Pitfalls in the Staging of Cancer of Oral Cavity Cancer

Ashley H. Aiken, MD

KEYWORDS

- Squamous cell carcinoma • Oral cavity • Retromolar trigone • Floor of mouth

KEY POINTS

- Staging OC tumors requires knowledge of OC anatomy, the OC subsites, and tumor spread patterns.
- Radiologists should always assess for features that would upstage to a T4a disease, including invasion of the extrinsic tongue muscles or mandible, and features that upstage to potentially unresectable T4b disease, including involvement of the masticator space, skull base, and encasement of the internal carotid artery.
- This article reviews the detailed imaging anatomy of the OC, and epidemiology, staging, and surveillance for OCSCC.

INTRODUCTION AND EPIDEMIOLOGY

Oral cavity (OC) cancer comprises nearly 30% of all malignant tumors of the head and neck. A total of 90% of cases are squamous cell carcinoma (SCC). The remaining 10% represent minor salivary gland neoplasms, melanoma, lymphoma, and rare varieties of squamous cell and odontogenic tumors.[1] Oral cavity cancer is the sixth leading cause of cancer-related mortality in the world.[2] Although it only accounts for a small percentage (0.6%–5%) of cancers in Western societies, it represents nearly 45% of cancers in certain countries, such as India, secondary to risk factors, such as betel nut chewing. Oral cavity cancer occurs most commonly in middle aged and elderly individuals. However, recent evidence suggests an increased incidence in younger individuals (<40 years) from 3% in 1973 to 6% in 1993.[3] The primary causative risk factors in North America include alcohol and tobacco, which are independent and synergistic. Human papillomavirus is strongly associated with oropharyngeal cancers, but only a minority of OC cancers.[4] Oral cancer is often diagnosed at a late stage contributing to the low 5-year survival rates, hovering at 50 60% overall and as low as 22% for late stage.[5,6]

The OC is the most anterior subdivision of the aerodigestive tract with a wide variety of tissue types for such a small region. The posterior OC is separated from the oropharynx (OP) by an imaginary ring drawn across the circumvallate papillae, anterior tonsillar pillars, and junction of the hard and soft palate. This is a critical distinction because carcinomas in the OC versus OP differ in presentation, treatment, and prognosis. However, it is not uncommon for OC tumors to spread to the OP and vice versa. The remaining boundaries of the OC include the lips anteriorly; the cheeks laterally; the hard palate and superior alveolar ridge superiorly; and the inferior alveolar ridge and mylohyoid muscle inferiorly (**Figs. 1** and **2**). The oral mucosal space refers to the nonkeratinized stratified squamous epithelium lining the entire OC including the buccal (cheek), gingival (gums), palatal, and lingual surfaces.[7] These are the potential sites for SCC. In addition, subepithelial collections of minor salivary glands are found throughout the OC, most commonly along the inner surface of the lip, buccal
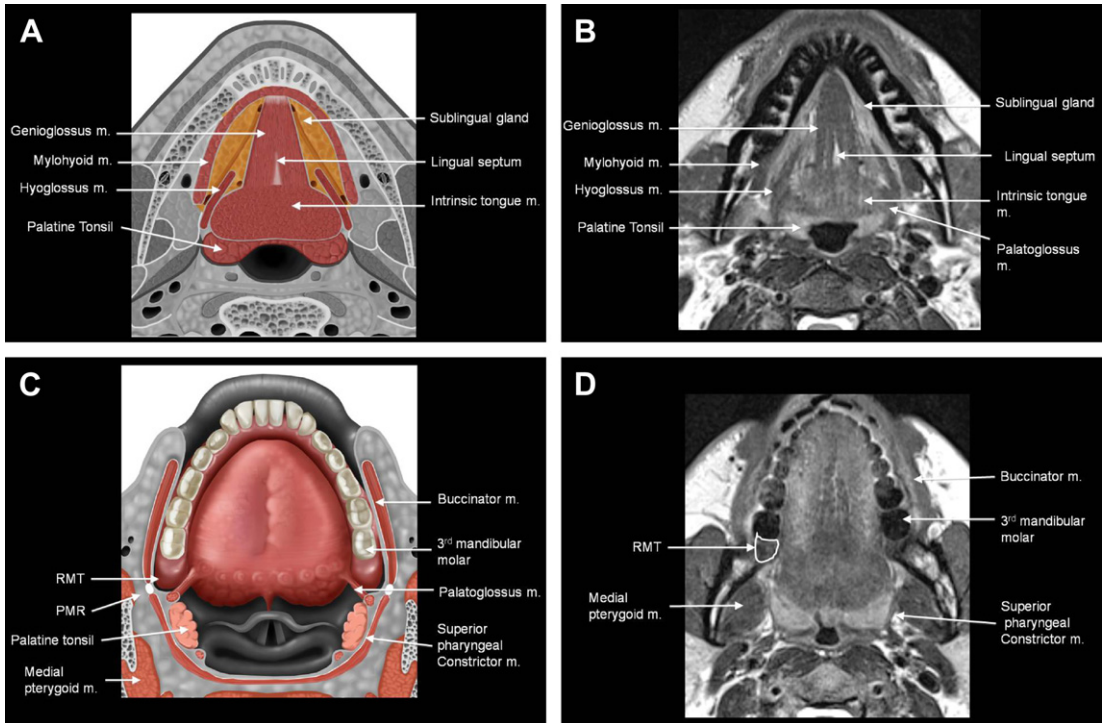
Department of Radiology and Imaging Sciences, Emory University, BG-21, 1364 Clifton Road, Northeast, Atlanta, GA 30322, USA
E-mail address: ashley.aiken@emoryhealthcare.org

Fig. 1. Normal OC anatomy: axial at the level of the floor of mouth and oral tongue. (*A*) Axial illustration at the level of the floor of mouth demonstrating the extrinsic tongue muscles and sublingual space. (*B*) Axial T2-weighted image at the level of the floor of mouth. (*C*) Axial illustration at the level of the oral tongue demonstrating the oral tongue and retromolar trigone (RMT). PMR, pterygomandibular raphe (facial band connecting the buccinator and superior constrictor muscles). (*D*) Axial T2-weighted image at the level of the oral tongue. (*Courtesy of* Eric Jablonowski.)

mucosa, and hard palate. These are potential sites for minor salivary gland neoplasms, such as adenoid cystic and mucoepidermoid carcinomas.

The OC is readily accessible, so oral cancer screening and initial evaluation should be accomplished by clinical examination. Changes in the mucosa are easily identified and evaluated. After a definitive diagnosis has been made, imaging is essential for staging the primary tumor by evaluating submucosal spread and invasion of adjacent structures, and to identify nodal or distant metastasis. OC anatomy is one of the most complex in the head and neck; therefore, knowledge of anatomic subsites and spread patterns is critical for accurate staging. This article begins with a discussion of imaging techniques, and then presents a detailed review of normal anatomy followed by imaging's role in tumor staging highlighting potential pitfalls (**Table 1**).

IMAGING PROTOCOLS

The choice of imaging modality is often determined by the clinical question and treatment options. Computed tomography (CT) is generally the workhorse modality for OC cancer. It can be acquired within minutes limiting motion artifact, and can easily be reformatted in coronal and sagittal planes. CT is also preferred to evaluate for early cortical bone involvement.[8] MR imaging may complement CT of the OC because it offers advantages in delineating soft tissue anatomy, especially where accurate tumor extent is critical for surgical planning and negative margins. MR imaging may also be preferable in patients with excessive dental amalgam artifact obscuring the primary tumor and tumor extent. The overall accuracy of CT versus MR imaging for T staging is comparable.[9] However, many subsites, especially the hard palate, can be understaged with CT and therefore MR imaging is invaluable for accurately defining margins and evaluating for perineural extension.[10] CT is more affected by artifact caused by dental metals, whereas MR imaging is more affected by artifact caused by movements of the patient. Most studies that have compared the accuracy of CT and MR imaging for the assessment of the neck have also found no difference.[11] Although
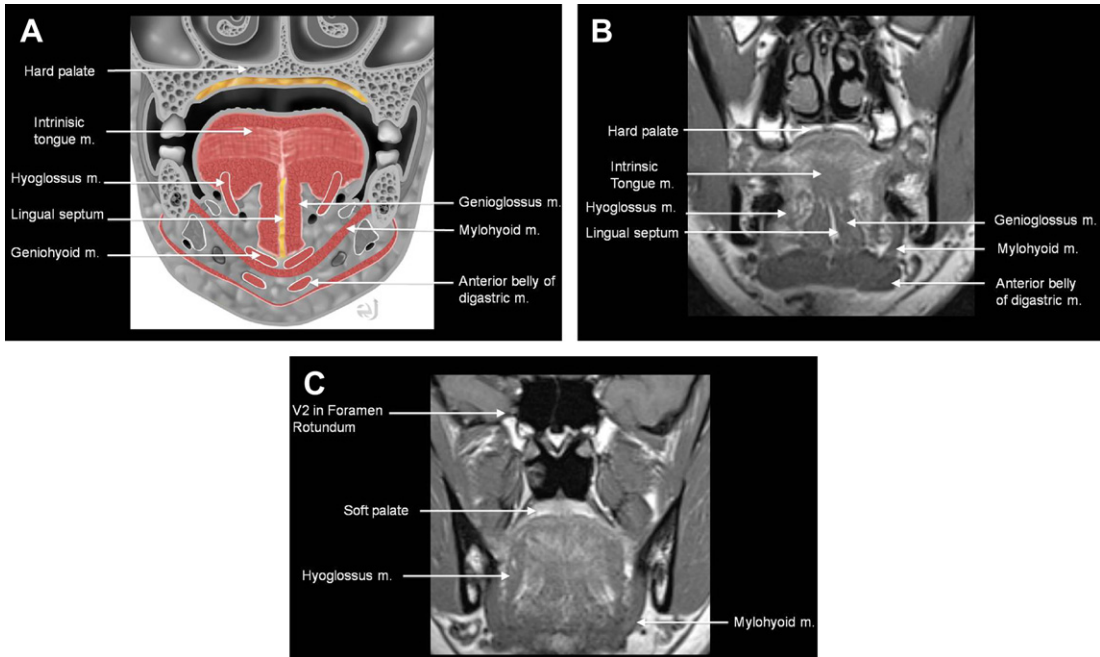
Fig. 2. Normal OC anatomy: coronal at the level of the hard and soft palate. (*A*) Coronal illustration through the hard palate. Note the mylohyoid muscle forming the inferior and lateral borders of the OC, the close relationship to the mandible, and the extrinsic tongue muscles (hyoglossus and genioglossus). (*B*, *C*) Coronal T1-weighted image through the hard palate and soft palate, respectively. (*Courtesy of* Eric Jablonowski.)

positron emission tomography (PET) and PET-CT have the potential to increase sensitivity for nodal disease, some authors have found that the diagnostic accuracy for OC nodal metastasis did not improve significantly compared with CT or MR imaging alone.[12–14]

Although protocols vary based on institution, my CT protocol includes 1.25-mm helical images after injection of intravenous contrast, reconstructed at 2.5 mm from the orbits through the thoracic inlet, with routine use of sagittal and coronal reformations. I also obtain a second set of images through

Table 1
Pitfalls in staging of OC SCC

Pitfall	Advice
Upstage to T4a: Misinterpreting odontogenic disease as mandible invasion	Thin section bone CT with multiplanar reformats
Upstage to T4a: Misinterpreting atrophic edentulous mandible as tumor invasion/ destruction	Thin section bone CT with multiplanar reformats
Upstage to T4a: Not recognizing extrinsic tongue muscle involvement significance rather than intrinsic	Know anatomy of hyoglossus and genioglossus MR imaging may help in difficult cases
Hard palate primary: Understaging with CT	Recommend MR imaging for all cases being considered for resection to delineate tumor spread
PET-CT too early after surgery or biopsy	Wait at least 8 wk
Upstaging to T4b: Overcalling involvement of masticator space	Tumor may bulge rather than invade medial pterygoid muscle. Most surgeons will still attempt resection for medial pterygoid involvement

the OC with delayed mucosal enhancement and butterfly angled images to decrease dental amalgam artifact (Fig. 3).

An ideal MR imaging protocol includes axial, sagittal, and coronal images obtained with a dedicated neck coil and section thickness of 4 mm or less.[15] Optimal field of view is 16 to 18 cm on T1- and 18 to 20 cm on T2-weighted images allowing for improved signal-to-noise ratio.[16] Three planes of precontrast T1-weighted imaging are desirable to delineate normal anatomy and obliteration of fat and muscle planes. Postgadolinium T1-weighted fat-saturated sequences are especially useful for delineating enhancing tumor margins from intrinsically high signal intensity fat, and in the evaluation for perineural tumor.[16,17] However, fat suppression can result in artifacts with signal loss and distortion.[18] In this case, I prefer to add postgadolinium sequences without fat saturation.

STAGING

The American Joint Committee on Cancer (AJCC) staging for lip and OC can be found in Table 2. This TNM staging system is only used for epithelial tumors including SCC and minor salivary gland carcinoma. T1, T2, and T3 lesions of the OC are distinguished based on 2-cm increments in size. Patterns of invasion are used to upstage to a T4a or T4b lesion. The primary considerations to upstage to T4a disease include bone invasion (mandible or maxilla) or involvement of the extrinsic tongue muscles. It is critical, therefore, that the radiologist be able to routinely identify the extrinsic tongue muscles. The sixth edition of the *AJCC Cancer Staging Manual* modified OC staging by the addition of T4b, which denoted unresectable disease. Since that time, the seventh edition of the AJCC has replaced the "resectable" versus "unresectable" terminology for T4a and T4b respectively to "moderately advanced" and "very advanced" disease. T4b still refers to tumor invasion of the masticator space, pterygoid plates, or skull base and tumor encasement of the internal carotid artery. The criteria for nodal staging of OC are identical to the criteria for other sites in the pharynx and larynx, with the exception of nasopharynx.

Additional Prognostic Indicators and Trends in Treatment Important for Staging

Tumor thickness and depth of invasion are important prognostic factors and surgical planning tools in OC cancer that are not included in the T staging of the AJCC. Tumor thickness and depth of invasion have been associated with local recurrence and survival for cancer of the oral tongue.[19] The exact depth of invasion that predicts nodal disease is not clear, but several studies have suggested that tumor thickness greater than 4 mm increases the chance of cervical metastasis.[20] Elective neck dissection for early T1-T2 N0 disease continues to be investigated. Clinically and radiographically occult nodal disease found only at surgery increases the risk of recurrence and decreases 5-year survival from 82% to 53%.[21] Furthermore, Kligerman and colleagues[22] showed that
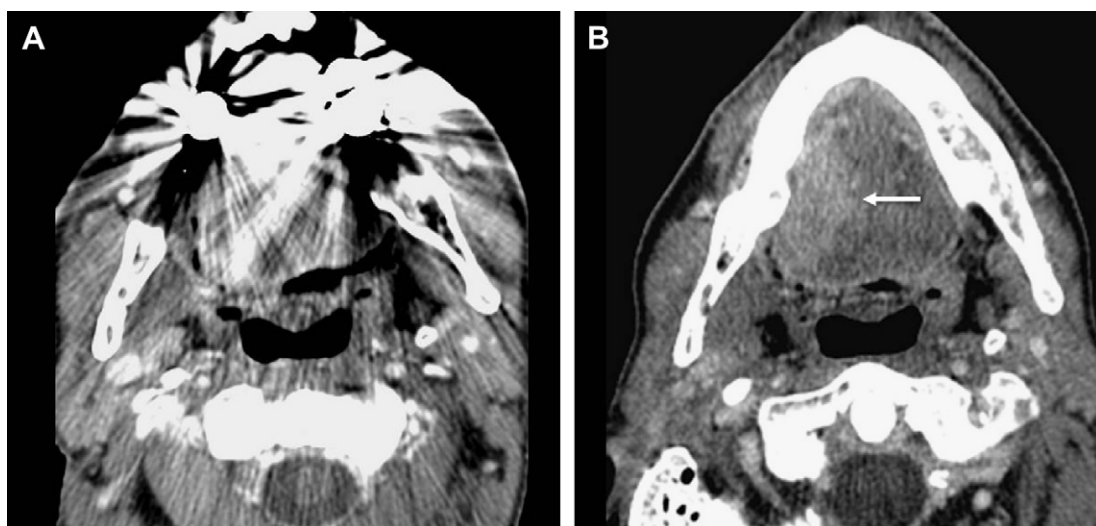
Fig. 3. SCC of the right oral tongue: usefulness of reangled images. (*A*) Axial contrast-enhanced (CE) CT through the oral cavity is nondiagnostic because of dental amalgam and extensive streak artifact. (*B*) Delayed and reangled axial CE CT image shows a large enhancing right oral tongue mass (*arrow*), effacing the right sublingual space.

Table 2
AJCC 7 lip and oral cavity staging

	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
T4a	Moderately advanced local disease (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face, i.e., chin or nose (oral cavity) Tumor invades adjacent structures only (e.g., through cortical bone, [mandible or maxilla] into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)
T4b	T4b Very advanced local disease Tumor invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery
	Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumor as T4
	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)
M0	No distant metastasis
M1	Distant metastasis

From Edge S, Byrd D, Compton C, et al. AJCC Cancer Staging Manual. 7th edition. Chicago (IL): Springer; 2010. p. 41–56; with permission.

a prophylactic neck dissection in patients with low-volume primary and N0 neck reduced recurrence rate from 33% to 12%, compared with those in whom the neck was treated with watchful waiting. Some authors advocate a prophylactic neck dissection for all OC cancers, regardless of depth of invasion.[14] Others recommend a staging supraomohyoid neck dissection for all patients with T2 disease at the primary site, and T1 disease with greater than 4 mm depth of invasion. Because 70% to 80% of neck dissection specimens are negative for regional metastatic disease, recently some authors advocate a sentinel node biopsy.[21,23]

Perineural invasion and lymphocytic response are additional histopathologic parameters that are not accounted for in the current AJCC staging system.[12] Extracapsular spread (ECS) may have a significant impact on the prognosis of patients with regional disease, with up to 50% reduction in survival.[24] On imaging, ill-defined margins of the lymph node and stranding are the biggest clues to ECS (**Fig. 4**). Patients with ECS are commonly treated with adjuvant radiation and chemotherapy.

Superficial carcinomas of the OC can be treated with excellent cure rates with either radiation or

Fig. 4. SCC of the floor of mouth with lymph node metastasis. Axial CE CT shows multiple level IB and IIA nodes that are pathologically enlarged. The IB nodes show central necrosis (*arrow*). The IIA nodes have extensive surrounding stranding (*arrowheads*) suggesting extracapsular spread. This pattern of nodal drainage suggests an OC primary.

surgery. However, because surgical cure can be achieved rapidly with minimal morbidity, it is often preferred.[12] Advanced disease is often managed with multimodality therapy. Surgery with or without reconstruction coupled with preoperative or postoperative radiation therapy is often used. Most centers perform surgery followed by postoperative radiation because of the higher rate of postoperative complications with preoperative radiation treatment.[12] Although primary surgical management has been advocated for most advanced OC cancer, recent evidence suggests that primary chemoradiotherapy may be effective for selected T4 patients, especially in cases of "functional irresectability," such as patients requiring total glossectomy.[25]

T STAGE

Primary SCCs in the OC are usually infiltrative mucosal lesions with variable enhancement on CT and MR imaging. Larger tumors may have central necrosis. On MR imaging, the precontrast T1-weighted sequence is often particularly helpful to show the T1 hypointense tumor, especially to contrast the signal intensity of the fibrofatty oral tongue. These tumors are minimally T2 hyperintense and variably enhancing postgadolinium.

Conversely, minor salivary gland tumors are submucosal and often more well circumscribed. The most common minor salivary neoplasms are adenoid cystic and mucoepidermoid carcinomas.

Adenocarcinoma is less common. On MR imaging, these tumors are T1 isointense to muscle, mildly T2 hyperintense, and avidly enhancing.

IMAGING ANATOMY AND PATTERNS OF SPREAD BY SUBSITE

OC cancers are classified into the following subsites: (1) lip, (2) buccal mucosa, (3) upper and lower gingiva, (4) retromolar trigone (RMT), (5) hard palate, (6) oral tongue, and (7) floor of mouth (FOM) (**Fig. 5**).

Lip Carcinoma

Keratinizing squamous epithelium covers the outer lips, whereas the inner surface and gingiva are covered by nonkeratinizing stratified squamous epithelium. The motor branch of cranial nerve (CN) VII innervates the lips. The primary lymphatic drainage is to submental (level IA) and submandibular (level IB) nodes.

The lip is the most common site of SCC in the OC, representing roughly 40% of cases.[26] Carcinomas of the lip usually arise from the vermillion border and may spread laterally to adjacent skin or deeply to the orbicularis oris muscle. If the tumor invades skin or bone, it becomes upstaged to a T4a.

Buccal Mucosa and Gingiva

The gingiva or "gums" refers to the mucosal covering of the lingual (medial) and buccal (lateral) surfaces of the alveolar mandible and maxilla. The junction between the gingival and the buccal mucosa lining the cheek is called the gingivobuccal sulcus.

Buccal carcinomas often originate along the lateral margins of the buccal mucosa lining the
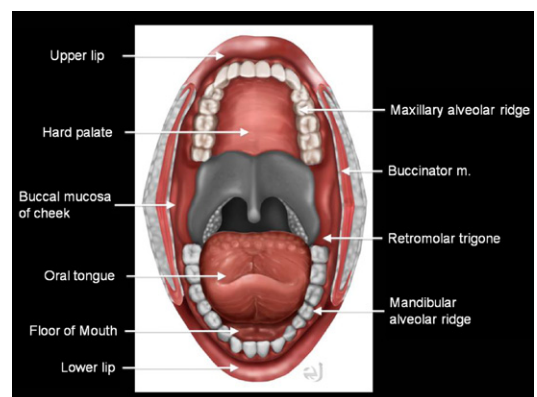
Fig. 5. Graphic drawing illustrating the mucosal subsites for oral cavity SCC. (*Courtesy of* Eric Jablonowski.)

cheeks. Some authors find it helpful to have patients puff their cheeks outward to reveal more subtle mucosal lesions (**Fig. 6**). I do not routinely use this technique, because it is primarily the clinician's role to identify mucosal extent. Imaging is critical to identify submucosal tumor, bone involvement, perineural extension, or extension to the masticator space. A common route of spread is lateral extension along the buccinator muscle to the RMT and ptergomandibular raphe. Buccal tumors that invade the buccinator muscle and have nodal disease or other poor prognostic indicators should undergo postoperative radiation. Therefore, it is important that the radiologist identifies involvement of the buccinator muscle and RMT, because involvement of the RMT provides numerous paths of tumor spread and makes surgical management more difficult (**Fig. 7**). More than half of buccal tumors present as deeply invasive tumors that may track along the parotid duct (**Fig. 8**), masseter muscle, or into the palate. Involvement of the parotid duct requires the surgeon to trace the duct retrograde to ensure negative margins. These lesions also spread along the submucosal surface and may eventually involve the skin.

Tumors of the gingiva along the maxillary or mandibular alveolar ridges account for less than 10% of OC carcinomas.[16,27] Because of the proximity to cortical bone, it is critical to assess for bone invasion and perineural extension, particularly along the inferior alveolar nerve for SCCs of the lower alveolar ridge (**Fig. 9**).

Fig. 6. Puffed cheek technique. Axial CE CT shows a patient "puffing" their cheeks, which may demonstrate the mucosal buccal space with better detail. Note the margins of the buccinator muscle are also better defined (*arrow*).

Retromolar Trigone

The RMT refers to the small triangular-shaped mucosa overlying the area just posterior to the last mandibular molar. The RMT is an important subsite of the OC because it represents a crossroads for tumor spread to and from the OC, OP, buccal space, FOM, and masticator space. The RMT refers to the small triangular-shaped mucosa overlying the area just posterior to the last mandibular molar. The pterygomandibular raphe lies just beneath the mucosa of the RMT and provides attachment for the buccinator and superior pharyngeal constrictor muscles (**Fig. 10**). This fibrous band connects the posterior mylohyoid line of the mandible to the hamulus of the medial pterygoid plate, and thereby it serves as a route of tumor spread superiorly from the RMT to the pterygoid process or posterior maxillary alveolus (**Fig. 11**). Tumors of the RMT are in close proximity to the mandible and maxilla, and therefore have a high propensity to invade bone.

Hard Palate

The hard palate is a thin horizontal bone formed by the palatine processes of the maxillae and the horizontal plates of the palatine bones (see **Fig. 2**). It spans the arch formed by the alveolar ridges and upper teeth. Posteriorly, the hard palate is contiguous with the soft palate, which is a subsite of the OP. It forms the superior margin of the OC and inferior margin of the nasal cavity. The greater palatine foramen is located medial to the posterior third molar within the lateral border of the bony palate.[28] The greater palatine nerve runs through this foramen and is a potential source of perineural spread of tumor along branches of CN V2 into the ptergopalatine fossa.[29] The incisive canal houses the nasopalatine nerves and arteries, and is found within the hard palate, just posterior to the incisor teeth.

Unlike other areas of the OC where SCC predominates, the palate is rich in minor salivary glands. OC minor salivary gland tumors are most commonly found at the junction of the hard and soft palate. Preoperative imaging is a key to assess invasion of the maxillary sinus, palatal bone, and nasal cavity. Important features to identify on CT are erosion of the hard palate and widening of the greater palatine foramen, suggesting perineural spread (**Fig. 12**). MR imaging is critical to define the extent of these infiltrating tumors and to assess for perineural spread, because these tumors have a propensity to spread along the greater and lesser palatine nerves into the pterygopalatine fossa, allowing intracranial access along V2 through foramen rotundum or the vidian nerve in the vidian
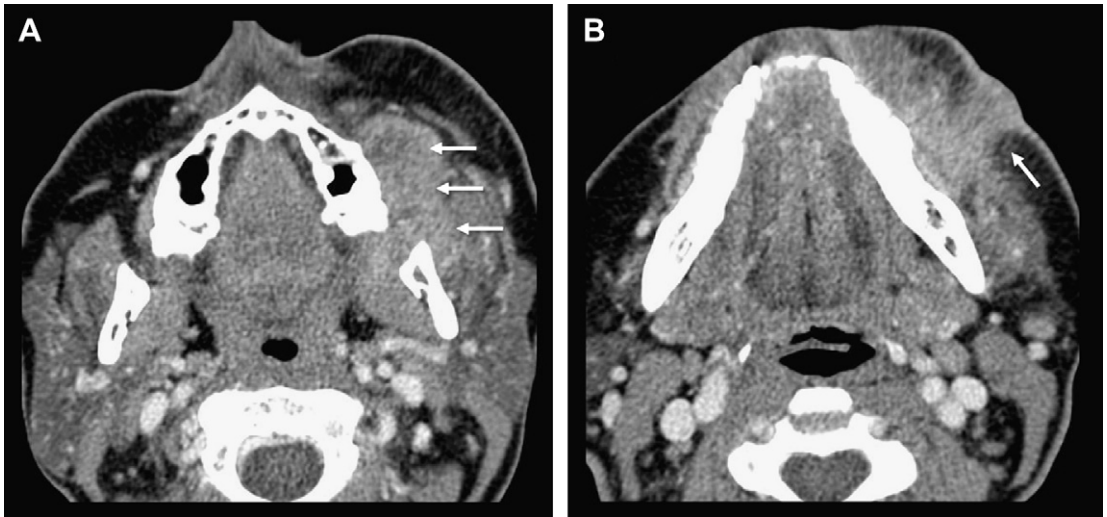
Fig. 7. SCC of the left buccal mucosa, T4a. (*A*) Axial CE CT shows large left buccal mass (*arrows*) extending to maxillary RMT. (*B*) Axial CE CT (inferior to *A*) shows inferior and lateral extension to involve the skin (*arrow*). Involvement of the skin critical to note, because the tumor is upstaged to T4a.

canal. Achieving negative margins at surgery is essential to a good outcome. Minor salivary gland tumors of the hard palate rarely metastasize to the neck, so that a neck dissection is rarely warranted in the absence of gross disease.

Oral Tongue

The oral tongue denotes the anterior two-thirds of the tongue separated from the base of tongue (OP)

by a line across the circumvallate papilla. The tongue is composed of intrinsic and extrinsic muscle fibers. The four interdigitating intrinsic tongue muscles include the superior and inferior longitudinal, transverse, and oblique muscles. The extrinsic tongue muscles originate from bony or soft tissue attachments outside the tongue and have distal fibers that interdigitate with the intrinsic tongue muscles. They are the genioglossus, stylogossus, hyoglossus, and palatoglossus
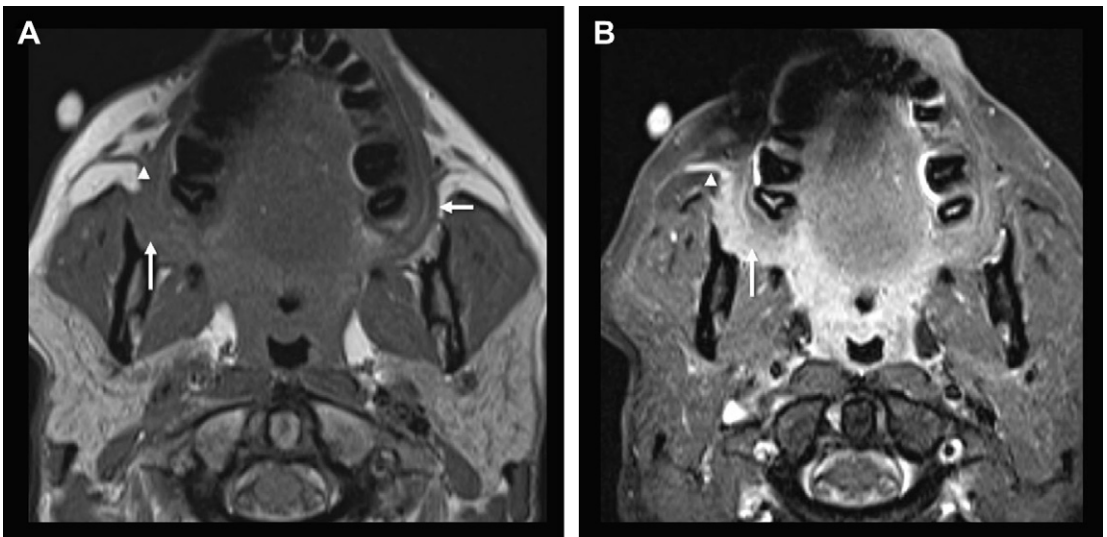

Fig. 8. Right buccal mucosa adenoid cystic carcinoma. (*A*) Axial T1-weighted image shows a right buccal mass (*arrow on right*), extending to the RMT and invading the buccinator muscle (*arrow on left* shows normal buccinator muscle) and extending to distal parotid duct (*arrowhead*). (*B*) Postcontrast fat-saturated axial T1-weighted image results in increased conspicuity of the mass (*arrow*) and parotid duct involvement (*arrowhead*). Note this example of limitation of fat saturation with increased artifact from dental amalgam.
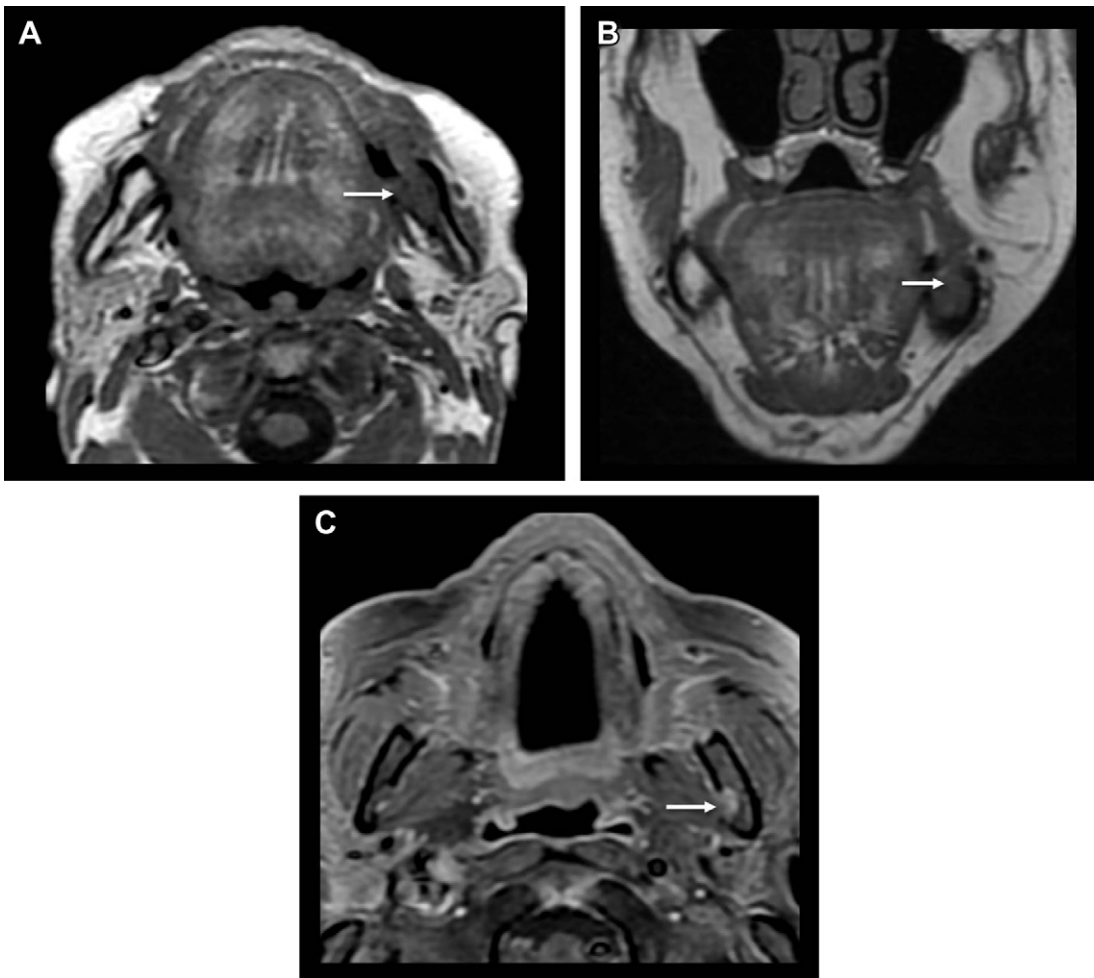
Fig. 9. SCC of the left posterior alveolar ridge, T4a. (*A*) Axial T1-weighted image shows an isointense mass with cortical and medullary cavity invasion of the mandible (*arrow*). Notice the interruption of the T1 hypointense line of the cortex, but also replacement of normal T1 hyperintense marrow signal intensity. (*B*) Coronal T1-weighted image also shows involvement and near complete replacement of normal marrow signal in the mandible (*arrow*). Cortical involvement was confirmed on a CT (not shown). Bone involvement upstages to a T4a. (*C*) Postcontrast fat-saturated T1-weighted image shows perineural spread along the inferior alveolar nerve (*arrow*). It is important to assess foramen ovale for intracranial extension.
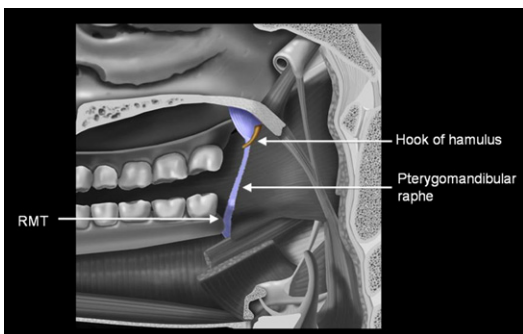
Fig. 10. Normal anatomy of pterygomandibular raphe.

muscles and originate from the genial tubercle of the inner mandible, anterior styloid process, cornua of the hyoid bone, and soft palate, respectively (see **Fig. 1**). The extrinsic tongue muscles are crucial to evaluate because involvement upstages OC carcinomas to at least a T4a.

The intrinsic and extrinsic tongue muscles are innervated by the hypoglossal nerve (CN XII), which emerges from nasopharyngeal carotid space and runs in the sublingual space with the lingual artery between the hyoglossus and mylohyoid muscles. The palatoglossus also receives supply from the vagus nerve (CN X) and the pharyngeal plexus. The sensory supply to the anterior two thirds of the tongue is by the lingual nerve, a branch of the trigeminal nerve (CN V)
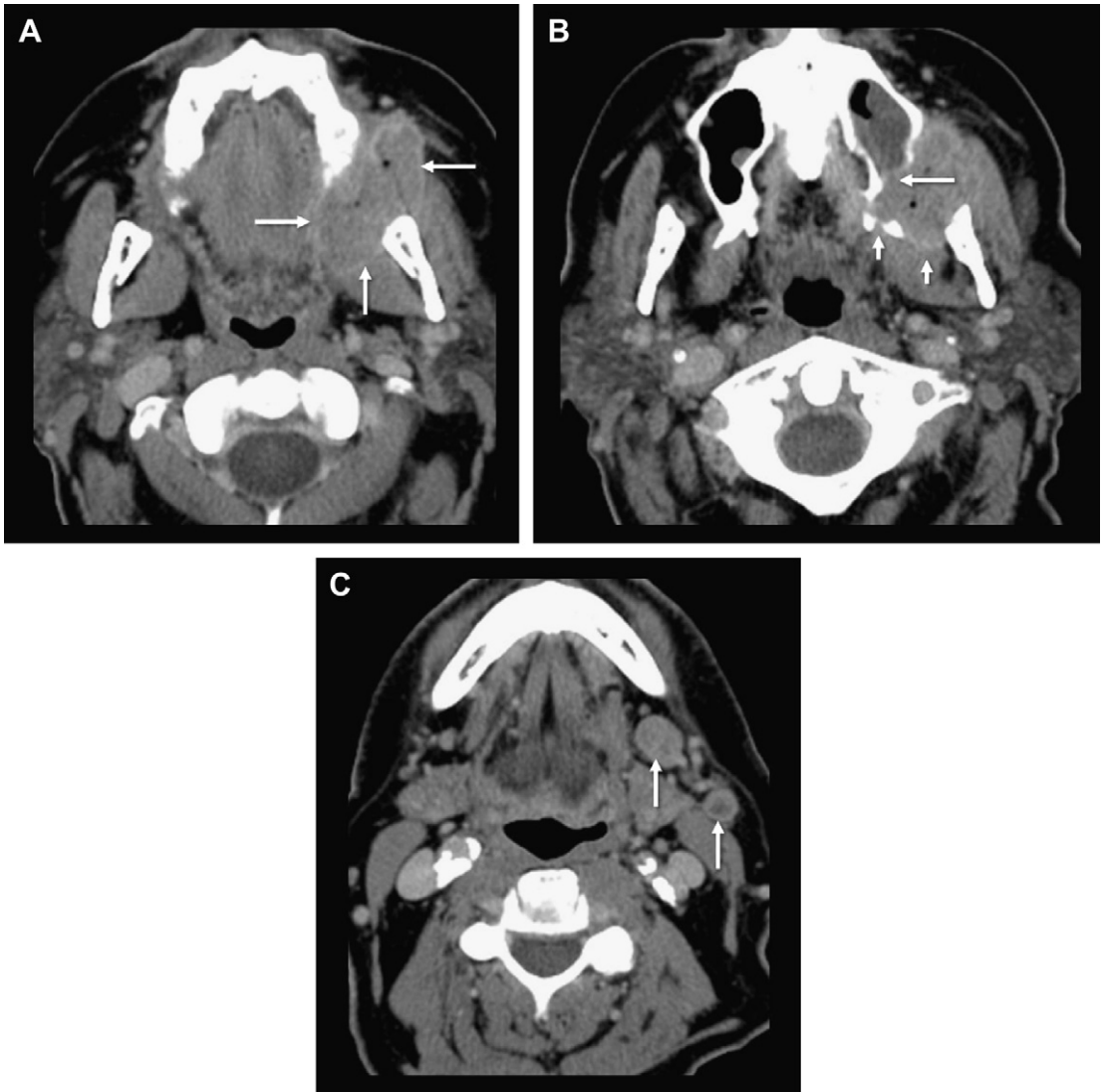
Fig. 11. SCC of the left RMT, T4b N2b. (*A*) Axial CE CT demonstrates large tumor centered in the left RMT (*arrows*). (*B*) Axial CE CT (cranial to *A*) shows obvious invasion of the posterior maxilla involving the maxillary sinus (*long arrow*) from tumor growing superiorly along the pterygomandibular raphe. Tumor is therefore upstaged to T4a. Also note tumor extension to medial pterygoid plate and masticator space (*short arrows*), resulting in overall T4b stage. (*C*) Axial CE CT shows metastatic level I and II nodes (*arrows*). Some have central low density, a very specific sign for metastasis.

and taste fibers from the chorda tympani nerve, a branch of the facial nerve (CN VII). The primary lymphatic drainage is by the superficial mucosa and deep collecting system, which both drain into anterior submandibular nodes (level IB). The superficial lymphatics are directed to level IB and IIA nodes, whereas the deeper lymphatics of the oral tongue have pathways to both sides of the neck. For this reason, tumor depth of 4 to 5 mm or greater has increased risk of bilateral lymphadenopathy.[12]

Nearly all tongue carcinomas occur along the lateral margin or undersurface. Prognosis and treatment depends on depth of invasion. Although superficial tumors are not easily seen on CT or MR imaging, it is not the radiologist's role to diagnosis mucosal lesions. It is critical that the radiologist assess the extrinsic tongue muscles as discussed previously to upstage to T4a. Assessment of involvement of the midline lingual septum is critical to determine whether the patient requires a hemi-glossectomy or total glossectomy. Advanced
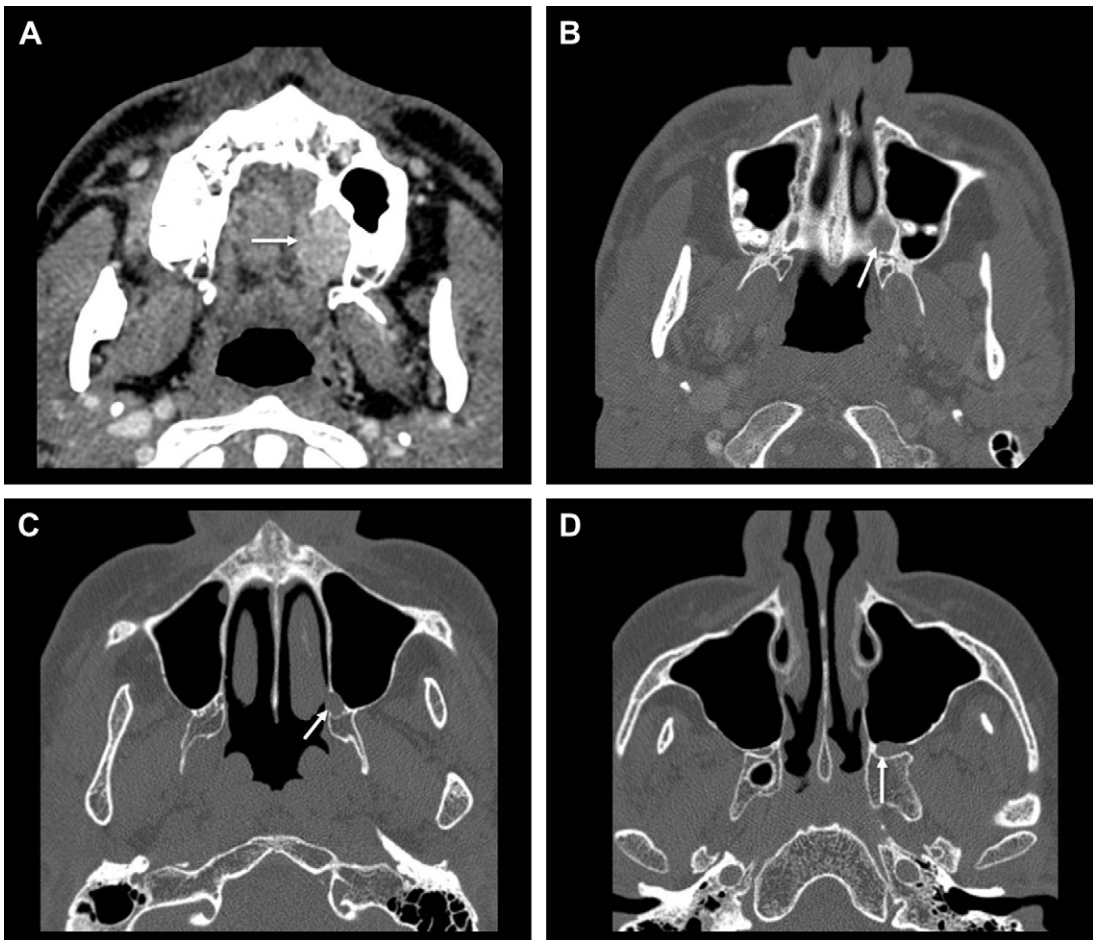
Fig. 12. Left hard palate mucoepidermoid carcinoma. (*A*) Axial CE CT shows 2-cm enhancing mass with fairly well-circumscribed borders (*arrow*) in the left hard palate. Well-circumscribed borders are common in minor salivary gland malignancies, making it difficult to differentiate them from benign minor salivary gland tumors. (*B*, *C*) bone window from axial CE CT images (at the level of the hard palate [*B*] and just above) show asymmetric widening of the left greater palatine foramen (*arrow*), compatible with perineural tumor extension. (*D*) Bone window from axial CE CT images shows extension of abnormal widening to the left pterygopalatine fossa (*arrow*). An MR image is needed to assess for proximal intracranial extension to determine if this tumor was resectable.

tumors have defined routes of infiltration. Anterior third tumors tend to invade the FOM (**Fig. 13**). Middle-third lesions invade the musculature of the tongue and subsequently the FOM (**Fig. 14**). Posterior-third tumors grow into the anterior tonsillar pillar, tongue base, and glossotonsillar sulcus.[8] Involvement of the tongue base is critical to note, because it may necessitate a total laryngectomy to prevent aspiration.[30]

Up to 35% of patients have nodal metastasis on presentation (see **Fig. 13**). Even in the clinically N0 neck, 30% have occult metastasis.[8] The first nodal drainage group is level IB or submandibular, then level IIA or high jugular chain. Most authors suggest that greater than 4 mm depth (some advocate 5 mm) is associated with an increased risk of cervical nodal metastasis and therefore recommend

elective treatment of the clinically N0 neck.[20] Multiple studies have demonstrated the impact of tumor size on overall survival, thus the importance of the T factor on the AJCC chart. Overall survival decreases from 90% for tumors less than 2 cm to 60% to 63% for tumors greater than 2 cm.[31]

Floor of Mouth

The mylohyoid muscle forms the inferior border of FOM and divides the sublingual space from the submandibular space. It arises from the mylohyoid line of the mandible and inserts into the hyoid bone. This U-shaped sling is best visualized in the coronal plane (see **Fig. 2**). The mylohyoid muscle is innervated by the mylohyoid nerve, a branch of the inferior alveolar nerve (CN V3). Primary FOM
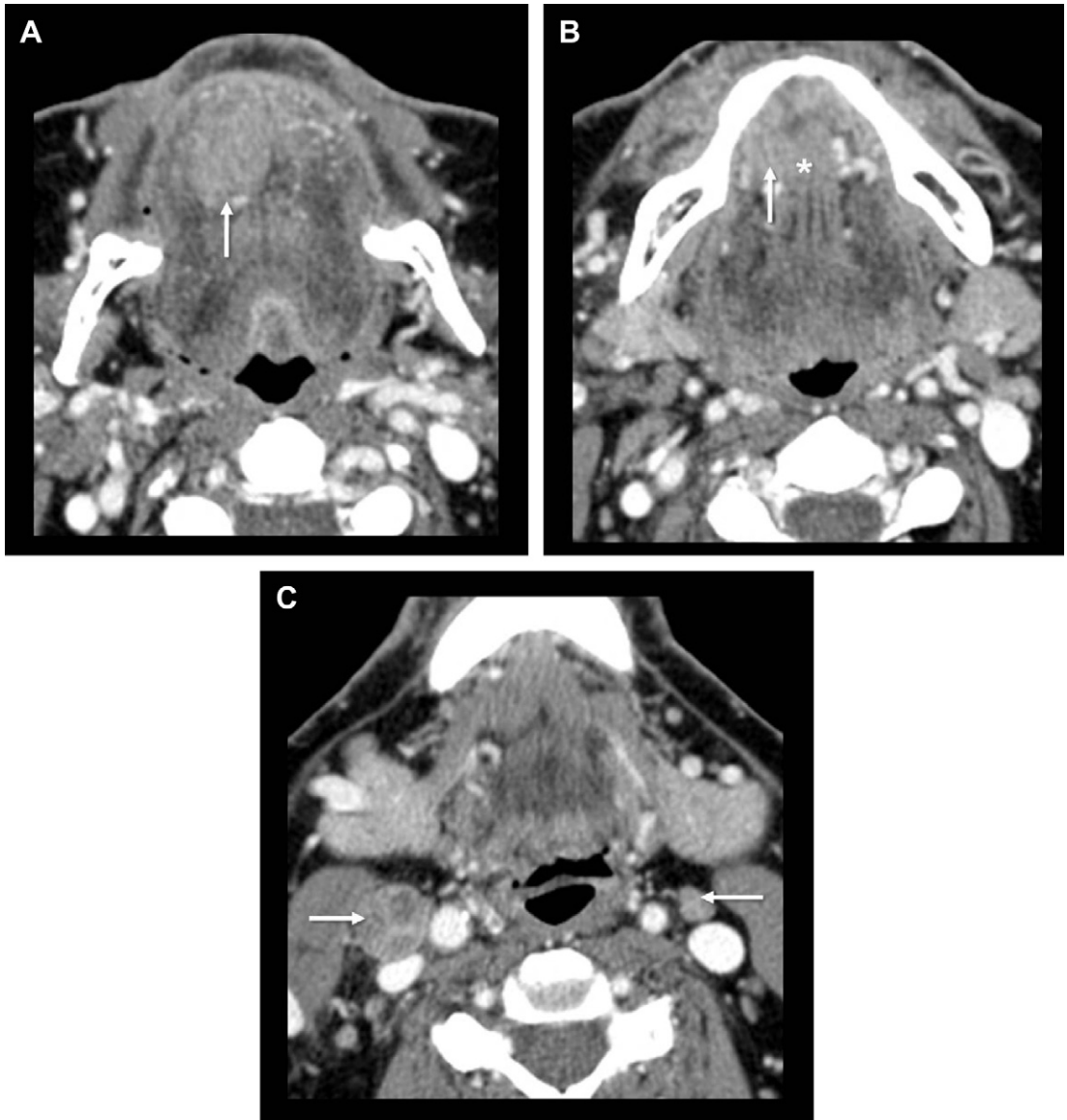
Fig. 13. SCC of the right anterior oral tongue, T4aN2c. (*A*) Axial CE CT shows a large mass in the anterior right oral tongue (*arrow*). (*B*) Axial CE CT (slightly inferior to *A*) shows extension to the floor of mouth (*arrow*), with efface-ment of sublingual space fat and involvement of genioglossus muscle (*asterisk*). The genioglossus muscle is an extrinsic tongue muscle and involvement upstages to T4a. (*C*) Axial CE CT shows abnormal bilateral level IIA nodes (*arrows*). Both have areas of low density consistent with necrosis, a morphologic abnormality with high speci-ficity, even though the left level IIA node is not abnormal by size criteria. The right level IIA node has surrounding fat stranding suggesting ECS. This is compatible with N2C disease.

carcinomas arise along the mucosal surface, including the crescent-shaped mucosa overlying the mylohyoid, sublingual space, and undersurface of the anterior two-thirds of the tongue.[28] FOM carcinomas tend to arise within 2 cm of the anterior midline and spread laterally to the adjacent mandible or ipsalateral or contralateral neurovas-cular bundle (**Fig. 15**). The neurovascular bundle, including the lingual artery and hypoglossal nerve, traverses the sublingual space. Ipsilateral tumor involvement necessitates sacrifice, but the remain-ing contralateral supply preserves viable tongue function. However, if tumor extends to the contra-lateral neurovascular bundle, this necessitates sacrifice of both bundles and total glossectomy. Nonsurgical management is often considered in these cases. Because the FOM is rich in neurovas-cular structures, frequent metastases occur to the
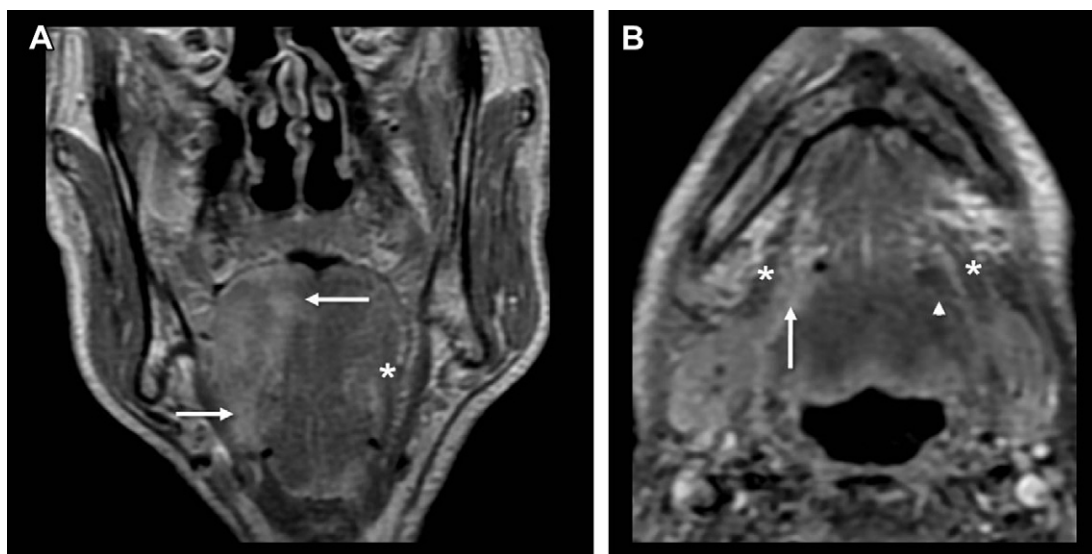
Fig. 14. SCC right oral tongue, T4a. (*A*) Coronal postcontrast T1-weighted image (fat saturation was not used secondary to excessive dental artifact) shows a large right oral tongue mass (*arrows*) extending to midline and inferiorly to involve the hyoglossus muscle. Note the normal left hyoglossus muscle (*asterisk*). (*B*) Axial postcontrast fat-saturated T1-weighted image shows the enhancing mass invading the right hyoglossus muscle (*arrow*). Note normal left hyoglossus muscle (*arrowhead*). Involvement of the hyoglossus (extrinsic tongue muscle) upstages to a T4a. The more lateral right and left mylohyoid muscles can also be seen (*asterisks*), but seem to have normal signal.

level I and II nodal groups. MR imaging provides better delineation of tumor extent in the FOM or toward the tongue base, but CT may be complementary to evaluate bone involvement.

Mandibular Invasion (T4a)

The presence of osseous involvement upstages OC carcinomas to at least stage T4a. Such subsites as the FOM, RMT, and the lower alveolus can invade the mandible directly. CT and MR imaging may be complementary for evaluation of mandibular involvement. In the RMT, one study suggests that CT is specific with a high positive predictive value (90%), but limited sensitivity (50%).[32] Other authors report high diagnostic accuracy for predicting mandibular invasion with thin-section CT Dentascan (sensitivity 95% and specificity 79%).[33] MR imaging offers superior evaluation of the medullary cavity, but may overestimate marrow involvement, secondary to adjacent odontogenic disease or edema. Although MR imaging may have good sensitivity, pitfalls result in low specificity.[34] The radiologist should closely examine the mandible for signs of invasion, including T1 hypointensity replacing normal fatty marrow, loss of low signal intensity cortex, and contrast-enhancement within the bone or along the inferior alveolar nerve. However, one potential

pitfall on MR imaging occurs in the setting of odontogenic disease, which can cause false-positive marrow replacement and even enhancement. Another pitfall on CT occurs in the evaluation of the edentulous patient, who may have a demineralized or even heterogeneous appearance of the mandible at baseline, making evaluation for subtle cortical invasion more difficult. Reformations in the oblique sagittal and coronal plane are often useful in these cases (**Fig. 16**).

Tumors invading the mandible can be managed with a marginal or segmental resection. Tumor invasion of only the periosteum without gross cortical invasion or involvement of the medullary cavity can be managed with a marginal mandibulectomy, which provides an adequate resection while maintaining the integrity of the bone. Tumors with gross cortical erosion or invasion of the medullary cavity require a segmental resection, meaning resection of the entire involved segment of mandible.[12] MR imaging may be complementary to CT to assess for medullary involvement. The segmental resection necessitates a more complex reconstruction, requiring vascularized bone and soft tissue, often a fibular free flap. In many cases, the most accurate measure of bony invasion is determined at the time of surgery. Unless there is frank invasion of the bony cortex on imaging or examination, wide excision and
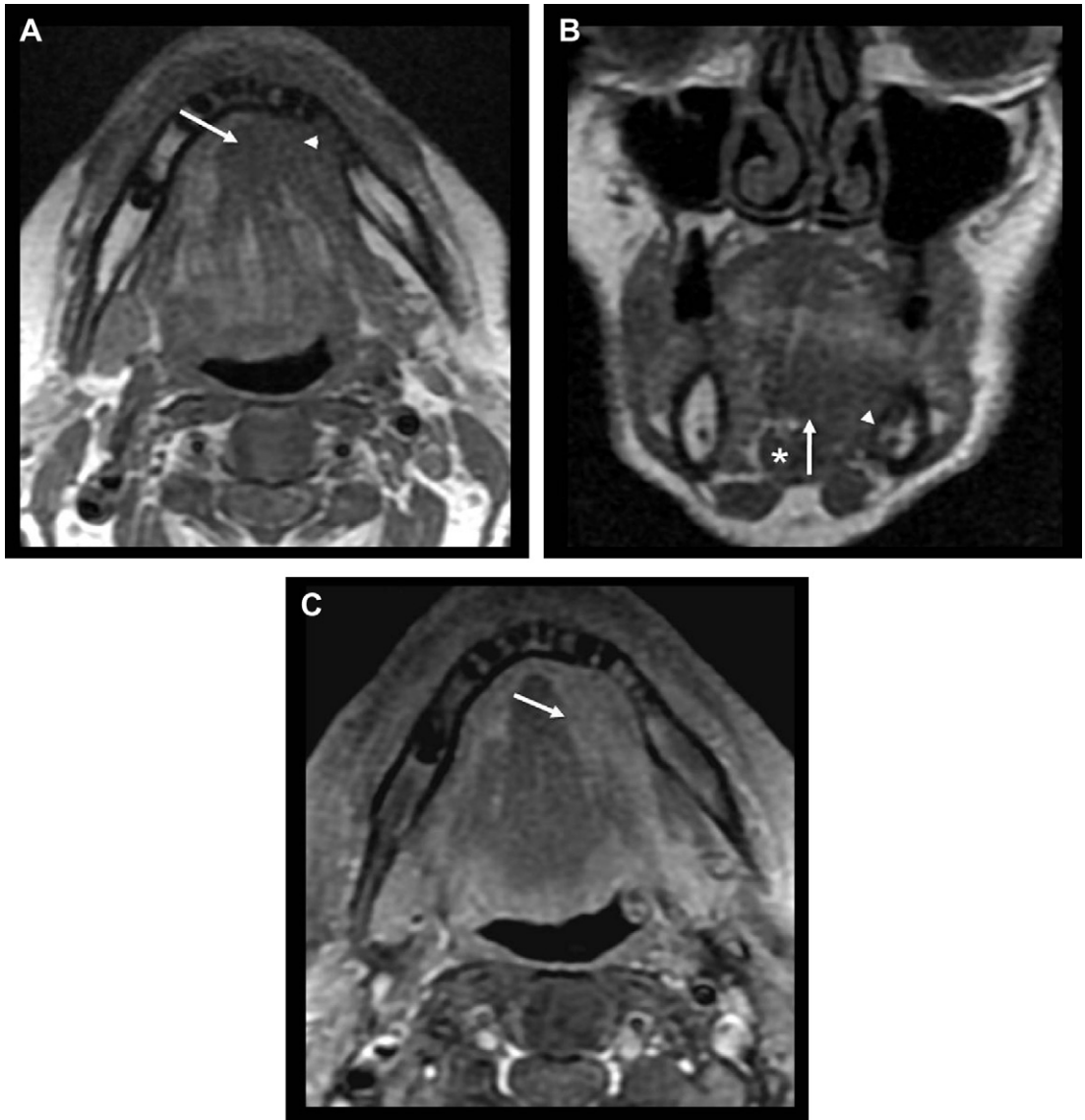
Fig. 15. SCC of the left floor of mouth, T4a. (*A*) Axial T1-weighted image shows a left anterior floor of mouth mass with medial extension to invade the anterior genioglossus (*arrow*) and lateral extension to invade the mandible (*arrowhead*). Both the genioglossus (extrinsic tongue muscle) and mandible invasion upstage to T4a. (*B*) Coronal T1-weighted image shows interruption of the mandible cortex (*arrowhead*) and medial extension to genioglossus muscle (*arrow*). The normal right geniohyoid muscle (*asterisk*) is seen just inferiorly. (*C*) Axial postcontrast fat-saturated T1-weighted image shows the borders of the mass and interface with midline genioglossus musculature (*arrow*).

periosteal stripping followed by frozen section examination at the time of surgery is often the most reliable measure of bone invasion.[12] If there is no cortical invasion, wide excision with periosteal stripping may suffice.

T4 DISEASE

The primary role of imaging in assessing the primary tumor is determination of T4a or T4b disease. The presence or absence of the following criteria should be reported for all OC tumors.

Extrinsic Muscle Invasion (T4a)

Invasion of the extrinsic tongue muscles should be assessed for all OC and OP primary tumors, because of the importance in upstaging to a T4a. Extrinsic tongue muscles include only the genioglossus, hyoglossus, styoglossus, and palatoglossus.
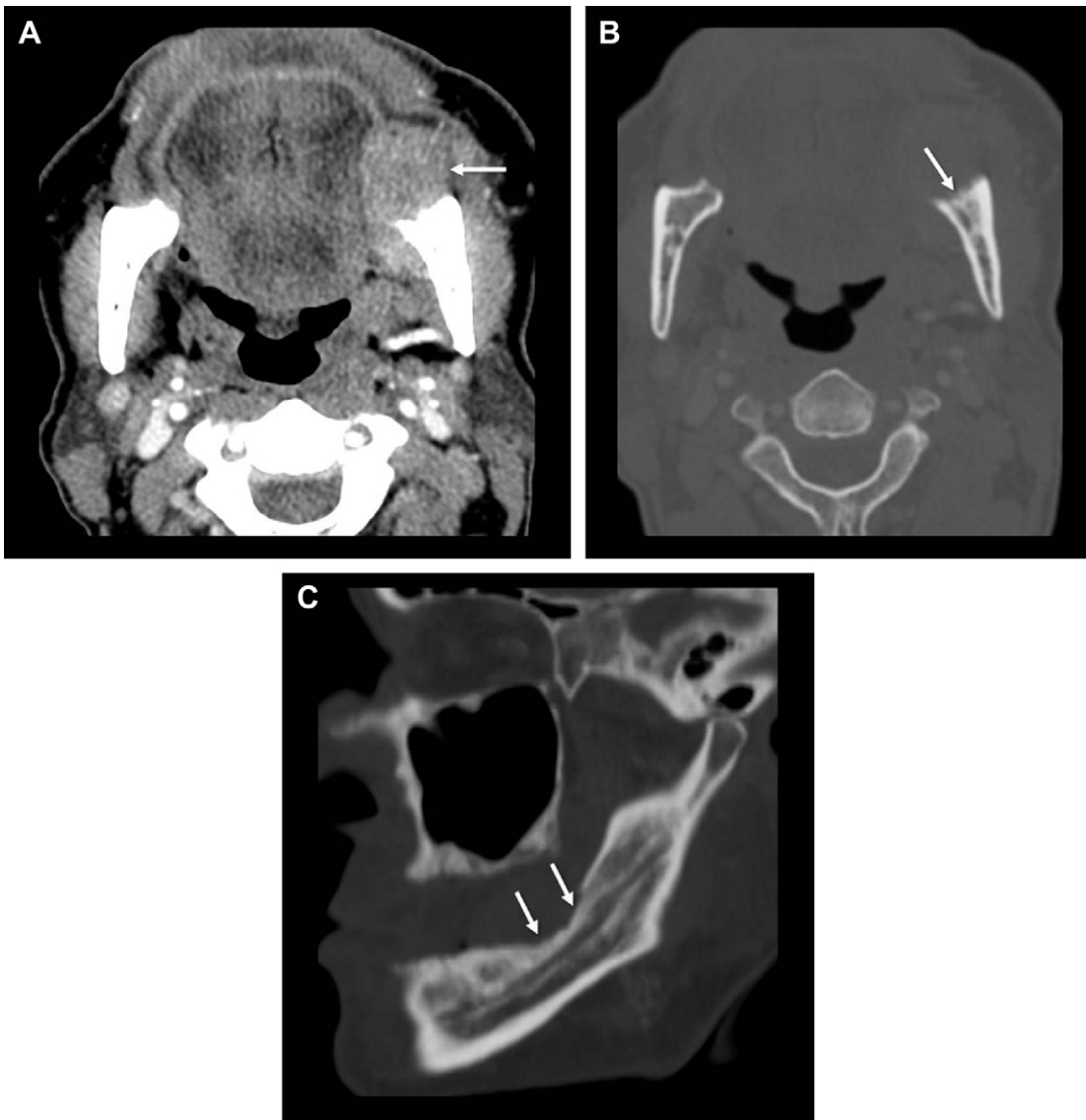
Fig. 16. SCC of the left posterior mandibular alveolar ridge, T4a: importance of reformations. (*A*) Axial CE CT shows a large mass along the posterior left mandibular alveolar ridge (*arrow*). (*B*) Axial CE CT in bone window demonstrates subtle cortical irregularity along the anterior mandibular angle/ramus junction (*arrow*). (*C*) Reformatted sagittal image confirms the focal cortical erosion (*arrows*).

The genioglossus and hyoglossus are most often involved and easily visualized on imaging to upstage to T4a. The hyoglossus muscle can be found just medial and parallel to the mylohyoid; it divides the sublingual space into medial and lateral portions (see **Figs. 1** and **2**). The paired genioglossus muscles can be found on either side of the lingual septum, just below the intrinsic tongue muscles (see **Figs. 1** and **2**). One potential pitfall is not understanding the anatomy or "speaking the same language" as the surgeons. The mylohyoid and geniohyoid are not extrinsic tongue muscles and their involvement does not upstage, but involvement is useful to report to surgeons.

Very Advanced Disease (T4b)

Tumor invasion of the masticator space, pterygoid plates, skull base, or encasement of internal carotid artery upstages to T4b (see **Fig. 11**). Resection may still be attempted for T4b disease, based upon masticator space invasion, but invasion of the skull base or internal carotid artery often deems a patient unresectable. Therefore, it is critical to

assess these structures for every OC tumor and clearly outline their involvement. However, it is important not to "overcall" because this may preclude surgery in a potentially resectable patient. For example, large tumors often seem to "bulge" into the masticator space and displace the medial pterygoid muscle, but this often does not translate into true invasion at surgery.

N STAGE

The N status of the cervical lymph nodes is the most important predictor of outcome in patients with SCC of the OC.[10] Most studies that have compared the accuracy of CT and MR imaging for assessment of lymph nodes have found no difference.[11,35–37] For lymph node staging of OC carcinoma it is important to remember that many surgeons perform prophylactic neck dissections for certain thickness of invasion (4–5 mm). Knowledge of the surgeons' practice at a particular institution dictates when careful discrimination of nodes is most critical to plan surgery and when it is not. Ultrasound-guided fine-needle aspiration of a suspicious node may be helpful for the clinically N0 neck, if this would affect surgical management. Level I and II lymph nodes are often the first involved. In the untreated neck, metastases to levels IV or V are rare in the absence of known metastasis at levels I to III. Among different subsites, the RMT and FOM show the strongest predilection for lymphatic involvement, with nearly 50% patients presenting the metastatic nodes.[26] Oral tongue SCCs present with regional lymph node metastasis in up to 40% cases, whereas primaries in the lip, buccal mucosa, and hard palate are less likely to have nodal involvement.[38] The imaging assessment of cervical lymphadenopathy is complex and includes not only determination of size, but also evaluation of morphology, borders, density, and number. A commonly used size criterion is no more than a maximal long axis diameter of 15 mm for levels I and II and no more than a maximal longitudinal diameter of 10 mm for all other levels.[39] If minimal diameter is used, then the threshold of 11 mm for level II nodes and 10 mm for all other levels has been used.

Regardless of the size, central low density is indicative of central necrosis and a metastatic node. Other highly suspicious features include rounded morphology with loss of the fatty hilum, heterogenous enhancement, clustering, and ill-defined margins. Ill-defined margins and soft tissue stranding indicate ECS. A more detailed discussion of lymph node drainage and metastatic lymphadenopathy is found elsewhere in this issue.

M STAGE

Distant metastasis from the OC is rare at presentation, so there is no cost-effective role for PET-CT in most patients with oral SCC. However, for more locally advanced cases PET-CT can be helpful to assess lymph nodes status, distant metastasis, or a second primary tumor, especially in the chest.

SURVEILLANCE

Most recurrences occur at the local site, so this should be the focus of surveillance imaging. Recurrence can be challenging to assess on imaging because of posttreatment changes, such as edema, fibrosis, and distortion of anatomy after surgical manipulation. It is standard to wait at least 10 to 12 weeks after surgery before imaging to reduce false-positive results. This is especially important when PET-CT is used for surveillance after surgical resection (or for staging after biopsy), because it is a common pitfall to see avid fluorodeoxyglucose uptake in areas of postsurgical inflammation (Fig. 17). The role of PET-CT has been assessed in other head and neck tumors, such as laryngeal and hypopharyngeal, but has not been established in OC SCC surveillance.[40] Nevertheless, it is not uncommon for surgeons to
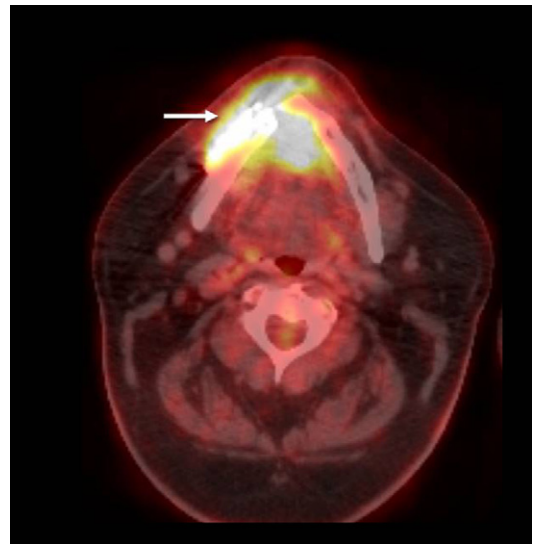
Fig. 17. Pitfall in PET-CT at the OC primary site. Axial fused PET-CT demonstrates intense fluorodeoxyglucose uptake 4 weeks after resection of floor of mouth. SCC (*arrow*). The patient had negative margins on pathology and a negative clinical examination. The increased fluorodeoxyglucose activity is caused by postoperative inflammation and is a common, expected postoperative appearance in this time frame. This examination was performed for lymph node staging.
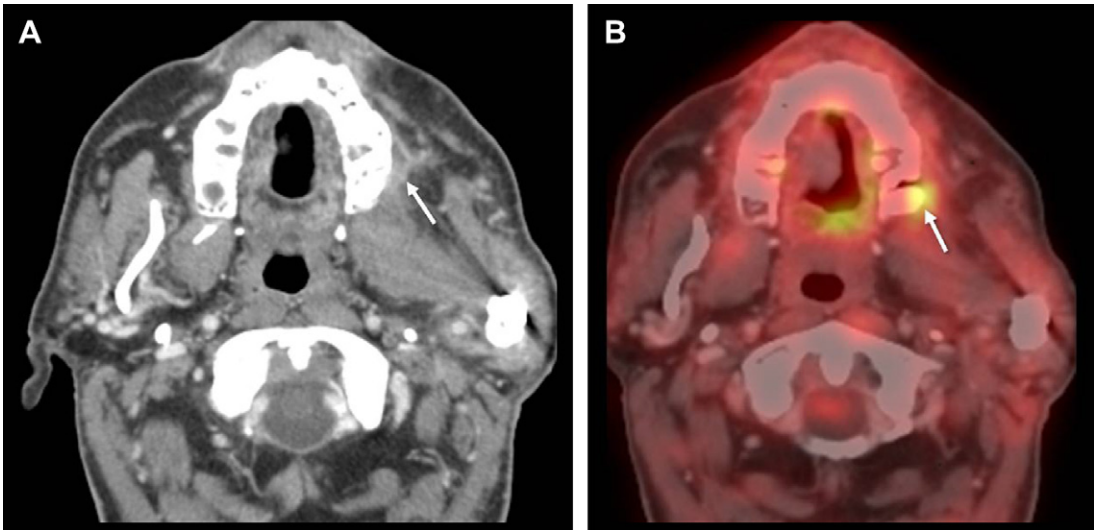
Fig. 18. Role of combined PET-CT to find early left RMT recurrence. (*A*) Axial CE CT showing postoperative changes after segmental mandibulectomy for an RMT primary. There is some effacement of buccal fat and mild prominence of soft tissue posterolateral to the maxillary alveolus (*arrow*); however, the findings are subtle and fairly nonspecific on this first postoperative baseline study. (*B*) The fused PET-CT image clearly identifies a focal area of increased uptake in this region (*arrow*). This was a pathologically proved recurrence. PET can add sensitivity to the CE CT, but it is important to be aware of false-positives.

use PET-CT surveillance after treatment for advanced OC tumors. In this setting, a diagnostic CT neck with contrast is performed and fused with PET images, interpreted by nuclear medicine and head and neck radiologists, and can be a powerful tool to detect recurrences in the complicated postoperative neck (**Fig. 18**).

Patients with advanced OC SCC treated with composite (removal of bone and soft tissue) resection and flap reconstruction present a particular challenge to the radiologist. The radial forearm flap is a fasciocutaneous flap commonly used to reconstruct the OC. The free fibula composite flap is often used to reconstruct after mandible
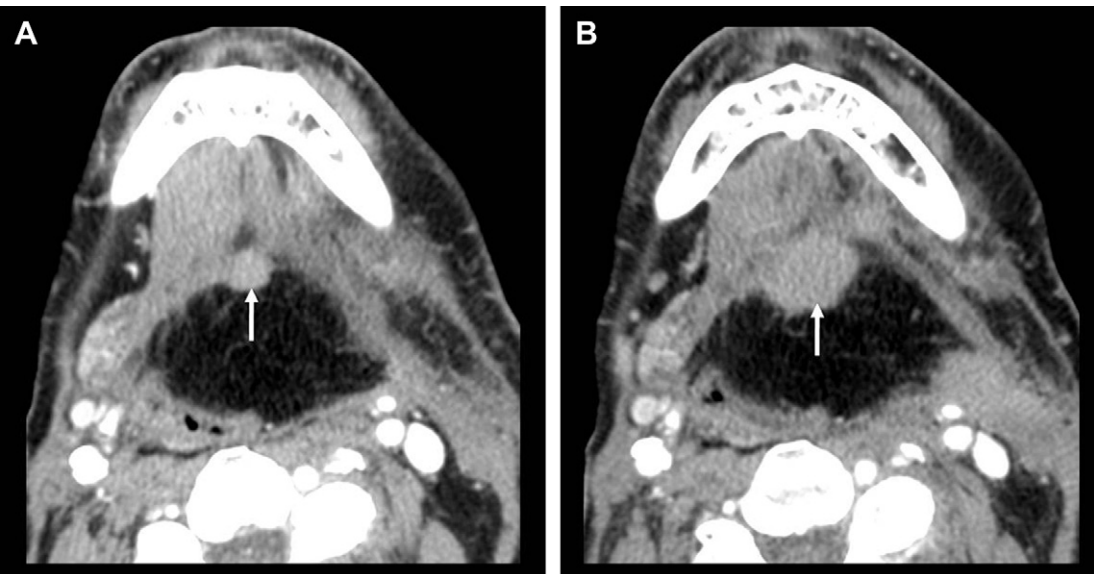
Fig. 19. Flap recurrence. (*A*) Axial CE CT shows a minimally enhancing 1-cm nodular density (*arrow*) along anterior aspect of the fatty portion of the flap at the interface between the flap and native floor of mouth structures. (*B*) Axial CE CT 2 months later shows interval increase in size of the mass (*arrow*).

resection. The radiologist should be aware of complications, such as seroma, hematoma, infection, fistulas, and recurrent tumor. Knowledge of the surgical procedure, type of flap used, and familiarity of the expected appearance of a flap greatly aid in interpreting the image. Therefore, reading operative reports is very useful. Tumor recurrence is commonly along the flap margins in the primary tumor bed. Focal nodular masses along the flap in the recipient bed, progressive soft tissue thickening, and local invasion are the strongest indicators of recurrent tumor (**Fig. 19**).[41]

Recurrence in the lymph nodes should also be assessed. Lymphatic metastasis after treatment can be unpredictable because of alterations in the normal lymphatic pathways, so even usual nodal groups, such as retropharyngeal, mediastinal, and even contralateral nodes, should be carefully assessed.

SUMMARY

Staging OC tumors requires knowledge of OC anatomy, the OC subsites, and tumor spread patterns. Radiologists should always assess for features that would upstage to a T4a disease, including invasion of the extrinsic tongue muscles or mandible, and features that upstage to T4b disease, including involvement of the masticator space, skull base, and encasement of the internal carotid artery. Although it is also important to assess for nodal metastasis, most surgeons perform a prophylactic neck dissection for T2-T4 disease and T1 disease with a depth of invasion greater than 4 mm. Radiologists should be familiar with important pitfalls and the complementary roles of CT, MR imaging, and PET-CT in the staging and surveillance of OC SCC.

REFERENCES

1. Cooper JS, Porter K, Mallin K, et al. National Cancer Database report on cancer of the head and neck: 10-year update. Head Neck 2009;31(6):748–58.
2. Landis SH, Murray T, Bolden S, et al. Cancer statistics, 1999. CA Cancer J Clin 1999;49(1):8–31, 1.
3. Llewellyn CD, Johnson NW, Warnakulasuriya KA. Risk factors for squamous cell carcinoma of the oral cavity in young people: a comprehensive literature review. Oral Oncol 2001;37(5):401–18.
4. Hennessey PT, Westra WH, Califano JA. Human papillomavirus and head and neck squamous cell carcinoma: recent evidence and clinical implications. J Dent Res 2009;88(4):300–6.
5. Jemal A, Thun MJ, Ries LA, et al. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. J Natl Cancer Inst 2008;100(23): 1672–94.
6. Steele TO, Meyers A. Early detection of premalignant lesions and oral cancer. Otolaryngol Clin North Am 2011;44(1):221–9, vii.
7. Laine FJ, Smoker WR. Oral cavity: anatomy and pathology. Semin Ultrasound CT MR 1995;16(6): 527–45.
8. Chong V. Oral cavity cancer. Cancer Imaging 2005; 5(Spec No A):S49–52.
9. Leslie A, Fyfe E, Guest P, et al. Staging of squamous cell carcinoma of the oral cavity and oropharynx: a comparison of MRI and CT in T- and N-staging. J Comput Assist Tomogr 1999;23(1):43–9.
10. Stambuk HE, Karimi S, Lee N, et al. Oral cavity and oropharynx tumors. Radiol Clin North Am 2007; 45(1):1–20.
11. Curtin HD, Ishwaran H, Mancuso AA, et al. Comparison of CT and MR imaging in staging of neck metastases. Radiology 1998;207(1):123–30.
12. Genden EM, Ferlito A, Silver CE, et al. Contemporary management of cancer of the oral cavity. Eur Arch Otorhinolaryngol 2010;267(7):1001–17.
13. Pohar S, Brown R, Newman N, et al. What does PET imaging add to conventional staging of head and neck cancer patients? Int J Radiat Oncol Biol Phys 2007;68(2):383–7.
14. Stuckensen T, Kovacs AF, Adams S, et al. Staging of the neck in patients with oral cavity squamous cell carcinomas: a prospective comparison of PET, ultrasound, CT and MRI. J Craniomaxillofac Surg 2000; 28(6):319–24.
15. Mack MG, Vogl TJ. MR imaging of the head and neck. Eur Radiol 1999;9(7):1247–51.
16. Kirsch C. Oral cavity cancer. Top Magn Reson Imaging 2007;18(4):269–80.
17. Escott EJ, Rao VM, Ko WD, et al. Comparison of dynamic contrast-enhanced gradient-echo and spin-echo sequences in MR of head and neck neoplasms. AJNR Am J Neuroradiol 1997;18(8): 1411–9.
18. Curtin HD. Detection of perineural spread: fat suppression versus no fat suppression. AJNR Am J Neuroradiol 2004;25(1):1–3.
19. Yuen AP, Lam KY, Wei WI, et al. A comparison of the prognostic significance of tumor diameter, length, width, thickness, area, volume, and clinicopathological features of oral tongue carcinoma. Am J Surg 2000;180(2):139–43.
20. Asakage T, Yokose T, Mukai K, et al. Tumor thickness predicts cervical metastasis in patients with stage I/II carcinoma of the tongue. Cancer 1998;82(8): 1443–8.
21. Coughlin A, Resto VA. Oral cavity squamous cell carcinoma and the clinically N0 neck: the past, present, and future of sentinel lymph node biopsy. Curr Oncol Rep 2010;12(2):129–35.

22. Kligerman J, Lima RA, Soares JR, et al. Supraomo-hyoid neck dissection in the treatment of T1/T2 squamous cell carcinoma of oral cavity. Am J Surg 1994;168(5):391–4.

23. Goerkem M, Braun J, Stoeckli SJ. Evaluation of clinical and histomorphological parameters as potential predictors of occult metastases in sentinel lymph nodes of early squamous cell carcinoma of the oral cavity. Ann Surg Oncol 2010;17(2):527–35.

24. Takes RP, Rinaldo A, Silver CE, et al. Future of the TNM classification and staging system in head and neck cancer. Head Neck 2010;32(12):1693–711.

25. Cohen EE, Baru J, Huo D, et al. Efficacy and safety of treating T4 oral cavity tumors with primary chemo-radiotherapy. Head Neck 2009;31(8):1013–21.

26. Trotta BM, Pease CS, Rasamny JJ, et al. Oral cavity and oropharyngeal squamous cell cancer: key imaging findings for staging and treatment planning. Radiographics 2011;31(2):339–54.

27. Kimura Y, Sumi M, Sumi T, et al. Deep extension from carcinoma arising from the gingiva: CT and MR imaging features. AJNR Am J Neuroradiol 2002;23(3):468–72.

28. Moore KL. Clinical oriented anatomy. 3rd edition. Baltimore (MD): Williams and Wilkins; 1992.

29. Ginsberg LE, DeMonte F. Imaging of perineural tumor spread from palatal carcinoma. AJNR Am J Neuroradiol 1998;19(8):1417–22.

30. Ong CK, Chong VF. Imaging of tongue carcinoma. Cancer Imaging 2006;6:186–93.

31. Tytor M, Olofsson J. Prognostic factors in oral cavity carcinomas. Acta Otolaryngol Suppl 1992;492:75–8.

32. Lane AP, Buckmire RA, Mukherji SK, et al. Use of computed tomography in the assessment of mandibular invasion in carcinoma of the retromolar trig-one. Otolaryngol Head Neck Surg 2000;122(5):673–7.

33. Brockenbrough JM, Petruzzelli GJ, Lomasney L. DentaScan as an accurate method of predicting mandibular invasion in patients with squamous cell carcinoma of the oral cavity. Arch Otolaryngol Head Neck Surg 2003;129(1):113–7.

34. Imaizumi A, Yoshino N, Yamada I, et al. A potential pitfall of MR imaging for assessing mandibular invasion of squamous cell carcinoma in the oral cavity. AJNR Am J Neuroradiol 2006;27(1):114–22.

35. van den Brekel MW, Castelijns JA, Snow GB. Detection of lymph node metastases in the neck: radiologic criteria. Radiology 1994;192(3):617–8.

36. van den Brekel MW, Stel HV, Castelijns JA, et al. Cervical lymph node metastasis: assessment of radiologic criteria. Radiology 1990;177(2):379–84.

37. Don DM, Anzai Y, Lufkin RB, et al. Evaluation of cervical lymph node metastases in squamous cell carcinoma of the head and neck. Laryngoscope 1995;105(7 Pt 1):669–74.

38. Wein R, Webber R. Malignant neoplasms of the oral cavity. In: Cummings C, Flint P, Harker L, editors. Cummings otolaryngology: head and neck surgery. Philadelphia: Elsevier Mosby; 2005. p. 1591–607.

39. Som P, Brandwein M. Lymph nodes. In: Som P, Curtin H, editors. Head and neck imaging. 4th edition. St Louis (MO): Mosby; 2003. p. 1912.

40. Ryan WR, Fee WE Jr, Le QT, et al. Positron-emission tomography for surveillance of head and neck cancer. Laryngoscope 2005;115(4):645–50.

41. Hudgins PA. Flap reconstruction in the head and neck: expected appearance, complications, and recurrent disease. Eur J Radiol 2002;44(2):130–8.