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Oral Cavity Cancer

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Oral cavity cancer is the sixth leading cause of cancer worldwide. In the United States alone, there are over 21,500 oral carcinomas diagnosed each year, and 6,000 Americans die of oral cancer each year.[1] The incidence of oral carcinoma varies throughout the world, with estimates exceeding 40 in 100,000 in parts of France, Southeast Asia, Hungary and Singapore.[2] Thus oral cancer is a major cause of morbidity worldwide. Ninety percent of oral malignancies are squamous cell carcinomas and therefore are the principal topic of this chapter. However, the treatment of some other oral malignancies, like sarcoma and minor salivary gland carcinoma, is also primarily surgical excision, and the surgical principles are applicable to the treatment of these other tumors as well.

The etiology of oral cancer is exposure to carcinogens in tobacco and the tumor-promoting effects of alcohol. Ninety percent of the risk of oral cancer in the United States is directly attributable to smoking.[3] Tobacco smoke and alcohol are synergistic in their carcinogenic effects in the oral cavity. The relative risk of oral cancer for heavy smokers is 7 times that of nonsmokers. The risk for heavy drinkers is 6 times that of nondrinkers. The risk for patients abusing both alcohol and tobacco is 38 times that of those who abstain from both.[4] Chewing tobacco and betel quid also increase the risk of oral cancer.[5] Chronic carcinogen exposure creates a field effect and the entire mucosa of the upper aerodigestive tract is at risk for malignancy in smokers and drinkers.[6] After successful treatment of oral cancer, the risk of a second primary cancer is 3.7 percent per year and increases to 24 percent at ten years.[7] Cessation of alcohol and tobacco exposure reduces the risk of second aerodigestive carcinoma.

Chronic carcinogen exposure causes mucosal cells to acquire genetic abnormalities. When these genetics abnormalities result in the activation of proto-oncogenes and the inactivation of tumor-suppressive genes, the cells may be afforded a growth advantage. Dysregulated proliferation due to aberrant cell cycle control leads to clonal populations of premalignant, genetically abnormal mucosal cells. These populations of cells have a high tendency to accumulate additional genetic abnormalities due to genomic instability. Genomic instability is the result of rapid cell cycling with decreased genomic surveillance, decreased capacity to repair genetic defects and ineffective signalling of apoptosis or programmed cell death. In these cell populations the rate of accumulation of acquired genetic abnormalities increases logarithmically with time.[8]

Eventually these abnormal cells acquire the malignant phenotype in which they lose normal differentiation, invade the basement membrane, become locally destructive, and metastasize regionally or distantly. These cells evade immune surveillance of the body, produce angiogenic factors allowing ingrowth of blood vessels, and become clinical carcinomas.

ANATOMY

The critical functions normally accomplished by oral tissues include articulation of speech, facial expression and cosmesis, respiration, mastication, deglutition, and taste. Ablative surgery for oral cancer removes the malignant tumor en bloc with a margin of normal tissue, and the integrity of functionally important structures is not violated unnecessarily.

The oral cavity is bounded anteriorly by the skin and the vermilion border of the upper and lower lips. The oral cavity extends posteriorly to the circumvallate papillae of the tongue, the junction of the hard and soft palates, and the anterior faucial arch. The tonsil, soft palate and posterior one-third of the tongue are oropharyngeal structures and are not considered in our discussion of the oral cavity. Laterally the oral cavity is bounded by the buccal mucosa.

The oral cavity is divided into the following subsites: the lip, anterior two-thirds of the tongue, floor of mouth, gingiva, retromolar trigone, buccal mucosa, and hard palate (Figure 5–1). Figure 5–2 demonstrates the distribution of oral tumors by subsite. Tumors of different subsites demonstrate distinct clinical behavior.

The lip is a common site of skin cancer. The layers of the lip, from external to internal, include the epidermis, dermis, subcutaneous tissue, the orbicularis oris and attached musculature, the oral submucosa and the oral mucosa. The oral submucosa contains minor salivary glands, copious lymphatic vessels, blood vessels and sensory nerves. The lip is supplied by the labial arteries and veins, which are branches of the facial vessels. The generous lymphatics of the lower lip cross and drain bilaterally to level I nodes of the submental and submandibular triangles. Pre- or post-facial nodes lie anterior and posterior to the facial vessels in the superior aspect of the submandibular triangle and are potential sites of metastasis of lip cancers. Lymphatic channels of the upper lip respect the midline and drain to submandibular, periparotid, or preauricular nodes. The upper lip possesses two peaks forming a "cupid's bow" where the filtrum ascends to the columella of the nasal septum.

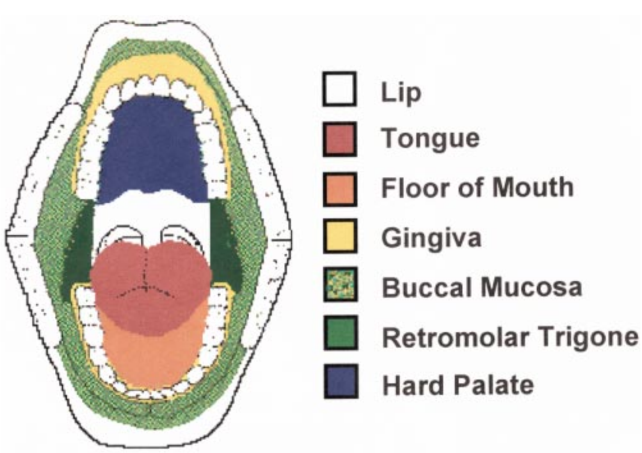


Figure 5–1. Diagram of the oral cavity and subsites.

The orbicularis oris muscle receives motor innervation from the marginal and buccal branches of the facial nerve and performs a sphincteral function to maintain oral competence and to facilitate articulation of speech. This muscle has many attachments from other muscles of facial expression that elevate and depress the lips. Of clinical importance is the innervation of the depressor anguli oris muscle by the marginal mandibular branch of the facial nerve.

Sensation of the lower lip is provided by the mental nerve, the terminal segment of the alveolar branch of the mandibular division of the trigeminal nerve. The nerve exits the mental foramen of the mandible near the root of the canine tooth. Paresthesia of the chin suggests extensive mandible invasion and inferior alveolar nerve involvement by oral carcinoma.

The anterior two-thirds of the tongue is called the oral or mobile tongue and is bounded posteriorly by the V-shaped line of the circumvallate papillae. Posterior to this line is the base of tongue, which is part of the oropharynx. The oral tongue has ventral and dorsal surfaces. The mucosa of the tongue is simple stratified squamous epithelium with interspersed papillae or taste buds of four morphologies: filiform, foliate, fungiform, and circumvallate.

The tongue is comprised of intrinsic and extrinsic muscles. The intrinsic muscles are arranged in vertical and horizontal fascicles that allow the mobile tongue to change shape and consistency. There are three pairs of extrinsic muscles that provide mobility of the tongue: genioglossus, hyoglossus, and styloglossus. Protrusion of the tongue is primarily accomplished by the action of the genioglossus muscle which originates from the mandibular tubercles on the lingual surface of the arch of the mandible, and inserts diffusely into the substance of the intrinsic musculature on each side of the tongue. The motor supply to the intrinsic and extrinsic tongue muscles is the hypoglossal nerve (CN XII), which exits the skull through its own hypoglossal canal and courses laterally and anteriorly between the external and internal carotid arteries, immediately inferior to the occipital artery.

The sensation of the tongue is supplied by the lingual nerve, a branch of the mandibular division of the

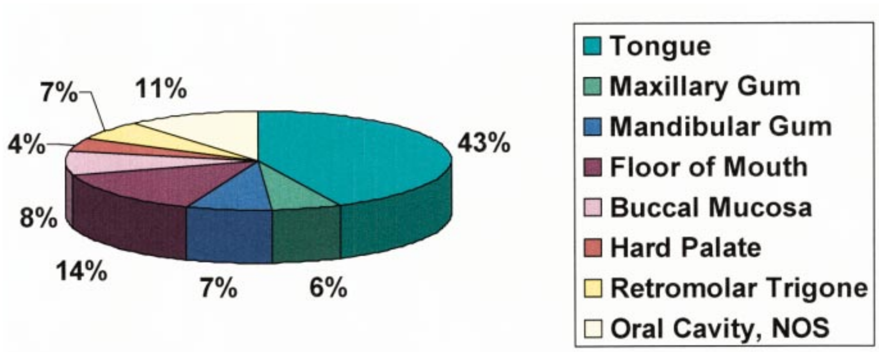


Figure 5–2. Distribution of oral cancers by subsite. A selected series of cases presenting to the head and neck service of Memorial Sloan-Kettering Cancer Center, New York.

trigeminal nerve (CN V_3). The lingual nerve also transports parasympathetic fibers from the chorda tympani branch of the facial nerve to the submandibular ganglion. The blood supply to the tongue is derived from the paired lingual arteries.

The lymphatic drainage of the tongue begins in a rich submucosal plexus, which may drain bilaterally when lesions approach the midline, the tip, or especially the base of the tongue. Tumors of the lateral mid-tongue drain predictably to the ipsilateral lymph nodes. The first echelon nodes for lesions of the tip include the submental nodes. The lateral and ventral tongue lesions metastasize to submandibular or jugulodigastric nodes while the base of tongue drains to the jugulodigastric and deep jugular nodes. Lesions of the anterior tongue may metastasize directly to the low jugular lymph nodes (level IV) of the neck.

The buccal mucosa lines the lateral oral cavity and blends with the gingiva superiorly and inferiorly and with the retromolar trigone posteriorly. The mucosa is pierced by the Stensen's duct of the parotid gland at the papilla adjacent to the second maxillary molar tooth.

The gingiva consists of thick keratinized mucosa with deep rete pegs and submucosal adherence to the periosteum. The mucosa covers the alveolar processes of the mandible and the maxilla.

The mandible possesses lingual and buccal cortices which envelop cancellous bone, dental sockets, and the mandibular canal transmitting the mandibular vessels and nerves (branch of CN V_3). The mandibular surface is innervated by branches of the lingual and mental nerves while the maxillary surface is innervated by alveolar branches of the second and third divisions of the 5th cranial (trigeminal) nerve.

The retromolar trigone is that portion of adherent keratinized mucosa covering the ascending ramus of the mandible from the third mandibular molar to the maxillary tubercle. It represents the area between the buccal mucosa laterally and the anterior tonsillar pillar medially and posteriorly. Tumors of this small region spread readily to the adjacent mandibular bone, alveolar foramen, masticator space, oropharyngeal tonsil, floor of mouth and base of tongue.

The hard palate lies within the horseshoe shape of the maxillary alveolar process. Keratinized adherent mucosa covers the palatal bone, which is divided into the primary and secondary bony palate. The primary palate consists of the palatal processes of the maxillary bones and represents the premaxilla anterior to the incisive foramen. The secondary palate is made up of the horizontal processes of the L-shaped palatine bones. On the posterior hard palate, near the maxillary second or third molar, are found the greater and lesser palatine foramina which transmit their respective vessels and nerves which are the terminal branches of the sphenopalatine vessels (branches of the internal maxillary artery) and nerves (branches of V_2). Anteriorly, the midline incisive foramen near the incisors transmits the terminal branches of the nasociliary nerve and vessels to supply the primary palate region. Lymphatic drainage of the palate includes the deep jugular chain as well as the retropharyngeal nodes. Anterior lesions may metastasize to pre-vascular facial lymph nodes of the submandibular region.

The floor of the mouth is a soft thin layer of U-shaped mucosa overlying the insertion of the mylohyoid muscle laterally, the hyoglossus muscle medially, and the insertion of the genioglossus muscle anteriorly. It covers the sublingual salivary glands, submandibular (Wharton's) duct, and the lingual nerve. The blood supply is from the lingual vessels. Its lymphatic plexus is copious and drains bilaterally in the midline. The lymphatic drainage patterns include the submental and bilateral submandibular nodes, as well as the ipsilateral jugulodigastric nodes posteriorly.

DIAGNOSIS

The diagnostic evaluation of a patient with oral carcinoma consists of the history and the physical examination, histopathologic tissue diagnosis, and imaging—when indicated.

The clinical history begins with the present illness and includes the duration and location of symptoms such as non-healing ulcer, mass in the oral cavity or neck, pain, bleeding, and any symptoms of cranial nerve deficits. A thorough exploration of the patient's past medical and surgical history, and the review of systems yield operative risk data. A thorough history of etiologic risk factors for squamous carcinomas not only reflects the patient's relative risk of malignancy but also suggests factors that affect the patient's overall health, fitness for surgery and emotional state. Current and distant abuse of tobacco and alcohol are critical factors and may be underreported by the patient. In many parts of the world the use of oral chews ("pan," betel nuts, etc.) is the chief etiologic factor.[9] These may contain tobacco, slaked lime and other irritants and may be retained in the oral cavity nearly constantly. An occupational exposure to heavy metals such as nickel,[10] and previous radiation exposure to head and neck are other important risk factors of head and neck cancer that are elicited in the history.

The social history impacts strongly on the patient's ability to comply with and tolerate treatment and rehabilitation programs, and these issues are resolved during the treatment planning phase. The family history reflects any familial tendencies toward malignant disease and completes the historical data.

A complete examination of the head and neck is performed to assess the precise location and extent of the primary tumor, identify regionally metastatic disease and to rule out multiple primary malignancies. Grossly, the earliest cancers may present as nonulcerous white or red patches. More advanced oral squamous cell carcinomas (SCC) present as mucosal lesions, although occasionally an SCC may present as predominantly submucosal with little or no mucosal involvement. Firm submucosal lesions are often minor salivary gland neoplasms. SCC may be ulcerative and invasive, fungating and exophytic or both (Figure 5–3). They may arise within premalignant lesions such as leukoplakia or erythroplakia. The following characteristics of the lesion should be documented: appearance and character, location, size in centimeters, texture to palpation, mobility, proximity to surrounding structures—especially bone, and the estimated palpable thickness (superficial vs. deeply infiltrating).

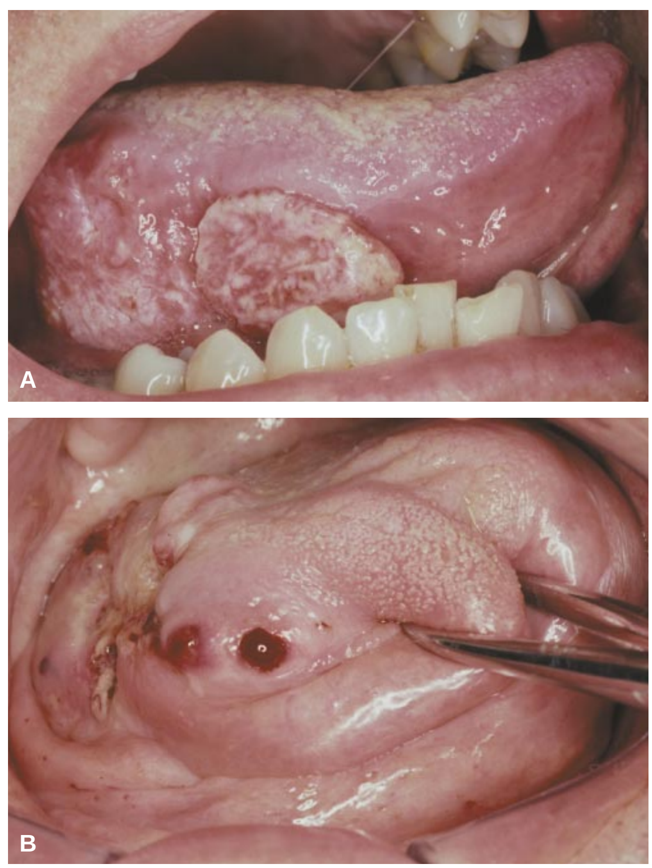


Figure 5–3. *A*, An exophytic lesion involving the right lateral border of the tongue. *B*, An endophytic lesion of the right lateral border of the tongue.

Trismus suggests ominous pterygoid and masticator space involvement. The condition of the dentition should be noted as tumors may, as the first sign, displace or loosen teeth. The distance from the tumor to the mandible and the mobility of the lesion in relation to the mandible are critical elements in determining the management of perimandibular cancers. A complete examination of the cranial nerves is performed, emphasizing sensation over the chin for mandibular nerve deficit, tongue mobility for hypoglossal nerve deficit, facial nerve function, palatal elevation and gag reflex, and function of the accessory nerve. A mirror or a flexible or rigid telescope is needed to document vocal cord mobility and to ensure that no lesions exist in the oropharynx, nasopharynx, endolarynx, and visible hypopharynx. Small lesions of the hypopharynx may only be visible by direct examination under anesthesia with the rigid laryngoscopes.

The neck should be thoroughly palpated for metastatic disease in the nodal groups at risk, and for other abnormalities of the great vessels and the thyroid gland which might impact treatment. Masses of the neck should be measured in centimeters, characterized for site (level), mobility, consistency, skin involvement, and proximity to vital structures. Normal neck structures commonly mistaken for metastatic masses include: the transverse process of C2 in the jugulodigastric region of thin patients, the scalene muscles, a tortuous carotid artery, a carotid aneurysm, a prominent carotid bulb, a cervical rib, and ptotic submandibular glands.

A complete general physical examination should be performed emphasizing the cardiovascular and pulmonary systems, which are commonly abnormal in this oral cancer population. The systemic effects of malnutrition or excessive alcohol intake should also be noted.

The history and physical examination with or without adjunctive imaging and histopathologic tissue diagnosis are sufficient to plan and execute surgical treatment for many patients with oral cancer. However, some patients will benefit from examination under anesthesia including direct palpation with or without biopsy, laryngoscopy, esophagoscopy, and bronchoscopy. The indications for examination under anesthesia include an inadequate assessment of the extent of the disease by history and physical examination and imaging, or the presence of symptoms referable to the trachea, larynx, hypopharynx and esophagus that need endoscopic assessment. It is not cost-effective screening to perform panendoscopy on all patients with head and neck cancer.[11–13] Symptoms suggesting lesions of the trachea, larynx, hypopharynx, or esophagus include: dysphagia, odynophagia, pain, hoarseness, hemoptysis or stridor. A careful history and meticulous head and neck exam is necessary to identify these lesions.

Evaluation of the deep extent of oral cancer often requires the use of imaging modalities. Imaging studies, however, will not adequately identify the superficial mucosal extent of disease, which must be established by visualization, palpation and biopsy. Plain radiographs such as panorex, dental films or a submental occlusal film may demonstrate gross bone involvement but do not show early cortical invasion.

Computed tomography (CT) is the most common modality employed to assess the extent of oral cancers (Figure 5–4). Advantages of CT include good soft-tissue discrimination and vessel identification and excellent definition of bone soft-tissue interfaces. CT scans are readily available and affordable. Cortical destruction and tumor in the alveolar canal and the bone marrow can be seen on CT. Special coronal reconstructions of dedicated mandible CT

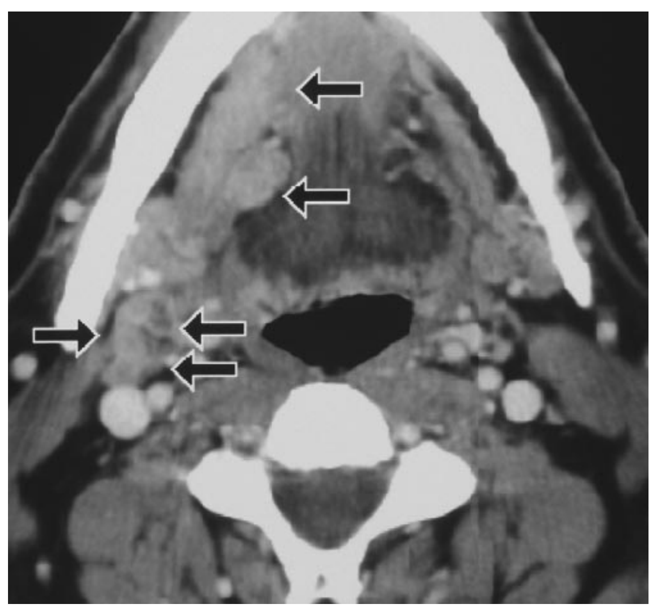


Figure 5–4. CT scan demonstrating an invasive carcinoma in the right half of the tongue with involvement of lymph nodes at level II.

scans (Dentascan) is particularly helpful in imaging the mandible. CT scans of the oral cavity should be combined with neck CT to assess for suspicious subclinical metastatic nodes. Axial and coronal views with bone and soft-tissue windows with contrast from the orbital floor to the base of the tongue as well as axial views of the neck are obtained. Disadvantages of CT scanning include radiation exposure, possible contrast dye sensitivity, dental amalgam interference, difficult positioning for coronal views, and no direct sagittal views.

Compared to CT scanning, magnetic resonance imaging (MRI) offers enhanced soft-tissue discrimination, excellent skull base and CNS assessment, sagittal views, and no radiation exposure (Figure 5–5). Disadvantages are that the examination takes longer, is more expensive, is poorly tolerated by some, and the black signal of bone makes cortical bone abnormalities difficult to see. An experimental imaging modality with promise is positron emission tomographic scanning. Positron emission tomography (PET) is a nuclear medicine study that demonstrates the difference in metabolism of radiolabeled glucose molecules between normal and malignant tissues. The clinical usage of this modality is currently not well-defined, but will likely aid in the diagnosis of recurrent and metastatic lesions.[14]

The appropriate metastatic evaluation of the patient with oral carcinoma is chest radiographs and serum liver function tests. The routine use of CT scanning of the chest, abdomen, and brain, or radionuclide bone scanning to evaluate oral cancer patients is not cost-effective and should be discouraged.

When all of the data from the history, physical examination, biopsy, imaging, and metastatic work-up are available, the tumor is staged according to the AJCC staging system (Table 5–1).

TREATMENT GOALS AND ALTERNATIVES; FACTORS AFFECTING CHOICE OF TREATMENT

The surgeon's goal is complete removal of all cells of the primary tumor and any cancer cells in regional lymph nodes, while preserving the integrity of uninvolved structures. Similarly, the radiotherapist endeavors to damage the abnormal cells irreparably while sparing the normal tissue. Either modality is effective in controlling early oral carcinomas, but the use of both modalities in combination is necessary to control locally advanced disease. The role of chemotherapy alone in localized disease is palliative. Currently, distantly metastatic disease is incurable but can often be effectively palliated with chemotherapy and radiation.

Treatment choices are best made after considering tumor factors, patient factors and resources factors. Tumor factors include subsite, T stage, N stage, histologic characteristics, endophytic vs. exophytic morphology, and proximity to bone. Patient factors include the patient's age, co-morbidities, convenience, rehabilitation potential, and the patient's wishes. Resource factors include the availability of a well-trained surgeon or radiotherapist with a dedicated interest in head and neck cancer, availability of advanced hardware for the planning and delivery of radiation, and the availability of funds to pay for the treatment.

The mainstay of treatment of early oral cancer is surgery. External beam radiation therapy alone can be effective for some early superficial lesions of the tongue or floor of mouth but sequelae of xerostomia

Figure 5–5. A T2N0 squamous carcinoma of the left lateral border of the tongue seen infiltrating the superficial musculature of the tongue on an MRI scan.

and mandible irradiation, and long duration and expense of treatment make radiation a poor choice. Also, bone involvement by oral cancer limits the effectiveness of external beam radiation, so lesions of the gingiva and hard palate are best treated with surgery due to the close proximity of bone and the high incidence of bone invasion. Advantages of surgery for T1 and T2 oral cancer compared to radiation include decreased cost, decreased time of treatment, the generation of a surgical specimen for examination of potential prognostic features and, in some instances, an opportunity to sample the regional clinically negative nodes for occult disease. Advantages of radiation therapy for early lesions are preservation of tissue and no need for general anesthetic.

Table 5–I. UICC/AJCC STAGING SYSTEM FOR ORAL CANCER

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
T4	Tumor (lip) invades adjacent structures (eg, through cortical bone, tongue, skin of neck) Tumor (oral cavity) invades adjacent structures (eg, through cortical bone, into deep [extrinsic] muscle of tongue, maxillary sinus, skin)

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 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	Presence of 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 IV	T4	N0	MO
	T4	N1	M0
	Any T	N2	M0
	Any T	N3	M0
	Any T	Any N	M1

Advanced T3 and T4 lesions are best treated with a combination of surgery and radiation therapy. Improvement in locoregional control of advanced oral cancer is attributable to the addition of postoperative radiation.[15,16]

Brachytherapy can sometimes be employed for oral cancers (especially tumors of the tongue) utilizing after-loading catheters.[17] However, resection of small lesions is usually simpler and less morbid, and surgery followed by radiation is more appropriate for treating the large volume T3 or T4 lesion. Close proximity of the tumor to the mandible, complex surface anatomy, and uncertainty of the tumor margins are tumor factors that also limit use of brachytherapy for oral cavity cancers. Tumors of the oral cavity are poorly responsive to traditional organ sparing approaches combining either sequential or concomitant chemotherapy and radiation therapy. The control rates for oral cavity cancers using these regimens are the lowest of all head and neck sites.[18] Chemotherapy alone for oral cavity cancers is palliative. While some complete clinical responses can be obtained, they are not durable. Preoperative chemotherapy for oral cancers is usually not helpful because adequate resection margins do not shrink with the clinical response of the tumor. Studies show that microscopic tumor foci exist where previous gross tumor has been shrunken by chemotherapy treatment. It is therefore not ordinarily possible to reduce the extent of surgical resection and the morbidity of oral cancer surgery by tumor shrinkage with preoperative chemotherapy.[19]

It is important that all head and neck cancer patients and their cases be discussed in a multimodality treatment conference setting to insure appropriate management.

SURGICAL TREATMENT

Most patients with oral cancer are in their fifth to seventh decades of life with a history of tobacco and alcohol abuse, and therefore warrant preoperative clearance by the patient's medical doctor, a cardiologist, and/or an anesthesiologist prior to surgery. All patients require preoperative chest radiographs, EKG, CBC and blood chemistry evaluation.

A significant portion of oral cancer patients will present in the malnourished state due to odynophagia or alcoholism. The malnourished patient will not withstand aggressive surgical and postoperative radiation treatment without complications. For this reason, preoperative nutritional support should be considered for patients with weight loss greater than 10 percent of body weight and those with low serum albumin. The benefits of 2 or 3 weeks of enteral feeding supplementation, to place the patient in a positive nitrogen balance, outweigh the risk of treatment delay in these patients. Nasogastric tube placement is the most common route of enteral supplementation. However, if patients require significant cancer resection, complex reconstruction, postoperative radiation therapy and extended swallowing rehabilitation, the temporary placement of a gastrostomy tube is safe and well-tolerated. The benefits of consistent nutrition and hydration during treatment and rehabilitation cannot be overemphasized.[20]

In patients with oral cancer undergoing general anesthesia, the management of the airway is the responsibility of both the surgeon and the anesthesiologist. Preoperative communication and preparation are critical. Patients may be difficult to orally intubate due to trismus, hemorrhage, or tumor bulk, and the presence of the oral endotracheal tube may interfere with the resection. The appropriate solution is nasal intubation with or without flexible fiberoptic nasopharyngoscopic guidance. Another option for airway management is preoperative tracheostomy under local anesthetic. In the event of an airway emergency the surgeon must be prepared to secure a surgical airway via cricothyroidotomy or an emergent tracheostomy. This must be performed within minutes of desaturation to prevent anoxic brain injury or cardiac arrest.

Similarly, postoperative airway management is critical to safe surgery of the oral cavity. Indications for tracheostomy after oral cancer surgery include: (1) the anticipation of significant postoperative edema of the pharynx, floor of the mouth or the base of the tongue, (2) a significant risk of postoperative hemorrhage, (3) the presence of any bolster or other aspiratable dressing material, (4) pre-existing pulmonary disease or obstructive sleep apnea, or the simultaneous operation or compromise of the nasal airway, and (5) the need for frequent endotracheal suctioning or ventilation support.

The anesthetist should be instructed to avoid paralyzing agents if nerve stimulators are to be used to help identify motor nerves. Also, fluid overload should be avoided in oral cancer cases. Patients undergoing head and neck surgeries have a decreased need for intraoperative fluid replacement, compared to patients undergoing abdominal surgeries of similar duration. This is due to less third spacing of fluid and less insensate losses of fluid in head and neck cases compared to abdominal cases.

Management of Leukoplakia

During the carcinogenic process, some abnormal clonal populations of mucosal cells form clinical premalignant lesions. These are manifested as leukoplakia or erythroplakia. Leukoplakias are common lesions in smokers and patients with a previous history of head and neck cancer. These are also noted in patients without heavy carcinogenic exposure. In general, dysplastic leukoplakia should be treated while lesions harboring only hyperplasia and hyperkeratosis may be observed. Clinical characteristics of lesions suggesting the presence of dysplasia include large size, tongue or floor of the mouth location, red color, friability, and the patient's prior history of oral cancer or dysplasia. It should be emphasized that any lesion which is red or red-speckled (erythroplakia) is of the highest risk for dyplasia or carcinoma and should be biopsied.

Treatment of dysplastic leukoplakia is generally surgical. While the vitamin A analogue isotretinoin (13 *cis*-retinoic acid or Accutane™) has been shown to be effective in the treatment of dysplastic oral leukoplakia, most lesions will recur after therapy has been stopped and many patients do not tolerate the mucocutaneous toxicity of isotretinoin treatment. [21,22]

Small dysplastic leukoplakia lesions may be easily excised in the office under local anesthesia with millimeter margins. All excised leukoplakia should be submitted for histopathologic assessment. Laser excision of oral leukoplakias can also be accomplished with good hemostasis and little tissue reaction.[23] Other treatment options for leukoplakia include destruction by electrodesiccation, and cryotherapy with liquid nitrogen. Local recurrence is common and occurs in up to one-third of cases.[24]

SURGERY FOR ORAL CANCER

The lip is the most common site for oral cancer. It is usually considered separately from cancers of other oral subsites as it behaves more like skin cancer. It occurs in sun-exposed surfaces and more commonly on the lower lip than upper lip. It is usually diagnosed early due to bleeding and a visible ulcer. Large lesions may rarely invade the mandible or the mental nerve and foramen.

T1 and T2 lesions are usually cured by wedge resection of the lip with primary closure, (Figure 5–6) although primary radiation therapy is also highly effective. Large T3 or T4 lesions require resection of involved tissues, bilateral upper neck dissections, complex reconstruction, and postoperative radiation therapy.

Depending on the size of the mouth and the presence of dentition, up to 50 percent of the lower lip can be resected and closed primarily in three layers with care to close the orbicularis oris muscle securely. Re-approximation of the vermilion line is important cosmetically. If greater than 40 to 50 percent of the lip is to be resected an Abbe or Estlander lip switch reconstruction borrows lip tissue from the normal upper lip. Karapandzic advancement flaps can also be useful for large lip reconstructions.[25] Free flap reconstruction is sometimes necessary but always inferior cosmetically and functionally due to the lack of orbicularis oris function and difficulty with commissure reconstruction.[26]

The anterior two-thirds of the tongue is the most common site of primary lesions accounting for 40 percent of oral cancers. Most malignancies occur on the lateral borders and ventral surface but are occasionally confined to the tip or the dorsum. Even small lesions of the oral tongue are visible and usually symptomatic, so oral tongue lesions tend to present in earlier stages: 37 percent stage I, 34 percent stage II, 21 percent stage III, and 8 percent stage IV.[27]

Tongue cancer may spread along the mucosal surface to involve the floor of the mouth and the mandible, or the oropharynx, or it may spread by deep invasion between muscle fascicles which offer little resistance to tumor spread (Figure 5–7). It is

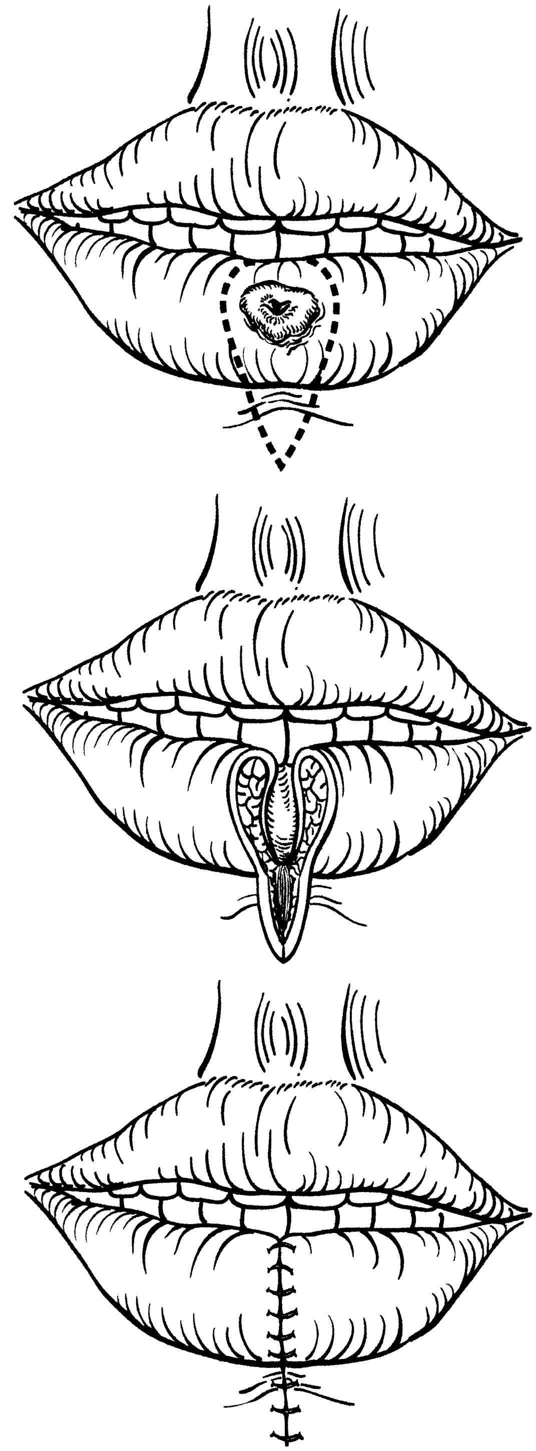


Figure 5–-6. *A* to *C*, Wedge resection of lower lip carcinoma with primary closure in layers.

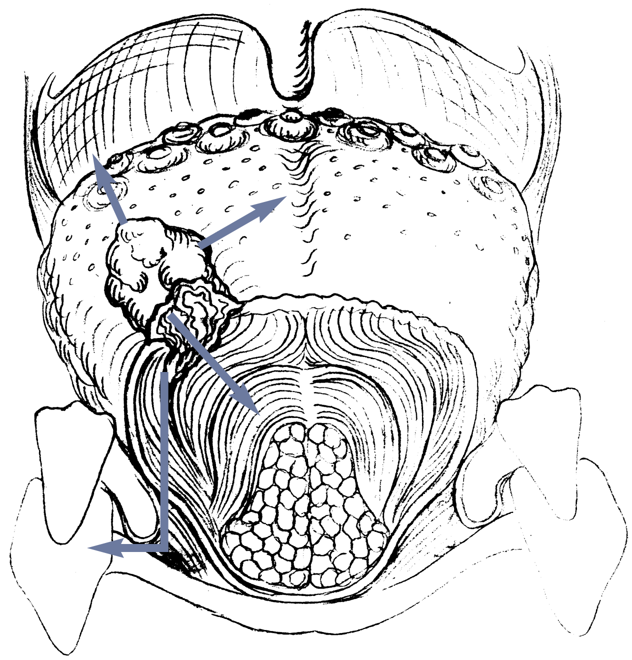
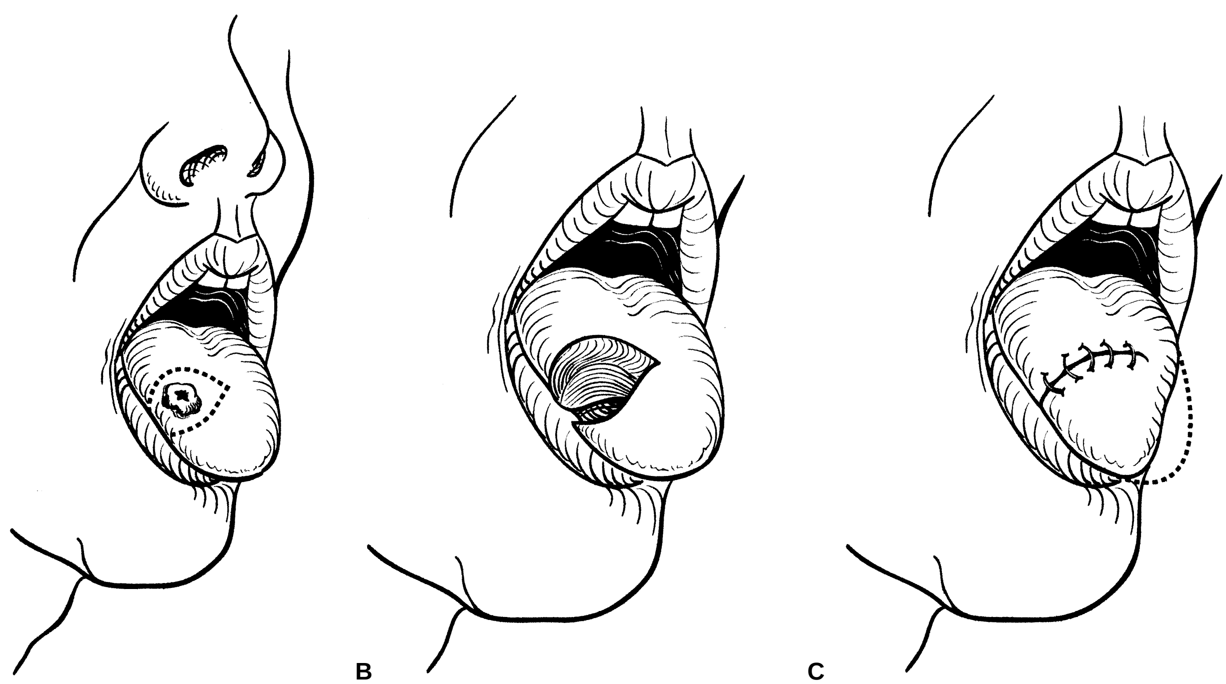


Figure 5–7. The anatomical routes of spread of oral tongue cancer.

easy to underestimate the deep extension of tongue tumors and great care should be exercised to take more than 1 cm cuff of normal tongue musculature as the margin of surgical resection. The midline raphe of the tongue does not provide any substantial resistance to tumor spread for lesions approaching or crossing the midline.

Peroral resection is the most common approach for T1 and T2 lesions of the oral tongue (Figure 5–8). A partial glossectomy is easily performed using electrocautery to maximize hemostasis. A 1 to 1.5 cm margin of normal tongue tissue is maintained in all dimensions, and both visual assessment and palpation of the tongue guide the resection. Intraoperative margin specimens for frozen section are taken with a scalpel to minimize cautery artifact. Resection can be performed with a carbon dioxide laser. Whenever feasible, the resection is planned in a transverse wedge fashion. Intraoperative frozen sections of the margins are mandatory. The defect of a partial glossectomy is closed in the horizontal direction causing a foreshortening of the tongue. The appearance and function after horizontal closure are excellent. This is preferable to a longitudinal closure, which results in a thin pointed tongue. The size and the extent of the tumor will determine the orientation of the resection.

For many T2 and T3 oral tongue tumors, and for any sized tumor in the posterior portion of the tongue or floor of mouth, the mandibulotomy approach provides the exposure required to perform an oncologically sound resection. The low morbidity of paramedian mandibulotomy is always preferred to the poor visualization and inadequate assessment



A **B** **C**

Figure 5–8. *A* to *C*, Peroral wedge excision and primary closure of a T1 cancer of the tongue with horizontal closure.

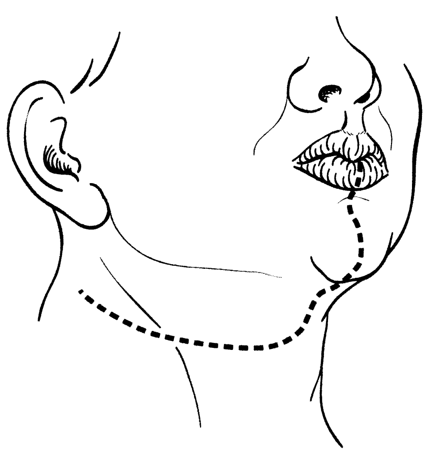
of the deep and posterior margins that result from inappropriate peroral excision.[28,29] In addition, the majority of these patients benefit from staging elective supraomohyoid neck dissection, which provides the neck exposure needed for the mandibulotomy approach (Figure 5–9).

This procedure begins with elective supraomohyoid or modified radical neck dissection, in which the skin and muscle flaps of the neck are raised exposing the lower border of the mandible. The floor of the mouth is exposed via the submandibular triangle. Next the lower lip splitting incision is performed. The vermilion border is marked to ensure accurate realignment, and the lip is split sharply in the midline and connected with the anterior extent of the neck incision. The periosteum of the mandible is left undisturbed while the soft tissues of the lip and cheek are elevated to identify and preserve the mental nerve. The gingival mucosa and periosteum are incised at the mandibulotomy site anterior to the mental foramen and lateral to the insertion of the digastric muscle. The cut is planned either between the lateral incisor and the canine tooth, or directly through the root of a lateral incisor tooth that is extracted. Cuts between tooth roots may damage both roots and both teeth may be lost subsequently. Prior to performing the bone cut, the 4-hole reconstructive plates for the lateral and inferior margin of the mandible are molded and the screw holes drilled to ensure accurate realignment. The cut is performed at right angles to the alveolar ridge and angled 45 degrees anteriorly below the tooth roots for better stabilization. Taking care to avoid the lingual nerve, the floor of mouth mucosa and mylohyoid muscles are divided posteriorly up to the anterior tonsillar pillar, and one centimeter from the medial aspect of the mandible.[28] Appropriate tumor resection is performed through the exposure thus provided (Figure 5–10).

The reconstruction requires the floor of mouth incision to be closed in layers, and the bone reapproximated with the preformed plates and screws (Figure 5–11). The lip is closed meticulously in three layers with attention to the orbicularis oris muscle and the exact apposition of the vermilion border. The best reconstructive options for partial and hemiglossectomy are primary horizontal closure if the defect is not too large, or free flap reconstruction. Other options include closure by secondary intention, split-thickness skin grafting and pedicled flaps. After large resections of the oral tongue, patients require speech and swallowing therapy for functional recovery.

Every effort should be made to achieve negative margins with the initial resection. Intraoperative positive frozen-section margins in tongue surgery significantly reduce local control and survival, even when additional resection and ultimately negative frozen and permanent sections are obtained.[30] When intraoperative positive frozen sections occur it reflects a tumor biology that is more invasive and aggressive than is estimated by the surgeon and thus warrants consideration of postoperative radiation therapy.

Final histopathology report of margins may show foci of premalignant change, carcinoma in situ (CIS), close surgical margins (less than 5 mm) or the presence of microscopic foci of invasive cancer. The presence of any of these findings at the surgical mar-



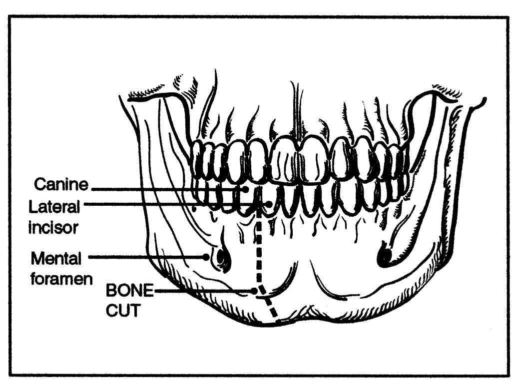


Figure 5–9. The mandibulotomy approach to tumors of the posterior oral cavity.

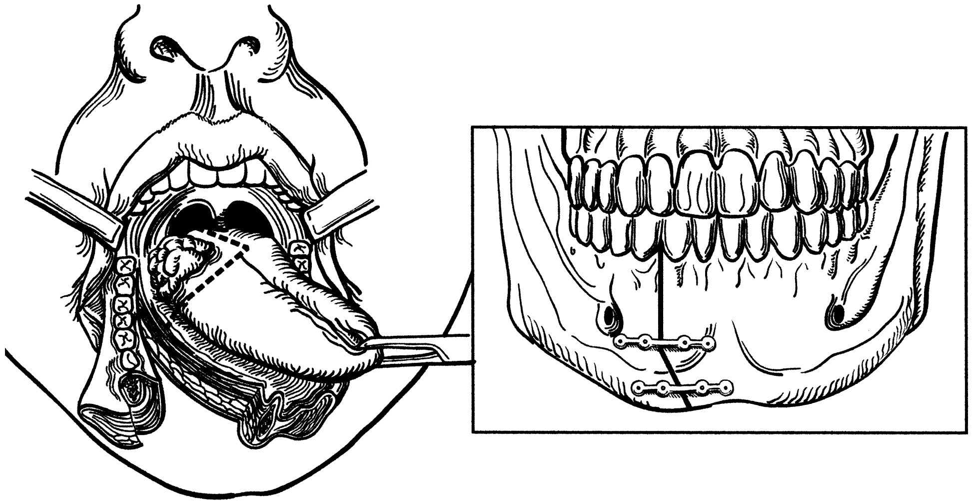


Figure 5–10. The mandibulotomy approach to tumors of the posterior oral cavity. Biplane fixation of the mandible is necessary.

gin increases the risk of local recurrence twofold, and significantly increases the mortality from oral cancers. Any of these histologic findings suggest a role for postoperative radiation therapy.[31,32]

Early tongue cancers demonstrate occult spread to the cervical lymph nodes in 20 to 30 percent of cases. The frequency of metastasis is related to the T stage and depth of invasion of tongue cancers. Increasing T stage correlates with increasing incidence of metastatic disease. A depth of invasion by tongue cancer of greater than 5 mm is associated with an increased incidence of occult metastasis.[33] Tumor depth greater than 2 mm is correlated with significantly lower survival and control of disease in the neck. In a study of early staged cancers of the tongue and floor of the mouth, the 5-year survival of patients with thin lesions was greater than 95 percent, while survival of patients with thick lesions was less than 80 percent, regardless of T stage (Table 5–2).[34] An appreciation of tumor depth can aid in the decision to perform elective neck dissection. Except for oral cancers less than 2 mm thick, all early staged oral cancer patients should receive elective supraomohyoid neck dissection (SOHND). On the other hand, elective radiotherapy to the neck should be employed if radiation therapy is the treatment selected for the primary tumor.

Survival after treatment for tongue cancers has improved over the last 15 years, due to the use of combined modality treatment for advanced disease, and the aggressive treatment of the neck in early stage disease. Franceschi reported 5-year survival of 82 percent for patients treated between 1978 and 1987 with stage I and II disease and 49 percent for

Figure 5–11. The mandibular osteotomy is fixed using miniplates which provide accurate dental occlusion, and stability.

Table 5–2. THICKNESS OF ORAL CANCER PREDICTS SURVIVAL AND TREATMENT FAILURE

Tumor Thickness	5-year Disease Specific Survival (%)	Treatment Failure (%)
< 2mm	97	2
2–8mm	83	45
>8mm	65	

Data from Spiro RH, et al. Predictive value of tumor thickness in squamous cacinoma confined to the tongue and floor of the mouth. Am J Surg 1986,152:345–50.

stage III and IV disease. These are improvements over the survival rates in their experience from the period 1967 to 1978 (Figure 5–12).[27]

The floor of the mouth is the second most common subsite accounting for 20 percent of oral cancers. Due to its dependent location, carcinogens may pool in the floor of mouth leading to high rates of cancer. Because of the small size of this area, floor of the mouth lesions often extend to involve the tongue and the mandibular gingiva. The size distribution of floor of mouth cancers at the time of diagnosis is 30 percent T1, 37 percent T2, 19 percent T3, and 14 percent T4.[28] Forty-one percent of patients present with regional neck metastasis, and micrometastases are identified histologically in 17 percent of elective neck dissection specimens. Of all treatment failures, 21 percent recur locally, 37 percent recur in the neck and 29 percent at both sites. Staging elective supraomohyoid neck dissection is appropriate for all but very superficial T1 lesions of the floor of the mouth, and bilateral staging neck dissection is indicated for midline lesions. Finally, survival for floor of mouth lesions is 88 percent, 80 percent, 66 percent, and 32 percent for disease of stages I to IV respectively.[35]

Because of the frequent involvement of the mandible by floor of the mouth tumors, management of the mandible is an important aspect of planning resections of the floor of the mouth. The key clinical question is: does the mandible require resection, and if so how much—the periosteum, a marginal mandibular resection or a segmental resection? Management of the mandible depends on the lesion's proximity to the mandible, whether the mandible is dentate or edentulous, the degree of atrophy of the alveolar ridge, whether the mandible has been irradiated, and whether there is mandibular invasion.

Historically, a segmental mandibular resection was often performed not only for bone involvement by cancer, but also to accomplish a monobloc resection of the primary carcinoma with cervical lymph nodes. It was incorrectly presumed that lymphatics from the oral cavity passed through the periosteum of the mandible to the neck and that in-transit metastasis could be resected with the mandible. The elegant histologic work of Marchetta and colleagues[36,37] has conclusively demonstrated that the lymphatic drainage of the tongue and floor of mouth does not pass through the mandibular periosteum nor through the substance of the mandible.

An additional advantage to routine mandibular resection in decades past was improved access and visualization of oral cancers. However, the morbidity and reconstructive challenges of segmental mandibulectomy led surgeons to reconsider the indications for this procedure, and to explore the possibility of partial-thickness mandibular resections. In these procedures only the alveolar ridge and/or the lingual plate of the mandible is resected (marginal mandibulectomy), and the inferior alveolar artery and nerve and the continuity of the mandibular arch are spared. In order to justify the oncologic soundness of marginal mandibulectomy, studies were undertaken to understand the routes of invasion and spread of cancer in the mandible. The results allow a rational approach to management of the mandible in oral cancer.

McGregor and colleagues have reported that the primary route of SCC invasion of the edentulous mandible is through cortical deficiencies of the occlusal surface of the bone.[38] The route of spread in the dentate nonirradiated mandible is via the tooth sockets, and the presence of teeth is a relative barrier to tumor infiltration. Also, the dentate mandible has a greater height from the floor of the mouth than does the edentulous mandible due to the resorption of the alveolar ridge after tooth loss. Therefore, tumors of the floor of the mouth must advance farther up the gingival mucosa to reach the occlusal

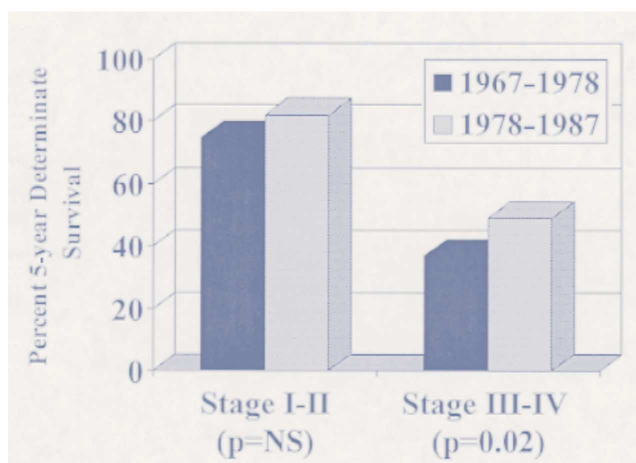


Figure 5–12. Graph demonstrating improved survival in tongue cancer from the years 1967 through 1978 to the years 1978 through 1987. Data from Franceschi et al. Improved survival in the treatment of squamous carcinoma of the oral tongue. Am J Surg 1993;166:360–5.

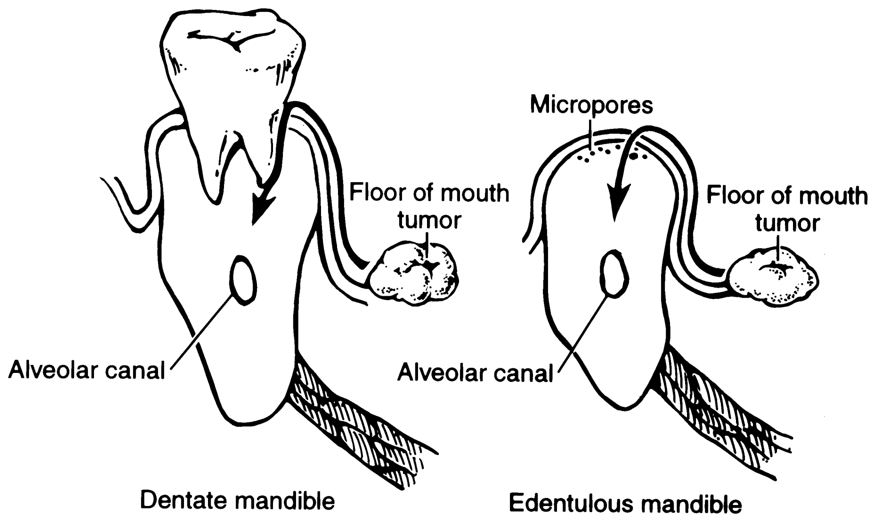


Figure 5–13. The routes of spread of oral cancer to the mandible in the dentate and edentulous mandible.

surface of the dentate mandible than the edentulous mandible (see Figure 5–13).

Cancer invasion of the *irradiated* mandible occurs not only through the occlusal surface but also directly through cortical bone of other surfaces.[39] This suggests the loss of barrier function of the periosteum after irradiation.

In both radiated and nonirradiated mandibles, the spread of squamous carcinoma within the cancellous bone is generally directed inferiorly toward the inferior alveolar nerve canal. Brown and colleagues reported that the early phase of mandibular invasion is erosive and that this phase progresses to an infiltrative phase as the depth of invasion increases.[40] In the histologic studies by McGregor and McDonald, tumor spread proximally and distally within the cancellous bone of the mandible was observed to be no farther than 5 mm beyond the region of overlying soft-tissue involvement, suggesting that a 5 to 10 mm bony margin, beyond the extent of the soft-tissue tumor, is oncologically sound.[40] On the other hand, invasion of the alveolar canal by oral cancer allows extensive perineural spread. By this route, disease can travel distally or proximally to the skull base, but does not tend to seed the bone along the course of the nerve or form skip lesions. Invasion of the ramus via the body of the bone occurs readily, especially in the irradiated mandible.[41]

With these principles in mind, one can develop a rational approach to management of the mandible in oral carcinoma. Because the dentate mandible is relatively resistant to cancer infiltration by adjacent lesions, marginal resection of the alveolar ridge and/or the lingual plate, sparing the alveolar artery, is sometimes acceptable treatment for disease in proximity to the bone. First, the proximity of the tumor is assessed by observation, palpation, and by CT scan if the lesion is fixed to the bone. If the tumor is greater than 1 cm away from the bone, then no mandible resection is needed. If the tumor is less than 1 cm from the mandible, then a marginal resection of the mandible will ensure 1 cm margins. If the tumor involves the gingival mucosa and the periosteum without clinical or radiologic evidence of cortical or cancellous bone involvement, then a marginal resection of the mandible is satisfactory, because any subclinical bone involvement is likely to be localized to the alveolar process. If the tumor is fixed to the occlusal surface with clinical or radiologic evidence of cortical or cancellous bone involvement, then a segmental resection is performed because, once the occlusal cortex is breached, there is no barrier to the vertical spread of tumor through cancellous bone to the alveolar canal. Totsuka and colleagues published studies showing that marginal mandibular resection was safe for some tumors with minimal gross bone invasion if there was a histologically "expansive" rather than "infiltrative" pattern of invasion. However, this pattern of invasion was not readily predictable based on radiographic findings.[42,43]

When extensive involvement of the cancellous bone is noted, the alveolar nerve must be assessed by frozen section, and further resection along the course of the nerve to the inferior alveolar foramen, the mental foramen, or the skull base is considered.

Contraindications to marginal resection of the mandible include gross involvement of the cortical or cancellous bone of the mandible, inability to preserve the inferior alveolar artery, significant resorption of the mandible—suggesting very thin and weak residual bone, a previously irradiated mandible, and cancer abutting the mandible on more than two surfaces.

Small T1 lesions that are 1 cm from the mandible are amenable to wide local excision via the peroral approach. This is easier in the edentulous patient due to better visualization. The mucosal margin is at least one centimeter. The deep margin is just below the sublingual salivary gland for superficial lesions. Wharton's duct may be ligated, but the authors prefer to reroute the duct to the posterior edge of the resection if the submandibular gland is not resected in the neck dissection. Caution is taken to identify and preserve the uninvolved branches of the lingual nerve as anesthesia of the tip of the tongue will result from their sacrifice. Small defects may be closed primarily but many can be allowed to granulate and heal by secondary intention. A split-thickness skin graft is an excellent reconstruction for small defects in the floor of mouth that expose the mylohyoid muscle.

Excision of small lesions of the floor of the mouth may require local resection with en bloc marginal resection of the mandible (Figure 5–14).[44] This may be accomplished via a peroral approach. The mucosal and soft-tissue excision is left attached to the mandible, the extraction of teeth at sites of alveolar cuts is performed, and the bone cuts are performed with the sagittal saw and ultra-thin blades. Smooth cuts rather than right-angle cuts are favored to evenly distribute forces of mastication and pre-

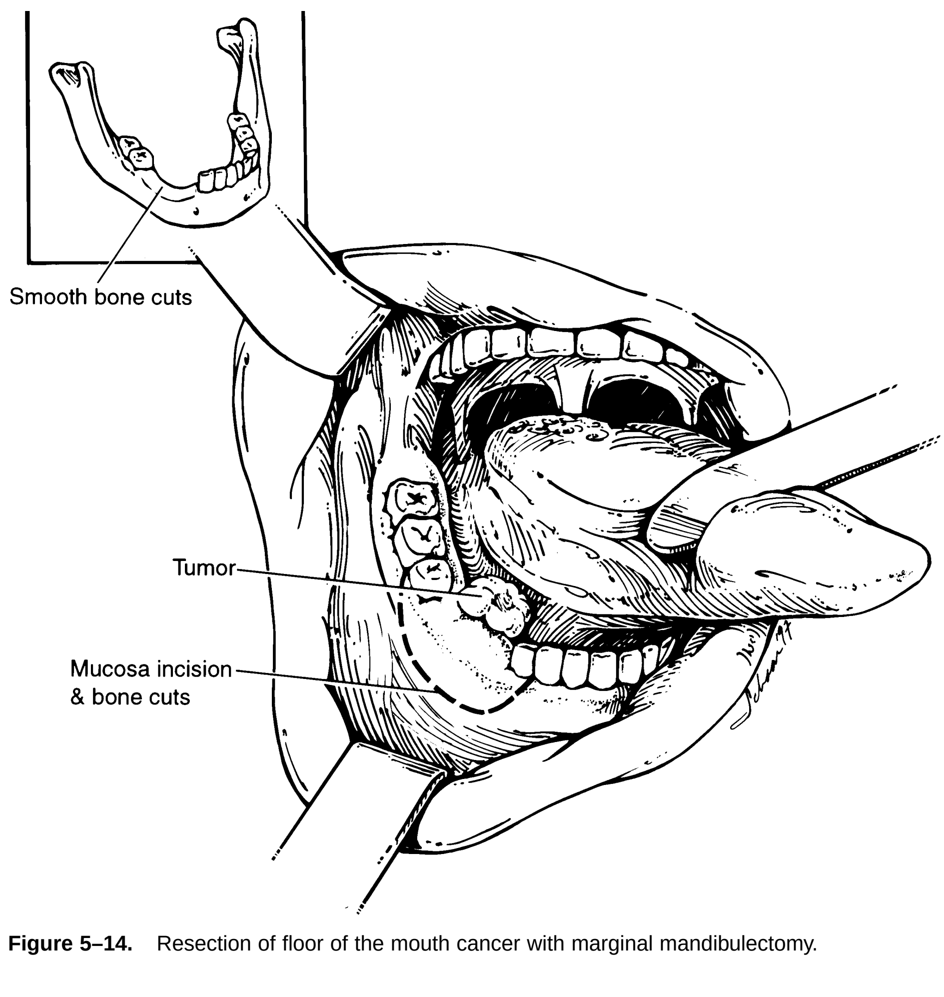


Figure 5–14. Resection of floor of the mouth cancer with marginal mandibulectomy.

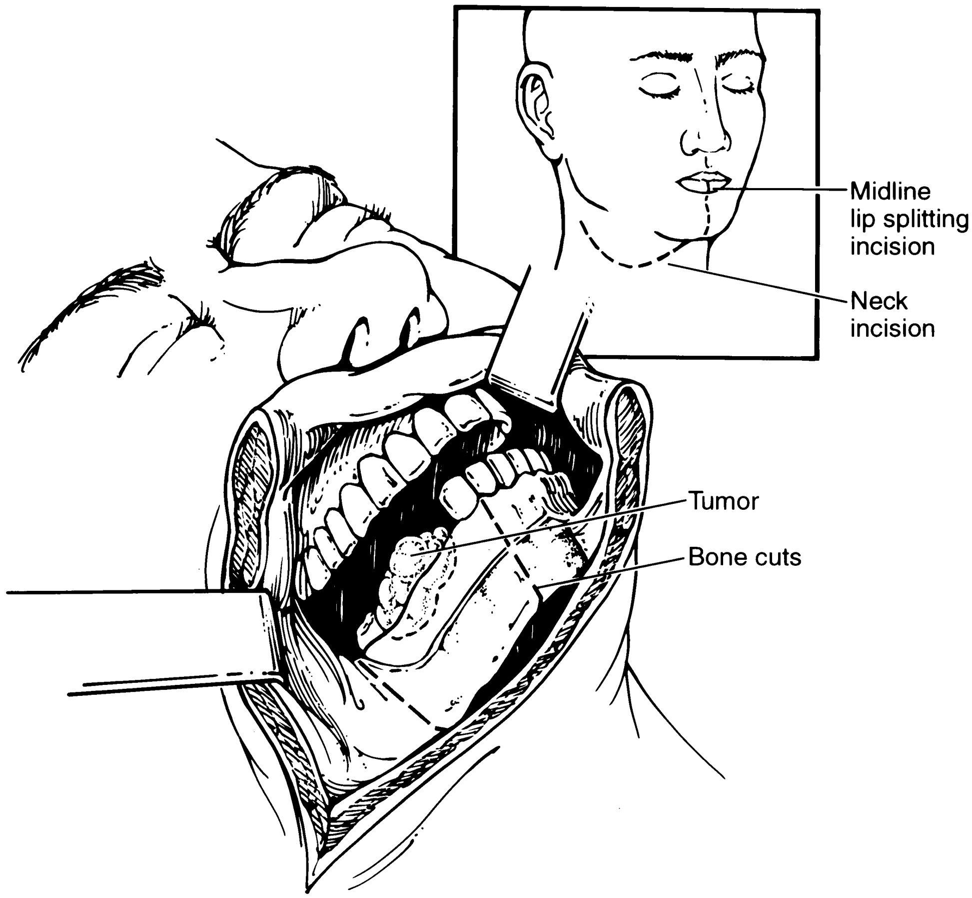


Figure 5–15. Segmental resection of the mandible through a lower cheek flap approach for a large floor of the mouth carcinoma with gross mandibular bone involvement.

vent subsequent fractures. When the dentate mandible is encroached upon by tumor at the lingual plate only, a vertical partial mandibular resection can be accomplished using the tooth roots as the vertical plane of resection. The related teeth are extracted and the right-angle saw blade is used to resect only the lingual plate, exercising caution to preserve the alveolar artery. Elective or therapeutic neck dissection improves the exposure of the lower mandible. The specimen is delivered en bloc. The resulting defects of the floor of the mouth and the mandible can be left to granulate, however mucosal advancement flaps or a split-thickness skin graft can often close these defects well.[45,46]

Most T3 and T4 floor of mouth cancers require extended local resections including partial glossectomy or a segmental mandibular resection, which is performed through a lower lip splitting incision and a lower cheek flap exposure (Figure 5–15). The mental nerve is sacrificed. An elective or therapeutic neck dissection is always indicated in surgical treatment of large floor of the mouth tumors and this provides good inferior exposure for the resection of the mandible. Tooth extractions and gingival mucosal incisions are then performed. Mandibular reconstruction plates may be pre-bent and screw holes drilled. With the soft-tissue portion of the tumor well defined and protected, the bone cuts are performed with the sagittal saw and the specimen removed en bloc, often with the neck specimen attached as well.[44] A frozen-section assessment of the alveolar nerve is prudent. Reconstruction of lateral mandibular defects with reconstruction plates or free bone grafts requires excellent soft-tissue coverage with myocutaneous flaps although the failure rate is 50 percent. Exposure of reconstruction plates used for anterior arch reconstruction approaches 100 percent. The free tissue transfer of fibula with attached muscle and skin is the state of the art reconstruction for large composite resections, especially when the anterior arch is involved.

An alternative surgical approach to T3 and T4 floor of the mouth lesions that do not require segmental mandibular resection is the transcervical pull-through procedure.[47] The primary tumor specimen is delivered into the neck with or without marginal mandibular resection. Bilateral upper neck dissections are usually performed. If necessary a marginal or lingual plate resection of the mandible is accomplished. The remaining soft-tissue attachments to the mandible, including the mylohyoid muscles, are divided and the oral contents delivered inferiorly into the neck. This provides good visualization of the tumor for the remainder of the soft-tissue resection. It is critical that the oral tissues are properly re-suspended and that the remaining extrinsic tongue musculature is appropriately attached to the mandible for postoperative swallowing function.

Maxillary and mandibular gingival lesions are often reported in the literature together as gingival lesions. Surgically, lesions of the mandibular gingiva and retromolar trigone are similar and will be discussed together. Lesions of the maxillary gingiva are surgically similar to those of the hard palate and so these two subsites will subsequently be addressed.

Three-quarters of gingival lesions involve the mandibular alveolus and one-quarter involve the maxillary alveolus. A report of 283 mandibular alveolar lesions from Memorial Sloan-Kettering Cancer Center showed the distribution of these primary tumors to be 30 percent T1, 48 percent T2, 17 percent T3 and 11 percent T4.[48] Only 5 percent were resected without bone, 32 percent were amenable to marginal resection and 63 percent required segmental bone resection. Local recurrence was 25 percent when the mandible was initially involved with tumor. Occult neck metastasis was found in only 6 of 107 elective radical neck dissections, indicating a low incidence of occult neck disease compared to tumors of other subsites of the oral cavity. Staging elective supraomohyoid neck dissection is indicated for T2 or larger lesions in conjunction with segmental mandibular resection. Five-year survival for all alveolar cancers was 77 percent stage I, 70 percent stage II, 42 percent stage III, and 24 percent stage IV.

Overholt[49] reviewed the M.D. Anderson Hospital experience of 155 mandibular alveolar lesions and determined that parameters affecting local control and survival were: size greater than 3 cm, bone involvement, and positive surgical margins. As discussed above, marginal mandibular resection is appropriate for periosteal involvement and segmental resection indicated when the cortical bone is involved with cancer.

Peroral wide local resection with marginal mandibular resection can be performed for smaller lesions, while segmental resection requires lip splitting incision and lower cheek flap elevation as described previously.

Tumors of the retromolar trigone occur with a disproportionately high frequency considering the small surface area (Figure 5–16). Fifteen percent of oral cancers occur in the retromolar trigone. This site is difficult to assess clinically because of its posterior location, mucosal irregularity, small area, and visual interference by the dentition. Trismus, if present, may also inhibit the examination, and is indicative of pterygoid involvement. Retromolar lesions are relatively difficult to treat because they spread early to deep structures such as the ascending ramus of the mandible, pterygoid muscles, the masticator space, and the skull base. Another avenue of local spread is the foramen of the inferior alveolar nerve into the ramus of the mandible. Tumor may also spread proximally along the perineurium or within the nerve to the trigeminal ganglion and the CNS. Surgical access to this region is challenging. Bone resection is nearly always indicated, and recurrence is difficult to diagnose.

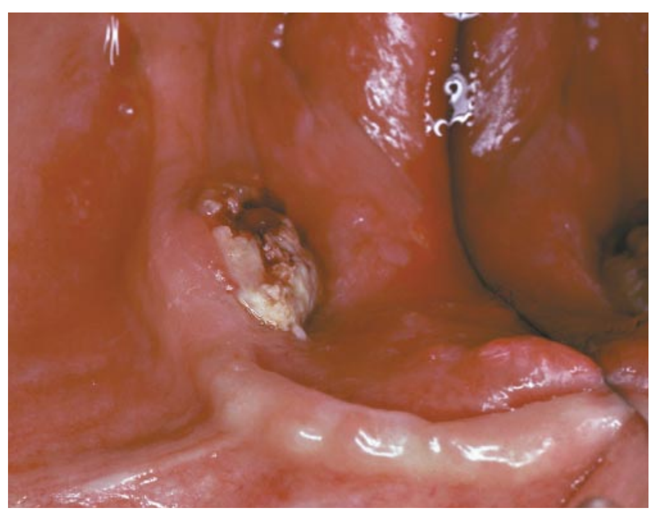


Figure 5–16. An exophytic lesion in the retromolar trigone.

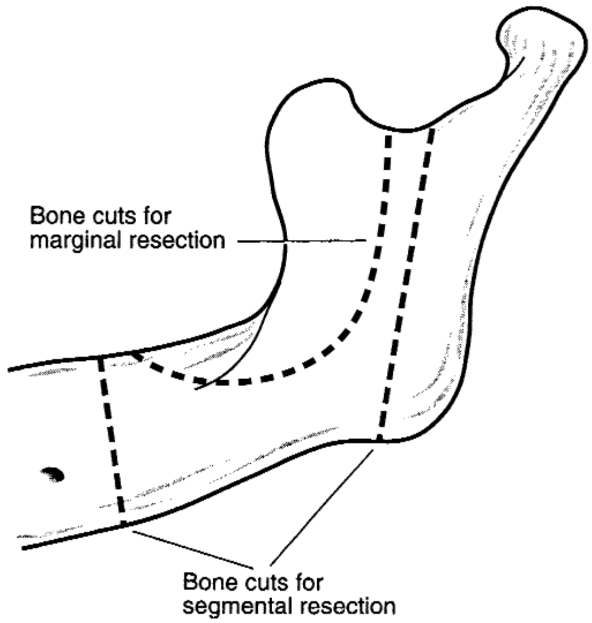


Figure 5–17. Bone cuts for marginal and conservative segmental resections of the mandibular ramus and body.

The peroral approach to the retromolar region is rarely satisfactory due to the posterior location of the trigone and the necessity for bone resection since the periosteum or bone is usually involved with cancer. Often a segmental resection of the ascending ramus of the mandible and part of the pharynx is necessary. Mandibular rim resection of the molar alveolus and the ascending ramus of the mandible is acceptable for small lesions without gross bony involvement. Marginal mandibular resection of the ascending ramus through the open mouth is not satisfactory.

If bone is grossly involved by clinical or imaging evaluation, then segmental resection of the ramus and/or body is required. If superficial involvement of the molar alveolus or ascending ramus is identified, then conservative segmental mandibular resection sparing the condyle and a posterior strut of ascending ramus is satisfactory bone resection.[41] Cuts are performed through the mandibular notch and the coronoid process (Figure 5–17). The alveolar foramen and nerve are included in the resection. Intraoperatively, a frozen-section margin on this nerve is important. Assessment of the superior extent of the disease, including the coronoid process of the mandible, the temporalis muscle, maxillary tubercle, masticator space, and pterygomaxillary space is necessary. Marginal resection of the maxillary alveolus or partial maxillectomy may be necessary if they are involved with cancer.

Soft-tissue reconstruction with primary closure, or healing by secondary intention over the retromolar trigone is occasionally satisfactory. Posteriorly-based buccal mucosal random-pattern rotational flaps, soft palate, tongue, and masseter muscle flaps are all described for this area. The need for thin tissue here suggests an advantage for skin grafting and radial forearm free flap reconstructions. If the ramus is sacrificed, a bulkier pectoralis pedicled flap may cover reconstructive hardware but tends to pull inferiorly with time. The excellent bone stock of the fibular free flap is detracted from by its association with bulky muscle, and variable survival of the overlying skin paddle. It is infrequent today that a lateral mandibular defect is left unreconstructed, but this defect is tolerated well by many patients and it allows easier assessment of the region for recurrence. Defects that are small, posterior and occur in the edentulous patient are tolerated well.

Carcinomas of the hard palate (Figure 5–18) and upper alveolus are relatively uncommon, accounting for 10 percent of oral cancers,[50] except in areas of Southeast Asia where reverse smoking is practiced.[51] In the United States, carcinoma of the hard palate is only half as common as carcinoma of the soft palate[52,53] and carcinoma of the maxillary alveolar ridge is only one-third as common as carcinoma of the mandibular alveolar ridge.[48] These areas are lined with adherent keratinized mucosa, which pro-

Figure 5–18. Squamous cell carcinoma of the hard palate.

vides protection from the trauma of mastication, and may provide relative protection of the basal nuclei from the effects of carcinogens.

Histologically, carcinomas of the upper alveolar ridge are nearly all squamous cell carcinomas, but up to one-third of hard palate cancers are of minor salivary gland origin.[54] In contrast to squamous cell carcinomas, palatal minor salivary gland tumors are often submucosal masses rather than ulcerative or fungating mucosal lesions. Kaposi's sarcoma can be seen on the hard palate of patients with acquired immunodeficiency syndrome. Malignant melanoma of the oral cavity, while rare, occurs most frequently on the palate.

Lesions of the maxillary alveolar ridge are symptomatic, thus allowing early diagnosis. Eighty-two percent of maxillary alveolar ridge carcinomas are T1 or T2 at the time of diagnosis, and 86 percent are N0.[48] Palatal carcinomas tend to be larger when diagnosed but only 13 percent have regional metastases when diagnosed.[49] The presence of regional metastases to the neck or locally advanced disease decreases 5-year survival from approximately 70 percent to approximately 30 percent.[53]

Surgery is the treatment of choice for cancer of the maxillary alveolus and the hard palate, and it is frequently necessary to resect periosteum and bone in order to ensure an adequate margin. The mucosa and the underlying periosteum are fused in this region forming a mucoperiosteum. Invasive carcinomas of this area frequently involve the periosteum or the underlying bone, thus reducing the effectiveness of primary radiation therapy for these lesions. However, postoperative radiation therapy for aggressive minor salivary gland malignancies or advanced squamous carcinoma is recommended.[54,55]

T1 and T2 lesions may be amenable to peroral wide local excision with resection of the involved mucoperiosteum and usually the underlying bone. Mucosal incisions are performed with electrocautery, allowing a 1 cm margin of normal tissue. Teeth are extracted at the osteotomy sites, and bony cuts are performed with an oscillating saw. Many small defects granulate well and close by secondary intention. Primary closure is usually not possible due to the immobility of the surrounding adherent mucosa. A posteriorly-based buccal mucosa flap

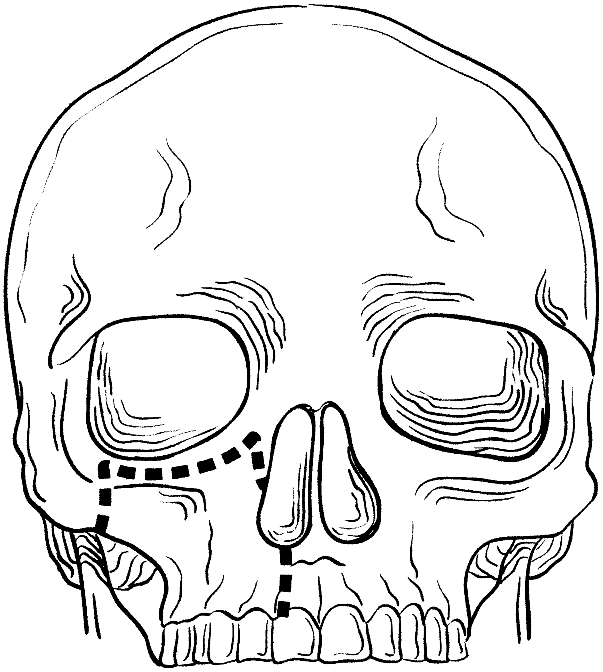


Figure 5–19. Bone cuts for subtotal maxillectomy preserving the inferior orbital rim and floor of the orbit.

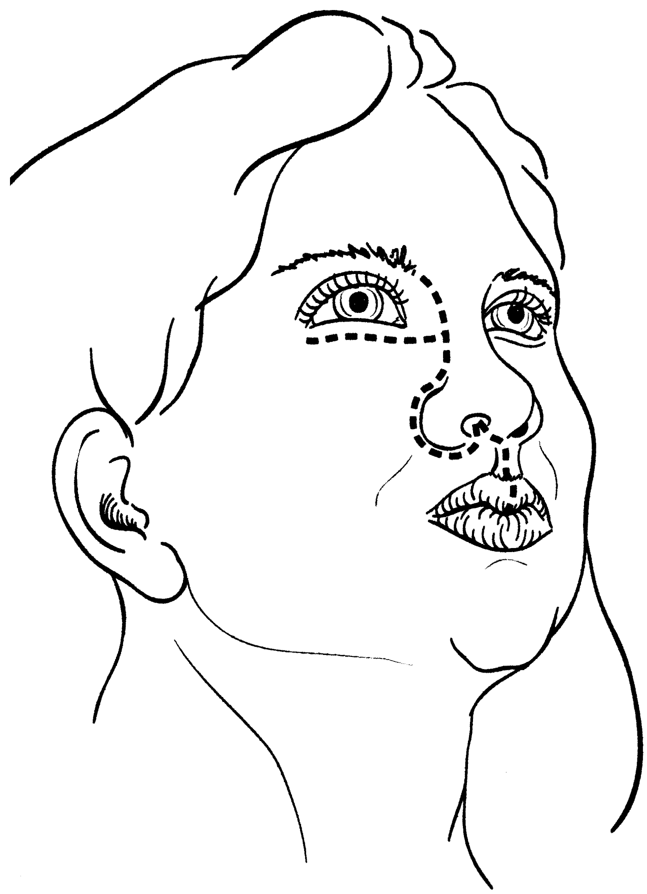


Figure 5–20. The Weber-Ferguson incision and its subciliary and brow extensions for maxillectomy.

with random blood supply is effective in closing lateral palatal and alveolar defects. A flap of the palatal mucoperiosteum, based on the greater palatine artery in the posterior aspect of the hard palate, can be rotated to cover a small defect, and the donor site left to granulate or be skin grafted. If the nasal and antral mucosa are intact after the resection, the oral defect can be closed with a local flap with a low risk of oronasal fistula formation.

T3 or T4 cancers with invasion of the maxillary antrum or nasal cavity often require partial or subtotal maxillectomy. Advanced lesions invade the nasal cavity, maxillary sinus, the pterygomaxillary space, pterygoid plates and skull base. T3 and T4 cancers requiring subtotal maxillectomy (preservation of the infraorbital rim and floor of the orbit) (Figure 5–19) need exposure via an extended Weber-Ferguson incision and an upper cheek flap for maximum exposure (Figure 5–20), or exposure via the midface degloving approach. A midface degloving approach provides excellent exposure for anterior lesions involving the lower maxilla and nasal cavity bilaterally without any external incisions, but superior exposure is limited above the orbital rim.[56,57] After the exposure is obtained, the soft-tissue cuts and dental extractions are performed as needed. Alveolar cuts should be made through the sockets of extracted teeth and not between them. This allows good bony support for the remaining teeth that will bear considerable forces from dental rehabilitation. The following cuts are performed using the oscillating saw: (1) from the lateral maxillary wall to the infraorbital rim preserving the latter, (2) from the infraorbital rim to the nasal cavity through the lacrimal fossa, (3) from the nasal cavity through the alveolar ridge, and (4) through the hard palate (see Figure 5–19). The remaining cuts are the lateral nasal wall cut, which joins the lacrimal cut to the nasopharynx using a thin osteotome and Mayo scissors, and finally the posterior cut. The posterior cut is performed only after all other aspects of the maxilla are freed. This is because significant bleeding can occur from the pterygoid venous plexus and the internal maxillary artery after this cut is performed. The expedient removal of the specimen and prompt packing of the maxillectomy defect are necessary to adequately control bleeding. The final cut is made anterior to the pterygoid plates if the posterior wall of the antrum is not involved, and posterior to the pterygoid plates if the posterior wall and the pterygomaxillary space are involved with cancer. The cut is made using a curved osteotome and the heavy curved Mayo scissors under palpation guidance with cognizance of the proximity of the internal carotid artery in the deep aspect of the parapharyngeal space, and the apex of the orbit superomedially. Hemostasis is obtained, the lacrimal sac is tacked open with chromic suture and/or the lacrimal duct cannulated with silastic tubing, and the cavity is skin grafted. The graft is supported by packing with xeroform gauze, which is supported by a preformed dental obturator that is wired to the remaining maxillary teeth or the alveolar bone.

Only rarely is total maxillectomy (including the orbital rim and floor) or radical maxillectomy (including orbital exenteration) necessary for oral cavity cancers.

REHABILITATION

The rehabilitation of function after oral surgery is a critical element in effective oral cancer surgery. After major oral resections the patients need rehabilitation of speech, swallowing, dentition and mastication as well as cosmesis. This process is best accomplished in a multidisciplinary environment which include the head and neck surgeons, plastic surgeons, speech and language therapists, nurses, dentists, prosthodontists and oral and maxillofacial surgeons.

Perhaps the most important element of rehabilitation is optimizing the patient's resection and reconstruction at the time of surgery. While the oncologic soundness of the tumor resection must not be compromised for functional reasons, neither should excessive resection of uninvolved soft tissue, nerve or bone be performed. Whenever oncologically possible, preservation of the hypoglossal, lingual and mental nerves should be attempted. Gentle handling of tissues, hemostasis, and obliteration of dead space are general principles of surgery which should be adhered to. This, in combination with antiseptic preparation of the oral cavity preoperatively and the use of perioperative antibiotics, may reduce inflammation and improve healing and reduce scar tissue formation, which will tend to maximize postoperative function.

Reconstruction of oral defects after ablative surgery is critical for oral rehabilitation. Perhaps the most important advance in head and neck surgery in the last 15 years has been the safe and effective use of free tissue transfer for reconstruction. Free tissue transfer techniques now allow the excellent reconstruction of the mandible, skin, and mucosa of the oral cavity. Bone flaps from the fibula, iliac crest and scapula are available to the reconstructive surgeon. Soft tissue from the radial forearm, lateral arm, trapezius, rectus abdominis and other sites provide vascularized, nonirradiated soft tissue for reconstructive purposes. It is clear that the appropriate use of these reconstructive tissues has dramatically improved the functional outcome of oral cancer patients. They should be employed whenever necessary. Adequate reconstruction of the mandibular arch, and soft tissues of the tongue and floor of mouth will significantly increase the likelihood of acceptable speech and swallowing after major oral cavity cancer surgery.

Rehabilitation of swallowing after oral cavity surgery is important. Swallowing can be divided into the preparation phase, the oral phase and the pharyngeal phase. Oral cavity surgery impacts most on the preparatory phase and the oral phase. The preparatory phase of swallowing begins with lubrication of the food bolus by saliva. This is impaired when pre- or postoperative radiation therapy is employed. Significant xerostomia results in the majority of irradiated patients. The xerostomia significantly limits the types and consistencies of food that can be swallowed. Most patients with oral cavity radiation require frequent sips of water to maintain moisture and liquid to wash down the food at mealtimes. One experimental strategy to try to limit xerostomia is to use a salivary gland protectant such as Salagen (pilocarpine hydrochlonde) during radiation. The benefit of Salagen™ is not yet proven and it is contraindicated in the presence of coronary artery disease. Amifostine is approved for the prevention of radiation-induced xerostomia. It is not widely used. A number of preparations are marketed for xerostomia but are not superior to water for the majority of patients.

Mastication is critical to an effective preparatory phase of swallowing. Certainly the quality and quantity of the teeth are important for mastication. Mastication requires intact sensation of the dentition, gingiva, tongue and buccal mucosa, and intact motor function of the hypoglossal nerve for tongue musculature, the facial nerve for oral competence and the third division of the trigeminal nerve for buccinator function. This combination of sensory and motor functions allows the food to be kept in the plane of the molars without biting the soft tissues.

Continuity of the mandibular arch provides great advantage for mastication. However, a patient with a segmental defect of the body of the mandible can frequently masticate some foods satisfactorily. Occasionally a guide plane prosthesis is helpful to maximize occlusion of the teeth in a patient with a lateral mandible defect. These guide plane prostheses help overcome the deviation of the mandible to the resected side from the unopposed action of the intact contralateral pterygoids. An unreconstructed defect of the anterior mandible is uncommon today. This defect will prohibit mastication of solids and patients will tolerate no more than a puréed diet. The combination of poor mastication, swallowing, speech and articulation, cosmetic defect and oral incompetence makes the anterior mandibular arch defect something to be avoided in almost every circumstance. The oral preparatory phase of swallowing can also be inhibited by trismus, which is common after surgery and/or irradiation of the posterior oral cavity and oropharynx.

The oral phase of swallowing consists of preparation of the food bolus followed by presentation to the oropharynx, where the swallowing reflex is initiated during the oropharyngeal phase. The oral phase is volitional. Preparation of the bolus is accomplished by the tongue, cheek, teeth and palate. After mastication and lubrication, the bolus is then propelled to the oropharynx by elevation of the tongue against the hard palate. When the bolus is sensed in the oropharynx the reflexive portion of the oropharyngeal phase of swallowing is initiated. Tongue elevation can be restricted due to either loss of tissue volume or motor function after surgery. Patients with near total glossectomy can be sometimes well rehabilitated with a palatal drop prosthesis, which lowers the level of the hard palate so that the residual tongue tissue can articulate with it to propel the bolus posteriorly (Figure 5–21).

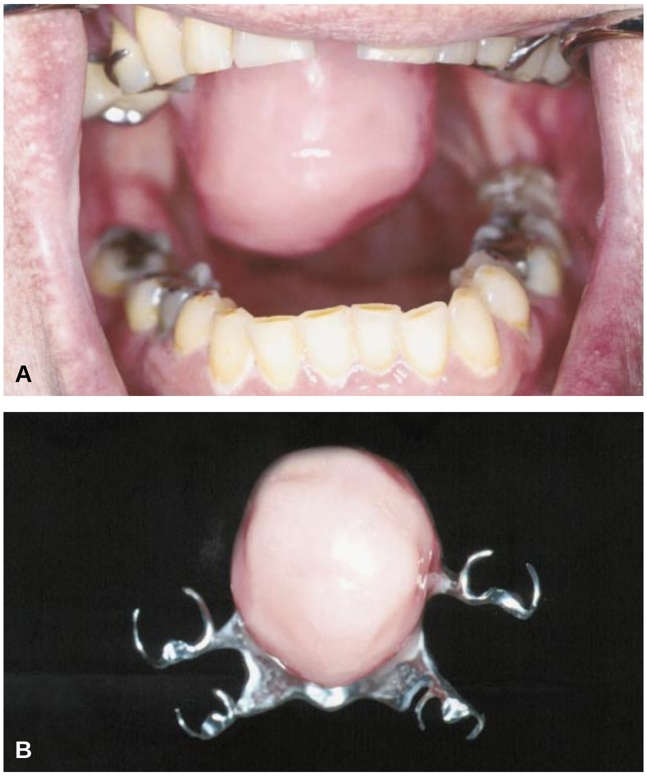


Figure 5–21. *A*, Patient with poor tongue mobility with a palatal drop prosthesis in place. *B*, Palatal drop prosthesis.

The oral prosthodontist plays a critical role in the rehabilitation of swallowing after oral cancer treatment. The proper number and quality of teeth and their alignment can be restored by maxillary and/or gingival dentures. After resection of the maxilla or hard palate, a dental obturator to cover the oro-antral and oronasal fistulae is necessary for swallowing without nasal regurgitation (Figure 5–22). Patients with large maxillary defects can attain excellent functional results with an obturator. For defects of the soft palate, dysphagia due to nasal regurgitation, hyponasal speech and difficulty with articulation of speech sounds, an obturator with a nasopharyngeal bulb is effective in minimizing nasal regurgitation and improving hyponasal speech. The bulb is properly positioned in the nasopharynx articulating with the posterior pharyngeal wall at the prominence of the body of C2, allowing the remainder of the soft palate to seal off the nasopharynx during swallowing (Figure 5–23).

Osseointegrated implants are an important advance in oral rehabilitation. If adequate bone stock exists, titanium posts can be placed in a multistaged process and the ingrowth of healthy bone into and around the implants results in a very secure foundation for oral prostheses.[58] Osseointegrative implants can be placed in fibula free flap reconstructions of the mandible after the healing and removal of the fibula fixation hardware (Figure 5–24). Osseointegrative implants should be avoided in the atrophic edentulous mandible especially after

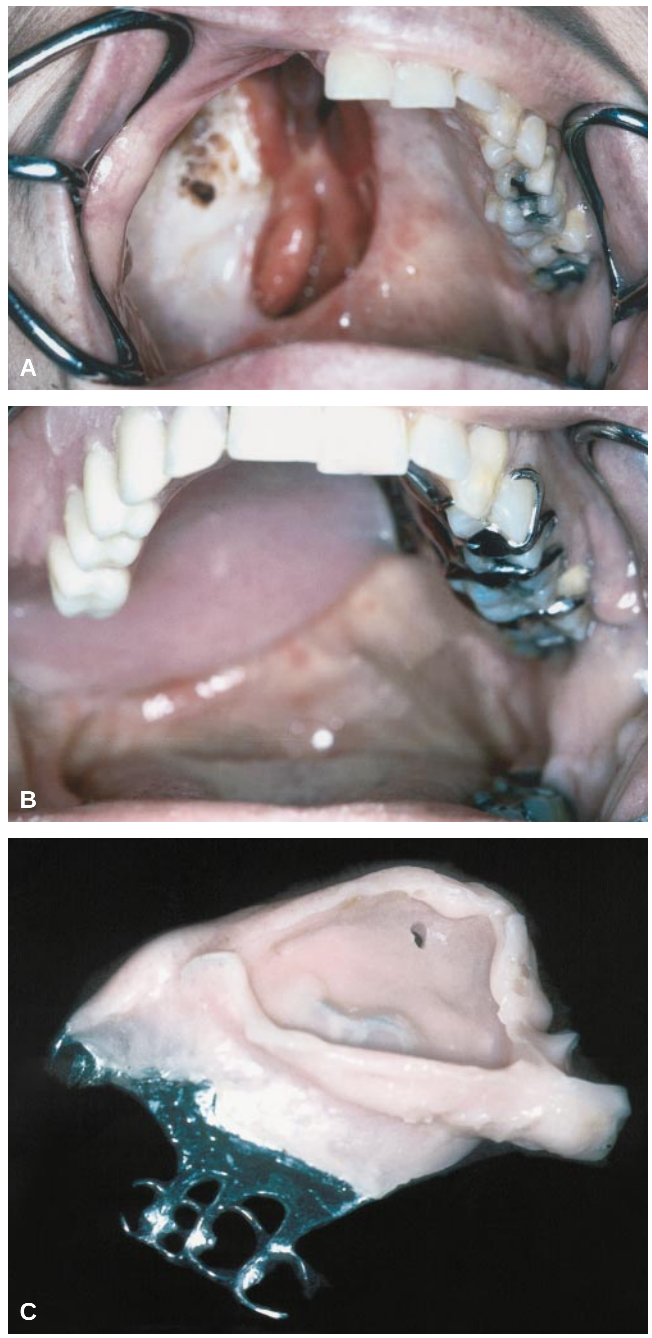


Figure 5–22. *A*, Maxillectomy defect with split-thickness skin graft. *B*, Prosthesis in place. *C*, Prosthesis.

radiation. Osseointegration can also be utilized effectively for external fixation of cosmetic prostheses after extended surgery for oral cavity cancer, which includes soft tissues of the face. It is important for the patient's rehabilitation that they have an acceptable cosmetic appearance in public.

Many patients benefit from evaluation and therapy by certified speech and swallowing therapists. They can often recommend exercises for the articulation of speech and can help both the patient and prosthodontist to optimize prostheses and to recommend alternative methods of phoneme formation.[59] Patients with significant resections of the lips, maxilla, tongue and palate will often benefit from speech therapy.

Speech and swallowing therapists can also help improve swallowing in patients who have undergone oral surgery.[60] A modified barium swallow under fluoroscopic observation by a radiologist and a speech therapist may be helpful diagnostically.[61] From this study, abnormalities of mastication, bolus preparation and bolus presentation of the oropharynx can be observed and studied frequently from this data. Strategies for improved function can be devised and taught to the patient and exercises implemented. Accompanying abnormalities of the pharyngeal phase of swallowing can also be diagnosed. Based on

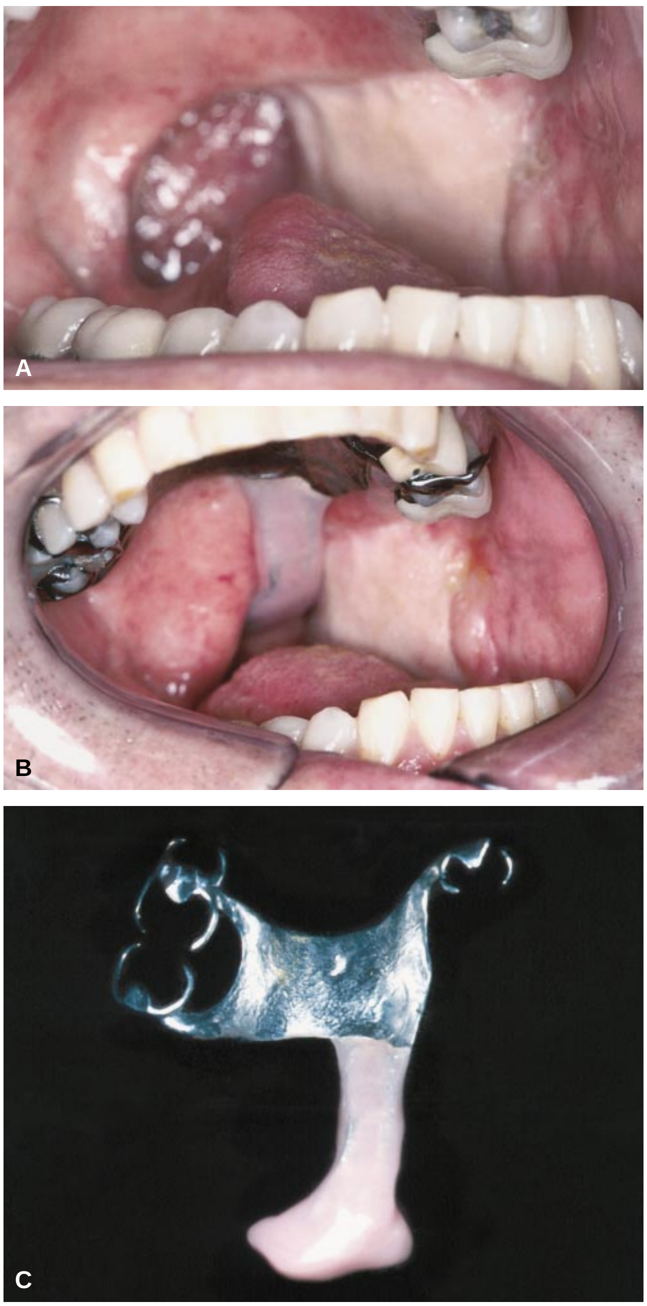


Figure 5–23 *A*, Soft palate defect after surgical resection and free flap reconstruction of the lateral pharyngeal wall. *B*, Prosthesis in place. *C*, The nasopharyngeal bulb prosthesis.

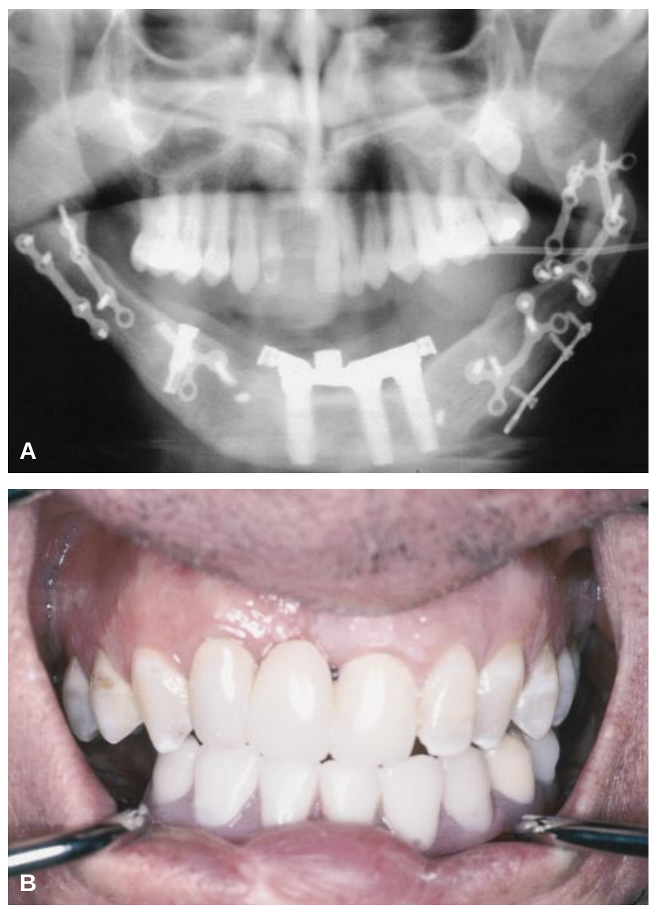


Figure 5–24. *A*, Panorex of osseointegrated implants in the anterior and right lateral aspects of a fibula free flap reconstruction of the mandible. *B*, The prosthesis in place.

the clinical findings and the modified barium swallow, therapists can also suggest optimal consistencies, and temperatures of food that can be best managed.

Consultation with a trained nutritionist with experience in treating head and neck cancer patients is essential to provide patients with information and suggestions regarding optimal foods to maintain a balanced nutrition within the patient's consistency restrictions. Patients with impaired oral function risk nutritional deficiency unless an appropriately varied diet is maintained. Many patients benefit from prepared commercial supplements, which are formulated specifically as a balanced diet. Some patients may subsist on liquid dietary supplements alone, while the majority benefit from regular foods as tolerated with additional dietary supplements as needed. Nearly any everyday food can be puréed with liquid in a blender and drunk. Patients should be weighed frequently in the postoperative period to monitor for weight loss. Supplemental tube feeding may be necessary while the patient is relearning swallowing.

Members of the rehabilitation team must educate the oral cancer patient regarding oral hygiene. Teeth brushing and fluoride treatments should be done at least twice daily. The patient should perform these fluoride treatments at home regularly using molded dental trays. Patients with post-radiation xerostomia require frequent sips of water, and may benefit from sialagogues such as lozenges or chewing gum; however it is critical that these be sugar free as the risk of caries is dramatically increased after radiation treatment. All patients with impaired oral function should be instructed to cleanse the oral cavity after eating. This may involve simple rinsing with water or saline solution or irrigation with a hanging bag and warm saline solution. Reconstruction flaps with skin lining the oral cavity may require frequent brushing to eliminate accumulated skin debris and sometimes trimming of the hair growing on the skin flaps is necessary for patient comfort and to decrease the adherence of food. Reconstructive flaps that have been irradiated no longer grow hair. Mouth washes, which contain alcohol, should be avoided as they dry the tissues and cause burning and discomfort. Normal saline or saline with bicarbonate of soda is preferred. Successful oral rehabilitation after oral cancer surgery requires a dedicated team of specialists working together. Each can contribute significantly toward the rehabilitation of speech, swallowing and appearance of the oral cancer patient.

SEQUELAE, COMPLICATIONS AND THEIR MANAGEMENT

Complications can be minimized by appropriate preoperative evaluation including medical cardiology and anesthesia consultation as indicated. Since the majority of oral cancer patients are elderly, many will have significant co-morbidities which need assessment, diagnosis or intervention prior to, or after, surgery. A preoperative medical evaluation is recommended for all patients over the age of 60 regardless of their health status. Routine preoperative testing should screen for previously undiagnosed major organ diseases and should consist of at least a preoperative chest radiograph, serum tests of renal and hepatic function and electrocardiography. Patients in negative nitrogen balance due to poor nutrition would be considered for a nasogastric feeding tube placement and several weeks of nutritional therapy prior to surgery. Properly selected patients should have a low incidence of major complications.[62]

The most common complications after oral surgery are wound related. The excellent blood supply to the oral cavity helps to ensure good healing of soft tissues and to resolve infection. Careful surgical technique can help to minimize complications. It is important to handle tissues atraumatically, avoid excessive char from electrocautery, observe careful hemostasis, obliterate any dead spaces and to minimize bacteria colony counts by gentle antiseptic preoperative preparation and copious irrigation with saline with or without antibiotics. Careful techniques of closure will help to minimize postoperative wound complications. Closure under tension should be avoided, especially of an irradiated tissue. Separate suture layers of muscle and mucosa should be performed. Oral wounds closed by primary intention will heal best. Many oral lesions will granulate well over several days to several weeks. Skin grafts can be helpful but are frequently lost when placed over mobile surfaces or directly over cortical bone. Any exposed bone or cartilage in the oral cavity will lead to granulation tissue formation and delay of healing.

Obviously carious or infected teeth should be removed at the time of surgery. Twenty-four hours of IV antibiotics, initiated at least 1 hour prior to surgery, may help to reduce the wound infection rate.

Other intraoperative measures to decrease complications include consideration of procedure duration to minimize the time of general anesthesia. Judicious intraoperative use of crystalloid will prevent postoperative complications of fluid overload. Insensate fluid loss in oral cavity surgery is significantly less than in abdominal surgery, which results in a lower requirement of intravenous fluid for oral cavity surgery patients than for abdominal surgery patients.

Postoperative management impacts significantly on complications of oral surgery. Aggressive oral irrigation should begin on the first day of the surgery. It should be accomplished with normal saline or normal saline and bicarbonate of soda solution in hanging irrigation bags or via compressed air-sprayer.

Major systemic complications are uncommon in oral cavity surgery. Cardiopulmonary complications occur due to pre-existing co-morbidities, the physiologic stress of surgery and fluid overload. Respiratory complications such as pneumonia can be minimized by appropriate early mobilization and the use of sequential compression devices, and careful observation for aspiration of liquids. Due to early mobilization, oral cavity cancer patients rarely suffer from deep venous thrombosis (DVT) or pulmonary embolism, however, immobilized patients should be placed on appropriate DVT prophylaxis, such as subcutaneous heparin or sequential compression devices.[63]

The majority of wound complications will heal with aggressive cleansing and infection control. Management of co-morbidities, such as diabetes mellitus, malnutrition and hypothyroidism, in order to maximize wound healing is critical. Poor healing or a persistent oral cutaneous fistula may result from the presence of a foreign body such as hardware, non-absorbable suture or sequestered bone. Persistent or recurrent tumor must be ruled out by biopsy in any non-healing wound after oral cancer surgery. The frequency, complexity and duration of wound complications are greater in the irradiated patient.

In summary, the incidence of major complications in oral cancer surgery can be minimized by appropriate patient selection, preoperative evaluation, meticulous technique and appropriate postoperative care.

OUTCOMES AND FUNCTION

Outcomes in oral cavity surgery may be divided into survival and functional outcomes. Five-year survival rates for early (T1 and T2) oral cancers are reported to be in the 70 to 90 percent range. In all head and neck sites, the presence of metastatic nodes to the neck decreases the survival by 50 percent. Five-year survival for patients with stage IV disease, especially with bulky or bilateral lower neck metastases, is less then 20 percent.[27]

In resectable stage III and stage IV tumors with N0 or N1 disease, 5-year survival has been increased to the 50 to 60 percent range by the aggressive addition of postoperative radiation therapy.[15,16] With improved local control rates a higher percentage of deaths are due to distant disease and second primary carcinomas rather than from uncontrolled locoregional disease.

Factors that predict survival of oral cancer patients are low T stage, low N stage, low overall stage, and the absence of significant co-morbidities. While the study of the molecular genetics of oral cancer is rapidly evolving, there are currently no molecular markers which have been shown to predict survival in head and neck cancer patients in large prospectively gathered series. It is however likely that in the next several years valid molecular markers will be developed which can predict tumor behavior, response to surgical and non-surgical treatment and patient survival rates.

Functional outcomes for surgery for early oral cancers is excellent. It is rare for patients to suffer significant loss of speech and swallowing function after surgical resection for T1 or T2 lesions. Even large T2 lesions of the tongue rehabilitate extremely well due to the plasticity of the tongue as well as its good blood supply, copious sensory innervation and the presence of intact musculature. Over 6 to 12 months, the patients invariably find dramatic improvement in articulation of speech sounds, mastication and swallowing. Aggressive and appropriate rehabilitation with speech and swallowing therapy and prosthodontics is critical to these results.

With increasing volumes of resected tissue, functional outcomes diminish. Tissues impacting most on function include tongue muscle, hypoglossal nerve, lingual nerve, anterior mandibular arch, and soft palate. When extensive or multiple resections of the above structures are undertaken for advanced disease, patient function may be poor even with the most advanced reconstructive and rehabilitative techniques. Despite improvements in postoperative function attributed to free flap reconstruction, the degree of coordination of motor and sensory function necessary for good oral function cannot be attained with the current technology. These patients are gastrostomy tube-dependent and speak poorly. Xerostomia from oral radiation therapy and trismus from surgery or radiation are also factors that can dramatically compromise function.

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