



## Provincial Oral Cavity Cancer Treatment Guidelines

Approved at the Provincial Head and Neck Cancer Guideline Meeting  
May 8, 2015

*Clinical practice guidelines have been developed after multi-disciplinary consensus based on best available literature. As the name suggests, these are to be used as a guide only. These guidelines do not replace physician judgment which is based on multiple factors including, but not limited to, the clinical and social scenario, comorbidities, performance status, age, available resources and funding considerations. The Saskatchewan Cancer Agency disclaims all liability for the use of guidelines except as expressly permitted by the Agency. No portion of these guidelines may be copied, displayed for redistribution to third parties for commercial purposes or any non-permitted use without the prior written permission from the Agency.*

*Recommendations for drug treatment presented in the Cancer Agency guidelines for a cancer site may not reflect provincial cancer drug funding. Please refer to the current Saskatchewan Cancer Agency drug formulary at [www.saskcancer.ca](http://www.saskcancer.ca) for information on cancer drug listing and funding.*

*Benefits and risk of the proposed should be discussed with patient.*

*Participating in clinical trials is encouraged when available. Involvement of a multidisciplinary team is strongly recommended.*

### Content:

- [Background](#)
- [Staging](#)
  - [Primary](#)
  - [Regional](#)
  - [Distant Metastases](#)
  - [Stage Grouping](#)
- [Pre-Treatment Investigations](#)
- [Management](#)
- [Stage I & II Oral Cavity Cancer](#)
- [Treatment of Advanced Stage \(T3\)](#)
- [Treatment for Very Advanced Stage \(T4B\)](#)
- [Site specific Treatment](#)
  - [Anterior Tongue](#)
  - [Buccal Mucosa](#)
  - [Floor of Mouth](#)
  - [Retromolar Trigone](#)
  - [Hard Palate and Alveolar Ridge](#)
- [Follow Up](#)

## BACKGROUND

Cancer of the oral cavity comprises nearly 30 % of all malignant tumours of head and neck (1). Most common histology is squamous cell carcinoma representing about 90% of oral cavity cancer cases and management is discussed with reference to this particular histology. Minor salivary gland cancers, melanomas, lymphomas and sarcomas are less common.

The oral cavity consists of the following sub sites:

- Lips
- Anterior 2/3 of tongue
- Buccal mucosa
- Floor of mouth
- Alveolar ridge
- Retro molar trigon
- Hard palate

Life style, habits, demographics and genetics influence the geographic variation in incidence of disease. Tobacco smoking and alcohol abuse are principal factors for developing oral cavity cancer. Oral tobacco use, periodontal disease, radiation and immune deficiency have also been implicated (2).

Treatment goal is to eliminate cancer, preserve or restore form and function, minimize treatment complications and to prevent and /or early detect any recurrence and new primary cancer. Treatment modalities used to achieve these goals include surgery, radiation therapy, and chemotherapy and combined modality treatments. Treatment is selected considering tumour, patient, and treatment team factors such as anticipated functional and cosmetic outcome, extent and location of the tumour, patient's general condition, availability of particular expertise or facilities, and patient's preference.

Patients should be counseled to stop smoking before beginning radiation therapy.

Head and neck cancer treatment is complex and patients must be encouraged to participate in clinical trials.

All patient cases should be presented and discussed at a multidisciplinary tumour board.

## STAGING – AJCC 7th ED., 2010 (4)

### Primary Tumour (T)

TX:	Primary tumour cannot be assessed
T0:	No evidence of primary tumour
Tis:	Carcinoma in situ
T1:	Tumour 2 cm or less in greatest dimension
T2:	Tumour more than 2 cm but not more than 4 cm in greatest dimension
T3:	Tumour more than 4 cm in greatest dimension
T4a (lip):	Tumour invades adjacent structures (e.g. through cortical bone, inferior alveolar nerve, floor of mouth, skin of face like chin or nose)
T4a (oral cavity):	Tumour invades adjacent structures (e.g. through cortical bone mandible or maxilla into deep [extrinsic] muscle of tongue, maxillary sinus, skin of the face.

- Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify as T4)
- T4b: Very advanced local disease. Tumour invades masticator space, pterygoid plates, or skull base, and or encases internal carotid artery.

### Regional Lymph Nodes (N)

- NX: Regional lymph nodes cannot be assessed.
- N0: No regional lymph node metastasis.
- N1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
- N2: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension; or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension; or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
- N2a: Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension.
- N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
- N2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
- N3: Metastasis in a lymph node more than 6 cm in greatest dimension.

### Distant Metastasis (M)

- MX: Distant metastasis cannot be assessed.
- M0: No distant metastasis.
- M1: Distant metastasis.

### Stage Grouping

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage IVA	T4a	N0	M0
	T4a	N1	M0
	T1-T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	any N	M0
Stage IVC	Any T	Any N	M1

## PRE-TREATMENT INVESTIGATIONS

1. History and physical examination including complete head and neck exam: mirror and fibre-optic endoscopic examination.
2. EUA with endoscopy as indicated.
3. Biopsy of the primary site.
4. CT scan/MRI with contrast of the primary site and neck, as indicated.
5. Consider PET- CT scan as indicated
6. Dental /Prosthetic evaluation.
7. Chest imaging.
8. Pre anesthetic studies as needed
9. Nutrition, Speech and swallowing evaluation/therapy (3).

## MANAGEMENT

For early stage disease surgery is considered the preferred treatment because it requires a single intervention with less morbidity than radiation. RT is recommended for patients with contraindications to surgery .It can achieve similar rates of local control and survival however multiple treatments are delivered over a period of several weeks and the incidence of long term sequelae are high (e.g., Xerostomia, Osteoradionecrosis ).

### Stage I and II oral cavity cancer (T1N0, T2N0)

The treatment options are:

1. Resection of the primary tumour (preferred) ± ipsilateral (guided by tumour thickness) or bilateral (guided by tumour location) neck dissection.
  - a. Elective neck dissection is recommended especially for tumours with a depth of invasion ≥4mm (5, 6) Recent data presented at ASCO shows survival benefit with elective neck dissection for oral cavity early cancers (10).
  - b. After elective neck dissection if only one node is involved by tumour and without adverse risk features then radiation is optional.
  - c. Presence of extra capsular spread ± positive margin will require adjuvant chemo radiation (7, 8).
  - d. Positive margin: consider re-resection to achieve negative margins. If re-resection is not possible consider chemo radiation (7, 8).
  - e. Close margin <5mm, Perineural invasion or vascular embolism: Radiation may be considered using clinical judgment and after discussion in multidisciplinary tumour board (3).
2. Definitive radiation therapy.
  - a. High risk areas including primary tumour and involved nodes are treated with dose of 66-70Gy (2Gy /fraction); daily Monday to Friday in 6-7 weeks (3).
  - b. Low to intermediate risk disease; sites of subclinical spread are treated to 54-63Gy (1.6-1.8Gy /fraction); daily Monday to Friday over 6-7 weeks (3).

Acute toxicities of radiation therapy include skin erythema, dry or moist desquamation, mucositis, altered taste, dry mouth and dysphagia, nausea and fatigue. Late complications

include skin and soft tissue atrophy, swallowing dysfunction, dryness of mouth, Trismus, osteo radio necrosis and neck stiffness (2).

### **Treatment of Advanced Stage (T3, N0; T1-3, N1-3; T4a.Any N) oral cavity cancer:**

In locally advanced tumours, treatment is individualized. Inclusion of patients in multimodality clinical trials is recommended. In lieu of trials most patients require combined modality treatment. The treatment options are:

1. Surgery of the primary disease and clinically involved neck .Postoperative treatment is considered in following situations.
  - a. Presence of extra capsular spread  $\pm$  positive margin will require re-resection to achieve negative margins and adjuvant chemo radiation.
  - b. pT3, pT4, and/or N2 or N3or nodal disease in level IV or V, and / Perineural/vascular invasion and close margins will be considered for adjuvant Radiation (3).
  - c. For pT3 or T4, level IV or V nodal disease from, N2 or N3, Perineural invasion and/or vascular embolism; ChemoRadiation may be considered, the decision should be based on clinical judgment and in discussion with the multidisciplinary group.
2. Radical course of concurrent chemo radiation is considered if patient is not a candidate for surgery or refuses surgery.

If patient has none of the above adverse risk features RT is optional before proceeding with follow-up and surveillance (e, g T1N1).

In the instance of residual neck disease and primary site controlled after above treatment; neck dissection should be considered if feasible.

### **Treatment for very Advanced stage T4b, Any N or Unresectable disease or unfit for surgery:**

Patient participation in clinical trials is recommended. In lieu of a clinical trial, patient should undergo treatment dependent on their performance status:

PS 0-1 patients should be considered for concurrent chemo radiation, induction chemotherapy followed by RT or chemo radiation.

PS 2 patients should be considered for definitive RT / Chemo radiation.

PS 3 patients should be considered for Palliative RT/ palliative chemotherapy/ best supportive care (3).

## **SITE-SPECIFIC TREATMENT**

### **Anterior Tongue**

The incidence of tongue cancer exceeds all other sites in the oral cavity, accounting for 30% of oral cavity cancer patients. Surgery is recommended for small, anterior and well lateralized lesions. Elective neck dissection is recommended especially if depth of invasion is  $\geq 4$  mm

because of the high incidence of occult cervical nodal disease and the staging information provided by the neck dissection to determine the need and type of post-operative treatment (3). The role of contralateral neck dissection in patients with T1 disease and clinically negative neck is difficult to define.

### **Buccal Mucosa**

In south East Asia, buccal mucosa squamous cell cancer is the most common type of oral cavity cancer due to betel nut chewing. In North America and Western Europe it accounts for about 10% of the oral cavity cancers (9). Literature is limited, mostly from Asia and may relate to different disease biology and treatment approach.

Buccal mucosa cancers have high tendency to recur loco regionally.

### **Floor of Mouth**

Floor of mouth squamous cell cancers are aggressive neoplasms that can quickly metastasize to cervical nodes due to lack of any substantial anatomical barriers. Risk of occult nodal disease is high so elective neck dissection is recommended in most cases.

Preferred treatment approach is usually surgery due to the risk of radiation induced bone necrosis. Post-operative radiation is usually indicated for patients who have positive margins, nodal involvement and mandibular bone erosion.

### **Retromolar Trigone**

Retro molar trigone is the area just behind the back molars in the lower jaw. Squamous cell cancer of retro molar trigon is relatively uncommon. Patients present with pain that is exacerbated by chewing. Local recurrence is higher with these tumours as they invade into maxilla and mandible early in the course of disease.

### **Hard Palate and Alveolar Ridge**

Malignant neoplasms of hard palate and alveolar ridge comprise approximately 5 percent of oral cavity malignancies. Due to less common nature of disease and paucity of data, there is no evidence to support superiority of one treatment over the other. Palate is rich in salivary gland carcinomas and other rare malignancies.

### **FOLLOW UP**

There are no Randomized controlled trials which have compared predefined follow up strategies with no follow up. Thus there is no evidence that any specific program is better or more efficient at detecting recurrence or improving survival or quality of life. Oral cavity cancer behaves differently in each person and follow up plans should take into consideration the individual's situation.

These recommendations are to manage complications, detect recurrence/new primary cancers.

1 <sup>st</sup> Year	– every 1-3 month
2 <sup>nd</sup> Year	– every 2-6 months
3-5 Year	– every 4-8 months
>5 Year	– annually

- On each visit, clinical assessment should include a symptom review, weight measurement and a careful physical examination of the region (mirror and fiberoptic examination).
- Post treatment baseline imaging of primary and neck within 6 months of treatment. Further imaging is considered to investigate signs and symptoms as indicated and not routinely recommended
- Chest imaging.
- Thyroid function tests in patients who had neck irradiation.
- Speech, hearing and swallowing evaluation and rehabilitation as needed.
- Smoking cessation and alcohol counselling.
- Dental evaluation at regular intervals to ensure compliance with a hygienic routine.
- Physiotherapy is indicated for all patients undergoing major head and neck resection during first 3-6 months post-surgery (3).

### References:

1. Rapidis A. Multimodality management of oral cavity and maxillary sinus cancers. In: Bernier J, editor. Head and neck cancer: Springer Science + Business Media, LLC: 2011. p. 363.
2. Uptodate.com/contents/ treatment of oral cavity cancers.
3. National comprehensive cancer Network. Head and Neck cancers. Version 2.2014. Available at [http://www.nccn.org/professional/physician\\_gls/pdf/head-and-neck.pdf](http://www.nccn.org/professional/physician_gls/pdf/head-and-neck.pdf).
4. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL., Trotti A editors. AJCC Cancer staging Manual. 7<sup>th</sup> ed. New York, NY: Springer: 2010.
5. Spiro RH, Huvos AG, Wong GY, Spiro JD, Geneco CA, Strong EW, Predictive value of tumour thickness in squamous carcinoma confined to the tongue and floor of mouth. Am J Surg 1986 Oct; 152 (4):345-350.
6. Yuen AP, FHKAM, Lam KY, HO CM, Chow T L, Prognostic factors of clinical stage I and II oral tongue carcinoma-A comparative study of stage, thickness, shape, growth, pattern, invasive front malignancy grading, Martinez-gimeno score, and pathological features. Head and Neck June 2002, 513-520.
7. Bernier J, D'Amico C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, et al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 2004 May 6; 350(19):1945-1952.
8. Cooper J S, Pajak T, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, et al. Postoperative concurrent radiotherapy and chemotherapy for high risk squamous cell carcinoma of the head and neck. N Engl J Med 2004 May 6; 350 (19):1937-1944.
9. Parkin DM, Pisani P, Ferlay J. Estimates of the world wide incidence of eighteen major cancers in 1985. Int J of cancer 1993 Jun 19;54(4):594-606.
10. Anil D'CRUZ presentation at ASCO plenary session May 31<sup>st</sup>, 2015. Elective neck dissection improved survival in early oral cancers.

**Chairperson:** Dr. Shazia Mahmood

**Presenters:** Dr. Shazia Mahmood, Dr. Evgeny Sadikov, Dr. Debra Korol, Dr. Ali El-Gayed, Dr. Derek Suderman, Dr. Rick Jaggi, Dr. Adnan Zaidi, Dr. Bryan Brunet, Dr. Wojciech Dolata, Dr. Kamal Haider

**Attendees:** Dr. Aisha Ahmed, Joe Andreas, Dr. Monica Behl, Dr. Janine Benoit, Dr. Bryan Brunet, Jennifer Cameron-Turley, Lorna Campbell, Dr. Peter Chang, Dr. Tineyi Chikukwa, Dena Colleaux, Dr. Wojciech Dolata, Dr. Ali El-Gayed, Lacey Fondrick, Christel Foord, Bertha Foote, Pauline Fox, Josh Giambattista, Dr. Kamal Haider, Dr. Rick Jaggi, Dr. Miroslav Jancewicz, Dr. Debra Korol, Lana Kruger, Dr. Shazia Mahmood, Courtney McKay, Dr. Mohamed Mohamed, Dr. William Moyer, Lori Muz, Dr. Mark Ogrady, Dr. Lenny Pillay, Dr. Florence Plaza Arnold, Dr. Evgeny Sadikov, Dr. Muhammad Salim, Judy Shaw, James Smetaniuk, Dr. Derek Suderman, Dr. Niranjana Venugopal, Brenda Wilde, Michelle Zahayko, Dr. Adnan Zaidi, Dr. Bill Ziegler