM
- Tonsil
- Nasopharynx
- Ethmoid
- Pyriform
- Other
## Parotid Tumors

Pathology – Memorial Hospital, 1939-1973  
(N=1973)

<table>
<thead>
<tr>
<th>Category</th>
<th>Benign (n=1342)</th>
<th>Malignant (n=631)</th>
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</thead>
<tbody>
<tr>
<td>Pleomorphic adenoma</td>
<td>1133</td>
<td>Mucoepidermoid</td>
</tr>
<tr>
<td>Warthin’s</td>
<td>183</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>20</td>
<td>Acinic cell</td>
</tr>
<tr>
<td>Monomorphic</td>
<td>6</td>
<td>Adenoid cystic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca ex pleomorphic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Undiff</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Epidermoid</td>
</tr>
</tbody>
</table>

Spiro, 1986, *Head and Neck Surg*
Presentation

Lump

Pain

Facial weakness

Neck metastases

Parapharyngeal mass – deep lobe tumors
Salivary Gland Tumors

- Dumb bell tumor
- Deep lobe tumor
- Parapharyngeal space
- Extraparotid salivary tissue
Parotid Carcinoma: Obvious Signs

- Facial nerve palsy
- Cervical metastasis
- Skin involvement
Investigations

- Clinical evaluation
- Sialogram
- CT scan
- CT sialogram
- Needle biopsy
- Sialendoscopy
Parotid Tumors Indications for CT Scan

- Clinical uncertainty of findings
- Deep lobe presentation
- Extraglandular extension
- Cervical nodal involvement
- Facial palsy or fixed mass
- Recurrent Tumor
- Parapharyngeal Tumor
Role of Imaging

1. CT scanning is superior to MRI for osseous and skull base involvement but MRI is superior for intracranial extension of tumour.

2. MRI is superior to CT for assessment of primary disease and regional recurrence, as well as characterising extra parotid extension. Perineural invasion is best characterised with MRI.

3. Minor salivary gland tumours are best imaged with MRI, with irregular margins.
Role of Needle Biopsy in Salivary Tumors

- To suspect malignancy
- To distinguish from metastatic carcinoma
- To suspect lymphoma
- To distinguish salivary from non-salivary tumors
  - In poor risk pt - if suspect Warthin’s tumor
  - To confirm pre-op suspicion of malignancy in pts with facial palsy
- In bilateral tumors
- Minimum risks

Shaha AR. Am J Surg
Mass in Parotid Region

History/Head & Neck Exam

<table>
<thead>
<tr>
<th>FNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salivary</td>
</tr>
</tbody>
</table>

- **Benign**
  - Mixed tumor
  - Warthin’s

- **Malignant**
  - Primary
  - Ad-Cystic
  - Adeno Ca.

- **Metastatic**
  - Sq Ca.
  - Melanoma

- **Lipoma**
  - Seb. Cyst
  - Lymph Nodes

- **Benign**
  - Melanoma

- **Met Ca.**
  - Lymphoma
Salivary Gland Tumors

General Principles of Treatment

• Tumor factors
• Patient factors
• Physician factors
Parotid Tumor Surgical Principles

Every attempt should be made to remove all gross tumor. Radiation therapy does not compensate for inadequate surgery.
Parotid Tumor Surgical Principles

• The extent of parotidectomy depends more upon the extent of the tumor than the histology of the tumor.
• Superficial Parotidectomy
• Extra-Capsular Dissection
Salivary Gland Carcinoma Treatment Principles

The anatomic relationship of the tumor to the nerve dictates the extent of surgery, not the histologic classification of the neoplasm.
Malignant Tumors

Surgical treatment of the primary tumour

- Parotid Gland:

- Size and location determine extent of resection
- Most T1/T2 lesions lateral to the nerve are suitable for a superficial parotidectomy
- Larger and deep lobe tumours usually require a total conservative parotidectomy with preservation of the facial nerve
- Patients with high grade extensive disease (i.e. skin involvement or facial palsy) may require extended radical parotidectomy
- In one series, facial nerve dysfunction was apparent initially in 14% of patients and complete nerve sacrifice was required in about 30% of parotidectomies
Indications of Facial Nerve Resection

- Pre-op facial palsy
- Large tumor adherent to the nerve
- Direct tumor involvement into the nerve
- Recurrent malignant tumor
Resection of Facial Nerve

- Nerve graft
- Great auricular nerve
- Ansa Cervicalis
- Sural nerve
- Nerve transfer-hypoglossal transfer
- Tarsorrhaphy
- Facial reanimation - facial slings
Problem Areas in Salivary Tumors: Parotid Gland

- Deep lobe parotid tumors
- Accessory parotid tumors
- Regional node metastases
- Local recurrences
- Facial nerve?
DEEP PAROTID TUMORS

INCIDENCE

Lateral 1087

89%

Deep 130

PRESENTATION

"Dumbbell" Palate

7%

External

12%

1875 Parotid Tumors/157 Deep: 1939-1968
Prognostic Factors

- Clinical Stage (TNM)
- Histological grade
- Age
- Gender
- Anatomical site
- Experience of the surgeon
## Ca of the Parotid, MSKCC 1939-1968

Factors Influencing “Cure”

<table>
<thead>
<tr>
<th>Cervical node metastasis:</th>
<th>Pts Eligible</th>
<th>NED</th>
<th>%</th>
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<tbody>
<tr>
<td>Never documented</td>
<td>213</td>
<td>157</td>
<td>74</td>
</tr>
<tr>
<td>Present on admission</td>
<td>57</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Appeared later</td>
<td>18</td>
<td>3</td>
<td>17</td>
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</table>

<table>
<thead>
<tr>
<th>Local recurrence*:</th>
<th>Pts Eligible</th>
<th>NED</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>194</td>
<td>153</td>
<td>79</td>
</tr>
<tr>
<td>Yes</td>
<td>71</td>
<td>15</td>
<td>21</td>
</tr>
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</table>

*No data or palliation only in 23
Ca of the Parotid, MSKCC 1939-1968
Factors Influencing “Cure”

<table>
<thead>
<tr>
<th>Stage of primary:</th>
<th>Pts Eligible</th>
<th>NED</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage of primary:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>104</td>
<td>88</td>
<td>85</td>
</tr>
<tr>
<td>(92)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>83</td>
<td>57</td>
<td>67 (75)</td>
</tr>
<tr>
<td>III</td>
<td>99</td>
<td>19</td>
<td>19 (20)</td>
</tr>
<tr>
<td>Facial nerve status:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Function intact</td>
<td>212</td>
<td>139</td>
<td>66</td>
</tr>
<tr>
<td>Partial/complete palsy</td>
<td>43</td>
<td>6</td>
<td>14</td>
</tr>
<tr>
<td>Not recorded</td>
<td>31</td>
<td>18</td>
<td>58</td>
</tr>
<tr>
<td>Unrelated dysfunction</td>
<td>2</td>
<td>2</td>
<td>100</td>
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</table>

*Determinate cases only
### Major Salivary Ca 1939-1982

Node Metastasis (26%)

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th># Pts*</th>
<th>Nodes +</th>
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<tbody>
<tr>
<td>Anaplastic</td>
<td>6</td>
<td>5 (83%)</td>
</tr>
<tr>
<td>Squamous</td>
<td>26</td>
<td>15 (58%)</td>
</tr>
<tr>
<td>Mucoep grades 2,3</td>
<td>123</td>
<td>54 (44%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>46</td>
<td>18 (39%)</td>
</tr>
<tr>
<td>Malig mixed</td>
<td>62</td>
<td>12 (19%)</td>
</tr>
<tr>
<td>Adenoidcystic</td>
<td>50</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Acinic cell</td>
<td>56</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>Mucoep grade 1</td>
<td>68</td>
<td>2 (3%)</td>
</tr>
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*439 determinate pts
Cancer of the Major Salivary Glands: Nodal Status & 5 Yr Survival
Elective Neck Treatment in Salivary Gland Cancers

- High grade tumors
- T3 (?) & T4 tumors
- Tumors >3 cm
- Facial paralysis
- Age >54
- Extraparotid extension
- Perilymphatic invasion
Management of the Neck in Parotid Cancer

Elective neck dissection should be reserved for those histologic diagnoses having the highest risk of nodal metastases plus selected patients whose primary tumor resection may be facilitated by Lymphadenectomy.

Indications for Postoperative Irradiation-Parotid Cancer

- Aggressive, highly malignant tumors
- Invasion of adjacent tissues outside parotid capsule
- Regional lymph node metastases
- Deep lobe cancers
- Gross residual tumor following resection
- After resection recurrent tumor
- Tumor invasion of facial nerve
Salivary Ca. - Impact of Post-op R.T. on Survival

- Stage I, II
- Stage I, II w/ RT
- Stage III, IV
- Stage III, IV w/ RT

Time (years)

0 5 10

%
## Adjuvant Radiotherapy: Impact on Prognosis

<table>
<thead>
<tr>
<th>Survival</th>
<th>Surg Alone</th>
<th>Surg+RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I/II</td>
<td>96</td>
<td>82</td>
</tr>
<tr>
<td>Stage III/IV</td>
<td>10</td>
<td>51</td>
</tr>
<tr>
<td>Lymph node mets</td>
<td>19</td>
<td>49</td>
</tr>
<tr>
<td>High-grade tumors</td>
<td>28</td>
<td>57</td>
</tr>
<tr>
<td>Overall</td>
<td>55</td>
<td>69</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Local control</th>
<th>Surg Alone</th>
<th>Surg+RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I/II</td>
<td>79</td>
<td>91</td>
</tr>
<tr>
<td>Stage III/IV</td>
<td>17</td>
<td>51</td>
</tr>
<tr>
<td>Lymph node mets</td>
<td>40</td>
<td>69</td>
</tr>
<tr>
<td>High-grade tumors</td>
<td>44</td>
<td>63</td>
</tr>
<tr>
<td>Overall</td>
<td>66</td>
<td>73</td>
</tr>
</tbody>
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Salivary Carcinoma - Survival by SITE

- Parotid
- Sub-max
- Minor

Time (years)

%
Salivary Carcinoma - Survival by GRADE

- Low
- Intermediate
- High

$p < 0.0001$
Salivary Carcinoma - Survival by STAGE

Stage I

Stage II

Stage III

Time (years)

P < 0.0001
Prognostic Factors in Salivary Gland Cancer
Important Prognostic Factors in Salivary Tumors

- Age at diagnosis
- Pain at presentation
- T stage
- N stage
- Skin invasion
- Facial nerve dysfunction
- Perineural growth
- Positive surgical margins
- Soft tissue invasion
- Treatment type

Vander Poorten, 2002.
Radiation Therapy: Fast Neutron Radiation

• Available in few centers

• High LET radiation

• RBE especially high for adenoid cystic ca

• Uncertain benefit in completely resected vs conventional photon RT

• Definite advantage residual, recurrent unresectable disease
Fast Neutrons as Treatment for Salivary Gland Carcinoma*

- 53 pts (24 gross resid p.o.; 13 inop; 16 rec p.o.)
- Locoreg control in Rx field in 48 (>90%)
- ACC = 14 pts (42 mos med f/u – min 1 yr)
- Actuarial 5 yr survival 33% (42% No)
- 17% serious acute complic (Incl 1 death)

*Buchholz et al. Cancer 1992
Salivary Tumors Molecular Biology

- Warthin’s tumor showed low SPF+G$_2$M and low Ki67
- Pleomorphic adenoma showed low SPF+G$_2$M and high Ki67
- Malignant tumor showed high SPF+G$_2$M and high Ki67
- MIB 1 and PCNA immunohistochemistry may help distinguish benign/low grade/ACC
Salivary Diseases

- Outpatient parotidectomy
- Extracapsular Dissection
- Needle biopsy
- Sialoendoscopy
- Sialocholeolithotomy
- Molecular markers
- Radiation therapy
Salivary Gland Carcinoma Rx

Principles

- Adequate local excision of tumor based on extent of the primary
- Preserve the nerve, if possible
- Elective neck dissection reserved for selected patients
- Post-operative radiotherapy when indicated (appropriate fields)
- Most important prognostic factors: stage & grade
“In seventh nerve paralysis, joy, happiness, sorrow, shock, surprise, all the emotions have for their common expression the same blank stare.”

Sterling Burnell, 1927