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Automatic classification and detection of oral cancer in photographic images using deep learning algorithms

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Abstract

Background: Oral cancer is a deadly disease among the most common malignant tumors worldwide, and it has become an increasingly important public health problem in developing and low-to-middle income countries. This study aims to use the convolutional neural network (CNN) deep learning algorithms to develop an automated classification and detection model for oral cancer screening.

Methods: The study included 700 clinical oral photographs, collected retrospectively from the oral and maxillofacial center, which were divided into 350 images of oral squamous cell carcinoma and 350 images of normal oral mucosa. The classification and detection models were created by using DenseNet121 and faster R-CNN, respectively. Four hundred and ninety images were randomly selected as training data. In addition, 70 and 140 images were assigned as validating and testing data, respectively.

Results: The classification accuracy of DenseNet121 model achieved a precision of 99%, a recall of 100%, an F1 score of 99%, a sensitivity of 98.75%, a specificity of 100%, and an area under the receiver operating characteristic curve of 99%. The detection accuracy of a faster R-CNN model achieved a precision of 76.67%, a recall of 82.14%, an F1 score of 79.31%, and an area under the precision-recall curve of 0.79.

Conclusion: The DenseNet121 and faster R-CNN algorithm were proved to offer the acceptable potential for classification and detection of cancerous lesions in oral photographic images.

KEYWORDS
artificial intelligence, deep learning, oral cancer, telemedicine

1 | INTRODUCTION

Oral cancer is a deadly disease which is the 17th most common cancer worldwide and the 11th in Asia, with approximately 380 000 new cases and nearly half of the number of these new cases of death in 2020.[1] Two-thirds of oral cancers have been found in developing and low-to-middle income countries, especially in Southeast Asia and South Asia which may be attributable to lifestyle behaviors such as smoking, alcohol consumption, and betel quid chewing.[2] The management of oral cancer, including surgery radiotherapy and/or chemotherapy, especially at an advanced stage, can lead to more morbidities and be very costly.[3] In addition, the prognosis for oral cancer is poor. The current study showed that the overall 5 years survival rate for oral cancer is approximately 52% but will decrease to 31.2% and 12.5% if there are regional and distant metastases, respectively.[4] Early diagnosis of oral cancer is very important so that the morbidity and mortality rate of patients can be reduced.

As mentioned earlier, oral cancer occurs mainly in low-to-middle income countries where the number of oral cancer specialists is limited.[2] Patients in remote areas also have limited access to appropriate diagnosis and treatment. Although the gold standard of oral cancer diagnosis is pathologically proven,[3] an abnormality in clinical appearances may also be a clue for the clinician to screen suspected malignant lesions in the oral cavity. Nowadays, telemedicine plays an important role in helping oral cancer specialists communicate with general practitioners and patients in remote areas. This remote consultation may improve the accuracy of oral cancer screening and appropriate referral.[5] It would be of great benefit to take this concept a step further by integrating an automated recognition system utilizing artificial intelligence[6] to analyze oral photographic images.

Artificial intelligence (AI) is a branch of computer science which can be defined as the ability for a computer to mimic the cognitive abilities of a human being. AI corresponds to a large array of techniques. Among them, deep learning is a potential disruptive technology that attempts to model high-level abstractions in medical images to determine diagnostic meaning. Deep learning, specifically as implemented using convolutional neural networks (CNNs), has become a conventional technique for classifying, detecting, and segmenting the objects in medical images.[7] A deep learning-based image classification is one of the useful tools for classifying medical diseases in clinical images and X-rays. For example, the DenseNet algorithm has been used to classify mass in breast mammography images.[8] A regional convolutional neural networks (R-CNN), which is part of CNNs, have been proven to have the highest accuracy for object detection.[9] Faster R-CNN, in particular, works reasonably well with a small dataset.[10] In medicine, Faster R-CNN has been used for automated detection of the abnormality in X-ray and clinical images such as lung nodules in computerized tomography scans (CT-scans), esophageal adenocarcinoma in high-definition white light endoscopy (HD-WLE) images,[11] and skin diseases from clinical photography.[12] In dentistry, there are a few studies on automated detection using Faster R-CNN mainly for the detection of abnormalities on the radiograph. The faster R-CNN trained on a limited amount of labeled imaging data performed satisfactorily in detecting periodontally compromised teeth in digital panoramic radiographs.[13] Another study used CNN models for detecting and classifying the presence of impacted supernumerary teeth in the maxillary incisor region on panoramic radiographs.[14]

The purpose of this study is to develop an automated classification and detection system for oral cancer screening using the DenseNet121 and Faster R-CNN algorithm. The use of this system is expected to assist clinicians in detecting suspected malignant lesions in the oral cavity. In combination with telemedicine, remote detection of oral cancer can help clinicians detect oral cancer at an early stage and improve the accuracy of referral systems.

2 | MATERIALS AND METHODS

2.1 | Ethical approval

This study was approved by the ethics review board of our university and was performed in accordance with the tenets of the Declaration of Helsinki. Informed consent was waived because of the retrospective nature of the fully anonymized images.

2.2 | Dataset

The dataset consisted of 700 clinical oral photographs retrospectively collected from our oral and maxillofacial surgery center between 2009 and 2018. The 700 images were divided into 350 images of oral squamous cell carcinoma (OSCC) and another 350 normal oral mucosae. All of the OSCC images were biopsy proven as the gold standard for oral cancer diagnosis.

2.3 | Reference data

Our reference data were clinical oral photographs of OSCC and normal oral mucosa. The OSCC images that were used for analysis in this study are OSCC stage I-IV according to the TNM clinical staging system as proposed by the American Joint Committee on Cancer (AJCC).[15] The OSCC images are characterized as ulcerative, exophytic, or endophytic in various areas of the oral cavity,[16] including the lip, upper and lower alveolar ridge, buccal mucosa, tongue, and hard palate. All OSCC images have been pathologically proven. The images of normal oral mucosa were also selected from the various area in the oral cavity.

All photographic images were uploaded to the VisionMarker server. VisionMarker is a private web application for image annotation. The public version is available on GitHub.[17] The lesion boundaries of the OSCC images were annotated by three oral and maxillofacial surgeons. Due to the differences in manual segmentation from one expert to another, we used the largest area of intersection between all of the surgeon's annotations in combination with the pathological result of OSCC as the ground truth in the deep learning model training, validation, and testing (Figure 1).

2.4 | Experiments

Deep learning, especially convolutional neural network (CNN), has been shown to be effective in object classification and detection. In this work, we adopt DenseNet121 to classify OSCC apart from the normal oral mucosa and used Faster R-CNN to detect OSCC on the oral photograph.

Faster R-CNN was developed by Ren et al.[10] as a deep learning-based object detection system by combining region proposal network (RPN) and the previous object detection system, Fast R-CNN,

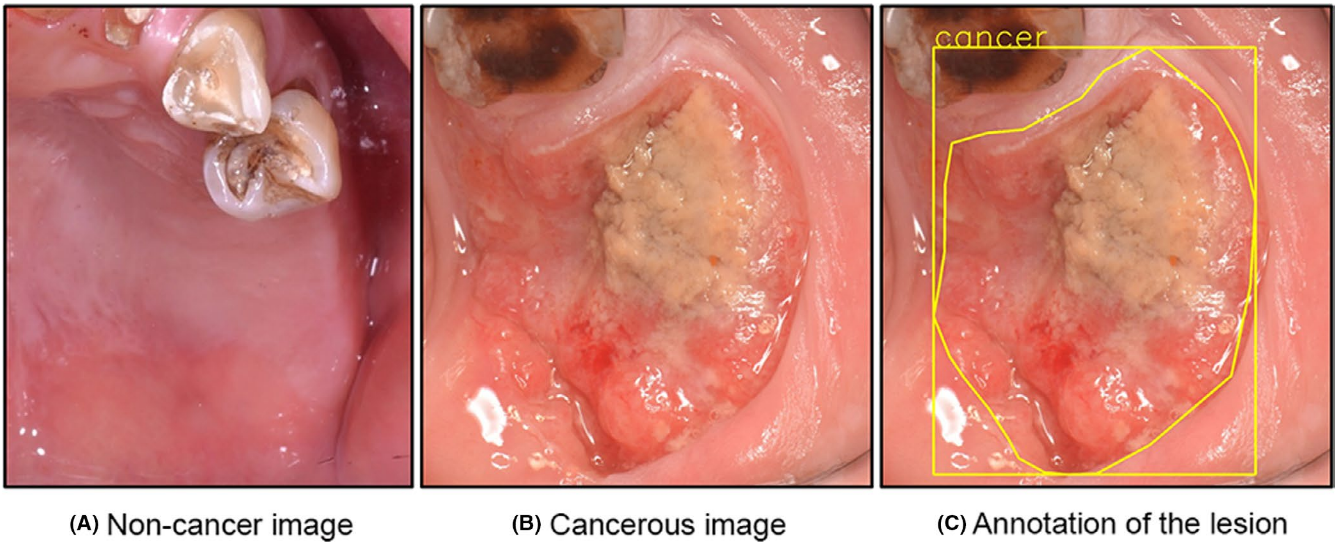

FIGURE 1 Examples of the oral photographic images from the dataset showing (A) non-cancer image, (B) OSCC image, and (C) the largest intersection area between the annotations from three different surgeons

into one single network by sharing their convolutional features leading to a more real-time method. The proposed RPN generates region proposals for each location using the last feature map produced from the CNN based on anchor boxes. The anchor boxes are detection boxes that have different sizes and ratios that are compared to the ground truth during the training process.

Dense convolutional network or DenseNet was introduced by Huang et al.[18] as a new convolutional network architecture which connects each layer to every other layer in a feed-forward fashion. DenseNet incorporates the properties of identity mappings, deep supervision, reduced feature redundancy, and diverse depth to enable feature reuse, making it a good feature extractor for various computer vision tasks which improve the accuracy of object classification.

Due to the limited amount of publicly available datasets, we performed an additional data augmentation to the training data by scaling, rotation, horizontal flipping, and adjustment of the saturation and exposure.[19] The manually cropped input images of OSCC were used to train the network in a minibatch manner.

Of these 700 photographic images, 490 (70%) were randomly assigned as training data (245 images of OSCC and 245 of normal oral mucosa), 70 (10%) were used as validation (35 images of OSCC and 35 of normal oral mucosa), and 140 (20%) were used as testing data (70 images of OSCC and 70 of normal oral mucosa) to confirm the accuracy. Fivefold cross-validation was applied to evaluate the robustness of the faster R-CNN performance.

For implementation, the experiments are divided into two categories: image classification and object detection. The image classification experiment was tested on Google Colab using a Tesla P100, Nvidia driver: 460.32, and CUDA: 11.2. The image was preprocessed by augmentation using Keras ImageDataGenerator; then, the framework resized an input image to 224 by 224 pixels to feed into a deep learning neural network. The neural network architecture in this experiment is DenseNet121 with pre-trained weight from ImageNet. The object detection experiment used the annotated image from VisionMarker. The annotated images were identified bounding boxes locations of the lesion areas; then, the pairs of image and annotation were ready for the training process. The training was performed on an on-premise server with 2 of GPU, TitanXP 12GB, Nvidia Driver: 450.102 and CUDA: 11.0. The neural network architecture was Detectron Faster R-CNN with the pre-trained weight from COCO Detection with Faster R-CNN.

2.5 | Evaluation measures

The metrics used to evaluate the machine learning algorithms in bioinformatics were used in this study.[20] To evaluate the performance of the DenseNet121 classification method in the classifying OSCC apart from the normal oral mucosa on the oral photograph, we use the precision, recall, F1 score, sensitivity, specificity, and area under the receiver operating characteristics (ROC) curve (AUC) to measure the classification performance of the algorithm. For the object detection, we evaluated the accuracy of the Faster R-CNN to detect a bounding box relative to the ground truth region in the cancerous images by the precision, recall, F1 score, and AUC of precision-recall curve. Furthermore, 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 as follows:

IoU = area of overlap/area of union.

Precision = TP/TP + FP = TP/all detections.

Recall = TP/TP + FN = TP/all ground truths.

F1 score = 2 x (Precision x Recall)/Precision + Recall.

Sensitivity = TP/TP + FN.

Specificity = TN/TN + FP.

TABLE 1 Binary image classification and object detection results “OSCC” vs. “normal oral mucosa”

Models	Precision (%)	Recall (%)	F1 score (%)	Sensitivity (%)	Specificity (%)	AUC of ROC curve
DenseNet121	100.00	99.00	99.00	98.75	100.00	0.99 (ROC curve)
Faster R-CNN	76.67	82.14	79.31	–	–	0.79 (precision-recall curve)

Abbreviations: AUC, area under the curve; R-CNN, regional convolutional neural networks; ROC, receiver operating characteristics.

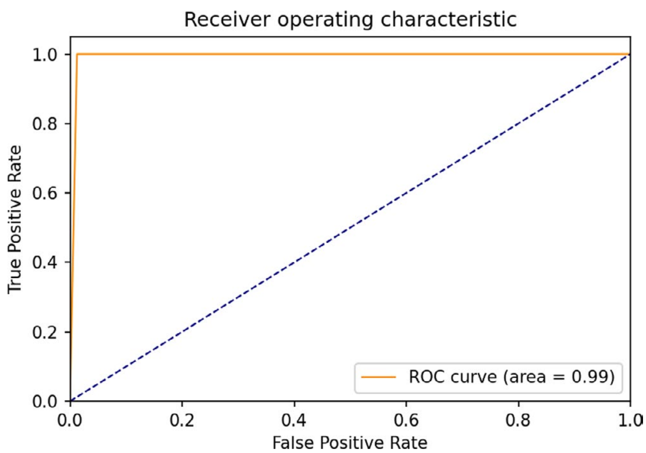

FIGURE 2 The receiver operating characteristic (ROC) curve of the DenseNet121 classification model showed the AUC of 0.99

- True positive (TP): The model classifies as positive, and the actual label is also positive which IOU >0.5.
- False positive (FP): The model classifies as positive, but the actual label is negative which IOU <0.5.
- True negative (TN): The model classifies as negative, and the actual label is also negative.
- False negative (FN): The model classifies as negative, but the label is actually positive.

3 | RESULTS

The evaluation was performed on the test set, and the results of the image classification model are reported in Table 1. The identification of images which contained cancerous lesions achieved a precision of 100%, a recall of 99%, an F1 score of 98.75%, a sensitivity of 99%, and a specificity of 100%. The AUC of the ROC curve of this model achieved a relatively high accuracy of 0.99 (Figure 2). The model's performance was also evaluated by generating a heat map visualization using the gradient-weighted class activation mapping (Grad-CAM)[21] to see how the model identifies the region of interest and how well the model distinguishes cancer from normal classes. Figure 3 shows a sample Grad-CAM output of normal and cancer classes and prediction probability. From the output, we observe that the model perfectly focuses on the key areas of images to classify cancers.

The object detection model trained by the faster R-CNN algorithm was evaluated on the test set, and the results are shown in Table 1. The detection of lesions achieved a precision of 76.69%, a recall of 82.14%, and an F1 score of 79.31%. The AUC of the precision-recall curve also achieved a high accuracy of 0.79 (Figure 4). Figure 5 shows examples of the output from the object detection model. The figure shows different samples of the true and false positives detection of cancerous and non-cancerous from oral images. The analysis was based on the bounding box generated by the faster R-CNN algorithm in comparison with the bounding box of the ground truth. One image, which achieved IoU of 0.49 (less than 0.5), was falsely predicted as a cancerous lesion by the model (Figure 5H). Figure 5J shows the false positive detection of a cancerous lesion in a non-cancer image.

4 | DISCUSSION

Oral cancer screening is an examination performed by a general dental practitioner or physician to look for signs of cancer or precancerous conditions in the oral cavity. In the primary care hospital, healthcare providers under the consultation of the dentist will help with screening and refer patients with suspected oral cancer to the cancer center hospital for diagnosis confirmation and treatment. In this work, we proposed the model for automatic classification and detection of cancerous oral lesions in oral photographs that will help in oral cancer screening. The algorithm used in this study was based on deep CNN via DenseNet121 to classify oral cancer apart from the normal oral mucosa and to detect this malignant lesion in photographic images via Faster R-CNN. The dataset consisted of photographic images with biopsy results as the gold standard for oral cancer diagnosis. All lesion boundaries were identified by three oral and maxillofacial surgeons as the ground truth for model training, validation, and testing.

The classification performance of our study is relatively high as seen in the result which achieved a precision of 100%, a recall of 99%, an F1 score of 98.75%, a sensitivity of 99%, a specificity of 100%, and AUC of ROC curve of 0.99. To our knowledge, there are only 2 studies using a CNN-based classification algorithm to classify oral cancer from an oral photograph.[22,23] The performance of DenseNet121 used in our study was similar to that of the algorithm in the study of Qiuyun et al.[23] but relatively higher than those of ResNet-10 used by the study of Rochan et al.[22] Deep CNNs have been used in several studies to classify head and neck lesions and have shown acceptable results for classification: for example,

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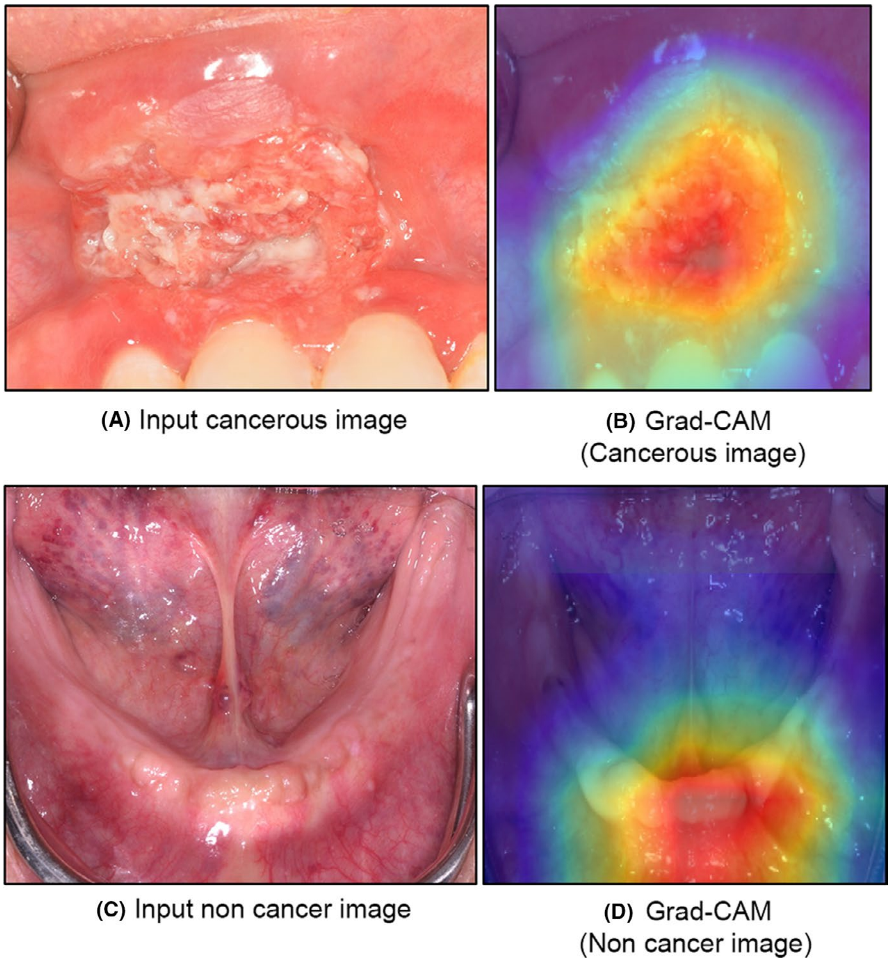


FIGURE 3 The Grad-CAM visualization of the deep learning-based classification model. The model correctly classified a cancerous image input (A) with high probability of 0.99 and labeled the correct location (B). The model correctly classified a non-cancer image input (C) with high probability of 0.98 and labeled the correct location (D)

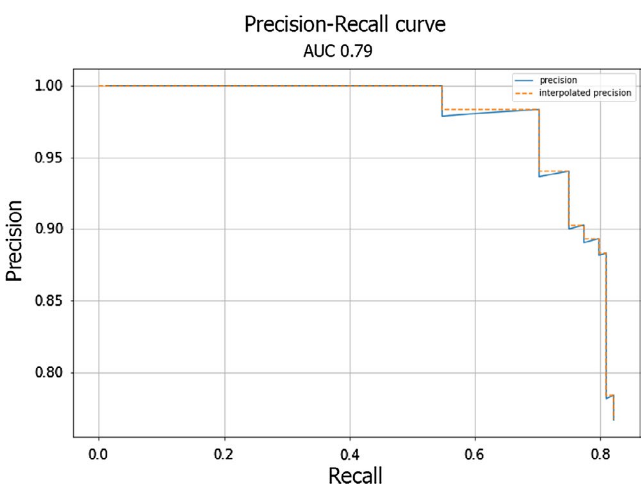
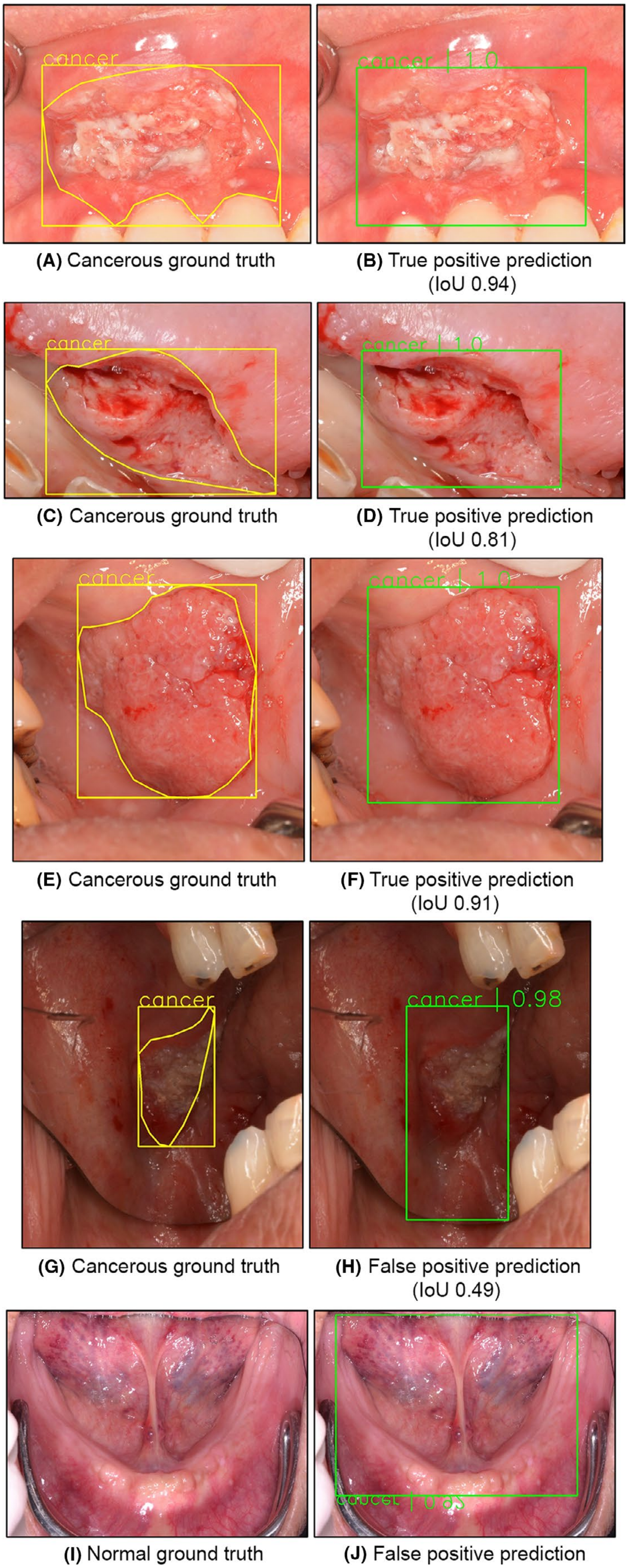


FIGURE 4 The precision-recall curve of the faster R-CNN detection model showed the AUC of 0.79

classification of esophageal adenocarcinoma using VGG-16,[11] and diagnosis of thyroid nodules in ultrasonography images using CNN-based classification algorithm.[24] DenseNet121 is one of the latest CNN-based classification algorithms which has advantages in improving information flow and gradients through the network and could reduce overfitting on tasks with small data training set size. These properties are significant for deep learning in medicine which is most often limited by the dataset size.[18] Although oral cancer lesions in the oral photograph may be obvious for cancer specialists, they might be difficult to identify by general physicians or healthcare providers. Thus, this classification model will be beneficial for oral cancer screening via telemedicine used by general practitioners in remote regions.

For oral cancer detection, our study showed a good performance for the detection of the lesion on the oral photograph with a precision of 76.67%, a recall of 82.14%, an F1 score of 79.31%, and AUC of precision-recall curve of 0.79. The detection performance was higher than that of the study by Rochan et al.[22] which also used Faster R-CNN for detecting oral cancer in photographic images. The difference may be due to the imbalance in class distribution between the number of oral cancer images and normal oral mucosal images used in their study. Faster R-CNN has been widely used in object detection in medical and dental images, that is, detection of lymph node metastases from rectal cancer on magnetic resonance imaging (MRI),[25] identification of lung nodules on chest X-rays,[26] and detection of periodontal defect on panoramic radiographs.[13] Currently, there are other CNN models used for object



(A) Cancerous ground truth

(B) True positive prediction (IoU 0.94)

(C) Cancerous ground truth

(D) True positive prediction (IoU 0.81)

(E) Cancerous ground truth

(F) True positive prediction (IoU 0.91)

(G) Cancerous ground truth

(H) False positive prediction (IoU 0.49)

(I) Normal ground truth

(J) False positive prediction

FIGURE 5 Bounding box ground truth based on experts annotation and the output from the faster R-CNN when using fivefold cross-validation from different oral photographic images showing correct prediction in (B), (D), and (F) and a false prediction in (H) and (J) detection in medical images that show promising results; that is, the Mask R-CNN model used for the detection of a lung tumor on a positron emission tomography (PET) image,[27] the You Only Look Once (YOLO) model used for the detection of a dental restoration in an oral photograph,[28] and the Single Shot MultiBox Detector (SSD) model used for the detection of temporomandibular joint arthritis in a panoramic radiograph.[29]

Our study also had one of the common deep learning problems in medicine, which was the limited amount of data.[7] This small dataset of oral cancer photographs is due to the fact that the data came from only one cancer center. In the training dataset to develop the model, we solved this problem by using a data augmentation method.[19] As we know, the key for deep learning is a large dataset which will improve the performance model. For future study, advanced augmentation techniques and recent deep CNN algorithms should be implemented to further improve the model performance. The dataset could be expanded by collecting cases from multi-cancer centers and gathering more image data from an oral cancer screening program via telemedicine.

In conclusion, we found that the combination of DenseNet121 and the Faster R-CNN algorithm gives acceptable results for the classification and detection of oral cancer in oral photography. Therefore, we expect that this research will be a fundamental model for the development of the application for oral cancer screening, especially through telemedicine, which will help inexperienced clinicians and healthcare providers in remote areas to detect malignancy lesions in the oral cavity.

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CONFLICT OF INTEREST

All authors declare that they do not have any conflict of interests.

AUTHOR CONTRIBUTION

Kritsasith Warin: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Validation; Writing-original draft; Writing-review & editing. **Wasit Limprasert:** Formal analysis; Methodology; Software; Validation. **Siriwan Suebnukarn:** Conceptualization; Methodology; Supervision; Validation; Visualization; Writing-review & editing. **Suthin Jinaporntham:** Resources. **Patcharapon Jantana:** Software; Validation.

ETHICAL APPROVAL

This study was approved by the institute research ethics committee (COE No. 020/2563) in accordance with the 1964 Helsinki Declaration and its later amendments.

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