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An automated diabetic retinopathy disorders detection model based on pretrained MobileNetv2 and nested patch division using fundus images

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ABSTRACT

Aim: Fundus images are very important to diagnose some ophthalmologic disorders. Hence, fundus images have become a very important data source for machine-learning society. Our primary goal is to propose a new automated disorder classification model for diabetic retinopathy (DR) using the strength of deep learning. In this model, our proposed model suggests a treatment technique using fundus images.

Material and Method: In this research, a new dataset was acquired and this dataset contains 1365 Fundus Fluorescein Angiography images with five classes. To detect these disorders automatically, we proposed a transfer learning-based feature engineering model. This feature engineering model uses pretrained MobileNetv2 and nested patch division to extract deep and exemplar features. The neighborhood component analysis (NCA) feature selection function has been applied to choose the top features. k nearest neighbors (kNN) classification function has been used to get results and we used 10-fold cross-validation (CV) to validate the results.

Results: The proposed MobileNetv2 and nested patch-based image classification model attained 87.40% classification accuracy on the collected dataset.

Conclusions: The calculated 87.40% classification accuracy for five classes has been demonstrated high classification accuracy of the proposed deep feature engineering model.

Keywords: Diabetic retinopathy, fundus image processing, biomedical image classification, artificial intelligence

INTRODUCTION

Diabetic Retinopathy (DR) is specific angiopathy involving retinal capillaries, arterioles, and venules, which occurs as a result of hyperglycemia, insulin deficiency, or insulin resistance (1, 2). The term diabetic retinopathy is used to describe microvascular abnormalities (microaneurysms, hemorrhage, exudates, neovascularization (NVE, NVD, preretinal/vitreous hemorrhage) found in clinical examination or fundus images, and according to the presence of these findings in the fundus, Nonproliferative Diabetic retinopathy (NPDR) and Proliferative diabetic retinopathy (PDR). It is divided into two main groups diabetic retinopathy (PDR). Macular edema is also one of the important causes of low vision in diabetic patients and can be found together with NPDR or PDR (3-5). Diabetic retinopathy (DR) is a common and serious complication of diabetes that can result in blindness. It is known to affect approximately 100 million people worldwide, and it will affect an estimated 600 million people in 2040. Studies have shown that with early intervention of DR, good results can be achieved in preventing the development of the disease and the rate of blindness can decrease significantly (6-8). Early scanning is very important for diagnosis and timely intervention. Clinical DR screening and diagnosis are typically based on Color Fundus Photograph (CFP) or Fundus Fluorescein Angiography (FFA) images (9). CFP is a rapid, non-invasive, and widely used method for DR screening (10). However, FFA can detect typical pathological changes such as

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microaneurysms, non-perfusion sites, and vascular leakage, and provide dynamic information about the retinal vascular structure that CFP cannot identify. FFA is a more powerful tool than CFP in fully assessing the severity of DR, which directly guides individual treatment plans and plays an important role in the diagnosis of DR (11). Many studies have confirmed the efficacy of lowering HbA1c level with the stability of tight glycemic index, control of blood pressure, and lipid profile in stopping DR progression (12-14). However, in cases where progression cannot be prevented, various treatments are applied to prevent vision loss. Laser photocoagulation, one of these treatment methods, is used to treat two main complications in diabetes: 1) neovascularization of the retina and 2) severe or clinically significant macular edema (15). Panretinal laser photocoagulation (LPC) is an effective method for regressing neovascularization performed in sessions (5). Apart from this, intravitreal injections and various lasers such as focal, grid, and subluminal lasers are applied in the treatment of macular edema. In resistant cases that do not respond to all these treatments, pars plana vitrectomy is applied (16).

Artificial intelligence (AI) is a branch of computer science in which machines mimic the cognitive function of the human mind. Artificial intelligence has widespread use in health and medical sciences. AI has been used in medicine since the early 1950s when doctors sought to improve the accuracy of their diagnoses using computer-assisted algorithms (17). AI has been applied in image-based medical fields such as Radiology and Ophthalmology, as it is suitable for processing complex images (18, 19). Various studies have been conducted in the field of ophthalmology to assist in the diagnosis of diseases such as DR, glaucoma, age-related macular degeneration, and retinopathy of prematurity (20). AI is planned to be used as a potential alternative to DR screening to help reduce the burden on ophthalmologists and overcome barriers with telemedicine. AI helps the right patients be seen at the right time and managed in the right place. However, there are shortcomings in using artificial intelligence to optimize DR management. In this research, we collected a new FFA dataset and we proposed a machine learning model to propose treatment techniques for helping medical professionals.

Motivation and Our Model

In the last decade, an important image classification methodology has been presented and this methodology is named deep learning. By proposing deep learning, great advances have been made in the field of computer vision. Also, computer vision models have been applied to biomedical images to generate/develop intelligence assistants. In this research, we proposed a pretrained deep learning – we used a pretrained MobileNetv2 (21) – based image classification model to contribute to DR disorders classification. Fundus images have circular structures. Therefore, we used four nested patches to extract features. Moreover, the last pooling layer of the pretrained MobileNetV2 has been used to extract deep features. The used layer (global average pooling layer of the MobileNetV2) has been applied to each patch and the features have been generated. In the feature selection layer, we used NCA (22) selector and the top 512 features have been selected. These 512 features have been used as input for the kNN classifier. The rough block diagram of our proposal is demonstrated in **Figure 1**.

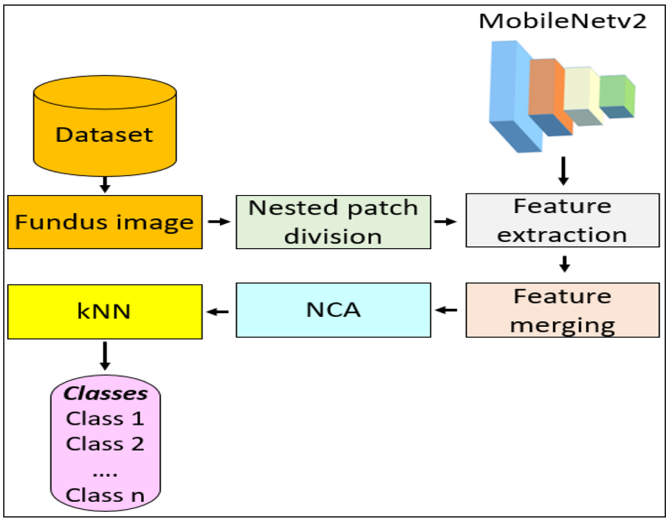

Figure 1. Block diagram of the proposed MobileNetv2 and NCA-based fundus image classification based model

Contributions

In this research, we collected a new Fundus Fluorescein Angiography images dataset to classify groups of the DR and we presented a deep feature-based model. The contributions of this research are given below.

Contributions:

- DR is one of the most commonly seen ophthalmologic disorders and groups of this disorder are very important to the selection cure method. In the literature, there are many PDR, NPDR, and healthy fundus classification models but there is no PDR/NPDR categorization/cure proposal model (machine learning based) in the literature as our knowledge.
- Deep networks are the flagships of computer vision models. Thus, the usage area of the deep networks is wide. Moreover, by using transfer learning, users/developers/scientists have used advantages of the deep networks with low time complexity. In this research, we proposed a new patch-based deep feature engineering image classification model. In the literature, fixed-size patches generate exemplar features. However, fundus images have a circular structure. Thus, we used nested patch division to detect local abnormalities.

Further, we used a lightweight CNN – MobileNetv2 – to generate features. Our proposal attained 87.40% accuracy on the used dataset.

MATERIAL AND METHOD

The study was carried out with the permission of Fırat University, Non-Interventional Research Ethics Board (Date: 13.03.2022 Decision No: 2022/04-10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. We collected a new FFA image dataset from Fırat University Hospital. This dataset contains 1365 FFA images with five categories and these categories are (i) NPDR+macular edema and intravitreal injection/macular laser treatment are recommended, (ii) PDR without macular edema and retinal laser recommended, (iii) PDR+macular edema and intravitreal injection/macular laser+retinal laser recommended, (iv) Metabolic regulation without ocular treatment –NPDR patient without macular edema requiring follow-up, early stage and (v) healthy. The format of these FFA images is dicom and we converted them to jpg images. These FFA images have variable sizes. In our proposal, we resized these images to 224 × 224 sized images. The sample images are given in **Figure 2**.

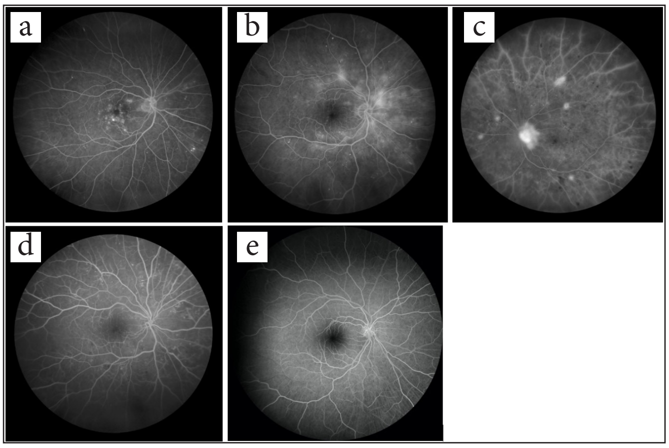

Figure 2. Sample FFA images from each category. **(a)** Intravitreal injection/macular laser **(b)** Retinal laser **(c)** Intravitreal injection/macular laser+ Retinal laser **(d)** Metabolic regulation without ocular treatment **(e)** Healthy

Distributions of the FFA images are also given in **Table 1**.

Table 1. Properties of the collected FFA dataset

Number	Class	Number of images
1	Intravitreal injection/macular laser (II/ML)	126
2	Retinal laser (RL)	339
3	Intravitreal injection/macular laser+ Retinal laser (II/ML+RL)	372
4	Metabolic regulation without ocular treatment (MR-OT)	179
5	Healthy	349
Total		1365

The Proposed Model

We proposed a new generation model of deep transfer learning-based fundus image classification model. This model is directly about feature engineering since it has feature extraction, feature selection, and classification layers. Nested patch division and pretrained MobileNetv2 have been used in the feature extraction layer. The used MobileNetv2 was trained on the ImageNet1K (23) (this dataset contains approximately 1.3 million images with 1000 object categories) and the last global average pooling layer has been utilized as a feature extractor. We generated four nested patches in this section since the sizes of our patches are 56 × 56, 112 × 112, 168 × 168, and 224 × 224. These patches have been generated from a fundus image with a size of 224 × 224. The top 512 features of the generated features have been chosen by deploying the NCA feature selection function. The chosen 512 features have been utilized as input of the kNN (24) classifier. The schematic expression of the proposed nested MobileNetV2-based model has been demonstrated in **Figure 3**.

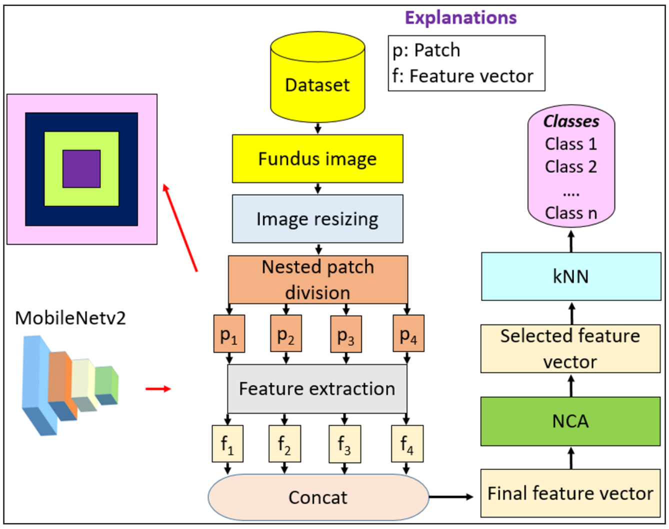

Figure 3. Graphical explanation of the proposed MobileNetv2-based fundus image classification model

In order to better express the proposed model, the steps of this model are given below.

Step 1: Read/load each image from the collected fundus angiography dataset.

Step 2: Resize each image to 224 × 224.

Step 3: Create nested patches from the resized image. This process is given below.

$$p_k = Img(c - s_k + 1 : c + s_k, c - s_k + 1 : c + s_k, l), l \in \{1,2,3\}$$
$$k \in \{1,2,3,4\}, s \in \{28,56,84,112\}, c = 112 \quad (1)$$

where Img defines the used fundus image, p_k represents kth patch and s is an increasing array to generate nested patches.

Step 4: Extract deep features from the generated patches in Step 3.

$$f_k = Mv2(p_k, GAP) \quad (2)$$

Herein, f_k defines kth feature vector with a length of 1280, $Mv2(.)$ pretrained MobileNetv2, and GAP represents the global average pooling layer and we used this layer to extract features.

Step 5: Merge/concatenate the generated feature vectors to obtain the final feature vector.

$$F(j + 1280 \times (k-1)) = f_k(j), j \in \{1,2,\ldots,1280\} \quad (3)$$

Here, F defines a merged feature vector with a length of 5120 (=1280×4).

Step 6: Apply NCA to these generated 5120 features and select the top 512 out of 5120 features.

Step 7: Classify the selected 512 features using the kNN classifier with 10-fold cross-validation. The attributes of the kNN classifier are given as follows. k is 1, distance metric: L1-norm, and voting is no-voting.

RESULT

We proposed a new MobileNetv2-based model and this model applied to the collected fundus angiography images. In the classification, the kNN classifier was used to get classification results. We used 10-fold cross-validation for validation. Furthermore, we used a simple configure computer (this computer has a 3.6 GHz processor, 16 GB memory, and Windows 10.1 operating system) and our used programming environment is MATLAB 2021a. Firstly, the pretrained MobileNetv2 was installed in MATLAB 2021a. A deep feature generation function was created using this library. Moreover, we created the main function to implement our proposed model.

In order to evaluate the classification ability of our proposal, we used unweighted average recall (UAR), unweighted average precision (UAP), and overall F1 score (25, 26). Further, we gave class-wise recall, precision, and F1 scores. The calculated confusion matrix of this model is also given in **Figure 4**.

According to this confusion matrix (see **Figure 4**), our model was tested on a fundus angiography dataset with five classes. These classes are enumerated from 1 to 5. These classes are 1: Intravitreal injection/macular laser, 2: Retinal laser, 3: Intravitreal injection/macular laser+ Retinal laser, 4: Metabolic regulation without ocular treatment, and 5: healthy. The overall results using this confusion matrix are listed in **Table 2**.

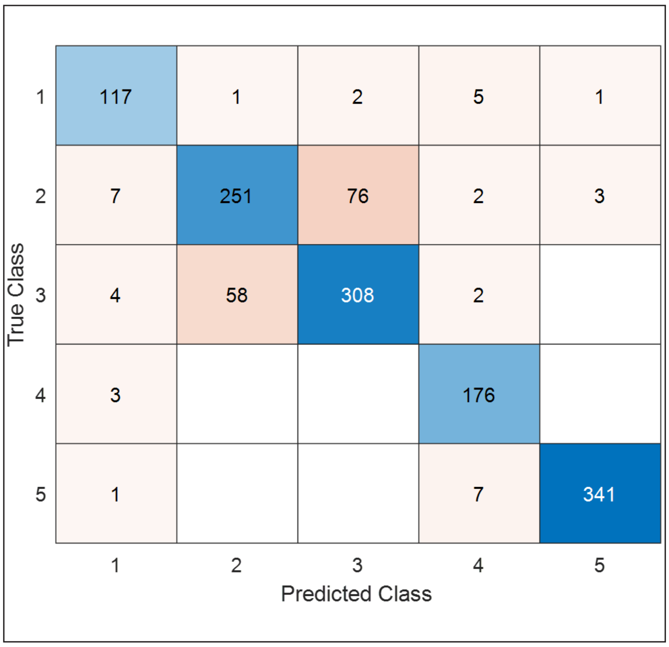

Figure 4. The calculated confusion matrix

Table 2. Overall results (%) of the proposed MobileNetv2-based model	
Performance metric	**Result (%)**
Accuracy	87.40
Unweighted average recall	89.15
Unweighted average precision	87.98
F1-score	88.49

Class-wise performances of the proposed model are demonstrated in **Figure 5**.

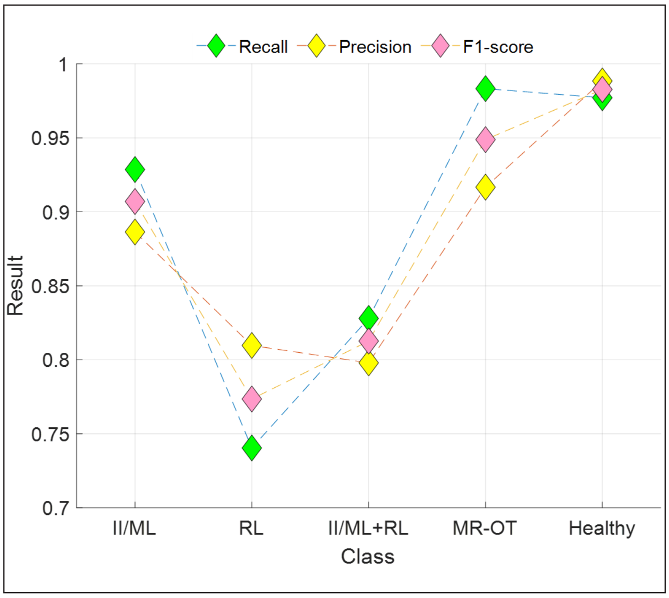

Figure 5. Class-wise results

Figure 5 demonstrated that the best accurate class is a healthy class. The worst two classes are Retinal laser and Intravitreal injection/macular laser+ Retinal laser since these types of disorders are very close to each other.

DISCUSSION

In this work, we have proposed a cure proposal mechanism using fundus angiography images. We used a deep transfer learning model and this model uses MobileNetV2 and nested patch division. In the feature extraction phase, 5120 features have been extracted from each fundus angiography image. By deploying NCA, 512 out of 5120 features have been selected. These features have been classified using a kNN classifier with a 10-fold CV. Our model attained 87.40% classification accuracy on the collected dataset. Moreover, class-wise results were calculated. According to this calculation (class-wise result calculation), results of the Retinal laser and Intravitreal injection/macular laser+ Retinal laser are lower than 85%. Results of other classes were over 85% (see **Figure 5**).

- As our knowledge, we are the first team to propose an automated classification model to propose treatment techniques using fundus angiography images. The important points of this research are listed below.
- Transfer learning was used for feature extraction. Thus, the time complexity of this model is low.
- Our proposed model attained 87.40% classification accuracy. Moreover, a 10-fold CV supports robust results calculation.
- This model is a simple and effective model.
- We used methods with default settings. There is no fine-tuning operation. Thus, this model is a cognitive model.
- The application of this model is very easy. Other image classification problems can be solved through this model.
- An intelligent cure proposal assistant can be used using our model in the near future.
- We collected this dataset from a single medical center. By collaborating with more medical centers, larger datasets can be collected.

Our study has some limitations. First, multimodal imaging modalities such as optical coherence tomography (OCT) and OCT-Angiography were not used. Second, the study was conducted in a single center. Finally, the number of samples was small.

CONCLUSION

In this research we proposed a new automated disorder detection model using computer vision model. We collected a FFA dataset and this dataset contains five classes. The collected FFA images were utilized as input of the proposed nested-patch based model. The nested patches have been used to generate features from local areas. These generated all feature vectors were concatenated to obtain final feature vector. The top features were selected by deploying NCA. The selected feature vector was utilized as input of the kNN classifier. Our proposed model attained 87.40% classification accuracy for the collected FFA dataset. This result obviously depicted that the presented nested patch-based deep feature engineering model is a good model for FFA classification.

Soon, we are planning to develop an automated disorder detection application using FFA images. Therefore, we will use attention-based models in the near future.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Fırat University, Non-Interventional Research Ethics Board Decisions (Date: 13.03.2022 Decision No: 2022/04-10).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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