

APPLICATION OF ARTIFICIAL INTELLIGENCE IN DIAGNOSIS OF POTENTIALLY MALIGNANT LESIONS

Comment [Tsehay.A1]: The title is too broad all of the AI applications cannot be covered within a single paper? Focus on specific AI areas instead.

Abstract:

Artificial intelligence (AI) is a technological breakthrough that is rapidly progressing and has captivated the minds of researchers all over the world. AI can be used to make a diagnosis of oral cavity lesions, detect and identify suspicious changed oral mucosa undergoing premalignant and malignant transformations. The purpose of this review is to give a comprehensive summary of developing optical **imaging technologies**, innovative artificial intelligence-based techniques. The concepts of **image-based techniques** for identifying oral cancer are defined in terms of clinical requirements and features. Although artificial intelligence (AI) is beginning to have a significant impact on increasing diagnosis accuracy in a variety of fields of medicine, there has been **limited research on oral cancer to date**. These results suggest that combining artificial intelligence with imaging can improve oral cancer outcomes, applications ranging from very low-cost oral cancer screening with Smartphone-based probes to algorithm-guided identification premalignant lesion heterogeneity and margins using optical coherence tomography. Oral cancer outcomes can be improved by combining imaging and artificial intelligence technologies for better detection and **diagnosis**.

Keywords: Machine learning, identifying malignant lesion, diagnosis of oral cancer, optical coherence tomography, Smartphone-based probes to algorithm, and artificial neural networks.

Comment [Tsehay.A2]: 1. Please make it clear, which technologies? Which image based techniques?
2. Do not mention scarcity as research gap you have already said AI is breaking through and what does limited research referring?

Introduction:

Malignancies of the buccal mucosa, hard palate, the floor of the mouth, upper and lower gingiva, anterior two-thirds of the tongue and lips are term to as "oral cancer. " Whereas malignancies of the posterior third of the tongue, tonsils, and soft palate are referred to as "oropharyngeal cancer (OPC)." Squamous cell carcinomas (SCC) account for 95% of all oral and oropharyngeal malignancies [1]. Oral potentially malignant diseases (OPMD) are abnormal lesions on the oral mucosa that appear during malignant transformation [2]. These mucosal diseases are described as morphologically changed tissue with a higher risk of malignancy than normal tissue. Only some of this OPMDs progress towards oral cancer thus, commonly used other terms such as "oral premalignant disease," and "oral premalignant conditions" that indicate a more predetermined path of progression are no longer recommended [3]. **The according** to pathologies are considered OPMD, oral leukoplakia, proliferative verrucous leukoplakia, erythroplakia, oral submucous fibrosis, oral lichen planus, actinic keratosis, palatal lesions in reverse smokers, oral lupus erythematosus, dyskeratosis congenital, epidermolysis bullosa, oral lichenoid lesion, and oral chronic graft vs. host disease [1-3].

Comment [Tsehay.A3]: English error or correct the grammar

Early clinical evaluation is expected to important risk factors for malignant transformation such as alcohol and smoking, genetic factors, immunosuppression, and infections, by health care providers, particularly dentists and dental hygienists [4]. The changes in the oral mucosa, head and neck area, and cervical lymph nodes must be recorded after a thorough intraoral and extraoral examination, as well as a tactile examination under incandescent light [5]. Toluidine blue staining has been found to have different specificity and sensitivity depending on the staining procedure, the quality of the solution used, and the investigator's experience. Low specificity has also been reported for autofluorescence and chemiluminescence imaging methods, as well as concerns about failure to assist doctors in selecting the biopsy location and relatively expensive for chemiluminescence-based approaches [6].

When compared to the conventional oral examination, white-light endoscopy and narrow band imaging was prove to be a sensitive and non-invasive methods for optical biopsies of OC and oral lichen planus, with significantly decreased false positive and false negative rates. The most significant factor in this regard is early detection of lesions while they are still in the early stages, as this increases the likelihood of successful treatment. Late-diagnosed or difficult-to-cure cancers have a lower survival rate, more treatment-related problems, and higher medical costs. Because of the advanced loco-regional stage at the time of diagnosis. [4–6].

OC is the sixth most commonly reported malignancy in LMICs, including the Pacific Islands, India, Southern Asia, Eastern Europe, Southern Africa, and Sri Lanka with very high disease-related morbidity and mortality rates. Every year, 354,864 new records of lip and oral malignancies are detected, resulting in 177,384 deaths worldwide. Those with localized cancer have a five-year survival rate of 75–83 % in the United States, but patients with metastasized cancer have a rate of 16–32 % [7]. When advanced malignancies (stages III and IV) are diagnosed, they have a 45 % in two-year survival rate with combination of surgery and chemoradiotherapy. Early cancers (stages I and II) are highly curable (nearly 90% of patients survive two years when treated with a single modality) and have significantly less morbidity and mortality. [6-7].

Currently, the diagnosis is based on a comprehensive clinical examination, which is included in any routine medical consultation and provides excellent discriminating capability while spending little time in the clinic. Autofluorescence investigated in population screening programs is recommended as a supplement to traditional oral examination for detection of oral potentially malignant disorders (OPMDs), with oral biopsy remaining the gold standard in all cases [8]. The significant cause of poor OC outcomes is a lack of inadequate assessment and monitoring at the local point-of-care level – typically the dentist or hygienist – which leads to difficulty in professional diagnosis and treatment. Patients with oral cancer who spent less time between noticing a suspicious lesion and having a histological diagnosis had a better prognosis [9].

Artificial intelligence

Artificial intelligence (AI) is defined as "a branch of research and engineering concerned with the computational understanding of what is often referred to as intelligent behavior, and the production of artifacts that exhibit such behavior." It's a field of computer science that focuses on

the development of intelligent machines that think and act like humans. As a result of increased interaction with new information and communication technologies, the arrival of digital medicine is likely to change the practices of healthcare professionals [10]. Throughout the 1980s and 1990s, AI techniques such as ambiguous intelligent machines, artificial neural networks (ANNs), Bayesian networks (BNs), and hybrid intelligent systems grew in popularity. Healthcare applications received the most investment in 2016 compared to other industries, as AI techniques continue to pique interest as a means of improving image-based diagnostics [11].

Machine learning has gained in popularity in recent years as a result of technological advancements that have provided more digitization of patient records by electronic case studies and image files, including in radiology and pathology departments. It entails transforming imaging data to detect variations that aren't apparent to the visual. Deep learning (DL) is a sub-discipline of machine learning, and it is the most recent evolution of machine learning. Its operation is more complicated, but it can manage large amounts of data and make decisions [10-12]

AI is also being utilized in the criminal justice system to identify people in images or films that are linked to criminal behavior. For the time being, the role of AI in shaping the future of modern society is still debatable, but it is fairly certain that these technologies will dramatically improve efficiency and performance in our workplaces [10-11].

HISTORY:

In 1955, a mathematician named John McCarthy created the term "artificial intelligence, and " he is renowned as the "Father of Artificial Intelligence." He coined the term to describe machines' capacity to perform that are defined as "intelligent." John McCarthy held a notable Dartmouth symposium in 1956, which was formally on the artificial intelligence research project [12]. The conference sparked a crucial period of research, from the 1950s to the 1970s. Artificial intelligence was defined by Richard Bellman, an applied mathematician, in 1978 as the automation of activities related to human cognitive capacities such as learning, decision making, and problem-solving [13].

There are three basic processes to using AI in medical imaging: preprocessing, segmentation, and postprocessing.

Preprocessing:

Unwanted visual information must be removed from raw photographs in order to reduce noise. To reduce optical noise, a variety of filters can be used. The contrast is adjusted at this point to aid in the identification and delineation of different structures, such as healthy versus diseased structures. OPSCC is well-suited to cutting-edge imaging methods that map several levels and types of biomarkers. The large volume of complicated data collected by these devices, on the other hand, is incompatible with the diagnostic requirements and workflow characteristics of the settings where OPSCC is identified, diagnosed, and treated. Deep learning excels at identifying complicated features of images, converting image interpretation from a qualitative subjective

task with ambiguous cutoffs and no decision-making guidance to a quantitative, repeatable, and customized process that provides only the necessary information for decision-making [14].

Image Segmentation:

The region of interest is identified and delineated at this stage. Pathological areas of the lesion are identified from non-pathological sites in cancer imaging. While there are four main classes of segmentation, there are many different ways to this process, and hybrid models incorporating various techniques are frequently used to increase accuracy [15].

Postprocessing:

Convolutional neural networks (CNNs), recurrent neural networks (RNNs), multiscale convolutional neural networks (M-CNN), and multi-instance learning convolution neural networks are among the postprocessing techniques used in medical imaging (MIL-CNN). Additional data sets are used to test network performance, and the resulting output was compared to the gold standard diagnosis (such as histopathology)[16]. In all circumstances when the outputs do not meet the gold-standard criterion, an error signal is generated. This erroneous signal travels in the other direction. To decrease error while avoiding overfitting the data in this step is repeated. The number of research examining the utility of these techniques for identifying and mapping various types of malignancies is rapidly expanding, particularly in the areas of breast, lung, brain, and skin cancer

Squamous cell carcinoma of the oral and oropharynx is imaged.

Many phenomena associated with the presence, progression, and recurrent malignancy can be shown in the image. Metabolic rates, oxygenation, blood flow, tissue architecture spatial, structural properties, biochemical pathways, and cell viability are examples of biomarkers (O'Connor et al. 2015). Screening, early detection, and surveillance of OPSCC using imaging-based approaches are appealing because they allow for a fast, noninvasive assessment of the oral tissues. Imaging can be repeated as needed because it is fully noninvasive [18].

Several innovative high-resolution imaging approaches that are specifically developed for usage by specialists have also been investigated. Although this equipment has often performed well in clinical studies, none have been adopted for use in specialized practice regularly [19]. Instead of diagnostic performance, their failure to bridge the gap between diagnostic performance and clinical acceptance is related to overall logistics and the impact on outcomes. A good illustration of this observation is OCT (optical coherence tomography). In 1991, OCT was introduced as an imaging technology for the first time. Ultrasound imaging was used to make a comparison [20].

An optical coherence tomography (OCT) image is a two-dimensional representation of the optical reflection within a tissue sample with great histological resolution. By combining these

images, three-dimensional reconstructions of the target tissue can be generated. A flexible fiber-optic probe is placed on the tissue surface to produce real-time surface and subsurface pictures, which are used to acquire images of tissue microanatomy and cellular structure. OCT can image to a depth 2 to 3 mm in oral mucosa [18, 19, and 20].

Several studies have examined the diagnostic value of OCT in identifying, diagnosing oral premalignancy and malignancies with diagnostic sensitivities ranging from 80% to 90% and 85% to 98% respectively (Sunny et al. 2016; Tran et al. 2016; Munir et al. 2019; Doi 2007; Tsai et al. 2008; Wilder-Smith et al. 2009;). OCT has struggled to gain widespread acceptance as a clinical tool for the diagnosis of OPSCC for various reasons: 1) the images are difficult to interpret; 2) the device is big, heavy, and fragile; 3) the operating software and user interfaces are scary; and 4) the price is expensive. A prototype OCT system was built for 10% of the cost of a standard commercial OCT technology. Despite good performance, dentists will benefit from increased diagnostic accuracy and a better user interface. The necessity to learn to read and write, according to those who tried the device, interpreting the visuals remained a considerable challenge to the system's clinical adoption [21].

Artificial Intelligence in Oral Cancer Screening, Identification, and Diagnosis:

Using a simple visual examination, risk indicators, and community health professionals may almost reduce OC and OPC-related mortality in high-risk groups. This type of screening has been shown to be expensive in people with a high OC risk in several trials. Other major OC screening studies, on the other hand, found no effect on result including death, morbidity, or cost [22]. In the last decade, several AI-based algorithms and methodologies have been developed to improve oral cancer screening accuracy. Without the need for experienced, qualified, and retrained screeners, they have the potential to achieve screening efficacy and accuracy on par with or better than traditional approaches. As early as 1995, artificial intelligence was used to identify people who were at risk of developing OC. A trained ANN's specificity and sensitivity for detecting oral lesions were reported to be 0.80 and 0.77, respectively. Using targeted simulation modeling techniques, this method was subsequently shown to identify high-risk individuals and identify all lesions by screening only 25% of the population [23]. AI facilitates promotes health care interactions, which may improve screening reach, particularly in low- and middle-income countries (LMICs), where screening has the largest impact. The significance of AI as a tool for remote oral screening has been stressed in recent years as interest in AI-based healthcare applications has increased. [22-23]

In a multiphase, multicenter study, and a very low-cost DL-supported Smartphone-based oral cancer probe was developed for high-risk persons in remote places with limited infrastructure. The auto fluorescence and polarization images from the probe were coupled with OSCC risk variables and analyzed using a proprietary DL-based algorithm to provide a screening output that gives the screener triage instructions [24]. The researches indicate that screening by non-specialist health care professionals such as nurses, general practitioners, dentists, hygienists, and community health workers using AI-enabled mobile phone applications is possible, potentially useful, especially in neglected and rural areas. The degree of agreement between intraoral photographs of mucosal lesions recorded by mobile phones and clinical examination has been

classified as moderate to strong, with low-resolution images showing a lower degree of agreement [25].

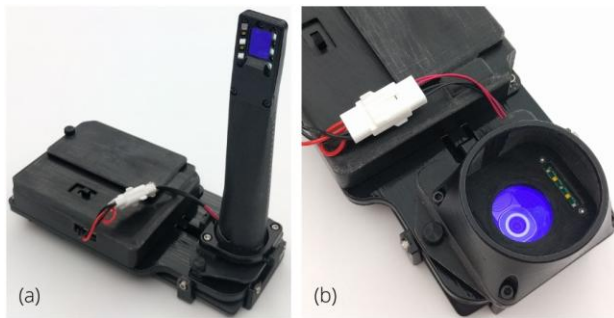


Fig. 1. Oral cancer screening devices

Oral cancer screening devices based on a smartphone that uses both auto-fluorescence imaging and a white image. (a) Intraoral image and (b) whole cavity. [25]

Using intraoral photographic images of OSCC, leukoplakia, lichen planus lesions, and a fuzzy inference-based discriminating system was able to identify OSCC and lichen planus lesions with an accuracy of 87%, while leukoplakia was identified with 70 % accuracy [26]. Deep CNN (DCNN) models trained on a small number of digital images of tongue lesions were able to diagnose early signs of OC as well as people [27]. On the internal validation dataset, an automated DL technique that was recently developed using 44,409 photographic images of biopsy-proven OSCC lesions and healthy mucosa achieved an AUC of 0.983 (95 % CI 0.973–0.991), sensitivity of 94.9 percent, and specificity of 88.7% [25-26].

Van Staveren et al. evaluated the performance of an ANN-based classification system for analysing autofluorescence spectra from 22 oral leukoplakia lesions and six healthy mucosal sites in a recent study. ANN's sensitivity and specificity for distinguishing between sick and normal tissues using spectral pictures have been reported to be 86% and 100%, respectively [28]. Wang et al. used a partial least squares and artificial neural network (PLS-ANN) classification algorithm to differentiate the autofluorescence spectra of premalignant (epithelial dysplasia) and cancerous (SCC) lesions from benign tissues, with a sensitivity of 81 %, specificity of 96 %, and positive predictive value of 88%. When utilizing an ANN classifier in a similar experimental design, others have reported greater sensitivity (96.5%) and specificity (100%) findings [29].

To discriminate between oral leukoplakia and OSCC, an SVM-based technique was developed using fourier-transform infrared (FTIR) spectroscopy applied to paraffin-embedded tissue slices from 8 healthy, 16 leukoplakia, and 23 OSCC samples [30]. When compared to the histopathological gold standard, the automated cancer screening platform distinguished between healthy, dysplastic, and malignant tissues with 87 percent sensitivity and an 83 percent specificity [30, 31]

Conclusion

Artificial intelligence will be improve research into early diagnosis of oral cancer, OPMD, as a result, and clinical practice in general. AI algorithms combined with telemedicine technologies, AI supported, and Smartphone-based technologies. AI can serve as effective as well as valuable methods for reducing both professional and health-care system delays, allowing patients to be triaged appropriately in the future to receive appropriate and timely treatment. In this review is crucial to facilitate the interdisciplinary incorporation of such techniques, and improvements in this field may open the door to further studies in the future.

Comment [Tsehay.A4]: AI is a broad area or field under AI which sub filed are you working on please be specific.

Comment [Tsehay.A5]: To be corrected as This review is crucial to...

Comment [Tsehay.A6]: What did you found from your review and what does it imply, what are the shortcomings?

References

1. Carreras-Torras C, Gay-Escoda C. Techniques for early diagnosis of oral squamous cell carcinoma: Systematic review. *Medicina oral, patologia oral y cirugiabucal*. 2015 May;20(3):e305.
2. Speight PM, Farthing PM. The pathology of oral cancer. *British dental journal*. 2018 Nov; 225(9):841-7.
3. Carreras-Torras C, Gay-Escoda C. Techniques for early diagnosis of oral squamous cell carcinoma: Systematic review. *Medicina oral, patologia oral y cirugiabucal*. 2015 May;20(3):e305.
4. Goyal D, Goyal P, Singh HP, Verma C. An update on precancerous lesions of oral cavity. *International Journal of Medical and Dental Sciences*. 2018 Jan 23;2(1):70-5.
5. Agarwal A, Bhola N, Kambala R, Borle RM. Touch imprint cytology: can it serve as an alternative to frozen section in intraoperative assessment of cervical metastasis in oral squamous cell carcinoma?. *Journal of Oral and Maxillofacial Surgery*. 2019 May 1;77(5):994-9.
6. Piazza C, Bon FD, Peretti G, Nicolai P. 'Biologic endoscopy': optimization of upper aerodigestive tract cancer evaluation. *Current opinion in otolaryngology & head and neck surgery*. 2011 Apr 1;19(2):67-76.
7. Ilhan BE, Lin K, Guneri P, Wilder-Smith P. Improving oral cancer outcomes with imaging and artificial intelligence. *Journal of dental research*. 2020 Mar;99(3):241-8.

8. Amarasinghe HK, Usgodaarachchi US, Johnson NW, Laloo R, Warnakulasuriya S. Public awareness of oral cancer, of oral potentially malignant disorders and of their risk factors in some rural populations in Sri Lanka. *Community dentistry and oral epidemiology*. 2010 Dec;38(6):540-8.
9. Epstein JB, Güneri P, Boyacioglu H, Abt E. The limitations of the clinical oral examination in detecting dysplastic oral lesions and oral squamous cell carcinoma. *The Journal of the American Dental Association*. 2012 Dec 1;143(12):1332-42.
10. Baliga M. Artificial intelligence-The next frontier in pediatric dentistry. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*. 2019 Oct 1;37(4):315-.
11. Nimbalkar, G., Keshwani, H., Katakwar, T., Chhabra, K.G., Deolia, S., Reche, A., 2020c. Artificial intelligence: a dental odyssey. *Indian Journal of Forensic Medicine and Toxicology* 14, 6776–6781. <https://doi.org/10.37506/ijfmt.v14i4.12683>.
12. Bindushree V, Sameen RJ, Vasudevan V, Shrihari TG, Devaraju D, Mathew NS. Artificial intelligence: In modern dentistry. *Journal of Dental Research and Review*. 2020 Jan 1;7(1):27.
13. Khanagar SB, Al-Ehaideb A, Maganur PC, Vishwanathaiah S, Patil S, Baeshen HA, Sarode SC, Bhandi S. Developments, application, and performance of artificial intelligence in dentistry—a systematic review. *Journal of dental sciences*. 2021 Jan 1;16(1):508-22.
14. Ilhan B, Lin K, Guneri P, Wilder-Smith P. Improving oral cancer outcomes with imaging and artificial intelligence. *J Dent Res* 2020;99:241–8.
15. Ilhan B, Guneri P, Wilder-Smith P. The contribution of artificial intelligence to reducing the diagnostic delay in oral cancer. *Oral Oncology*. 2021 May 1;116:105254.
16. Khanagar SB, Al-Ehaideb A, Maganur PC, Vishwanathaiah S, Patil S, Baeshen HA, Sarode SC, Bhandi S. Developments, application, and performance of artificial intelligence in dentistry—a systematic review. *Journal of dental sciences*. 2021 Jan 1;16(1):508-22.
17. Kalappanavar A, Sneha S, Annigeri RG. Artificial intelligence: A dentist's perspective. *Journal of Medicine, Radiology, Pathology and Surgery*. 2018 Mar 1;5(2):2-4.
18. Wang X, Yang J, Wei C, Zhou G, Wu L, Gao Q, He X, Shi J, Mei Y, Liu Y, Shi X. A personalized computational model predicts cancer risk level of oral potentially malignant disorders and its web application for promotion of non- invasive screening. *Journal of Oral Pathology & Medicine*. 2020 May;49(5):417-26.

19. Schwendicke FA, Samek W, Krois J. Artificial intelligence in dentistry: chances and challenges. *Journal of dental research*. 2020 Jul;99(7):769-74.
20. Nguyen TT, Larrivée N, Lee A, Bilaniuk O, Durand R. Use of Artificial Intelligence in Dentistry: Current Clinical Trends and Research Advances. *J Can Dent Assoc*. 2021;87(17):1488-2159.
21. Khanagar SB, Naik S, Al Kheraif AA, Vishwanathaiah S, Maganur PC, Alhazmi Y, Mushtaq S, Sarode SC, Sarode GS, Zanza A, Testarelli L. Application and Performance of Artificial Intelligence Technology in Oral Cancer Diagnosis and Prediction of Prognosis: A Systematic Review. *Diagnostics*. 2021 Jun;11(6):1004.
22. Sankaranarayanan R, Ramadas K, Thomas G, Muwonge R, Thara S, Mathew B, Rajan B, Trivandrum Oral Cancer Screening Study Group. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *The Lancet*. 2005 Jun 4;365(9475):1927-33.
23. Speight PM, Elliott AE, Jullien JA, Downer MC, Zakzewska JM. The use of artificial intelligence to identify people at risk of oral cancer and precancer. *British dental journal*. 1995 Nov;179(10):382-7.
24. García-Pola M, Pons-Fuster E, Suárez-Fernández C, Seoane-Romero J, Romero-Méndez A, López-Jornet P. Role of Artificial Intelligence in the Early Diagnosis of Oral Cancer. A Scoping Review. *Cancers*. 2021 Jan;13(18):4600.
25. Uthoff RD, Song B, Sunny S, Patrick S, Suresh A, Kolar T, Keerthi G, Spires O, Anbarani A, Wilder-Smith P, Kuriakose MA. Point-of-care, smartphone-based, dual-modality, dual-view, oral cancer screening device with neural network classification for low-resource communities. *PloS one*. 2018 Dec 5;13(12):e0207493.
26. Nishi Y, Horio K, Saito K, Habu M, Tominaga K. Discrimination of oral mucosal disease inspired by diagnostic process of specialist. *Journal of Medical and Bioengineering Vol*. 2013 Mar;2(1).
27. Shamim MZ, Syed S, Shiblee M, Usman M, Ali S. Automated detection of oral pre-cancerous tongue lesions using deep learning for early diagnosis of oral cavity cancer. *arXiv preprint arXiv:1909.08987*. 2019 Sep 18.
28. de Veld DC, Skurichina M, Witjes MJ, Duin RP, Sterenborg DJ, Star WM, Roodenburg JL. Autofluorescence characteristics of healthy oral mucosa at different anatomical sites.

Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery. 2003 Jun;32(5):367-76.

29. Wang CY, Tsai T, Chen HM, Chen CT, Chiang CP. PLS- ANN based classification model for oral submucous fibrosis and oral carcinogenesis. Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery. 2003 Apr;32(4):318-26.
30. Banerjee S, Pal M, Chakrabarty J, Petibois C, Paul RR, Giri A, Chatterjee J. Fourier-transform-infrared-spectroscopy based spectral-biomarker selection towards optimum diagnostic differentiation of oral leukoplakia and cancer. Analytical and bioanalytical chemistry. 2015 Oct 1;407(26):7935-43.
31. Heidari AE, Sunny SP, James BL, Lam TM, Tran AV, Yu J, Ramanjinappa RD, Uma K, Birur P, Suresh A, Kuriakose MA. Optical coherence tomography as an oral cancer screening adjunct in a low resource settings. IEEE Journal of Selected Topics in Quantum Electronics. 2018 Sep 10;25(1):1-8.

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