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Review

Artificial Intelligence and Oral Cancer Diagnosis: Current Evidence, Critical Limitations, and the Basic Science Priorities Essential for Improving Diagnostic Accuracy

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Abstract

Oral cancer remains one of the deadliest malignancies with more than half of late-stage patients dying within five years of diagnosis globally. Late presentation before initial diagnosis is a principal driver of poor outcomes for the disease. Artificial intelligence (AI), particularly deep learning systems, has emerged as a promising tool to improve the sensitivity and timeliness of oral cancer detection. This narrative review examines the current state of AI-assisted oral cancer diagnosis, evaluating the performance of image-based approaches [including convolutional neural networks (CNNs) applied to clinical photographs, histopathological slides, and cytology workflows] and critically analyzes where these systems fall short. Of note is the fact that AI models are functionally blind to submucosal and early infiltrating lesions without visible surface change, and their detection of high-grade epithelial dysplasia remains poor. Model generalizability across institutions is further compromised by the absence of large-scale standardized oral cancer image repositories. This review argues that the next frontier must shift from morphology-based learning to biologically informed AI [specifically through multiomics integration, tumor microenvironment characterization, and molecular imaging biomarkers] in order to detect oral cancer earlier and more reliably.

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Introduction

Oral squamous cell carcinoma (OSCC) accounts for the overwhelming majority of oral cavity malignancies and continues to carry one of the highest mortality rates among cancers for which established screening pathways exist [1]. The five-year survival rate for oral cancer in low and middle-income countries (LMIC) remains approximately 25-45% [2,3], a figure that has not improved meaningfully over several decades despite significant advances in surgical, radiation, and systemic oncology [4]. The primary driver of this persistent mortality burden is the disproportionately high rate of late-stage [III-IV] diagnosis [5]. When oral cancers are detected at Stage I or II, five-year survival rates exceed 70–80%; unfortunately, this figure drops dramatically with advanced-stage disease [6].

Some of the barriers to early detection are embedded in our current diagnostic standards. Conventional clinical visual examination [which is the the predominant screening method in most healthcare settings] has a pooled sensitivity of approximately 70% [7], for detecting dysplastic and malignant oral lesions, meaning that a substantial proportion of early lesions are still missed even by trained clinicians. Oral potentially malignant disorders (OPMDs) such as leukoplakia and erythroplakia represent important targets for secondary prevention, but their clinical heterogeneity

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and the inter-examiner variability inherent to conventional visual assessment create a well-documented diagnostic gap that the current standard of care cannot consistently close [8].

Artificial intelligence offers a credible and increasingly well-supported pathway to addressing these gaps. Machine learning approaches [particularly deep learning architectures] have demonstrated meaningful performance advantages over conventional diagnostic techniques across multiple oncologic applications [9]. In the oral cancer space, the pace of research has accelerated considerably over the past decade, with multiple meta-analyses now available characterizing the aggregate performance of AI systems in oral cancer detection [10,11]. However, translation of promising research outputs into generalizable clinical tools has been inconsistent [12], and a clear-eyed analysis of where the technology works, where it does not, and what basic science focus should be prioritized is necessary to guide both research investment and implementation strategy.

This narrative review synthesizes current evidence on AI-assisted oral cancer diagnosis, offers a structured critique of the field's principal limitations, and proposes a forward-looking framework for the biological and computational advances required to meaningfully improve oral cancer outcomes.

Literature Search Strategy

This narrative review synthesizes peer-reviewed literature on artificial intelligence applications in oral cancer diagnosis. Relevant publications were identified through searches of PubMed, Scopus, and Google Scholar using combinations of keywords including "oral cancer," "oral squamous cell carcinoma," "artificial intelligence," "deep learning," and "machine learning." Studies were selected based on relevance to diagnostic performance, biological limitations, and translational clinical applicability.

Current Landscape of AI-Assisted Oral Cancer Detection

In the oral cancer domain, the predominant AI-assisted diagnostic strategy is image-based deep learning; of which the most common is convolutional neural networks trained on clinical photographs, histopathological whole-slide images, and oral endoscopic images [13]. CNNs are a class of artificial neural networks well-suited to visual pattern recognition due to their ability to learn hierarchical spatial features from raw pixel data through successive convolutional layers [14]. These models have been trained across a range of input types, from standardized photographic archives to whole-slide images digitized from biopsy specimens.

Published meta-analyses show that AI-based, predominantly CNN-driven oral cancer detection systems achieve pooled sensitivities around 87–90% and specificities around 81–90% [9,15]. One meta-analysis of mixed AI models for oral cancer and OPMDs reported a pooled sensitivity of 0.87, specificity of 0.81, and a diagnostic odds ratio (DOR) of 131.6, while a CNN-focused meta-analysis in oral squamous cell carcinoma found a DOR exceeding 260 with an area under curve (AUC) of 0.98 [16]. This performance profile represents a clinically meaningful advantage over unaided conventional oral examination, which shows a pooled sensitivity of about 70% for detecting dysplastic and malignant oral lesions and is highly operator dependent [7]. Additionally, emerging comparative data indicate that deep learning models now often outperform earlier machine learning classifiers [including logistic regression and support vector machines] on many published oral cancer detection benchmarks, particularly for image-based tasks [10]. Hybrid approaches combining CNN-based feature extraction with ensemble classifiers have pushed accuracy above 95% on some OSCC datasets [17].

Beyond static image classification, AI-assisted endoscopy has begun to exploit advanced segmentation architectures [such as U-Net and related deep semantic segmentation models] to differentiate intraoral tissue types in endoscopic hyperspectral imaging, achieving high F1-scores [around 0.84–0.86] across multiple tissue classes in *in vivo* settings [18]. AI-integrated cytology workflows are also increasingly being evaluated alongside conventional histopathology as a complementary diagnostic modality [19].

High-Performing Applications

CNNs applied to digitized histopathological slides represent the highest-performing application currently available in the AI oral cancer literature [20]. These models excel because histopathology provides standardized, high-resolution input in a training environment where deep learning architectures are naturally suited to exploit subtle morphological differences in cellular architecture, nuclear pleomorphism, and tissue organization [21,22]. The performance characteristics of histopathology-based AI are broadly reproducible across datasets and represent the most mature area of the field.

Clinical image analysis has also matured considerably. Systems trained on OPMDs, particularly leukoplakia, perform with high consistency, and smartphone-integrated AI platforms have demonstrated near-expert-level diagnostic accuracy in community screening settings [23]. This is a particularly meaningful development for resource-limited environments, where limited specialist access and high rates of late-stage presentation converge to create the greatest unmet diagnostic need. Custom-designed CNN architectures built specifically for oral cancer [rather than adapted from general image classifiers] have reported precision above 91%, sensitivity of 94%, and categorization accuracy of 95% for oral tumors, suggesting that disease-specific model design confers meaningful performance advantages over repurposed general architectures [20].

Table 1. AI Performance Benchmarks in Clinical Imaging.

Metric	Repurposed General AI (e.g., VGG/ResNet)	Custom Oral Cancer CNNs
Categorization Accuracy	85.0% – 88.4% [20]	**95.2%** [20]
Sensitivity	84.1% – 87.0% [20]	**94.5%** [20]
Precision	86.0% – 89.2% [20]	**91.1%** [20]
Global Applicability	Limited by demographic bias [24]	High potential for LMIC screening [23]

Critical Limitations of Current AI Approaches

A key limitation of many current AI oral-cancer detection systems [particularly those based on clinical photographs or white-light imaging] is that they primarily model surface-visible features and therefore may not reliably identify pathology whose most salient signal is submucosal [25]. This is clinically important because depth of invasion is incorporated into the American Joint Committee on Cancer staging system (AJCC) 8 staging and is an important predictor of nodal metastasis and adverse outcomes, including extracapsular spread [26].

Detection of high-grade epithelial dysplasia, which is arguably the highest-value target for secondary prevention, also underperforms in current AI workflows [27]. One AI-integrated cytology platform reported sensitivity of only 18% for high-grade dysplasia, a figure comparable to conventional cytology alone and insufficient for meaningful clinical utility [28]. The major biological explanation for this failure is that cells exfoliated from deeper epithelial layers in highly keratinized squamous mucosa are both difficult to sample adequately and morphologically ambiguous, creating noise in training data that confounds even well-optimized classifiers [29].

General-purpose large language model-based image recognition tools have also been evaluated with some sobering results. GPT-4-based image recognition performed inconsistently on OSCC

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images when clinical history was not provided as context, making it unreliable for clinical decision-support in its current form [24]. Across the broader field, model generalizability across institutions remains a structural problem due to majority of published AI systems being trained and validated on single-center datasets, which constrains external reproducibility and limits the evidence base for multi-site deployment [30]. The absence of large-scale, standardized, and annotated oral cancer image repositories compounds this, functioning as a structural bottleneck that limits both the diversity of training data and the rigor of benchmarking [23].

Table 2. Comparative Diagnostic Utility and Primary Limitations.

Modality	HGD Sensitivity	Primary Limitation
Conventional Cytology	~18% – 25%	Sampling depth; manual observer fatigue; keratinization. [28]
AI-Integrated Cytology	~18% (in specific platforms)	Reliance on surface morphology; inability to access deeper tissue layers. [27]
Histopathology (Gold Standard)	~90% – 100%	Invasive; captures full-thickness architecture. [31]

Basic Science Priorities for Next-Generation Ai Oral Cancer ToolS

As we have stated earlier, the fundamental constraint on current AI performance is that these systems learn from morphology alone [31]. However, oral carcinogenesis [like any other tissue-specific cancer] is driven by molecular events such as transcriptional reprogramming, epigenetic dysregulation, and immune microenvironment remodeling that precede visible tissue change by months to years [32–34]. For AI to detect oral cancer earlier and more reliably, the field must transition toward training models on biologically meaningful molecular signals.

Three scientific urgencies are clear and should be prioritized in order to make the leap towards the next generation of diagnostic AI products in oral carcinogenesis. First, multiomics integration. Machine learning models that incorporate transcriptomic, proteomic, and epigenomic data consistently outperform image-only models on cancer classification tasks [35]. Convergent biological processes involved in oral carcinogenesis; like metabolic reprogramming, immune-inflammatory remodeling, microbiome dysbiosis, and epithelial-stromal disruption, are now identifiable as molecular signatures that precede histologic transformation [36]. AI models trained to recognize these molecular patterns could substantially compress the diagnostic window and identify malignant progression before a visual phenotype emerges [37].

Second, tumor microenvironment (TME) characterization. Advances in spatial transcriptomics and single-cell RNA sequencing now enable characterization of the OSCC cellular architecture at resolutions previously unavailable [22]. AI models encoding TME features [including immune cell composition, cancer-associated fibroblast activation states, and extracellular matrix remodeling signatures] can capture information directly relevant to invasion risk and immune evasion [38], dimensions that image-based AI is structurally incapable of accessing [39].

Third, molecular imaging biomarkers. TME-targeted molecular imaging enables detection of functional tissue changes before structural alterations become visible on standard clinical or radiological examination [40]. Integrating these signals into AI training pipelines represents a direct strategy for addressing the submucosal blind spot and could extend the clinical detection window into the preclinical invasive phase of oral carcinogenesis.

Table 3. Comparison of Diagnostic Modalities in AI Development.

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Feature	Surface Image-Based AI	Multi-Omics & TME-Informed AI
Primary Input	Morphology (RGB/Optical) [20]	Transcriptomics, Proteomics, Spatial data [37]
Detection Timing	Visible phenotype (Stage I-IV) [23]	Pre-clinical molecular shifts [40]
Biological Depth	Surface-level only [25]	Submucosal & cellular architecture [22]
Key Limitation	Submucosal blind spot [25]	High cost and data complexity [12]

Conclusions

Artificial intelligence has demonstrated meaningful diagnostic performance in oral cancer detection, particularly in histopathological slide analysis and clinical image-based classification of OPMDs, and the performance advantage relative to unaided clinical examination is now well-established and clinically significant. However, the current generation of AI tools operates within a narrow morphological paradigm that cannot detect the molecular events driving early invasion, cannot reliably identify high-grade dysplasia, and lacks the cross-institutional generalizability required for broad clinical deployment. Addressing these gaps requires coordinated progress in basic cancer biology, multiomics methodology, spatial transcriptomics, and molecular imaging. The extent to which the field advances on these fronts in the coming years will determine whether AI can genuinely change oral cancer survival outcomes or not.

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