

# Improvement of oral cancer screening quality and reach: The promise of artificial intelligence

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## Abstract

Oral cancer is easily detectable by physical (self) examination. However, many cases of oral cancer are detected late, which causes unnecessary morbidity and mortality. Screening of high-risk populations seems beneficial, but these populations are commonly located in regions with limited access to health care. The advent of information technology and its modern derivative artificial intelligence (AI) promises to improve oral cancer screening but to date, few efforts have been made to apply these techniques and relatively little research has been conducted to retrieve meaningful information from AI data. In this paper, we discuss the promise of AI to improve the quality and reach of oral cancer screening and its potential effect on improving mortality and unequal access to health care around the world.

## KEYWORDS

artificial intelligence, early detection, machine learning, oral squamous cell carcinoma

## 1 | INTRODUCTION

Squamous cell carcinoma of the oral cavity is the sixth most common malignancy in the world. The WHO estimates an incidence of 529 000 new cases of oral cancer each year, causing more than 300 000 deaths.<sup>1</sup> A majority of these tumors arise in low- and middle-income countries (LMICs), specifically those of Southeast Asia and the Indian subcontinent, where consumption of causative tobacco products is highest. Although significant advances in clinical management of oral cancer have been achieved, early detection retains the most significant potential to reduce mortality rates, as the vast majority of oral cancers present late.<sup>2</sup> For example, an Indian study showed an 82% 5-year survival rate in patients diagnosed at an early stage, while only 27% of patients survived 5 years after an advanced stage diagnosis.<sup>1</sup> Although different strategies for early detection have been proposed, the optimal approach remains subject of debate, and none has been firmly established.

The vast majority of oral cancers does not arise de novo. Rather, oncogenesis in the oral cavity follows a stepwise process which is hallmarked by a progressive deterioration of the genetic content of initially benign mucosal cells, under the influence of extrinsic (tobacco) and intrinsic mutagenic factors. Phenotypic manifestations of this process can often be followed visually, by the occurrence and sequential development of well-defined premalignant changes to the oral mucosa. The oral cancer tumor progression model (Califano et al,<sup>3</sup> Cancer Research, 1996) is well established and may be exploited to improve early detection. However, determination of those oral lesions with a propensity for malignant transformation is not always straightforward by visual or histologic assessment.<sup>3</sup> The advent and continuous development of information technology, such as artificial intelligence (AI) techniques in dental informatics, combined with recent progress in data mining algorithms provide potential to facilitate both the quality and the reach of this process, and highly sensitive technology facilitates remote access.

The present review describes the potential impact of AI on improvement of oral cancer screening, and its anticipated effect upon reduction of mortality and unequal healthcare access around the world.

## 2 | IMPACT OF UNEQUAL ACCESS TO HEALTH CARE ON DELAYED DIAGNOSIS OF ORAL CANCER

Application of information technology to the early detection of oral cancer may be most beneficial in rural and/or low socioeconomic status (SES) populations, as these populations are disproportionately affected by late-stage oral cancer. Optimal management of oral cancer requires specialized management which is often only provided by the public tertiary healthcare setting or private hospitals, especially in the third world. In India, several regional cancer centers are located throughout the country. Although these are dispersed in a relatively equal geographical fashion, their sheer number is too low to cover the immense distances on the Indian subcontinent. Private hospitals are predominantly located in urban areas, and care is expensive. Accessibility to specialized health care and associated late diagnosis of oral cancer therefore tends to disproportionately affect poor and/or rural populations in India and the third world at large.<sup>4</sup>

Consumption of tobacco products amplify this issue, as its association with low socioeconomic status, and some of its derivatives like reduced income and education levels, has increased over the course of the last decades. This is not only true for many western countries such as the United States and Canada, but also for lower middle-income countries (LMIC) such as India and Southeast Asia. Johnson et al assessed whether the awareness of oral cancer screening in the United States correlated with socioeconomic status (SES) and found that higher SES individuals are more likely to be aware of and screened for oral cancer.<sup>5</sup> Auluck et al<sup>6</sup> reported approximately 50% of oropharyngeal and oral cancers cases of in both sexes resided in SES-deprived neighborhoods in Canada. More significant proportions of cancer cases were diagnosed at later stage disease for both sexes residing in deprived neighborhoods.<sup>6</sup> In India, national surveys and community-based studies have shown that tobacco consumption among the poor has continued, while it has decreased among higher socioeconomic subpopulations.<sup>7</sup> As an example, although government-sponsored tobacco control efforts have significantly reduced overall tobacco consumption, there is still widespread among middle-aged adults, less educated individuals, and people are living in rural and tobacco-cultivating areas of India.<sup>8</sup>

For these reasons, it is the lower SES populations that are likely to benefit from the potential application of mobile and remote access information technology devices to the early detection of oral cancer most.

## 3 | SCREENING FOR ORAL CANCER

Several established cancer screening programs for a variety of malignancies, such as cervix, colon, and breast cancer, have been

shown to reduce patient morbidity and mortality significantly (REF). Traditional screening for oral cancer includes visual and palpation (self) assessment of the oral cavity and neck by medical professionals (or patients), ideally before symptoms occur. Screening for OSCC can also involve cytological assessment of oral cavity cells derived from brush examinations or saliva, vital or fluorescent staining/visualization (with or without application of optical instruments), and assessment of biopsy specimens for microscopic or molecular features. Although the latter means Biopsy, as it is the gold standard for diagnosis and investigation, it has some disadvantages like being invasive in nature.<sup>9</sup>

The viability of government-funded oral cancer screening programs in the western world has not been deemed high, due to the low incidence of oral cancer, high frequency of dental visits, high costs and limited anticipation of survival impact, even in high-risk groups. This may be different for high-risk regions such as Southeast Asia and the Indian subcontinent, where oral cancer incidence consistently ranks among the most common cancers. A randomized-controlled trial on oral cancer screening conducted in India concluded indeed that visual examination was useful in high-risk subjects like chronic smokers or alcoholics.<sup>10</sup> Another Indian study reported visual screening of 96 517 eligible participants with significant reduction of mortality in high-risk individuals. Extrapolation of these data suggested the potential of preventing at least 37 000 oral cancer deaths worldwide.<sup>11</sup>

## 4 | ARTIFICIAL INTELLIGENCE FOR ORAL CANCER SCREENING

Although traditional oral cavity screening appears viable in LMIC, in particular the high incidence countries, disproportionate accessibility of health care of high-risk groups within these countries forces us to identify alternative screening methods, in order to improve the reach and therefore the success of screening. Modern technology such as artificial intelligence (AI) offers the potential to perform medical activity at remote distance, circumventing issues related to physical presence requirements, which promises to improve expedited reach of screening, specifically into the remote lower SES regions around the world where screening is deemed most successful.

Beyond increasing the reach of screening and improving accessibility to early cancer diagnosis, AI application in disease screening may further improve diagnosis by virtue of its expedited workflow, and its improved sensitivity compared with conventional human-derived screening methods. For example, in contrast to conventional screening methods, observational fatigue is absent, and minute changes in the range of a single pixel can be detected at improved rate compared with the naked eye.<sup>12</sup>

Early application of AI in medicine was provided by IBM's Watson, which received considerable attention in the media for its focus on precision medicine in cancer diagnosis and treatment. Watson, named after IBM's founder Thomas J. Watson, is a question-answering computer system capable of answering questions

posed in natural language, developed in IBM's DeepQA project. Watson employs a combination of machine learning (ML) and natural language processing (NLP) capabilities. However, early enthusiasm for the application of this technology in the field of medicine has faded as customers realized the difficulty of teaching Watson how to address particular types of disease<sup>10</sup> and the difficulty of integrating Watson into care processes and systems.<sup>13</sup>

Recently, newer AI applications have been applied to the detection of cancer. McKinney et al<sup>14</sup> reported the development of an AI system for interpretation of screening mammograms and showed it to outperform expert radiologists. In oral cancer, Morikawa et al reported the utility of optical instruments in oral screening finding that high-quality medical AI can be established as an oral cancer screening system.<sup>14</sup>

This study was one of the first suggesting that AI could serve as a useful modality in the detection of (pre)malignant lesions of the oral cavity and suggested significant potential for population-based screening. Shamim et al proposed to automate the screening process to detect oral cavity cancer using deep convolutional neural network (DCNN) models using a small dataset of clinically annotated photographic images. Although the work represents a positive step toward an effective and inexpensive oral cancer screening method for daily clinical practice, the study was restricted to detection of tongue lesions only.<sup>15</sup> Rosma et al suggested that both fuzzy regression and fuzzy neural network models provide improved prediction of oral cancer susceptibility compared with human expert analyses. Hence, the use of AI prediction models was proposed as a suitable filtering system in identifying people at risk of oral cancer, based on their risk habits and demographic profiles.<sup>16</sup> Others concluded that the field of clinical decision support systems (CDSS) applications in different types of cancer have indicated that ML methods have a high potential to manage the data and diagnostic improvement in oral cancer intelligently and accurately.<sup>17</sup>

Artificial intelligence has also been applied to biopsy-based analysis of oral (pre)cancerous specimens. A deep learning algorithm has been developed based on partitioned convolution neural network (CNN) for automatic oral cancer specimen diagnosis by investigating hyperspectral images from patient biopsy specimens. The accuracy of this regression-based partitioned algorithm was 94.5%, with a specificity of 98% and a sensitivity of 94%. This outperformed more conventional classifiers including the support vector machine (SVM) and the deep belief network (DBN). This algorithm improves both the accuracy of detection and the differentiation between benign and malignant lesions and hence increases the quality of diagnosis.<sup>18</sup>

Other have proposed methods for efficiently training CNNs for tissue classification using active learning (AL) instead of the more common random learning (RL). One hundred and forty-three digitized images of hematoxylin-and-eosin-stained whole oral cancer sections were classified using both methods and the compared data found that the AL strategy provided an average 3.26% greater performance than RL for any given training set size and tissue type.<sup>19</sup>

An oral cancer identification and detection system using a Deep Neural based Adaptive Fuzzy System (DNAFS) has been reported. The proposed algorithm was trained and tested on medical datasets of several oral cancer biopsy specimens. Although the algorithm had limitations in terms of its accuracy in diagnosis and detection of oral cancer, the performance of this classifier was far superior to any other cancer detection classifier.<sup>20</sup>

Artificial intelligence has also been applied extensively in the molecular analysis of oral cancer biopsy specimens including applied machine learning methods to predict the development of oral cancer in patients with oral potentially malignant lesions. Fisher discriminant analysis was used to select relevant features from a gene expression array. The results showed highly accurate performance of this program compared with other classification method.<sup>21</sup> AI may also contribute positively to prognostic evaluation of oral cancer patients. For example, ML techniques for the analysis of genomic data can play a role in the prognostic prediction of head and neck squamous cell carcinomas.<sup>22</sup>

Altogether, various AI methods have been applied to both the diagnostic and prognostic evaluation of cancer patients, assisted by the development of artificial neural networks, fuzzy logic programs, genetic algorithms, support vector machine learning, and other hybrid techniques. These applications have been shown to generate more accurate diagnostic and prognostic information as compared to traditional statistical methods.<sup>23</sup> However, most studies evaluating AI as a diagnostic tool in oral oncology and other branches of medical oncology have not been strongly validated for its reproducibility and generalizability. Currently, the 4 main types of AI or AI-based systems include reactive machines, limited memory machines, theory of mind, and self-aware AI applications. In the field of health care at large, and oral cancer screening specifically, the limited memory machine-type of AI has been studied most, and continuous improvement in accuracy, computing power, algorithm development, and accumulation of training data is anticipated to improve the applicability of AI to the analysis of patients significantly.

## 5 | CONCLUSION

Oral screening is essential for the early detection of oral cancers and such screening plays a vital role in reducing the proportion of SCC mortality which results from diagnostic delay. This is especially pertinent in LMICs, specifically those of Southeast Asia and the Indian subcontinent. These countries feature high rates of oral cancer, but low rates of early detection as a result of decreased access to health care of their most at risk subpopulations. Although AI promises to improve both the quality and reach of oral cancer screening in such countries, there are significant considerations that need to be addressed before further implementation can be established. There are essentially three stages in the evolution of AI-based decision-making systems. At present, we have reached stage II (general intelligence level) in which the relationship between healthcare providers and AI remains unequal with regard to an existing power difference

that favors the healthcare provider. Integrating these systems into clinical practice necessitates building a mutually beneficial and thus more equalized relationship between AI and clinicians. Such a relationship is characterized by AI offering clinicians greater efficiency or cost-effectiveness, while clinicians offer AI the required clinical exposure to improve its education in complex clinical case management in return. Along this process, we anticipate the biggest impediment of further AI development will come from the public, who are expected to become increasingly hesitant to accept an increasingly self-sufficient technology.<sup>24</sup> It will therefore be critical to ensure that AI does not obscure the human face of medicine in order to avoid ethical issues that may arise from implementation of this technology. Given these considerations, it remains to be seen whether AI will be successfully applied to the screening of oral cancer and medicine at large, despite its enormous potential.

### CONFLICT OF INTEREST

None.

### AUTHOR CONTRIBUTIONS

Ankita Kar: Design, Data Acquisition, Manuscript Drafting and editing. Volkert B. Wreesmann: Data Acquisition, Data Analysis, Manuscript Design, drafting and editing. Shwetha V: Data Analysis, Manuscript Drafting and editing. Shalini Thakur: Manuscript Design, Data analysis, Manuscript editing. Vishal U.S. Rao: Data Analysis and Interpretation Concept, Manuscript Review. Gururaj Arakeri: Data Analysis, Manuscript Review and Revision. Peter A. Brennan: Critical Revision, Data Analysis, Interpretation.

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