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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.

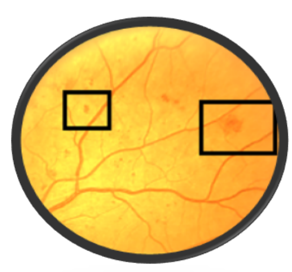

Fig 1. Microaneurysms [7]

- **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.

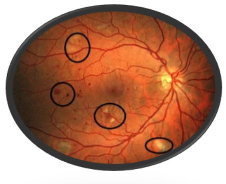

Fig 7. Moderate NPDR [8]

- **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]

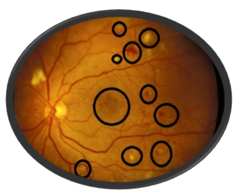

Fig 8. Severe NPDR [8]

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.

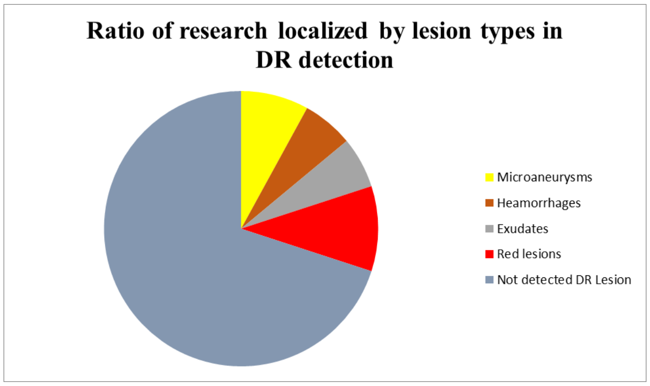

Fig 9. Ratio of research localized by lesion types in DR detection

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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