



**PRINCESS MARGARET CANCER CENTRE  
CLINICAL PRACTICE GUIDELINES**

**HEAD AND NECK**

**SALIVARY GLAND CARCINOMAS**

## Head & Neck Site Group – Salivary Gland Carcinomas

<b>1.</b>	<b><u>INTRODUCTION</u></b>	<b>3</b>
<b>2.</b>	<b><u>PREVENTION</u></b>	<b>3</b>
<b>3.</b>	<b><u>SCREENING AND EARLY DETECTION</u></b>	<b>3</b>
<b>4.</b>	<b><u>DIAGNOSIS</u></b>	<b>3</b>
<b>5.</b>	<b><u>PATHOLOGY</u></b>	<b>3</b>
<b>6.</b>	<b><u>MANAGEMENT</u></b>	<b>5</b>
	<b>MANAGEMENT ALGORITHMS</b>	<b>5</b>
6.1	<b>SURGERY</b>	<b>7</b>
6.2	<b>CHEMOTHERAPY</b>	<b>8</b>
6.3	<b>RADIATION THERAPY</b>	<b>8</b>
6.4	<b>ONCOLOGY NURSING PRACTICE</b>	<b>9</b>
<b>7.</b>	<b><u>SUPPORTIVE CARE</u></b>	<b>10</b>
7.1	<b>PATIENT EDUCATION</b>	<b>10</b>
7.2	<b>DENTAL CARE</b>	<b>10</b>
7.3	<b>SYMPTOM MANAGEMENT</b>	<b>10</b>
7.4	<b>CLINICAL NUTRITION</b>	<b>10</b>
7.5	<b>PALLIATIVE CARE</b>	<b>10</b>
7.6	<b>SPEECH PATHOLOGY</b>	<b>10</b>
<b>8.</b>	<b><u>FOLLOW-UP CARE</u></b>	<b>10</b>

## 1. Introduction

- The epidemiology of salivary gland tumors (SGTs) is not well documented and does vary considerably with geographical location and ethnicity.
- About 70% of SGT's arise in the parotid gland, 10% submandibular gland, and the remainder in the minor salivary glands, with <1% arising in the sublingual glands<sup>1</sup>.
- About two-thirds of SGTs are benign, whilst around one-third are malignant.

## 2. Etiology and Prevention

- Etiology: several factors have been implicated in the development of SGT's<sup>1</sup>:
  - Link between EBV and lymphoepithelial carcinomas, in Asian and Inuit people.
  - Radiation exposure for both benign and malignant tumors (based on data from both survivors from atomic bomb exposures; and also exposure to therapeutic radiation).
  - Smoking and Warthin's tumors.
  - Industrial exposures (e.g. silica, nickel, rubber manufacturing).
- Avoidance or minimization of exposure to the above agents may have a role in reduction of SGT's.

## 3. Screening and Early Detection

- There is currently no role for screening and/or early detection in SGT's.
- An awareness of individuals at risk for development of SGT's (e.g. previous radiation exposure) should confer an index of suspicion and appropriate investigation for those individuals detected to have salivary gland abnormality.

## 4. Diagnosis / Initial Assessment

All patients should be assessed prior to treatment intervention, by the multidisciplinary Head & Neck Team.

### *History and Physical evaluation:*

- Record height, weight and ECOG performance status.
- History and Physical examination, including evaluation of:
  - Trismus.
  - CN involvement (CNVII, V-2, V-3).
  - Skin involvement.
- Record stage (current edition TNM):
  - Note that tumors in the minor salivary glands are staged according to anatomic site of origin (e.g. oral cavity, paranasal sinus etc).
- Specify location of primary by anatomic subsite:
  - Parotid.
  - Submandibular.
  - Sublingual.
  - minor salivary gland.

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<sup>1</sup> IARC "Pathology and Genetics of Head and Neck Tumors" 2005

- Documentation of specific nodal level (s) involved:
  - Size and extent of nodal involvement (e.g. fixed/mobile)
- Assess evidence of recent or remote radiation exposure.
- Record smoking and alcohol history
  - Smoking
    - Non-smoker / Current / ex-smoker
    - pack years
    - For current smokers smoking cessation is to be advised and a referral to cessation services made
  - alcohol history in standard drinks/week;
    - None / Light <10 drink/wk/ Mod 10-20 / Heavy >20

***Investigations (Baseline):***

- Panendoscopy if deemed necessary.
- Biopsy:
  - UHN pathology review including pathological subtype, histological grade.
  - Molecular diagnostic testing as indicated.
- Surgical specimen [see further detail, section 5, below]:
  - Establish resection margins in mm
- CT scan Head and Neck and/or MRI Head & Neck ( MR+ gadolinium preferred for skull base/major nerve involvement, or adenoid cystic carcinoma)<sup>2</sup>.
- PET scan in selected cases (high grade malignant tumors)<sup>3</sup>.
- CT thorax.
- Bloodwork: CBC, creatinine, electrolytes, liver function, glucose, coagulation studies (APTT, INR).
- Other staging investigations as clinically indicated (abdominal CT, bone scan etc).

**5. Pathology**

- Salivary gland tumors are a heterogeneous group of neoplasms; additionally, the presence of hybrid tumors, de-differentiation and potential for some benign tumors to progress to malignancy can present diagnostic difficulties.
- Fine needle aspiration biopsy (FNAB) can assist in identifying benign vs malignant tumors, and lymphoma vs epithelial neoplasms, however correct classification of malignant tumors may be difficult and false-negatives may occur due to sampling error.
- The most common salivary gland carcinomas are mucoepidermoid, adenoid cystic, salivary duct carcinoma, adenocarcinoma NOS, and acinic cell carcinoma, while the remaining comprise more than 20 different histological subtypes:
  - grading of salivary gland carcinomas into low-grade and high-grade (e.g. salivary duct and high-grade mucoepidermoid carcinoma) is an important prognostic factor.

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<sup>2</sup> Thoeny 2007

<sup>3</sup> Otsuka et al 2005

- molecular genetic changes characterize some tumors (e.g. EGFR and HER-2 over-expression in mucoepidermoid and salivary duct carcinomas), and the clinical significance of these changes are currently being investigated; hence reporting of these molecular changes is optional.
- review by a pathologist with experience in salivary gland neoplasms is recommended due to the diversity and complexity of these tumors.
- Pathology reporting should follow a standard format for salivary gland neoplasms, and include the following SYNOPSIS DATA, as per the College of American Pathologists 2011 cancer protocols (see [www.cap.org](http://www.cap.org) for full detail):
  - Tumor Site:
  - Laterality:
  - Histologic Type:
  - Tumor Size (Greatest dimension):
  - Histologic Grade:
  - Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)
  - Perineural Invasion:
  - Extraglandular Invasion:
  - Additional Pathologic Findings:
  - Margins:
    - Margin site(s):
    - Distance from closest margin:
  - Pathologic Staging (pTNM):
    - Number of regional lymph nodes examined:
    - Number of regional lymph nodes involved:
    - Extranodal extension:

## 6. Management

### *Overall Management Approach*

- These guidelines apply to patients with tumors of primary major salivary gland origin; tumors metastatic to salivary gland / lymph nodes and lymphomas, require separate consideration and are not included in this guideline.
- Management of minor salivary gland tumors follows the general principles of carcinomas of the relevant anatomic subsite:
  - e.g. for carcinoma of the oral cavity (most common minor salivary gland site), surgical excision is the treatment of choice, with adjuvant radiotherapy for indications as per squamous cell carcinoma of the oral cavity
  - refer to appropriate treatment guidelines for further detail
- Surgery is the primary curative modality for benign and malignant salivary tumors:
  - Maximal resection with preservation of important neural structures such as the facial nerve or hypoglossal nerve, is employed unless the nerve is

encased or invaded by tumor where preservation would result in leaving gross disease .

- Post-operative radiotherapy is indicated for high risk features.
- Chemotherapy is not generally indicated for salivary tumors.
- Rarely, radiotherapy is used as a sole modality where disease is unresectable or if surgery cannot be employed for medical or other reasons.
- All patients should be assessed for inclusion on available current trial protocols and, if eligible and appropriate, offered inclusion on trial.

## **POST- OPERATIVE RADIOTHERAPY TREATMENT: MALIGNANT TUMORS**

### ***INDICATIONS:***

- High-risk pathology:
  - Adenocarcinoma, NOS
  - Salivary duct carcinoma
  - High-grade mucoepidermoid carcinoma
  - Adenoid cystic carcinoma
  - Carcinoma ex-pleomorphic adenoma
  - Other high-grade tumors
- Microscopic positive resection margin(s).
- Positive lymph nodes.
- Nerve involvement (microscopic or major nerve).
- Deep lobe parotid tumor.
- T3/T4 category (relative indication).
- Close margins < 5mm, (relative indication).
- Submandibular gland primary (relative indication).

### ***Dose fractionation schedules***

- 66Gy in 33 fractions, over 6.5 weeks (5 fractions/wk) for
  - positive margin.
  - extranodal extension.
- 60Gy in 30 fractions, over 6 weeks (5 fractions/wk)
- Elective regions:
  - 60 Gy in 33 fractions (post-operative bed)
  - 54 or 56 Gy in 30-33 fractions (undissected regions considered to be at risk)

### ***Treatment considerations***

- Frequently, ipsilateral target volumes are appropriate.
- For involvement of a major (named) nerve, consider coverage of the course of the nerve to skull base.

**POST- OPERATIVE RADIOTHERAPY TREATMENT: PLEOMORPHIC ADENOMA**

***INDICATIONS:***

- Recurrence (relative indication):
  - Special consideration for multiple recurrence, or multifocal disease
- ).Microscopic residual disease that cannot be managed surgically (e.g. pleomorphic adenoma with intact CNVII).

***Dose fractionation schedules***

- 50 Gy/25 fractions<sup>4</sup> for microscopic residual.
- 60 Gy/30 fractions for suspected gross residual disease / multi-nodular disease.
- Target volumes:
  - primary tumor bed i.e. no elective neck irradiation.
  - Attention should be paid to inclusion of surgical scar, and areas of potential dermal spread.
- Consider bolus to scar for tumor spill or open biopsies.

**PRIMARY RADIOTHERAPY TREATMENT**

***INDICATIONS:***

- Unresectable tumor due to:
  - Location e.g. minor salivary gland tumors of pharynx.
  - Invasion of adjacent structures.

**Standard Radiation Treatment (off clinical trial)**

***Dose fractionation schedules***

- 70Gy in 35 fractions, over 6 weeks (DAHANCA; 6 fractions/wk)
  - Intensification to HARDWINS schedule may be considered

**Patients not suitable for radical treatment**

Refer to separate guideline: Palliative Management of Patients with H&N malignancy (**SECTION 12**)

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## 6.1 Surgery

- Primary site
  - Surgical resection is treatment of choice.
  - Superficial vs total parotidectomy, +/- mastoidectomy or temporal bone resection depending on extent of disease.
  - Perform node sampling of level IIA if pathology not clear on FNA (for diagnostic purposes).
  - Special considerations:
    - In general, preservation of facial nerve is recommended.
      - Indications for facial nerve sacrifice:
        - Pre-operative facial nerve paralysis.
        - Invasion of nerve by tumor or encasement of the nerve where nerve preservation would result in leaving gross residual disease.
    - If facial nerve sacrificed, consider:
      - Nerve grafting i.e.).
      - Static sling to oral commissure ).
      - Treat lagophthalmos with: gold weight, tarsorrhaphy, and/or lower eyelid static sling.
    - If loss of significant soft tissue bulk from resection, consider microvascular free tissue transfer to restore bulk and/or skin; this is also helpful in hastening recovery in preparation for adjuvant radiotherapy.
- Neck
  - N0:
    - If low grade malignancy or not prone to regional metastases: observe neck.
    - If high grade malignancy and/or advanced stage disease: perform selective neck dissection (levels II – V).
  - N+: perform selective neck dissection (levels II – V) or dictated by location of neck disease.

## 6.2 Chemotherapy

- Chemotherapy is generally not indicated for salivary gland tumors.
- Patients are encouraged to participate in clinical trials. Optimal chemotherapy or systemic therapy is not well defined.

## 6.3 Radiation Therapy

### Pre-Treatment Assessment

- Dental assessment.



- Nutritional assessment and consultation (pre-treatment, or during first weeks of treatment).
- Audiology.
  - Patients receiving platinum-type chemoradiation.
  - Patients receiving high-dose adjacent to auditory apparatus.
- Medical Oncology assessment (in patients potentially eligible for chemotherapy).
- Ophthalmology consult as indicated.
- Written consent to be obtained prior to simulation.
- Pre-radiotherapy review: patients are reviewed by the radiation oncologist in the week prior to commencing treatment for assessment and to review the treatment plan.

#### CONTOURING:

- DEFINITION / DELINEATION of TARGETS:
  - PRIMARY
    - GTVp (unresected, or gross residual disease)
    - GTVp\_preop
    - CTVp:
      - High-dose
      - Low-dose
  - NECK:
    - GTVn(s) (unresected, or gross residual disease)
    - CTVn
      - High-dose
      - Intermediate-dose
      - Low-dose (elective neck)

### **TREATMENT**

- CLINICAL CARE DURING RADIOTHERAPY:
  - Patients shall be reviewed by the RO at least weekly during RT.
  - ASSESSMENT:
    - Acute toxicities (RTOG criteria) documented in MOSAIQ.
    - Weight and nutritional review (weekly nutritional review for patients with G-tube, or as clinically indicated).
    - Bloodwork prior to each cycle of chemoradiation, or as clinically indicated.
  - Management of acute toxicities: refer to Nursing / Supportive Care guideline.

#### **6.4 Oncology Nursing Practice**

Refer to [Head and Neck Nursing Care](#)

## **7. Supportive Care**

### **7.1 Patient Education**

Refer to [general patient education practices](#)

### **7.2 Dental Care**

Refer to [dental care for Head and Neck Cancers](#)

### **7.3 Symptom Management**

Refer to [general symptom management care guidelines](#)

### **7.4 Clinical Nutrition**

Refer to [general clinical nutrition care guidelines](#)

### **7.5 Palliative Care**

Refer to [palliative management of Head and Neck Cancers](#)

### **7.6 Speech Pathology**

Refer to [speech language pathology for Head and Neck Cancers](#)

## **8. Follow-up Care**

- Setting: Assessment in multidisciplinary clinic.
- Schedule:
  - 2-6 weeks post radiotherapy.
  - Q3 months or more frequent for two years.
  - Q4 months or more frequent for third year.
  - Q6 months or more frequent for years 4-5.
  - Annually for years 6-10, if indicated (long-term follow-up for adenoid cystic carcinoma).
- Investigations and assessment (follow-up):
  - Fibre-optic nasoendoscopy if indicated (e.g. dysphagia).
  - Imaging:
    - CT head and neck at 10-12 weeks post-treatment.

- MRI Head and Neck if indicated.
- Pharyngeal function (speech/swallow), if indicated.
- Dental assessment where applicable.
- Audiometry or ophthalmology where applicable.

**ASSESSMENT and MANAGEMENT of PERSISTENT / RECURRENT DISEASE (SALVAGE)**

- Biopsy / histological confirmation.
- Record site of failure (local, regional, distant).
- Date of failure/recurrence.
- Determine site of recurrence relative to the initial target volume.
- RE-STAGE:
  - CT Head, neck, thorax.
  - Other imaging as clinically indicated.
- salvage options:
  - RE-IRRADIATION: refer to guideline for re-treatment of pts with H&N malignancy for re-irradiation:
    - RT volumes.
    - Fractionation.
    - Use of concurrent Rx.