



Review Article

Artificial intelligence as a tool for improving oral cancer outcomes

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ABSTRACT

Oral cancer detection at an early stage remains a challenging situation for health professionals in the rural setup. This is due to lack of training and infrastructure facilities. In the era of modernization, when tools like artificial intelligence and machine learning are gaining acceptance, this article throws insight into the role of AI as a tool for improving oral cancer outcomes.

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1. Introduction

Worldwide, cancer is the main cause for mortality and Oral Cancer remains at the 6th most common malignancy in the world. Oral cancer can be defined as any malignant neoplasm affecting lips, floor of mouth, cheek lining, gingival, palatal or tongue mucosa. In India, 5 people lose their life of oral cancer every hour and it is one of the top three types of cancers in the nation. In India, there is no robust mechanism for cancer registration and it is not mandatory for hospitals to register cancer cases in the National data pool, so the true nature of the disease is underestimated. Current National Cancer Registry program provides population-based data from 28 cancer registries which are located across the country at urban and rural levels and the data is alarmingly high.

Most of the oral cancers include oral and oro-pharyngeal squamous cell carcinomas (OPSCC). In India, the main etiology behind OPSCC is consumption of tobacco (both smoking & smokeless forms), betel quid and alcohol. In western world, especially in countries like Europe & North America, human papilloma virus (HPV) induced oral

cancers are also on a rise and they pose an additional burden on the healthcare facilities.

Early diagnosis remains a key feature for improving any disease outcome. In South-Asia, especially India, there is an increased incidence of oral potentially malignant lesions (OPML) which can be attributed to rampant use of tobacco and gutka. Most of the OPSCC remain undetected in initial stages or are diagnosed at the stage when they have metastasized to other body parts. After metastasis, OPSCC outcome remains poor leading to increased morbidity and mortality.¹

Oral cancer research is continuously evolving in different ways like early screening methods, classification of oral cancer patients into high-risk, moderate-risk and low-risk groups, the prediction of cancer susceptibility (risk assessment) especially when diagnosing OPML's like Leukoplakia, OSMF etc., the prediction of cancer recurrence / local control and cancer survival rates.²

In the recent past, many novel imaging modalities are being studied to check their sensitivity & specificity in early detection of oral cancer so as to improve the outcome of the disease. Artificial intelligence (AI) too has gained lot of momentum in the past decade. AI approaches have also been showing remarkable results in enhancing

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diagnostic accuracy in many fields of medicine, but very little research has been carried out in the field of oral cancer. AI applications in medical field require three steps namely, Preprocessing, Image Segmentation and Post processing. AI has two variants namely Deep learning (DL) and machine learning (ML). Both the sub sets are different but many a times they have been used reciprocally. In short, machine learning algorithms often require precisely separated data entries, while deep learning networks rely on artificial neural network layers to reproduce their domains by identifying margins (differences). Machine learning will require discreet data or predictive models, whereas in deep learning also, data is required to be fed in to the computer, but the quantity of data is quite high. ML usually requires human intervention for coding and training the computer; however, in DL specific computer algorithms are used to learn from vast data. Thus, both ML & DL being smart and within the realm of AI, deep learning techniques require complex data sets, less of human intervention & more robust supercomputers than traditional machine learning algorithms, which can work efficiently with simpler and fewer data sets to match to the gold standards or specific conditions of interests.¹

2. Research Problem

2.1. Lack of knowledge and training lapses

More than 28% of adults visit the dentist annually, which makes general dental care a good option to enhance timely OPSCC diagnosis. Dentists during their routine practice of oral hard tissue & mucosal examination should primarily diagnose OPSCC and should be able to refer the suspected malignancy patients to the specialist for further intervention. Figure 1 shows an ideal traditional approach to an Indian dental care setting. (Ilhan B et al. 2020) The approach states that, any patient seeking dental care should be examined by oral health care provider for oral cancer risk assessment especially for high-risk group patients who are having a positive habit history. Dentists with the help of visual, tactile examination and non-invasive adjuncts should provide a suitable diagnosis for pathologies affecting oral mucosa. Once the positive diagnosis is made, a specialist referral is made who will further decide the course of action like invasive biopsy procedure or surveillance. Research has shown that there is lack of knowledge and screening skills in the dentists to diagnose OPML's, OPSCC and normal variants of oral mucosa which often leads to under and over diagnosis of such lesions. There is a grave need to incorporate specific continuing dental education programs like workshops for enhancing diagnostic skills and raise general awareness amongst dental practitioners about specialist's referrals. In addition, especially in rural population, there are many hurdles like inaccessibility to health care, affordability and lack of information and

awareness, which serves as a roadblock for seeking early diagnosis. Due to these reasons, in the current scenario, oral cancer screening accuracy remains very poor.

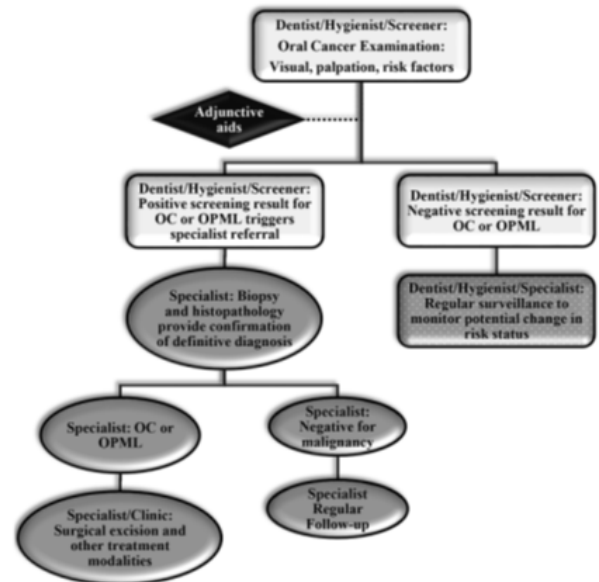


Figure 1: Traditional diagnostic process of a dental office. Courtesy: Dr. Diana Messadi

2.2. Diagnostic dilemma to differentiate benign & malignant lesions

Oral diagnosis of mucosal lesions is very challenging and it is quite subjective. Dentists or specialist usually come to a provisional diagnosis of a lesion by analyzing their clinical features like color, extent, surface texture, margins, and consistency, therefore, initial or subclinical lesions can go unnoticed. Most of the lesions which appear clinically benign may have some degree of dysplasia. Clinical diagnosis, alone, is difficult to differentiate benign lesions from dysplastic lesions. There are other factors also responsible in it like lack of knowledge, inability to differentiate OPSCC and OPML's from benign lesions, atypical lesions and delay in referral to a specialist. Dentists are shown to have only 31% specificity in differentiating OPSCC and OPML's from other benign lesions according to a recent published meta-analysis.

2.3. Biopsies remain gold standard for diagnosis but they are invasive

For confirmatory diagnosis of OPSCC and OPML's, biopsy remains the golden standard. However, it is the invasive procedure. Many a times dentists are not trained or are hesitant to perform such chair side investigations or specialist are not available on the site to perform this

procedure. OPML's are heterogenic lesions wherein few areas might depict dysplasia and rest of the lesion will be benign. Visually, choosing the biopsy site again remains very subjective and can lead to false-negative results. Additionally, 3-dimensional mapping of lesion, point-based histological mapping and intraoperative histopathological analysis is rarely being done for oral cancer due to increased surgical risks, duration and cost. Subsequently, recurrent lesions are not diagnosed at an initial stage to prevent morbidity and mortality.

3. Solution

In today's modern world, biomedical field and AI have received remarkable achievements. For any technology to succeed it should fulfill two basic requisites. Firstly, AI augmented technology should cater to user's needs especially which involve the decision making. If any AI equipped device won't aid the dentist in improved decision-making, then it will just add to the unprecedented cost and waste clinician's time. Secondly, technology should be such that it can be gauged precisely to meet the end users' factors for expenditure, training, expertise, time and space. For example, if there is an AI enhanced device developed for screening oral cancer, it should be able to:

1. Differentiate benign lesions from malignant lesions,
2. Should be able to quantify change in lesion status in subsequent follow up visits,
3. Should assist in choosing biopsy site,
4. Should assist dentist in decision making whether to provide a specialist referral or not,
5. It should be cost effective, portable, robust.
6. Should have friendly user interface.
7. Guiding the patient with future care and follow ups.

4. Application of Ai to Improve Oral Cancer Outcomes

4.1. Oral cancer screening using simple smartphone probe imaging with DL algorithms

Imaging remains very crucial in diagnosing oral cancers. Being non invasive in nature it can be repeated. They can be readily available for community setups and can aid in screening, early detection and surveillance of OPSCC & OPML's. Many studies recommend the use of imaging-based adjuncts like auto fluorescence in detection of Oral cancer.

Visual examination of the oral cavity makes use of dental light source attached to the dental unit. It could be either a halogen lamp or a natural white LED light. But most of the times, the white light intensity is not enough to reach to a conclusive diagnosis especially when examining similar looking red and white lesions. Autofluorescence is a property in which certain cellular structures like mitochondria and lysosomes emit natural

light when they are subjected to a source of light of a particular wavelength. Fluorophores are naturally present in the human cellular tissues and they become excited when a light of a particular wavelength falls on them and then they start re-emitting light of a varying wavelength. This autofluorescence based diagnostic techniques for oral cancer include; Autofluorescence imaging (AFI), Autofluorescence spectroscopy and Visual autofluorescence [VELscope].

AFI is one of the better chair side investigations for early diagnosis of oral cancer and has a less subjective error as compared to VELscope. In this modality, oral tissues are illuminated at the wavelength of 400-410nm, which comes under the green spectrum and digital images are captured of the tissues using a camera. Normal and dysplastic tissues both appear green on the final image. OPML's having lower stromal collagen will appear dark green as compared to healthy tissues which will have light green hue in them and can be easily delineated using computer algorithms. Previous autofluorescence imaging (AFI) studies have gained a sensitivity of more than 71% and a specificity of 15.3% -100% although few studies have shown rather reduced sensitivity of only 30-50%.³ Increased sensitivity will enable the clinicians to catch the disease in its initial stages, enabling immediate treatment of the disease, and specificity should also be considerably high for AFI imaging. Such a technology is a boon especially for the rural primary health care set ups and far-flanged remote areas where doctor to patient ratio is less, health care facilities are inaccessible and where trained specialists are not available. AFI system should be developed in such a way that it is easily operable by community worker, dentist, nurse or a social worker without the formal training.

In today's time smartphones are readily available which has a very user-friendly camera tool. The advancements in the pixel size and camera quality enable the operator to capture the digital images which are portable and transferrable. Smartphones having features of Bluetooth connectivity, simple touch screen interface and internet connectivity can be easily incorporated as a cancer screening device. Using smartphone data transfer capabilities, captured images can be uploaded to a central cloud server, where a panel of specialists from the fields of Oral Medicine & Oral Pathology can access these images and make appropriate diagnosis. Additionally, in-depth learning tools like Convolutional Neural Network (CNN) can be deployed in the cloud at the pre-processing phase which will be used for automated image analysis, fragmentation and differential diagnosis.

Recently, a multi-centre study has demonstrated successful use of an economical, DL-supported smart phone based oral cancer probe which can be easily used by dentists or interns posted in remote rural locations. This kind of probe can be used to screen all high-risk group

patients and it is able to reach most inaccessible sites which have a high incidence to develop HPV-related oral cancer. The probe has a unique design and it incorporates technologies of auto fluorescence and polarization. (Figure 2) Images captured by the probe along with the basic patient data (like habit history, signs, symptoms, other systemic co-morbidities) are analyzed by a specific DL-based algorithm to generate an output which will guide the screener about the outcome of the disease.

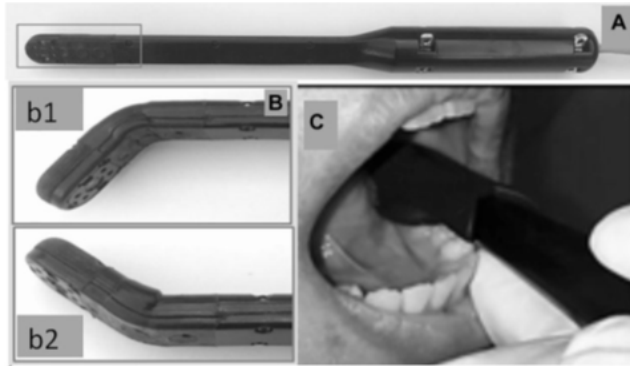


Figure 2: Fourth generation OPSCC screening probe prototype

Field study has been carried out to test the accuracy of this DL-driven probe. The results showed that there was increased mean diagnostic reliability from 59% (clinical evaluation alone) to 86.6% (Machine learning diagnosis).¹

4.2. Use of OCT with machine learning & deep learning algorithms

Optical coherence tomography (OCT) is one of the high-resolution imaging approaches being used in cancer screening. It was first introduced as an imaging modality in the year 1991 in the field of ophthalmology and ever since has been compared with ultrasound imaging as both of them work on almost the same principle of backscatter signals. They have performed really well in specialty clinics, and their use at grass root level is quite low. There are few drawbacks of this technology, being, difficulty in interpretation of the images, cost & size of the machine, operating software and user interfaces and requirement of a specialist. Principle of OCT image capturing is OCT image is basically a 2-D representation of a 3-D object through the virtue of optical reflection of a tissue sample which is very close to the histological resolution. The digital images can then be stacked up to provide a three-dimensional mapping of the lesion. The OCT images have the capacity to capture images at a depth of 2-3mm in oral tissues. The OCT makes use of a probe which can be kept close to the tissue surface to apprehend real time dynamic images of the epithelial and sub-epithelial surface.

To overcome the limitations of traditional OCT, DL-driven OCT prototype has been developed at only 10% of

the total cost and has been successfully used at clinical setting. The prototype has been added with DL-algorithms so that end user don't find cumbersome to interpret the images. Recent study which made use of such a prototype revealed that DL-driven OCT was able to differentiate healthy lesions with that of lesions with dysplasia and frank malignancy with a sensitivity of 87% and specificity of 83%.⁴

4.3. Use of machine learning in oral cancer prediction / prognosis

Several tools have been developed for medical researchers which make use of ML methods. The integration of various factors like family history, age, diet, weight, habit history, exposure to other environmental carcinogens, molecular biomarkers (cancer biomarkers), genomics, etc. can produce huge data for oral cancer and can be made available for researchers. Example of such a data bank is The Cancer Genome Atlas Research network (TCGA) which aids diagnosticians in better understanding of the molecular basis of cancer and support for personal medicine.²

5. Machine Learning Applications in Oral Pathology

Computer-Assisted Diagnosis (CAD) can be very promising in the field of histopathology. In super specialty hospitals where there is excessive load on the histopathology tissue banks, CAD not only will reduce the subjective errors by pathologists, but it will also help in segmentation of area of interest, automated scoring of immune-staining, classifying & sub-classifying various features, automated cancer staging and detection of vascular invasion. Content Based Image Retrieval (CBIR) is based on such novel technology which using computerized algorithms compares & evaluates similar looking images to an image in question. In digital pathology, CBIR systems are very useful in numerous situations, especially in early diagnosis, for improved teaching methodologies, and for innovative research. ML methods can be used in discovering novel clinico-pathological relationships. In this digital world, when medical data like patient demographics, clinical history, genomic data, biomarkers, blood profile, digital pathological images, DICOM images of CT & MR are available online, using ML techniques will lead to new discoveries.

6. Conclusion

It is encouraging to see how AI is expanding its wings in various fields of dentistry especially in the field of oral cancer detection, prediction and outcome. However, there will be requirement of pools of data to develop ML related techniques so that the devices which are made out of it are flawless. To interpret and analyze such a massive pool of data, it is impractical for an unaided human mind without

computational assistance. One should also remember that AI cannot replace the job of an oral pathologist but on contrary will ease their job as they will be more equipped with tools of AI and DL which may lead to novel research ideas.

7. Scope for Future Work

Histopathological images have their unique characteristics which can lead to specific problems and hence make a way for future work in those areas. Examples being:

1. Very large image sizes and specific region of interest (ROI).
2. Insufficient labeled images – very limited training data is available.
3. Variable magnification levels (eg. 1x, 10x, 100x, and so on) result in different degrees of information.
4. Presence of color variations and artifacts.

Other potential future research topics can include like discovery of novel objects / software which are more economical according to Indian setup, interpretable deep learning models, intra-operative diagnosis and tumor infiltrating immune cell analysis.

8. Source of Funding

None.


9. Conflict of Interest

None.

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