



## Contemporary Approaches to Oral Cancer Screening and Early Detection: A Narrative Review

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### ABSTRACT

Oral cancer is a significant global health burden, and delayed diagnosis remains a major factor contributing to poor outcomes. Early detection through effective screening and timely diagnosis is essential for improving survival. This narrative review summarizes contemporary approaches to oral cancer screening, including visual and tactile examination, vital staining, autofluorescence, brush cytology, salivary biomarkers, molecular diagnostics, optical imaging, and artificial intelligence-assisted analysis. The diagnostic potential, clinical applications, advantages, and limitations of these methods are discussed, with emphasis on their role in detecting oral potentially malignant disorders and early oral squamous cell carcinoma. Although emerging technologies show promising results, conventional clinical examination and histopathological evaluation remain fundamental. Integrating validated adjunctive technologies with routine clinical assessment may enhance early detection and risk-based referral.

## INTRODUCTION

Oral cancer is a major global health concern and represents a significant cause of cancer-related morbidity and mortality.<sup>1</sup> Oral squamous cell carcinoma (OSCC) accounts for the majority of oral malignancies and is frequently diagnosed at an advanced stage, resulting in poorer treatment outcomes and reduced survival.<sup>2</sup> Despite advances in surgical, radiotherapeutic, and systemic treatment, prognosis remains strongly influenced by the stage at diagnosis. Early detection of oral cancer and its precursor lesions, particularly oral potentially malignant disorders (OPMDs), therefore remains

a critical component of oral healthcare.<sup>2,3</sup>

Conventional oral cancer screening primarily relies on systematic visual and tactile examination of the oral mucosa, followed by biopsy and histopathological assessment of suspicious lesions. Although this approach remains the clinical standard, subtle or early mucosal changes may be difficult to recognize, and diagnostic accuracy can vary with the experience of the examiner. Consequently, several adjunctive techniques have been developed to improve the detection and characterization of suspicious lesions.<sup>3</sup>

Recent advances have introduced a range of approaches, including vital staining, autofluorescence, tissue reflectance, brush cytology, optical imaging, sali-

vary biomarkers, molecular diagnostics, and artificial intelligence-based image analysis. These technologies have the potential to support earlier recognition, improve risk assessment, and facilitate appropriate referral. However, differences in diagnostic accuracy, cost, accessibility, and clinical validation have limited their widespread implementation.<sup>4</sup>

This narrative review discusses contemporary approaches to oral cancer screening and early detection, focusing on established and emerging diagnostic modalities, their clinical applications, advantages, limitations, and potential role in improving early diagnosis and patient outcomes.

## CONVENTIONAL ORAL CANCER SCREENING

Conventional oral cancer screening primarily involves a systematic visual and tactile examination of the oral cavity and associated cervical lymph nodes. The clinician should assess the lips, buccal mucosa, gingiva, tongue, floor of the mouth, hard and soft palate, and oropharyngeal region for abnormalities such as persistent ulcers, induration, red or white lesions, unexplained swellings, and changes in mucosal texture or color. Particular attention should be given to lesions that persist for more than two weeks, especially in individuals with recognized risk factors such as tobacco and alcohol use. Palpation helps identify induration, fixation, submucosal masses, and regional lymphadenopathy that may not be apparent during visual examination. Although conventional examination is simple, inexpensive, and widely accessible, its accuracy can be influenced by lesion characteristics and examiner experience. Suspicious or persistent lesions require appropriate referral and tissue biopsy for histopathological evaluation, which remains essential for definitive diagnosis. Thus, conventional screening continues to serve as the foundation of oral cancer detection, while adjunctive technologies may provide additional information in selected clinical situations.<sup>5,6</sup>

## ADJUNCTIVE SCREENING AND DETECTION METHODS

Adjunctive screening methods have been developed to assist conventional oral examination by highlighting clinically suspicious mucosal changes that may not be readily apparent on routine inspection. These techniques are generally intended to support clinical assessment rather than replace biopsy and histopathological examination.

### *Toluidine Blue Staining*

Toluidine blue is a vital dye that preferentially stains areas with increased cellular activity, nuclear abnormalities, and altered epithelial architecture. It may help identify areas of dysplasia or malignancy, particularly when lesions are clinically subtle. Its low cost and simple application make it useful as an adjunct; however, inflammatory, traumatic, and ulcerative lesions may also produce false-positive staining.<sup>7</sup>

### *Lugol's Iodine*

Lugol's iodine staining is based on the glycogen content of epithelial cells. Normal mature squamous epithelium containing glycogen takes up iodine and appears brown, whereas dysplastic or malignant epithelium may show reduced staining. Although potentially useful for identifying suspicious areas, variations in staining and limited specificity restrict its use as a standalone screening method.<sup>8</sup>

### *Autofluorescence*

Autofluorescence devices use specific wavelengths of light to detect changes in tissue fluorescence associated with alterations in epithelial structure, stromal composition, and cellular metabolism. Abnormal tissues may appear as areas of reduced fluorescence. Autofluorescence can improve visualization of potentially suspicious lesions, but loss of fluorescence is not specific for malignancy and may occur with inflammation or trauma.<sup>9</sup>

### *Tissue Reflectance*

Tissue reflectance techniques use differences in the scattering and reflection of light from normal and abnormal oral tissues. Changes in epithelial thickness, cellular organization, and stromal characteristics can alter the reflected light and help identify suspicious areas. These methods are non-invasive and can provide real-time assessment, although their diagnostic performance varies among lesions and clinical settings.<sup>10</sup>

### *Brush Cytology*

Brush cytology is a minimally invasive technique that collects epithelial cells from suspicious mucosal lesions for cytological evaluation. It can be particularly useful when conventional biopsy is difficult or when an additional assessment is required. However, because tissue architecture cannot be evaluated adequately, positive or suspicious findings generally require confirmation by conventional biopsy and histopathology.<sup>11</sup>

### **Chemiluminescence**

Chemiluminescent screening involves applying a chemical solution to the oral mucosa after rinsing, followed by examination under a specialized light source. Abnormal tissues may appear as acetowhite or more prominently illuminated areas due to differences in light scattering. The technique is relatively simple and non-invasive, but its limited specificity and potential for false-positive findings mean that it should be considered an adjunct rather than a definitive diagnostic method.<sup>12</sup>

### **Advanced Optical Imaging Techniques**

Advanced optical imaging techniques are increasingly being investigated for the early detection and characterization of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC). These technologies provide real-time, non-invasive or minimally invasive assessment of tissue architecture, vascular changes, cellular morphology, or biochemical composition. Although many remain primarily investigational, they may complement conventional clinical examination and histopathological diagnosis.

#### **Narrow-Band Imaging**

Narrow-band imaging (NBI) uses selected wavelengths of blue and green light to enhance the visualization of superficial mucosal vasculature. Neoplastic transformation can produce characteristic alterations in vascular patterns, which may assist in identifying suspicious areas and defining lesion margins. NBI has shown potential in detecting early mucosal changes and improving visualization of lesions that are difficult to appreciate under conventional white light.<sup>13</sup>

#### **Optical Coherence Tomography**

Optical coherence tomography (OCT) is a non-invasive imaging technique that produces high-resolution, cross-sectional images of epithelial and subepithelial tissues using near-infrared light. It can demonstrate changes such as epithelial thickening, disruption of tissue architecture, and alterations at the epithelial-stromal interface. OCT has potential for real-time assessment of suspicious lesions and may assist in selecting appropriate biopsy sites; however, its clinical application is currently limited by equipment availability and the need for standardized interpretation.<sup>14</sup>

### **Confocal Laser Endomicroscopy**

Confocal laser endomicroscopy (CLE) provides high-resolution images at or near the cellular level by focusing laser light on specific tissue planes. It can potentially demonstrate cellular and architectural abnormalities associated with dysplasia and malignancy in real time. CLE may facilitate targeted examination of suspicious lesions and provide an optical biopsy-like assessment, although its relatively high cost, technical complexity, and limited clinical availability remain important barriers.<sup>15</sup>

### **Raman Spectroscopy**

Raman spectroscopy evaluates the molecular composition of tissues by analyzing changes in the scattering of incident light. Because malignant transformation is associated with biochemical alterations in proteins, lipids, nucleic acids, and other cellular components, Raman spectroscopy may distinguish normal, potentially malignant, and malignant tissues based on their molecular signatures. Its ability to provide biochemical information without tissue removal makes it a promising emerging technology, although further clinical validation is required before routine application.<sup>16</sup>

### **Other Emerging Optical Technologies**

Several other optical approaches are being explored, including hyperspectral imaging, fluorescence lifetime imaging, multiphoton microscopy, photoacoustic imaging, and multimodal optical imaging. These technologies aim to improve the detection of subtle structural, vascular, metabolic, or biochemical changes associated with malignant transformation. Integration of optical imaging with artificial intelligence and machine-learning algorithms may further improve automated lesion detection and risk classification. However, variations in imaging protocols, equipment, interpretation criteria, and clinical validation currently limit widespread clinical implementation.<sup>17,18</sup>

### **Salivary and Molecular Biomarkers**

Saliva has emerged as a promising, non-invasive diagnostic fluid for the detection of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC). It contains nucleic acids, proteins, metabolites, extracellular vesicles, and other molecules that may reflect local and systemic pathological changes. Salivary and molecular biomarkers have therefore attracted considerable interest as potential tools for early detection, risk assessment, and disease monitoring.<sup>19</sup>

### **DNA and RNA Biomarkers**

Alterations in DNA and RNA associated with malignant transformation can be detected in saliva and oral tissues. Changes in gene mutations, DNA methylation, messenger RNA (mRNA), and other RNA molecules may provide molecular indicators of oral carcinogenesis. These biomarkers have potential for identifying high-risk lesions and supporting early diagnosis; however, differences in sampling methods and molecular assays require further standardization.<sup>20,21</sup>

### **MicroRNAs**

MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression and play important roles in cellular proliferation, apoptosis, invasion, and tumor progression. Abnormal miRNA expression patterns have been reported in OSCC and may help differentiate malignant from normal tissues. Their stability in saliva makes them particularly attractive as non-invasive biomarkers, although their diagnostic accuracy varies among individual miRNAs and patient populations.<sup>20,21</sup>

### **Proteins and Inflammatory Markers**

Salivary proteins and inflammatory mediators may reflect tumor-associated changes and local immune responses. Potential biomarkers include cytokines, growth factors, enzymes, and tumor-associated proteins. Alterations in molecules such as interleukins, matrix metalloproteinases, and other inflammatory mediators have been investigated for their association with oral malignancy. Their clinical usefulness may be enhanced when multiple biomarkers are combined rather than relying on a single marker.<sup>20,21</sup>

### **Metabolomics**

Salivary metabolomics involves the comprehensive analysis of small-molecule metabolites associated with cellular metabolism. Cancer-related metabolic alterations can produce characteristic changes in metabolites such as amino acids, lipids, organic acids, and energy-related compounds. Metabolomic profiling may therefore provide an opportunity for early detection and molecular characterization of OSCC. However, dietary factors, medications, oral hygiene, and systemic conditions can influence salivary metabolite levels.

### **Liquid Biopsy**

Liquid biopsy refers to the detection of tumor-derived material in body fluids, including circulating tumor DNA, cell-free DNA, RNA, extracellular vesicles, and circulating tumor cells. In oral cancer, saliva offers particular advantages because of its direct contact with oral lesions. Liquid biopsy may potentially support early detection, molecular profiling, treatment monitoring, and identification of recurrence. Nevertheless, low biomarker concentrations and technical variability remain important challenges.

### **ADVANTAGES AND LIMITATIONS**

Salivary and molecular biomarkers offer several advantages, including non-invasive sampling, ease of collection, relatively low cost, repeatability, and potential for point-of-care testing. They may also complement clinical examination and provide molecular information that cannot be obtained through visual inspection alone. However, biomarker levels can be affected by age, diet, smoking, oral hygiene, inflammation, medications, and systemic diseases. Variability in sample collection, processing, analytical platforms, and diagnostic thresholds also limits comparison between studies. Therefore, despite promising findings, large prospective studies and standardized protocols are needed before salivary and molecular biomarkers can be routinely incorporated into oral cancer screening.

### **Artificial Intelligence in Oral Cancer Detection**

Artificial intelligence (AI) is increasingly being explored as an adjunctive tool for the early detection, classification, and risk assessment of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinoma (OSCC). By analyzing clinical, photographic, histopathological, radiographic, and molecular data, AI-based systems may assist clinicians in identifying suspicious lesions and improving diagnostic consistency.<sup>22</sup>

### **AI-Based Image Analysis**

AI-based image analysis uses computer algorithms to evaluate intraoral photographs and other digital images for features associated with potentially malignant and malignant lesions. These systems can identify changes in color, texture, lesion borders, and tissue patterns that may be difficult to recognize consistently during routine examination. Automated image analysis may facilitate rapid screening and help prioritize patients requiring further clinical evaluation or biopsy.<sup>22</sup>

## **Machine Learning and Deep Learning**

Machine learning enables algorithms to identify patterns within clinical and imaging datasets and generate predictions based on previously analyzed cases. Deep learning, particularly convolutional neural networks, has gained considerable attention for image-based diagnosis because of its ability to automatically extract complex visual features. These approaches can potentially support lesion classification without requiring manual identification of every diagnostic feature.<sup>22</sup>

### **Detection of OPMDs and OSCC**

AI has been investigated for differentiating normal oral mucosa from OPMDs and OSCC using clinical and photographic images. Deep-learning models may identify subtle visual characteristics associated with dysplasia or malignancy and assist in distinguishing suspicious lesions from benign conditions. AI may therefore have particular value in screening and referral, especially when integrated with conventional clinical examination.

### **Diagnostic Accuracy**

Several studies have reported promising sensitivity, specificity, and overall classification performance for AI-based oral cancer detection. However, reported accuracy can vary substantially depending on the dataset, image quality, disease spectrum, algorithm, and reference standard used. Performance obtained from retrospective or curated datasets may not necessarily reflect real-world clinical performance. External validation using independent and diverse patient populations is therefore essential before widespread clinical implementation.

### **Clinical Decision Support**

AI can function as a clinical decision-support tool by combining patient history, risk factors, clinical findings, and imaging characteristics to assist in risk stratification and referral decisions. Such systems may help clinicians identify lesions requiring urgent evaluation and potentially improve consistency between practitioners with different levels of experience. Importantly, AI-generated assessments should complement rather than replace professional clinical judgment and histopathological confirmation.

## **Current Limitations and Ethical Considerations**

Despite its potential, AI-based oral cancer detection faces several limitations, including small datasets, inadequate representation of different populations, variations in image acquisition, algorithmic bias, overfitting, and limited external validation. Differences in cameras, lighting conditions, image resolution, and clinical documentation can also affect model performance. Ethical concerns include patient privacy, informed consent, secure handling of clinical images, transparency of algorithms, accountability for diagnostic errors, and the risk of over-reliance on automated predictions. Future research should prioritize standardized datasets, multicenter prospective validation, explainable AI, and integration with established

## **CHALLENGES AND LIMITATIONS**

Despite advances in oral cancer screening, several challenges limit the widespread clinical adoption of adjunctive and emerging technologies. Variability in diagnostic accuracy, operator expertise, image quality, and interpretation criteria can affect clinical performance. Many technologies have been evaluated using small, retrospective, or highly selected datasets, with limited external and prospective validation. False-positive results may lead to unnecessary referrals and biopsies, whereas false-negative results can delay diagnosis. Additional barriers include cost, equipment availability, technical expertise, lack of standardized protocols, and limited evidence regarding cost-effectiveness. For AI-based systems, concerns regarding algorithmic bias, data privacy, transparency, explainability, and accountability further require attention. Therefore, emerging technologies should complement rather than replace conventional clinical examination and histopathological assessment.

## **FUTURE PERSPECTIVES**

The future of oral cancer screening is likely to involve an integrated approach combining clinical examination with digital imaging, optical technologies, molecular biomarkers, and artificial intelligence. Development of portable and affordable point-of-care devices may improve screening accessibility, particularly in resource-limited settings. AI-based systems may facilitate automated lesion recognition, risk prediction, and personalized referral pathways when trained and validated using diverse multicenter datasets. Integration of imaging findings with salivary and molecular biomarkers may further improve diagnostic precision. Tele-oral

medicine and cloud-based platforms may also support remote screening and specialist consultation. Future research should prioritize prospective clinical validation, standardized protocols, explainable AI, and evaluation of real-world clinical and cost-effectiveness outcomes.

## CONCLUSION

Early detection remains essential for improving outcomes in oral cancer. Conventional visual and tactile examination, supported by biopsy and histopathological evaluation, continues to form the foundation of diagnosis. Adjunctive technologies such as vital staining, optical imaging, brush cytology, salivary biomarkers, molecular diagnostics, and artificial intelligence offer promising opportunities to improve lesion detection and risk assessment. However, most emerging approaches require further standardization and clinical validation before routine implementation. A multidisciplinary and integrated screening strategy that combines established clinical methods with appropriately validated technologies may enhance early detection, facilitate timely referral, and ultimately contribute to improved outcomes in patients with oral cancer.

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