

OPINION PAPER

VITAL STAINING AND ARTIFICIAL INTELLIGENCE IN ORAL CANCER DETECTION: A HYBRID DIAGNOSTIC APPROACH FOR GLOBAL HEALTH EQUITY

Abhijeet Satpathy, Rupsa Das, Satya Ranjan Misra *

Department of Oral Medicine and Radiology, Institute of Dental Sciences, Siksha 'O' Anusandhan University, Bhubaneswar, Odisha, India

* Correspondence to: ✉ satyamisra@soa.ac.in; <https://orcid.org/0000-0002-1994-543X>

ABSTRACT: Oral squamous cell carcinoma (OSCC) remains a major public health challenge, particularly in low- and middle-income countries (LMICs), where early detection infrastructure is limited. Vital staining is affordable and chairside-simple but is undermined by operator variability and modest specificity. Artificial intelligence (AI)-assisted image analysis offers reproducibility and scale but is constrained by technological and logistical barriers in resource-poor settings. Our position in this Opinion is straightforward: neither modality alone will close the diagnostic gap in rural India, and withholding a low-cost triage layer from village populations while urban centers benefit from AI-assisted histopathology is inequity by omission. We argue for a hybrid workflow in which frontline workers apply a standardized dye, capture the stained lesion on a smartphone, and route the image through a cloud-hosted deep-learning classifier to a specialist hub. We defend this position with a pragmatic implementation pathway and a four-step, milestone-driven research agenda covering image repositories, prospective accuracy trials, cost-and-equity metrics, and regulatory-sandbox validation.

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Impact statement: This Opinion proposes a pragmatic hybrid approach combining vital staining and artificial intelligence to strengthen early oral cancer triage, enhance diagnostic access, and decrease inequities in resource-limited settings.

Key words: *Artificial intelligence; early diagnosis; hybrid diagnostic model; oral squamous cell carcinoma; oral potentially malignant disorders; vital staining.*

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INTRODUCTION

Consider Kamala, a 52-year-old woman in rural Odisha who has chewed areca-nut-tobacco quids for two decades. A frontline health worker visiting her hamlet notices a white patch on her buccal mucosa, applies toluidine blue, photographs the stained lesion on a smartphone, and uploads it to a cloud-hosted classifier that flags it as high-risk within seconds. Within a week, an oral-medicine specialist at the district hub reviews the image and Kamala is scheduled for biopsy. This is not a technology story. It is an equity story: a triage layer that costs pennies

per image, delivered by workers who already visit her village, is either offered to Kamala or it is not. Oral squamous cell carcinoma (OSCC) is one of the most prevalent malignancies globally and disproportionately burdens South Asia. India recorded 143,759 new lip and oral cavity cancer cases and 79,979 deaths in 2022 – roughly a third of the global burden – with men bearing an age-standardized rate of 15.6 *versus* 5.0 per 100,000 in women (1, 2). That burden is overwhelmingly attributable to modifiable behavioral exposures: smokeless tobacco, areca-nut chewing, bidi smoking and alcohol together account for the great majority of Indian cases (3).

Human papillomavirus (HPV), while carcinogenic at the oropharynx, has neither a strong nor consistent causal association with cancer at the oral cavity subsite in Indian populations (4), which is why India's National Programme for Prevention and Control of Non-Communicable Diseases (NP-NCD, formerly NPCDCS) targets tobacco cessation and opportunistic oral, breast and cervical screening rather than viral prophylaxis; HPV vaccination sits under the Universal Immunisation Programme and is being introduced in phases for cervical cancer prevention (5). The implication for policy is unambiguous: any early-detection strategy for OSCC in India must be built around behavioral risk factors and the visible mucosal lesions they produce, and it must reach the villages in which those exposures occur.

The persistent challenges in early diagnosis stem from limited infrastructure, insufficient trained personnel, and lack of population-wide screening implementation. Even where NP-NCD has been rolled out, rural and underserved populations often lack access to timely screening, specialist consultation, and definitive diagnosis. What is needed is a diagnostic strategy that is cost-effective, scalable, and adaptable to varying health system capacities – one that meets this gap directly with a hybrid workflow combining a low-cost dye-based screen with an AI-assisted classification layer capable of running on a smartphone.

THE EXISTING LANDSCAPE OF OSCC DETECTION

Vital staining methods –Toluidine Blue, Methylene Blue, Lugol's Iodine – have long been used as adjuncts to clinical examination in OSCC detection. Their appeal in LMICs rests on affordability, simplicity and chairside use. They suffer, however, from operator

variability and reduced specificity, generating false positives and, less often, false negatives (6).

AI-assisted image analysis offers the reverse profile: reproducibility and scale when supported by adequate infrastructure. Convolutional neural networks and related deep-learning architectures have demonstrated strong classification performance for oral potentially malignant disorders (OPMDs) and OSCC on clinical, histological and radiographic images (7). Most such systems, however, are confined to academic or urban settings with the technological readiness to support them, while in LMICs – where the majority of OSCC deaths occur – the digital divide continues to hinder frontline deployment. A context-appropriate pairing of the two, rather than a choice between them, is the pragmatic path forward.

A TIERED GLOBAL OVERVIEW: DIAGNOSTIC CHOICES BY HEALTH SYSTEM STRENGTH

Diagnostic choices in OSCC do not diverge across settings by accident; they track health-system capacity in ways that matter for how any new tool is deployed. In high-resource tertiary centers, workflows are anchored by biopsy with histopathology, adjunct optical technologies and, increasingly, AI-assisted histopathology or radiology, in which specificity is prioritized over cost and where a false positive is absorbed as an additional pathology review. In middle-resource settings – urban and semi-urban public hospitals in India among them – clinicians rely on visual and adjunctive examination, opportunistic screening within NP-NCD, and referral pathways whose bottleneck is specialist availability rather than the screening step itself. In resource-limited village and outreach settings, the dominant modality remains visual inspection by non-specialist staff,

Table 1. *The diagnostic capabilities of countries with maximum oral cancer burden.*

COUNTRY TYPE	EXAMPLES (TOP 10 BURDEN)	DIAGNOSTIC PREFERENCE AND RATIONALE
Developed, robust healthcare systems	Japan, France	AI is increasingly adopted due to solid digital infrastructure and insurance-backed health systems.
Developed but inequitable	USA	Feasible AI use but hindered by high costs and disparities in healthcare access.
Rapidly developing	China, Brazil	Hybrid models are emerging with expanding digital literacy and infrastructure.
Resource-limited/developing	India, Bangladesh, Indonesia	Vital staining remains primary due to cost-effectiveness; AI integration is slowly emerging.

supplemented in some programs by vital staining and, where connectivity permits, by smartphone photography. **Table 1** summarizes this landscape. Two features of this comparison bear directly on the position we develop below. First, the diagnostic tools chosen at each tier reflect what is affordable and delegable, not what is most accurate; where health workers rather than clinicians perform the screen, sensitivity and low training burden matter more than headline specificity. Second, the transition between tiers – village screen to district hub to tertiary confirmation – is where preventable delay accumulates in Indian OSCC and where a triage layer, if it is standardized and digitally linked, does the most work per rupee spent. It follows that the design question is not whether to introduce AI, but where in the tiered pathway to place it so that the modality complements rather than displaces the human screen at the village end (8).

VITAL STAINING: STRENGTHS, LIMITATIONS, AND CURRENT EVIDENCE

Standardizing the pre-application decontamination, dye concentration and rinsing sequence, and documenting deviations at the time of image capture, may improve consistency in field-based staining (9, 10). Its utility as a low-cost triage tool in areas lacking biopsy facilities remains uncontested. Clinicians commonly use it to delineate biopsy sites, track lesion progression, or screen large populations during outreach programs. It is safe, requires minimal training, and yields immediate visual feedback – qualities that make it ideal for field-level application. Limitations persist: dysplastic changes may go unstained if the lesion is keratinized.

ARTIFICIAL INTELLIGENCE IN OSCC DETECTION: A NEW FRONTIER

AI applications in dentistry are rapidly evolving. Deep-learning algorithms trained on large image datasets have achieved sensitivity approaching 100% and specificity above 90%, in histopathologic and clinical imaging tasks (7, 11). A 2024 systematic review and meta-analysis by Li and colleagues reported a notably high diagnostic odds ratio for AI-assisted clinical photography, suggesting transformative

potential in early oral cancer detection (11). That pooled estimate, however, carries substantial caveats: recent meta-analyses report between-study heterogeneity of $I^2 > 98\%$ for both sensitivity and specificity, and the majority of primary studies are rated high or unclear risk of bias for patient selection under QUADAS-2, largely because of retrospective designs, convenience sampling and lack of external validation (12). Headline accuracy figures therefore reflect model performance under favorable conditions, not real-world screening performance in an unselected village population.

Given more than 6.5 billion smartphone users globally, even rural clinics can potentially implement AI-assisted imaging with modest resources. Two published pilots make this concrete. Birur and colleagues deployed a smartphone-based oral cancer screening application with frontline health workers across four Indian states from 2010 to 2018, screening 42,754 individuals in door-to-door, workplace and village programs and identifying 5,406 OPMDs, of which 516 were biopsy-confirmed at remote locations (13). In their initial targeted cohort, however, only 61% of images captured by frontline workers were deemed interpretable – a stark reminder that image quality, not model architecture, is the rate-limiting step. Uthoff and colleagues developed a dual-modality (autofluorescence plus white-light) smartphone probe and evaluated it in 190 patients from Indian oral-oncology clinics; the CNN classifier trained on data from 99 patients achieved point-of-care performance suitable for remote diagnosis but again required careful attention to acquisition geometry and lighting (14). These pilots demonstrate that smartphone-AI screening in rural India is feasible; they also show that interpretability rates and calibration drift, not headline AUCs, are the metrics that determine field utility.

AI performance in this domain depends on image quality and standardization, algorithm training across diverse populations, and clinician interpretation and validation. Challenges such as poor lighting, lesion retraction, anatomical complexity and image resolution all affect diagnostic accuracy (15–17), and models developed in homogeneous populations may generalize poorly across ethnic groups or lesion types. **Table 2** compares vital staining and AI across principle, cost, training, sensitivity, specificity and scalability; neither tool is sufficient alone, but synergizing both can improve diagnostic accuracy in both resource-rich and resource-poor environments.

Table 2. Comparison between vital staining and artificial intelligence as adjunct diagnostic tools.

PARAMETER	VITAL STAINING	ARTIFICIAL INTELLIGENCE (AI)
Principle	Dye retention in dysplastic epithelial cells	Pattern recognition from image datasets
Techniques	Toluidine Blue, Lugol's Iodine	CNNs, supervised/unsupervised learning
Application	Chairside adjunct to clinical exam	Image analysis, prediction models
Cost	Very low	High initially, cost reduces with scale
Invasiveness	Non-invasive	Non-invasive
Training needed	Moderate (clinical judgment)	High (AI model development, validation)
Turnaround Time	Immediate	Fast post-deployment
Sensitivity and specificity	Variable across studies; dependent on dataset, imaging modality and validation setting	
Accessibility	High in LMICs	Limited by infrastructure in LMICs
Use in mass screening	Highly feasible	Growing feasibility with mobile AI
Suitability in LMICs	Very high	Currently limited
Scalability	Proven	Uncertain, but promising

Our proposal differs from earlier hybrid concepts in a specific way. Most published integrations treat toluidine-blue uptake as a categorical input to a decision rule (positive stain $\rightarrow$ biopsy) or feed unstained clinical photographs into a CNN. We propose that the stained image itself – the spatial pattern, intensity gradient and border characteristics of dye retention – becomes the CNN input. This preserves the biological signal the dye captures (nucleic-acid-rich dysplastic epithelium) while adding the pattern-recognition capacity of deep learning to distinguish genuine dysplastic uptake from candidal, inflammatory or traumatic false-positive uptake.

CHALLENGES AND THE NEED FOR CLINICAL OVERSIGHT

AI systems face validation, ethical and legal barriers in clinical deployment. Misclassification mistaking benign lesions for malignancies, or *vice versa*, could have severe implications. AI must therefore be integrated as a decision-support tool, not a replacement for clinician judgment. Oral medicine specialists play a pivotal role, from standardized image acquisition to interpreting ambiguous outcomes; centralized repositories and biobanks can improve AI training, and protocols for intraoral photography (lighting, retraction, resolution) can standardize diagnostic inputs (15-18).

Beyond model validation, three governance issues warrant attention. First, data privacy: intraoral images

uploaded from village camps carry facial and identifying features and must be handled under India's Digital Personal Data Protection Act, 2023, with explicit consent for research reuse. Second, maintenance and calibration: classifier drift over time and across handset generations is well documented in real-world medical AI and mandates a scheduled re-validation cadence with locally acquired hold-out data. Third, training and accountability: frontline workers require a defined competency threshold before they upload images, and the clinician of record – usually the oral-medicine specialist at the hub – retains diagnostic responsibility for every flagged case, with the AI output treated as advisory. These governance elements are not optional add-ons; they are the difference between a research pilot and a system that survives public-sector procurement.

IMPLEMENTATION STRATEGY

A decision-tree protocol (**Figure 1**) can be employed in primary care settings. Where the frontline worker observes no dye retention, the patient is placed under routine monitoring, with a biopsy triggered only where clinical suspicion overrides the negative stain. Where dye is retained, a smartphone image of the stained lesion is captured under standardized conditions (fixed working distance, retracted field, ring-lit or flash-lit white balance) and uploaded to the AI classifier. Cases stratified as low-risk return to observation with a follow-up interval of eight

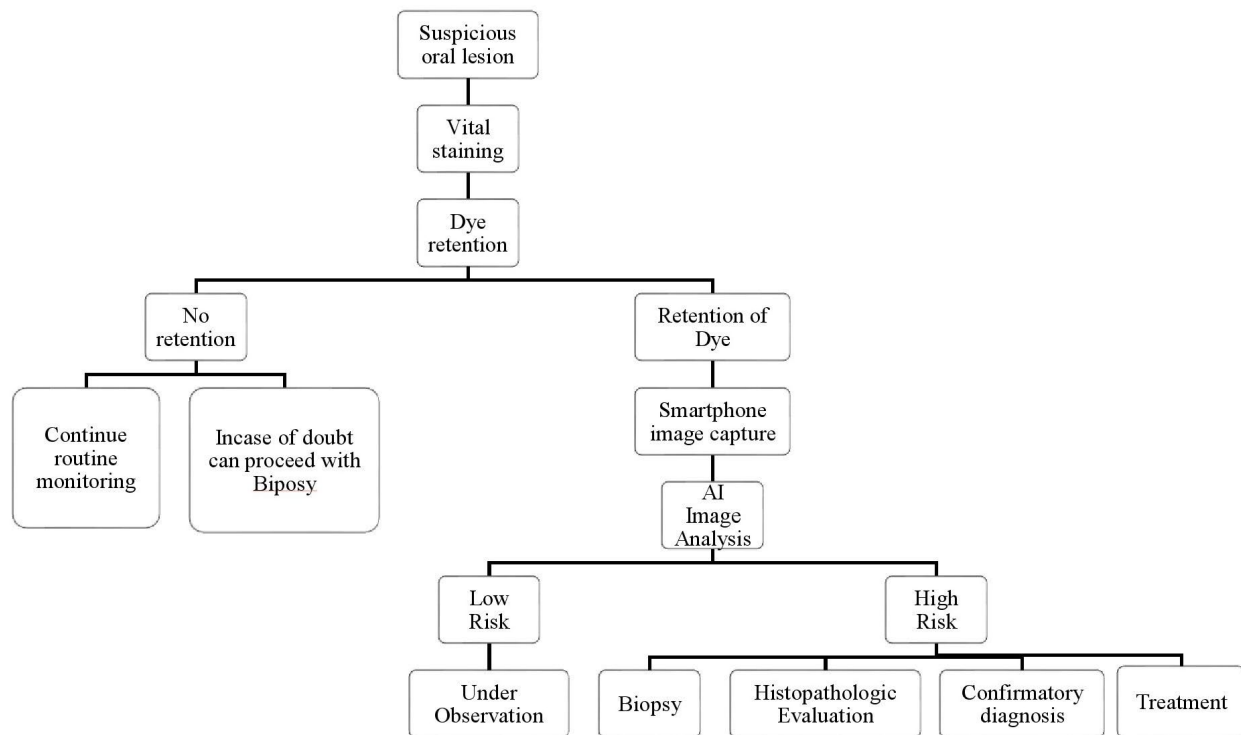


Figure 1. A flow chart describing the workflow of a hybrid model using vital staining integrating artificial intelligence for oral cancer diagnosis.

to twelve weeks; cases stratified as high-risk are referred through the tele-network to the specialist hub for biopsy, histopathology and definitive management.

FUTURE DIRECTIONS: A HYBRID, CONTEXTUALIZED APPROACH

The equity claim opened this Opinion; it also determines what research is worth doing next. If a smartphone classifier that costs pennies per image can shift even 10% of Indian OSCC diagnoses from stage IV to stage II, the mortality reduction dwarfs any conceivable investment in additional specialist infrastructure. That is the arithmetic. What follows from it is a hybrid workflow in which vital staining is the first-line screen at primary health centers and community camps, AI-based imaging is the second-line support that guides referral and remote consultation, and centralized diagnostic hubs, staffed by specialists, deliver review and intervention. Research over the next 24-36 months should follow four sequential, measurable milestones rather than the diffuse partnerships-and-repositories language of ear-

lier commentaries. In months 0-6, curate a population-representative image repository of at least 10,000 paired white-light and toluidine-blue-stained lesion images from at least four Indian states, with structured metadata (age, sex, tobacco and areca history, lesion site, histopathology ground truth, staining protocol used) following FAIR data-sharing standards. In months 6-18, conduct prospective, pre-registered diagnostic-accuracy trials enrolling at least 2,000 community-screened participants in a multi-center STARD-compliant study, with pre-specified classifier operating threshold, primary sensitivity and specificity endpoints, and subgroup analyses by state, sex and lesion site. In months 12-30, embed cost-effectiveness and equity metrics: incremental cost per OPMD detected, per stage-shift achieved and per disability-adjusted life-year averted, with equity reported as the ratio of rural-to-urban uptake, the reduction in the proportion of OSCC diagnosed at stage III/IV, and the time from screen-positive to biopsy result. In months 24-36, work with the Central Drugs Standard Control Organization and state health authorities to pilot the classifier as a software-as-a-medical-device under a phased regulatory sandbox, with periodic external audits. None of

this is speculative; each step has an owner, a time-frame and a measurable output.

CONCLUSIONS

No single diagnostic strategy will close the OSCC gap in India. Vital staining is indispensable for its simplicity and cost; AI adds precision and reproducibility. Together they can bridge the distance between advanced urban hospitals and resource-deprived rural clinics. The next step is not another position paper, but a coordinated four-step research program – image repository, prospective diagnostic-accuracy trial, cost-and-equity metrics, and regulatory sandbox – that converts the hybrid concept into evidence a district hospital can act on.

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Conflicts of interest

The authors declare no competing interests.

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Authors' contributions

AS: conceptualization. RS, SRM: writing – original draft, writing, review & editing.

Publications ethics

Plagiarism

We hereby declare that this manuscript has not been published or submitted for publication elsewhere. All appropriate references have been cited wherever required. This manuscript does not contain plagiarism.

Data falsification and fabrication

The authors declare that no data fabrication, falsification, or manipulation has been carried out in the preparation of this work. Generative AI was used only for language editing and formatting checks; all scientific content, interpretation, and references were drafted, verified and approved by the authors.

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