A Review on Non-invasive Tools and Deep Learning/Machine Learning Methods for the Early Identification of Oral Cancer

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The most common type of cancer in India is called "oral cancer." Poor lifestyle choices like chewing tobacco, binge drinking, smoking cigars or pipes, getting an HPV infection, and being in the sun can cause irreversible cell proliferation and the formation of cancer. Oral cavity cancers are becoming more common and need to be treated right away. While a visual examination by a specialist and a gold standard "biopsy" carried out under expert supervision and using the detection instrument can detect an oral cancer lesion, this method is not ideal because it is invasive. There is a summary of various invasive and non-invasive tools, and there is a review of machine and deep learning techniques used by numerous researchers. It was found that some models with pre-defined networks and transfer learning techniques were used on a small dataset during the review process. However, there is an urgent need for non-invasive early diagnosis of multiple types of lesions in the early stages of oral cancer.

Keywords: Oral cancer, machine learning, deep learning, transfer learning, CNN.

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1 Introduction

Worldwide, the incidence of menaces of the mouth and throat is rising worryingly. This disease has the ability to invade and spread to other sections of the body, causing unregulated and aberrant cell proliferation in surrounding tissue. Oral cancer is India's biggest cause of death for both men and women. Mouth cancer begins as a painless, swelling white area that eventually transforms into a red patch if it is not identified and treated quickly. Then, there are non-healing ulcerations and lump formations over the palate, cheeks, sinuses, pharynx (throat), lips, tongue, and floor of the mouth. Oral cavity cancer is twice as common in males as in females, with men over 50 having the highest risk. According to WHO estimates, there are 657,000 new cases and around 330,000 deaths from oral and pharyngeal cancer per year. Thirty percent of mouth cancer cases recorded worldwide originate from India. About 177,757 people died, and 377,713 new cases were reported in 2020 [1].

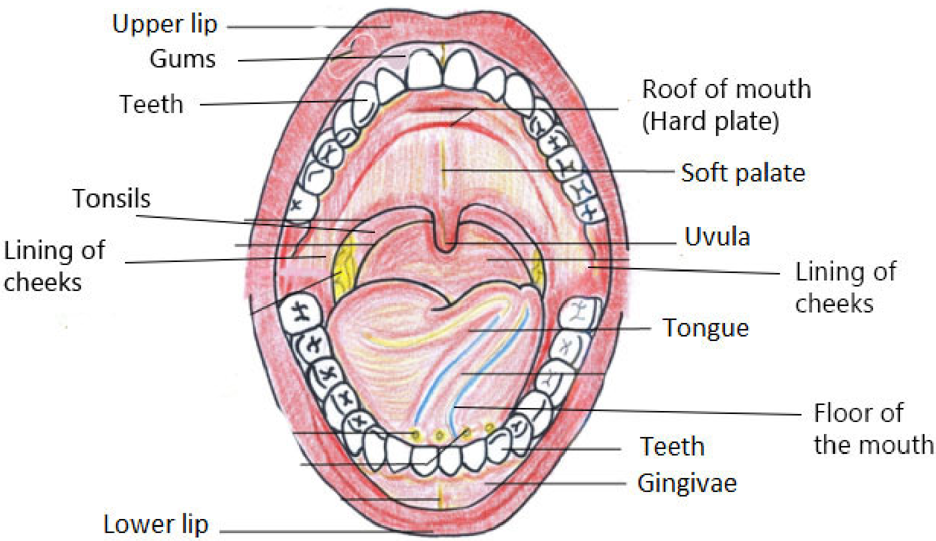

Figure 1. Potential oral surface area where cancer could grow [25]

From the above Figure 1, it can be observed that oral cancer development may occur in various regions, like floor of the mouth, the gums, lining of the cheeks, soft and hard plate, upper and lower lip, tongue, and gingivae.
The primary sites where mouth cancer may begin are as follows:

1. The area behind the tongue could be the cause of a canker sore, often known as the floor of the mouth.
2. Gum disease, often known as gingivitis, is very common in the gums.
3. A buccal mucosal carcinoma that might develop in the inner cheek.
4. Carcinoma developed inside hard palate or a roof of the mouth ulcer.
5. Tongue and lip [2]

Oral cavity tumors and oropharyngeal carcinoma can be of many different forms. In the oropharynx, oropharyngeal carcinoma first appears. This is the area directly behind the mouth in the throat.

There are, in general, 3 categories:

Benign growths: it is not much of a cancer. They do not spread to other areas of the body or impact other tissues. Pre-cancerous conditions termed dysplasia, which are innocuous growths that can progress into cancer over time. Unusual growths, known as cancer tumors, have the ability to invade neighboring tissues and other regions of the body [3].

Every patient with oral cancer is different. In medical terms, this type of cancer is mainly divided into the following types:

Oral Squamous Cell Carcinoma (OSCC): In about 90% of cancer cases, squamous cells lining the mouth and throat are visible. It may arise from aberrant squamous cell mutations. A patch of white and red inside the lips and mouth is indicative of this kind of malformation.

Verrucous carcinoma: This kind of tumor makes up roughly 5% of all tumors and grows slowly. It may infect adjacent tissues, , but it does not often spread.

Minor salivary gland carcinomas: The small salivary glands that border the inside of the mouth and throat may develop them.

Lymphoma: It could appear in immune system tissue called lymph tissue.

Tumors that arise in the oropharynx and oral cavity that are benign include fibromas, leiomyomas, papillomas, rhabdomyomas, and many more.

Leukoplakia and Erythroplakia are cancers characterized by the formation of abnormal cells in the mouth and throat. Precancerous stages are reached by 25% of leukoplakia and approximately 70% of erythroplakia. A section exhibiting erythroleukoplakia has red and white patches [4].

Oral submucous fibrosis (OSF) is a chronic oral disease brought on by submucosal tissue fibrosis and swelling. Eventually, rigidity is the cause of the mouth's inability to open [5].

There are basically four stages of oral cancer displayed in Figure 2: [6]

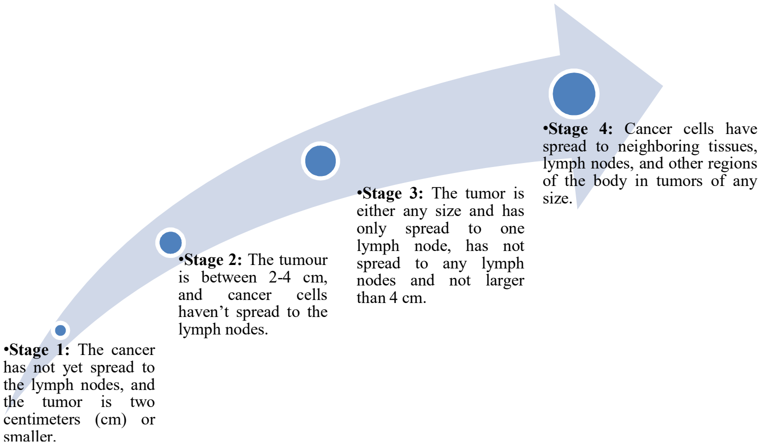

Figure 2. Oral cancer stages

As of late, the most dependable technique for identifying these lesions is the Clinical Oral Examination (COE), which involves the widely accepted process of a skilled visual examination and biopsy. The gold standard for diagnosing oral cancer is a biopsy; however, because of its invasive nature, the lack of knowledge at the point-of-care, and the significant discrepancies in practitioner diagnoses, it is frequently not the best option as a screening tool. An objective point-of-care oral screening approach is therefore urgently needed. Many forms of mouth cancer spread to the cheeks, lips, tongue, and other regions of the mouth, including the floor and surface, due to dangerous cells in the mouth area developing out of control. This causes swelling in the places that have been eroded, red or white patches in the mouth, and soreness and tenderness. Primitive diagnosis contributes significantly to reduced mortality rates and functional loss, both of which result in severe loss and a terrible quality of life. There are several ways to identify oral cancer early on, such as by taking samples from the affected area or using non-invasive approaches [7]. Many scientists have worked on techniques to detect cancerous cells in many kinds of samples.

After the invention of Artificial Intelligence techniques, researchers have applied Machine Learning as well as Deep Larning to different types of diagnosis for cancer tissue detection in a reliable manner. Deep Learning and CNN (Convolutional Neural Networks) are now frequently used mainly in medical imaging, which will help the medical field connect with IT and get non-invasive disease detection at an early stage. There are some alternative tests that are non-invasive but use optical diagnostic equipment. This literature review focuses on the machine and deep learning techniques applied to dental diseases in recent years.

2 Literature Review

2.1 Research Based on X-ray and Biopsy Microscopic Images

Biopsy sample collection is an uncomfortable procedure that requires a high-definition imaging instrument. In addition, the analysis of MRI and X-ray pictures takes a lot of time. There is a great need for restricted surface area and non-invasive equipment that may be completed faster without requiring tedious procedures. Because the disease-specific indicators used in biopsy-based histopathological image categorization are imprecise, they require frequent updating. Andrew E. Heidari and his colleagues have distinguished between normal and pathological head and neck mucosa tissues using OCT (Optical Coherence Tomography) pictures. They received 100% sensitivity and 70% specificity from CNN, respectively. After all, the removal of mucosal tissues makes this procedure invasive [8].

In their most recent application of CNN, Bibek Goswami et al. were able to determine normal and different phases of oral submucous fibrosis using microscopic images of stained biopsy samples acquired from the oral department and images taken under a microscope, with an overall accuracy of 99.4%. There are 100 photos in the dataset. This process's drawback is that it cannot identify cancer in its extremely early stages [9]. Using the given dataset (290 normal and 934 OSCC images), Ibrar Amin and his colleagues have employed histological images to distinguish between oral squamous cell carcinoma (OSCC) and normal. The paper offers three deep learning models for evaluating oral biopsy images: Resnet50, InceptionV3, and VGG16. The combined model performed better than the separate models, attaining 96.66% recall, specificity, accuracy, and precision. With only 120 photos available for assessment, this study's tiny and unbalanced OSCC dataset-which included 934 malignant patients and 290 normal instances—might not be the best choice for practical use [10]. RutwikPalaskar et al. employed massive CNN and transfer learning with InceptionNet V3, ResNet, and MobileNet. They were able to obtain an AUC of 0.75 with ResNet and 83.66% accuracy with InceptionNet. Using a big CNN yields worse results, while gathering higher-quality images takes longer [11]. Others have obtained less than 6% of losses by extracting cancer cell images based on their morphological features using CNN and predefined networks with a novel approach.

2.2 Using Different Algorithms

Additionally, algorithms such as GLCM and Feed Forward Neural Network (FNN) are used to forecast the occurrence of oral cancer. Using FNN in Matlab, N. Kripa et al. created the DSS (Decision Support System), which can diagnose oral squamous cell cancer with 90% accuracy. They have identified photos that are malignant and normal; however, they do not state how many photographs made up the input sample size [12]. The best results were obtained by adding more methods, such as the Cox proportional hazard model (CPH), the multi-layer feed-forward network, and comparing them with random survival forest (RSF) and DeepSurv, an open-source Python package based on prediction. These methods led to predictions that were 81% more accurate. The algorithm's potential has been evaluated by applying it to patients who have undergone surgery at various stages [13].

In addition to varying algorithms, the most recent deep learning trend has also been tested on a variety of cancer tissues, including oral tissue.

2.3 Machine Learning and Deep Learning

Images obtained from the electromagnetic spectrum using hyperspectral imaging (HSI) essentially process each pixel. For the purpose of identifying organs at risk, hyperspectral imaging (HSI) is widely utilized. In order to classify oral cancer filtering into HSI images, Pandia Rajan Jeyaraj and his colleague used a deep CNN regression-based algorithm. They compared their results with SVM and DBN methods and obtained 91.4% accuracy [14]. Using majority voting of chosen features and spanning trees, they also increased the sensitivity and mixed pixel detection on the same hypercube dataset and raised their accuracy to 94.75% [15].

Some have worked with specific tissues in addition to recognizing the overall structure of the tissue. Chronic physical stress and smoking can lead to elevated levels of keratin, a biological protein found in mucosal epithelial layers. In OSCC, keratin content is less than 20%. Devkumar Das et al. used deep CNN with several layers on 10 pictures of oral tissue histopathology slides that had keratin in them to find that level. The segmentation accuracy obtained varied, with an overall 96.88%. One can tell the difference between the regular keratin structure and the pearl keratin structure, which is already present in OSCC, using a random forest tree classifier that is based on Gabor texture characteristics [16]. The nucleus from oral tissue histology images, which are used in the diagnosis of OSCC, was also described by the same individual and his associates. They proposed a two-step computer-aided tool for automatic detection of the detected nucleus, which is in the second stage of OSCC diagnosis. In order to do this, they downsampled and used CNN on randomly chosen patches (81*81) from the original RGB images that showed parts of the nucleus, which is a part of cells [15]. This approach showed promising results in accurately identifying the presence and characteristics of OSCC.

Rajaram Anantharaman et al. limited their scope to cold sore and canker sore, which are types of oral implications caused by Herpes simplex virus type 1 (HSV-1). The images they have collected are from the public domain and limited to 40. They applied the Mask-RCNN model, which was developed in 2017, and extended the Faster-RCNN model for semantic segmentation, achieving a pixel accuracy of 74% [17].

Using different types of images is not useful in real-time detection of such diseases, and delaying treatment may cause major issues related to health. For that, there are many such instruments developed to get real-time images of oral cancer.

Marco Mascitti et al. have conducted surveys of the various tools used in the examination of oral cancer. The ViziLite R, manufactured by Zila Pharmaceuticals in Phoenix, AZ, is a chemiluminescence-based diagnostic tool that uses light with a wavelength of 430–580 mm to help in the early diagnosis of PMD and OSCC. This device's high percentage of false-positive and false-negative tests is its main drawback. The primary oral examination tool is called Identafi, and it has three distinct light sources with varying wavelengths. GOCCLES is an inexpensive, user-friendly tool that may be used with any dental curing light to identify anomalies in autofluorescence within the oral cavity. Although these tools work effectively, their usage is restricted to practitioners with extensive training in oral pathology due to their non-negligible inter observer variability [18].

Another study by Navarun Das et al. used oral biopsy images, the CNN model and, transfer learning to do a multi-class classification of OSCC. There are pre-trained networks used, such as Alexnet, VGG-16, VGG-19, and Resnet-50, with multiple layers, and they were compared with the proposed CNN model, which gave an accuracy of 96.6% for 50 epochs. There is no real-time decision support system provided, and the images used are also of biopsy [19].

Various techniques on biopsy images has been stated in Table 1.

Table 1. Summary of detection techniques and its analysis

Type of Detection	Techniques	Advantages	Disadvantages
OPG, OCT, CLE, X-ray, and Cellular image dataset	CNN, ResNet, VGG, Random forest and SVM	Non-invasive techniques used	This kind of image gathering involves expensive technology, professionals, and data limitations because of ethical constraints
Biopsy microscopic images	CNN, 2DCNN, 3DCNN, AlexNet and VGG-16	This method is more accurate than others	Invasive in nature, early-stage detection is not possible due to stained samples
Histopathological slide images and HIS imaging	Deep learning, SVM DBN methods	Precise as on pixel detection	Invasive in nature

2.4 Images taken by a mobile camera

Some researchers are ignorant of how images can be presented and processed in the medical field because the majority are not up-to-date on the latest imaging techniques. Because of this, the researchers have employed a range of data, such as tissues, microscopic photos, and datasets. Several recognized approaches are available for the examination of pictures of the oral cavity.

To detect oral cancer, Bofan Song et al. have used hybrid dual-model imaging in conjunction with autofluorescence and white light imaging. The first pictures were taken with an Android phone and an external peripheral intraoral attachment LED. A success rate of 86.9% was reached using transfer learning, data enhancement of the VGG-CNN-M module with 4-fold cross validation, and the open-source toolkit MatConNet [20]. There is no coverage of multi-stage performances, and there was an overfitting problem due to the small image size.

The majority of the researchers using this data set are working with medical images.However, Shah R et al. have used the public domain, differentiated two types of oral cancers (Leukoplakia and Erythroplakia), and compared the results of CNN and pre-defined networks [21]. The same researchers looked at pictures to find diseases automatically on binary and multiclass datasets using CNN architecture, stratified K-fold validation, and transfer learning in a different study.The proposed CNN architecture achieves F1 scores of 84%, 78%, and 87% for hygienic mouths or ulcers, and 83%, 87%, and 84% for normal mouths, ulcers, and leukoplakia, respectively. The idea is to classify ulcers, healthy mouths, and precancerous type "Leukoplakia" using non-invasive techniques, hence diagnosing patients without the need for them to see a physician [22]. Roshan Alex and his colleagues then went one step further, applying the Bounding Box Method to composite annotations created by combining annotations from multiple clinicians and further applying transfer learning to multiple images, yielding encouraging results [23].

Some have applied pre-defined network weights to classification tasks using transfer learning on photos. Eman Shawky Mira et al. used HRNet-W18 and CNN to achieve 96.6% specificity, 84.3% accuracy, and an 83.6% F1 score by differentiating between Aphthous ulcer, low-risk OPMD, high-risk OPMD, and oral cancer on 232 patient-captured photographic images. However, they used a smaller dataset, and the quality of the smartphone camera is also not mentioned [24]. Santisudha Panigrahi et al. achieved 96.6%, precision and recall of 97% and 96%, respectively, using deep transfer learning to categorize histological pictures of OSCC, focusing on normal mucosa and malignant cases. They have used transfer learning with pre-defined networks such as VGG16, VGG19, ResNet50, InceptionV3, and MobileNet. Here, changes in the photos are handled by using more hierarchical models. Despite this, they were limited to using histopathology pictures [25].

Based on photographic images, Wenjing Wang et al. have employed a more recent kind of algorithm to distinguish between cancer and noncancer from the Kaggle dataset. They achieved an F1 score of 94.65%, a Matthews Correlation Coefficient of 94.65%, an accuracy rate of 97.71%, and a sensitivity rate of 92.37%. Despite using numerous techniques, such as combined group teaching optimization algorithms and deep belief networks, they were only able to distinguish between cancer and non-cancer types [26].

A predefined network is essential to deep learning.Using weights from CNN and VGG16, VGG19, Alexnet, ResNet50, ResNet101, Mobile Net, and Inception Net, Madhusmita Das et al. distinguished between Normal and OSCC on 1224 histological images from the collection. The accuracy values for Alexnet, Resnet50, ResNet101, Mobile Net, and Inception Net were, 0.88, 0.91, 0.89, 0.93, and 0.92 respectively. The result of the 10-layer CNN is 0.97. The study's principal benefit is its ability to quickly distinguish between normal and OSCC types of cancer; nevertheless, it was limited to primary cancers [27].

To shorten clinical times, more sophisticated procedures are employed for photographic images. OPMD and OSCC are the two main cancer forms that Kritsasith Warin et al. distinguished from 980 oral cancer photo images. Using CNN, pre-trained networks, and faster R-CNN, they were able to obtain AUC values of 0.98 for OPMD and 1.0 for OSCC. They covered a bigger dataset, and the outcomes are satisfactory [28]. The annotation's primary disadvantage is that it was only made feasible with the assistance of surgeons. Additionally, by employing Mask R-CNN with pre-defined networks, Tanriver Gizem et al. wereable to distinguish between benign, OPMD, and cancer on 162 photos from hospitals and the public-domain, achieving an 86% to 90% F1 score. Various CNN models have been utilized. The photographs in this dataset are from public domain sources [29].

The comparison of these techniques and their results is displayed in Table 2.

Table 2. Comparison of techniques applied to camera images by researchers

Algorithm	Accuracy	Advantages	Drawbacks
CNN, Stratified k-fold validations and Transfer learning	CNN F1-score 74%-87%, Stratified K-fold validation F1-score 77%-97%, Transfer learning F1-score 73%-98%	Binary and Multi class classification	Smaller dataset and not real time images
HRNet-W18 and CNN	83.0% sensitivity, 96.6% specificity, 84.3% accuracy, and 83.6% F1 Score	Covered multiple types of cancers	Smaller dataset and the quality of smartphone camera is also not mentioned
Transfer Learning with VGG16, VGG19, ResNet50, InceptionV3, and MobileNet,	96.6%, precision and recall values 97% and 96%	Used more general models to handle variations in images	Images used are histopathological which are time consuming
ANN, Bayesian, CNN, GSO-NN, and End-to-End NN	Precision rate :97.71%, sensitivity rate : 92.37%, Matthews Correlation Coefficient : 94.65%, and F1 score 94.65%	Used different approach like Deep belief networks and Combined group teaching optimization algorithm	Only cancer and noncancer differentiation
CNN and VGG16, VGG19, Alexnet, ResNet50, ResNet101, Mobile Net and Inception Net.	Net accuracy of 88%, 91%, 89%, 93% and 92% respectively for AlexNet, Resnet50, ResNet101, MobileNet and InceptionNet, 10 layer CNN 98%	quick detection of normal vs OSCC type of cancer	focused on primary type of cancer only
CNN and pre-defined networks	Accuracy: 83.54%, F1 score 87% and 78%	Able to cover different types of cancer	Smaller dataset and not real time images
CNN, pre-trained networks and faster R-CNN	AUC 1.0 for OSCC and 0.98 for OPMD	Covered large dataset and results are good	Annotation could only be possible with the help of surgeons
Mask R-CNN with pre-defined networks	86% to 90% F1 score	Different type of CNN models has been applied	dataset is small and images are taken from public domain
Faster R-CNN and Mask R-CNN	Binary class: 87.07% and 78.30%, Multi class: 41% to 66%	Covered risk of oral cancer	Results are less in terms of F1 score

References	Author	Year	Type of tumor	Dataset	Types of images
[21]	Shah R et al.	02-2024	Normal vs Ulcer, Normal vs Ulcer vs Leukoplakia	505 images	Photographic images
[24]	Eman Shawky Mira et al.	12-2023	Aphthous ulcer, low risk OPMD, high risk OPMD and oral cancer	232 patient captured images	Photographic images
[25]	Santisudha Panigrahi et al.	02-2023	Oral Squamous Cell Carcinoma (OSCC)	1035 sample patches of normal mucosa (Benign) and 1154 sample patches of OSCC (Malignant) cases	Histopathological images
[26]	Wenjing Wang et al.	07-2023	Cancer and noncancer	Kaggle dataset	Photographic images
[27]	Madhusmita Das et al.	01-2023	Normal and OSCC	1224 histopathological images from repository	Histopathological images
[22]	Shah R et al.	07-2022	Leukoplakia and Erythroplakia	550 images	Photographic images
[28]	Kritsasith Warin et al.	08-2022	OPMD and OSCC	980 oral cancer images	Photographic images
[29]	Gizem Tanriver et al.	06-2021	Benign, OPMD and carcinoma	162 images from public domain and hospital	Photographic images
[23]	Roshan Alex welikala et al.	07-2020	Risk of OPMD	2155 images of oral mouth	Photographic images

While several methods have been employed by researchers to identify various forms of malignant tissues in the mouth, a basic diagnostic tool ought to be created so that patients can be informed about when to see a physician and whether or not an ulcer can progress to a precancerous lesion.

3 Challenges and Future Outcomes

This kind of research could provide several difficulties. Getting real-time photos will be the main difficulty facing the researchers. Patient privacy and medical ethics may permit this to happen. Many people remain untreated because there are insufficiently skilled diagnostic tools and doctors in many places, especially in developing and/or remote areas. Many cancer patients consequently went without medical attention. Deep learning and non-invasive methods can be used in future research to help provide a risk analysis for various types of oral cancer. It might result in the creation of clinical applications that give patients access to initial recommendations.

4 Conclusion

Depending on the stage of oral cancer, there are different effects on oral health. Researchers have used a range of methods, with the highest accuracy ranging from x-ray imaging to pap-smear biopsies to smartphone photos. Deep learning, a modern technique, has also been applied, and on such images, it performed well for early predictions of such malignant lesions. Given the current situation and the limits of predicting oral cancer, a non-invasive instrument that can aid with mouth region detection, which is expensive and requires expert observation, is desperately needed. In addition, there is little chance that the methods used up to this point for detecting oral cancer will be able to distinguish between different types of oral cancer and regular ulcers in terms of early diagnosis. Determining the extent of the spread of oral cancer without considering radiological and his to pathological pictures is also necessary. More attempts should be made to design powerful AI systems that can overcome the issue of limited dataset availability, and there is an immediate need to develop a specific framework incorporating all of the models that can be utilized to do classification tasks. Moreover, the application of such frameworks is necessary prior to deploying them in everyday prognosis practice as a clinical assistant to provide another viewpoint to the doctor. Deep learning algorithms have the capacity to improve the quantity of clinical data available and create a valuable tool for accurately identifying oral cancer and its subtypes. Future research should focus on the overall outcome with the use of deep learning models to help improve the accuracy of early-stage oral cancer diagnosis and its type. This will allow professionals to treat the condition quickly.

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