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Diabetic retinopathy classification via Generative Adversarial Networks

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Diabetic retinopathy is a disease that affects many people around the world. So an optimal way to diagnose the degree of diabetes on retinal images is essential in the prevention of acute illness and vision loss. But the dataset is imbalanced, then we introduce a new solution for facing to imbalanced data challenge. This study is a new method in medical image classification applying the Kaggle dataset of a hospital in England. This dataset consists of 5 classes that a major class (normal eyes) accounting for about 73% of the total data, and minor classes in a low percentage of the total data. To solve imbalanced data problems, first the number of minor classes is increased via training of designed Generative Adversarial Network (GAN), then classification is done in both proliferative and non-proliferative classes by using the designed deep model. Three general methods have been reviewed, then the problem of degree diagnosis is solved with 89% accuracy via deep model training that improvements have been made about 7% compared to the top Kaggle Challenge participants. Then GANs are distributed in several processors, it results in Run time decreasing about 60%. In the last two decades, three methods of screening for diabetic retinopathy, retinal imaging, and deep models have been used, and deep learning techniques have been more efficient than other methods. The proposed model is optimized by solving the problem of imbalanced data by generating new images via the designed deep generative model.

Keywords: Diabetic Retinopathy, Medical Image Classification, Deep Learning, Model Distributing, Generative Adversarial Network.

INTRODUCTION

Diabetic retinopathy (DR) is the main cause of blindness associated with diabetes (Aboderin et al., 2002).The majority of people suffering from diabetes mellitus will eventually develop DR. Diabetic retinopathy is a complication of diabetes caused by changes in the retina blood vessels that at the proliferative level damage the retina blood vessels, cause blood leakage, growth of fragile and clogged vascular branches, and damage to the retina. Damage to the retina causes blurred images to be sent to the brain. Diabetic retinopathy is one of the leading causes of vision loss and people who have untreated diabetes are many times more likely to develop blindness.

Early diagnosis through regular screening has been shown to prevent visual loss and blindness. Color fundus photography is characterized by low-cost and patient friendliness which are a prerequisite for large scale screening (Abràmoff et al., 2008). However, a large number of diabetic patients need to be screened annually, which poses a huge workload for ophthalmologists.

Therefore, developing an automatic DR diagnosis system is necessary, which can not only reduce the workloads of ophthalmologists but also improve the accuracy of classification(Acharya et al., 2008).

In this paper, we mainly focus on the diagnosis of PDR, which present at the severe stage of DR, it leads to blindness.

The various *components of the retina images* include the four major components of the optic disc, macula, fovea, and blood vessels. In addition to normal retina structures, retina fundus images contain information on diabetic retinopathy lesions include microaneurism, hemorrhage, exudate, macula edema, and Neovascularization.

The severity of diabetic retinopathy is divided into five levels:

Degree 0 (NPDR0): At this stage, there are no signs of disease in the retina images.

Mild non-proliferative (NPDR1): At this stage of the disease, at least one microaneurism develops on the retina surface.

Moderate non-proliferative (NPDR2): At this level of the disease, some of the retinal nutrient blood vessels are blocked.

Severe non-proliferative (NPDR3): At this stage, blood vessels are blocked in more areas than the retina. These areas send signals to the brain to grow new blood vessels to feed the retina.

Proliferative (PDR): This is the most advanced stage of the disease that develops new blood vessels that are very thin and fragile. Leakage of blood by these vessels can cause severe weakening of the eyes or may even lead to blindness.

Numerous approaches have been proposed for DR classification, which always involves three fundamental processing phases: preprocessing with the normalization of the images, feature extraction, and classification based on features computed on each candidate(Acharya et al., 2009)

In all the researches, certain methods of classification have been used. In general, the classification stages of the degree of diabetic retinopathy can be visualized as preprocessing, feature extraction and classification.

Methods of feature extraction of diabetic retinopathy images are generally divided into the following three categories:

• Diabetic retinopathy screening
• Retinal imaging
• Applying deep models

A screening method for diabetic retinopathy is designed to capture the original retinal images, provide an image output that specifies the location of the lesions, then based on image pixels of the learning and classification (Li Q et al., 2008).

In the retina imaging method, classification is performed using image processing techniques and then mapping with certain algorithms based on the characteristics of the different regions.

In the sample shown in Figure 6, after the discovery of blood vessels, optic disc and fovea sites are diagnosed and then the lesions are identified in green and blue, and finally, the pixels of the image are classified (Abràmoff et al., 2010).

In the above two methods, retinal feature extraction is performed using image processing techniques and with the presence of an expert, but with deep modeling methods due to the ability to train the model, a fundamental transformation in feature extraction is achieved and the classification was done.

Since 2014, with the development of deep models and high image processing power of these models, research has also been undertaken in the field of medical image analysis, including to solve the problem of diabetic retinopathy with these models. In this method, after training the model, the retina images are given as a set of input images to the deep layers, and after passing through the layers of the model, the image features are automatically extracted.

It should be noted that in this method retina properties can be determined without using image processing techniques and only using a suitable architecture. After extracting the features of the retina datasets, the classification stage is performed.

But since the dataset of diabetic retinopathy is imbalanced, the training of these models have trouble. In imbalanced DR dataset often the number of images of individuals with lesions is significantly lower than the number of normal eyes, this poses a significant trouble during model training.

In general, the *methods for dealing with imbalanced data challenge* are:

-Data-level approaches that change the distribution of data through the representation of the data space.

-Algorithm-level approaches that change learning algorithms to help the learning process towards a minority class.

-The cost-sensitive learning framework that lies between the algorithms and data-driven approach. This will change both at the data level and the algorithm level (Ali A et al., 2015, More A. 2016).

To solve the challenge of imbalanced classes in data-level approach, some methods have been proposed to balance the datasets by adding the pre-processing step before classifying. Pre-processing of sampling is done in either an under-sampling of the majority class, oversampling of the minority class, or a combination of both. In the Under-sampling randomly deletes samples from the majority class, until the minority class receives an acceptable percentage of the majority class, and in the oversampling method balance the class distribution through the sample generation of minor class (Sun Y et al., 2009).

The problem of imbalanced data and some of the general strategies proposed to address this challenge are discussed. But in deep models, researchers have suggested oversampling a more efficient and successful resampling strategy (Buda M et al., 2018).

Therefore, in this study, deep generative adversarial models called GANs were used for oversampling minor data.

MATERIALS AND METHODS

Deep learning allows computational models that are composed of multiple processing layers to learn representations of data with multiple levels of abstraction. These methods have dramatically improved the state-of-the-art in computer vision, speech recognition, visual object recognition, object detection and many other domains such as drug discovery and genomics.

Deep learning discovers intricate structure in large data sets by using the back propagation algorithm to indicate how a machine should change its internal parameters that are used to compute the representation in each layer from the representation in the previous layer.

Generative adversarial nets approach that introduced by Good fellow et al., 2014 is a framework for training generative models. They consist of two 'adversarial' models: a generative model G that captures the data distribution, and a discriminative model D that estimates the probability that a sample came from the training data rather than G. Both G and D could be a nonlinear mapping function, such as a multi-layer CNN (Goodfellow et al., 2014, Radford et al.,2015, Dosovitskiy et al.,2015). (Figure 1)

G and D are both trained simultaneously: we adjust the parameters for G to minimize log(1 - D(G(z)) and adjust parameters for D to minimize log D(X), as if they are following the two-player min-max game with value function V(D,G):

$$\min_G \max_D V(D,G) = E_{x \sim p_{data(x)}} [\log D(x)] + E_{z \sim p_{z(z)}} [\log(1 - D(G(z)))] \quad (1)$$

In 2017, Buda systematically studied and investigated the impact of class imbalance on the classification performance of convolutional neural networks (CNNs) and compared frequently used methods to address the issue. The results from their experiments on CNN conclude that: the effect of class imbalance on classification performance is detrimental and the method of addressing the class imbalance that emerged as dominant in almost all analyzed scenarios was oversampling.

So, it can use GANs for oversampling the small class in the dataset classification via deep neural networks.

In our *experiment*, the dataset used is approximately 35,000 Kaggle Retina images for diabetic retinopathy of hospital information in the UK comprising five classes. This dataset has a very high number images of NPDR classes(classes 0,1,2,3) about 98% of the total data and a very low number images of PDR class (class 4) about 2% of the total data. (Table 1)

Table 1: Dataset of DR Kaggle

Class	Name	Number of images	percentage
0	Normal	25810	73.48%
1	Mild NPDR	2443	6.96%
2	Moderate NPDR	5292	15.07%
3	Sever NPDR	873	2.48%
4	PDR	708	2.01%

Due to the imbalanced data, the model training stages don't perform correctly.

Table 2: The experimental hardware and software setting

API	Python
OS	Ubuntu
CPU	Intel Core i7
GPU	NVidia GTX 1050 Ti
	NVidia GTX 1080
	NVidia GTX 1080 Ti
RAM	16 GB
	20 GB
	20 GB
Disk	2 TB
	250 GB
	250 GB

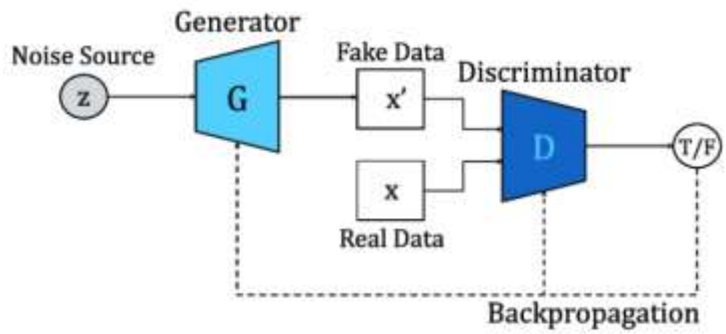

Figure 1:The Framework of GAN

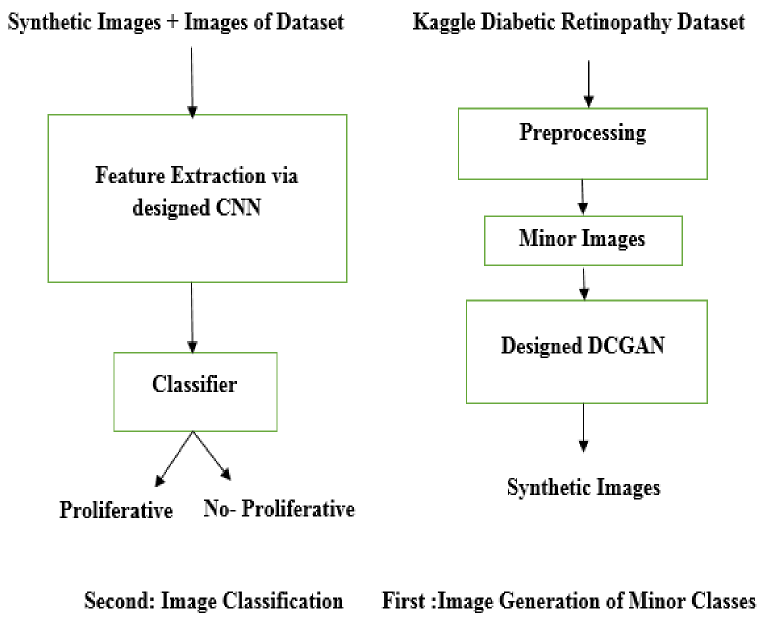

Figure 2:Block Diagram of Proposed Method

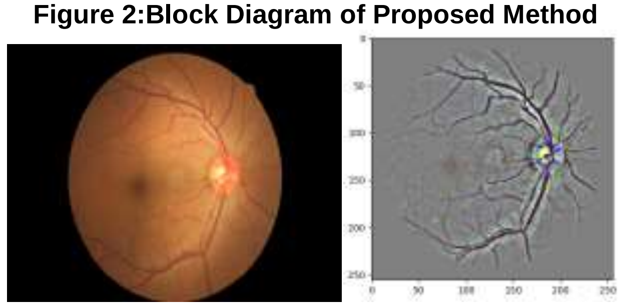

Figure 3: Image '17_ right.jpeg 'before and after preprocessing

Therefore, using GAN for image generation of minor classes and then classifies dataset and generating images by training designed CNN. The proposed solution to DR classification is shown in Figure 2.

These experiments used certain hardware and software as shown in Table 2.

The first step is to make the necessary preprocessing on the datasets used in the experiments to normalize the images from the Open CV library. After preprocessing, in addition to providing seamless and sharp images, they also reduced their size from about 40 GB to about 2.2 GB. An example of the retinal image before and after the preprocessing operation is illustrated in Figure 3.

RESULTS

The classification accuracy after completing the second stage was 89%, while the top contestants of the Kaggle Competition achieved about 82%, thus improving the accuracy of the proposed method to about 7%. On the one hand, oversampling and generation new images from several classes are done by using one GPU and then the distribution of multiple GPUs was investigated, resulting in accuracy tests performed in different modes with several nodes. Various run times and accuracy of experiments are presented in Figures 4, 5.

As a review of research in solving the problem of diabetic retinopathy: in 2000, Wang presented a new method for the diagnosis of exudate using image processing techniques (Wang H et al., 2000). In 2003, the researchers classified retinal images into four stages. In this solution, the necessary preprocessing was done on the images in terms of light intensity, etc. Then the optical disc and blood vessels were positioned in the image. In the third stage, diabetic retinopathy lesions including exudate, hemorrhage, produced veins, and micro aneurysm was diagnosed and finally, the whole dataset was classified and labeled into two classes of health and patient cases (Sinthanayothin et al., 2003). The following year this problem solved by using neural networks (Fleming et al., 2007). Then in 2005, using image processing and pattern recognition techniques, the lesions were examined and labeled in three non-proliferative states (Lee SC et al., 2005) and some incorporate optimization in the classification using the Bayesian method (Kahai P et al., 2006). The following year, the researchers made the diagnosis in three stages. In the first stage, they collected 600 normal and 300 diabetic eye images, and in the second stage analyzed the retina features by examining the lesions and obtained the results of these three types of healthy, diseased and unknown labels. Finally, the results were evaluated (Singalavanija et al., 2006). In 2007, they performed exudative grading (Philip S et al., 2007) and others used filtering and statistical methods to identify different components of the retina in images of both healthy and diseased retina and tested 90% accuracy (Estabridis et al., 2007). The following year, researchers classified the data into proliferative and non-proliferative, using luminous lesions and capillary patterns in the retina image (Li Q et al., 2008) and some performed a three-layer neural network image processing and classification (Yun WL et al., 2008). Elsewhere, morphological classification was performed (Nayak J et al., 2009). In 2009, retina images were classified by 5 labels using the Support Vector Machine technique (Acharya et al., 2009). The following year, a system was introduced to diagnose the degree of diabetic retinopathy as well as the risk of macular edema (Dupas et al., 2010). In 2011, a Decision Support System was introduced that STARE dataset classifies 40 retinal images into two classes of healthy and diseased and non-prolife ratively classified into three classes of mild, moderate, and severe (Reza AW et al., 2011). In 2014, it determined the existence of micro aneurysm and hemorrhages in each sample by local binary patterns and using Support Vector Machine techniques (Ashraf MN et al., 2014) and some were better achieved by the Gaussian method (Akram MU et al., 2014). But in 2015, the Kaggle dataset was launched at https://www.kaggle.com/c/diabetic-retinopathy-detection with about 35,000 images and a deep learning approach challenge and top people in this challenge reached an accuracy of about 82%. (Lunscher N et al., 2017) The following year, the Kaggle dataset with another design of the deep model achieved 70% accuracy (Pratt H et al., 2016), and another group classified the problem with the Messidor-2 dataset containing 1475 retinal images of macula edema lesion passage (Abràmoff MD et al., 2016). From 2017 onwards, with the deep learning approach on the Kaggle dataset, methods were presented that each method solved the problem one way (Wang Z et al., 2017, Zhou W et al., 2017, Quellec G et al., 2017).summery of the algorithms are shown in table 3.

As shown in the chart, the classification accuracy of the proposed method was 89%, while the top contestants of the Kaggle Competition achieved about 82%, thus improving the accuracy of the proposed method to about 7%. with the distribution of training operations among inter-clustering machines, training time is dramatically about 60% reduced and the accuracy of the distributed run operation decreased a low amount (about 3%). the accuracy of this model with several GPUs is about 86% achieved.

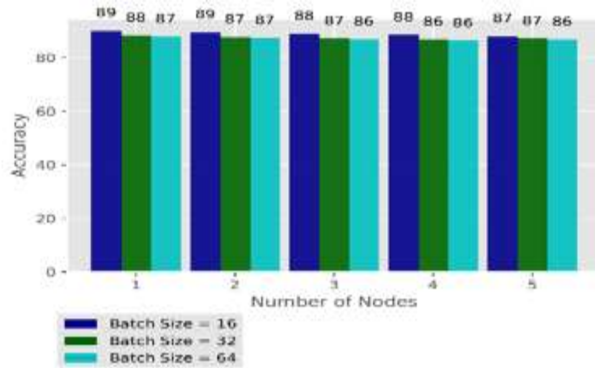

Figure 4: Classification accuracy for different number of nodes and size of batch on Kaggle dataset

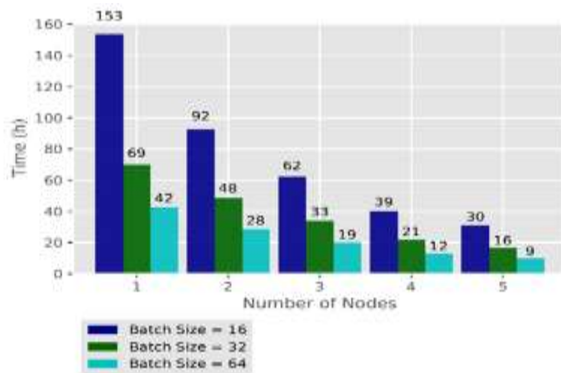

Figure 5: Runtime variation for different number of nodes and size of batch on Kaggle dataset

Table 3: Different Diabetic Retinopathy Algorithms

Algorithm	Image processing techniques	Database	Accuracy /AUC	Lesions detection /No of Class
Kahai et al., 2006 (9)	Decision support system (DSS)	143 retinal images provided by theLouisiana State University Eye Center	63%	Classification 2Classes
Ashraf et al.,2014 (19)	SVM Imaging	DIARETB	86.15% 87%	NPDR detection
Reza,Eswaran 2011(18)	Rule based classifier screening	STARE	97%	NPDR detection
Singalavanija et al., 2005 (10)	Blood vessels, exudates, haemorrhages, microaneurysms	182 patients, 336 eyes 221 eyes had a normal fundus and 115 eyes had NPDR	83%	Classificatio n2Classes
Philip et al., 2007 (11)	Exudates	14 406 images from 6722 patients	67%	Classification2Classes disease/health
Estabridis and Figueiredo 2007 (12)	Fovea, blood vessel network, optic disk, bright and dark lesions	UCLA 20 images training 20 images tested	90%	Classification2Classes
Pratt et al.,2016 *(22)*	CNN approach to diagnosing DR from digital fundus images	Kaggle	75%	Classification 5Classes
Wang et al.,2017 (24)	regression activation map CNN	Kaggle	-	detection
Abràmoff et al.,2016 *(23)*	CNN	Messidor-2	-	NPDR, PDR, or ME detection
Quellec et al.,2017 (26)	CNN	Kaggleand a private dataset of almost 110,000	-	All lesions detection
Antony et al.,2015 (21)	CNN	Kaggle	84.5%	detection
Proposed Method	GAN,CNN	Kaggle	89%	2Classes: PDR,NPDR

Table 4: Accuracy of Classification in paralleling

Number of Classifiers Inter clustering	Classifiers	Average accuracy of Classification in initial state	Accuracy of Classification after ensembling
3	AlexNet(Adam), VGG16(Adam), UNet	88.62	89.77
4	AlexNet(Adam), VGG16(Adam), UNet, AlexNet(RMSprop)	87.78	89.08
5	AlexNet(Adam), VGG16(Adam), UNet, AlexNet(RMSprop), VGG16(RMSprop)	87.19	88.68

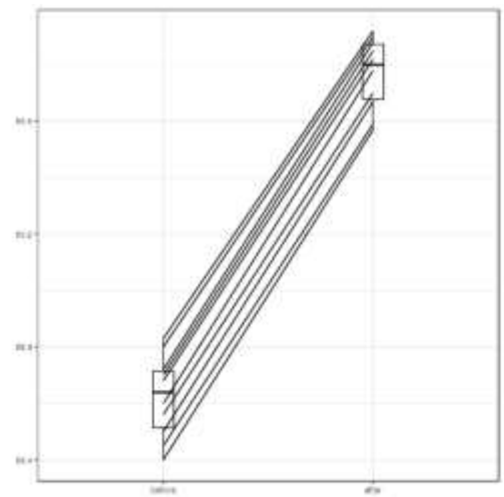

Figure 6: Degree of improvement of the classification accuracy in the 3-classifier by 10 times

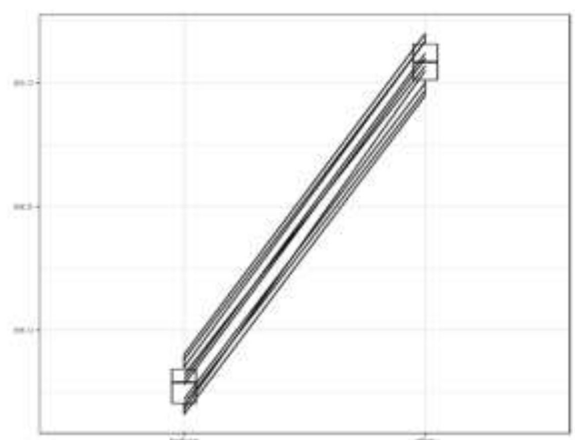

Figure 7: Degree of improvement of the classification accuracy in the 4-classifier by 10 times

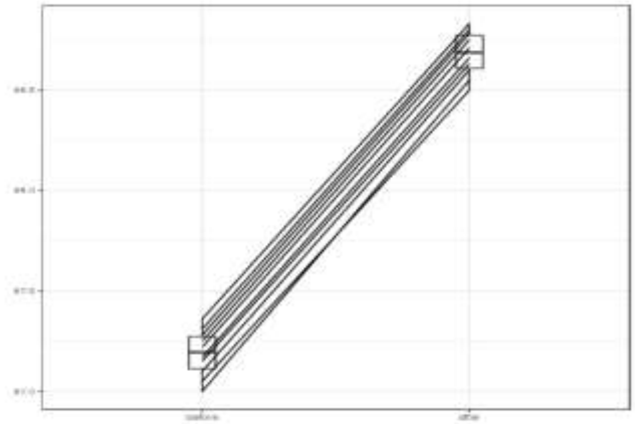

Figure 8: Degree of improvement of the classification accuracy in the 5-classifier by 10 times

DISCUSSION

The results of the paired sample T-test of the experiments are as follows:

Table 4 shows the accuracy of the classification in the case of using a single-classifier and multi- classifier mode. Since at least three data sets are required to vote, at least three classifier and a machine inter clustering are required to implement this algorithm. In order to evaluate, the paired sample T-test is evaluated separately on 3 to 5 classifier networks. The results of this assessment are shown in Figures 6-7-8.

The accuracy of classification was 89% after completing the first and second stages, which improved by approximately 7% compared to the top participants in the competition. In these experiments performed oversampling and generate new images from minor classes. Also, the use of one GPU and then the model distribution on multiple GPUs were investigated.

These techniques utilize imaging, screening and deep models to determine detection and classification of two or five classes. But in all ways, the problem of imbalanced data causes the disorder to be diagnosed, each of which has somehow resolved the problem. The proposed approach presents a novel approach to solving the problem of imbalanced data by using deep-based generative models and also tests the performance of multiple processors. The classification accuracy of a processor was about 89%, which was 7% better than the top Kaggle participants.

Also by increasing the number of nodes the runtime was significant (about 60%) saved and the accuracy decreased by 3% to 86% that it can be neglected by a 3 percent reduction. It is worth noting that since healthy class images are much more abundant in medical images than in with the diseased ones, this approach can be applied to other medical datasets as well, it is considered in the medical field

CONCLUSION

As stated above, many efforts have been made to identify the degree of diabetic retinopathy since 1996, but since 2014 after the amazing results presented by training in deep models in the field of machine vision. There have also been many efforts to process medical images, including retinal images, to solve the problem of diabetic retinopathy, which due to the optimal performance of this approach tends to improve the resolution of medical problems and diagnoses through training in deep models. It is growing rapidly, and these efforts have significantly helped patients and professionals to recognize the extent of the disease. It should be noted that since healthy class images are much more abundant in complex medical images than in complex ones, this approach can be applied to other medical datasets as well, so it is considered in the medical field.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

MK advised the road of research and experiments. JM was a consultant of the road of research. SM participated in data collection and analysis of the data and designed model architecture and experiment and research. All authors read and approved the final version.

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