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Appendix L2

(Item No 5 of Check List) Details of Research Publications

Verified mam.

S.No	Article	Journal	Other Details Vol/No/Page No/ Year	Published in UGC-CARE / Scopus Indexed/ Web of Science
1	Exploration of AI powered Densenet 121 for effective diabetic retinopathy detection	International ophthalmology (SCIE)	(2024) 44:90 (1)	Web of science and Scopus Indexed
2	The Role of Artificial Intelligence in Enhancing Diabetic Retinopathy lesion Detection : A Review	Journal of clinical and Biomedical sciences	14(4) 121-128 2024	UGC Care

*Proof of list of Journals from Internet to be attached along with copies of reprints.

Scholar :

Supervisor : 26/3/25

Checked By: 26/3/25

HoD/Dean of Respective School

3

The scholar Miss Santhiya Lakshmi, K. [21 PHELF 001]
has published her research articles in the following journals:

1. International ophthalmology - indexed in Scopus from 2007 to present.
2. Journal of Clinical and Biomedical Sciences - indexed in UGC Care Group I from July 2024 to present.

This may be considered.

J. [signature]
26.03.25
Asst. Librarian.

Master Jour

Int Ophthalmol (2024) 44:90
https://doi.org/10.1007/s10792-024-03027-7

ORIGINAL PAPER

Exploration of AI-powered DenseNet121 for effective diabetic retinopathy detection

K. Santhiya Lakshmi · B. Sargunam

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Abstract
Objective Diabetic Retinopathy (DR) is a severe complication of diabetes that damages the retina and affects approximately 80% of patients with diabetes for 10 years or more. This condition primarily impacts young and productive individuals, resulting in significant long-term medical complications for patients and society. The early stages of diabetic retinopathy often advance without noticeable symptoms, resulting in delayed identification and intervention. Therefore, develop approaches employing transfer learning methodologies to enhance early detection capabilities, facilitating timely diagnosis and intervention to mitigate the progression of diabetic retinopathy.
Methods This study introduces a transfer learning approach for detecting four stages of DR: No DR, Mild, Moderate, and Severe. The methods AlexNet, VGG16, ResNet-50, Inception v3, and DenseNet121 are utilized and trained using the Kaggle DR dataset.
Results To assess the efficiency of the suggested improved network, the Kaggle dataset is employed to analyze four performance metrics: Sensitivity, Precision, Accuracy, and F1 score. DenseNet121 demonstrated superior accuracy among the two models, outperforming other models, making it a suitable option for automatic DR sign detection.
Conclusion The integration of the DenseNet121 model shows great promise in transforming the timely identification and treatment of DR, resulting in enhanced patient results in the long run and alleviating the burden on society.

Keywords Diabetic retinopathy · Diabetes · Retina · DenseNet121 model · Kaggle dataset

Introduction

Diabetes is a medical condition that impairs the body's ability to regulate blood sugar. Globally, there are approximately 425 million people with diabetes, with about 82 million residing in the South East Asia. Projections indicate this number will increase to 151 million by 2045 [1–3]. In India alone, there were over 72,946,400 reported cases of diabetes in 2020. DR is a complication that affects the blood vessels in the retinal tissue, potentially leading to vision disability and blindness, particularly in older individuals. A challenging aspect of DR is that there may be no visible signs in its early

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stages, making early detection even more difficult [4]. According to the report, the prevalence of DR is 18.6% among individuals aged 60–69, 18.3% among those aged 70–79, and 18.4% among individuals over 80. In the age range of 50–59 years, a lower prevalence of 14.3% is observed. States with economic solid and epidemiological advancements, such as Tamil Nadu and Kerala, showed a high prevalence of diabetes. These states also host various research centers conducting studies on the frequency of occurrence [5].

The four stages are categorized as Non-Proliferative DR (NPDR) or pre-proliferative DR. If left untreated, NPDR may progress to the Proliferative DR (PDR), the fifth stage, with a high risk. The early signs of DR include lesions such as Microaneurysms, Hemorrhages, and Exudates, as illustrated in Fig. 1. Accurately detecting these lesions is a crucial step in analyzing DR. In NPDR, the stages are determined based on the severity of the lesions, as described below: Level 0: No DR. This represents a non-severe case and does not require immediate attention for retinopathy. Level 1: Mild NPDR. Patients exhibit at least one microaneurysm, with or without the presence of other lesions. Level 2: Moderate NPDR. Patients have hemorrhages and multiple microaneurysms. Level 3: Severe NPDR. Patients display hemorrhages and multiple microaneurysms in four sections or quadrants of the retina, along with cottonwood spots in two or more quadrants and intraregional microvascular abnormalities in at least one quadrant. The lesions and stages are depicted in Fig. 1.

Classifying and detecting DR is time-consuming, which becomes crucial when dealing with severe patient cases. Instead of relying solely on Machine Learning techniques, an automated system is essential to identify the stages of DR. Several research papers have been explored to understand better Pre-trained Models for building such a system. A comprehensive survey of numerous articles on the diagnosis of DR reveals various methods employed for retinopathy detection. Currently, the detection of DR relies on trained doctors reviewing individual fundus images of patients' eyes. Fundus photography involves capturing images of the back of the retina (fundus) using a specialized microscope with an attached camera known as a Fundus camera. While this approach is practical, it demands considerable resources. The expertise and equipment required may not be easily accessible in certain regions. Thus, there has long been a recognized need for automated and accurate detection of DR.

The primary objective of this study is to conduct a comparative analysis between Pre-trained Models in the detection of DR. Deep learning is employed, involving training a model from scratch using the dataset. In contrast, transfer learning entailed pretraining a model utilizing the ImageNet dataset and then transferring the weights to the DR dataset. Subsequently, the model underwent fine-tuning, and the outcomes of the five approaches were compared. The

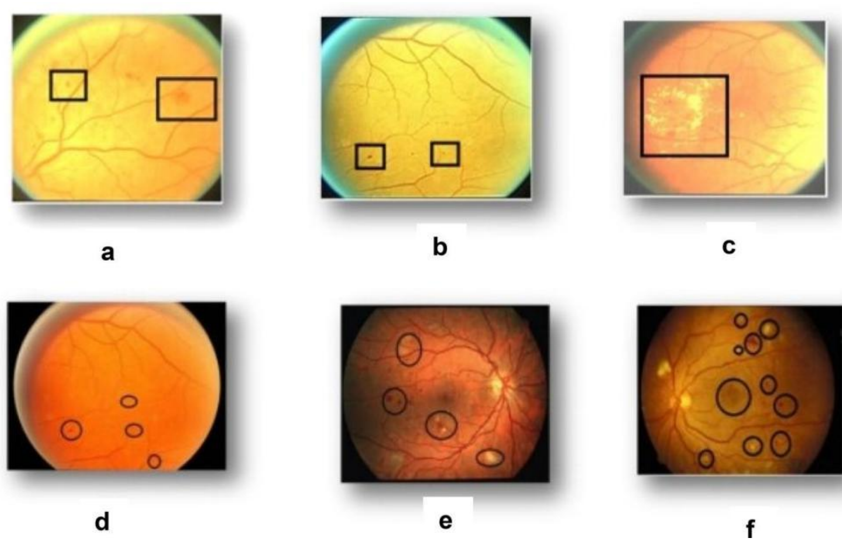


Fig. 1 Lesion Classification [6] **a** Microaneurysm, **b** Hemorrhages, **c** Exudates and Stages of DR [7], **d** Mild, **e** Moderate, **f** Severe

other sections of this research paper are structured as follows: Section "Methods" discusses the network architectures, Section "Implementation details" elaborates on implementation details, Section "Results" presents the results and discussions, Section "Conclusion" provides the conclusion, and the references are included.

Diabetic eye disease (DED) is a major contributor to blindness, and its prevalence is expected to increase steadily. Different forms of DED can damage various parts of the eye's retina. Among adults aged 20–70, severe DED is the leading cause of blindness. In response to this challenge, researchers have developed several algorithms to investigate DR reports to diagnose DR [8, 9]. This article accurately discusses some relevant papers in this field. A comparison of different methods [10] for detecting exudates was evaluated using CNN, a Discriminative Restricted Boltzmann Machine, and deep features extracted from a ResNet-50, combined with various Machine Learning classifiers.

Utilizing learnable features obtained the most promising results in conjunction with an SVM classifier. A standalone U-Net [11] was trained on fundus patches to segment relevant DR lesions from the images. Two different partitioning approaches were investigated for creating these patches. The first approach involved randomly selecting a pixel that belonged to an exudate lesion and extracting a patch of 48×48 pixels around it. This method ensured that the chosen patches contained an exudate; however, some patches might have overlapping exudates. The second approach, on the other hand, involved iteratively cropping discrete patches from the image. Although this approach avoided overlapping areas among the patches, the percentage of patches containing an exudate was small. After experimentation, the model achieved the best F1 score of 92.8% when trained with a combination of 75% patches from the first and 25% from the second approaches. A two-stage pipeline [12] was used to detect Microaneurysms (MA). In the first stage, they used a CNN model to generate a probability map of potential MA regions from the input image. In the second stage, this probability map was combined with the original image, and another CNN was employed to detect specific MA spots and non-MA regions.

The authors argue that this approach overcomes the challenges of imbalanced datasets, reducing the model's false positive rate. A study [13] using the STARE dataset was performed using binary classification (normal and abnormal) for ten retinal diseases. They utilized SGD optimizer with random forest classifier achieving an AUC of 90.3%, sensitivity of 80.3%, and specificity of 85.5%. The VGG-Net architecture [14] was utilized to identify DR and other diseases like Age-related Macular Degeneration (AMD) and Glaucoma (Gl). They gathered the dataset from the Singapore National DR Screening Program (SIDRP) between 2010 and 2013, achieving an AUC of 93% and specificity of 91.6%, with a sensitivity of 90.5% for DR. For glaucoma, they obtained an AUC of 94.2%, specificity of 87.2%, and sensitivity of 96.4%.

Methods

Network architecture

Transfer learning

Although Deep Learning has proven to be a powerful tool for solving complex problems, it often demands significant computational resources to train a new network for each new task [15, 16]. Another common challenge in deep learning is overfitting, wherein the web tends to "memorize" the training dataset [17]. This issue becomes more severe when the dataset is small, making it easier for large networks to overfit the entire dataset. Consequently, the network's performance on unseen test data could be better due to its failure to generalize effectively.

To address these challenges, transfer learning comes to the rescue. Transfer learning involves transferring the learned parameters (weights) from networks trained on other datasets to a new network trained on a different dataset. This process provides beneficial regularization to the network, mitigating overfitting issues. In this study, the pre-trained models are used, which first undergoes training on large available datasets and then receives further training on the new dataset [18]. The choice of pre-trained models for diabetic retinopathy detection involves a detailed exploration of selection criteria for each model, namely AlexNet, VGG16, ResNet-50, Inception v3, and DenseNet121, along with an elucidation of why these models were preferred over others for this particular task are discussed along with their architecture as below:

a. AlexNet model.

In 2012, Alex Krizhevsky and their team introduced a CNN model called AlexNet, which was more profound and broader than the LeNet model [19]. AlexNet achieved remarkable success by winning the prestigious ImageNet Large Scale Visual Recognition Challenge (ILSVRC) that same year. It outperformed traditional machine learning and computer vision approaches, establishing a new state-of-the-art accuracy for visual recognition and classification tasks. This makes AlexNet a promising candidate for diabetic retinopathy detection, especially in settings with resource limitations. Figure 2 illustrates the architecture of AlexNet.

b. VGG16 model.

The Visual Geometry Group (VGG16), Oxford Net, stands out as exceptional convolutional neural network architecture in computer vision [14]. This network is 16 layers deep and is characterized by a substantial number of hyper-parameters, primarily concentrated within its convolutional layers featuring 3 × 3 filters with a stride of 1 and consistent employment of the same padding, along with max-pooling layers using 2 × 2 filters and a stride of 2 [20].

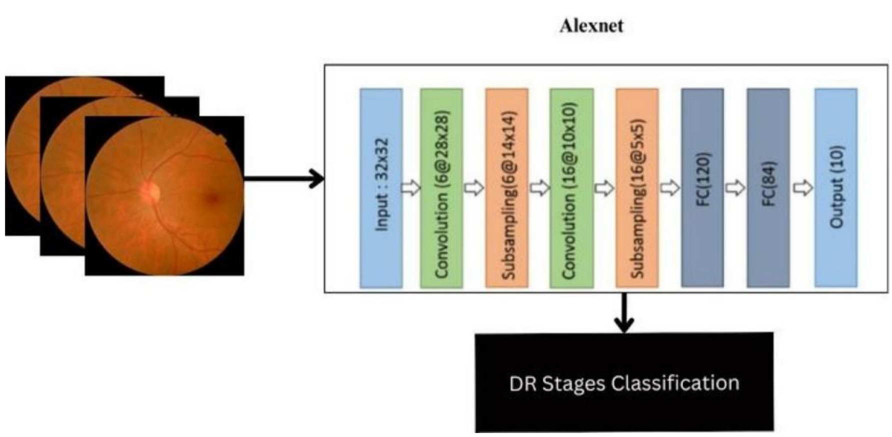
The prominent use of 3 × 3 convolutional layers stands out as a distinctive characteristic of VGG16, and this design choice yields several noteworthy impacts. VGG16 maintains a consistent and uniform structure by employing 3 × 3 convolutional filters throughout its architecture. This simplicity contributes to a clearer understanding of the model, facilitates effective training, and streamlines deployment processes. Additionally, the stacking of 3 × 3 convolutional layers within VGG16 allows the network to acquire hierarchical features progressively. Starting with the capture of basic features in the initial layers, the depth of the network leads to the learning of more abstract and complex features.

It is worth acknowledging, however, that while VGG16's architecture, featuring extensive use of 3 × 3 convolutional layers, has demonstrated effectiveness in image classification tasks, it is imperative to recognize that the resultant model can be computationally intensive. This is particularly notable in terms of memory requirements and processing power, considerations that warrant attention in practical implementations. Thus, the uniform structure of VGG16, coupled with its proven success in image classification tasks, renders it an appealing choice for transfer learning in diabetic retinopathy detection. A visual representation of the VGG16 method can be found in Fig. 3.

c. ResNet-50 model.

Residual learning empowers the neural network to delve deeper into its layers, extracting higher-level features from images and achieving classification with a reduced error rate [21]. The ensemble model of the residual neural network further improved the performance, earning a 3.57% error rate. The core idea behind the ResNet-50 architecture lies in its skip

Fig. 2 Architecture of AlexNet model



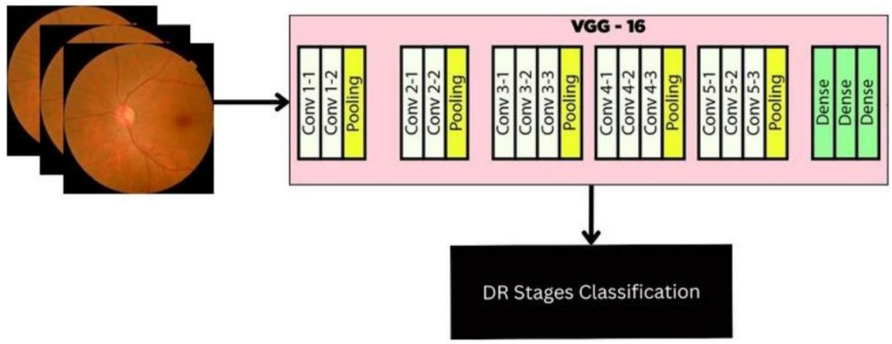


Fig. 3 Architecture of VGG16 model

connections, which effectively address the problem of vanishing gradients. These connections enable the network to learn from deeper layers. For this study, the ResNet-50 architecture has been adopted, shown in Fig. 4, with an input size of 224 × 224 × 3, where the channel width is 3. The residual network incorporates numerous basic residual blocks, and the operations within these blocks are altered depending on the type of residual network architecture. One significant advantage of ResNet-50 is its ability to mitigate the issue of gradient diminishing. The shortcut connections (residual links) play a crucial role in accelerating the convergence of deep networks, ensuring that the slopes do not vanish during training [22] and

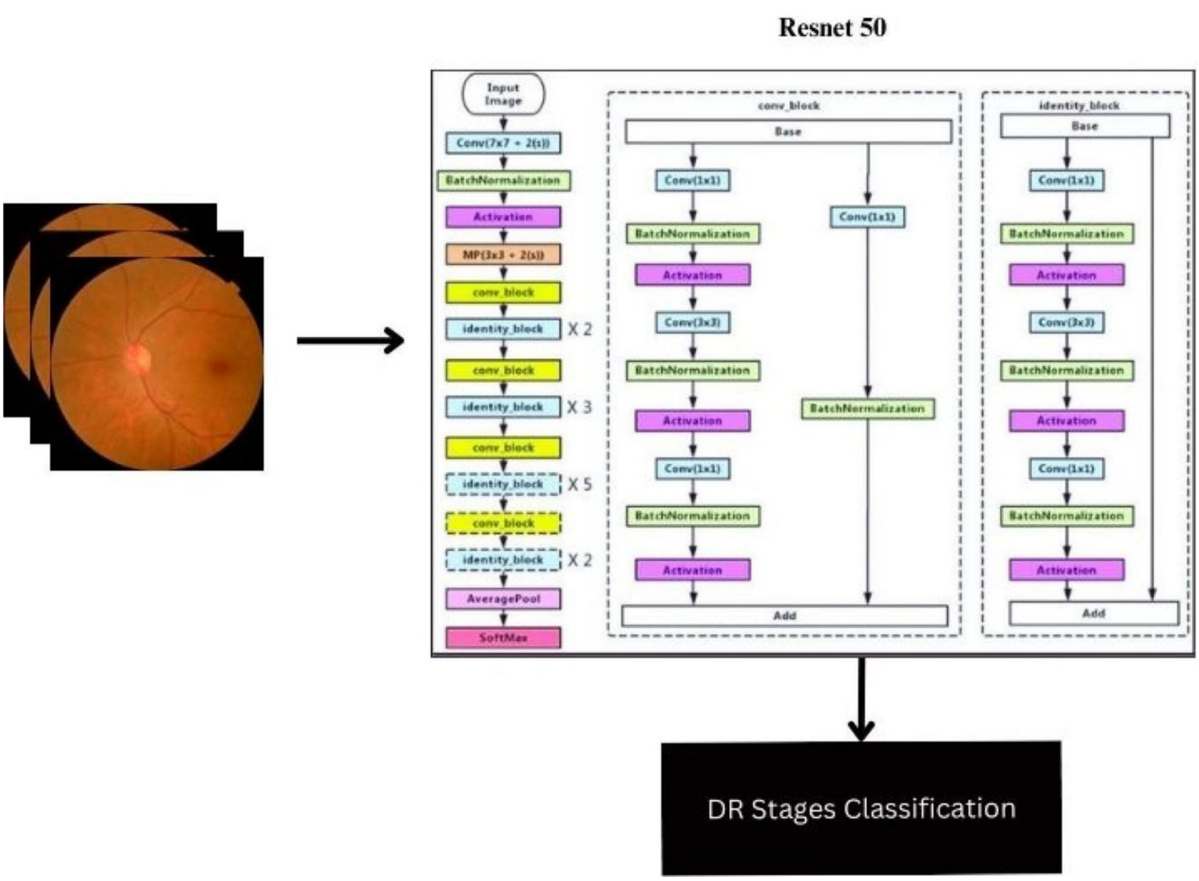


Fig. 4 ResNet-50 model's architecture

making it well-suited for addressing the intricacies of diabetic retinopathy detection, particularly in tasks necessitating deeper network architectures.

d. Inception v3.

Szegedy et al. [23] introduced Inception v3, a revision of the earlier Inception architectures, primarily emphasizing optimizing computational resources. The Inception v3 architecture (Fig. 5) is constructed in a step-wise fashion, gradually. In Inception v3, the utilization of factorized convolutions, also referred to as depth-wise separable convolutions, plays a crucial role in optimizing computational efficiency.

In the context of Depth-wise Convolution, the process involves independently applying convolution to each channel of the input. Instead of employing a unified convolutional filter spanning all input channels, a distinct filter is utilized for each channel. This results in the generation of a set of feature maps specific to each input channel. Subsequently, a point-wise convolution is implemented, essentially representing a 1 × 1 convolution. This step combines information derived from the output of the depth-wise convolution, facilitating the creation of new features through linearly combining the information across channels.

Hence, the factorized convolutions in Inception v3 enhance computational efficiency by significantly reducing the number of parameters and computations. This design choice not only contributes to a more lightweight and efficient model but also allows for effective deployment in scenarios with limited computational resources. In addition, the inclusion of an auxiliary classifier acts as a form of regularization by preventing the network from becoming overly reliant on the final classification layer for learning. This regularization effect helps prevent the model from memorizing the training data and encourages it to capture more generic features that are applicable to a broader range of inputs. It is a deep architecture, and training very deep networks can be challenging. The auxiliary classifier facilitates the training of deeper networks by providing additional gradient flow paths and helping to combat issues related to vanishing gradients.

The efficient capture of multi-scale features by Inception v3 aligns seamlessly with the diverse characteristics found in retinal images. This, coupled with its competitive accuracy and lower computational cost, positions Inception v3 as a compelling option for diabetic retinopathy detection.

e. DenseNet121 model.

In the year 2017, Huang and colleagues (Huang et al. [24]) introduced DenseNet, a convolutional neural network distinguished by its densely connected architecture, as illustrated in Fig. 6. DenseNet121 is a particular version of the DenseNet architecture, incorporating 121 layers. The designation "121" in its nomenclature indicates the overall count of layers

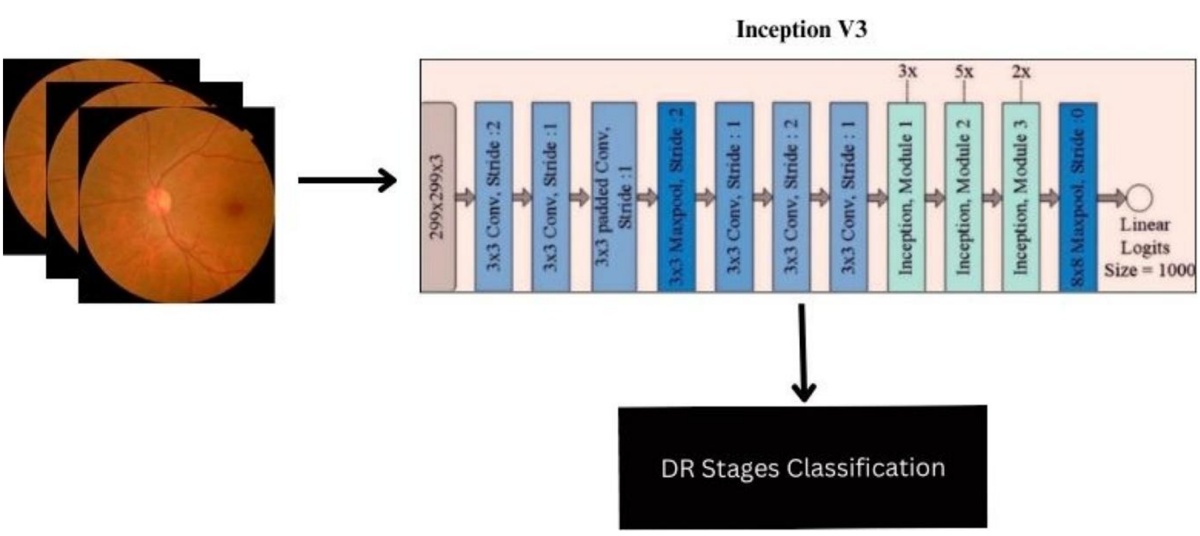


Fig. 5 Architecture of Inception v3 model

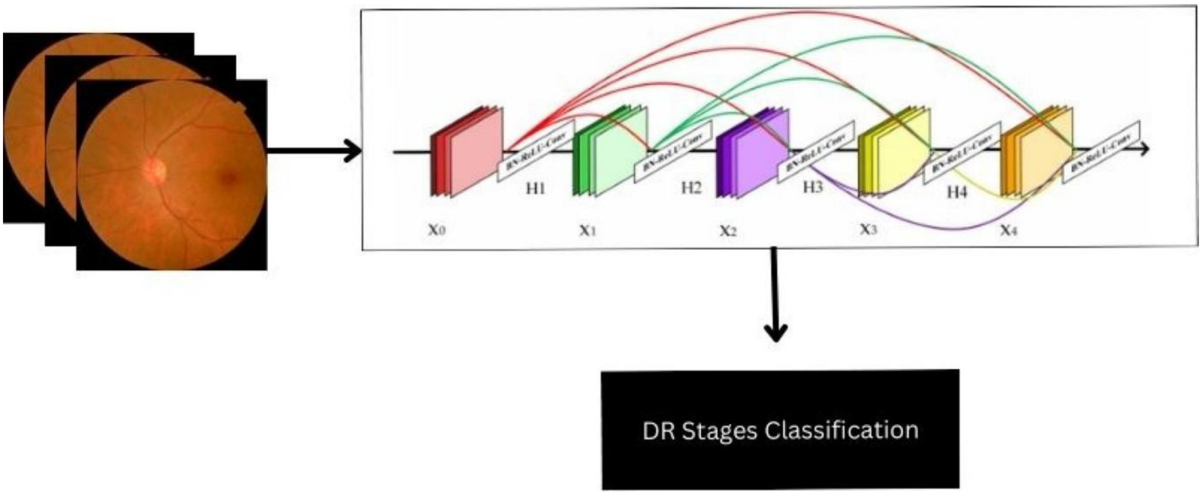


Fig. 6 Architecture of DenseNet121 model

within the network. Within DenseNet121, each layer establishes connections with every other layer in a forward-flow manner, contributing to a reduction in parameters while preserving the richness of features acquired by the network. The essential elements of DenseNet121 encompass:

1. Dense blocks

DenseNet exhibits distinctive dense blocks, serving as the foundational components of its architecture. Each dense block comprises numerous densely connected layers. Within a dense block, every layer receives as input the concatenated feature maps from all preceding layers.

2. Transition layers

Following each dense block, transition layers are employed to diminish the spatial dimensions of the feature maps. These layers commonly integrate a blend of batch normalization, 1 × 1 convolutions, and pooling operations to downsample the feature maps.

3. Bottleneck layers

Within each dense block, bottleneck layers are employed to decrease the number of input feature maps prior to establishing dense connectivity. A typical bottleneck layer includes a batch normalization layer, a 1 × 1 convolution layer (for dimensionality reduction), and a subsequent 3 × 3 convolution layer.

4. Global average pooling (GAP)

Instead of utilizing fully connected layers at the conclusion of the network, DenseNet employs global average pooling. Global average pooling reduces the spatial dimensions of the final feature maps to a 1 × 1 size, with the resulting values serving as input to the ultimate softmax layer for classification.

5. Dropout

In certain implementations, dropout layers may be incorporated to mitigate overfitting during training. Dropout randomly zeroes a portion of input units during the training process.

6. Batch normalization

Batch normalization is applied uniformly across the network to normalize the input of each layer, facilitating accelerated convergence during training. The fundamental structure of DenseNet121 involves the arrangement of multiple dense blocks and transition layers. The dense connectivity inherent in these blocks fosters feature reuse, aids in the smooth flow of gradients, and enhances the model's capacity to discern intricate patterns in the data. The core idea behind the DenseNet architecture is the concept that the feature maps generated by each layer can be concatenated to compose the input for the subsequent layer. This implies that the output of each layer serves as the input for all subsequent layers. Additionally, DenseNet incorporates a transition layer between each dense block to diminish spatial dimensionality and the quantity of feature maps. This transition layer comprises a batch normalization layer, a 1 × 1 convolutional layer, and a pooling layer. Moreover, DenseNet's dense connectivity promotes feature reuse and addresses vanishing gradient issues, making it particularly suitable for training deeper networks, and its ability to achieve commendable performance with fewer parameters enhances efficiency, making DenseNet121 advantageous for diabetic retinopathy detection, especially in resource-efficient scenarios.

Implementation details

(a) Hardware.

The system employed for model implementation and training features an NVIDIA Tesla K20 GPU boasting 5 GB of memory. The operating environment is Windows 10, running on a 64-bit Intel i3 processor.

(b) Software.

For the implementation of pre-trained architectures using an open-source language, this work recommends leveraging TensorFlow. TensorFlow, a freely available self-learning platform primarily developed by Google and based on the Python language, offers a comprehensive set of libraries. Among these is Keras, a deep learning application programming interface (API) for Python, built on top of TensorFlow. With Keras, the creation of equivalent models is facilitated effortlessly.

(c) Integrated Development Environment (IDE).

The experimental evaluation takes place within the Jupyter Notebook environment.

Table 1 The details of DR Dataset

Dataset subsets	Kaggle dataset
Training set	2697 images
Validation set	335 images
Test set	335 images

Table 2 The number of retinal images available in the dataset under Severity Level

Severity level	Samples
Class-0 (normal)	37
Class-1 (mild stage)	99
Class-2 (moderate stage)	180
Class-3 (severe stage)	19
Total	335

Data collection

The dataset used in the research is an open-source DR detection dataset obtained from Kaggle [25] consisting of 3367 images. The classification task involved categorizing the images into four classes, namely: No DR, Mild DR, Moderate DR, and Severe DR, and it is graded on a scale of 0–3 (0-No DR, 1-Mild, 2-Moderate, 3-Severe) to indicate different severity levels. The dataset is further divided to accommodate pre-trained models; the details of the split are provided in Tables 1 and 2 which give the number of retinal images available in the dataset under each level of severity.

Model configuration

Data pre-processing techniques are applied before feeding the images to the network to account for the significant variation in image quality within the dataset. The Keras Image Data Generator function performs data pre-processing and augmentation for this task. This class also supports essential data augmentation, such as randomly flipping images horizontally. The generator is also used to transform the values in each batch, ensuring that their mean is 0 and their standard deviation is 1. This will facilitate model training by standardizing the input distribution. Once the data are set up, data generators are created for training, testing, and validation of data using Keras's Image Data Generator class. With the data preparation complete, the model is loaded using the pre-trained function from Keras. The layers are kept frozen to prevent the already trained layers from being altered. On top of the pre-trained model, a custom output layer using the Sequential class from Keras is added.

Next, the model is compiled, specifying the optimizer, loss function (chosen for better accuracy with a low value), and evaluation metric. Subsequently, the model is trained using the fit process and evaluated on its performance on the validation data using the evaluate function. In addition, hyperparameters played a crucial role. Hyperparameters are variables predefined or tuned by a human designer or using hyperparameter optimization methods. In this instance, the manual hyperparameter tuning expedites the process. The configuration values for the models are given in Table 3.

The selection of optimizer, learning rate, and loss function is a crucial aspect in the training of neural network models. Let us delve into the specifics of the chosen components, such as the Adam optimizer—an optimization algorithm widely applied in deep neural network training, known for fostering rapid convergence and efficient optimization. Additionally, the learning rate, a pivotal hyperparameter determining the optimization step size, is worth considering. Opting for a smaller learning rate, like 0.0001, tends to yield slower but more stable convergence, proving advantageous for training stability and preventing overshooting during the optimization process. This learning rate is often favored in scenarios involving fine-tuning or specific tasks where a cautious approach to learning rate selection is preferred. Lastly, the utilization of Categorical Cross-Entropy loss stands out for models engaged in multi-class classification tasks. This loss function plays a crucial role in penalizing misclassifications effectively, thereby promoting precise predictions in the context of multi-class classification challenges.

Table 3 Hyperparameters for the pre-trained models

Optimizer	Adam
Loss function	Sparse categorical cross-entropy
Batch size	8
Learning rate	0.0001
Epochs	10
Momentum	0.9
Mode	Triangular
Class weight	Auto
Dropout	0.5

Evaluation metrics

Accuracy [26, 27] is a crucial classification model metric. Its simplicity and ease of understanding make it popular for binary and multi-class classification problems. Accuracy measures the proportion of correct predictions from the total number of records tested and is calculated using Eq. (1). This metric is effective in evaluating classification models constructed from balanced datasets. However, caution should be exercised when interpreting accuracy for skewed or imbalanced datasets, as it may lead to incorrect assessments due to the disproportionate representation of classes.

$$\mathrm{ACC} = \frac{\text{True Positives} + \text{True Negatives}}{\text{True Positives} + \text{False Negatives} + \text{True Negatives} + \text{False Positives}} \tag{1}$$

Sensitivity, also known as Recall, is a metric used to optimize the prediction of a specific class. It quantifies the proportion of positive voxels from the ground truth correctly identified as positive during the segmentation process. Sensitivity is calculated using Eq. (2),

$$\text{Sensitivity} = \text{Recall} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Negatives}} \tag{2}$$

Precision is a statistical measure employed to evaluate the precision of a classification model, like a diagnostic test. Put differently, precision gages the model's capacity to refrain from categorizing negative instances as positive. The precision formula is expressed in Eq. (3),

$$\text{Precision} = \frac{\text{True Positives}}{\text{True Positives} + \text{False Positives}} \quad (3)$$

The F1 score is an evaluation metric used to assess the effectiveness of classifiers. It quantifies a classifier's ability to perform classification tasks by harmonizing precision and recall, resulting in a unified performance measure. It is calculated using the following equation:

$$\text{F1} - \text{score} = \frac{2\ \text{Precision} * \text{Recall}}{\text{Precision} + \text{Recall}} \quad (4)$$

Results

Diabetic Retinopathy (DR) is a leading cause of vision loss among people with diabetes. Early detection is crucial to prevent further damage and provide timely treatment. With advancements in deep learning and computer vision, new techniques are emerging to revolutionize the detection of DR. One such technique is the use of DenseNet121, a powerful pre-trained model that has shown promising results in discriminating between the presence and the absence of DR, as well as identifying the specific stages of DR. Pre-trained models are pre-trained on large datasets, such as ImageNet, and have learned to extract meaningful features from images. These models can be fine-tuned and adapted to specific tasks like DR detection. By leveraging the knowledge and representations learned from ImageNet, pre-trained models can quickly adapt to new datasets with relatively small amounts of labeled data.

Table 4 The obtained metrics for the pre-trained models

Models	Accuracy	Precision	Recall	F1 score
AlexNet	0.52	0.70	0.58	0.63
VGG16	0.66	0.78	0.61	0.68
ResNet-50	0.73	0.80	0.65	0.71
Inception v3	0.76	0.84	0.73	0.78
DenseNet121	0.87	0.89	0.78	0.83

Various performance metrics such as Precision, Recall, F1 score, and Accuracy were computed to evaluate the performance of different pre-trained models for DR detection. These metrics provide insights into the effectiveness and reliability of the models in accurately classifying DR cases. Table 4 displays the achieved outcomes of these metrics for the suggested pre-trained models. The result shows that DenseNet121 outperformed other models in its potential to detect and classify DR. This pre-trained model accurately has shown remarkable results and holds great promise for improving the diagnosis and management of diabetic retinopathy.

The training and validation loss for all pre-trained models are depicted in Figs. 7 and 8. Notably, the loss for DenseNet121 consistently decreased throughout

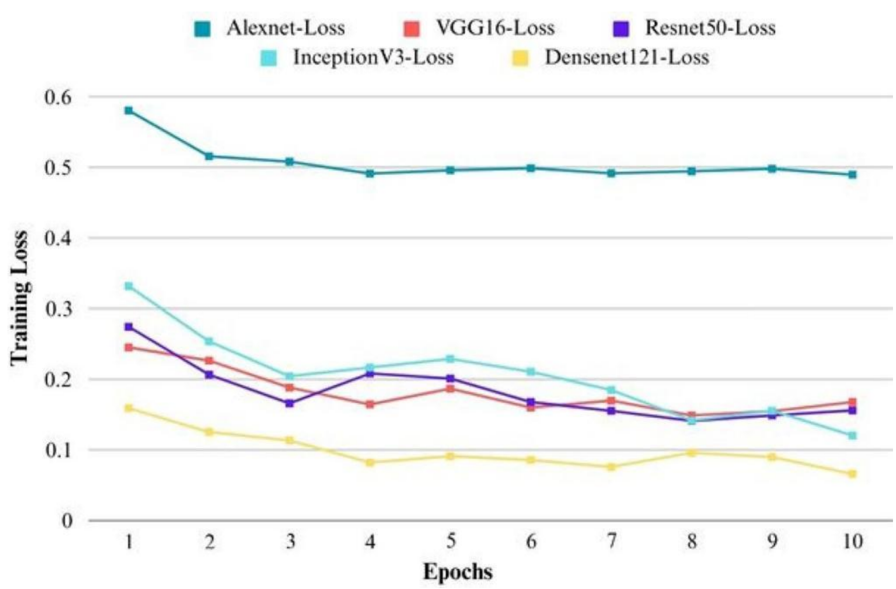


Fig. 7 The training loss per epoch for all models

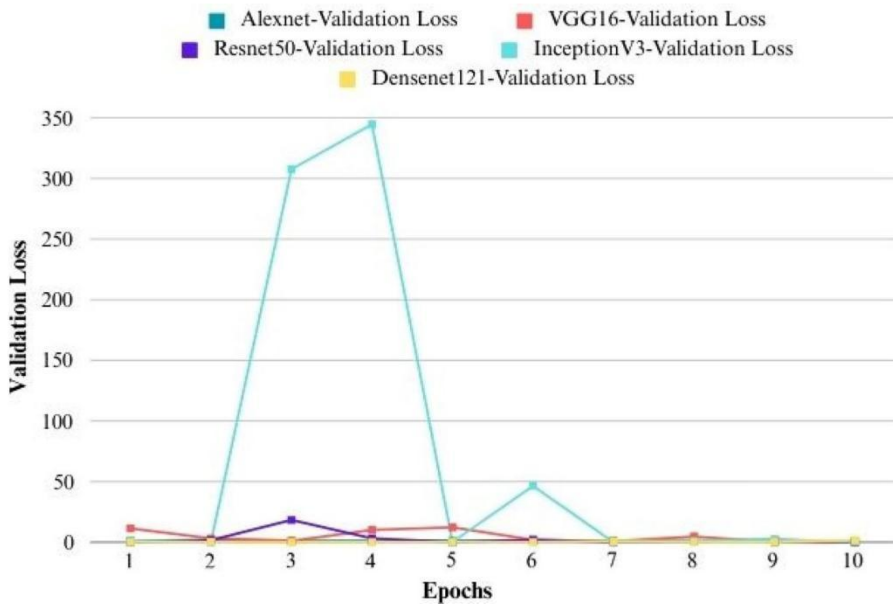


Fig. 8 **The** validation loss per epoch of all five models

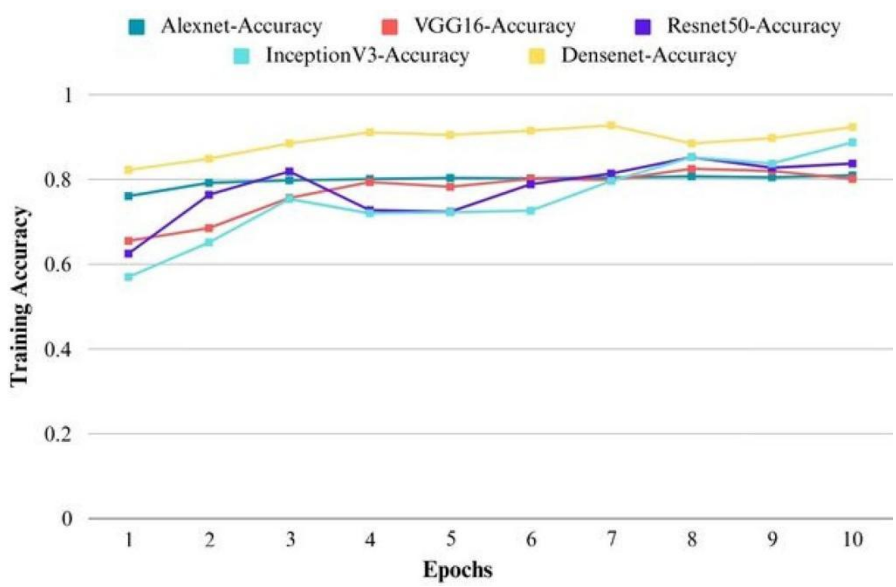


Fig. 9 The training accuracy per epoch of all five models

the epochs, underscoring the model's effectiveness in minimizing errors and enhancing overall performance.

Additionally, Fig. 9 illustrates the training accuracy for all pre-trained models. The AlexNet model exhibited a gradual accuracy improvement during training, reaching its peak around the eighth epoch. Similarly, VGG16 demonstrated a steady accuracy increase, peaking around the eighth epoch. In contrast, ResNet-50 rapidly improved in accuracy in the initial epochs but plateaued after the fifth epoch. Inception v3 showcased a gradual accuracy increase, reaching its peak around the ninth epoch. DenseNet121, on the other hand, displayed a sharp accuracy increase initially, leveling off after the sixth epoch.

Furthermore, Fig. 10 presents the validation accuracy for all pre-trained models. The validation accuracy of the AlexNet model suggests strong generalization to unseen data. The validation accuracy closely mirrored the training accuracy for VGG16, indicating

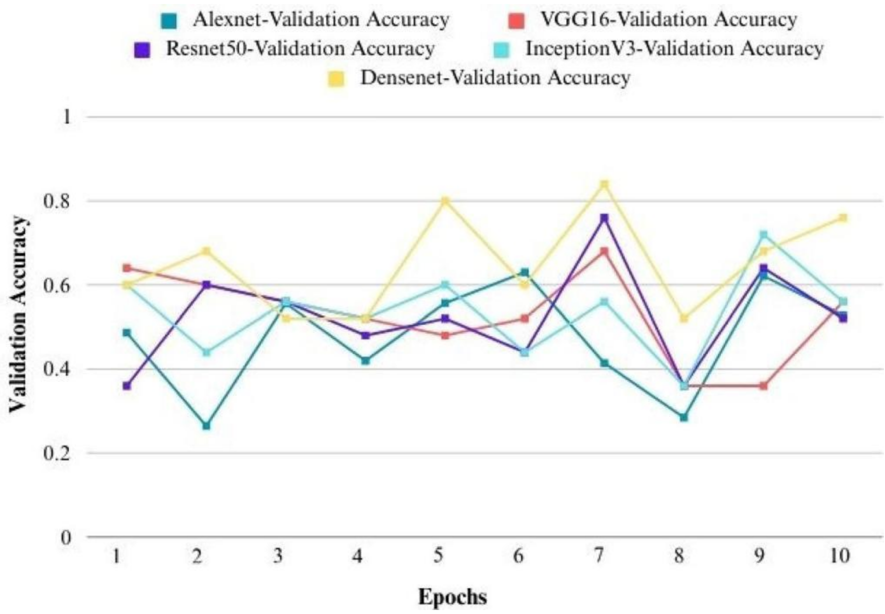


Fig. 10 The validation accuracy per epoch of all five models

effective generalization. ResNet-50's validation accu- racy closely tracked its training accuracy, reflecting good generalization. Notably, DenseNet121 exhibited close alignment between validation and training accu- racy, suggesting better generalization compared to Inception v3. Figure 11 represents Confusion Matri- ces of pre-trained models, whereas confusion matrix provides information about the performance of a clas- sification model.

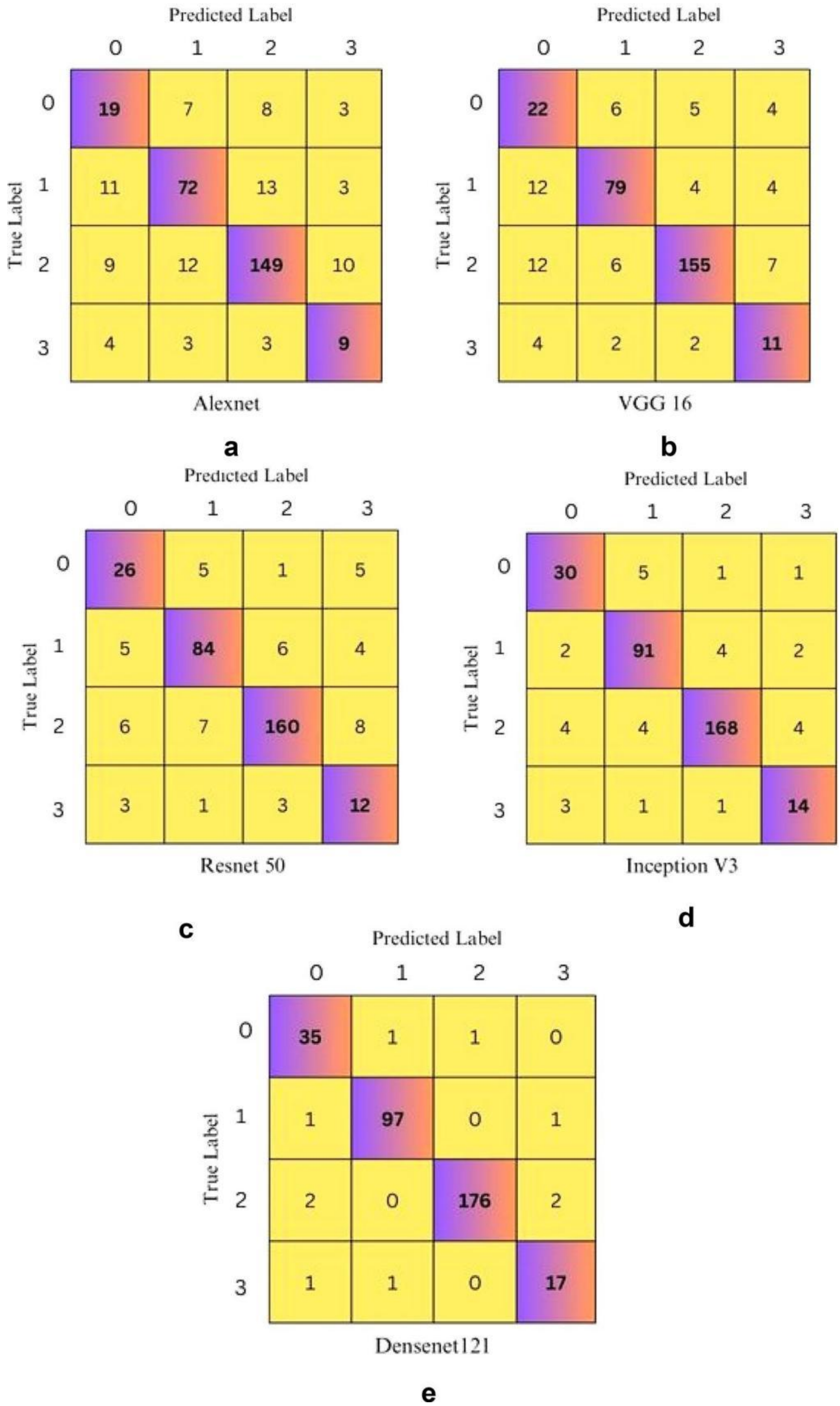
Based on the training and validation accuracy/ loss analysis for each pre-trained models and the confusion matrices, it is evident that DenseNet121 is a highly effective model for diabetic retinopathy detection. Its unique architecture and dense connectivity pattern allow for efficient information flow, resulting in accurate identification of diabetic retinopathy. However, it is essential to note that other pre-trained models, such as AlexNet, VGG16, ResNet-50, and Inception v3, also show promise. This research demonstrates the power and effectiveness of DenseNet121 in accurately classifying images related to diabetic retinopathy. Accuracy alone is not sufficient when it comes to medical image analysis. Precision and recall are equally essential metrics to consider. Precision measures the ability of the model to correctly identify positive samples, while recall measures the ability to identify all positive samples.

Table 4 shows that DenseNet121 achieves the highest values for Precision, Recall, F1 score, and Accuracy among all the pre-trained models. This suggests that DenseNet121 is recommended for identifying the specific stages of DR and detecting the different levels of severity with higher accuracy and precision. DenseNet121 is a convolutional neural network model that has been pre-trained on a large dataset and fine-tuned for image classification tasks. Its architecture and design allow for more efficient use of parameters, reducing the risk of overfitting and improving performance in generalization tasks. This makes DenseNet121 ideal for medical image analysis, including detecting diabetic retinopathy.

Discussion

Diabetic Retinopathy (DR) is a common eye disease caused by diabetes [28]. It is a leading cause of vision loss and blindness among adults. Early detection and accurate classification of DR stages are crucial for effective treatment and prevention of further vision deterioration. In recent years, deep learning models have shown great promise in automating the detection and classification of DR stages. One such model that has gained attention is DenseNet121. This study proposed a model of different depths in terms of architecture. DenseNet121 is a deep learning model that offers a compact design and superior performance in image classification tasks. It

Fig. 11 The Confusion Matrices of all five models **a** AlexNet, **b** VGG16, **c** ResNet-50, **d** Inception v3, **e** DenseNet121



achieves higher performance than other pre-trained models due to the limited depth in its architecture. This narrow depth, along with the size of the training data used, makes DenseNet121 more efficient and less time-consuming. To train the DenseNet121 model for DR detection, the researchers utilized the ImageNet dataset for fine-tuning. The experiment involved comparing different domains and tuning parameters. They also opted to immobilize the lower-level layers and select portions of the higher-level layers while introducing new layers, including a softmax layer, to generate class probabilities.

AbdelMaksoud et al. [29] developed a computer-inspired diagnostic tool for the early detection of diabetic retinopathy. Their method is based on a hybrid deep learning approach, combining CNN models with other machine learning techniques. Specifically, they employed the DenseNet121 architecture, which has proven to be a powerful tool for image recognition tasks. In a recent study, Rafid et al. [30] proposed an ensemble framework for the early diagnosis of diabetic retinopathy. Their method extended the work of Abdel Maksoud et al. by incorporating multiple deep learning models and ensemble techniques.

Additionally, the lower network layers extract simpler, low-level features, while the higher layers capture intricate and high-level features. As a result, the study opted to immobilize the lower-level layers and certain portions of the high-level layers while introducing new layers, including a softmax layer, to generate class probabilities. Furthermore, when fine-tuned DenseNet weights were applied to classify medical images related to diabetic retinopathy using the Kaggle dataset, impressive results were achieved. These outcomes can be attributed to the network's depth, width, and the substantial size of the training dataset, ImageNet, used for fine-tuning the model. DenseNet is particularly noteworthy for its compact design, allowing feature reuse and providing a concise and diverse set of input features through shortcut connections of varying lengths.

When applying the fine-tuned DenseNet121 model to classify medical images related to diabetic retinopathy using the Kaggle dataset, Das et al. [31] conducted a groundbreaking research study to explore the potential of DenseNet121 in diagnosing diabetic retinopathy. They utilized the widely recognized Kaggle dataset, which consists of retinal images labeled with various stages of the disease. The network's depth, width, and the substantial size of the training dataset, ImageNet, contributed to the potential outputs. DenseNet121's feature reuse and shortcut connections of varying lengths provided a concise and diverse set of input features. This approach yielded superior results, especially when working with images of size $224 \times 224 \times 3$, surpassing the performance of other models.

On the contrary, Inception v3 and ResNet-50, considered state-of-the-art in computer vision and image classification, demonstrated a convergence of their results, even when considering the differences across epochs. Our approach involved the utilization of the pre-trained model, DenseNet, with fine-tuning executed in the following manner: a) fine-tuning the pre-trained models on a layer-wise basis, with the lower layers and selected portions of the higher layers being frozen, and new layers introduced, all while working with images at a resolution of $224 \times 224 \times 3$; b) employing the Adam optimizer; c) when selecting hyperparameters, it is essential for transfer learning to use a low learning rate to take advantage of the weights of the pre-trained model. It is recommended to use batch sizes with powers of 2 (8, 16, 32, 64, 128) because it fits the computer's memory.

In Keras, one can use callbacks in their model to perform specific actions during training, such as weight saving, and to avoid overfitting; it is expected to use Batch Normalization and Dropout layers in between the dense layers. During Optimization methods, Adam and RMSProp are tested. RMSProp, with a meager learning rate, required more epochs than 30 to complete reasonable training. Adam is employed for 10 epochs to obtain the desired result. The choice of optimizers significantly affects the number of epochs needed to achieve a successfully trained model.

Various AI-based supporting systems are available to detect the severity of diabetic retinopathy [32]. Batch Normalization and Dropout serve as synergistic methods crucial for averting overfitting in the training process. While Batch Normalization contributes to stabilizing and expediting training, Dropout provides a form of regularization by randomly deactivating neurons. This prevents the model from memorizing the training data and encourages the generalization of knowledge to unseen data. Employing these techniques concurrently can yield more resilient and adaptable deep learning models.

The present study paves the way for developing a comprehensive automatic follow-up system for DR. DR is a chronic condition with a prolonged potential phase; regular patient follow-ups can effectively prevent blindness and delay vision deterioration. Compared to other state-of-the-art methods applied to the Kaggle datasets, the DenseNet121 model achieved significantly higher and superior results than the other models. The successful implementation and performance of the DenseNet121 model in accurately detecting and classifying DR stages opens doors to developing a comprehensive automatic follow-up system for DR. Regular patient follow-ups can effectively prevent blindness and delay vision deterioration in this chronic condition.

Conclusion

This work represents an earnest effort in that direction, employing transfer learning and fine-tuned DenseNet121 to classify various DR stages. The pretrained model architectures are utilized for the present work, and their performance is evaluated using different metrics, including Accuracy, Sensitivity, Precision, and F1 score. Harnessing the power of DenseNet121 in DR detection represents a significant advancement in leveraging AI for early diagnosis and treatment. The fast, accurate, and extensive diagnosis provided by AI-based systems holds immense potential for large-scale screening, particularly in rural areas with limited access to specialized healthcare professionals. The high accuracy achieved by DenseNet121 in classifying DR stages highlights its effectiveness as a tool for enhancing the detection and intervention of this disease. By continuing to explore and refine AI-based systems, researchers can revolutionize the field of DR detection and improve the lives of individuals with diabetes. Upon analyzing the evaluation metrics for both DenseNet and other models, it is observed that DenseNet121 outperformed other models, achieving an accuracy of 87%. This high accuracy indicates the reliability and robustness of DenseNet121 in identifying various stages of DR. Its ability to accurately distinguish between standard retinal images and those with signs of DR makes it a valuable tool in the medical field. The success of leveraging DenseNet121 in the context of DR detection opens up possibilities for further advancements in AI-based systems. By continuing to refine and improve the models, the accuracy and efficiency of DR detection can be enhanced, benefiting individuals at risk of developing this severe eye disease.

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Authors' contributions The corresponding author contributed to the study conception, design, data collection, and analysis. The first draft of the manuscript was written by KSL. The second author BS read and approved the final manuscript.

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Data availability All analysis-based data generated in the study have been included in the manuscript, and the dataset used in the study is available in the Kaggle platform.

Declarations

Conflict of interest The authors declare no competing interests.

Consent to participate Informed consent was obtained from authors included in this study.

Consent for publication The authors approved the final manuscript for submission.

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The Role of Artificial Intelligence in Enhancing Diabetic Retinopathy Lesion Detection: A Review

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Abstract

Diabetic retinopathy represents a significant microvascular complication associated with prolonged diabetes mellitus and serves as a leading cause of blindness, particularly in developing nations. For the patient's vision to be adequately preserved, early identification of DR is essential. In order to treat the disease, the patient must maintain his or her current level of vision since the disease is irreversible. The Clinical diagnosis demands significant time and the specialized knowledge of an experienced ophthalmologist and also identifying the disease features in images is also more challenging, particularly in the early stages of the disease when disease features are less noticeable. Therefore, deep learning algorithms have been used for the early diagnosis of DR in recent years, and medical image analysis utilising machine learning has demonstrated to be effective in evaluating retinal fundus images. This review's objective is to go over the numerous Deep learning techniques for automated computer-aided analysis of microaneurysms, haemorrhages, and exudates were also addressed, along with a knowledge gap in DR identification. As part of future research, this review seeks to systematize the available algorithms for ease of use and guidance by researchers.

Keywords: Diabetic Retinopathy Review; Microaneurysms; Haemorrhages; Exudates; Red Lesions; Deep Learning

1 Introduction

Diabetes is the leading cause of blindness among people under the age of 50 years. Diabetes Mellitus (DM) is a direct cause of Diabetic Retinopathy (DR) which is a complication of diabetes where prolonged hyperglycemia leads to endothelial damage in blood vessels and triggers vascular inflammation, known as microangiopathy, which, when affecting the retinal blood vessels, results in retinopathy due to reduced blood supply to the retina. In order to avoid complications associated with chronic diseases such as Diabetes, early detection is vital.

According to statistics collected by the International Association for the Prevention of Blindness (IAPB), there are approximately 1.1 billion persons worldwide who are visually impaired, and by 2050, that number is expected to rise to 1.7 billion. [1] The main contributors to the vision loss include: Uncorrected refractive error (671 million), Cataract (100 million), Glaucoma (8 million), Age and related macular degeneration (8 million), DR (4 million). [1]

The major two forms of Diabetes Mellitus include the following: Type-1 and Type-2 diabetes: Type-1 commonly manifests in children and adolescents. It is due to the combined interactive effects of immune and environmental factors, leading to a complete deficiency of insulin secretion. [2] Type-2 usually appears in middle-aged adults whose cells become resistant to insulin. The characteristics of DR appear in 60% of subjects with more than 15 years of disease with diabetes. DR can result in rapid loss of vision; the condition does not have symptoms in its early diagnosis. The improvement of no blindness and modification of disease in diabetic patients require regular monitoring and early detection with consistent treatments.

2 AI-Powered Detection of Diabetic Retinopathy

Artificial Intelligence has indeed given a new dimension to medical imaging, which enabled the automation of identification and classification of complex patterns within visual information. Machine Learning and Deep learning within AI have emerged as the most powerful tools that allow the computer to garner knowledge through big datasets and enhance their capability without explicit programming. [3] Deep learning, in particular, uses a type of artificial neural network composed of many interrelated layers, called Convolutional Neural Networks, which are specifically developed to perceive and analyze visual data such as images.

Basically, while comprising several layers to extract effective features from the image, a CNN comprises convolutional layers, pooling layers, and fully connected layers.

The convolutional layers apply filters on the input images to extract important features such as edges and textures, extracted at an increasingly higher level of complexity with a deeper network. The pooling layers decrease the spatial dimensions of data while keeping crucial information and reducing computational burdens. Finally, fully connected layers take the features learned from the previous layers and use them to make some kind of prediction, for example, whether any anomalies exist in the images.

Concretely speaking, a CNN updates its internal parameters during training by means of backpropagation on labelled datasets that may consist of both training and classification data. A training dataset teaches it to recognize certain features present in every class, while a classification dataset evaluates its performance on unseen data. This hierarchical learning enables CNNs to locate and classify objects in images with high accuracy.

These range from the detection and classification of various abnormalities, such as DR lesions in retinal fundus images, for which CNNs and other deep learning approaches are widely used in medical imaging. Diabetic retinopathy is one of the most common complications of diabetes. It affects the blood vessels of the retina and may lead to severe visual loss. The main types of DR lesions have been identified as microaneurysms, hemorrhages, exudates, and neovascularization, each having different visual characteristics, which may make their detection by humans difficult. [4] AI-powered algorithms significantly enhance the accuracy and speed of such lesion detection to assist the clinicians for early diagnosis and management of DR. Training of CNNs using large-scale annotated datasets helps them in the detection of subtle changes within the retinal images and enhances diagnostic capability while reducing the workload for health professionals. [5,6]

This paper is aimed at discussing the integration of AI, notably deep learning and CNNs in detecting DR lesions on fundus images; more importantly, how the inception of these technologies has transformed modern diagnostics.

3 Fundoscopic appearance of DR lesions

Diabetic retinopathy (DR) has two main stages: Non-proliferative DR (NPDR) and Proliferative DR (PDR). In NPDR, damaged retinal blood vessels leak fluid, causing swelling and symptoms like microaneurysms, hemorrhages, exudates, and inter-retinal microvascular abnormalities. PDR is a more severe stage marked by the growth of abnormal blood vessels, potentially leading to complete blindness.

- **Microaneurysms (MAs)**

For an ophthalmologist, MAs are the first indication of DR, which result from leakage from the retina's small blood vessels. They are red in colour, smaller in size, and circular in shape.

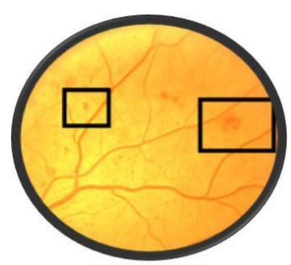

Fig 1. Microaneurysms [7]

- **Dot blot hemorrhages (DBHs)**

When the walls of MAs rupture, Hemorrhages (HMs) occur. Blot haemorrhages are larger red lesions, whereas dot haemorrhages resemble bright red dots. A clear sign of moderate DR and these outperform MAs with indistinct margins in size.

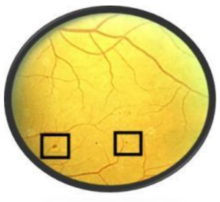

Fig 2. Dot blot hemorrhages [7]

- **Hard Exudates (HEs)**

Hard exudates (yellow dots visible in the retina) and soft exudates (pale yellow or white areas with ill-defined edges) are two types of exudates. The lipid and proteinaceous components of the hard exudates, including albumin and fibrinogen, leak from the damaged blood-retinal barrier. They are typically deposited in the retina's outer plexiform layer.

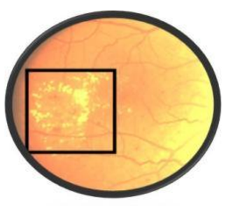

Fig 3. Hard Exudates (HEs) [7]

- **Cotton Wool Spots (CWS)**

Cotton wool spots (CWS) due to vascular occlusion, also known as soft exudates, occurs if the lipid buildup is on the macula or nearby, they can result in total blindness. Exudates (EXs) (Hard and Soft) are referred to as bright lesions and MAs and HMs as dark lesions.

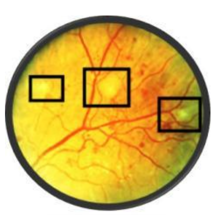

Fig 4. Cotton Wool Spots (CWS) [7]

- **Venous beading (VB) and IntraRetinal Microvascular Abnormality (IRMA)**

Venous beading (VB), It shows damaged walls of major retinal vessels and is a delayed indication in non-proliferative DR. This is one of the best indicators that a person may develop proliferative DR (PDR).

Intra Retinal Microvascular Abnormality (IRMA), These are tiny blood arteries with unusual shapes that divert blood from arterioles to venules. [7]

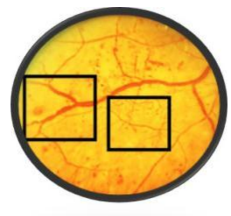

Fig 5. Venous beading (VB) and IntraRetinal Microvascular Abnormality (IRMA) [7]

4 Classification Level of DR

We primarily focus on NPDR lesions that are MAs, HMs, or EXs in this paper. According to the location and frequency of the lesions, ophthalmologists typically classify NPDR into three categories: Mild, Moderate, and Severe. Below we discuss about DR Level and Clinical features of DR level.

- **Mild NPDR**

Few Microaneurysms.

Fig 6. Mild NPDR [8]

- **Moderate NPDR**

At least one hemorrhage or Microaneurysms and/or at least one of the following: Retinal hemorrhages, Hard exudates, Cotton wool spots, Venous beading.

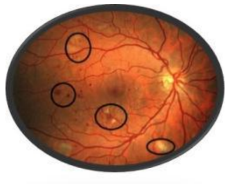

Fig 7. Moderate NPDR[8]

- **Severe NPDR**

Use the 4-2-1 rule below. Only one of these criteria have to be met to be considered severe, 4 quadrants with microaneurysms or dot blot haemorrhages, ≥2 quadrants with venous beading, ≥1 quadrant with intraretinal microvascular abnormality (IRMA).[8]

Fig 8. Severe NPDR[8]

5 Microaneurysms lesion detection

Microaneurysms (MA) are early indicators of DR, appearing as tiny red dots with sharp margins, usually not exceeding 125 micrometres, due to focal dilations in small retinal arteries. When MAs rupture, they result in haemorrhages. Retinal lesions like MAs, exudates, and haemorrhages occur in approximately 77-90% of diabetics who have had the disease for 15 years or more. This review aims to categorize these DR lesions and identify research gaps in DR detection for future studies.

- Long[9] et al focuses on MAs detection. The median filter is first applied to the green channel with a filter size bigger than the largest blood vessel width in the fundus picture to perform shade corrective preprocessing. Following the extraction of directional local contrast (DLC) characteristics from each candidate patch, Naive Bayes is utilised as a classifier. The stated sensitivity value at the average 8 FPIs is 0.7. The high dimensional DLC properties of this method's principal drawback is their poor performance.
- A unique deep convolutional encoder-decoder network was created by Liao[10] for the purpose of detecting microaneurysms by locating the MAs using variations in the network's skip connections. Finally, a precise probability map for MA detection is generated using an activation function with a long tail. Numerous tests, carried out on the e-ophtha-MA and Retinopathy Online Challenge datasets, show that the suggested model achieves the comparable performance to the current state-of-the-art methods on microaneurysm identification with just one hundredth the running time compared with its counterparts.
- Mateen[11] uses VGG-19 and Inception-v3 pre-trained CNN models in a hybrid feature embedding strategy to achieve early detection of MAs. Using two publicly accessible datasets, "E-Ophtha" and "DIARETDB1," the performance of the suggested approach was assessed, and it obtained classification accuracy of 96% and 94%, respectively.

6 Haemorrhage lesion detection

Haemorrhages (HM), like microaneurysms, appear as large patches on the retina with irregular edges up to 125 micrometres wide. They are classified into two types- flame and blot based on their depth and surface area. The frequency and pattern of haemorrhages reflect the severity of diabetic retinopathy. Below, we provide an overview of literature using deep learning approaches for haemorrhage detection in DR.

- Huang[12] proposed a system to extract haemorrhages consists of three components: image pre-processing, training data improvement, and object detection using a convolutional neural network with label smoothing.
- A novel technique for precise bleeding detection from retinal fundus pictures was put out by Maqsood.[13] The convolutional sparse image decomposition method is used to fuse all retrieved feature vectors in the third stage. When evaluated on 1509 images from the HRF, DRIVE, STARE, MESSIDOR, DIARETDB0, and DIARETDB1 databases, the suggested solution exceeds past attempts with an average accuracy of 97.71%.
- An automatic bleeding detection technique based on two-dimensional gaussian fitting was presented by Wu[14] Using Sensors 2021, 21 and 3865, the image is improved. A candidate for haemorrhages is subjected to the two-dimensional Gaussian adaptation in order to extract visual characteristics. With 219 retinal fundus images from the DIARETDB1 database, this approach was able to achieve sensitivity, specificity, and accuracy values of 100%, 82%, and 95.42%, respectively.

7 Exudates lesion detection

Exudates (EXs), caused by fluid leaks from retinal blood vessels, are a significant contributor to vision loss in diabetic retinopathy. They are classified into- hard exudates yellow spots with sharp edges due to plasma leakage and soft exudates, which are swollen nerve fibres appearing as white, oval regions with blurred edges on the retina. Below, we summarize literature using deep learning methods for detecting these exudates in DR.

- A ten-layered CNN was created in 2015 by Prentasi'c and Loncaric [15] to find exudates. However, its sensitivity was modest (0.77). In order to classify data, trained deep convolutional neural networks are fed the immediate region surrounding the seed points. As a result, exudate detection at the pixel level is realised.
- Although Yu [16] and Prentasi'c [17] used an approach that needed manual pre-processing procedures for optic disc removal and vessel segmentation, they nevertheless managed to attain a respectable sensitivity (0.88). They employed deep convolutional neural networks to detect exudate. The results of the optic disc detection and vascular detection algorithms are merged with the results of the convolutional neural network in order to include high level anatomical knowledge regarding probable exudate locations. The validation step's results had a maximum F1 measure of 0.78 and were based on a manually segmented image database.
- Convolutional Neural Network (CNN) algorithms and the circular Hough transform were combined, according to Kemal [18] to detect exudates, one of the symptoms of DR. In comparison to results achieved using CNN or image processing techniques alone, the outcomes of the suggested strategy are more successful. The proposed method is more efficient than those achieved using only CNN or image processing approaches.

8 AI-Based Classification and Food and Drug Administration (FDA)-Approved Algorithms for Diabetic Retinopathy: From Detection to Stage Differentiation

The following studies focuses on AI-based classification techniques applied to diabetic retinopathy, including those for both the detection of diabetic retinopathy versus non-diabetic retinopathy and nuanced stages. It also evaluates FDA-cleared algorithms that have demonstrated success in clinical settings, underlining their contribution to improving diagnostic precision and accessibility in the screening and management of diabetic retinopathy.

8.1 AI-Based Classification of Diabetic Retinopathy: From DR Detection to Stage Classification

- Mohammadian [19] et al., compared the performance of InceptionV3 with Xception architecture to classify the DR in two classes-DR or No DR using Waggle dataset. The authors have used the complete dataset consisting of 35,126 images and reserved 20% of images to test the performance of an algorithm. The last two blocks of the two architectures were compared for fine-tuning, using two optimizers with different learning rates. Image augmentation was performed to enhance the robustness of the model, which included horizontal and vertical flipping, image shifting, and rotation. The metric used in evaluation will be accuracy. It reported accuracy of 87.12% for the InceptionV3 architecture and 74.49% for Xception.
- Zago [20] et al., during their research work, focused on diabetic retinopathy (DR) red lesions and DR images by applying augmented 65x65 patches. They used two CNN models for this purpose: one pre-trained VGG16 and one proposed CNN consisting of five CONV layers, five max-pooling layers, and an FC layer. These models were trained using the DIARETDB1 dataset and then tested for classification of patches into red lesions or non-red lesions on the datasets DDR, IDRiD, Messidor-2, Messidor, Kaggle, and DIARETDB0. After the patch-level classification, a probability map of test image lesions was generated that classified the images into DR or non-DR categories. The results of their work reached very high sensitivity of 0.94 and 0.912 AUC for the Messidor dataset, which showed the effectiveness of their approach for DR lesion detection.
- Gulshan [21] et al. aimed to develop and validate a deep learning algorithm that can detect and classify various stages of diabetic retinopathy by using retinal fundus images. The investigators, in a study published in JAMA, focused on developing a CNN capable of determining different stages of diabetic retinopathy, including no DR, mild NPDR, moderate NPDR, severe NPDR, and proliferative DR. The algorithm, trained on a large, annotated dataset, was able to recognize the disease and its severity with an AUC of 0.95. This study accentuated the role of deep learning to improve diagnostic accuracy and help healthcare professionals in managing diabetic retinopathy in a better way.
- Grzybowski [22] et al. published an extended review of AI applications regarding DR. This review discusses the development and performance of various AI technologies, especially deep learning algorithms, for the screening and diagnosis of diabetic retinopathy. Several AI systems are analyzed that utilize images of the retinal fundus as raw material for the detection and staging of DR, underlining their potential for the valid detection, and staging of this disease. The review emphasizes significant advancements in artificial intelligence-based screening instruments, contrasting their efficacy with conventional approaches and assessing their capacity to enhance diagnostic efficiency and accessibility. This study highlights the increasing importance of artificial

intelligence in improving diabetic retinopathy screening methods, providing an analysis of how these technologies can be incorporated into clinical processes to promote early identification and improved management of diabetic retinopathy.

- Kanagasingam[23] et al. assessed the performance of an AI-driven grading system for diabetic retinopathy. The work intended to determine how well the AI algorithm could identify the stages of diabetic retinopathy from the imaging of the retina. The AI system was tested for its ability to correctly identify and grade various stages of the disease, from no DR to severe NPDR and proliferative DR. The study concluded that the algorithm achieved high accuracy in staging the disease with strong agreement by expert human graders. The present study demonstrates the potential of AI in improving diabetic retinopathy screening by providing accurate staging and increasing diagnostic efficiency at the level of primary care.

8.2 Some of the studies that consist of FDA-Approved Diabetic Retinopathy Detection Algorithms

- Abràmoff[24] et al. introduced the IDx-DR algorithm, which had a high level of accuracy in detecting referable DR by examining retinal fundus photographs. The area under the receiver operating characteristic curve was 0.95, indicating high diagnostic performance. The FDA approved IDx-DR to be used autonomously; thus, it is able to enhance diagnostic efficiency and accessibility in clinics.
- Gulshan[25] et al. evaluated the EyeArt AI system, finding it to be highly effective in detecting diabetic retinopathy and diabetic macular edema (DME). The EyeArt system achieved an AUC of 0.94 for detecting referable DR, demonstrating high diagnostic accuracy. The results underscore EyeArt's capability to reliably classify DR severity and support efficient screening processes in clinical environments.
- Ting[26] et al. discuss AEYE, which is an AI-driven diagnosis system for diabetic retinopathy and diabetic macular edema. Among the general review, AEYE's performance is underlined for its high accuracy in detecting and classifying DR. While specific AUC values regarding AEYE are not reviewed, this paper underlines the role of such a system in improving diagnostic precision and streamlining current practices of DR screening.

9 Future Perspectives on AI in Diabetic Retinopathy: Clinical Applications and FDA-Approved Algorithms

As artificial intelligence (AI) continues to advance, its role in diabetic retinopathy (DR) is becoming increasingly pivotal. Future perspectives on AI in DR should emphasize the practical clinical applications of FDA-approved algorithms, rather than focusing solely on in silico evaluations. AI systems such as IDx-DR, EyeArt, and AEYE have already received FDA approval, demonstrating their effectiveness in real-world settings. These algorithms are transforming DR screening by providing reliable, automated detection and stage classification, which enhances diagnostic efficiency and accessibility, especially in underserved areas. Looking ahead, the integration of these AI tools into routine clinical practice promises to improve patient outcomes through earlier and more accurate detection of diabetic retinopathy, ultimately facilitating better management and prevention of vision loss.

10 Clinical Application and Limitations of AI in Diabetic Retinopathy Detection

The field of Artificial Intelligence has made great strides in promoting early detection for diabetic retinopathy (DR) by offering significant advantages in clinical settings, particularly, in areas of the world with limited access to ophthalmologists. Therefore, AI-powered systems like IDx-DR, EyeArt, and AEYE enable the analysis of retinal fundus photographs with the intention of detecting and grading DR at various levels. This feature has great potential in peripheral and under-resourced areas where specialized eye care services might be short in supply, thus facilitating early detection and timely referral of cases for further evaluation and management. Artificial intelligence in community practices enhances early diagnostic capabilities and optimizes patient management to minimize the risk of visual impairment through early intervention.

Nonetheless, in spite of their progress, artificial intelligence systems possess certain constraints. The challenges encompass the necessity for extensive and varied datasets for training purposes to guarantee generalizability across distinct populations and imaging conditions. Moreover, artificial intelligence algorithms may encounter difficulties arising from discrepancies in image quality and patient demographics, which could adversely affect diagnostic precision. In addition, the deployment of AI tools necessitates meticulous evaluation regarding their incorporation into current clinical workflows, as well as continuous validation to uphold efficacy and dependability. Addressing these limitations is crucial for optimizing AI's role in DR detection and ensuring its equitable application in diverse healthcare settings.

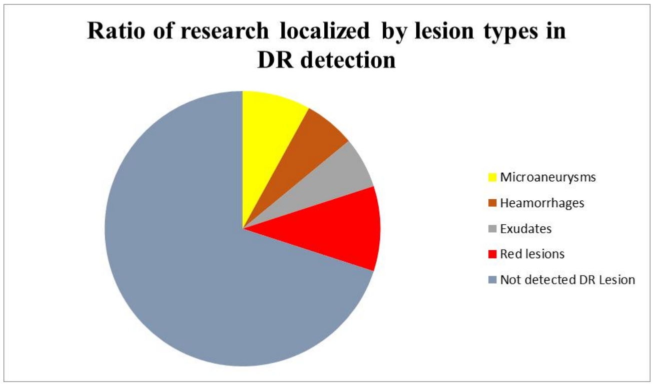

Fig 9. Ratio of research localized by lesion types in DR detection

11 Discussion

Recent developments in medical image processing are facilitating quick and automated disease screening. Statistics show that DR affects 80% of diabetes patients who have had the disease for 15 to 20 years or longer. Worldwide, there is concern about diabetes and gestational diabetes (GDM). A serious case of DR during pregnancy or a worsening of an existing DR are potential outcomes of GDM. [27] Diabetes affects more than 171 million individuals globally. According to a poll by the World Health Organization (WHO), there will be 366 million cases of diabetes worldwide by 2030. [28]

DR identification in the early stages of the illness must be improved by a multidisciplinary collaborative approach. With advancements in AI algorithms, this technique will enhance early detection of many additional retinal diseases in addition to DR screening. Automated screening techniques are not just useful for DR; they may also be used for other diseases, including as glaucoma and age-related macular degeneration, where early diagnosis would probably lead to better clinical outcomes. Such algorithms are widely available nowadays. All such algorithms should undergo thorough validation testing to verify their suitability for clinical application.

The initial sign of DR is blood vessel lesions with tiny, circular red patches. MAs, HEMs, EXs, and CWs are moderate indications of DR. To distinguish between mild and severe levels, it is crucial to consider the ratio of these symptoms. The visual resemblance of symptoms between No-DR, Mild-DR, and occasionally Moderate-DR makes it challenging to recognise in the early stages of diagnosis, which is a significant problem in identifying the level of DR severity. Finally, if DR worsens and reaches an advanced stage, may lead to vision loss.

Although DR cannot be reversed, it is crucial to identify it early to limit future suffering. For instance, early signs of DR will almost always be present in non-proliferative DR stages, and being able to recognise and categorise those stages using the right diagnostic technique may allow one to save their vision.

In this review paper, a major portion of the work focuses on the study of Haemorrhages, Microaneurysms and Exudates and the Figure 9 shows about the Current Research ratio papers localized by lesion types in DR detection.

These DL-based strategies could be incorporated into screening systems that are currently being developed to improve and categorise the DR stage using lesion detection methods on a variety of fundus images. The primary problem raised in the studies under examination is the weak NPDR lesions detection research ratio in comparison to other lesion DR detection research.

Additionally, the variations of fundus images that can be utilised to evaluate indications are constrained by dataset limits. The analysis of retinal scans has grown quicker, more inclusive, and more generalizable as a result of the effectiveness of Deep Learning techniques, yet the criteria employed to assess the outcomes and the corresponding datasets are still skewed and uneven between researches. These developments allow for the generalisation of DL-based models and the evaluation of a wider variety of symptoms and signs, which may aid in the discovery of the underlying pathologies underlying retina-based disorders. Due to the lack of publicly available datasets, DR lesions screening is still a problem. While most recent DL improvements achieve encouraging classification scores, some are still unable to distinguish impacted lesions.

Additionally, we believe that in the future, our assessment can be expanded to offer a comprehensive and current review of the difficult and rapidly expanding field of DR detection.

12 Conclusion

Artificial intelligence in the analysis of medical images has greatly enhanced early detection and screening for diabetic retinopathy, among other retinal diseases. Nonetheless, difficulties persist, including the need for extensive validation, a lack of significant datasets, and further refinement to detect stages of non-proliferative conditions. Continuing improvements in deep learning technologies and growing databases are likely to make diabetic retinopathy screening methods more robust and efficient. This includes a number of challenges that must be overcome if clinical outcomes are to be improved, and AI technologies fully utilized in the timely diagnosis and treatment of diabetic retinopathy.

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