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# Research Paper Deep Learning

# Performance of deep convolutional neural network for classification and detection of oral potentially malignant disorders in photographic images

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Abstract. Oral potentially malignant disorders (OPMDs) are a group of conditions that can transform into oral cancer. The purpose of this study was to evaluate convolutional neural network (CNN) algorithms to classify and detect OPMDs in oral photographs. In this study, 600 oral photograph images were collected retrospectively and grouped into 300 images of OPMDs and 300 images of normal oral mucosa. CNN-based classification models were created using DenseNet-121 and ResNet-50. The detection models were created using Faster R-CNN and YOLOv4. The image data were randomly selected and assigned as training, validating, and testing data. The testing data were evaluated to compare the performance of the CNN models with the diagnosis results produced by oral and maxillofacial surgeons. DenseNet-121 and ResNet-50 were found to produce high efficiency in diagnosis of OPMDs, with an area under the receiver operating characteristic curve (AUC) of 95%. Faster R-CNN yielded the highest detection performance, with an AUC of 74.34%. For the CNN-based classification model, the sensitivity and specificity were 100% and 90%, respectively. For the oral and maxillofacial surgeons, these values were 91.73% and 92.27%, respectively. In conclusion, the DenseNet-121, ResNet-50 and Faster R-CNN models have potential for the classification and detection of OPMDs in oral photographs.

Key words: precancerous conditions; oral neoplasms; artificial intelligence; deep learning; neural network models.

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Oral potentially malignant disorders (OPMDs) are a group of conditions that have a risk of developing into oral squamous cell carcinoma (OSCC)<sup>1</sup>. Previously, these premalignant conditions were grouped under the term 'precancer'. Since 2007, the World Health Organization Collaborating Centre for Oral Cancer/Precancer has introduced new terminology for 'precancer of oral cavity', to be used under the term 'OPMDs'<sup>2</sup>. Clinically, OPMDs usually present as white, red, or white-red lesions in the oral cavity; these include oral leukoplakia, erythroplakia, erythroleukoplakia, proliferative verrucous leukoplakia, oral submucous fibrosis, and oral lichen planus<sup>3</sup>. OPMDs have a global prevalence of 4.47%, with the highest prevalence of 10.54% found in Asian populations<sup>4</sup>. OPMDs have a potential for malignant transformation of approximately 1%, which may be a relatively low rate, but the development of a malignant lesion leads to higher morbidity and mortality, and more invasive treatment for the patient<sup>1,5</sup>. Furthermore, the cost of oral cancer management is approximately three to seven times higher than that of OPMDs, which is markedly different<sup>6</sup>. Early detection of these premalignant lesions is therefore very important, because it not only increases the survival rate but also reduces the cost of treatment.

The clinical appearances of OPMDs make them difficult to diagnose accurately. Their features, with the presentation of primarily white/red lesions, resemble those of inflammatory lesions, and they are difficult to recognize and are often misdiagnosed by inexperienced clinicians. Even experienced specialists may fail to detect these lesions in the oral cavity, leading to late detection, which may result in premalignant lesions developing into cancer. The gold standard for confirming the diagnosis of OPMDs is a pathological examination. Adjunctive diagnostic tools have been developed to help clinicians detect these challenging lesions in the oral cavity, e.g., vital staining with toluidine blue, cytological testing, light-based detection using autofluorescence (VELscope), and fluorescence visualization in combination with adjunctive tests<sup>8,9</sup>. These diagnostic adjuncts with different clinical accuracy may help clinicians better evaluate OPMDs before definitive biopsy<sup>8</sup>.

Deep learning or convolutional neural networks (CNNs) is a subset of artificial intelligence (AI) that learns from the data itself and has the ability to classify and predict outcomes of the data<sup>10</sup>. Recent CNN-based algorithms have been used

to detect and classify clinically pathological lesions in the medical field, with promising results. Moreover, CNNs play a role in assisting in the detection of lesions of precancerous neoplasms. CNN-based classification algorithms, e.g., GoogLe-AlexNet, Residual Network (ResNet), and VGGNet, have been used to classify precancerous skin lesions<sup>11</sup>. Faster Regional-CNN (Faster R-CNN), one of the CNN-based object detection algorithms, has shown a high accuracy rate in detecting precancerous cervical lesions<sup>12</sup>. In addition, a study using a CNN-based model to detect laryngeal tumours in laryngoscopic images showed results comparable to those of the expert with 10-20 years of work experience<sup>13</sup> This demonstrates that the CNN-based algorithm has high accuracy in the detection of precancerous lesions, no less than experienced experts. The detection of OPMDs is another challenge, as the oral cavity has many structures such as the tongue, gingiva, and teeth, which make it more difficult to identify lesions. This often misleads the clinicians in the search for OPMDs. With the advantages of AI technology accelerated by computing power, big data, and new learning algorithms<sup>14</sup>, the diagnosis of OPMDs may enter a period of change.

The aim of this study was to evaluate the most appropriate models of CNN-based classification and detection algorithms for the detection of OPMDs. The use of these models is expected to assist clinicians in detecting these lesions, in combination with clinical patient data, to aid decision-making during treatment planning, and to improve the referral system for these premalignant lesions.

## Materials and methods

#### Data acquisition

The image datasets used in this study were collected retrospectively from the oral and maxillofacial surgery centre, covering the period from January 2018 to December 2020. The images were captured using a digital dental camera (Nikon D5200; Nikon, Tokyo, Japan) with a resolution of 1920 × 1280 pixels. A total of 600 images were collected and grouped into 300 images of OPMDs and 300 of normal oral mucosa. All of the OPMD images were biopsy proven as the gold standard for diagnosis.

The reference data used in this study were clinical oral photographs of OPMDs and normal oral mucosa. The OPMDs were located in various areas of the oral

cavity, including lip (36 images), buccal mucosa (95 images), upper alveolar ridge (27 images), lower alveolar ridge (46 images), tongue (45 images), retromolar trigone (34 images), and hard palate (17 images). The images of normal oral mucosa were chosen to cover the same areas as the OPMDs. All OPMD images had been pathologically proven. The OPMD images used for analysis in this study included oral leukoplakia (59 images), erythroplakia (79 images), and erythroleukoplakia (116 images), with pathological results of mild, moderate, and severe epithelial dysplasia and hyperkeratosis. Images of white striae (22 images) and erythematous lesions surrounded with white striae (24 images) had the pathological result of oral lichen planus<sup>3</sup>.

All photographic images were uploaded to the VisionMarker server (Digital StoreMesh, Bangkok, Thailand). VisionMarker is a private web application for image annotation. The public version is available on GitHub (GitHub, Inc., San Francisco, CA, USA)<sup>15</sup>. The boundaries of the lesions in the OPMD images were annotated by three oral and maxillofacial surgeons. Due to the differences in manual segmentation between the surgeons, the ground truth used in the CNN training, validation, and testing was the largest area of intersection between all of the surgeons' annotations (Fig. 1).

#### **Experiments**

The experiments conducted in this work were divided into two categories: image classification and object detection. Two recent CNN models were used in order to classify and detect lesions in the photographic images.

Of the 600 photographic images, 420 (70%) were randomly assigned as training data (210 images of OPMDs and 210 of normal oral mucosa), 60 (10%) were used for validation (30 images of OPMDs and 30 of normal oral mucosa), and 120 (20%) were used as testing data (60 images of OPMDs and 60 of normal oral mucosa) to confirm the accuracy. Five-fold cross-validation was applied to evaluate the robustness of the performance of the algorithms.

#### Image classification

Two CNN-based classification algorithms – DenseNet-121 and ResNet-50 – were adopted to create the binary image classification models of 'OPMDs' and 'normal oral mucosa' on oral photographic images. The image classification experiment was tested in Google Colab (Google Inc.,

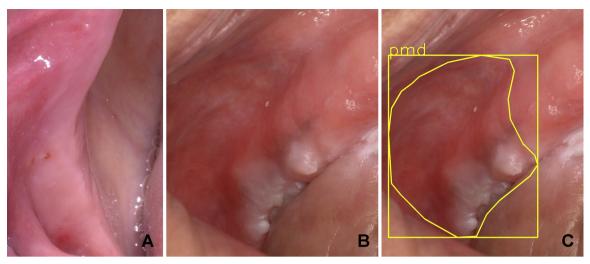


Fig. 1. Examples of oral potentially malignant disorder (OPMD) images from the dataset, showing (A) normal oral mucosa, (B) OPMD, and (C) the largest intersection area between the annotations of three different surgeons.

Mountain View, CA, USA) using a Tesla P100 (Nvidia Corporation, Santa Clara, CA, USA), Nvidia driver 460.32 (Nvidia Corporation), and CUDA 11.2 (Nvidia Corporation). The image was pre-processed by augmentation using Keras Image Data Generator (open-source software); then the framework resized the input image to  $224 \times 224$  pixels to feed into a deep learning neural network. The neural network architecture in this experiment was DenseNet121 and ResNet50 with pre-trained weight from ImageNet<sup>16</sup>. The Dense Convolutional Network or DenseNet was introduced by Huang et al. 17 as a CNN-based classification architecture. DenseNet is operated by incorporating each layer into other layers in a feed-forward fashion to improve the accuracy of object classification. ResNet, which is another respected CNN-based classification model, was presented by He et al. 18 as an architecture that explicated a reformulation of the layers as learning residual functions with reference to the layer inputs, instead of learning unreferenced functions to gain more accuracy in object classification.

DenseNet-121 and ResNet-50 were modified with the softmax activation function to have a two-dimensional output vector for two classes: OPMDs and normal oral mucosa. The hyper parameters were the following: maximum number of epochs was 100, batch size was 32, and learning rate was 0.00001. The training took just under 60 epochs before stopping. The validation loss was very close to the training loss, and there was no significant indication of over-fitting. The confusion

matrix was then calculated from the test set before calculating further metrics.

## Object detection

Two CNN-based object detection algorithms - Faster R-CNN and YOLOv4 were used to locate the OPMD lesions in the oral photographic images. Faster R-CNN was developed by Ren et al. 19 as a CNN-based object detection model by combining Region Proposal Network (RPN) and the Fast R-CNN, a previous object detection model, into one single network via sharing of their convolutional features, leading to a more real-time method that can improve the accuracy of object detection. You Only Look Once (YOLO), which was introduced by Redmon et al.20 as a CNN-based object detection, reframes object detection as a single regression problem, straight from image pixels to bounding box coordinates and class probabilities. YOLO is unlikely to predict false-positives on background and is extremely fast in object detection.

The object detection experiment used the annotated image from VisionMarker. The annotated images were identified with bounding boxes at locations of the lesion areas, then the pairs of image and annotation were ready for the training process. The training was performed on an onpremise server with two GPU, Titan Xp 12 GB (Nvidia Corporation), Nvidia Driver 450.102 (Nvidia Corporation), and CUDA 11.0 (Nvidia Corporation). The neural network architecture was Detectron Faster R-CNN with the pre-trained weight from COCO Detection (open-source soft-

ware) with Faster R-CNN<sup>21,22</sup>. The hyper parameters were as follows: 20,000 iterations, learning rate of 0.0025, and batch size per image of 128. The training loss was reduced and maintained between 15,000 and 20,000 iterations. The Intersection over Union (IoU) between detection and ground truth was calculated by a pairwise IoU operation in Detectron<sup>21</sup>.

## Evaluation

The precision, recall, F1 score, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC) were used to evaluate the diagnostic performance of the binary image CNNbased classification models of 'OPMDs' and 'normal oral mucosa' on the oral photograph. The accuracy performance of the CNN-based object detection models was evaluated by detecting a bounding box relative to the ground truth region in the OPMD images. If the IoU value between the generated bounding box and the ground truth was less than 0.5, then the produced bounding box was considered to be a false prediction. A separate test dataset with known pathological results was evaluated to compare the performance of the CNN-based classification model with that of six oral and maxillofacial surgeons who each had at least 5 years of experience in oral cancer surgery. None of these readers participated in the clinical care or assessment of the enrolled patients, nor did they have access to their medical records. The overall sensitivity and specificity of these experienced surgeons were calculated. Data analyses were conducted

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*Table 1.* Diagnostic performance of convolutional neural network models for the classification of oral potentially malignant disorders in oral photographs.

	Model	
	DenseNet-121	ResNet-50
Precision (%)	91	92
Recall (%)	89.51	98
F1 score (%)	95	95
Sensitivity (%)	100	98.39
Specificity (%)	90	91.67
AUC of the ROC curve (%)	95	95.03

AUC, area under the curve; ROC, receiver operating characteristic.

using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). The statistical analyses for image classification and object detection were calculated as follows<sup>22</sup>:

IoU = area of overlap/area of union

Precision = TP/(TP + FP)Recall = TP/(TP + FN)

F1 score =  $2 \times [(Precision \times Recall)/$ 

(Precision + Recall)]

Sensitivity = TP/(TP + FN)

Specificity = TN/(TN + FP)

True positive (TP) is the number of OPMD images that had a correct prediction. True negative (TN) is the number of normal oral mucosa images that had a correct prediction. False negative (FN) is the number of OPMD images that had no prediction. False positive (FP) is the number of normal oral mucosa images that had regions predicted as OPMDs.

#### Results

#### Image classification results

The evaluation was performed on the test set, and the results of the CNN-based image classification models are reported in Table 1. The image classification of DenseNet-121 achieved a precision of 91%, a recall of 89.51%, an F1 score of 95%, a sensitivity of 100%, a specificity of 90%, and an AUC of the ROC curve of 95%. The image classification of ResNet-50 achieved a precision of 92%, a recall of 98%, an F1 score of 95%, a sensitivity of 98.39%, a specificity of 91.67%, and an

AUC of the ROC curve of 95.03%. The overall sensitivity and specificity for the classification of OPMDs by the six oral and maxillofacial surgeons was 91.73% (standard deviation = 1.74%) and 92.27% (standard deviation = 5.93%), respectively.

## Object detection results

The object detection models were evaluated on the test set and the results are reported in Table 2. The detection performance of Faster R-CNN achieved a precision of 79.69%, a recall of 81%, an F1 score 80.31%, and an AUC of the precision–recall curve of 74.34%. The detection performance of YOLOv4 achieved a precision of 52.38%, a recall of 52.38%, an F1 score of 52.38%, and an AUC of the precision–recall curve of 44.18%. Examples of the detection outputs from Faster R-CNN and YOLOv4 object detection models are provided in Fig. 2.

#### **Discussion**

OPMDs are precancerous lesions that are often overlooked by many clinicians. Malignant transformation of OPMDs may not be high. However, early detection and prompt management will increase the patient's survival rate<sup>3</sup>. Deep learning, also known as deep neural networks, has achieved unprecedented success in detecting and classifying abnormalities in medical images<sup>10</sup>. CNNs are one of the most

*Table 2*. The detection performance of convolutional neural network models for the detection of oral potentially malignant disorders in oral photographs.

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	Model	
	Faster R-CNN	YOLOv4
Precision (%)	79.69	52.38
Recall (%)	81	52.38
F1 score (%)	80.31	52.38
AUC of precision-recall curve (%)	74.34	44.18

AUC, area under the curve.

successful deep learning algorithms in the medical field, due to their precise capacity to analyse information and recognize the object. CNNs are directly inspired by the visual cortex of the brain to process multiple types of data, e.g., two-dimensional images. CNNs are applied to mimic three key ideas: local connectivity, invariance to location, and invariance to local transition<sup>23</sup>.The CNN architecture process makes the model capable of accurately detecting and classifying an abnormal lesion in medical images. CNNs are highly effective when the amount of data is large. In this era of 'big data', the large amount of data increases the performance of CNNs in the accuracy and prediction of models<sup>24</sup>. Unfortunately, one of the main challenges of CNNs in analysing medical images is the small amount of data. This limitation can lead to overfitting of the CNN model. With the evolution of AI technology, the pre-training of the model and data augmentation method have been deployed to prevent overfitting and increase the performance of the model<sup>25,26</sup>.

In this study, CNN-based classification and detection models were used to detect OPMDs in oral photographs. The models achieved high accuracy in detecting and classifying features of OPMDs in the oral photographic images. Regarding the classification algorithm, DenseNet-121 and ResNet-50 achieved high accuracy in distinguishing the OPMDs from the normal oral mucosa, with an AUC of 95%, which is close to the performance found in the study using CNN-based algorithms to classify skin lesions<sup>11</sup>. With regard to the object detection algorithm, Faster R-CNN achieved higher accuracy than YOLOv4 in detecting OPMD in oral photographs, with AUC of the precision--recall curve of 74.34% and 44.18%, respectively. This showed that Faster R-CNN detected OPMDs more correctly than YOLOv4. However, in the detection process, YOLOv4, which has an operating time of only 0.06 seconds per image, was faster at detecting the lesion in images than Faster R-CNN. According to a review, only one study has used CNN-based algorithms, Faster R-CNN and ResNet-10, to detect and classify OPMDs in oral photographs, which achieved acceptable accuracy for the detection of oral lesions<sup>27</sup>. The performance of models used in this study and previous studies indicates that CNN-based algorithms are a reliable medical-aided diagnostic tool for the detection of precancerous lesions 11,12,27,28.

Regardless of the performance of the CNN-based algorithms, the practice of

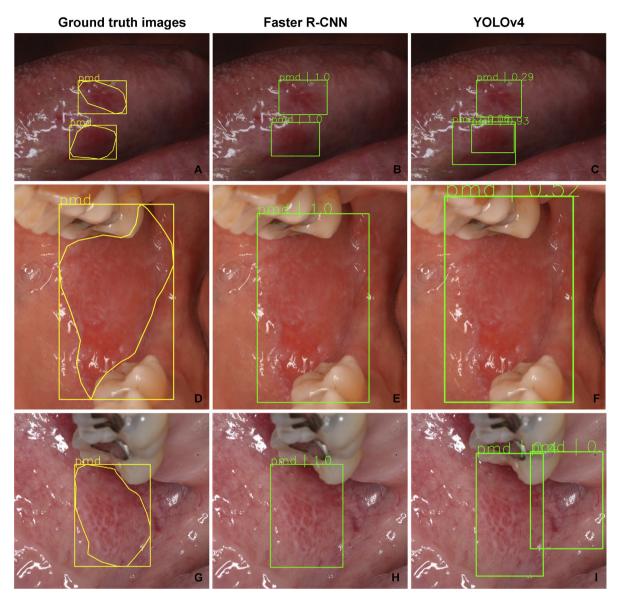


Fig. 2. Images A–C are from a patient with erythroplakia at the lateral tongue. Images D–I are from patients with oral lichen planus at the buccal mucosa. (A, D, G) Bounding box ground truth based on the surgeons' annotations. (B, E, H) True positive outputs from Faster R-CNN detection. (F) True positive output and (C, I) true positive with false positive outputs from YOLOv4 detection.

image-based diagnosis will continue to change as new technologies are introduced. One of the challenges of exploiting AI algorithms is that they are not a static product and continue to be modified and improved as new training data become available. At this point in time, the US Food and Drug Administration considers AI-based algorithms as medical devices<sup>29</sup>. The regulatory framework will allow rapid progress in this area while maintaining patient safety<sup>30</sup>. In the future, it is likely that AI will continue in a supporting role for diagnosis, helping to automate routine pathology detection and improve the workflow. Nevertheless, humans will remain responsible for all final decisions and reports. This technology will also neces-

sitate a shift in the training of diagnostic clinicians to better understand the computational techniques involved.

The results of this study showed that DenseNet-121 and ResNet-50 were good candidates for classifying OPMDs. Regarding the detection models, Faster R-CNN was better in the detection of lesions than YOLOv4 on oral photographic images. OPMDs could be detected based on photographic images using CNN-based classification algorithms with sensitivity and specificity comparable to those of manual diagnosis by oral and maxillofacial specialists with at least 5 years of experience in oral cancer surgery. It is expected that these models will be a fundamental assisted diagnostic tool to auto-

matically detect lesions and provide supplementary information to aid clinicians in decision-making for the early detection and precise management of OPMDs before their transformation into oral cancer.

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## **Competing interests**

The authors have no conflicts of interest to declare.

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## Ethical approval

Exemption was obtained from Thammasat University Research Ethics Committee (COE 020/2563).

#### Patient consent

Not required.

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