

Oral Cancer Review for Oral Healthcare Professionals

Regular Screening For Early Diagnosis and Management as Key to Better Outcomes

Prepared by: Ricardo J. Padilla, DDS

Dr. Ricardo Padilla is an oral and maxillofacial pathologist from Guatemala City and retired Distinguished Professor at the University of North Carolina. He currently practices oral and maxillofacial/head and neck surgical pathology in Charleston, South Carolina. He has taught dental and medical trainees at all levels and has published numerous peer-reviewed journal articles.

INTRODUCTION

Oral cancers, predominantly oral squamous cell carcinoma (OSCC), represent a significant public health concern in the United States. They are part of the broader category of head and neck cancers, which encompass a heterogeneous group of malignancies arising from the oral mucosa, skin of the head and neck, salivary glands, lymphoid tissue, connective tissues, and musculoskeletal functional and supporting structures of the craniofacial region. Within this broader group, the most common malignancies overall are ultraviolet (UV)-induced cutaneous cancers of sun-exposed head and neck skin. However, when focusing specifically on the oral cavity and oropharynx, the predominant malignancy is squamous cell carcinoma, accounting for approximately 90% of oral cancers, making it the type of oral cancer that most oral healthcare providers in the dental field may encounter in their patients.

Although squamous cell carcinoma accounts for most oral and oropharyngeal cancers, other malignancies may arise in these regions, including salivary gland cancers, lymphomas, sarcomas of soft tissues and bones, odontogenic malignancies, and even distant cancers may produce metastatic disease that may lodge in these areas. All these tumors may involve both soft tissues and underlying bone and often present with clinical features different from conventional mucosal squamous cell carcinoma. For this reason, dental professionals must consider any abnormal clinical finding a "lesion" that must be addressed and diagnosed, either by clinical, radiographical, chemical,

pathological, molecular, or genetic methods, or a combination of these methods. If the provider who identifies the lesion is not comfortable making the diagnosis, it is necessary to refer the patient for a consultation with a specialist with experience in the type of lesion that the patient has.

Within the oral cavity, cancers primarily affect the tongue (approximately 30–40%), floor of the mouth (15–20%), buccal mucosa (10–15%), gingiva and alveolar ridge (~10%), retromolar trigone (5–10%), hard palate (<5%), and the lip, as well as the oropharyngeal region.

A critical distinction exists between oral mucosal squamous cell carcinoma and oropharyngeal squamous cell carcinoma, as these represent biologically and epidemiologically distinct diseases. Oral mucosal squamous cell carcinoma is predominantly associated with tobacco use and excessive alcohol consumption, whereas oropharyngeal squamous cell carcinoma is largely driven by high-risk human papillomavirus (HPV), especially HPV-16 and 18. It is important to remember that for staging purposes, the anatomical oral mucosa is considered to include the non-sun-exposed mucosa of the lips, the buccal mucosae, vestibules, gingiva, hard palate, floor of mouth, and tongue mucosa anterior to the foramen cecum/circumvallate papilla/lingual tonsils; the oropharynx includes the soft palate, uvula, tonsillar pillars, tonsils, posterior pharyngeal wall, and the base of the tongue mucosa down to the epiglottis. The embryological origin of the oral mucosa and oropharyngeal mucosa are different, and that makes them susceptible to different carcinogens

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that if giving origin to squamous cell carcinoma will have significantly different risk factors, clinical presentations, treatment, and prognosis.

It is also important to distinguish between sun-exposed lip/vermillion squamous cell carcinoma, which arises through ultraviolet (UV)-induced carcinogenesis and resembles cutaneous squamous cell carcinoma, and inner lip mucosal squamous cell carcinoma, which shares risk factors with intraoral cancers. These are distinct disease entities yet occur in anatomical areas that dental professionals encounter and must evaluate routinely.

Despite advances in treatment modalities and resources, outcomes remain strongly stage-dependent. Early-stage disease demonstrates five-year survival of approximately 80–85%, whereas in people with regional disease it declines to approximately 55–65%, and those with distant metastatic disease is often below 30–40%.

Dental professionals are uniquely positioned to identify early lesions due to routine easy access to the oral cavity and their expertise in local anatomy, form and function, and familiarity with the appearance of the structures in the oral cavity, and the head and neck.

Epidemiology and Burden of Disease

Oral cavity and oropharyngeal cancers individually and combined represent a significant health burden in the United States, with greater than 60,000 new cases expected to be diagnosed in the USA in 2026. Survival is highly stage-dependent, with markedly improved outcomes in early-stage disease compared with advanced disease. Unfortunately, a substantial proportion of cases are still diagnosed at advanced stages, contributing to overall survival rates that remain suboptimal.

The distribution of oral cavity squamous cell carcinomas is not uniform. The tongue (30–40%) is the most common site, followed by the floor of the mouth (15–20%). The buccal mucosa (10–15%), gingiva and alveolar ridge (~10%), retromolar trigone (5–10%), and hard palate (~5%) follow in decreasing frequency.

Cancers of the lip vary by subsite. Vermilion border cancers are predominantly UV-driven, whereas mucosal lip cancers resemble intraoral squamous cell carcinoma.

Oropharyngeal cancers have undergone a major epidemiologic shift, with HPV-associated cancers now representing most cases.

Etiology and Risk Factors

Oral cancers arise through multiple etiologic pathways. Oral mucosal squamous cell carcinoma is strongly associated with tobacco and alcohol exposures, which act synergistically to increase carcinogenic risk. Oropharyngeal squamous cell carcinoma is predominantly driven by high-risk HPV infection. Vermilion lip (sun-exposed) squamous cell carcinoma is associated with chronic ultraviolet radiation exposure, whereas mucosal lip carcinoma shares the same risk factors as intraoral disease. Additional contributing factors include immunosuppression, immunodeficiency, prior malignancy, and possibly nutritional and oral microbiome influences. Importantly, some patients develop oral or oropharyngeal cancers without identifiable risk factors, reinforcing the need for universal periodic screening of all dental patients at least once per year, and more often if they have any high-risk factors.

Oral Potentially Malignant Disorders and Oral Epithelial Dysplasia

Clinically, oral potentially malignant disorders (OPMDs) encompass a spectrum of clinical findings and lesions associated with increased risk of malignant transformation, including leukoplakia (figure 1), erythroplakia (figure 2), erythroleukoplakia (figure 3), persistent non-healing ulcers (figure 4), proliferative verrucous leukoplakia, submucous fibrosis, and actinic cheilitis. Certain inflammatory conditions may also carry a small but clinically relevant risk, such as oral lichenoid lesions and oral lichen planus (figure 5). Rare genetic conditions such as Fanconi's anemia and Li-Fraumeni syndrome are associated with increased incidence of oral cancer development and therefore reviewing and frequently updating each patient's medical history and medications thoroughly may uncover some additional risk factors for oral cancers.

Histologically, oral epithelial dysplasia (OED) represents the microscopic correlation of premalignant change and is graded as mild, moderate, or severe; or as low-grade or high-grade. Infection with high-risk types of human papillomavirus is associated with a basaloid histomorphology of squamous cell carcinomas, especially in the oropharynx. The likelihood of progression to carcinoma increases with the severity of dysplasia, although clinical features such as size, type and number of lesions, persistence, heterogeneity, and anatomical location also influence risk.

Figure 1A: Oral leukoplakia involving the posterior floor of mouth, lingual gingiva, and glossotonsillar sulcus. Irregular, well-demarcated leukoplakic lesion spanning these sites, with focal areas of erythroplakia.

Figure 1B: Oral leukoplakia involving the right lateral ventral tongue. Thin, homogeneous leukoplakic lesion with well-delineated borders on the right lateral ventral tongue surface.

Figure 1C: Oral leukoplakia involving the left floor of mouth. Well-delineated, thin leukoplakic lesion with a slightly leathery surface texture.



Figure 2: Erythroplakia involving the left posterior lateral tongue at the junction with the base of tongue. Non-blanching, asymptomatic non-bleeding lesion.



Figure 3: Erythroleukoplakia involving the right posterior lateral ventral tongue. Mixed erythroleukoplakic lesion with areas of thick, corrugated leukoplakia; granular erythroplakia; and focal ulceration.



Figure 4: Invasive squamous cell carcinoma involving the right anterior ventrolateral tongue. Ulcerated lesion initially favored to be traumatic in origin; biopsy confirmed invasive squamous cell carcinoma.



Figure 5: Reticular Wickham striae involving the right anterior ventral tongue in a patient with a lichenoid reaction; biopsy showed no evidence of oral epithelial dysplasia.

Non-Squamous Malignancies of the Oral and Maxillofacial Region

Although most oral cancers are squamous in origin and arise from the surface epithelium, a minority represent non-squamous malignancies, including salivary gland tumors, lymphomas, sarcomas, mucosal melanoma, odontogenic malignancies, and metastatic disease. These tumors often clinically present differently, such as submucosal masses, non-healing ulcers, pigmentations, or intraosseous lesions.

Metastatic tumors to the oral region are rare but clinically significant and may represent the first manifestation of an undiagnosed primary malignancy. Identification of metastatic disease to the oral and maxillofacial areas is a finding that is critical to report to the patient's oncology team since additional cancer sites may influence staging, treatment, and prognosis.

Clinical Presentation

Oral cancers present across a spectrum from subtle mucosal changes (figure 6) to ulcerated or exophytic masses (figures 7-8). Early lesions may appear as leukoplakic, erythroplakic, or mixed lesions, with red lesions carrying a higher likelihood of dysplasia or carcinoma.

Symptoms may include pain, dysphagia, altered nerve sensation or motor function, or cervical lymphadenopathy, although early lesions are often asymptomatic. Lesions persisting beyond approximately two or three weeks or demonstrating concerning features should be considered suspicious.



Figure 6A: Invasive squamous cell carcinoma involving the floor of mouth. Minimally symptomatic but indurated lesion initially attributed by the patient and original provider to trauma from a poorly fitting denture; the lesion persisted after denture adjustment, and biopsy confirmed invasive squamous cell carcinoma.



Figure 6B: Invasive squamous cell carcinoma involving the right posterior floor of mouth, approximating the right retromolar pad and lingual gingiva. Erythroleukoplakic lesion with focal ulceration, discovered incidentally during a routine dental examination; biopsy confirmed invasive squamous cell carcinoma.



Figure 6C: Invasive squamous cell carcinoma involving the left posterior lateral and ventral tongue, extending toward the floor of mouth. Lesion presented as a heterogeneous, thick area of leukoplakia initially attributed to denture irritation; biopsy confirmed invasive squamous cell carcinoma.



Figure 8A: Advanced invasive squamous cell carcinoma involving the underlying bone with ipsilateral cervical lymph node metastasis. Lesion was initially attributed by the patient to denture irritation for several months, during which he attempted to adjust the denture himself.



Figure 8B: Invasive squamous cell carcinoma involving the right posterior palate and extending to the soft palate. Lesion occurred in a patient with several decades of chronic snuff use and no history of alcohol consumption or smoking.

Clinical Oral Examination and Risk Integration

A comprehensive clinical and radiographic examination combined with review and update of the patient's medical history remains the cornerstone of early disease detection. This includes systematic visual inspection and palpation of the head and neck structures and intraoral mucosal surfaces. Integration of findings with an updated patient history and risk factors enhances diagnostic accuracy.

Diagnostic Principles

All dental patients should receive a comprehensive head and neck and oral exam with medical history update at least on a yearly basis, and radiographic screening or correlation as indicated, upon identification of a lesion, either clinically, radiographically, or symptomatically, the oral healthcare provider must proceed to document, analyze, and diagnose all abnormal findings. If the patient's lesion is not within the scope of practice or level of comfort of the dental provider who identifies the lesion, a consultation or referral must be completed and assured in a timely fashion. Often, a tissue biopsy of a lesion may be necessary for a proper and actionable diagnosis. Biopsy with histopathologic evaluation remains the



Figure 7A: Invasive squamous cell carcinoma involving the right hard palate and tuberosity. Lesion presented as granular, elevated, exophytic erythroplakia associated with loose teeth, mild tenderness, and bleeding during brushing and flossing in a patient without traditional oral cancer risk factors but with a history of immunosuppression.



Figure 7B: Irregularly shaped erythroleukoplakia with granular surface involving the left buccal mucosa. The lesion extends from the left oral commissure to the left retromolar pad, left mandibular vestibule, and facial aspect of the posterior attached gingiva; biopsy confirmed invasive squamous cell carcinoma.

Disease subtype	Specimen	Biomarkers	Clinical use	Limitations
Oral mucosal SCC	Saliva/serum	IL-6, IL-8, TNF- α , MMP-9	Research	Not validated
HPV+ OPSCC	Plasma	ctHPV DNA	Surveillance	Limited scope
HPV- OPSCC	Plasma	ctDNA	Research	Limited evidence
UV lip SCC	Serum	MMP-13, miRNA	Research	No standard
Metastatic disease	Variable	Primary-specific	Diagnosis	No universal marker

Table 1. Examples of Current Biomarkers by Disease Subtype

Category	Examples	Mechanism	Clinical Role	Limitations
Vital dyes	Toluidine blue, iodine	Binding/contrast	Guide biopsy	False positives
Light-based	Autofluorescence, reflectance, NBI	Optical contrast	Visualization	Low specificity
Cytology	Brush cytology	Cell sampling	Triage	Not definitive
Imaging	OCT, confocal, Raman	Structural imaging	Research	Limited availability

Table 2. Examples of Adjunctive Diagnostic Tools

gold standard for diagnosis of any lesion that cannot be diagnosed with non-invasive methods. Salivary and serum biomarkers, including inflammatory mediators and circulating tumor DNA, and other molecules are under investigation but currently remain adjunctive rather than definitive diagnostic tools.

Adjunctive Diagnostic Tools

Adjunctive diagnostic tools are intended to enhance visualization and assessment of oral mucosal abnormalities but do not replace biopsy. These include vital staining, light-based detection systems, cytologic techniques, and emerging imaging technologies.

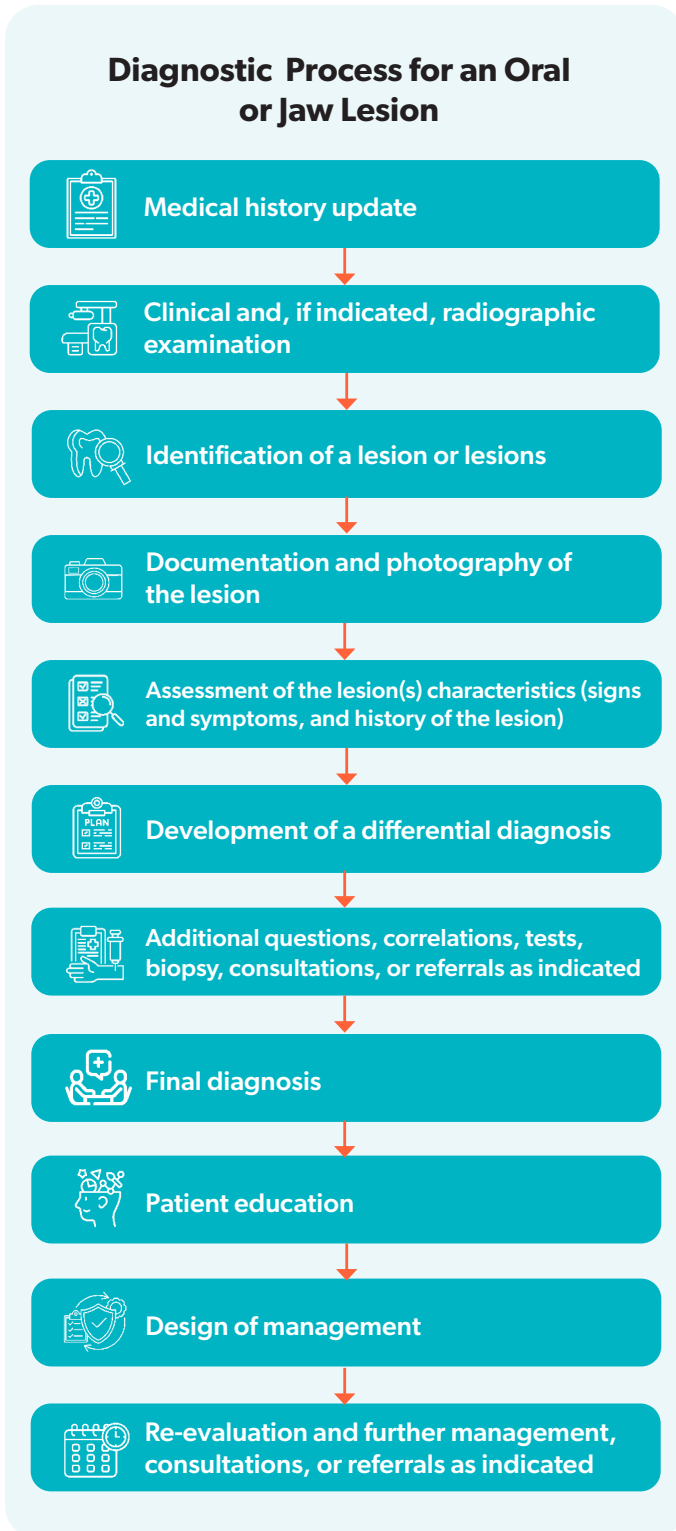
Vital staining methods such as toluidine blue selectively bind nucleic acids and may highlight dysplastic tissue, although false positives occur in inflammatory conditions. Light-based systems rely on optical changes in tissue, including autofluorescence and reflectance, but are limited by low specificity. Cytologic techniques such as brush cytology provide minimally invasive sampling but are not definitive nor provide a specific diagnosis. Emerging technologies, including optical coherence tomography (OCT), confocal microscopy, and Raman spectroscopy, offer promising structural and biochemical assessment but remain investigational.

Diagnostic Algorithms

Dental patients with suspicious lesions should be evaluated systematically, and persistent or high-risk lesions require a diagnostic biopsy for an actionable diagnosis. If trauma is a potential variable in the etiology or exacerbation of any oral or jaw lesion, the source of trauma should be resolved, and the patient reevaluated in 2-3 weeks. Adjunctive tools do not provide definitive information to confirm or exclude malignancy to the point of being actionable; they rather are a risk stratification tool that supports the use of a conventional diagnostic biopsy. If the lesion believed to be related to trauma does not resolve in that time, a representative tissue biopsy for diagnosis is indicated. If a lesion is very suspicious or the patient has high-risk factors for malignancy, a biopsy should be performed immediately regardless of the management of traumatic variables.

On the next page is an example of a diagnostic sequence for an oral mucosa lesion, but the same principles apply for lesions in other anatomical sites. Importantly, this process may require multiple cycles to reach a proper diagnosis and management or may need to be modified for highly suspicious lesions that require immediate diagnostic biopsy. The dental professional must expect this to be a process that may require more than one encounter.

Table 3.



Once diagnosed, the management of oral cancer is multidisciplinary and may include surgery, radiation therapy, chemotherapy, immunotherapy, or a combination of these. The goal of therapy can have either curative or palliative intent, based on each patient's disease stage, burden, and characteristics. Ideally, patients diagnosed with oral cancer should be evaluated by a multi-specialty team with experience and expertise in management of head and neck cancer. Academic centers and large community practices or medical centers have head and neck tumor boards that meet regularly and can provide a comprehensive evaluation and management suggestions and care for these patients. Outcomes depend on multiple factors including the patient's preferences and wishes, available treatment modalities and resources, and tumor stage and biology.

Dental Management in Oncology Care

Dental professionals play a critical role in reducing head and neck cancer treatment-related complications. Pre-treatment care includes comprehensive examination, elimination of dental and periodontal disease, management and prevention of infections, and fluoride therapy. During treatment, management focuses on symptom control and avoidance of invasive procedures. Post-treatment care includes lifelong preventive strategies and regular maintenance and follow-up with disease surveillance.

Oral Complications of Cancer Therapy

Oral complications of cancer therapy are common and can significantly affect quality of life and treatment outcomes. These include mucositis, xerostomia, dental caries, trismus, osteoradionecrosis, infections, and immune-mediated mucosal reactions. Some of these complications are transient, but unfortunately some are permanent.

Osteoradionecrosis (ORN) is a potential complication for patients treated with radiation that involves bone, and it is a dose-dependent problem. In addition to ORN, medication-related osteonecrosis of the jaw (MRONJ) is an additional important complication associated with antiresorptive and antiangiogenic therapies. It is characterized by exposed bone or bone that can be probed through a fistula persisting for more than eight weeks in patients without prior radiation to the jaws (figure 9). Prevention of ORN and MRONJ focuses on comprehensive dental evaluation prior to initiation of therapy, including elimination of infection and, if possible, avoidance of future invasive procedures that induce bacteremia and require bone healing. Diagnosis of ONJ and MRONJ is clinical, radiographical, and based on medication history and characteristic findings. Management is stage-dependent and ranges



Figure 9: Medication-related osteonecrosis of the jaw involving the right maxilla. Area of exposed bone following dental extraction in a patient receiving antiresorptive medication as part of antineoplastic treatment for metastatic prostate adenocarcinoma. The lesion had been present for 3 months with mild to moderate pain and clinical signs of infection, including suppuration; biopsy showed necrotic bone colonized by oral flora, with no evidence of metastatic disease.

from conservative care with antimicrobial rinses to surgical intervention in advanced cases.

Preventive dental care remains the most effective strategy for reducing ORN, MRONJ and chemotherapy, immunotherapy, and/or radiation-related complications such as dry mouth, trismus, and mucositis.

Surveillance and Follow-Up

Patients with OPMDs, OED, or head and neck cancer require long-term surveillance by both medical and dental providers due to the risk of recurrence, second primary tumors, metastatic disease, and complications of cancer treatment. Follow-up includes regular clinical, radiographic, and laboratory examinations, including regional lymph nodes, biomarkers, and monitoring for new or changing lesions. Dental professionals play an essential role in ongoing surveillance and prevention of late complications of antineoplastic treatment.

Prevention and Patient Education

Prevention focuses on reducing cancer risk factors and promoting early detection. Tobacco cessation, alcohol reduction, anti-HPV vaccination, and sun protection are critical. Patient education should emphasize recognition of early signs, maintenance of oral hygiene, and adherence to follow-up care. Dental professionals are in a privileged position to deliver most of these services to their patients, or to consult or refer to the appropriate provider as needed.

Emerging and Future Directions

Advances in molecular diagnostics, salivary biomarkers, liquid biopsy technologies, and artificial intelligence are promising for improving early detection and surveillance. However, these approaches remain adjunctive to conventional clinical examination and biopsy. The advent of transoral robotic surgery has

revolutionized the surgical care of previously hard to access lesions and decreased the collateral damage to adjacent anatomical structures from oncological surgical procedures. Similarly, the evolution of reconstructive techniques has allowed for grafting of viable tissues into surgical defects with improved form and function, including dentition rehabilitation. In the field of chemotherapy, immunotherapy, and individualized medicine, the advances have allowed for almost customized protocols for each patient. The role of the tumor microenvironment and oral microbiome are being explored with promising information accumulating in the literature. Invariably, the prognosis of patients with oral cancer will improve as the diagnostic and treatment tools continue to develop. Electronic medical records with improved communication tools for providers, health systems, medical and dental offices, and patients will undoubtedly contribute to more effective and efficient information sharing in a compliant way, medical history and medications review, screening, diagnosis, and management of OPMDs, OED, and head and neck cancers.

Conclusion

Oral cancers remain serious diseases with outcomes that depend heavily on early detection and effective and efficient diagnosis and treatment. Dental professionals play a critical role in screening, diagnosis, treatment preparation, and long-term survivorship care. A structured, evidence-based approach is continuing to evolve and is essential for improving patient outcomes. All oral healthcare providers can contribute to better patient outcomes and less complications of cancer treatment, especially if they maintain a routine oral cancer screening protocol as part of their clinical practice.

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Biography

Dr. Padilla is an oral and maxillofacial pathologist originally from Guatemala City, Guatemala. He earned his DDS degree from Universidad Francisco Marroquín, completed a three-year residency in Oral and Maxillofacial Pathology at the University of Florida, and subsequently completed a one-year fellowship in Head and Neck Surgical Pathology at the University of Texas Health Science Center in San Antonio. He joined the faculty in Oral and Maxillofacial Pathology at the University of North Carolina School of Dentistry, where he advanced to the rank of Distinguished Professor and retired after 23 years of academic service. During his tenure, he served as Residency Program Director in Oral and Maxillofacial Pathology for 19 years, taught dental and medical trainees at all levels, and provided numerous continuing education courses for healthcare providers on diseases of the oral cavity, head, and neck. He currently practices oral and maxillofacial, head and neck surgical pathology in private practice with his associate, Dr. Brad Neville, at Head and Neck Specialists and HCA Trident Hospital in Charleston, South Carolina, where he participates in an active biopsy and consultation service evaluating cases from Virginia, North Carolina, and South Carolina, with planned expansion into Tennessee and Georgia. He also evaluates patients across six clinical locations throughout South Carolina, with expansion into North Carolina planned in the near future. Dr. Padilla currently serves as a Director of the American Board of Oral and Maxillofacial Pathology and is expected to ascend to the position of President in 2030. He has also served in multiple leadership roles in the American Academy of Oral and Maxillofacial Pathology, is a life member of the American Head and Neck Pathology Society, and has published numerous peer-reviewed journal articles, many in collaboration with former trainees who are now colleagues and friends.