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Original Article

Artificial intelligence-assisted enhancement of diagnostic accuracy and efficiency in detecting cervical lymph node metastases in oral squamous cell carcinoma

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Abstract *Background/purpose:* Cervical lymph node metastasis represents a critical prognostic factor in oral squamous cell carcinoma (SCC); however, early-stage or subtle metastases often pose diagnostic challenges under conventional microscopy. Recent advancements in artificial intelligence (AI) offer promising solutions to enhance diagnostic accuracy and efficiency. This study aimed to evaluate the extent to which AI-assisted tools can improve diagnostic performance and efficiency in the detection of cervical lymph node metastases.
Materials and methods: Sixty-six hematoxylin-eosin-stained slides containing 621 lymph nodes from oral SCC cases were digitized. Four participants (two oral pathologists, one postgraduate year (PGY) resident, one fourth-year dental student) reviewed slides with and without the AI-assistant tool. Diagnostic accuracy and interpretation time were compared.
Results: AI assistance significantly improved diagnostic accuracy and efficiency across different participants. False positives and false negatives decreased notably, especially for junior participants. Review time was also significantly shortened for negative and

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macrometastatic slides ($P < 0.0001$ and $P < 0.05$, respectively), with the greatest benefit seen among less-experienced participants.
Conclusion: The AI-assisted tool improved diagnostic accuracy and efficiency in detecting cervical lymph node metastases in oral SCC. It may serve as a preliminary screening tool and a valuable educational aid for training junior pathologists, underscoring its potential for broader application in digital pathology.

Introduction

Oral cancer is prevalent in Taiwan, particularly among males.[1] In 2021, the combined incidence of oral cavity and oropharyngeal cancers ranked sixth among all cancers (fifth among males), while their combined mortality ranked fifth overall (fourth among males).[2] This is largely attributed prevalent cultural habits, including betel nut chewing, tobacco use, and alcohol consumption, which contribute to a higher incidence of oral cancer compared to other countries.[3] Over 90 % of oral cancers are histologically classified as squamous cell carcinoma (SCC).[4] Previous data indicate that nearly 32 % of patients with oral SCC present with cervical lymph node metastases at the time of pathological examination of surgical specimens.[5,6] Furthermore, cervical lymph node metastasis is a well-established adverse prognostic factor, with affected patients demonstrating a significantly poorer prognosis.[7] Consequently, these patients often require adjuvant radiotherapy or systemic chemotherapy postoperatively to improve treatment outcomes and overall prognosis.[8]

Currently, the detection of cervical lymph node metastasis depends on pathologists' interpretation of tissue sections. However, early-stage or subtle metastasis can be challenging to detect due to the small number of tumor cells and their frequent obscuration by surrounding lymphoid tissue. This may lead to diagnostic errors, even among experienced pathologists. Recent advances in AI have led to the development of AI-assisted tools that help detect micrometastases (<2 mm, ≥0.2 mm) hidden within lymph nodes. For example, the Taiwan-based company aetherAI has developed a platform known as "aetherAI-LNMD-GA," which is specifically designed to support pathologists in identifying subtle metastatic foci of gastric cancer in lymph nodes.[9] These tools have the potential to enhance diagnostic accuracy, reduce the risk of misdiagnosis, and facilitate optimal patient management, thereby improving clinical outcomes.

In this study, we utilized the aetherAI-LNMD-GA (aetherAI, Taipei City, Taiwan) tool for evaluation. Our study aimed to address two primary objectives: first, to assess whether this AI tool could help oral pathologists and trainees to identify SCC cells within cervical lymph nodes more easily and improve their diagnostic accuracy; and second, to evaluate whether its use could reduce the time required by oral pathologists and trainees for interpretation of slides.

Materials and methods

The histological dataset in this study comprised 66 hematoxylin-eosin-stained histopathological slides, encompassing a total of 621 lymph nodes. These slides were retrospectively retrieved from the archives of the Division of Oral Pathology, Kaohsiung Medical University Hospital approved with Institutional Review Board of our Institution (KMUHIRB-E(I)-20250078). All specimens originated from

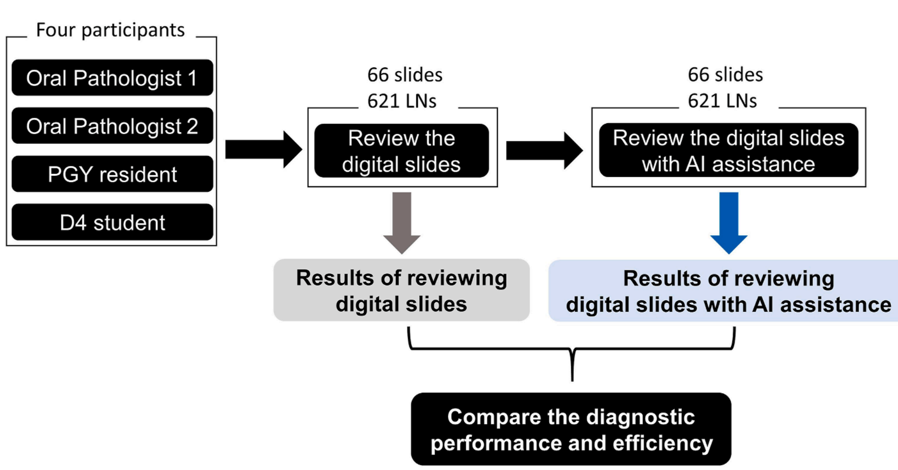

Figure 1 Workflow of this study. PGY, postgraduate year. D4, fourth-year dental. LN, lymph node. AI, artificial intelligence.

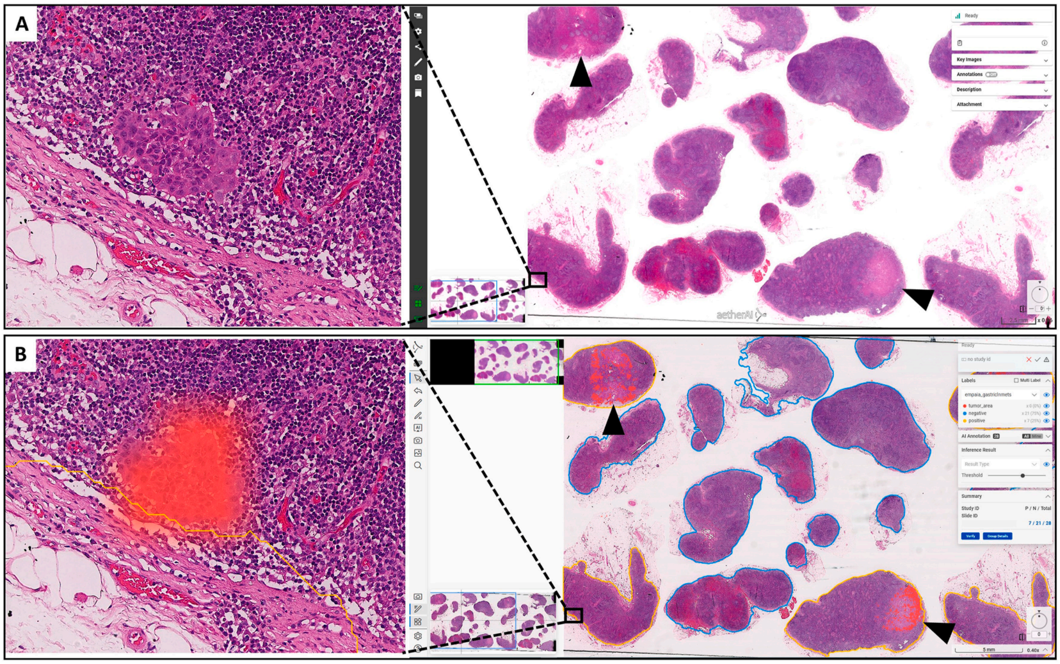

Figure 2 Representative images of digitized lymph node (LN) slides without and with artificial intelligence (AI) annotation. (A) Original digital slide without AI assistance. (B) Corresponding slide with AI annotation, where metastatic regions are highlighted in red (arrowheads indicate macrometastatic foci). A micrometastatic focus within a LN is indicated by a rectangular box.

cervical lymph node dissections conducted during surgical resections of oral SCC in adult patients between 2021 and 2023. Whole-slide images were acquired and digitized at 40× magnification (0.23 μm/pixel) using a NanoZoomer S360 digital slide scanner (Hamamatsu Photonics, Hamamatsu, Japan).

The methodological framework for evaluating the diagnostic utility of the AI-assisted tool in detecting metastatic SCC in cervical lymph nodes is illustrated in Fig. 1. Participants included two board-certified oral pathologists, one postgraduate year (PGY) resident, and one fourth-year dental student. In the first phase, all participants independently reviewed the digitized slides without AI assistance (Fig. 2A). This phase was designed to establish baseline diagnostic accuracy and efficiency, reflecting each participant's ability to identify pathological features unaided. The results from this phase served as the control dataset.

Following a two-week washout period, the same participants re-examined the same set of digital slides with the assistance of aetherAI-LNMD-GA. In this second phase, areas suspected to contain metastatic carcinoma were highlighted in red by the AI tool (Fig. 2B). This AI-assisted review aimed to assess the impact of the tool on diagnostic accuracy and efficiency, allowing for direct comparison with the baseline performance. Final diagnoses for all slides were determined by consensus among three board-certified oral pathologists.

Results

The study set comprised 66 slides in total, including 53 negative slides, eight slides with macrometastases (≥2 mm), three slides with micrometastases, and two slides containing both macrometastases and micrometastases (Fig. 2). The diagnostic outcomes with and without AI assistance are summarized in Table 1. Overall, AI assistance enhanced diagnostic accuracy across all participants. Reductions in false positives (FP) and false negatives (FN) served as key metrics reflecting improved diagnostic performance. For example, the fourth-year dental student showed a reduction in false negatives from four to zero and false positives from four to one, demonstrating a marked improvement in diagnostic precision with AI support.

Table 1 Summary of diagnostic performance of participants.

Model/participants	TP	FP	TN	FN	Sensitivity	Specificity
Pathologist 1	18	0	600	3	0.8571	1.0000
Pathologist 2	20	0	600	1	0.9523	1.0000
PGY resident	19	78	522	2	0.9047	0.8700
D4 student	17	4	596	4	0.8095	0.9933
Pathologist 1 with AI assistance	20	0	600	1	0.9523	1.0000
Pathologist 2 with AI assistance	21	0	600	0	1.0000	1.0000
PGY resident with AI assistance	19	3	597	2	0.9047	0.9950
D4 student with AI assistance	21	1	599	0	1.0000	0.9983

Abbreviations: PGY, postgraduate year; D4, fourth-year dental; TP, true positive; FP, false positive; TN, true negative; FN, false negative.

Similarly, the PGY resident experienced a substantial decrease in false positives, from 78 to three, underscoring the pronounced benefit of AI assistance for less experienced readers. Even among experienced oral pathologists, subtle micrometastases were occasionally missed without AI support. However, with the integration of AI, both oral pathologists exhibited notable improvements in diagnostic performance. A comparative analysis of diagnostic efficiency under normal (gray box plots) and AI-assisted (light blue box plots) conditions for all four participants is shown in Fig. 4. Each panel is subdivided into four categories: Macro (slides with macrometastases), Micro (slides with

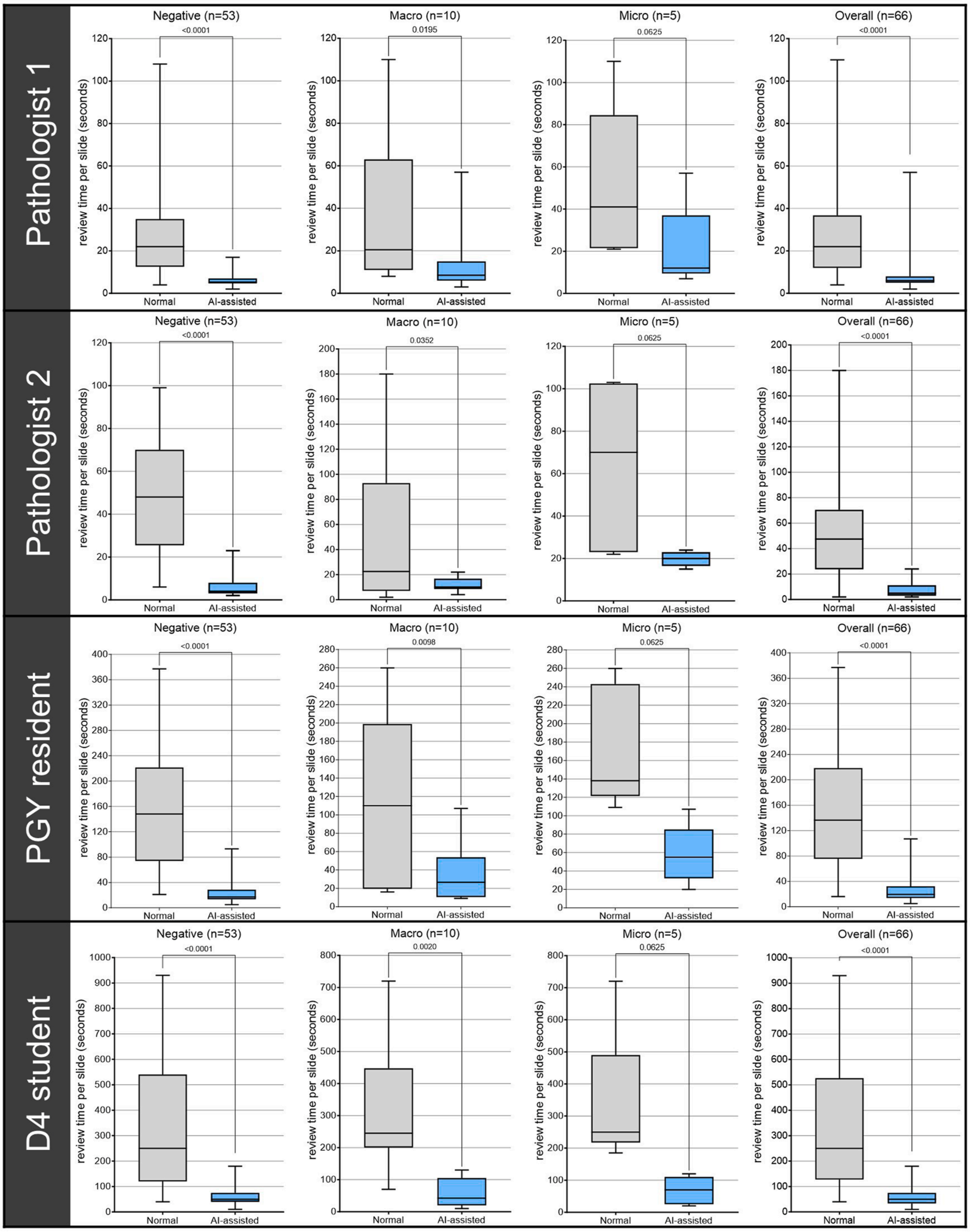

Figure 3 Plots of reviewing time of four participants with/without AI-assistance. AI, artificial intelligence. PGY, postgraduate year. D4, fourth-year dental. Macro, slides with macrometastatic foci. Micro, slides with micrometastatic foci. The box-and-whisker plots illustrate the distribution of data using several key components: the horizontal line inside each box represents the median, while the top and bottom edges of the box correspond to the first and third quartiles, respectively. The whiskers extend to the smallest and largest values. Statistical comparisons were performed using paired *t*-test.

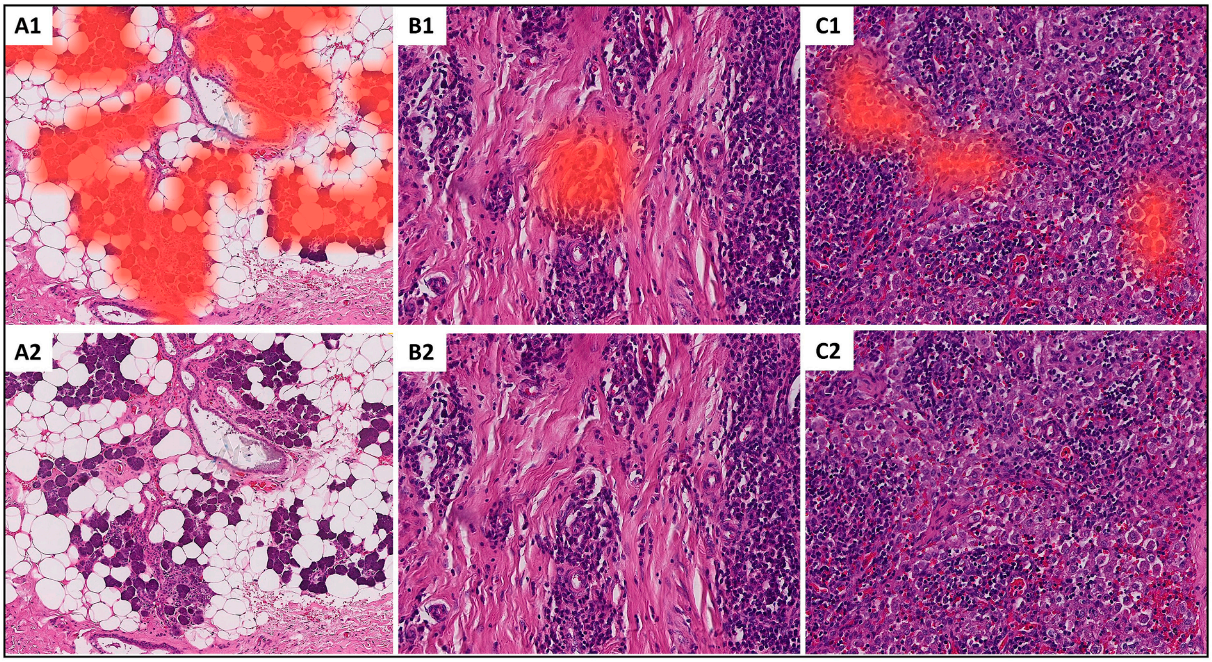

Figure 4 Examples of false-positive results by artificial intelligence (AI) model. (A1-2) Parotid gland tissue included in the specimen. (B1-2) Plump endothelial cells of blood vessels with adjacent aggregate of lymphoid cells. (C1-2) Aggregates of histiocytes.

micrometastases), Negative (non-metastatic slides), and Overall (all slides combined). A statistically significant reduction in review time was observed across participants for negative slides ($P < 0.0001$), slides with macrometastases ($P < 0.05$), and overall slides ($P < 0.0001$). These findings indicate that AI assistance markedly improves efficiency in slide interpretation, irrespective of the participant's level of expertise. The most substantial time savings were seen among less experienced participants, particularly the PGY resident and the dental student.

Discussion

In the current era of AI, the integration of AI technologies into the medical field has been rapidly advancing, particularly in the domain of histopathological diagnostics. AI is expected to assist pathologists in identifying potential lesions with enhanced accuracy and efficiency. Among its various applications, the detection of lymph node metastasis from malignant tumors remains a critical area where AI support is especially valuable. To date, numerous AI-assisted approaches for detecting lymph node metastases have been reported across a variety of tumor types, including breast,[10,11] colorectal,[12,13] gastric,[9,14] lung,[15] prostate,[16] and bladder[17] cancers. Although these studies employed diverse methodologies and technical frameworks, a common finding across them is the improvement in diagnostic accuracy and pathologists' workflow efficiency with the aid of AI.

In the present study, we applied a previously developed AI-based tool, originally designed for detecting lymph node metastases of gastric cancer, to the identification of cervical lymph node metastases in oral SCC. Our findings demonstrate a significant improvement in both diagnostic accuracy and efficiency. Notably, even experienced pathologists are at risk of overlooking subtle micrometastases due to their small size and inconspicuous presentation. With AI assistance, the detection rate of such challenging cases markedly increased. Furthermore, for novice pathologists who are still gaining experience in diagnostic pathology, the unaided interpretation of slides often results in a high false-positive rate. However, the use of AI substantially mitigated this issue. Therefore, beyond its role in improving diagnostic precision, AI-based diagnostic tools also show great promise as educational aids for training junior pathologists. By leveraging AI guidance, trainees can gain critical diagnostic insights and pattern recognition skills that traditionally require many years of clinical experience to acquire. In this digital era, such tools offer the potential to accelerate the learning curve by providing structured exposure to curated histological slides supplemented by AI-driven feedback. Beyond accuracy, diagnostic efficiency is another key advantage of AI assistance. In our study, the time required for slide interpretation was markedly reduced across all conditions of cervical lymph node samples when AI assistance was used, especially among less-experienced trainees. Although the reduction in interpretation time for micrometastatic slides did not reach statistical significance, a decreasing trend was still observed. This lack of statistical significance may be attributed to the relatively small number of micrometastatic slides included in the current study.

In this study, the threshold for the AI-assisted tool was intentionally set to a relatively sensitive level. During the evaluation process, we observed that under this setting, the AI system occasionally produced false-positive results. Specifically, structures such as salivary gland tissue (Fig. 3A), proliferation of immature endothelial cells (Fig. 3B), and aggregates of histiocytes (Fig. 3C) were sometimes misinterpreted by the AI model as SCC. This heightened sensitivity setting, while beneficial in detecting subtle micrometastatic foci, led to an increase in regions flagged as suspicious, requiring pathologists to spend additional time verifying whether these areas truly contained malignant cells. As a result, diagnostic efficiency could be temporarily impacted due to the need for more detailed review of AI-highlighted regions. However, despite these challenges, our findings indicate that the overall diagnostic efficiency remained significantly improved with AI assistance compared to unaided diagnosis. More importantly, this sensitive threshold enabled the detection of minute metastatic tumor cells that might otherwise be missed, effectively serving as an alert system for pathologists. Based on these observations, we recommend that the sensitivity threshold of AI-assisted diagnostic tools be set to favor higher sensitivity, especially in clinical scenarios where the detection of micrometastases is critical. This approach minimizes the risk of missing clinically significant lesions and reinforces the tool's value as a safety net for diagnostic vigilance.

In summary, the integration of AI-assisted tools in the diagnosis of lymph node metastases from malignant tumors has demonstrated clear benefits in both diagnostic accuracy and efficiency. Furthermore, such tools significantly enhance the diagnostic capabilities of less-experienced pathologists, serving as valuable aids in training and clinical decision-making. We anticipate that with further development and broader implementation, AI-assisted diagnostic systems will contribute to more accurate pathological diagnoses and help alleviate the growing workload faced by pathologists in routine practice. These findings highlight the potential of AI to transform histopathological workflows and underscore the importance of continued innovation in digital pathology.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

Acknowledgments

None.

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