



Research Paper

Artificial Intelligence-Assisted Histopathological Diagnosis of Oral Squamous Cell Carcinoma

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Abstract

Background:

Oral squamous cell carcinoma (OSCC) is a major malignant neoplasm of the oral cavity in which timely and accurate diagnosis is essential for appropriate management. Artificial intelligence (AI)-based image analysis has emerged as a promising approach for supporting histopathological evaluation.

Aim:

To evaluate the diagnostic performance of an AI-assisted system for detecting OSCC and recognizing important histopathological features, using expert histopathological diagnosis as the reference standard

Materials and Methods:

A total of 100 histopathologically evaluated OSCC cases were included. Incisional biopsy specimens were stained with hematoxylin and eosin (H& E) and assessed by an experienced oral and maxillofacial pathologist. The AI-assisted system was evaluated for OSCC classification, histopathological grading, and recognition of selected morphological features. Diagnostic performance was assessed using accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F1 score, and receiver operating characteristic–area under the curve (ROC-AUC). Agreement between AI classification and histopathological diagnosis was determined using Cohen's kappa statistic. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS), IBM SPSS Statistics version 26.0, with a p -value < 0.05 considered statistically significant.

Results:

The study population had a mean age of 56.8 ± 10.7 years, with males comprising the majority of participants. Well-differentiated OSCC was the predominant histopathological grade, followed by moderately and poorly differentiated tumors. The AI-assisted system demonstrated high overall diagnostic performance, with an accuracy of 92.0%, sensitivity of 93.1%, specificity of 90.4%, PPV of 91.8%, NPV of 92.1%, F1 score of 92.4%, and ROC-AUC of 0.94. Agreement with the histopathological reference diagnosis was substantial ($\kappa = 0.84$). Diagnostic performance remained consistently high across the three histopathological grades. Recognition accuracy for individual morphological features ranged from 89.0% to 94.0%, with increased nuclear-to-cytoplasmic ratio showing the highest performance.

Conclusion:

The AI-assisted system demonstrated strong diagnostic performance and substantial agreement with expert histopathological assessment in OSCC. Its ability to recognize important microscopic features further supports its potential as an adjunctive tool in oral cancer diagnosis. Larger multicenter studies and independent external validation are required before routine clinical implementation.

Keywords: Artificial intelligence, Diagnostic accuracy, Histopathology, Machine learning, Nuclear pleomorphism, Oral squamous cell carcinoma, Tumor invasion

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I. Introduction

Oral squamous cell carcinoma (OSCC) is the most frequently encountered malignant neoplasm of the oral cavity and continues to represent a significant challenge in oral healthcare. The disease is influenced by multiple etiological factors, particularly tobacco and alcohol exposure, betel quid consumption, and other environmental and behavioral determinants. Despite improvements in diagnostic techniques and cancer management, delayed recognition remains an important contributor to unfavorable outcomes. Consequently, the development of reliable approaches for accurate and timely identification of OSCC remains an important objective in oral oncology [1].

Histopathological assessment of an incisional or excisional biopsy continues to serve as the principal reference standard for establishing the diagnosis of OSCC. The pathological evaluation involves assessment of epithelial architecture, cellular differentiation, nuclear abnormalities, mitotic activity, keratinization, stromal invasion, and other microscopic characteristics. However, interpretation of histopathological sections is influenced by tissue heterogeneity, specimen quality, tumor morphology, and the experience of the reporting pathologist. These factors can create diagnostic difficulties, particularly in lesions exhibiting subtle malignant changes or considerable morphological variation [2].

The emergence of digital pathology has enabled conventional histological sections to be converted into high-resolution digital images that can be analyzed computationally. This development has created opportunities for artificial intelligence (AI) to assist in the interpretation of pathological specimens. Machine learning algorithms can identify patterns within large datasets, whereas deep learning methods, particularly convolutional neural networks (CNNs), can automatically extract relevant morphological characteristics from images without requiring every diagnostic feature to be manually defined. Such approaches have generated considerable interest in the development of computer-assisted systems for oral cancer diagnosis [3].

Histopathology-based AI has demonstrated encouraging potential in differentiating malignant from non-malignant oral tissues. Deep learning systems can analyze microscopic image characteristics and classify tissue according to patterns learned from previously annotated specimens. One investigation using a dedicated deep learning model for OSCC histopathological images reported high diagnostic performance, supporting the possibility that automated image analysis could function as an additional resource for pathologists during routine microscopic evaluation [4].

The broader evidence base has also indicated that AI can be applied to several stages of oral cancer assessment, including lesion classification, recognition of malignant regions, histological grading, and prediction of clinical outcomes. A systematic review of AI applications involving histopathological images reported substantial variation in the algorithms and datasets used across studies, while overall diagnostic performance remained promising. These findings suggest that computational analysis may complement conventional pathological assessment, although differences in study methodology must be considered when interpreting reported results [5].

Recent systematic reviews and meta-analyses have further strengthened the evidence supporting AI-assisted OSCC detection. Reported pooled estimates indicate that AI-based approaches can achieve high sensitivity and specificity, demonstrating their potential as supportive diagnostic technologies. Nevertheless, the considerable heterogeneity observed between studies emphasizes the importance of standardized image acquisition, appropriate training and testing strategies, independent validation, and evaluation using clinically representative datasets before these systems can be incorporated routinely into diagnostic practice [6].

Deep learning has become particularly prominent because of its ability to learn complex visual representations from digital histopathological material. Recent evidence indicates that deep learning models have been investigated not only for binary identification of OSCC but also for classification, segmentation, and other clinically relevant image-analysis tasks. Although the reported results are encouraging, variations in model architecture, image preparation, sample size, reference standards, and validation procedures continue to limit direct comparison between individual studies [7].

An important advantage of AI-assisted histopathological analysis is its potential to provide reproducible and quantitative assessment of digital slides while reducing some of the repetitive workload associated with manual examination. Rather than replacing the expertise of the pathologist, AI may serve as an adjunctive tool capable of highlighting suspicious areas, assisting with diagnostic classification, and providing an additional level of computational assessment. Such integration could be particularly valuable in settings where the workload is high or access to experienced specialists is limited [8].

Despite these advantages, several challenges must be addressed before AI-assisted histopathological diagnosis can achieve widespread clinical adoption. Differences in staining procedures, scanners, image resolution, patient populations, disease prevalence, and annotation practices can influence algorithm performance. Furthermore, the limited interpretability of some deep learning models, potential dataset bias, insufficient external validation, and uncertainty regarding generalizability to routine clinical specimens remain

important concerns. Recent evidence therefore supports AI as a promising adjunct to OSCC diagnosis while emphasizing the need for rigorous external validation and standardized methodologies [9].

This article represents a promising approach for integrating computational image analysis with conventional oral pathology. By evaluating microscopic morphological patterns through trained AI algorithms, such systems may assist in improving diagnostic consistency, accelerating identification of malignant tissue, and supporting pathologists in complex diagnostic situations. The present study therefore aims to investigate the utility of AI-assisted histopathological image analysis for the diagnosis of OSCC and to assess its potential as a complementary tool to conventional microscopic examination.

II. Materials & Methods

Study Design and Study Population

This study was conducted at a single tertiary care centre from March to May 2025 to evaluate the diagnostic utility of an AI-assisted system for the identification and histopathological assessment of OSCC. A total of 100 cases were included in the analysis. The study population comprised patients with clinically suspected oral malignant lesions for whom incisional biopsy specimens were available for definitive histopathological evaluation.

Inclusion Criteria

Patients were included if they met the following criteria:

- Patients presenting with a clinically suspected malignant lesion of the oral cavity
- Patients who provided consent for participation in the study
- Availability of an adequate incisional biopsy specimen for histopathological examination.
- Biopsy specimens with sufficient tissue for hematoxylin and eosin (H & E) staining and microscopic evaluation.
- Cases with a definitive histopathological diagnosis of OSCC
- Histological sections of adequate quality for digital imaging and AI-assisted analysis

Exclusion Criteria

Cases were excluded based on the following criteria:

- Cases with incomplete clinical or histopathological information
- Inadequate or insufficient biopsy specimens for definitive histopathological diagnosis
- Specimens showing poor tissue preservation or extensive processing artifacts
- Sections with suboptimal or inadequate H & E staining that interfered with microscopic assessment
- Specimens containing insufficient tumor tissue for AI-based image evaluation
- Duplicate biopsy specimens from the same patient
- Cases with a histopathological diagnosis other than OSCC
- Histopathological images that were of insufficient quality for reliable digital or AI-assisted assessment

Histopathological Assessment

Biopsy specimens were processed using standard histopathological procedures and stained with H & E. Each specimen was examined microscopically by an experienced oral and maxillofacial pathologist. The histopathological diagnosis was considered the reference or gold-standard diagnosis for comparison with the AI-assisted classification. Based on conventional histopathological criteria, OSCC cases were categorized as well-differentiated, moderately differentiated, or poorly differentiated.

AI-Assisted Image Evaluation

Digitized histopathological images were evaluated using the AI-assisted diagnostic system. The system was assessed for its ability to classify cases according to the reference diagnosis and to recognize selected morphological characteristics associated with OSCC. The evaluated histopathological features included keratinization, nuclear pleomorphism, increased nuclear-to-cytoplasmic ratio, abnormal mitotic activity, and tumor invasion. The diagnostic output generated by the AI system was subsequently compared with the corresponding histopathological findings.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Appropriate descriptive and inferential statistical methods were applied according to the type and distribution of the data. Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as

frequency and percentage. The diagnostic performance of the AI system was assessed using accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F1 score, and receiver operating characteristic–area under the curve (ROC-AUC). Agreement between AI-based diagnosis and the gold-standard histopathological diagnosis was evaluated using Cohen’s kappa (κ) statistic. Differences in diagnostic performance across histopathological grades were assessed using appropriate comparative tests. A p-value <0.05 was considered statistically significant, with 95% confidence intervals (CI) reported wherever applicable.

III. Results

Table 1 & Figure 1 summarize the demographic characteristics and anatomical distribution of lesions among the 100 patients included in the study. The participants had a mean age of 56.8 ± 10.7 years, with a clear male predominance: 72 (72.0%) were males and 28 (28.0%) were females. The buccal mucosa was the most commonly affected anatomical site, accounting for 38 (38.0%) cases, followed by the tongue, which was involved in 27 (27.0%) cases. Lesions were identified in the lower alveolus in 15 (15.0%) patients and in the gingivobuccal sulcus in 10 (10.0%) patients. The remaining 10 (10.0%) cases involved other anatomical sites. Overall, males constituted the majority of the study population, while the buccal mucosa represented the most frequent site of lesion involvement, followed by the tongue.

Table 1: Study population and demographic characteristics

	Parameter	n (%) / Mean $\pm$ SD
	Age (years)	56.8 $\pm$ 10.7
Gender	Male	72 (72.0%)
	Female	28 (28.0%)
Site	Buccal mucosa	38 (38.0%)
	Tongue	27 (27.0%)
	Lower alveolus	15 (15.0%)
	Gingivobuccal sulcus	10 (10.0%)
	Other sites	10 (10.0%)

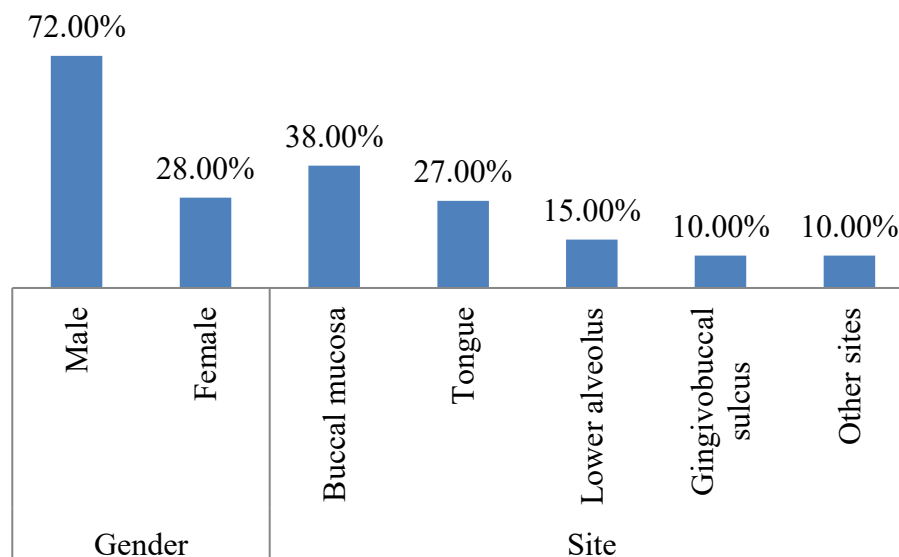


Figure 1: Demographic characteristics and anatomical distribution of lesions among the study participants

Table 2 & Figure 2 illustrate the histopathological grading of the OSCC cases. All incisional biopsy specimens were examined using H&E staining by an experienced oral and maxillofacial pathologist, with the histopathological diagnosis considered the reference standard. Among the 100 cases evaluated, 54 (54.0%) were diagnosed as well-differentiated OSCC, making it the predominant histological category. Moderately differentiated OSCC was observed in 34 (34.0%) cases, whereas poorly differentiated OSCC accounted for 12 (12.0%) cases. Overall, well-differentiated OSCC was the most frequently observed histopathological grade, followed by moderately and poorly differentiated tumors.

Table 2: Gold-standard histopathological diagnosis

Histopathological grade	n (%)
Well-differentiated OSCC	54 (54.0%)
Moderately differentiated OSCC	34 (34.0%)
Poorly differentiated OSCC	12 (12.0%)

■ Well-differentiated OSCC ■ Moderately differentiated OSCC
 ■ Poorly differentiated OSCC

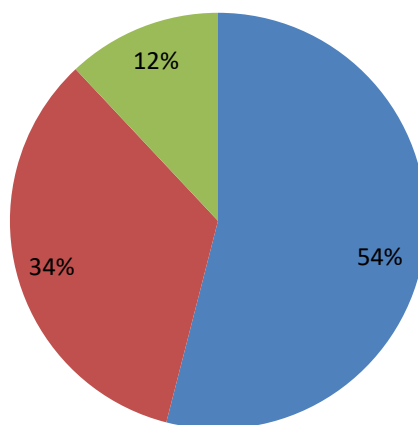


Figure 2: Distribution of study cases according to the histopathological grade of OSCC

Table 3 & Figure 3 summarize the diagnostic performance of the AI-assisted system in comparison with the reference standard based on histopathological examination. The system achieved an overall accuracy of 92.0%, indicating a high proportion of correctly classified cases. The sensitivity was 93.1%, demonstrating a strong ability to detect cases of OSCC, while the specificity of 90.4% indicated good performance in correctly identifying cases without OSCC.

The PPV was 91.8%, indicating that most cases predicted as OSCC by the AI system were confirmed by histopathological assessment. The NPV was 92.1%, suggesting a high likelihood that cases classified as negative were truly negative. The system also achieved an F1 score of 92.4%, reflecting a favorable balance between sensitivity and precision. Furthermore, the ROC-AUC was 0.94, demonstrating excellent discriminatory capability. Overall, the AI-assisted diagnostic system exhibited strong diagnostic accuracy and reliable discrimination when compared with expert histopathological evaluation.

Table 3: AI-assisted diagnostic performance

Diagnostic parameter	AI performance
Accuracy	92.0%
Sensitivity	93.1%
Specificity	90.4%
PPV	91.8%
NPV	92.1%
F1 score	92.4%
ROC-AUC	0.94

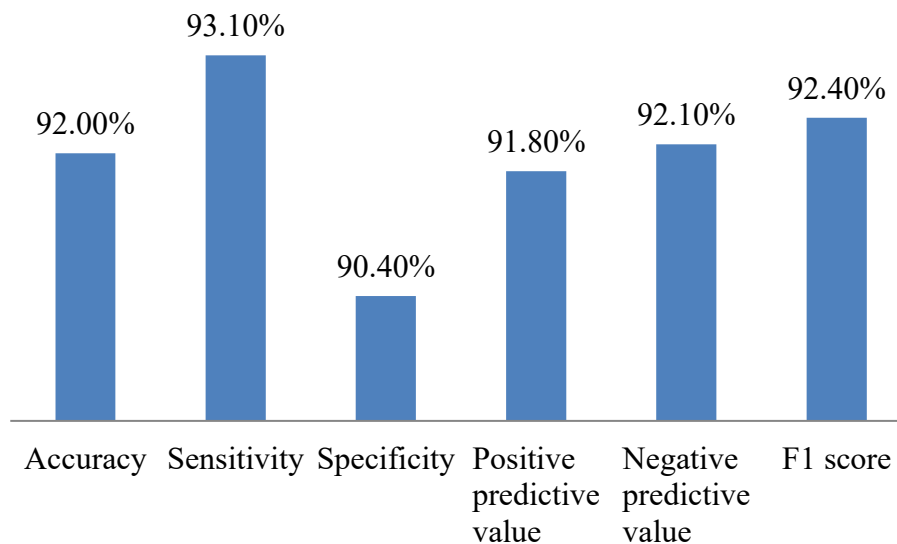


Figure 3: Diagnostic performance of the AI-assisted system compared with the histopathological reference standard

Table 4 presents the agreement between the AI-assisted diagnostic system and the histopathological reference diagnosis, assessed using Cohen's kappa (κ) statistic. The AI system demonstrated a κ value of 0.84 (95% CI: 0.75–0.93), reflecting a very good level of agreement with the diagnosis established by an experienced oral and maxillofacial pathologist. The observed agreement was statistically significant ($p < 0.001$), indicating that the concordance between the two diagnostic approaches was unlikely to be due to chance. These findings demonstrate a high degree of consistency between AI-based assessment and expert histopathological evaluation and suggest that the AI system may serve as a useful adjunctive tool for the detection of OSCC.

Table 4: Agreement between AI diagnosis and gold-standard histopathology

Measure	Value
Cohen's kappa (κ)	0.84
95% CI	0.75–0.93
P value	<0.001

Table 5 & Figure 4 summarize the diagnostic performance of the AI-assisted system across the three histopathological grades of OSCC. For well-differentiated OSCC, the system demonstrated a sensitivity of 94.4%, specificity of 91.3%, PPV of 92.7%, and NPV of 93.3%, indicating strong diagnostic performance in identifying this grade. For moderately differentiated OSCC, the sensitivity, specificity, PPV, and NPV were 91.2%, 92.7%, 88.6%, and 94.0%, respectively. These findings demonstrate that the AI-assisted system showed good discrimination for moderately differentiated OSCC, with a high NPV indicating reliable exclusion of cases not belonging to this category. For poorly differentiated OSCC, the system achieved a sensitivity of 91.7%, specificity of 96.6%, PPV of 78.6%, and NPV of 98.4%. This category showed the highest specificity and NPV among the three grades, reflecting a strong ability to correctly identify negative cases. Overall, the AI-assisted system exhibited consistently high sensitivity and specificity across all histopathological grades of OSCC. The highest sensitivity was observed for well-differentiated OSCC, whereas poorly differentiated OSCC showed the highest specificity and NPV.

Table 5: AI Performance According to Histopathological Grade

Histopathological grade	Sensitivity	Specificity	PPV	NPV
Well differentiated	94.4%	91.3%	92.7%	93.3%
Moderately differentiated	91.2%	92.7%	88.6%	94.0%
Poorly differentiated	91.7%	96.6%	78.6%	98.4%

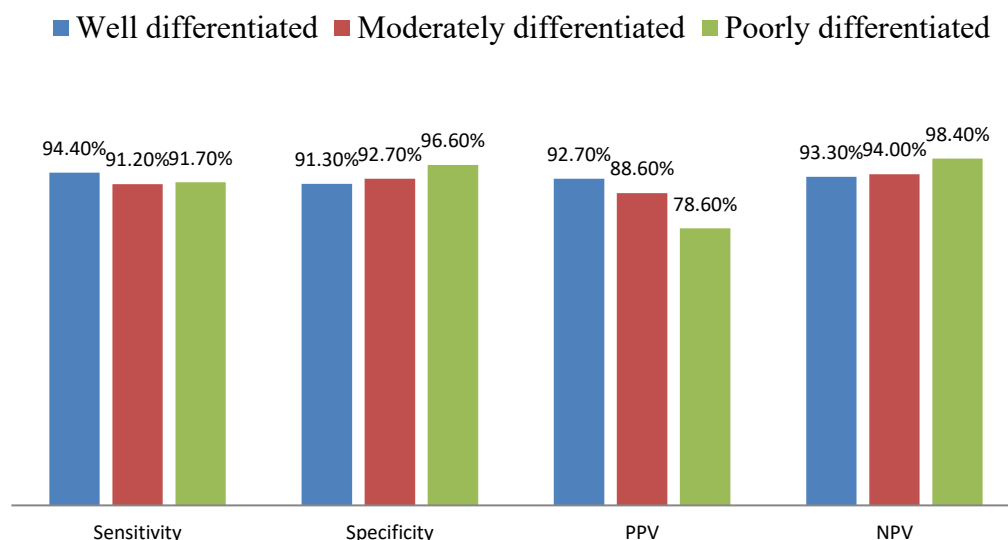


Figure 4: Diagnostic performance of the AI-assisted system across different histopathological grades of OSCC

Table 6 & Figure 5 present the performance of the AI-assisted system in recognizing key histopathological features associated with OSCC. The highest accuracy was recorded for increased nuclear-to-cytoplasmic ratio (94.0%), followed by keratinization (93.0%) and tumor invasion (92.0%). The system identified nuclear pleomorphism with an accuracy of 91.0%, whereas abnormal mitotic activity showed the lowest accuracy at 89.0%.

Overall, the AI-assisted system demonstrated good recognition of major histopathological features of OSCC, with accuracy values ranging from 89.0% to 94.0%. Its strongest performance was observed in detecting increased nuclear-to-cytoplasmic ratio and keratinization, which are important morphological characteristics considered during the histopathological evaluation of OSCC.

Table 6: Identification of Key Histopathological Features Based on AI

Histopathological feature	AI accuracy (%)
Keratinization	93.0
Nuclear pleomorphism	91.0
Increased nuclear-to-cytoplasmic ratio	94.0
Abnormal mitotic activity	89.0
Tumor invasion	92.0

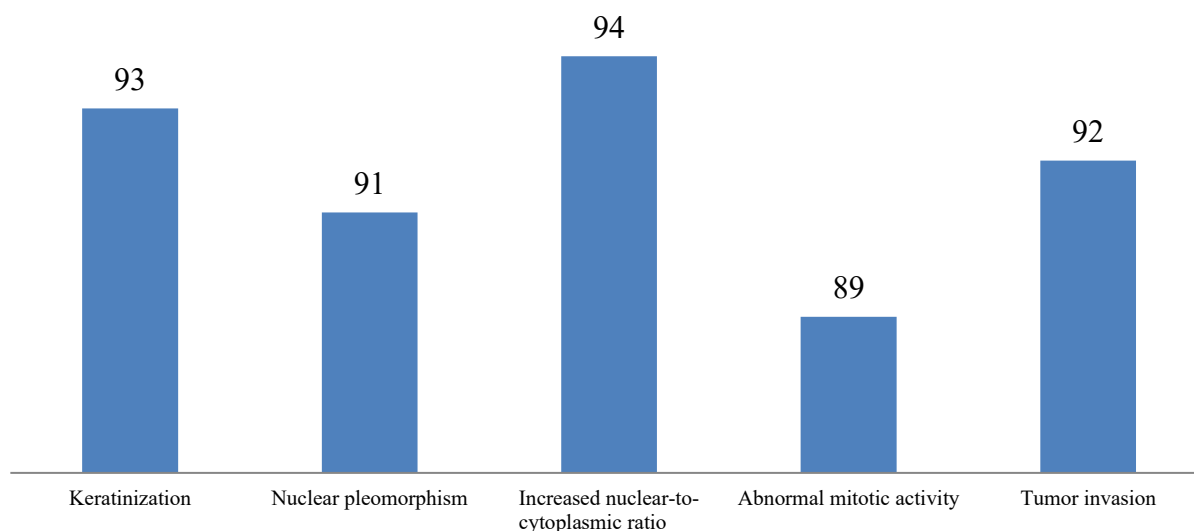


Figure 5: Accuracy of the AI-Assisted system in identifying key histopathological features of OSCC

Table 7 present the comparison of the AI-assisted diagnostic classification with the gold-standard histopathological diagnosis showed that 92 (92.0%) of the 100 cases were correctly classified by the AI system. A total of 8 (8.0%) cases showed discordance with the reference diagnosis. Among these discordant cases, 4 (4.0%) were false-negative classifications, in which the AI system failed to identify cases that were positive according to the gold-standard histopathological examination. The remaining 4 (4.0%) cases were false-positive classifications, in which the AI system classified the cases as positive despite the absence of the target diagnosis according to the reference standard. Overall, the findings demonstrate a high concordance of 92.0% between AI-based classification and expert histopathological diagnosis, with relatively low rates of both false-negative and false-positive classifications.

Table 7: Diagnostic classification of AI against the gold standard

AI classification outcome	n (%)
Correctly classified	92 (92.0%)
Discordant	8 (8.0%)
False negative	4 (4.0%)
False positive	4 (4.0%)

IV. Discussion

The present study highlights the potential role of AI-assisted histopathological image analysis in the diagnosis of OSCC. Conventional histopathological examination remains the established diagnostic approach for OSCC; however, interpretation may be influenced by tumor heterogeneity, differences in tissue morphology, staining characteristics, and observer experience. The incorporation of machine learning and deep learning into digital pathology provides an opportunity to support pathologists through automated recognition and classification of complex microscopic patterns.

Dixit et al. (2023) [10] reviewed the application of machine learning and deep learning techniques in oral cancer diagnosis and emphasized the increasing contribution of computational methods to oral cancer detection. Their review demonstrated that a variety of AI architectures have been investigated for image-based diagnosis, with deep learning approaches showing particular promise because of their ability to automatically identify diagnostically relevant features from complex image datasets. The authors also highlighted important challenges, including limited datasets, differences in image quality, lack of standardized protocols, and the need for external validation. These observations support the importance of developing AI systems using adequately representative histopathological datasets before their implementation in routine diagnostic practice.

The findings of the present study are also consistent with the work of Oya et al. (2023) [11], who evaluated CNN-based analysis of digitized histological images for OSCC diagnosis. Their study demonstrated that CNN technology could identify characteristic histopathological patterns associated with OSCC and distinguish malignant tissue within digitized pathological material. This finding is particularly relevant because conventional microscopic diagnosis depends on visual recognition of multiple architectural and cytological abnormalities simultaneously. AI-based image analysis may provide an additional computational layer that can assist in recognizing subtle or complex morphological patterns that may otherwise be difficult to evaluate consistently.

Fati et al. (2022) [12] investigated deep and hybrid learning approaches for the early diagnosis of OSCC using histopathological images. Their findings demonstrated the feasibility of combining different computational learning strategies to improve the automated recognition of malignant changes. The relevance of this approach lies in the possibility of detecting pathological abnormalities at an earlier stage, when morphological alterations may be relatively subtle. In the context of the present study, the use of AI-assisted analysis may therefore have clinical value not only for confirming established OSCC but also for supporting the recognition of suspicious histopathological patterns requiring further expert evaluation.

More recently, Panigrahi S et al. (2023) [13] compared five CNN architectures for automated detection of OSCC in histopathological images. Their comparative approach is important because AI performance is not determined solely by the availability of digital images but also by the selection and architecture of the computational model. Different CNN structures may vary in their ability to extract and classify morphological features. The findings of this study emphasize the importance of comparative model evaluation rather than assuming that a single deep learning architecture will provide optimal performance across all histopathological datasets. This is particularly relevant for future studies seeking to identify the most suitable AI architecture for OSCC diagnosis.

Another important development in AI-assisted pathology is the emphasis on interpretability. Parola M et al. (2024) [14] investigated an explainable deep learning approach for oral cancer recognition. The incorporation of multi-scale information is particularly valuable in histopathology because malignant transformation can be recognized through changes occurring at different levels, ranging from individual cellular abnormalities to alterations in tissue architecture. An interpretable AI framework may further improve clinical acceptance because pathologists can potentially understand which regions or morphological characteristics contributed to the algorithm's prediction. Thus, future OSCC diagnostic systems should ideally combine high classification performance with clinically meaningful explanations of their decisions.

The broader clinical implications of AI in OSCC were discussed by Alabi et al. (2021) [15], who reviewed the current status, clinical concerns, and future prospects of machine learning in OSCC. They emphasized that although machine learning has considerable potential in oral cancer diagnosis and prognostic assessment, several barriers must be addressed before widespread clinical application. These include dataset bias, variability in imaging and histopathological protocols, limited external validation, model interpretability, reproducibility, and the requirement for clinically relevant validation. The present findings should therefore be interpreted within the broader concept of AI as an adjunct to, rather than a replacement for, professional pathological expertise.

An important strength of AI-assisted histopathological analysis is its potential to provide standardized and reproducible assessment of digital images. Human observers may differ in their interpretation of borderline or morphologically heterogeneous lesions, whereas a trained computational model applies the same learned criteria consistently to each image. AI may also assist in reducing the workload associated with examination of large numbers of digital slides by directing attention toward regions with a higher probability of malignancy. Such capabilities could be particularly valuable in high-volume pathology services and in settings where access to experienced oral pathologists is limited.

Nevertheless, AI-based diagnosis should not be considered independent of conventional histopathological assessment. The quality of the algorithm is strongly dependent on the quality and representativeness of the training data. Differences in tissue preparation, fixation, staining, scanner characteristics, image resolution, and patient demographics can affect model performance. Furthermore, OSCC exhibits considerable biological and morphological heterogeneity, meaning that an algorithm trained predominantly on one tumor subtype or anatomical site may not perform equally well when applied to specimens from different populations or clinical settings. Therefore, multicenter datasets and external validation are essential for establishing the generalizability of AI-based diagnostic systems.

Another consideration is the distinction between high computational accuracy and actual clinical usefulness. An AI model may demonstrate excellent performance under controlled experimental conditions but still encounter difficulties when confronted with poor-quality biopsy material, limited tissue, inflammation, necrosis, or unusual histological variants. Consequently, future research should include prospective validation using consecutive clinical specimens and should assess not only sensitivity and specificity but also diagnostic agreement with expert pathologists, false-positive and false-negative patterns, processing time, and the practical effect of AI assistance on clinical decision-making.

Overall, the studies collectively demonstrate the rapidly developing role of AI in oral cancer histopathology. The progression from conventional machine learning toward deep learning, CNN-based classification, comparative architectural evaluation, multi-scale analysis, and interpretable models indicates that AI-assisted pathology is moving toward increasingly sophisticated diagnostic frameworks. However, successful translation into routine practice will require standardized datasets, transparent reporting, external validation, and continued collaboration between oral pathologists, clinicians, computer scientists, and AI researchers.

In conclusion, AI-assisted histopathological analysis represents a promising adjunctive approach for OSCC diagnosis. Its ability to analyze large digital datasets, identify complex morphological patterns, and potentially provide consistent quantitative assessment may complement conventional pathological examination. Rather than replacing the pathologist, AI is likely to be most valuable as a decision-support technology that enhances diagnostic efficiency and consistency while retaining expert clinical and histopathological judgment at the center of patient care.

V. Limitations

The present study has certain limitations that should be considered when interpreting the findings. The relatively small sample size of 100 cases may have limited the precision of the diagnostic estimates, particularly for individual histopathological grades, and the single-center design may restrict the generalizability of the

results to other populations and clinical settings. The unequal representation of histopathological grades, especially the smaller number of poorly differentiated OSCC cases, may also affect the reliability of grade-specific performance estimates. Selection of biopsy-confirmed cases could introduce selection bias and may not reflect the complete range of lesions encountered in routine practice. Although expert histopathological assessment was used as the reference standard, some degree of interobserver variability may occur in microscopic interpretation. The AI system was also evaluated using a limited set of histopathological features and did not encompass all morphological or prognostic characteristics of OSCC. Variations in tissue processing, staining quality, image resolution, and scanning procedures may influence AI performance. Furthermore, the absence of independent external validation limits assessment of the system's reproducibility across different institutions and laboratory conditions. The occurrence of both false-positive and false-negative classifications also highlights the need for cautious interpretation of AI-generated results, particularly when malignancy may be missed. In addition, the study focused primarily on diagnostic performance and did not assess the impact of AI assistance on reporting time, pathologist decision-making, clinical workflow, or patient outcomes. Therefore, larger prospective multicenter studies using diverse and independently collected datasets are required to validate these findings and establish the reliability, clinical utility, and applicability of the AI-assisted system in routine OSCC diagnosis.

VI. Conclusion

The present study demonstrated that the AI-assisted system provides effective and consistent performance in the detection and histopathological assessment of OSCC. The system showed strong diagnostic discrimination and good agreement with expert histopathological evaluation across different tumor grades. It also reliably recognized key morphological features of OSCC, including increased nuclear-to-cytoplasmic ratio, keratinization, nuclear pleomorphism, abnormal mitotic activity, and tumor invasion. These findings support the potential role of AI as a valuable adjunct to conventional histopathological assessment, helping to improve diagnostic consistency and efficiency. However, AI should complement rather than replace expert pathological judgment. Further multicenter studies with larger and independent datasets are required to confirm its reliability and clinical applicability in routine OSCC diagnosis.

Conflicts of Interest: Nil

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References

- [1]. Rich BJ, Samuels SE, Azzam GA, Kubicek G, Freedman L. Oral Cavity Squamous Cell Carcinoma: Review of Pathology, Diagnosis, and Management. *Crit Rev Oncog*. 2024;29(3):5-24. doi: 10.1615/CritRevOncog.2023050055. PMID: 38683151.
- [2]. Woolgar JA, Triantafyllou A. Pitfalls and procedures in the histopathological diagnosis of oral and oropharyngeal squamous cell carcinoma and a review of the role of pathology in prognosis. *Oral Oncol*. 2009 Apr-May;45(4-5):361-85. doi: 10.1016/j.oraloncology.2008.07.016. Epub 2008 Oct 11. PMID: 18849188.
- [3]. Khanagar SB, Alkadi L, Alghilan MA, Kalagi S, Awawdeh M, Bijai LK, Vishwanathaiah S, Aldhebaib A, Singh OG. Application and Performance of Artificial Intelligence (AI) in Oral Cancer Diagnosis and Prediction Using Histopathological Images: A Systematic Review. *Biomedicines*. 2023 Jun 1;11(6):1612. doi: 10.3390/biomedicines11061612. PMID: 37371706; PMCID: PMC10295336.
- [4]. Yang SY, Li SH, Liu JL, Sun XQ, Cen YY, Ren RY, Ying SC, Chen Y, Zhao ZH, Liao W. Histopathology-Based Diagnosis of Oral Squamous Cell Carcinoma Using Deep Learning. *J Dent Res*. 2022 Oct;101(11):1321-1327. doi: 10.1177/00220345221089858. Epub 2022 Apr 21. PMID: 35446176.
- [5]. Khanagar SB, Naik S, Al Kheraif AA, Vishwanathaiah S, Maganur PC, Alhazmi Y, Mushtaq S, Sarode SC, Sarode GS, Zanza A, Testarelli L, Patil S. Application and Performance of Artificial Intelligence Technology in Oral Cancer Diagnosis and Prediction of Prognosis: A Systematic Review. *Diagnostics (Basel)*. 2021 May 31;11(6):1004. doi: 10.3390/diagnostics11061004. PMID: 34072804; PMCID: PMC8227647.
- [6]. Elmakaty I, Elmarasi M, Amarah A, Abdo R, Malki MI. Accuracy of artificial intelligence-assisted detection of Oral Squamous Cell Carcinoma: A systematic review and meta-analysis. *Crit Rev Oncol Hematol*. 2022 Oct;178:103777. doi: 10.1016/j.critrevonc.2022.103777. Epub 2022 Aug 2. PMID: 35931404.
- [7]. Pirayesh Z, Mohammad-Rahimi H, Ghasemi N, Motamedian SR, Sadeghi TS, Koohi H, Rokhshad R, Lotfi SM, Najafi A, Alajaji SA, Khoury ZH, Jessri M, Sultan AS. Deep Learning-Based Image Classification and Segmentation on Digital Histopathology for Oral Squamous Cell Carcinoma: A Systematic Review and Meta-Analysis. *J Oral Pathol Med*. 2024 Oct;53(9):551-566. doi: 10.1111/jop.13578. Epub 2024 Sep 10. PMID: 39256895.
- [8]. Sahoo RK, Sahoo KC, Dash GC, Kumar G, Baliarsingh SK, Panda B, Pati S. Diagnostic performance of artificial intelligence in detecting oral potentially malignant disorders and oral cancer using medical diagnostic imaging: a systematic review and meta-analysis. *Front Oral Health*. 2024 Nov 6;5:1494867. doi: 10.3389/froh.2024.1494867. PMID: 39568787; PMCID: PMC11576460.
- [9]. Alabi RO, Youssef O, Pirinen M, Elmusrati M, Mäkitie AA, Leivo I, Almangush A. Machine learning in oral squamous cell carcinoma: Current status, clinical concerns and prospects for future-A systematic review. *Artif Intell Med*. 2021 May;115:102060. doi: 10.1016/j.artmed.2021.102060. Epub 2021 Mar 26. PMID: 34001326.
- [10]. Dixit, S.; Kumar, A.; Srinivasan, K. A Current Review of Machine Learning and Deep Learning Models in Oral Cancer Diagnosis: Recent Technologies, Open Challenges, and Future Research Directions. *Diagnostics* **2023**, *13*, 1353. <https://doi.org/10.3390/diagnostics13071353>

- [11]. Oya K, Kokomoto K, Nozaki K, Toyosawa S. Oral squamous cell carcinoma diagnosis in digitized histological images using convolutional neural network. *J Dent Sci.* 2023 Jan;18(1):322-329. doi: 10.1016/j.jds.2022.08.017. Epub 2022 Sep 8. PMID: 36643248; PMCID: PMC9831840.
- [12]. Fati SM, Senan EM, Javed Y. Early Diagnosis of Oral Squamous Cell Carcinoma Based on Histopathological Images Using Deep and Hybrid Learning Approaches. *Diagnostics (Basel).* 2022 Aug 5;12(8):1899. doi: 10.3390/diagnostics12081899. PMID: 36010249; PMCID: PMC9406837.
- [13]. Panigrahi S, Nanda BS, Bhuyan R, Kumar K, Ghosh S, Swarnkar T. Classifying histopathological images of oral squamous cell carcinoma using deep transfer learning. *Heliyon.* 2023 Feb 6;9(3):e13444. doi: 10.1016/j.heliyon.2023.e13444. PMID: 37101475; PMCID: PMC10123069.
- [14]. Parola M, Galatolo FA, La Mantia G, Cimino MGCA, Campisi G, Di Fede O. Towards explainable oral cancer recognition: Screening on imperfect images via Informed Deep Learning and Case-Based Reasoning. *Comput Med Imaging Graph.* 2024 Oct;117:102433. doi: 10.1016/j.compmedimag.2024.102433. Epub 2024 Sep 11. PMID: 39276433.
- [15]. Alabi RO, Youssef O, Pirinen M, Elmusrati M, Mäkitie AA, Leivo I, Almangush A. Machine learning in oral squamous cell carcinoma: Current status, clinical concerns and prospects for future-A systematic review. *Artif Intell Med.* 2021 May;115:102060. doi: 10.1016/j.artmed.2021.102060. Epub 2021 Mar 26. PMID: 34001326.