A Review of Salivary Gland Malignancies

Common Histologic Types, Anatomic Considerations, and Imaging Strategies

Remy Lobo, MD, Jeffrey Hawk, MD,
Ashok Srinivasan, MBBS, MD*

KEYWORDS

• Parotid • Submandibular • Sublingual • Minor salivary gland • Perineural tumor spread

KEY POINTS

- Most parotid neoplasms (approximately 4/5) are not malignant. Most sublingual neoplasms (approximately 4/5) are malignant. Approximately half of the minor salivary and submandibular neoplasms are malignant.
- The parotid gland has lymph nodes within its fascia, which makes it an important site in both primary and secondary malignancy evaluation.
- In addition to local aggressive features, important directions of spread for parotid malignancy include routes along the cranial nerves (CNs), most commonly trigeminal (CN V) and facial (CN VII), with their anastomotic connections. Knowledge of local tumor and nodal staging offers crucial prognostic and management information in tumor-node-metastasis staging of disease.

TUMOR EPIDEMIOLOGY AND PRESENTATION

Salivary gland malignancies are a rare group of heterogeneous neoplasms arising along the aerodigestive tract and its major secretory structures. They represent less than 8% of head and neck tumors and a total of less than 2500 new cases per year in the United States. Both viral and environmental factors have been implicated as potential causes of neoplasia.[1]

These tumors can present in various clinical scenarios. Major salivary gland malignancy typically manifests as a palpable abnormality to a clinician or patient. The major (parotid, submandibular, and sublingual) gland is often enlarged and may (or may not) be painful on examination. Pertinent features for the clinician involve the evaluation of the adjacent nervous structures. For example, cranial nerve (CN) VII (facial) should be scrutinized in the setting of parotid enlargement because facial muscle weakness can alert a clinician to a parotid neoplasm affecting CN VII as it passes through the gland. Minor salivary gland malignancies present according to the surrounding tissue affected. For example, a hard palate tumor may be quite small, but if it affects a branch of CN V (trigeminal), the patient may present with numbness. Other scenarios can be imagined: a minor neoplasm along the optic canal could present with vision complaints and a nasal mass could present with obstruction. Nasopharyngeal masses often present late to the clinician and may already have invasion at the skull base.[2] If the primary site is more occult, a nodal mass may be the presenting sign, leading to imaging evaluation. Certain salivary malignancies (eg, mucoepidermoid carcinoma

Department of Neuroradiology, University of Michigan, B2-A209D, 1500 East Medical Center Drive, Ann Arbor, MI 48109, USA
* Corresponding author.
E-mail address: ashoks@med.umich.edu

Neuroimag Clin N Am 28 (2018) 171–182
https://doi.org/10.1016/j.nic.2018.01.011

[MEC]) have a tendency for nodal metastases. Close attention should be paid to the aerodigestive tract and associated salivary glands in all cases of pathologic nodal enlargement.

Most salivary gland neoplasms arise in the parotid gland, approximately 73% in 1 large study,[3] but they are not usually malignant; merely one-fourth (15%–32%) of parotid neoplasms are malignant on histology.[4] Less than 11% of salivary gland neoplasms arise in the submandibular gland, where they carry a 41% to 45% chance risk of being malignant. Less than 0.5% of salivary neoplasms arise in the sublingual gland, but they carry a 70% to 90% chance of being malignant. Minor salivary glands account for the remaining approximately 14% of salivary tumors.[1] Among the 450 to 750 minor salivary glands overall, approximately half of the tumors found are malignant. Risk of malignancy is stratified among the minor salivary glands; approximately half of the palatal neoplasms found are malignant; however, in the floor of mouth, the risk increases to 90%.[5] Although most large population studies are somewhat dated, recent studies have generally held these percentages stable over time.[6] The 1 addition is that more cancers are now diagnosed, yet causative factors remain elusive.

In summary, and as a rule, the risk of malignancy increases as the gland decreases in size. Although tumors are most commonly found in the parotid, they are least likely to be malignant in that location; the majority are adenomas. Although the sublingual gland is a small structure, tumors found within it are usually (almost 90% of the time) malignant. Still, given the overall disproportionate distribution of tumors to the parotid gland, the parotid is the most likely major salivary gland in which malignancy arises.

TUMOR HISTOLOGY

According to the World Health Organization (WHO), there are more than 25 types of distinct salivary gland tumors. New histologic and biochemical techniques allow for identification of different molecular and genetic subtypes (including hallmark translocations), which can help direct targeted therapy. The WHO updated their 2005[7] *Classification of Head and Neck Tumours* with a new list of salivary gland malignancies in 2017.[8] The most common salivary malignancies (**Box 1**) still include adenocarcinomas, carcinoma ex pleomorphic adenoma, acinic cell carcinoma, adenoid cystic carcinoma (ACCa), MEC, and lymphomas. Important additions include the mammary analog secretory carcinoma (an acinic cell variant based on gene fusion) and several differences in grouping (eg, low-grade cribriform adenocarcinoma is now grouped in with intraductal carcinoma). The update grants pathologists increased flexibility to characterize the tumors according to which translocations and gene fusions are identified. Pathologists can also incorporate descriptions of high/intermediate/low-grade rates of mitoses into their analysis, and preference is now given to a new phrase, "high-grade transformation," which replaces dedifferentiation.[8] Genetic rearrangements are also described and help determine tissue of origin. Although much of the update revolved around primary neoplasms, it must be remembered that secondary malignant pathology can also occur in the salivary glands, specifically, malignant metastases to intraparotid lymph nodes.

Box 1
Common histologic types of salivary malignancies

Primary

Adenocarcinomas

Carcinoma ex pleomorphic adenoma

Acinic cell carcinoma

ACCa

MEC

Intraductal carcinoma

Mammary analog secretory carcinoma

Lymphomas

Secondary

Intraparotid lymph node metastases

Abbreviations: ACCa, adenoid cystic carcinoma; MEC, mucoepidermoid carcinoma.

IMAGING AND STAGING OF SALIVARY GLAND MALIGNANCIES

Major salivary gland malignancies have a separate, dedicated American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system. Minor salivary gland malignancies are staged according to the local site of origin. AJCC TNM classifications for malignancies of the paranasal sinuses/nasal cavity, nasopharynx, oral cavity, oropharynx, hypopharynx, or larynx (with subsites) are used. Proper radiologic assessment of salivary gland malignancies requires having familiarity with the AJCC TNM staging schemes in the head and neck and apply these guidelines when mapping the extent of tumors.[9] Simply identifying the presence of a tumor or speculating as to the histologic type of tumor is not the primary role of the radiologist in these cases.

When imaging salivary gland malignancies, the goal is to determine the extent of tumor for treatment planning purposes. Four forms of extension should be considered (**Box 2**). These include direct extension (direct invasive growth of the primary tumor), perineural extension (extension along CNs and their branches) and metastatic extension (typically lymphatic extension to cervical lymph nodes); hematogenous metastasis to bone or brain as seen on head and neck imaging does occur but is far less common. Techniques for imaging salivary gland malignancies include ultrasound, Computed tomography (CT), MR imaging, and nuclear medicine (fluorodeoxyglucose [FDG] PET-CT).

Ultrasound

Superficial palpable masses are amenable to ultrasound evaluation. High-frequency linear transducers provide exquisite detail of the superficial anatomy and can be used as a convenient screening tool for lymphadenopathy. Ultrasound provides an inexpensive and portable means of early evaluation of superficial parotid and submandibular lesions. Ultrasound-guided procedures are also a useful adjunct for obtaining histologic samples that may help direct future imaging examiantions.[10] Ultrasound is of limited utility in the deep lobe of the parotid and of the minor salivary glands. Rare sublingual neoplasms, given inherent risk of malignancy, are usually evaluated with other cross-sectional modalities.

Computed Tomography

Salivary gland malignancies are often first imaged with (or incidentally detected) on routine CT imaging of the neck. Unless there is a contraindication, contrast-enhanced imaging should always be used. Noncontrast imaging, either alone or in combination with contrast-enhanced imaging, is of limited value and is usually not indicated (discussed later).

CT imaging of the neck (**Table 1**) should begin at the midorbit and extend below the clavicular heads with the arms at a patient's side. A head holder may be helpful. The authors use a split bolus technique using a total of 125 mL of Isovue-300: an initial 50-mL bolus is followed 120 seconds later by a 75-mL bolus. The scan is initiated 60 seconds after the second bolus. Slice thickness is 1.25 mm with a 1.25-mm interval and a display field of view (DFOV) of 20 cm to 24 cm. Axial bone and soft tissue reformats are used in conjunction with the soft tissue sagittal and coronal reformats in all cases.

CT imaging is useful for identifying major and minor salivary gland tumors and determining the local direct extension of the tumor with attention to the nearby involved soft tissue and osseous structures. Bone algorithm CT nicely displays osseous cortical and trabecular destruction. Bone CT also demonstrates destruction of ossified cartilage from direct tumor extension. Perineural extension can be detected on CT by noting expansion of the respective skull base foramina or loss of fat on soft tissue images, but this occurs only after the nerves have been extensively involved by tumor. Direct and perineural extensions are critical components of the T component of TNM staging.

Lymphatic spread of tumor to cervical lymph nodes is well depicted with CT. Careful assessment of each cervical nodal level, including the retropharyngeal regions, should be performed after determining the local tumor extent. This determines the N component of the TNM staging. Presence or absence of extranodal extension was a new addition to the *AJCC Cancer Staging Manual, Eighth Edition*.[9] Extranodal extension (+) nodes have indistinct fat planes and may show strands of soft tissue directly invading the adjacent structures. Although many pathologic cervical nodes

Box 2
Imaging goals for assessing extent of salivary gland malignancies

Local extent (T staging, CT/MR imaging)

Direct extension

Perineural extension

Lymphatic spread (N staging, requires PET/dedicated chest, abdomen, pelvis imaging)

Nodal involvement

Hematogenous spread (M staging, requires PET/dedicated chest, abdomen, pelvis imaging, +/− MR imaging)

Anatomically remote structures (bone, brain, and so forth)

Table 1
Helical CT neck protocol

Slice thickness	1.25 mm
Interval	1.25 mm
Pitch	0.97:1
Kilovolt (peak)	100
Auto milliamperes (minimum/maximum)	100/450
DFOV	20–24 cm

are clinically palpable, retropharyngeal nodes are not. Imagers can add value by drawing attention to the retropharyngeal nodes, possibly altering surgical approach. Assessment of the visualized intracranial structures and osseous structures on neck CTs remote from the primary tumor also assists with M component of TNM staging, although full staging requires PET and/or dedicated imaging of the chest, abdomen and pelvis (with or without MR imaging).

Dual-Energy Computed Tomography

Dual-energy CT (DECT) can be a useful technique to determine true tissue enhancement and identify differences in attenuation within glandular structures.[11] This technique, although not in common use, has potential for application in salivary imaging. DECT can generate a virtual noncontrast (VNC) image. VNC sequences are most useful for identifying calcifications seen in inflammatory sialolithiasis. Several higher-grade neoplasms (like salivary ductal carcinoma) can have calcifications,[12] and VNC sequences can increase the conspicuity of these foci. CT is limited in its detection of perineural tumor; DECT can (in part) overcome this with bone subtraction, which can increase the conspicuity of enhancement at the skull base foramina by removing the adjacent hyperattenuating osseous structures,[11] leaving the enhancing tumor floating in the foramen of interest. In an area of ongoing research, DECT may be useful in evaluating cervical lymphadenopathy.[13] DECT also has a benefit in assessing the primary malignant site. By creating virtual monochromatic sequences at a low kiloelectron voltage (eg, 50–70 keV), the conspicuity of tumors can be increased within the salivary glands. Salivary neoplasms can be occult on regular contrast-enhanced CT and obvious on MR imaging; virtual monochromatic sequences bridge this gap by creating a lower profile of photons; the native gland often becomes slightly hypoattenuated and the enhancing tumor becomes more conspicuous.[14] In cases of MR imaging not available, DECT may be a useful modality for analysis.

MR Imaging

MR imaging is useful for precise tumor mapping in certain circumstances and adds additional information for further soft tissue characterization of the primary tumor. The main uses for MR imaging are in the evaluation of salivary gland malignancies that arise near or extend to the skull base (more often minor salivary gland malignancies), evaluation of perineural tumor spread (important for parotid malignancies and minor salivary gland malignancies near the skull base), and assessment for osseous marrow involvement, when applicable. MR imaging also provides better soft tissue resolution of head, neck, and intracranial structures.[15]

Dedicated MR imaging protocol (**Table 2**) for assessment of perineural spread, including protocols focused on the CN VII (for parotid malignancies) and CN V (for malignancies arising along the skull base or palate), should be performed in all applicable cases. This is particularly true when there is clinical evidence of CN deficits (eg, facial pain or numbness) or in the presence of a tumor with a high propensity (whether by location or histology) for perineural spread. MR imaging can detect perineural spread at a much earlier stage than CT and is the imaging standard in this assessment.[16]

Precontrast, non–fat-saturated T1 sequences are useful to detect intermediate to low T1-weighted image signal obliteration of high signal fat planes at the exocranial aspects of skull base foramina (stylomastoid foramen, foramen ovale, and so forth) or in the deep face (pterygopalatine fossa, inferior alveolar canal, orbital fissures, and so forth). Postcontrast, fat-saturated T1 sequences in the axial and coronal planes are useful for identifying abnormal enhancement in these same areas as well as asymmetric enhancement along the intraosseous and deeper courses of these nerves (intratemporal facial nerve, foramen rotundum,

Table 2
Skull base protocol

Slice thickness, interval	3 mm, 1 mm
DFOV (cm), matrix	20, 512 × 512
Whole brain	Ax DWI, Ax FLAIR, Ax GRE, Sag T1, and Ax post-T1 (spin echo)
Precontrast skull base (third ventricle–hyoid)	Ax T1, Cor T1, Ax T2 FS, Cor STIR
Postcontrast skull base (third ventricle–hyoid)	Ax T1 FS, Cor T1 FS
Optional general (whole) neck	Precontrast Sag T1, Ax T2 FS or STIR, Ax T1, Cor T1, Cor STIR or T2 FS; and postcontrast Ax T1 FS, Cor T1 FS
Optional advanced imaging	T1 DCE, DWI (full-neck axial)

Abbreviations: Ax, axial; Cor, coronal; FLAIR, fluid-attenuated inversion recovery; FS, fat saturated; GRE, gradient recalled echo; Sag, sagittal.

vidian/pterygoid canal, palatine foramina, cavernous sinus, trigeminal/Meckel cave, and so forth). Caution should be used when evaluating the intratemporal facial nerve, because variable segments of the intratemporal perineural venous plexus enhance normally.[17] Enlargement and marked asymmetry are the hallmarks of pathology.

Precontrast non–fat-saturated and postcontrast fat-saturated T1 MR imaging are also useful for detecting involvement of marrow spaces of the mandible and skull base. In cases of minor salivary gland tumors of the larynx, they are helpful in detecting tracheal and cricoid cartilage infiltration.[18] These sequences, along with fat-saturated T2/short tau inversion recovery (STIR), are also useful for assessing invasion of soft tissues of the neck and skull base.

Advanced imaging is not ubiquitously used in the evaluation of salivary gland malignancies, although it may yet prove useful.[19] Techniques like diffusion-weighted imaging (DWI)/apparent diffusion coefficient (ADC) are well researched in the brain and many studies look at the hypointense signal on ADC as a marker of hypercellularity and as a surrogate marker of malignancy. The caveat is that multiple nonmalignant neoplasms (eg, Warthin tumors, also known as papillary cystadenoma lymphomatosum [PCL]) can also be hypointense on ADC. Because Warthin/PCL tumors are far more common than malignant neoplasms, this confounds data and overwhelms most studies. Dynamic contrast-enhanced imaging (DCE) uses contrast-enhanced curves to characterize tumoral angiogenesis, and tissue enhancement. DCE (Time to maximal contrast enhancement) has been shown helpful in distinguishing benign from malignant minor salivary gland neoplasms.[20] This was not replicated in major salivary glands, however.[21] Despite this, groups have tried a combination approach using DWI and DCE with varying degrees of success.[22] Continued research is ongoing in this area.[23]

PET-Computed Tomography

PET-CT is often an adjunct to other anatomic imaging in the evaluation of salivary gland malignancies. Primary lesions may be FDG avid, although several salivary carcinomas are not. More commonly incidental salivary lesions are found when imaging patients with PET-CT for a different cause. A reported 2% of cases have focal FDG-avid signal, although PET-CT is not reliable in distinguishing benign from malignant tissue (Warthin tumors can also be FDG avid). Tissue sampling is usually indicated in these cases because there is a reported one-third risk of malignancy.[24]

HISTOLOGIC TYPES OF SALIVARY GLAND MALIGNANCIES

Adenocarcinoma

Adenocarcinomas most commonly occur in the minor salivary glands of the palate and can be treated with surgical resection if caught early. Care must be taken to ensure clear margins because there is a risk of perineural extension and (less commonly) osseous invasion. Histologic progression[25] and transformation are also risks.[8] These adenocarcinomas were previously described as polymorphous low-grade adenocarcinoma. They stain positive for S100 on pathology,[26] have gene rearrangements of PRKD, and can have a targetoid appearance on histopathology.[8] **Fig. 1** shows a 49-year-old woman who initially presented with right facial numbness. She was worked up for stroke, but the cause of her numbness was actually a palatal adenocarcinoma affecting the maxillary division of CN V. Note the expansile lesion centered at the junction of the hard and soft palate, which, coincidentally, also has a targetoid appearance,

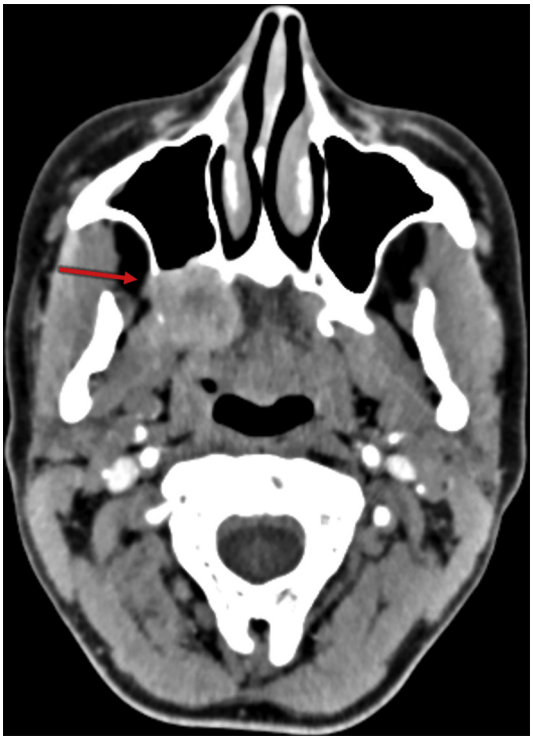

Fig. 1. Right palatal minor salivary gland neoplasm, adenocarcinoma, which initially presented with facial numbness in a 49-year-old woman. Axial image shows a right palate mass eroding the posterior right maxillary sinus and adjacent pterygoid plates (*arrow*). Incidental aerodigestive lesions can occasionally be identified on emergent stroke evaluation (CT angiogram, as shown, or MR imaging of the brain).

centrally hypoattenuating with increased peripheral attenuation/enhancement. Major salivary glands can also have adenocarcinomas, as shown in Fig. 2—a 51-year-old woman with left neck palpable lump. The parotid masses often present as painless abnormalities; key descriptions in Fig. 2 involve the cystic change in the adenocarcinoma and irregular margins, suggesting a degree of infiltration. These have a nonspecific appearance on MR imaging and variable T2 signal (often hyperintense to the gland, although they can be hypointense) and usually enhance.

Carcinoma Ex Pleomorphic Adenoma

Carcinoma ex pleomorphic adenoma is a carcinoma that arises from a preexisting pleomorphic adenoma. This occurs in approximately 1.5% of pleomorphic adenoma cases at 5 years and almost 10% at 15 years.[27] The classic history is a painless mass for many years that has recently grown. That story was true in Fig. 3—a 52-year-old man with lump near the right submandibular gland that grew over the previous year. The peripherally calcified mass was excised en bloc, with histologic features of carcinoma ex pleomorphic adenoma. Soft tissue invasion beyond the lesion capsule is common and should be quantified on pathology. Histologic hallmarks could include translocations of 8q12, 12q13-15, or 12q15.[8] Although most common in the parotid, they can occur in other secretory glands, even lacrimal. When positioned along bone, CT can show osseous erosions suggesting malignant degeneration.

Acinic Cell Carcinoma

Acinic cell carcinoma is a low-grade malignancy most commonly found in the parotid gland. The tumor is characterized by serous acinar differentiation and basophilic cytoplasmic granules on histology. Acinic cell carcinomas are not (typically) locally aggressive[28] and may be managed surgically. Fig. 4 is an image of a 56-year-old woman with palpable left parotid mass. It is homogeneously intermediate/low in signal (see Fig. 4A) precontrast T1, distinguishing it from the remainder of the glandular architecture. It enhances uniformly (see Fig. 4B) and is intermediate

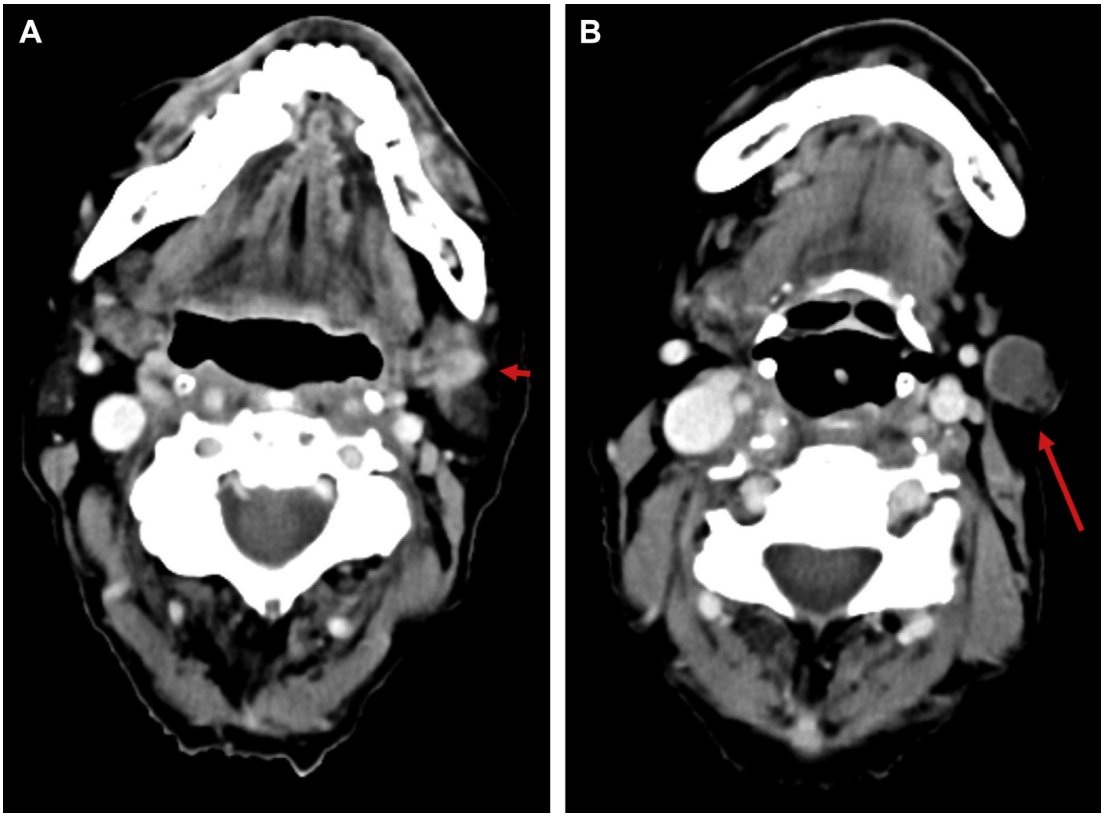

Fig. 2. Adenocarcinoma of the left submandibular gland in a 51-year-old woman with palpable nodule. Contrast-enhanced CT shows areas of hyperattenuation superiorly (*short arrow, A*) and cystic change more inferiorly (*long arrow, B*).

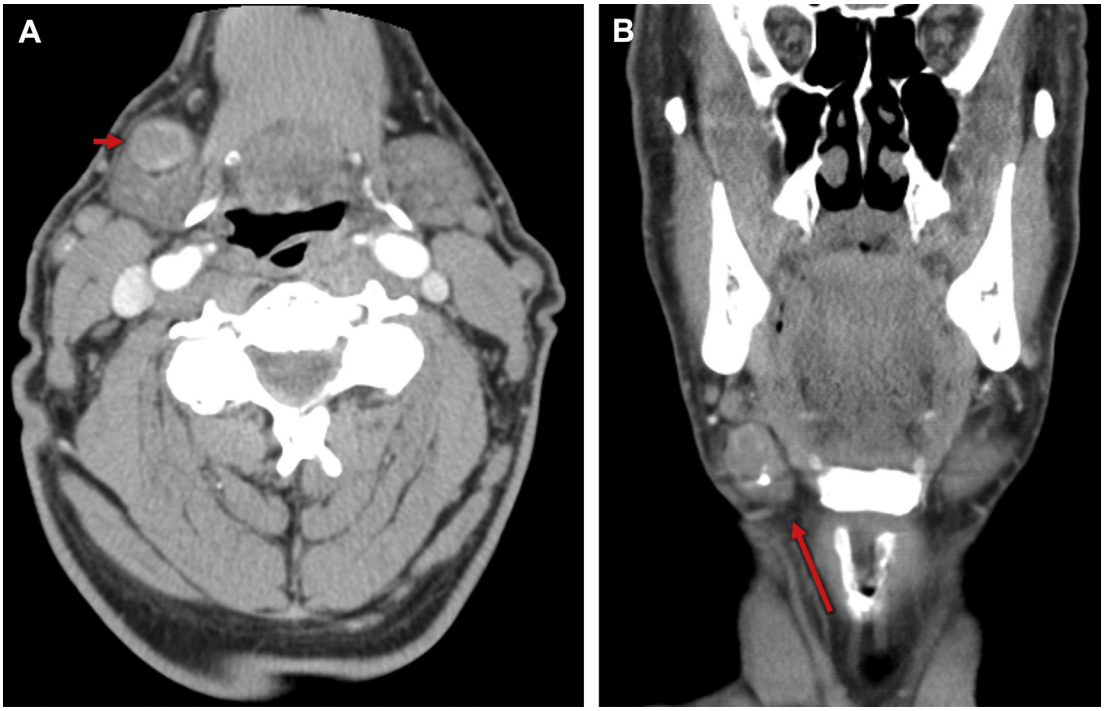

Fig. 3. Carcinoma ex pleomorphic adenoma in a 52-year-old man with "neck lump." Axial contrast-enhanced CT shows a peripherally hyperattenuating lesion (*small arrow, A*) in the right submandibular gland, with a punctate calcification on coronal contrast-enhanced CT (*long arrow, B*). Appearance is often nonspecific and requires histologic sampling.

on fluid-sensitive sequence (see Fig. 4C). Many malignancies previously believed acinic cell carcinomas are now characterized as mammary analog secretory carcinomas.[28]

Adenoid Cystic Carcinoma

ACCa occurs most commonly in middle-aged and elderly patients. ACCa occurs in both major and minor salivary gland tissue and has a strong propensity to spread by perineural growth. ACCa tumors are composed of ductal epithelial and myoepithelial cells. Architecturally, ACCa has 3 types, including solid, cribriform, and tubular, with cribriform the most common. ACCa can show distant metastasis as well as nodal metastasis.

On imaging, ACCa is intermediate to low signal on both T1 and T2. ACCa tumors enhance, and thickening and enhancement of CN V and/or CN VII raise concern for perineural tumor growth. Fig. 5 shows a right parotid lesion in an 82-year-old woman who presented with facial weakness. The tumor is low/intermediate on T1 (see Fig. 5C) and enhancing (see Fig. 5B). Although T2 bright on fluid-sensitive sequences (see Fig. 5A), these tumors can have intermediate signal, as well. Subtle although true asymmetric enhancement of CN VII was positive at histology for perineural tumor spread of ACCa. Lower-grade tumors often have better defined margins and high-grade tumors are generally more infiltrative on imaging. Histologically, they most commonly have 6q22-23 translocations, although they can also have 8q13 translocations.[8]

Mucoepidermoid Carcinoma

MEC is the most common salivary gland malignancy in both adults and children.[29] MEC originates from the epithelium of the salivary gland ducts and consist of a mixture of mucus-secreting cells, epidermoid cells, and intermediate cells. There can be cystic components and there is variability in the appearance of these tumors at pathology. MEC tumors are assigned a grade of low, intermediate, or high, based on features, such as necrosis, frequency of mitoses, and anaplasia. MEC metastasizes to lymph nodes and can show perineural tumor growth (although less frequently than ACCa).

On imaging, low-grade tumors may have a more circumscribed margin and higher-grade tumors may appear more infiltrative, ill-defined, and aggressive. MEC often demonstrates low to intermediate signal on both T1 and T2 imaging with cystic components appearing more T2

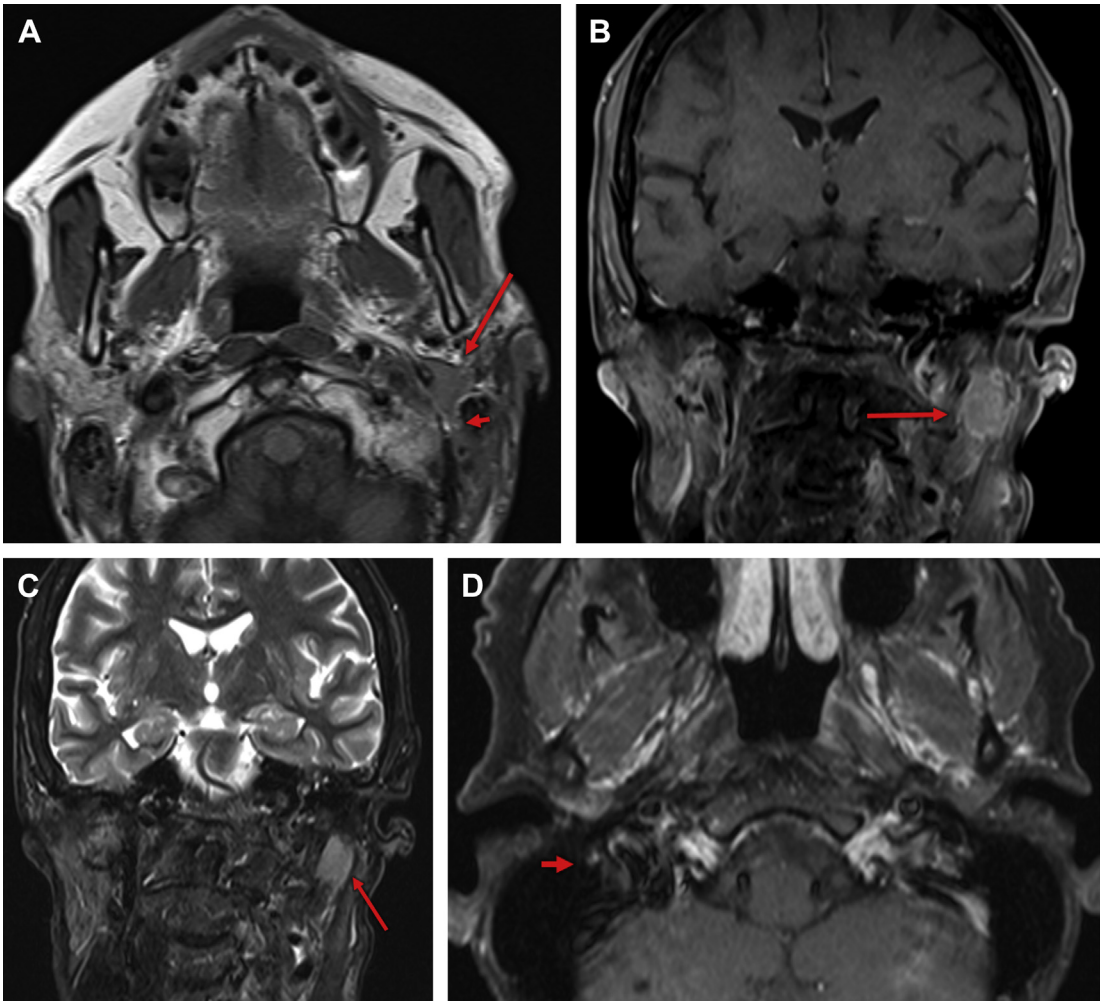

Fig. 4. Acinic cell carcinoma of the left parotid (*long arrows*) in a 56-year-old woman with facial swelling. Precontrast T1 axial shows a deep left parotid lobe lesion with intermediate to low T1 signal (*A*). Note the tail of tissue extending posteriorly toward the stylomastoid foramen (*short arrow, A*). Coronal postcontrast (*B*) shows uniform enhancement and slightly hyperintense T2/STIR (*C*) signal on coronal fluid-sensitive sequences. Note the asymmetric enhancement at the mastoid segment of the right facial nerve (*short arrow, D*).

hyperintense, as shown in Fig. 6—a 73-year-old man who presented with palpable right-sided neck mass. Low to intermediate on T1 (see Fig. 6A) and uniformly enhancing (see Fig. 6B), The MEC showed relatively lower signal on coronal STIR (see Fig. 6C). The presence of ipsilateral enlarged nodes (see Fig. 6C) helped direct the differential to MEC over other neoplasms.

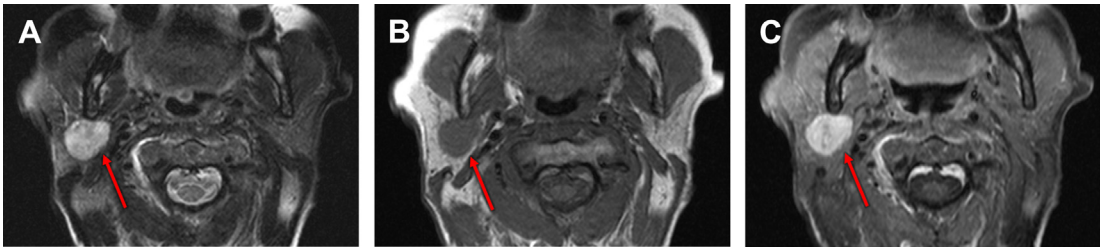

Fig. 5. ACCa of the right parotid in an 82-year-old woman. Axial T2 fat-saturated image (*A*) shows a slightly hyperintense lesion, precontrast T1 image (*B*) shows hypointense signal, and T1 with contrast fat-saturated image (*C*) shows homogenous enhancement (*long arrows*).

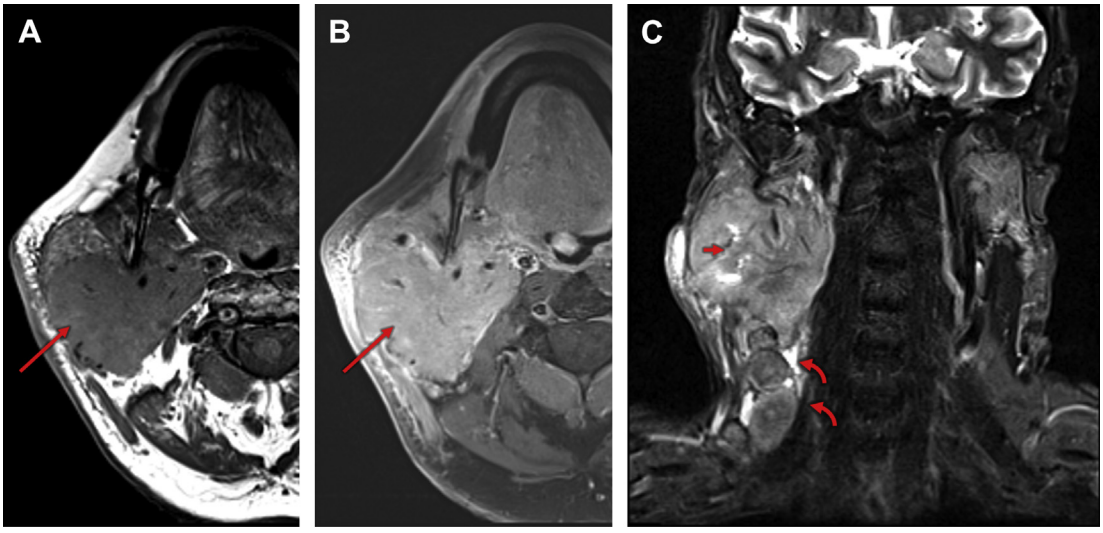

Fig. 6. Large MEC of the right parotid in a 73-year-old man who presented with slowly increasing neck masses. T1 hypointense on precontrast (*A*) and uniformly enhancing on T1 postcontrast (*B*) right parotid mass (*long arrows*) on initial scan. It had an almost stellate appearance on coronal STIR (*short arrow, C*) which raised concern for oncocytoma. Ipsilateral enlarged and metastatic nodes (*curved arrows, C*) helped cement the diagnosis as a parotid malignancy, MEC, with ipsilateral lymphadenopathy.

Mammary Analog Secretory Carcinoma

Mammary analog secretory carcinoma is a new addition to the WHO classification and is characterized by a gene translocation, ETV6-NTRK3. These nonaggressive tumors may have previously been misdiagnosed as nonparotid acinic cell carcinomas.[28]

Lymphoma

Lymphoma can involve the salivary glands. This is true for all of the major salivary glands, including the parotid gland, which has intraglandular lymph nodes. Lymphoma in the salivary glands can be primary or secondary. Primary lymphomas of the salivary glands are often infiltrative and enlarge the glands diffusely, as shown in **Fig. 7**—CT in an 85-year-old woman who presented with constitutional symptoms and a left parotid mass. The bilateral nodal involvement helped narrow the differential in this case. Secondary lymphomas can have this appearance as well or present as enlarged lymph nodes in the parotid glands.

Metastasis to Intraparotid Lymph Nodes

The parotid gland is the only salivary gland that contains lymph nodes within the gland itself. These nodes are seen in normal patients, although they also serve as the primary drainage site for skin malignancies of the upper face, ear, and scalp. Common skin malignancies to metastasize to the parotid lymph nodes include squamous cell carcinomas and melanomas. These typically manifest with lymph node enlargement in a parotid gland on the side of the primary skin malignancy.

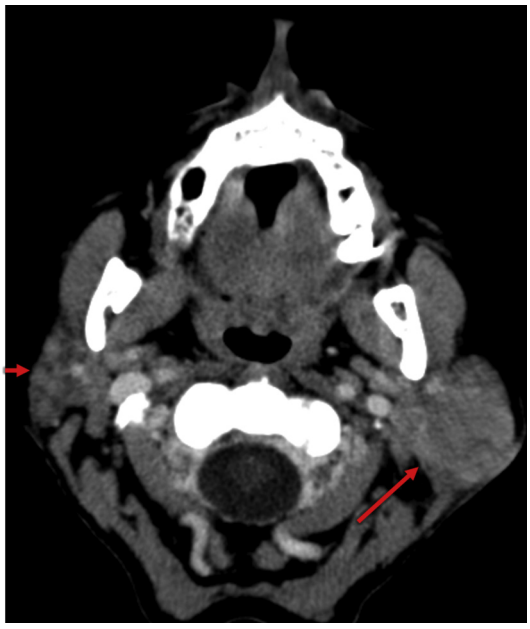

Fig. 7. Lymphoma, especially diffuse large B-cell variants, must be considered in the setting of enlarged parotid lymph nodes, especially with contralateral involvement (and systemic adenopathy, not shown). This 85-year-old woman presented with constitutional symptoms and a dominant left parotid mass (*long arrow*) with smaller contralateral intraparotid nodes (*short arrow*).

Parotid lymph nodes can also serve as the site of metastasis for systemic malignancies from other organs, such as kidney, breast, and lung. **Fig. 8** shows a case of osseous, parotid, and CN V (mandibular) lesions identified on a PET-CT for breast cancer staging. This 72-year-old woman had an FDG-avid palpable mass (a small left superficial lobe parotid nodule) and facial numbness under her chin due to tumor involvement on the mandibular division of CN V.

As with lymph node metastasis elsewhere, enlarged intraparotid lymph nodes or lymph nodes that are growing over time are a suspicious finding, particularly in patients with skin malignancies of the face, ear, and scalp. The nodes are often hypointense on T1 and intermediate to hyperintense on T2. They are most conspicuous on precontrast T1 sequences and on enhanced CT, where they contrast well with the fat in the parotid gland. Involved lymph nodes can become necrotic, demonstrating heterogeneity and areas of nonenhancement centrally, as can be seen elsewhere in the head and neck. PET-CT can be used to determine if nodes are involved, even those without suspicious morphologic features by CT assessment.[30,31]

Other Considerations

Hyperenhancement and/or enlargement in a salivary gland is not always a marker of malignancy. **Fig. 9** shows treatment-related changes from prior glossectomy and neck dissections for oral cavity squamous cell carcinoma. This 35-year-old man was treated with radiation; note the enlarged and hyperenhancing left sublingual gland, indicative of radiation-related inflammation. **Fig. 10** shows a complicated case of high-grade salivary ductal carcinoma in a 78-year-old man who had long-standing facial paralysis. The precontrast T1 image (see **Fig. 10**A) shows a T1 hypointense mass infiltrating the superficial and deep parotid lobes in the expected region of the auriculotemporal nerve. There was perineural spread of tumor from CN VII to CN V with spread intracranially through foramen ovale (mandibular CN V). There was also spread peripherally, with FDG-avid tissue along the pterygomaxillary fissure. Perineural spread of tumor can be central (toward the brain), peripheral (toward the end organ), or both, as in this unfortunate case.

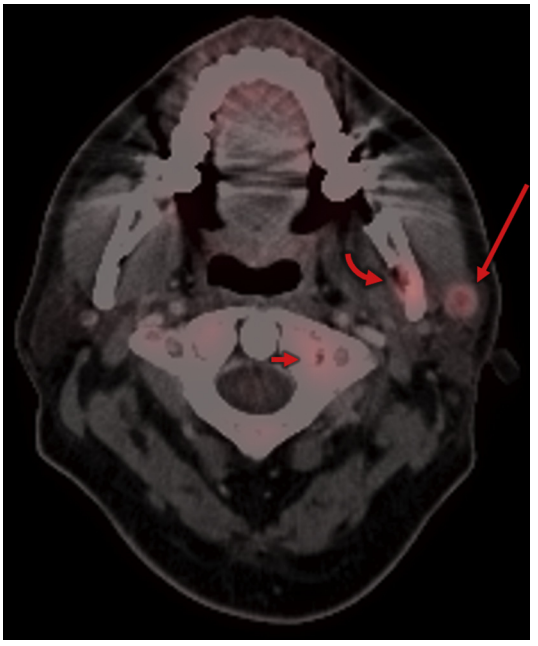

Fig. 8. Parotid glands have multiple lymph nodes; thus, metastatic disease can present with cheek swelling or facial numbness/pain as in this case. FDG-avid metastatic parotid nodule from breast cancer in a 72-year-old woman (*long arrow*). Note the adjacent involvement in the mandible, along the inferior alveolar nerve (*curved arrow*). Additional osseous lesions were also present (*short arrow*).

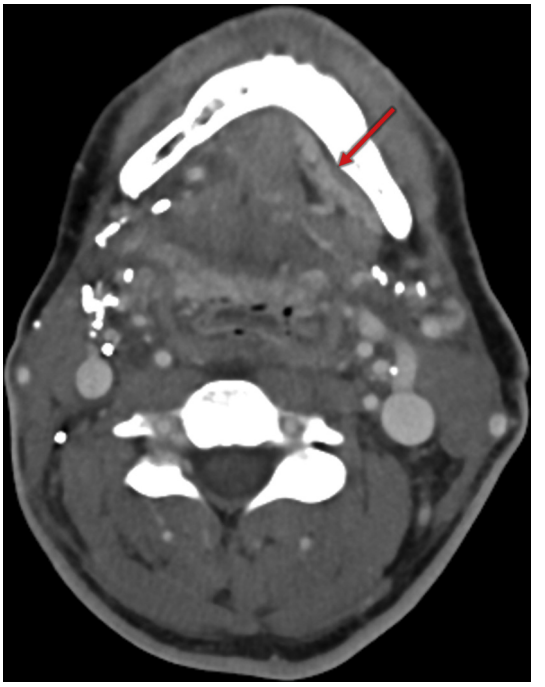

Fig. 9. Not all enlargement or enhancement is pathologic. Note the enlarged and hyperenhancing left sublingual gland (*arrow*) in a 35-year-old man with prior hemiglossectomy, bilateral neck dissections, chemotherapy, and radiation for oral cavity squamous cell carcinoma. Findings were related to treatment (radiation)-induced inflammation.

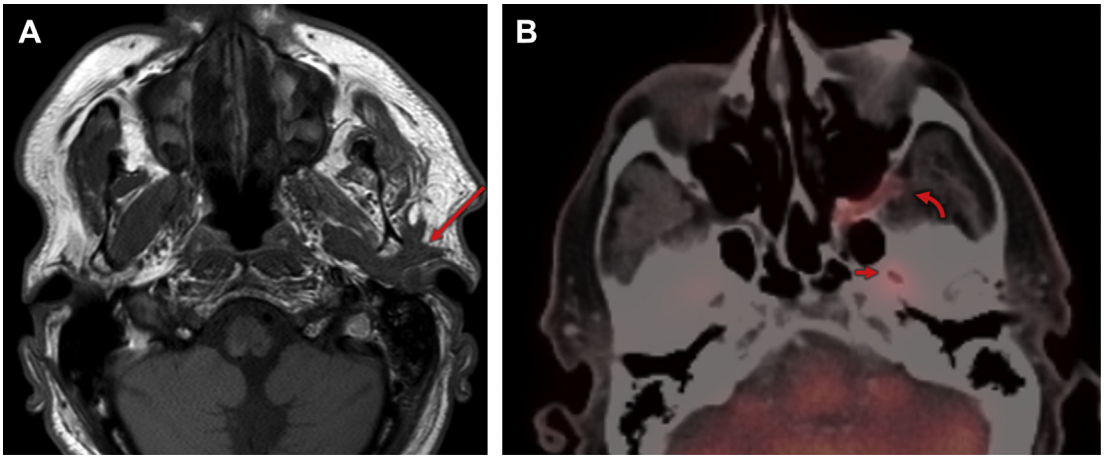

Fig. 10. Parotid malignancies often have an impact on facial nerve function (note the left eyelid gold weight). The trigeminal nerve can also be affected via anastomotic connections. This T1 hypointense mass (*long arrow, A*) insinuates along the expected path of the auriculotemporal nerve (connecting CN V and CN VII). FDG PET-CT showed avidity in the left foramen ovale (*short arrow, B*), pterygopalatine fossa, and pterygomaxillary fissure (*curved arrow, B*). This 78-year-old man also had direct brain parenchymal invasion (not shown) and was initially described as an "atypical schwannoma."

SUMMARY

Salivary gland malignancies represent a wide range of tumors from the indolent to the aggressive. The smaller the gland, the higher the malignant risk with (up to) 90% of sublingual gland tumors malignant. The most common location for a malignant tumor is the parotid gland because there are so many more parotid tumors overall. Patients may present with localized swelling, facial pain (suggesting trigeminal involvement), or facial paralysis (suggesting facial nerve involvement). CT and MR imaging both offer benefit in evaluating the extent of these tumors, although full staging (according to AJCC) may require additional imaging modalities.

REFERENCES

1. Guzzo M, Locati LD, Prott FJ, et al. Major and minor salivary gland tumors. Crit Rev Oncol Hematol 2010; 74(2):134–47.
2. Schramm VL Jr, Imola MJ. Management of nasopharyngeal salivary gland malignancy. Laryngoscope 2001;111(9):1533–44.
3. Eveson JW, Cawson RA. Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. J Pathol 1985;146(1):51–8.
4. Spiro RH. Salivary neoplasms: overview of a 35-year experience with 2,807 patients. Head Neck Surg 1986;8:177–84.
5. Batsakis JG, editor. Tumours of the head and neck. Clinical and pathological considerations. 2nd edition. London: Williams & Wilkins; 1982.
6. Boukheris H, Curtis RE, Land CE, et al. Incidence of carcinoma of the major salivary glands according to the WHO Classification, 1992 to 2006: a population-based study in the United States. Cancer Epidemiol Biomarkers Prev 2009;18(11):2899–906.
7. Barnes L, Eveson JW, Reichart P, et al, editors. Tumours of the salivary glands. Pathology and genetics of head and neck tumours. Lyon (France): World Health Organization; 2005.
8. Seethala RR, Stenman G. Update from the 4th edition of the World Health Organization classification of head and neck tumours: tumors of the salivary gland. Head Neck Pathol 2017;11(1):55–67.
9. Amin MB, Edge SB, Greene FL, et al, editors. AJCC cancer staging manual. 8th edition. New York: Springer; 2017.
10. Lee YY, Wong KT, King AD, et al. Imaging of salivary gland tumours. Eur J Radiol 2008;66(3):419–36.
11. Vogl TJ, Schulz B, Bauer RW, et al. Dual-energy CT applications in head and neck imaging. AJR Am J Roentgenol 2012;199:34–9.
12. Weon YC, Park SW, Kim HJ, et al. Salivary duct carcinomas: clinical and CT and MR imaging features in 20 patients. Neuroradiology 2012;54(6):631–40.
13. Tawfik AM, Michael Bucher A, Vogl TJ. Dual-energy computed tomography applications for the evaluation of cervical lymphadenopathy. Neuroimaging Clin N Am 2017;27(3):461–8.
14. Chawla A, Srinivasan S, Lim TC, et al. Dual-energy CT applications in salivary gland lesions. Br J Radiol 2017;90(1074):20160859.
15. Christe A, Waldherr C, Hallett R, et al. MR imaging of parotid tumors: typical lesion characteristics in MR imaging improve discrimination between benign

and malignant disease. AJNR Am J Neuroradiol 2011;32(7):1202–7.
16. Kato H, Kanematsu M, Makita H, et al. CT and MR imaging findings of palatal tumors. Eur J Radiol 2014;83(3):e137–46.
17. Gebarski SS, Telian SA, Niparko JK. Enhancement along the normal facial nerve in the facial canal: MR imaging and anatomic correlation. Radiology 1992;183(2):391–4.
18. Kuno H, Onaya H, Fujii S, et al. Primary staging of laryngeal and hypopharyngeal cancer: CT, MR imaging and dual energy CT. Eur J Radiol 2014;83(1):e23–35.
19. Yabuuchi H, Matsuo Y, Kamitani T, et al. Parotid gland tumors: can addition of diffusion-weighted MR imaging to dynamic contrast-enhanced MR imaging improve diagnostic accuracy in characterization? Radiology 2008;249:909–16.
20. Matsuzaki H, Yanagi Y, Hara M, et al. Minor salivary gland tumors in the oral cavity: diagnostic value of dynamic contrast-enhanced MRI. Eur J Radiol 2012;81:2684–91.
21. Aghaghazvini L, Salahshour F, Yazdani N, et al. Dynamic contrast-enhanced MRI for differentiation of major salivary glands neoplasms, a 3-T MRI study. Dentomaxillofac Radiol 2015;44(2). 20140166.
22. Eida S, Sumi M, Nakamura T. Multiparametric magnetic resonance imaging for the differentiation between benign and malignant salivary gland tumors. J Magn Reson Imaging 2010;31:673–9.
23. Hisatomi M, Asaumi J, Yanagi Y, et al. Diagnostic value of dynamic contrast-enhanced MRI in the salivary gland tumors. Oral Oncol 2007;43(9):940–7.
24. Seo YL, Yoon DY, Baek S, et al. Incidental focal FDG uptake in the parotid glands on PET/CT in patients with head and neck malignancy. Eur Radiol 2015; 25(1):171–7.
25. Seethala RR, Johnson JT, Barnes EL, et al. Polymorphous low-grade adenocarcinoma: the University of Pittsburgh experience. Arch Otolaryngol Head Neck Surg 2010;136(4):385–92.
26. Castle JT, Thompson LD, Frommelt RA, et al. Polymorphous low grade adenocarcinoma: a clinicopathologic study of 164 cases. Cancer 1999;86(2): 207–19.
27. Seifert G. Histopathology of malignant salivary gland tumours. Eur J Cancer B Oral Oncol 1992; 28:49–56.
28. Bishop JA, Yonescu R, Batista D, et al. Most nonparotid "acinic cell carcinomas" represent mammary analog secretory carcinomas. Am J Surg Pathol 2013;37(7):1053–7.
29. Jones AV, Craig GT, Speight PM, et al. The range and demographics of salivary gland tumours diagnosed in a UK population. Oral Oncol 2008;44(4): 407–17.
30. Razfar A, Heron DE, Branstetter BF, et al. Positron emission tomography-computed tomography adds to the management of salivary gland malignancies. Laryngoscope 2010;120:734–8.
31. Lee SK, Rho BH, Won KS. Parotid incidentaloma identified by combined 18F-fluorodeoxyglucose whole-body positron emission tomography and computed tomography: findings at grayscale and power Doppler ultrasonography and ultrasound-guided fine-needle aspiration biopsy or core-needle biopsy. Eur Radiol 2009;19(9): 2268–74.