Oral Cavity and Oropharyngeal Squamous Cell Cancer: Key Imaging Findings for Staging and Treatment Planning[1]

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CME FEATURE

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LEARNING OBJECTIVES FOR TEST 2

After reading this article and taking the test, the reader will be able to:

- Recognize imaging findings of SCC of the oral cavity and oropharynx.
- Describe the TNM classification of SCCs of the oral cavity and oropharynx and its implications for treatment planning.
- Determine the potential routes of spread of SCC on the basis of the primary tumor site within the oral cavity and oropharynx.

TEACHING POINTS
See last page

The imaging findings in squamous cell carcinoma (SCC) of the oral cavity and oropharynx vary widely, depending on the site of origin of the primary tumor and the extent of its involvement of other regions. Knowledge of the complex anatomy of the oral cavity and oropharynx, as well as the most common routes by which SCC spreads from various anatomic sites, allows the radiologist to accurately determine the extent of disease and help clinicians plan appropriate treatment. SCCs that originate in the oral cavity tend to behave differently than those that originate in the oropharynx, with the latter group exhibiting more aggressive growth. Furthermore, primary tumors in certain anatomic subsites within the oral cavity or oropharynx have a greater propensity to spread by direct extension along muscle, bone, or neurovascular bundles or to be disseminated along lymphatic drainage pathways to regional or distant nodes. Imaging findings of deep muscular, neurovascular, osseous, or nodal involvement are indicative of an advanced stage of disease for which management options are limited.

Abbreviations: HPV = human papillomavirus, SCC = squamous cell carcinoma

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Introduction

Squamous cell carcinoma (SCC) accounts for the vast majority of malignancies of the oral cavity and oropharynx and is commonly evaluated with radiologic imaging. The symptoms of disease, the routes by which it may spread, and the prognosis vary greatly, depending in large part on the anatomic site at which the primary tumor originates. The complexity of the anatomy in the oral cavity and oropharynx requires that clinicians and radiologists be able to distinguish among multiple anatomic subdivisions of these two regions. Knowledge of the anatomy and the most common routes of spread of SCC from each site of origin is essential information for diagnostic assessment, disease classification, and optimal treatment planning. Inaccurate assessment of the extent or stage of disease may lead to unnecessary or incomplete surgical or radiation therapy, with a negative outcome.

The article reviews the potential routes of spread of SCCs of the oral cavity and oropharynx according to the anatomic subsite in which the primary tumor originates, with an emphasis on imaging features that affect staging and treatment planning.

Epidemiologic and Etiologic Considerations

Most oral cavity and oropharyngeal lesions are benign. Among the malignant lesions occurring in this region, SCCs predominate, accounting for more than 90%. Other malignancies that may occur in the oral cavity or oropharynx include minor salivary gland tumors, lymphomas, and various mesenchymal tumors. The most commonly recognized risk factors for SCC include long-term overuse of alcohol and tobacco. In addition, human papillomavirus (HPV) was shown to be associated with the development of a unique papillary type of SCC within the upper aerodigestive tract, with HPV-16 accounting for 90%–95% of such cases.

Teaching Point

Studies have shown that approximately 25% of all head and neck cancers and 60% of all oropharyngeal cancers are HPV positive, a finding that may drastically alter treatment planning (1,2).

Anatomic Subdivisions

To accurately evaluate SCCs of the oral cavity and oropharynx, the radiologist and clinician must distinguish among multiple subdivisions of the anatomy. The most basic division is that between the oral cavity and oropharynx: The squamous epithelium within the oropharynx derives from endoderm and demonstrates a greater propensity for the development of poorly differentiated, aggressive carcinomas. In contradistinction, the squamous epithelium of the oral cavity derives from ectoderm and tends to give rise to more differentiated, less aggressive lesions. The ability to distinguish among specific sites of origin (subsites) within these larger anatomic divisions is important because routes of spread, lymphatic drainage patterns, and surgical approaches vary, depending on the subsite (see "Oral Cavity Subsites" and "Oropharyngeal Subsites").

Anatomy of the Oral Cavity

The oral cavity is the most ventral portion of the aerodigestive tract. It is separated from the oropharynx by a ring of structures consisting of the circumvallate papillae inferiorly, the soft palate superiorly, and the anterior tonsillar pillars on both sides. The anatomic subdivisions of the oral cavity are *(a)* the lips, *(b)* the floor of the mouth, *(c)* the oral tongue (ie, the anterior two-thirds of the tongue), *(d)* the buccal mucosa, *(e)* the upper and lower gingivae, *(f)* the hard palate, and *(g)* the retromolar trigone. Within the oral cavity, the lower lip, oral tongue, and floor of the mouth, in order of decreasing frequency, are the sites of the primary tumor in more than 75% of patients with SCC.

Anatomy of the Oropharynx

The oropharynx is the part of the pharynx that is posterior to the oral cavity, between the nasopharynx and the hypopharynx. The oropharynx contains the base (posterior one-third) of the tongue, palatine tonsils, soft palate, and oropharyngeal mucosa. The anterior border of the oropharynx is a plane formed by the circumvallate papillae, anterior tonsillar pillars, and soft palate. Its posterior border is the posterior pharyngeal wall. The oropharynx is bordered superiorly by the level of the elevated soft palate and inferiorly by the valleculae. The lateral borders of the oropharynx are the tonsillar regions, which contain the anterior and posterior tonsillar pillars (the palatoglossus and palatopharyngeus muscles, respectively) and the palatine tonsils. The anatomic subdivisions of the oropharynx are *(a)* the base of the tongue and *(b)* the tonsils. SCC of the pharyngeal wall is rare and is not described in this article.

Table 1
TNM Classification of SCCs of the Oral Cavity and Oropharynx

Disease Category	Defining Characteristics
	Primary Tumor of Oral Cavity
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor is seen
Tis	Primary tumor is carcinoma in situ
T1	Primary tumor has a maximal diameter of 2 cm or less
T2	Primary tumor has a maximal diameter of more than 2 cm but no more than 4 cm
T3	Primary tumor has a maximal diameter of more than 4 cm
T4a	
Lip	Primary tumor involves cortical bone, inferior alveolar nerve, floor of the mouth, skin
Oral cavity	Primary tumor involves cortical bone, intrinsic or extrinsic muscles of the tongue, maxillary sinus, skin
T4b	Primary tumor involves masticator space, pterygoid plates, skull base, internal carotid artery
	Primary Tumor of Oropharynx
Tx	Primary tumor cannot be assessed
T0	No evidence of primary tumor is seen
T1	Primary tumor has a maximal diameter of less than 2 cm
T2	Primary tumor has a maximal diameter of 2–4 cm
T3	Primary tumor has a maximal diameter of more than 4 cm
T4a	Primary tumor involves the larynx, intrinsic or extrinsic muscles of the tongue, medial pterygoid, hard palate, mandible
T4b	Primary tumor involves lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base, carotid artery
	Regional Metastasis
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis is evident
N1	Ipsilateral single enlarged node with a maximal diameter of less than 3 cm
N2a	Ipsilateral single enlarged node with a maximal diameter of 3–6 cm
N2b	Ipsilateral multiple enlarged nodes with a maximal diameter of less than 6 cm
N2c	Bilateral or contralateral enlarged nodes with a maximal diameter of less than 6 cm
N3	Enlarged node with a maximal diameter of more than 6 cm
	Distant Metastasis
M0	No distant metastasis is evident
M1	Distant metastasis is evident

Disease Staging

SCCs of the oral cavity and oropharynx and nonsquamous carcinomas of the minor salivary glands are staged by using the TNM classification system. There are currently 32 possible combinations of T, N, and M categories, which are aggregated into seven stages of SCC: 0, I, II, III, IVA, IVB, and IVC. The grouping of TNM categories into stages represents both homogeneous survival data and important variations in disease characteristics that may affect treatment options (Tables 1, 2). However, these disease stage groups have not yet been validated in any prospective multivariate trial. Differentiation between SCCs of stage I or II and those of stage III or IV is most important for treatment planning, because tumors of stage

I or II are typically treated with single-modality therapy (either surgical resection or radiation therapy), whereas those of stage III or IV may require multimodality therapy with a combination of chemotherapy, radiation, and surgical resection. The therapeutic modalities that are selected are often specific to the anatomic subsite in which the primary tumor originated (3).

The division of stage IV lesions into three distinct subcategories based on different therapeutic strategies is the result of revisions introduced in the sixth edition of the classification system in 2002. The terminology for T4 lesions and stage IV disease was also changed in the seventh edition in 2007. Stage IVA denotes moderately advanced local-regional disease; stage IVB, very advanced local-regional disease; and stage IVC, distant metastatic disease. T4a and T4b lesions are now referred to, respectively, as “moderately advanced” and “very advanced” instead of “resectable” and “unresectable.” Lesions of stage IVA or IVB may be treated with combined chemo- and radiation therapy for regional control, whereas stage IVC disease is characterized by distant metastases and therefore is treated with palliative therapy only.

Routes of Spread

Teaching Point

SCCs of the oral cavity and oropharynx may spread in three general ways: *(a)* by direct extension over mucosal surfaces, muscle, and bone, *(b)* by dissemination via lymphatic drainage pathways, and *(c)* by extension along neurovascular bundles (4). For accurate staging of SCCs of the oral cavity and oropharynx, evaluation of these three routes of spread is mandatory. Some anatomic structures must be routinely assessed for involvement in SCC if the primary tumor is in certain anatomic subsites (for details, see “Oral Cavity Subsites” and “Oropharyngeal Subsites”).

Direct Extension

Oral cavity and oropharyngeal SCCs are amenable to direct visualization, and the extent of mucosal spread is therefore best estimated with a physical examination. Superficial mucosal lesions are not often radiographically evident. However, the overall extent of a tumor is often underestimated at physical examination because of the inability to detect submucosal spread and direct invasion of adjacent structures.

Table 2
Oral Cavity and Oropharyngeal SCC Stages Based on TNM Classification

Cancer Stage	T Category	N Category	M Category
0	Tis	N0	M0
I	T1	N0	M0
II	T2	N0	M0
III	T1, T2	N1	M0
	T3	N0, N1	M0
IVA	T1, T2, T3	N2	M0
	T4a	N0, N1, N2	M0
IVB	Any	N3	M0
	T4b	Any	M0
IVC	Any	Any	M1

Teaching Point

The presence of osseous involvement is indicative of a T4 lesion. Subtle cortical erosions are best detected with computed tomography (CT), whereas the extent of marrow involvement may be better assessed by using magnetic resonance (MR) imaging. CT findings of osseous involvement include cortical erosion adjacent to the primary lesion, aggressive periosteal reaction, abnormal attenuation in bone marrow, and pathologic fractures. Typical CT examinations of the neck are performed with a section thickness of 2.5 mm. If there are equivocal findings of bone involvement on the initial CT images, thin-section CT may be performed with a commercially available application such as Dentascan (GE Healthcare, Milwaukee, Wis). CT of dental bone typically is performed with a section thickness of 1.0 mm, and multiple panoramic and cross-sectional views are reconstructed from the acquired image data. Using this technique, Brockenbrough et al (5) demonstrated a sensitivity of 95% (21 of 22 patients) for the detection of cortical erosions.

Study results indicate that although MR imaging has good sensitivity for the detection of osseous involvement, its specificity is not as high (6). MR imaging findings that are suggestive of osseous involvement include loss of low-signal-intensity cortex; replacement of high-signal-intensity marrow on T1-weighted images by intermediate-signal-intensity tumor; contrast enhancement within bone; and contrast enhancement of nerves traversing the mandible, especially the inferior alveolar nerve. Conditions that may lead to false-positive findings of osseous involvement in SCC include recent tooth extraction, radiation-induced fibrosis, and osteoradionecrosis. Imaizumi et al (7) showed that false-positive findings at MR imaging were due either to chemical shift artifacts in the evaluation of mandibular cortical invasion or to overestimation of inferior alveolar canal involvement secondary to adjacent inflammation from peritumoral edema, reactive changes, or fibrosis.

The osseous structures most commonly affected are the mandible and the maxilla. Evidence of osseous involvement seen at imaging precludes a wide local excision during surgical treatment. The treatment of choice is then a partial mandibulectomy or maxillectomy. The degree of osseous involvement dictates the extent of resection required for appropriate oncologic control. If the lesion abuts the mandible but is freely mobile on examination, then a wide excision with resection of the periosteum is undertaken. In cases where a lesion is fixed on examination and adherence with minimal or subtle cortical involvement is observed at imaging, a marginal mandibulectomy may be performed with excision of either the gingival aspect of the mandible or the lingual cortex, without sacrificing an entire segment. However, in the presence of gross cortical invasion or involvement of the mental or inferior alveolar nerves, a segmental mandibulectomy is required, necessitating a more complex reconstruction, most often with vascularized bone and soft tissue (ie, fibular free flap). The choice between a marginal and a segmental mandibulectomy is often challenging and is influenced by intraoperative assessment by the surgeon (8).

Lymphatic Dissemination

The lymphatic dissemination of SCC is often detectable clinically but is most accurately assessed with imaging. A large percentage of oral and oropharyngeal SCCs initially manifest with a neck mass that represents the involvement of cervical nodes. Because nodal involvement is the single most important prognostic indicator, an accurate assessment of all nodal chains at the same time is required. In cases of SCC within the oral cavity, the level I and II lymph nodes are often the first to be involved. Dissemination from the oropharynx is usually to the ipsilateral internal jugular nodes, particularly those at levels II and III, and retropharyngeal nodes. The rates of regional metastasis from primary SCCs in the oral cavity and oropharynx vary according to anatomic subsite and T category.

Teaching Point

Among SCCs of the oral cavity, those in the retromolar trigone and floor of the mouth show a strong predilection for lymphatic involvement, with nearly 50% of patients presenting with regional disease. SCCs in the oral tongue manifest with regional disease in 40% of patients, whereas SCCs in the lip, buccal mucosa, and hard palate are less likely to manifest with lymphadenopathy. Those in the lip manifest with lymphadenopathy in only 10% of cases. In such cases, lymph nodes on either side of the neck may be involved, as lymphatic drainage from the lip is bilateral. SCC in the hard palate manifests with lymphadenopathy in 10%–25% of cases (8).

Approximately 65% of patients with oropharyngeal SCCs present with cervical lymphadenopathy due to metastases. When the rates of regional metastasis of oropharyngeal SCCs are compared according to the anatomic subsite of the primary tumor, the base of the tongue is associated with the highest frequency of regional disease, followed by the tonsillar fossa, oropharyngeal wall, and soft palate (9).

The imaging assessment of cervical lymphadenopathy in patients with head and neck cancers includes a determination of node size, morphologic features, and margination. The cardinal imaging features of pathologic lymphadenopathy are large nodal size and the presence of central necrosis in the node. The usual size criterion is a maximal longitudinal diameter of more than 15 mm for jugulodigastric lymph nodes and more than 10 mm for other nodes (except retropharyngeal lymph nodes, which are considered pathologic at a diameter of more than 8 mm). However, if the minimal axial diameter is the parameter measured, a size of 11 mm for jugulodigastric (level II) nodes and 10 mm for other nodes is considered indicative of abnormality (10). The latter criterion changes to more than 8 or 9 mm when more than three enlarged nodes are seen in the same lymphatic drainage area. Regardless of size, enlargement of lymph nodes after surgical excision of a primary SCC may portend a poor outcome.

Assessment of nodal morphologic characteristics is equally important. Normal nodes tend to be reniform, whereas pathologic nodes are more likely to be round. Nodal necrosis may be identified as a central region of hypoattenuation with a rind of enhancing tissue on CT. If nodes appear with internal attenuation resembling that of water

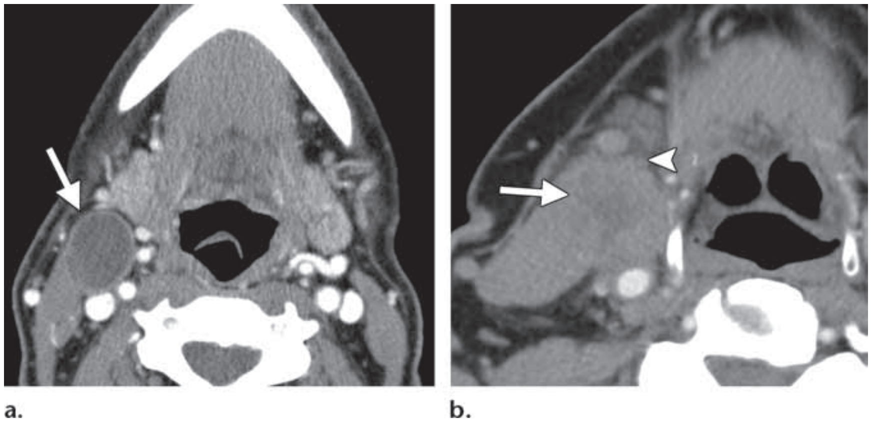


Figure 1. **(a)** Contrast-enhanced CT image depicts a cystic right-sided level IIA lymph node (arrow) in a patient with HPV-positive tonsillar SCC. The primary tumor is not shown. **(b)** Contrast-enhanced CT image obtained in another patient shows a right-sided level IIA lymph node with central hypoattenuation indicative of necrosis. Indistinct anterior nodal margins with soft-tissue infiltration of fat (arrow) and lack of margination between the lymph node and sternocleidomastoid muscle (arrowhead) are indicative of extracapsular spread of SCC.

on CT images or with signal intensity of fluid on MR images, the term *cystic adenopathy* may be applied. This finding, which is sometimes associated with HPV-positive SCC (Fig 1a), should not be confused with a branchial cleft cyst (11). A finding of extracapsular spread at CT or MR imaging is important because it is associated with a 3.5-fold increase in the local recurrence rate (12). Imaging features of extracapsular spread include poorly defined nodal margins and soft-tissue stranding around nodes (Fig 1b). At MR imaging with T2-weighted fat-suppressed and contrast material–enhanced T1-weighted techniques, the ranked predictive criteria for extracapsular spread include high signal intensity in tissues surrounding a node (so-called flare sign), a poorly defined nodal border, irregular rimlike enhancement of a node, and large nodal size (13).

Neurovascular Spread

Vascular and perineural invasion make local and regional control particularly difficult by allowing tumor extension beyond the expected treatment margins. The presence of vascular invasion is associated with an increased likelihood of nodal involvement, which, as previously mentioned, is the single most important prognostic indicator. Because perineural invasion is often clinically silent and cannot be detected at physical examination, it is particularly important that the radiologist be alert to this possibility. Perineural spread is more common in subsites such as the floor of the mouth, where the neurovascular bundles are particularly accessible. Perineural invasion is thought to be characteristic of aggressive SCCs. If the initial treatment is surgical resection, findings of perineural, lymphatic, or vascular invasion at pathologic analysis necessitate postoperative adjuvant radiation therapy (14). Imaging features of perineural spread include foraminal enlargement and replacement of normal fat within the neural foramen. The nerve may appear enlarged on contrast-enhanced MR images, a change that cannot be seen on CT images (15,16).

Teaching Point

Oral Cavity Subsites

Lip

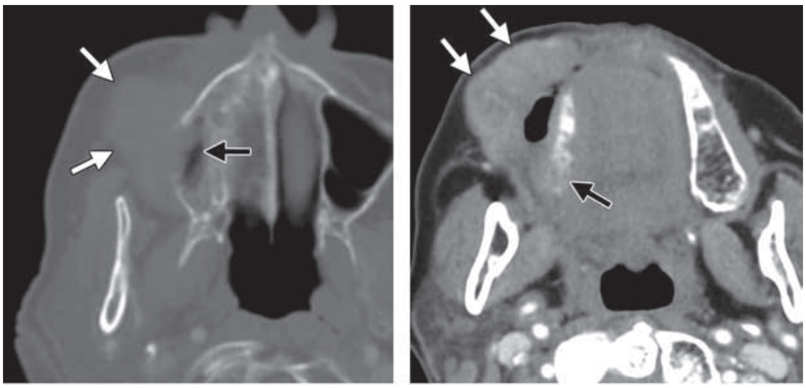
The lip is the most common site of SCC of the oral cavity (approximately 40% of cases). SCC of the lip tends to arise from the vermilion border and spread by lateral extension to the skin or by deep extension to the orbicularis oris muscle. Lip lesions are easily assessed with direct visualization, and only infiltrative tumors with uncertain margins require imaging. Even so, early-stage lesions are often difficult to differentiate from the normal orbicularis oris muscle.

The key features that should be sought in the presence of an SCC of the lip include osseous invasion and lymphatic involvement (17). Lymphatic spread is primarily through level I and II lymph nodes. Osseous involvement usually occurs along the buccal surface of the maxillary

RadioGraphics

a. b. c.

Figure 2. **(a)** Axial contrast-enhanced CT image (soft-tissue window) demonstrates an enhancing soft-tissue mass (arrows) along the right mandible, an extension of a primary SCC of the lip. **(b)** Axial contrast-enhanced CT image (bone window) shows cortical erosion (arrow) along the right buccal aspect of the mandibular alveolus. This finding led to reclassification of the tumor as a T4a lesion. **(c)** Three-dimensional volume-rendered CT image depicts postoperative changes in the mandible after a rim mandibulectomy, the preferred surgical treatment for SCCs involving cortical but not medullary bone.



a. b.

Figure 3. **(a)** Axial contrast-enhanced CT image (soft-tissue window) demonstrates an enhancing soft-tissue mass (white arrows) along the buccal mucosa, a finding consistent with SCC. Erosion of the adjacent maxilla (black arrow) also is seen. **(b)** Axial contrast-enhanced CT image (bone window) depicts a buccal lesion (white arrows) that has eroded and infiltrated the maxillary sinus (black arrow). Bone erosion and sinus invasion are indicative of a T4a lesion.

or mandibular alveolar ridge (Fig 2). Osseous infiltration creates the opportunity for perineural invasion along the alveolar nerves, which makes local-regional control particularly difficult.

Buccal Mucosa and Gingiva

The buccal mucosa covers the cheeks and lips. It is continuous with the buccal aspect of the gingiva of the maxillary and mandibular alveolar ridge, as well as the retromolar trigone. Buccal SCC tends to occur on the lateral walls and is often difficult to differentiate from the orbicularis oris muscle at imaging. The superficial spread of these lesions is best assessed clinically, but their detection at CT often can be improved by having the patient perform special maneuvers during image acquisition, such as puffing the cheeks outward (18).

Buccal SCC tends to be low grade and to spread submucosally, most commonly along the buccinator muscle. Evaluation of a buccal or gingival mucosal lesion should address the extent of submucosal spread, osseous involvement, involvement of the retromolar trigone and pterygomandibular raphe, and cervical lymphatic spread.

Involvement of the mandible, as opposed to the maxilla, introduces the possibility of perineural or intramedullary extension. Tumor involvement of the maxilla may also allow spread into the paranasal sinuses (Fig 3). Tumor extension into the retromolar trigone and pterygomandibular raphe is of particular concern because these structures provide numerous routes of spread, making surgical treatment more difficult; therefore, involvement of these structures is discussed further in the next section. Last, lymphatic spread tends to occur predominantly to level I and II lymph nodes.

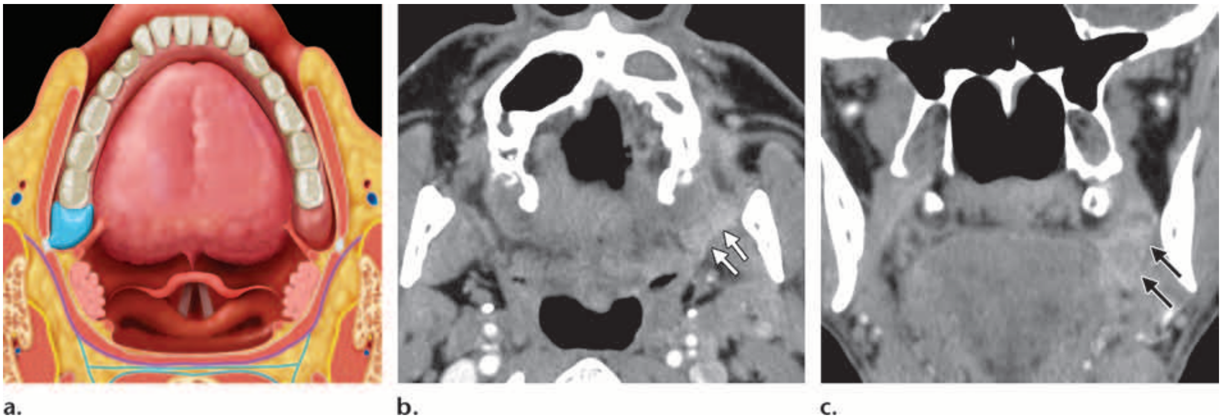


Figure 4. **(a)** Axial diagram of the mandible shows the retromandibular trigone (crescent-shaped blue region). (Reprinted with permission from Amirsys, Salt Lake City, Utah.) **(b, c)** Axial **(b)** and coronal **(c)** contrast-enhanced CT images show SCC involvement of the left retromolar trigone (arrows) and a normal appearance of the right retromolar trigone.

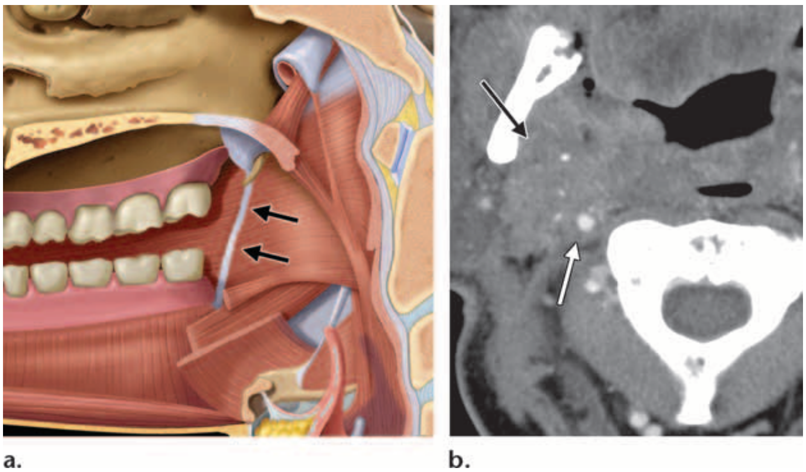
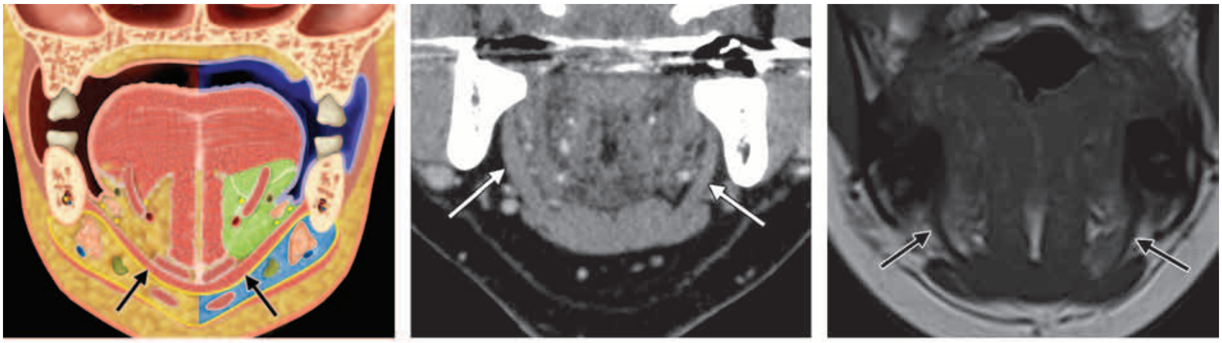


Figure 5. **(a)** Sagittal diagram demonstrates the pterygomandibular raphe (arrows) extending from the hamulus of the medial pterygoid plate to the mandibular mylohyoid ridge. (Reprinted with permission from Amirsys, Salt Lake City, Utah.) **(b)** Axial contrast-enhanced CT image shows a primary tonsillar SCC that has infiltrated the right pterygomandibular raphe, invading the right masticator space (black arrow). The white arrow indicates circumferential invasion of the internal carotid artery.

Retromolar Trigone

The retromolar trigone is a triangle-shaped area of mucosa posterior to the last mandibular molar that covers the anterior surface of the lower ascending ramus of the mandible (Fig 4a). Imaging evaluation of the retromolar trigone is critical because the extent of SCC involvement of this subsite cannot be determined clinically (Fig 4b, 4c). Evaluation of SCC involvement of the retromolar trigone should include assessments of submucosal spread, including involvement of the muscles of mastication; osseous involvement; neurovascular extension; and cervical lymphatic spread.

SCC of the retromolar trigone may be primary or may result from regional extension. The clinical significance of the retromolar trigone is that it provides easy access to numerous routes of spread. The tumor may spread to sites posterior to the mandibular ramus, the masticator space, the superior constrictor muscles, and the mandibular branch of the trigeminal nerve. Anterior spread occurs along the alveolar ridge, and infe-



a. b. c.

Figure 6. **(a)** Diagram shows the mylohyoid muscle (arrows), a muscular sling that separates the sublingual space superomedially from the submandibular space inferolaterally. (Reprinted with permission from Amirsys, Salt Lake City, Utah.) **(b, c)** Coronal contrast-enhanced CT image **(b)** and unenhanced T1-weighted MR image **(c)** obtained in two different patients show normal appearances of the mylohyoid muscle (arrows).

rior spread occurs along the mandible and inferior alveolar nerve. The tumor also may spread along the pterygomandibular raphe, a thick fascial band that extends between the posterior border of the mandibular mylohyoid ridge and the hamulus of the medial pterygoid plate (Fig 5a). The pterygomandibular raphe provides access to the masticator space superolaterally (Fig 5b) and the floor of the mouth inferomedially. Involvement of the medial pterygoid muscle is often clinically evidenced by trismus.

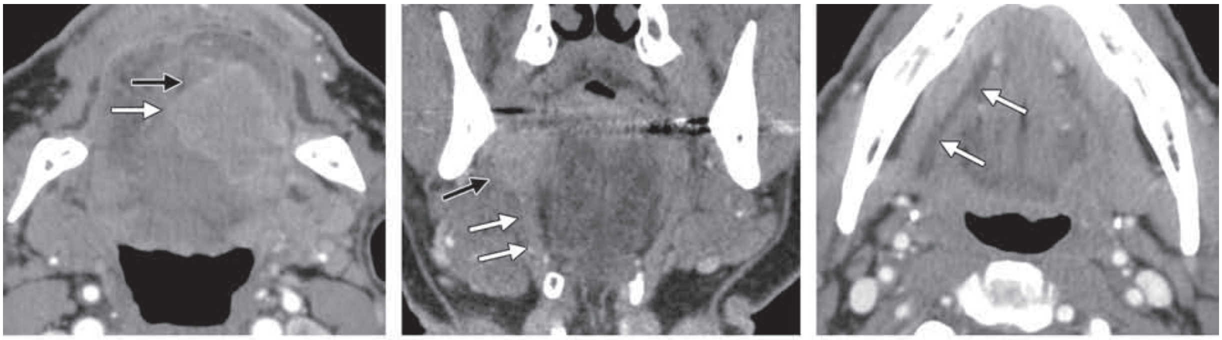
Contrast-enhanced CT allows evaluation of both the soft tissues and bones, but the image quality is often limited by artifact from dental amalgam. MR imaging is often useful for assessing invasive retromolar trigone lesions because it is less affected by dental amalgam artifact (19). In particular, axial T2-weighted images and axial T1-weighted fat-saturated images are useful for evaluating the extension of SCC cephalad when the pterygomandibular raphe is involved.

Floor of the Mouth

The floor of the mouth is the third most common subsite of SCC of the oral cavity. A crescent-shaped area, the floor of the mouth is bordered by the lingual aspect of the lower gingiva anteriorly, the alveolar ridge of the mandible laterally, the insertion of the anterior tonsillar pillar into the tongue posteriorly, and the free inferior aspect of the tongue medially. Anteriorly, the floor of the mouth is divided in half by the lingual frenulum. The sublingual and submandibular glands drain into the floor of the mouth via the major sublingual (Bartholin) ducts and submandibular (Wharton) ducts, respectively. The main supporting structure of the floor of the mouth is the mylohyoid muscle, which originates along the mylohyoid line of the medial surface of the mandible and inserts into a midline fibrous raphe and the body of the hyoid (Fig 6). The mylohyoid muscle serves as a key anatomic landmark separating the sublingual space from the submandibular space, although there is continuity between these spaces along the posterior aspect of the muscle.

Superficial lesions at this site are often difficult to assess at imaging. However, imaging is necessary to define the extent of disease because it is difficult to ascertain the depth of invasion at physical examination. Evaluations of SCC of the floor of the mouth should include a determination of the extent of submucosal invasion (whether the midline is crossed, whether the tumor extends into the submandibular space), involvement of the neurovascular pedicle, mandibular osseous involvement, and cervical lymphatic involvement.

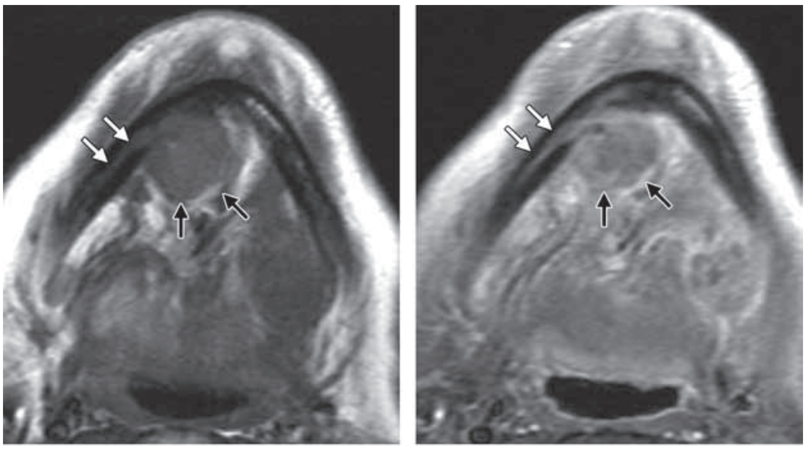
Submucosal involvement is often the most difficult parameter to assess because visualization of SCC is poor in this subsite, and the lesion may extend along multiple routes. Routes of spread include deep invasion of the adjacent neurovascular bundle, hyoglossus muscles, and mylohyoid muscle. The neurovascular bundle is particularly vulnerable to invasion by cancers in the floor of the mouth, a site that permits easy perineural extension. Close inspection of the neurovascular bundle and the midline lingual septum is therefore critical. As with SCCs in the tongue, crossing of the midline of the tongue by SCCs in the floor



a. b. c.

Figure 7. SCCs of the floor of the mouth. **(a)** Axial contrast-enhanced CT image depicts a tumor (white arrow) that crosses the midline of the tongue, which is demarcated by the fatty lingual septum (black arrow). **(b)** Coronal contrast-enhanced CT image obtained in another patient shows direct tumor extension (black arrow) through the superior aspect of the mylohyoid muscle (white arrows). **(c)** Axial contrast-enhanced CT image obtained in a third patient demonstrates dilatation of the right submandibular duct (arrows), a finding indicative of ductal involvement in SCC.

Figure 8. Axial unenhanced **(a)** and contrast-enhanced **(b)** T1-weighted MR images demonstrate an enhancing SCC (black arrows) of the floor of the mouth with invasion of the lingual cortex. A linear region of abnormal enhancement in the right hemimandible (white arrows) is suggestive of involvement of the mandibular canal and the right inferior alveolar nerve.



a. b.

of the mouth precludes a partial glossectomy (Fig 7a). Tumors may also extend beyond the sublingual space to infiltrate the submandibular space. Involvement of the mylohyoid muscle may be directly depicted on coronal images (Fig 7b) or signaled by secondary signs such as obstruction of the submandibular duct (Fig 7c).

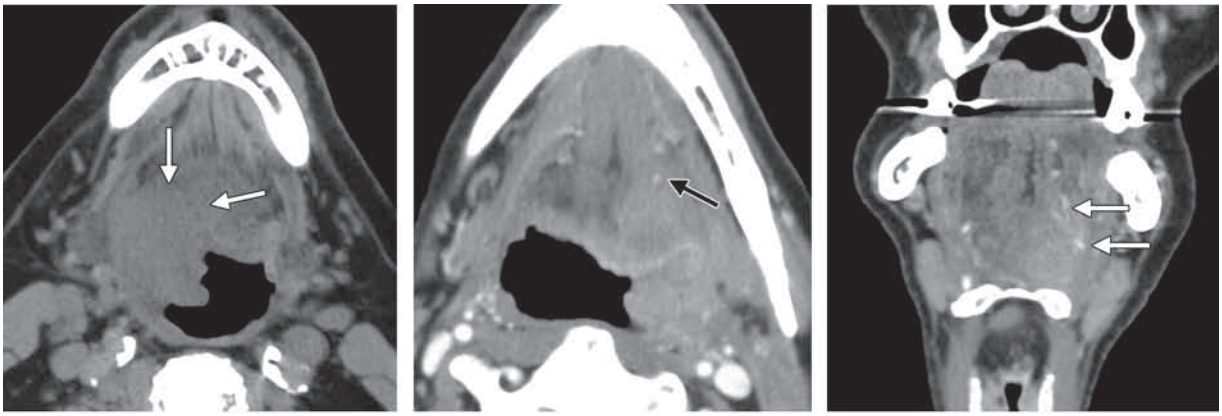
Osseous invasion by SCCs of the floor of the mouth has been previously described. A finding of mandibular bone invasion mandates an assessment of the inferior alveolar nerve (Fig 8). With regard to sites of frequent lymphatic spread, SCCs of the floor of the mouth spread primarily to level I and II lymph nodes.

Oral Tongue

The oral tongue consists of the anterior and middle thirds of the tongue; the posterior third (the base) of the tongue is considered part of the oropharynx. Evaluation of an oral tongue lesion requires assessments for involvement of the submucosa, the intrinsic musculature of the tongue, the neurovascular bundle, bone, and cervical lymph nodes, as well as invasion across the midline of the tongue.

SCCs of the oral tongue occur predominantly along its lateral and ventral surfaces. Oral tongue lesions tend to spread along the submucosa and may involve the floor of the mouth and the mandibular gingiva. Infiltration of the mandibular gingiva may lead to osseous involvement, which, as with oral cavity SCCs, mandates the classification of primary oropharyngeal SCCs as T4a lesions.

Oral tongue lesions also tend to invade the tongue musculature, which provides an easy route of spread deep into the intrinsic muscles of the oral tongue (Fig 9a) and along the extrinsic



a. b. c.

Figure 9. **(a)** Axial contrast-enhanced CT image depicts a primary SCC of the oral tongue (arrows). Invasion of the intrinsic muscles of the tongue is indicative of a T4a lesion. **(b, c)** Axial **(b)** and coronal **(c)** contrast-enhanced CT images obtained in another patient show a primary SCC of the oral tongue that encases the ipsilateral left neurovascular bundle and extends to the base of the tongue and lateral oropharyngeal wall. Arrows indicate blood vessels within the neurovascular bundle.

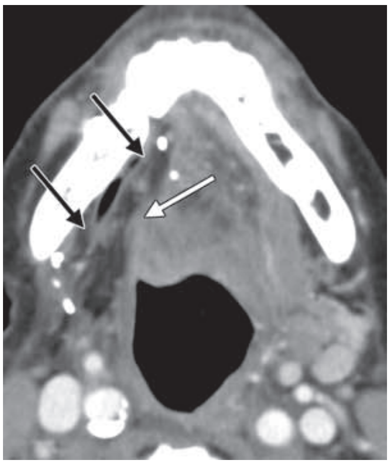


Figure 10. Contrast-enhanced CT image demonstrates a normal baseline postoperative appearance after a radial forearm myocutaneous free flap reconstruction of the floor of the mouth. Black arrows indicate the fatty component of the flap, and the white arrow indicates the muscular portion. Note the numerous surgical clips.

muscles to their sites of attachment. Involvement of the intrinsic muscles leads to categorization of a primary tumor as a T4a lesion (20). The intrinsic muscles of the tongue include the inferior and superior longitudinal muscles, the transverse muscle, and the vertical muscle. The extrinsic muscles (and their sites of attachment) include the genioglossus (mandible), styloglossus (styloid process), palatoglossus (soft palate), and hyoglossus (hyoid bone). Involvement of any of the extrinsic muscles necessitates evaluation of the muscle at the site of its attachment.

With SCCs of the oral tongue, as with SCCs of the floor of the mouth, evaluation of the neurovascular bundle is essential (Fig 9b, 9c). Evaluation of the midline of the tongue and the contralateral neurovascular bundle is important for surgical planning because any invasion of the midline precludes hemiglossectomy.

Various procedures might be used for surgical reconstruction of tongue defects after tumor excision, depending on the extent of tumor involvement and the resultant functional deficits. In general, the defect left by a partial glossectomy (excision of one quarter to one third of the tongue) may be reconstructed with primary closure, a skin graft (to prevent tethering of the tongue to the floor of the mouth if part of the mucosa was removed during tumor excision), or both. Involvement of the intrinsic musculature or more than a third of the tongue by a tumor often results in substantial deficits in speech and swallowing after resection, as the tongue may have insufficient length and substance to position food posteriorly or to contact the teeth, lips, and palate. The defects in such cases are frequently repaired with a free flap consisting of a thin layer of pliable fasciocutaneous tissue harvested from the radial forearm or anterolateral thigh. Reconstruction with a free flap is also indicated if significant portions of the floor of the mouth and the tongue are resected (Fig 10).

The pattern of lymphatic spread of SCCs of the oral tongue is similar to that of SCCs of the

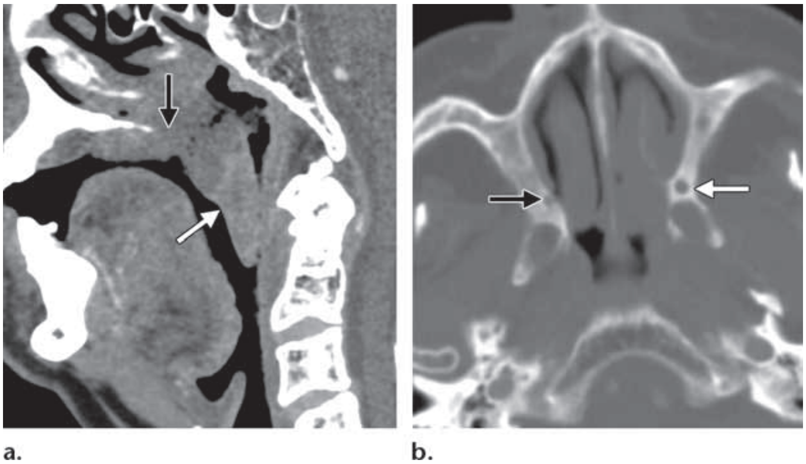


Figure 11. **(a)** Sagittal contrast-enhanced CT image depicts a primary SCC of the hard palate with erosion of bone (black arrow) and extension into the nasopharynx, as well as posterior spread along the soft palate (white arrow). **(b)** Axial contrast-enhanced CT image (bone window) demonstrates asymmetric enlargement of the left greater palatine foramen (white arrow) in comparison with the right (black arrow), a finding suggestive of tumor extension along the greater palatine nerve.

lip and floor of the mouth, predominantly involving level I and II nodes. However, studies have shown a tendency toward "skip lesions" (eg, regional spread to level III and IV nodes, without involvement of level I and II nodes) in 15% of SCCs in the lateral aspects of the oral tongue. Consequently, neck dissection in patients with SCCs in such sites typically involves the removal of nodes from level I through level IV (21). In addition, since there is significant cross drainage of lymph in the oral tongue, bilateral cervical lymph node involvement is common. Bilateral lymphadenopathy is frequently seen in stage IV lesions.

Hard Palate

Primary SCC of the hard palate is rare and often represents extension from an adjacent gingival lesion. Lesions in this subsite are best demonstrated on sagittal and coronal images because of the axial orientation of the hard palate. When such a lesion is found, the site should be evaluated carefully for evidence of osseous involvement and perineural spread. SCC of the hard palate may extend laterally to invade the maxillary alveolar ridge or superiorly to involve the nasal cavity and maxillary sinuses. Perineural spread tends to occur along the greater and lesser palatine nerves, which provide a pathway upward to the pterygopalatine fossa (Fig 11). Perineural spread of palatine lesions is best evaluated with MR imaging (22).

Oropharyngeal Subsites

Base of the Tongue

The base of the tongue extends from the circumvallate papillae anteriorly to the valleculae inferiorly. The detection of SCCs in this subsite is often challenging because the base of the tongue consists of dense musculature and lacks the fat planes that provide a contrasting background to SCCs in other subsites. In addition, the great variability in the size of the lingual tonsils makes evaluation difficult. For these reasons, direct visualization by the referring physician is vital before imaging is performed. Evaluation of SCCs of the base of the tongue should include a determination of the extent of *(a)* submucosal involvement, *(b)* involvement of the intrinsic muscles of the tongue, *(c)* crossing of the midline of the tongue, *(d)* invasion of the pre-epiglottic fat, *(e)* osseous involvement, and *(f)* cervical lymphatic spread.

SCCs in this subsite often manifest with dysphagia, odynophagia, or the sensation of a mass.

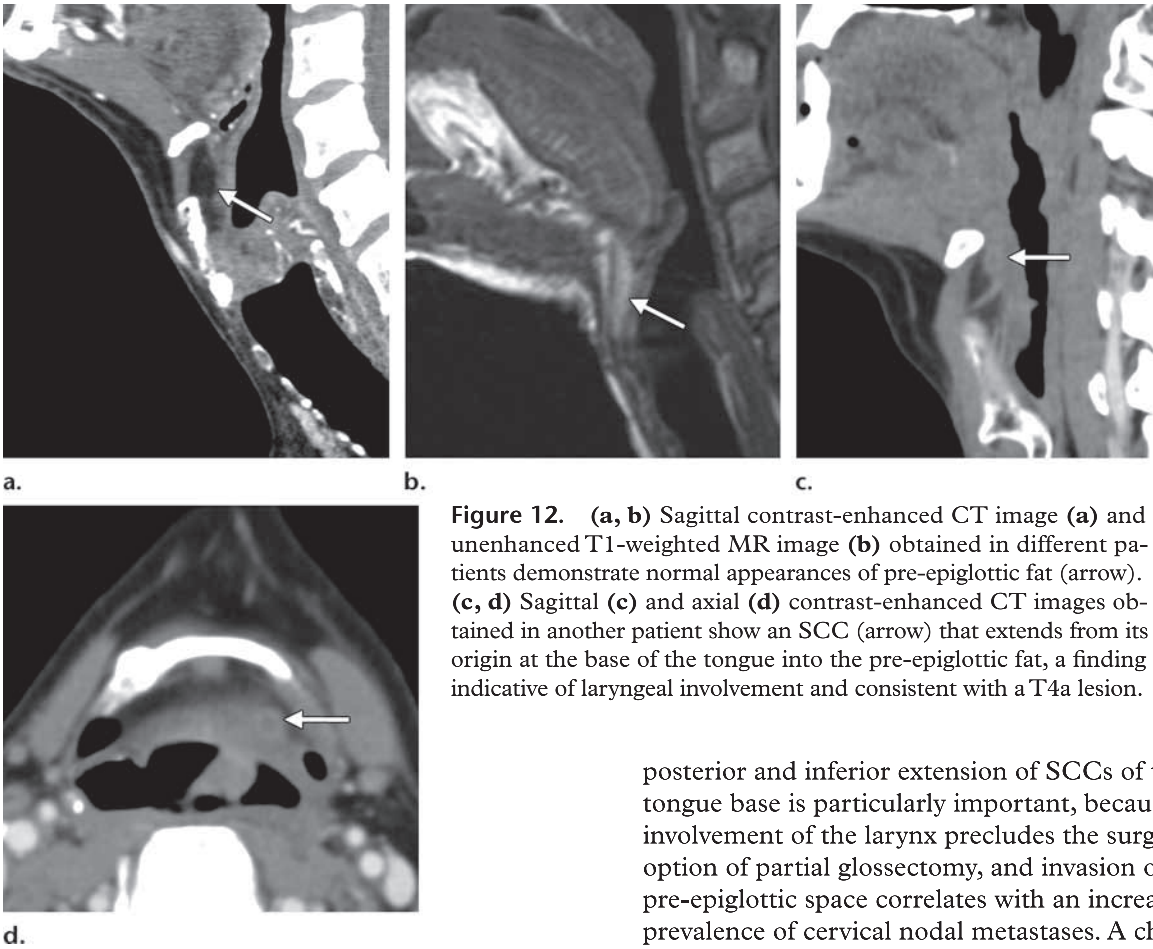


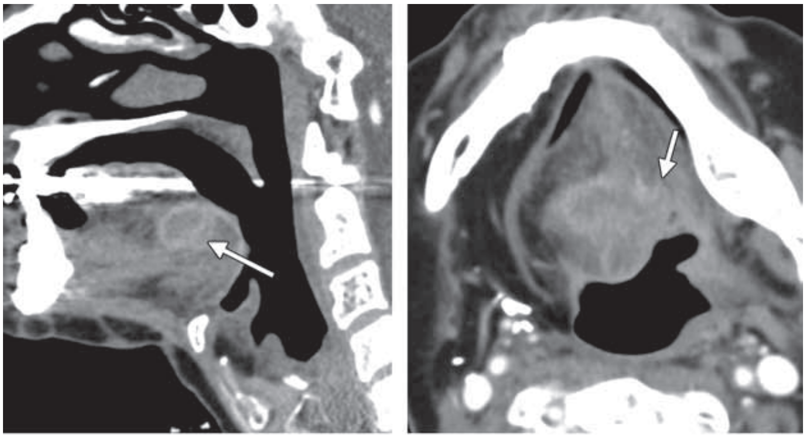
Figure 12. **(a, b)** Sagittal contrast-enhanced CT image **(a)** and unenhanced T1-weighted MR image **(b)** obtained in different patients demonstrate normal appearances of pre-epiglottic fat (arrow). **(c, d)** Sagittal **(c)** and axial **(d)** contrast-enhanced CT images obtained in another patient show an SCC (arrow) that extends from its origin at the base of the tongue into the pre-epiglottic fat, a finding indicative of laryngeal involvement and consistent with a T4a lesion.

However, many cases are clinically silent for an extended period and are not detected until the appearance of a neck mass representing nodal involvement (23). At presentation, approximately 60% of patients with SCC of the tongue base have nodal involvement, which is bilateral in approximately 30% and necessitates meticulous inspection with CT (24). The high rate of nodal involvement by SCCs in this subsite is due to a rich lymphatic network with significant cross drainage. The primary lymphatic drainage is to level II, III, and IV lymph nodes. Level V lymph nodes are infrequently involved. SCCs of the base of the tongue tend to be poorly differentiated and aggressive, with a survival rate of only 20%.

SCCs of the tongue base often originate on one side and spread laterally to the tonsillar pillars, anteriorly to the sublingual space, or posteriorly under the valleculae. Evaluation of the posterior and inferior extension of SCCs of the tongue base is particularly important, because involvement of the larynx precludes the surgical option of partial glossectomy, and invasion of the pre-epiglottic space correlates with an increased prevalence of cervical nodal metastases. A change in the normal appearance of pre-epiglottic fat may be indicative of extension into the larynx (Fig 12). The pre-epiglottic fat is a triangular or quadrangular region of fat just anterior to the epiglottis and just below the hyoepiglottic ligament. The pre-epiglottic fat may be evaluated with CT or MR imaging but is best depicted on T1-weighted axial and sagittal MR images, where the high-signal-intensity fat serves as a homogeneous background for evaluation of low-signal-intensity tumor infiltration. Loevner et al (25) demonstrated diagnostic accuracy of 90% with the use of this technique in a study of 40 patients in whom SCC was believed to have infiltrated the pre-epiglottic fat.

SCCs of the base of the tongue may extend deep into the intrinsic muscles, structures best evaluated with CT or T1-weighted MR imaging in the sagittal plane (Fig 13a). Invasion of

Figure 13. Recurrent SCC of the base of the tongue after a hemiglossectomy with a flap reconstruction. **(a)** Sagittal contrast-enhanced CT image demonstrates the anterior extent of the recurrent tumor (arrow), which involves the intrinsic muscles of the tongue. **(b)** Axial contrast-enhanced CT image shows that the recurrent SCC (arrow) has crossed the midline of the tongue base.



a. b.

the intrinsic muscles of the tongue is indicative of a T4a lesion. The tumor site should also be inspected for evidence of midline invasion, which usually occurs in an advanced stage of disease (Fig 13b). If the tumor crosses the midline, its relation to the contralateral neurovascular bundle must be determined, because partial glossectomy, the preferred surgical treatment for SCCs of the base of the tongue, requires the preservation of one lingual artery and one hypoglossal nerve. Tumor infiltration beyond the midline with proximity to the contralateral neurovascular bundle is a contraindication against partial glossectomy, and most surgeons consider total glossectomy an unacceptable alternative because of high associated morbidity (26).

Early-stage SCC of the base of the tongue is treated initially with surgical excision or radiation therapy. The tumor can be accessed transorally or with a lateral pharyngotomy or mandibulotomy with mandibular swing, or a transhyoid approach may be used. Repair of the subsequent defect may require primary closure, substantial secondary intention healing, or both. A thin, pliable, fasciocutaneous flap may be used to repair large defects. As much as one-half of the base of the tongue may be resected with acceptable functional outcomes (27). However, after a near-total or total tongue base resection, there is a significant risk of aspiration, which often necessitates a total laryngectomy. In the presence of negative prognostic factors such as perineural, lymphatic, or vascular invasion, postoperative radiation therapy is required after resection. Advanced-stage SCCs of the base of the tongue require treatment with a combination of chemotherapy, radiation therapy, and surgical resection (28).

Tonsils

Tonsillar subsites include the anterior and posterior tonsillar pillars, which overlie the palatoglossus and palatopharyngeus muscles, respectively, and the palatine tonsils. Evaluation of tonsillar SCC primarily involves the assessment of submucosal invasion because there are multiple unobstructed routes by which the tumor may spread into the nasopharynx, parapharyngeal space, masticator space, skull base, and tongue base. Because many of these regions are not amenable to endoscopic evaluation and are not surgically accessible, imaging examinations are particularly important for treatment planning. CT is usually the modality of choice for the initial imaging study; however, with tonsillar SCCs, as with SCCs of the retromolar trigone, MR imaging is more useful for a complete evaluation of soft-tissue extension. Evaluation of a tonsillar SCC should include a determination of the extent of *(a)* submucosal extension, *(b)* involvement of the pterygoid muscles, *(c)* extension along the pterygomandibular raphe to the skull base, *(d)* osseous involvement, and *(e)* involvement of the cervical lymph nodes.

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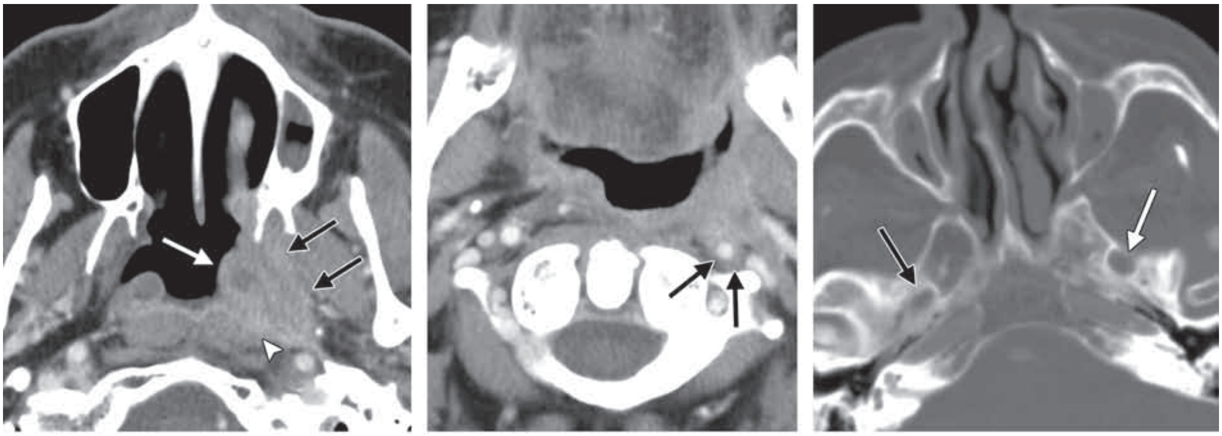
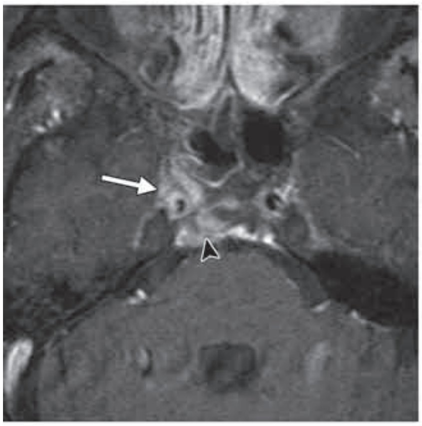
Figure 14. **(a)** Axial contrast-enhanced CT image shows a primary tonsillar SCC that extends upward into the medial pterygoid muscle (black arrows), the lateral part of the nasopharynx adjacent to the fossa of Rosenmüller (white arrow), and the retropharyngeal space, where the tumor is inseparable from the left longus colli muscle (arrowhead). Any of these imaging features is diagnostic of a T4a lesion. **(b)** Axial contrast-enhanced CT image obtained in the same patient as in **a** shows circumferential tumor involvement of the left internal carotid artery (arrows), a finding indicative of a T4b lesion. **(c)** Axial contrast-enhanced CT image obtained in another patient (same patient as in Fig 11) depicts asymmetric enlargement of the left foramen ovale (white arrow) relative to the right foramen ovale (black arrow), a finding indicative of perineural extension along the mandibular nerve (CN V3). **(d)** Contrast-enhanced T1-weighted fat-suppressed MR image obtained in a third patient demonstrates an enhancing tumor that involves the cavernous part of the internal carotid artery (arrow) and the petroclival fissure (arrowhead), findings indicative of a T4b lesion.



a. b. c.



d.

Most SCCs of the tonsil originate in the anterior tonsillar pillar. These tumors tend to spread superiorly along the palatoglossus muscle to the hard and soft palates. From there, they may continue to spread along the tensor and levator palatine muscles as well as the pterygoid muscles. Tonsillar SCCs also may spread upward to the nasopharynx (Fig 14a). Anterior and medial spread tends to occur along the superior constrictor muscles to the pterygomandibular raphe, by means of which the tumor may gain access to the skull base and cranial nerves (Fig 14b–14d). A tumor also may extend posteriorly to the retropharyngeal or carotid space or inferiorly to the tongue base.

Osseous involvement in tonsillar SCCs occurs primarily along the pterygoid plates and the maxilla and is assessed in the same fashion as osseous involvement in SCCs at other sites. Lymphatic involvement is common, occurring in nearly half of cases of tonsillar SCC. Level I, II, and III lymph nodes may be involved.

Summary

SCC accounts for approximately 90% of oral cavity and oropharyngeal malignancies. Familiarity with the anatomic subsites and potential routes of spread allows accurate staging of this disease. Accurate identification and reporting of key imaging findings allows referring physicians to choose the most appropriate treatment options and plan a surgical approach.

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Oral Cavity and Oropharyngeal Squamous Cell Cancer: Key Imaging Findings for Staging and Treatment Planning

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Page 340
Studies have shown that approximately 25% of all head and neck cancers and 60% of all oropharyngeal cancers are HPV positive, a finding that may drastically alter treatment planning (1,2).

Page 342
SCCs of the oral cavity and oropharynx may spread in three general ways: *(a)* by direct extension over mucosal surfaces, muscle, and bone, *(b)* by dissemination via lymphatic drainage pathways, and *(c)* by extension along neurovascular bundles (4). For accurate staging of SCCs of the oral cavity and oropharynx, evaluation of these three routes of spread is mandatory.

Page 342
The presence of osseous involvement is indicative of a T4 lesion.

Page 343
A large percentage of oral and oropharyngeal SCCs initially manifest with a neck mass that represents the involvement of cervical nodes. Because nodal involvement is the single most important prognostic indicator, an accurate assessment of all nodal chains at the same time is required.

Page 344
Imaging features of perineural spread include foraminal enlargement and replacement of normal fat within the neural foramen. The nerve may appear enlarged on contrast-enhanced MR images, a change that cannot be seen on CT images (15,16).