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A Convolutional Neural Network Based Deep Learning Algorithm for Identification of Oral Precancerous and Cancerous Lesion and Differentiation from Normal Mucosa: A Retrospective Study

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Abstract

Oral cancer is the sixth most common cancer associated with high diseases related mortality. The prime reason is that more than two-thirds of patients are diagnosed at later stages of cancer. The majority of oral cancers are preceded by noticeable changes in the oral mucosa known as oral potentially malignant disorders (OPMDs). Early diagnosis of OPMDs can elude cancer development in 88% of cases. Artificial intelligence (AI) has gained popularity in the field of medicine including oncology and has shown efficacy in the diagnosis and prediction of cancer prognosis. In the present study, pre-trained convolutional neural networks (CNNs) are used for identifying oral pre-cancerous and cancerous lesions and to differentiate them from normal mucosa using a dataset of clinically annotated photographic images. This study was conducted on clinical photographs of patients who presented with oral squamous cell carcinoma and OPMDs. A comparative analysis of these photographs was done with photographs of the normal oral mucosa. Transfer learning using various pre-trained CNN architectures was employed for image classification. An accuracy of 76% for VGG19, 72% for VGG16, 72% with MobileNet and 68% for InceptionV3, and 36% with ResNet50 was obtained. In the present study, VGG19 exhibited good performance when compared to other models.

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1. Introduction

Oral cancer encompasses all the malignant lesions of the lip, buccal mucosa, hard palate, floor of the mouth, gingiva, and anterior two third of the tongue.[1] It is the sixth most common cancer worldwide associated with high disease-related mortality and morbidity rates.[1] Global Cancer Statistics 2020 reported 377,713 new cases and 177,757 new deaths in 2020 making it a global health issue.[2] Despite various emerging treatment modalities, the overall mortality rate has not reduced and the prognosis remains poor with a five-year survival rate of 28-67%.[3] The prime reason for the aforementioned being more than 2/3rd of patients are diagnosed at later stages of cancer.[4] The probable causes for the late diagnosis include lack of early screening, public awareness, and knowledge among healthcare workers.[4]

The majority of oral cancer cases are preceded by noticeable changes in the oral mucosa termed oral potentially malignant disorders(OPMDs).[4,5] These usually present as non-scrapable white plaques, red patches, mixed red and white areas, and chronic ulcerations.[1] Early diagnosis and management of OPMDs can elude cancer development in 88% of cases. Also, early diagnosis of cancerous lesions can lead to a down-staging of the disease and mortality rate reduction.[4-6] Oral cavity unlike other organs is a very accessible site for detailed examination nevertheless, the conventional

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examination occasionally fails to differentiate between benign and OPMD lesions.[7] Therefore, with the increasing burden of oral cancer especially in low-income countries, designing a cost-effective and sensitive screening diagnostic tool is the need of the hour.[4] A practicable and sustainable solution would be the use of technology. Previous studies have shown good agreement with images using telemedicine and WhatsApp in clinical diagnosis and remote screening of OPMDs in comparison to conventional examination and analysis.[8-10] Inclusion of an automated detection system linked to artificial intelligence (AI) to telemedicine tools in the identification of OPMDs and the cancerous lesion can be notably beneficial.[4]

Over the last decade, artificial intelligence has gained popularity in the field of medicine including oncology. It has shown efficacy in the diagnosis and prediction of cancer prognosis. AI uses machines to mimic cognitive functions like humans.[3] Studies have shown the use of the convolutional neural network (CNN) such as AlexNet, GoogLeNet, MobileNet, VGG19, VGG16, InceptionV3, ResNet50, and SqueezeNet architecture in the diagnosis and classification of skin cancers as well as lung, breast and colon cancers and reported promising results.[11-23] Deep learning techniques have also outperformed human experts in identifying subtle visual patterns in photographic images[3,13] A few studies in the literature have developed AI-based algorithms for the diagnosis of Oral Squamous Cell Carcinoma (OSCC), with most of them using standardized images such as multidimensional hyperspectral images,[14] laser endomicroscopy images,[15] computed tomography images,[16] histological images,[17] and Raman spectra images.[18] However, there have been very few studies using photographic images,[7,19–23] with the majority of them focusing on identifying specific types of oral lesions. The feasibility study performed used pre-trained convolutional neural networks for identifying oral pre-cancerous (potentially malignant) and cancerous lesions and to differentiate them from normal mucosa using a dataset of clinically annotated photographic images.

2. Methodology

2.1 Data collection

This study was conducted by retrospectively collecting clinical oral photographs from the archives of the Department of Oral Medicine and Radiology and the Department of Oral and Maxillofacial Surgery from 2016 to 2021. Photographs retrieved included biopsy-proven oral squamous cell carcinoma cases (OSCC), oral potentially malignant lesions, and normal mucosa. Blurred images, images with shadows of other oral structures, and images of the same lesion with different angulations and orientations were excluded from the study sample. The photographs were labeled as ‘normal mucosa’, ‘OPMD’, and ‘OSCC’ based on the corresponding pathologic report. As the images were taken at different angulations and magnifications, they were manually cropped and resized. However, no manipulation was done concerning the contrast, saturation, and brightness of the images. The study was performed after obtaining the Institutional Ethics Committee clearance (IEC: 667/2020). A total of 329 images including 106 normal images, 102 OPMD images, and 121 OSCC images were used.

2.2 Method

Transfer learning using various pre-trained CNNs was employed for image classification. This approach facilitates the use of the knowledge acquired by pre-trained CNNs which are trained using a large number of non-medical data. The top layers of the pre-trained CNNs were removed and replaced with new layers as shown in Fig. 1. Bottom layers were frozen and newly added layers were fine-tuned using a new dataset until optimum performance is achieved.

Pre-trained CNN architecture namely MobileNet, VGG19, VGG16, InceptionV3, and ResNet50 were considered for experimentation using transfer learning. The model summaries of these CNNs are shown in Figs. S1 to S5.

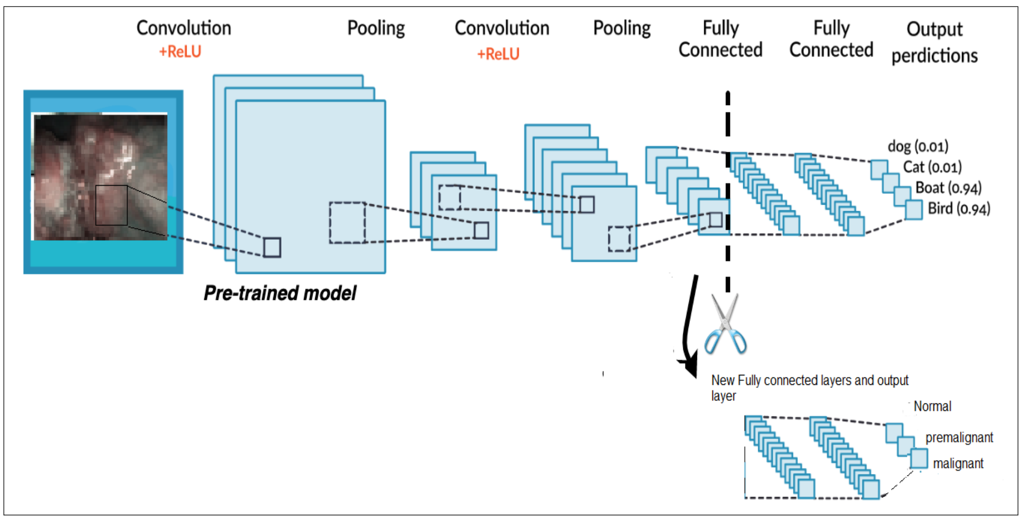

Fig. 1 Image classification using Transfer learning of the pre-trained CNN.

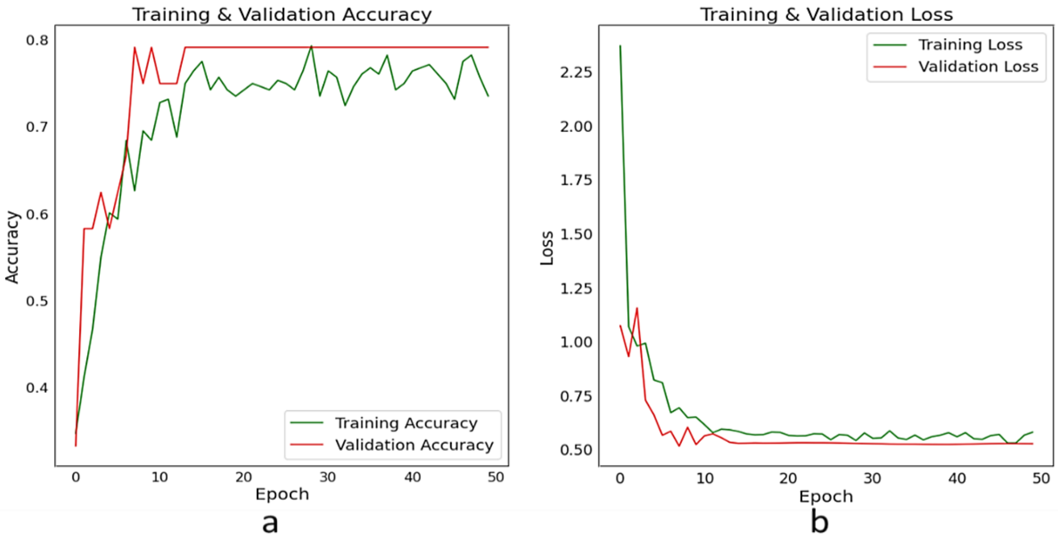

Fig. 2 VGG19 Training and Validation for each epoch (a) Model accuracy (b) Model loss.

All these CNNs were trained on ImageNet which is a dataset with 1.2 million images belonging to 1,000 classes.[24] The final dense layer of these CNNs was replaced with a new dense layer having three neurons which correspond to the number of classes in the application considered. 85% of the data were used for training the CNN's and 7.5% each for validation and testing. Training images were augmented by using random flipping, image zooming, and image rotation operations. During training, CNNs were trained for 50 epochs with a batch size of 16 and a learning rate of 0.001. The performance of these CNNs was compared the network with the best performance was selected.

3. Results and discussion

Experimentation was executed in a system with a Tesla 1xK80 graphics card. CNN's training was implemented in Google Colab using Python3 Tensorflow version 1.15.2. Classification accuracies for test images of different pre-trained networks are listed in Table 1.

Table 1. Classification accuracies of different pre-trained models.

Pre-trained CNN	Accuracy
VGG19	76%
VGG16	72%
MobileNet	72%
InceptionV3	68%
ResNet50	36%

VGG19 exhibits the best accuracy of 76% in comparison to other networks. A plot showing training and validation accuracy and loss for each epoch for VGG19 is shown in Fig. 2. From the learning curves of VGG19 for training and validation (Fig. 2), it can be observed that the VGG19 exhibits good learning as the gap between the training and validation loss curves is small. The per-class basis classification report of VGG19 is listed in Table 2. Table 2 shows the classification metrics precision, recall, and F1-score on a per-class basis. Precision indicates the ability of CNN to not label a normal image as malignant/pre-malignant. Recall indicates the ability of a classifier to find all positive instances. The correctness of positive predictions is indicated by the F1- score. Several instances used under each class for testing are indicated by support.

Table 2. Per-class basis classification report of VGG19 architecture.

Class	Precision	Recall	F1-score	Support
Malignant	0.6	0.43	0.5	7
Normal	0.9	1	0.95	9
Pre-malignant	0.7	0.78	0.74	9

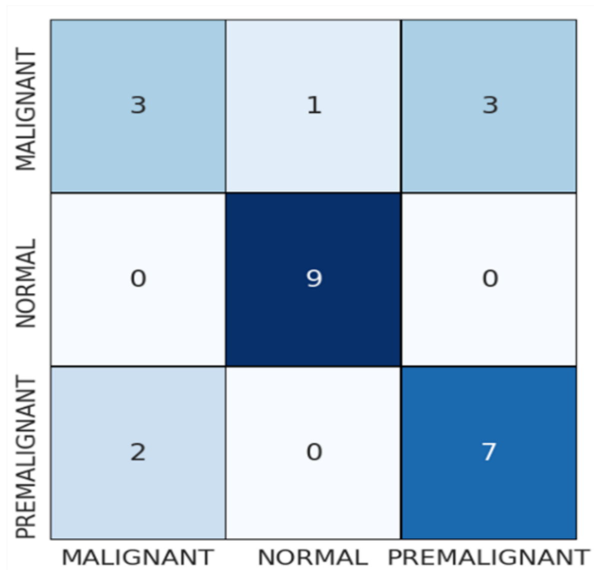

Fig. 3 Confusion matrix for VGG19 architecture.

A confusion matrix is a tabular way of visualizing the performance of a CNN (Fig. 3). It is used to obtain the comparison between actual and predicted classes. As depicted in Table 2, the number of images (indicated by support) under the malignant class is 7. Considering the first row of the confusion matrix, out of 7 malignant images, 3 were correctly classified as malignant, one of the images is classified as normal, and 3 images as pre-malignant.

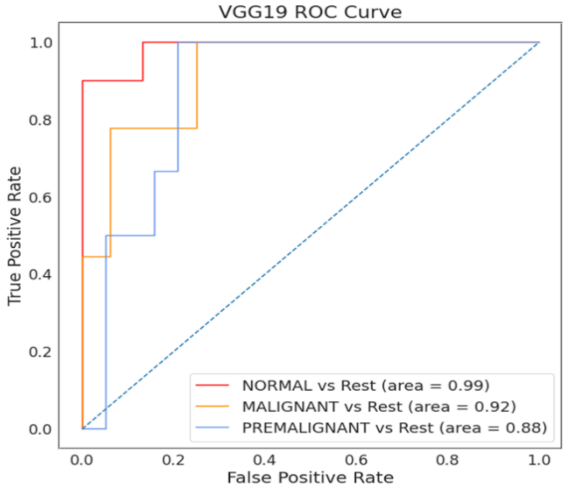

Fig. 4 ROC curve of VGG19 architecture over its operating range.

The receiver operating characteristic (ROC) curve, which is a plot of the false positive rate (x-axis) versus the true positive rate (y-axis) for several different candidate threshold values between 0.0 and 1.0 for VGG19 is shown in Fig. 4.

ROC curves can be used to assess the performance of the classifier over its entire operating range. The most widely-used measure is the area under the curve (AUC). An AUC of 0.5 indicates no discrimination, 0.7 to 0.8 is acceptable, 0.8 to 0.9 is excellent, and more than 0.9 is outstanding. A plot showing training and validation accuracy and loss for each epoch for VGG16 architecture is shown in Fig. 5.

From the learning curves of VGG16 for training and validation (Fig. 5), it can be observed that the gap between the training and validation loss curves is slightly more than VGG19.

A plot showing training and validation accuracy and loss for each epoch for MobileNet architecture is shown in Fig. 6. It can be observed from the learning curves for MobileNet architecture in Fig. 6, that both training and validation loss is improving, but there is a large gap between the two curves. This indicates that the model is overfitting and the training dataset lacks sufficient information to learn the problem in comparison to the validation dataset used to evaluate the problem.

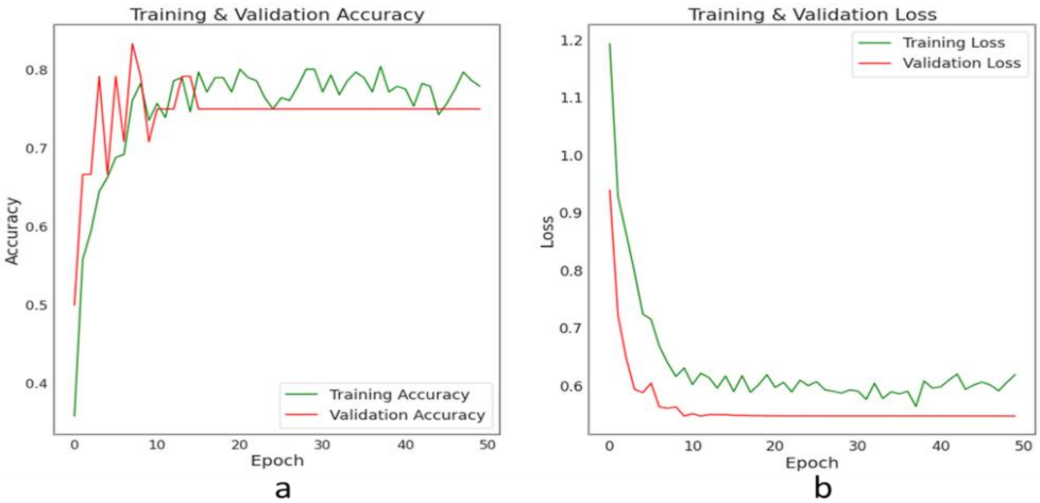

Fig. 5 VGG16 Training and Validation for each epoch (a) Model accuracy (b) Model loss.

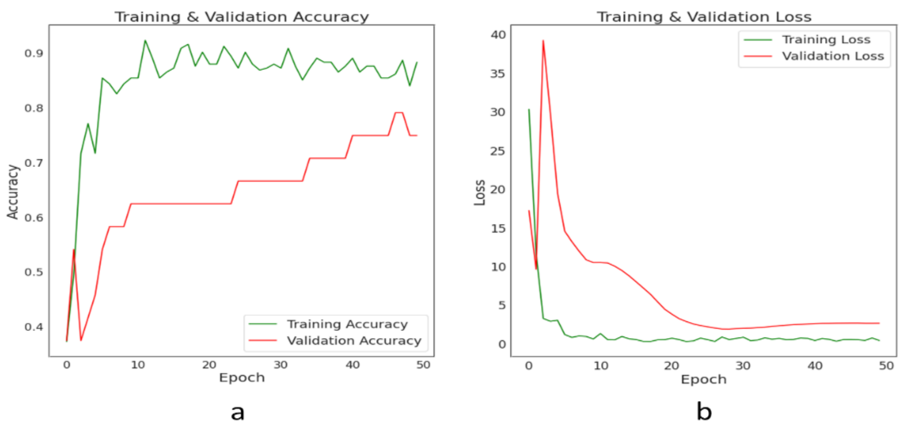

Fig. 6 MobileNet Training and Validation for each epoch (a) Model accuracy (b) Model loss.

Fig. 7 InceptionV3 Training and Validation for each epoch (a) Model accuracy (b) Model loss.

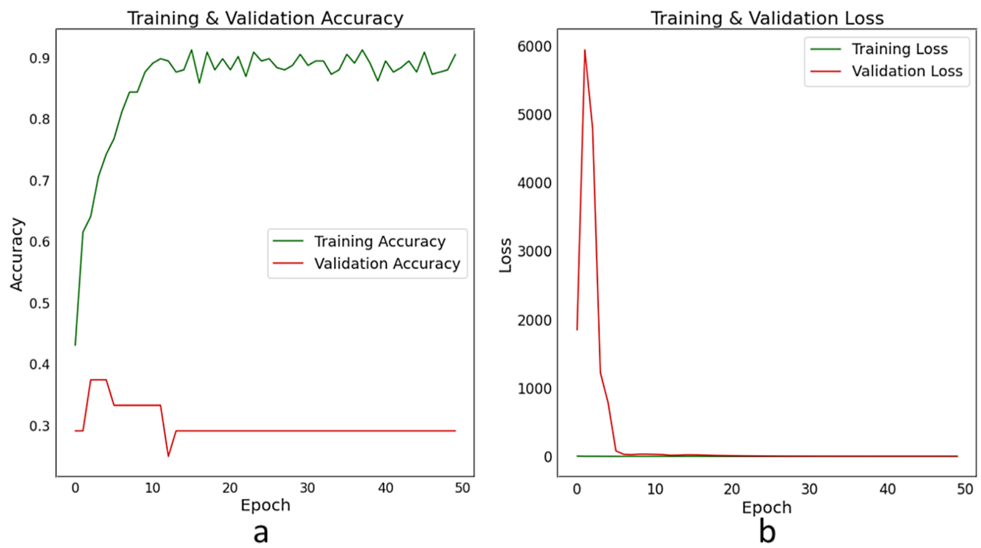

Fig. 8 ResNet50 Training and Validation for each epoch (a) Model accuracy (b) Model loss.

The learning curves of InceptionV3 and ResNet50 are shown in Fig. 7 and Fig. 8, respectively. It can be observed from the learning curves that both models overfit and need more data for better generalization.

Confusion matrices for MobileNet, VGG16, InceptionV3, and ResNet50 are shown in Fig. 9. It can be observed that normal cases are classified almost correctly by all CNNs. Misclassification occurs in the other two classes. This may be due to the overlapping of visual features in the images belonging to malignant and premalignant classes.

The ROC curve for MobileNet, VGG16, InceptionV3, and ResNet50 are shown in Fig. 10. All of the networks, except ResNet50, perform remarkably well in classifying images into various categories, as seen in Fig. 10.

In future work, these networks can be trained using more images to improve performance. A trained network can be saved and deployed as a mobile application embedded in an android device, which will analyze the acquired images to get instant results.

Computerizing the cancer screening process using artificial intelligence and its subtypes is a beneficial and reasonable approach to the management of oral cancer. This study assessed the accuracy of classifying clinically annotated smartphone and camera-captured photographic images in comparison to gold standard-biopsy reports. Pre-trained CNN models namely MobileNet, VGG19, VGG16, InceptionV3, and ResNet50 were considered in the present study. Training and testing for each epoch with the model accuracy, model loss, and confusion matrix for the models VGG19, VGG16, InceptionV3, and ResNet50 is shown in Figs. 4-7, respectively. Out of the considered five CNN models, VGG19 exhibited good performance with an accuracy of 76%. The results of the present study are supportive of the development of a low-cost, universally accessible, easy-to-handle mobile application.

Among the multiple reasons for poor prognosis of oral cancer, delay in referrals to cancer specialists is the foremost

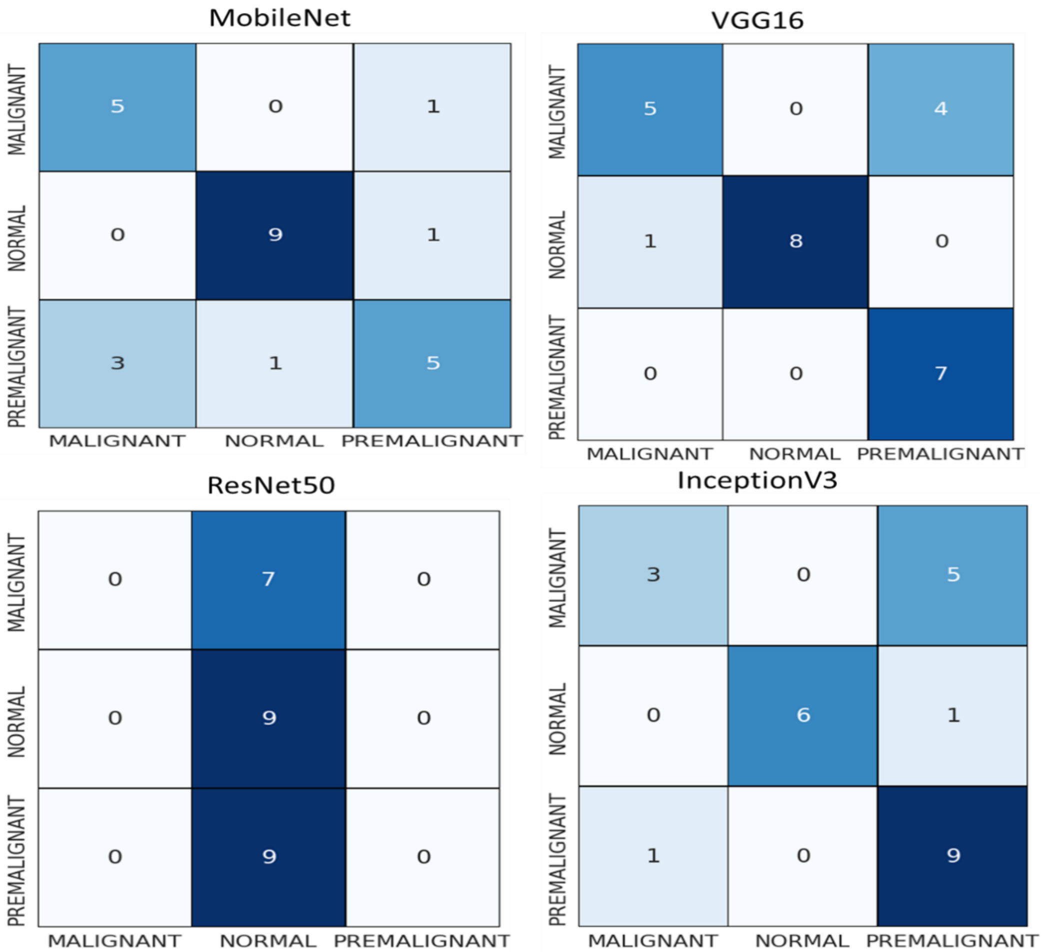

Fig. 9 Confusion matrices for MobileNet, VGG16, InceptionV3 and ResNet50.

causative factor.[6] Lack of awareness and expertise to identify subtle early signs and OPMDs also leads to delays in diagnosis.[1] Even though screening programs by trained healthcare workers have been shown to reduce mortality, they were reported to be less cost-effective, time-consuming, and strenuous.[7] Technological advances like multifactor analysis, conventional logistics, and cox regression models have improved the prediction models in cancer management. Likewise, artificial intelligence and its subfields like machine learning, and deep learning have brought in newer arrays in cancer diagnosis, management, and prognostication of its outcomes.[14]

Machine learning models have helped in the prediction of treatment outcomes in oral cancer.[15] Deep learning techniques are proven useful in estimating tumor infiltration and its prognosis. AI to identify genes related to OSCC has also been developed.[22] Still, there is a paucity of evidence regarding the use of AI in the early identification of OPMDs. Previous studies conducted were site-specific involving only tongue lesions or using histopathological sections.[23] Our study is a novel beginning, wherein the VGG19 algorithm shows good accuracy in differentiating OPMDs from normal mucosa and OSCC using photographic images of different oral mucosal sites.

VGG19 algorithm is a type of convolutional neural network using transfer-learning technology. CNN is a deep learning architecture widely used in image analysis. It is composed of several layers such as convolutional, pooling, activation, and fully connected layer. There are two ways of using deep learning for image analysis; full training and transfer learning. In full training, CNN is designed from scratch, and trained using several images to achieve the required functionality. This type of training needs a large number of the annotated dataset and high computations. In the transfer learning method, CNNs trained on different domain images are tweaked and retrained with images of different domains to achieve a given task. It is used in situations with fewer images and resources with lower computation capacities. Hence, we consider the transfer learning approach of deep learning for the classification of photographic images of the oral cavity into three classes namely normal mucosa, oral potentially malignant disorders, and OSCC. Photographs used in our study are from image-capturing tools like mobile cameras and professional cameras. However, we have to exclude a few images due to the poor quality insufficient for machine learning application. Hence resolution of the camera is one of the key factors in our view. The use of mobile phones as an adjunct is emerging with its increasing application in the field of telemedicine.[25]

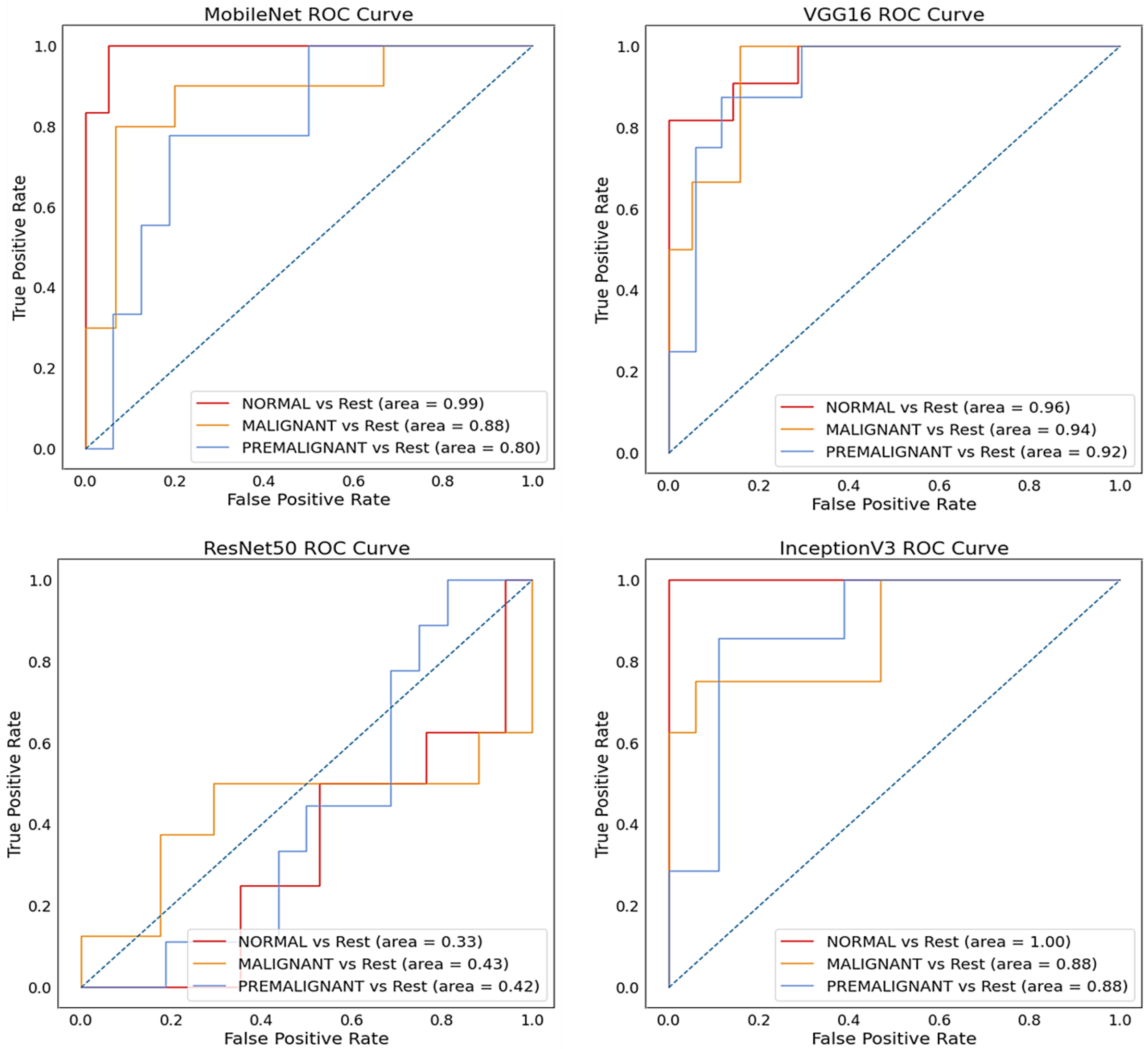

Fig. 10 ROC curve for CNN architecture (a) MobileNet, (b) VGG16, (c) ResNet50, and (d) InceptionV3.

The findings of the present study indicate that the overall performance of CNN developed using the VGG19 transfer model is comparable to CNN developed using conventional models such as VGG19 and ResNet101.[4,21] The maximum accuracy of 76% obtained in our study using MobileNet, in comparison to the previous studies, is better when the amount of study data set are compared (Table 3).

Table 3 summarizes and compares the recent studies, using transfer learning for classification for oral cancer detection. It is observed that images acquired using computed tomography (CT), digital cameras, smartphones, *etc.* are used in the previous studies.[3,4,21,22,25] Although deep learning algorithms can perform classification very efficiently, a large number of datasets are the key to their performance. Imaging modalities such as computed tomography (CT), and magnetic resonance imaging (MRI) are not suited to low-resource settings. Using a smartphone to obtain oral cavity images is very simple and economical. But there is no such large data set available. Hence, there is a requirement for the development of a larger dataset of annotated photographs of the oral cavity for developing an efficient algorithm. In addition, the basic ground truth types used for algorithm development differ in the various literature. CNNs provide the best performance in previous studies among which many have a less number of layers indicating the need for lightweight networks. Such types of networks are also useful when deploying them as a mobile application to be embedded in android devices.[3,4,21,22,25,26]

It can be observed from Table 3 that CNNs outperform when the number of images used for learning is increased. The present study obtains lower results than the published results due to this reason. Also, the quality of the images, clarity of features, and type of ground truth used to play a major role in the performance of the network. It can be observed that Shamim *et al.*[21] obtained an accuracy of 97% despite using only 300 images. The researchers used images of the different oral tongue lesions in which features were very distinct visually and an expert annotation as ground truth. Features of premalignant and malignant images were visually not distinct. The biopsy-verified diagnosis was considered as ground truth in the present study. This may be the reason for lower accuracy when compared to the accuracy obtained by Shamim *et al.*[21]

Table 3. Summary and comparison of studies using pre-trained CNN models.

Author	Pre-trained CNNs used for experimentation	Number of images	Image type	Ground Truth	CNN which provided the best result	Results
Xu *et al.*[22] 2019	2D CNN 3D CNN	7,000	CT images of early oral cancer	Lableme software	3D CNN	Accuracy: 75.4% Sensitivity: 81.8% Specificity: 73.9%
Welikala *et al.*[4] 2020	ResNet-101	2155	Oral cavity images acquired using smartphones	Expert in the field of Oral Medicine	ResNet-101	Precision: 84.77%, Recall: 89.51% F1 score: 87.07%
Shamim *et al.*[21] 2020	AlexNet, GoogLeNet, Vgg19, ResNet50, Inceptionv3 SqueezeNet	300	Images of the different oral tongue lesions downloaded from the internet	Expert in the field of Oral Medicine	ResNet50	Accuracy: 97% Sensitivity: 89% Specificity: 97%
Jubair *et al.*[3] 2021	EfficientNet-B0 VGG19 ResNet101	716	Tongue images acquired using digital cameras and smartphone	Expert in the field of Oral Medicine	EfficientNet-B0	Accuracy: 85% Specificity: 84.5% Sensitivity: 86.7%
Tanriver *et al.*[25] 2021	ResNet-152, DenseNet-161, Inception-v4, EfficientNet-b4	684	Photographic images of oral lesions	Expert oral pathologist	DenseNet-161	Precision: 87.9%, Recall: 84.1% F1 score: 84.4%
Present Study	MobileNet VGG19 VGG16 InceptionV3 ResNet50	329	Oral cavity images acquired using smartphones	Biopsy	VGG19	Accuracy: 76%

despite using a comparable number of images.

4. Conclusions

The novelty of the present study lies in the non-restricted sample size and the dataset consisted of lesions from the tongue, labial mucosa, and buccal mucosa and compared them with their biopsy reports (gold standard). The present study demonstrated the performance of CNN models in identification and classification comparable to a biopsy report. Although the limitation of the present study is the small dataset, studies in the past have suggested that a greater amount and variety of data can further strengthen CNN models. Further study demands more evidence from different lesions and different oral sites to automate the identification of potentially malignant oral disorders and OSCC. This work is a progressive step towards obtaining a cost-effective and accurate oral cancer screening tool.

5. Future scope

There is a need to train and optimize the network with the larger dataset for obtaining improved performance. Further research includes the use of the trained network and deploying it as a mobile application to be embedded in an android or iOS device. The acquired images can be analyzed using the mobile application to get an instant result. This would help in the quick diagnosis of oral cancer in rural settings with having lack of accessibility and expertise.

Acknowledgments

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Conflict of interest

There are no conflicts to declare.

Supporting information

Applicable.

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