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Automatic Detection and Classification of Diabetic Retinopathy from Optical Coherence Tomography Angiography Images using Deep Learning-A Review

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***Abstract*: Diabetic retinopathy (DR), a microvascular complication of diabetes, has become a major global health problem, affecting vision and potentially leading to blindness if left untreated. Optical Coherence Tomography Angiography (OCTA) has become a transformative imaging technique for the detection and analysis of the choriocapillaris and retinal microvasculature, enabling the identification of preclinical microvascular abnormalities that precede visible DR symptoms. This review examines the role of machine learning (ML) and deep learning (DL) learning methods in OCTA-based DR classification. We summarize recent advances in convolutional neural networks (CNNs) for automated feature extraction and accurate diagnosis, as well as the various OCTA datasets used in these studies. The advantages of OCTA imaging over fundus photography, particularly for early-stage DR detection, are highlighted. Furthermore, we propose a novel DL-based system for DR classification that compares its performance with traditional ML methods based on manual feature extraction. Challenges related to clinical delivery, such as data variability, model interpretability, and integration into clinical workflows, are also discussed. Finally, we highlight future research directions to address these challenges and improve the adoption of Deep Learning models for OCTA-based DR diagnosis.**

***Keywords*: Diabetic retinopathy, Convolutional Neural Networks, Fluorescein Angiography, Machine learning, Deep learning, Optical Coherence Tomography Angiography, Computer-aided Diagnostic, Artificial intelligence**

I. Introduction

Diabetes, also known as hyperglycemia, is a group of metabolic diseases that affect both insulin secretion and function. Diabetes-induced chronic hyperglycemia has been linked to kidney, blood vessel, eye, nerve, heart, and kidney damage over time. It should be emphasized that the worldwide occurrence of diabetes is projected to increase in the forthcoming years. In 2017, diabetes diagnosis incurred a total cost of $327.01 billion in the United States, encompassing $237 billion in direct clinical expenses and $90.01 billion attributed to low efficiency. [1]. Diabetes is expected to affect 642 million people in the world by 2040, according to some estimates [2].

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Diabetes wreaks havoc on the body's arteries and nerve cells, including those in the eyes. Diabetic retinopathy is a negative health outcome of long-term diabetes and poor blood sugar control for the eyes (DR). According to reports [3,4], DR was responsible for 0.8 million cases of blindness worldwide in 2020, ranking sixth overall. The two major types of DR are PDR, which is linked to the formation of NV, and NPDR, which is divided into three levels: severe, moderate, and mild. [5,6]. Patients exhibit various ocular changes at each stage [7].When DR is routinely evaluated [8], it has been discovered that the prevalence of blindness among diabetes patients decreases [9], [10], [11]. Retinal imaging, commonly referred to as retinal screening, is acrucial method for the precise, early diagnostics of eye illnesses, which possesses the ability to decrease the prevalence of blindness worldwide. The importance of this screening has only grown with technological advancements over the past few decades. Currently, dye-based FA is the benchmark for determining the amount of vascular leakage and the existence of ischemia [12], [13], [14]. FA can detect vascular integrity, MA, blood vessel perfusion loss, and raised artery permeability, causing edema and NV. But, FA is an intrusive examine that, in a small proportion of patients, may cause serious negative effects [15]. Therefore, it is not frequently used as a screening procedure because of its potential side effects.

Technology advancements have made it possible to use OCTA as a quick, non-invasive imaging modality to look at capillary microvascular changes. Without the use of fluorescein dye, OCTA delivers depth-resolved imagining of the ocular microvasculature [16], [17]. OCTA has proven to serve as a useful instrument in the treatment of diabetics with or without microvascular disease abnormalities. Currently, a non-invasive vascular imaging technique known as OCTA has the benefit that it is capable of anticipating the initial stages of retinopathy caused by diabetes. The benefits of early detection of retinal microaneurysms in a microvascular system are included. However, a few studies continue to classify DR using retinal fundus images rather than retinal OCTA images. However, OCTA images can provide precise information about blood vessels that exist in the retinal capillary system.

With the assistance of OCTA images and a CNN[72], we aim to construct an automated DR detection and classification system and test the system's viability. Recent results from a DL application for retinal image automation processing have shown expert-level precision in the detection of DR severity.

We aim to further facilitate access to DR screening and enhance diagnostic precision. This review aims to utilize DL and ML methods to identify diseases in the retina related to DR. We anticipate that by creating these algorithms and using them on real patients, we will be able to identify serious diseases early. The prompt intervention that results from this early discovery can then stop blindness. DL is a subset of AI that is built on DNN. It has produced great advances in clinical imaging, notably in picture categorization and pattern acknowledgment. In eye medicine, there is a growing interest in using DL algorithms to evaluate OCTA images. According to the investigation, DL algorithms performed well on OCTA image evaluation for disease detection, future estimation, and image quality monitoring, implying that incorporating the DL method might enhance disease assessment accuracy and medical process efficiency.

A. Drawbacks of Fluorescein Angiography (FA)

The invasive imaging procedure known as fluorescein angiography (FA) requires continuous dye injection and takes 10 to 30 minutes to complete [17]. It provides two-dimensional views about an extensive field of view, which permits dynamic blood flow visualization. Although retinal capillaries can be seen, the basic intra-retinal aspects of capillary networks are not visible on their own. FA, in particular, corresponded to surface retinal veins while not revealing deeper retinal capillaries, most likely caused by light dispersion in the retina [18-21]. The choroidal vessels, which are difficult to see in DM eyes, are also difficult to see in FA. Still, FA can be used to detect dye leakage, pooling, and staining patterns [22]. FA is not a good procedure to use frequently in clinical practice because it is invasive, expensive, and time-consuming. Furthermore, while FA is generally thought to be safe, the dye can cause nausea, allergic reactions, and, in rare cases, anaphylaxis. Patients who require periodic check-up scans or who are unable to deal with the negative consequences of dye injections may not be fit for the FA procedure.

B. Pros of Optical Coherence Tomography Angiography (OCTA)

The most recent simple angiography method, OCT angiography (OCTA)[61,62], does not involve ocular dilation. Images of the choriocapillaris (CC) and retinal capillary plexuses are produced at high resolution without the need for contrast. Modern technology and the acquisition of hardwires have made it possible to image blood flow in the retina in grayscale using OCTA. Both averages as well as specialized perfusion density maps may be generated. OCTA can identify MA, non-perfusion areas, IRMA, and NV[63,64], all of which are DR variations. OCTA outperforms FA in revealing non-capillary perfusion regions because the imaging is not distorted by leakage. [64]. Fig. 1 shows optical coherence tomography angiography (OCT-A) images illustrating various severities of diabetic retinopathy.

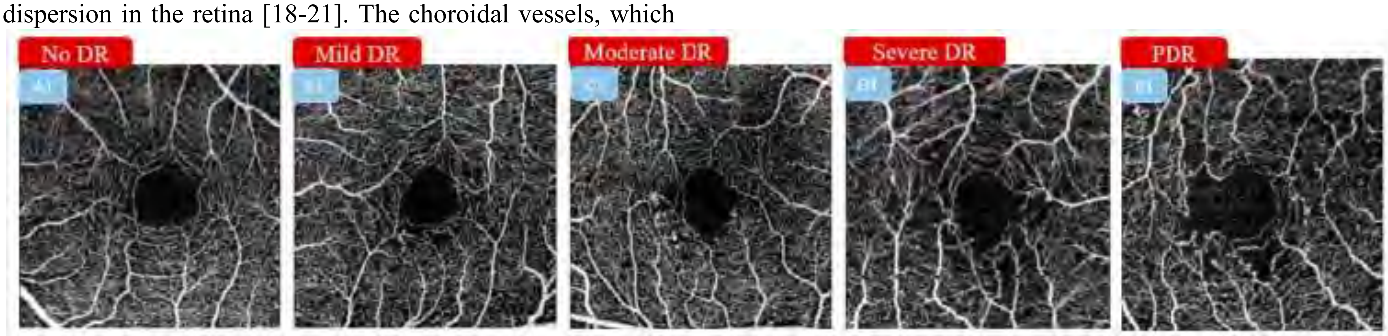

Fig. 1. Examples of a series of 3 × 3 mm2 superficial capillary plexus (SCP) and deep capillary plexus (DCP) optical coherence tomography angiography (OCT-A) images illustrating different severities of diabetic retinopathy. (A1–E1): SCP OCT-A images illustrating the alteration of the FAZ area and the surrounding vasculature from no DR to PDR.[67]

Even before the disease is symptomatic, OCTA offers a dye-free technology that can be employed to spot angiographic symptoms of DR. OCTA techniques enable imaging and thorough assessment of alterations in the retinal microvasculature [67]. This is important because OCTA can more commonly be utilized than FA to check patients' eyes consistently. Moreover, OCTA gathers data faster than FA. The OCT platform OCTA was created based on the conventional OCT and is often utilized. Furthermore, 3-D resolution is a feature of OCTA data. Individual capillary plexuses are visible and can be assessed. The segmentation of the ocular vasculature can also be further altered and customized to produce images of additional layers, like the intermediate capillary plexuses (ICP), which aid in the visualization of diseased characteristics not seen in customary dye-based angiography[68,69].

In this study, we discuss the requirement of a technology like OCTA in the diagnosis of DR and discuss developments that have a significant influence on the therapy and early identification of DR. Knowing the frequency of diabetes and the enormous burden that DR imposes, we attempt to provide an accurate depiction of the numerous works emphasizing the significance of OCTA usage in DR patients. In this paper, we will present a summary of ML in OCTA for retinal disease categorization. The next part discusses the fundamental concepts of machine learning, as well as the ML implementation pipeline and the distinctions amid classic ML methodologies and DL. It has been established that quantitative OCTA [73] characteristics may be used for machine learning categorization of various retinopathies. DL-based solutions for automated OCTA picture processing and illness categorization have also been investigated. In this study, we discuss recent advances in measuring OCTA features, ML and DL image analysis, and classification.

Color fundus photography has been the primary data source for most published AI diagnostic system experiments to date. One of the most widely used forms of clinical imaging, fundus photography has long been accepted as a reliable method of diagnosing and monitoring retinal disorders. When it comes to microvascular aberrations around the fovea, for example, and layer information of the retina, fundus images fall short.

The following is the outline of this paper: The materials and procedures of the study are described in Section 2, while its results and interpretations are offered in Section 3. Part 4 describes the accessible OCTA datasets, while Section 5 details the discussion and conclusions from the review of DR classification models and datasets. Section 6 discusses the research gap of the method. Section 7 explains the proposed methodology. The various performance indicators for categorization are detailed in Section 8, while the research and potential future scope are presented in Section 9. In Section 10, we conclude this systematic review.

II. Materials And Methods

A. Search Criteria

We conduct the recommendations in the PRISMA declaration [24] when conducting this systematic review. The analysis involved the search of several databases, comprising PubMed and GoogleScholar, Scientific direct for the following phrases, along with MeSH terms and synonyms: OCTA or as well as NPDR and proliferative Diabetes Mellitus due to diabetes or diabetics retinopathy PDR as well as DL or ML or CNN.

B. Inclusion and Exclusion Criteria

The purpose of the study was to identify analyzes that addressed the need for using OCTA to identify diabetics with DR as well as its automated applications. To ensure the breadth of the study, only recent studies from 2015 to 2024were selected. Case reports, letters, and studies employing time-domain OCT were excluded; only English-language, peer-reviewed journal articles were considered.

B. Literature Review

A total of 325hits in PubMed, 115 in Google Scholar, and 110 in Science Direct were found employing the search mentioned above, yielding 550 records. Due to 225 items being duplicates, we removed them and the remaining 325 titles and abstracts were then subjected to the predefined screening process. We followed a strict screening for population, image modality algorithm type, and publication category because the goal at this time was not to be over-inclusive. As a result, 82 final articles were included and 243 titles were excluded.

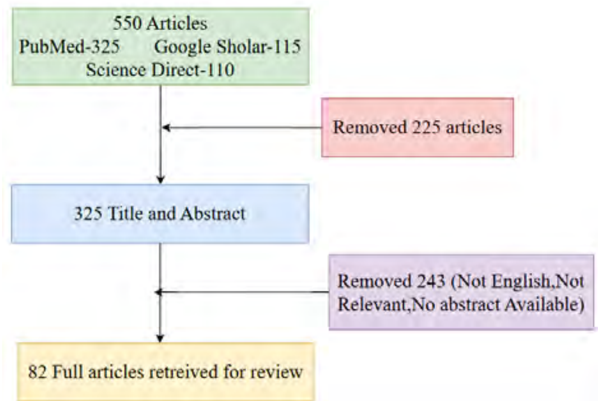

Fig. 2.PRISMA Diagram Illustrating the Systematic Article Selection Process for the Literature Review.

III. Results And Discussions

There are a variety of ways to automatically diagnose and grading of DR in the state of the art. Most previous research relied on fundus images for detecting DR and segmenting retinal blood vessels. The recently developed retinal scanning technology known as OCTA may extract far more information from the retina than conventional fundus imaging. Particularly, when compared to a traditional fundus image, OCTA can resolve even the smallest vessels of blood in the retina, making all microaneurysms visible with a great deal greater clarity. However, practically all of the research on automated DR identification up to the end of 2020 remained primarily focused on using traditional fundus images, and all DR identification techniques produced by OCTA are still in the early stages of advancement. As technology advances, it is expected that OCTA will eventually be another traditional fundus imaging. Thus, it is essential to create new techniques that can make use of OCTA to enable the early diagnosis of DR.

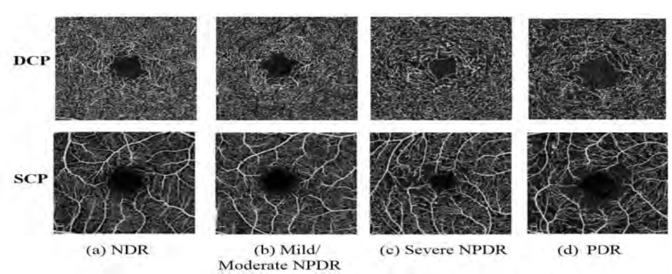

Fig. 3.FAZ structure in the eyes of NDR, mild/ moderate NPDR, severe NPDR, and PDR participants from OCTA image.

A. Application of OCTA in Diabetic Retinopathy Diagnosis

Different researchers have adopted several segmentation and classification strategies to accurately identify the presence and development of the DR. Nonetheless, the use of powerful OCTA in diagnostic methodologies is limited. Most of the authors have selected color fundus images for the automated prediction of DR. So, there is a shortage of works in the literature using OCTA, and we strongly believe that this non-invasive technology could create wonders in the field of automating ophthalmological disease predictions such as DR.

In this article, we discuss the usage of ML and DL for the categorization of diabetic retinopathy.

1)Machine learning in Optical Coherence Tomography Angiography for DR prediction and classification

Quantitative parameters of OCTA samples, which have been employed in many investigations, are examined in the background of retinal disorders in a current evaluation of the literature. Machine learning is an AI method that uses a classifier like a neural network, SVM, or random forest supplied with characteristics that were manually created (RF). Over the years, several machine learning algorithms have been developed. Popular methods include linear regression, k-nearest neighbors, and SVMs. Typically these algorithms for categorising retinal images need two steps. Computer vision and automatic learning. To extract attributes or measures from an image, the person who using it needs to first carry out digital image processing. After the features have been collected, the second component may be utilized to train the ML prototype. The efficiency of the prototype must be evaluated following training. Machine learning models are typically evaluated using common metrics like accuracy, Particularity as well and sensitivity. The sensitivity of the prototype is defined as its capacity to recognize examples with the disease, while the specificity is defined as its ability to isolate instances without the sickness.

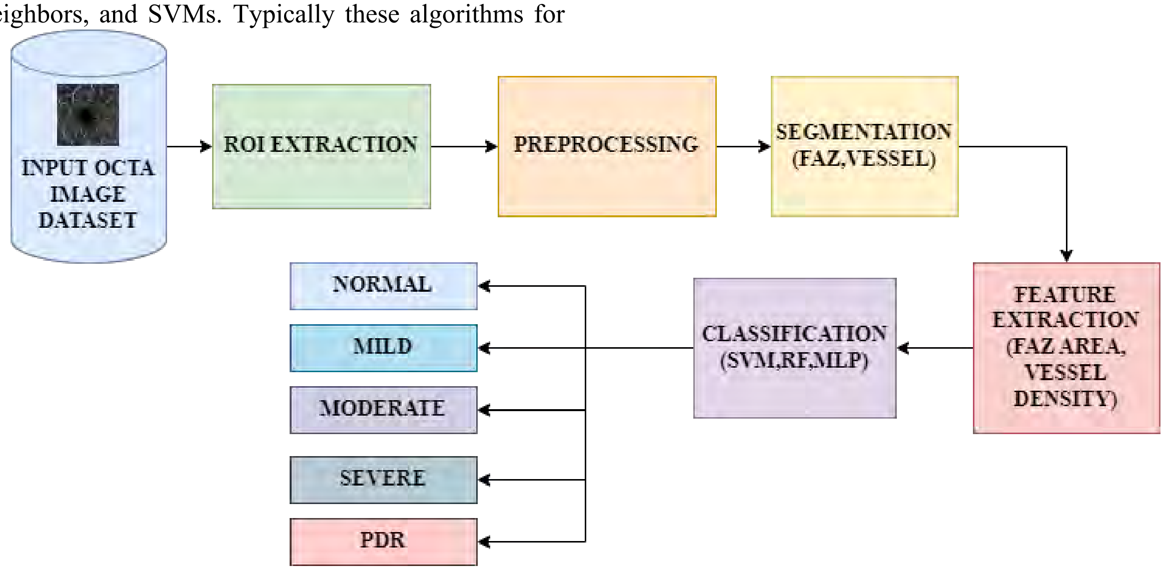

Fig.4.Classification of DR using OCTA images based on machine learning.

Sandhu et al. [25] were able to identify DR by analyzing OCTA images using an SVM classifier. These characteristics included vasculature density, vasculature caliber, and FAZs. Eladawi et al.[26] developed an OCTA-based CAD system for diagnosing diabetic retinopathy, employing RV division, image-derived makers, and an SVM-based categorization. Utilizing a combined MGRF prototype, the system delineates the development of deep and superficial blood vessels in vessels in both diabetic and non-diabetic individuals, based on a stochastic method. Their method, which uses biomarkers derived from OCTA images, can be used to recognize a wide range of choroid and retinal diseases. The AUC, VVD, and DSC for the original picture without the GGMRF and RDHE models are 56.71, 58.33, and 54.56, respectively. For the improved picture, the AUC was 0. 96percent, the VVD was 0. 79 percent, and the DSC was 0.96 percent.

The study conducted by Eladawi et al. [27] involved 23 healthy eyes and 82 diabetic retinopathy (DR) eyes. The authors extracted features such as vessel density (VD), blood vessel complexity (BVC), and the width of the foveal avascular zone (FAZ). They made use of an SVM for classification purposes, overall with a radial basis function (RBF) kernel. The model achieved an accuracy of 94.3%, with a sensitivity of 97.9% and specificity of 87.0%. AUC was 92.4% with a Dice Similarity Coefficient (DSC) of 95.8%. Alam et al. [28] showed that localized quantitative OCTA analysis might be used to stage Limits, NPDR patients, and PDR patients (proliferative DR). This paper compared measurements taken throughout the entire picture to those taken using a moving window. In this investigation, we employed eight parameters, including foveal density (FD), blood vessel density (BVD), and vessel complexity index (VCI) for the SVP, alone and FAZ area (FAZA) for the DCP. Using localized complexity maps, researchers were able to pinpoint regions of the PDR eye with a higher concentration of blood vessels. In this study, we employed a total of 16 attributes, including both global and local aspects of the images. To choose the best iteratively qualities for categorization, the investigation used a logistic regression model with backward elimination. This study found that, out of a total of 16, the FD, shifting-window features VCI, and BVT performed the best, with stated accuracy levels of 85.10, 91.26, and 87.62 percent, respectively. The combination of these three characteristics led to a 94.75% accurate categorization performance.

Aslam et al.[29] used machine learning to categorize healthy individuals as either diabetic or nondiabetic based on several variables. Decision trees, logic regression, random forests, and other ML approaches were compared in this study. The classifier based on random forests accomplished an AUC of 0.80 for binary identification of diabetes-related eyes from healthy eyes, whereas the logistic retrogression prototype yielded an AUC of 0.91. Overall, the findings of the review indicate that ML may be used for both the early staging of NPDR and the diagnosis of diabetes. According to the results of this research, a vascular and vessel density areas are the most telling features for classifying DRs. Capillary vascular intensity changed quantitatively, indicating a reduction in blood flow. This suggests that features based on OCTA intensity may one day be employed for illness detection. Working together to generate a 94.75% accurate categorization performance. A CAD system combining OCTA and OCT features for the categorization of NPDR was investigated in another study [30]. The research gathered data on four Optical Coherence Tomography Angiography features, including FAZA, BVD, BVC, and bifurcation points, and three OCT characteristics, including curvature, reflectivity, and thickness. In addition to these demographic factors, we additionally factored in age, gender, HbA1c, hypertension, dyslipidemia, and edema prevalence. To do classification using machine learning, a multi-stage random forest classifier was used. The first random forest separates eyes with DR into those with the disease and those without using a binary classification. If the eye is determined to have DR, a second casual forest classifies the severity of the condition as either mild or severe. Using only OCTA characteristics, the study claims 0.94% accuracy; with more detail, including OCT and the medical data, the categorizer reaches a 0.98% accuracy.

Moreover, recent research Alam et al.[31] has revealed that retinopathies possess multiple classification methods. Six quantitative OCTA parameters- namely, VPI, BVD, BVC,FAZCI, BVT, and FAZA were used to classify and individually stage retinopathy in a group of well participants, NPDR patients, and SCR patients. Both the SVP and DCP were mined for all of their characteristics. In addition to distinguishing between nasal retinal quadrants, superior, temporal, and inferior, we also measured BVD at varying eccentricities. As a result, the research used backward omission to choose the most effective optical feature sets for multi-task categorization. It was found in this research that FAZCI(D), BVT, BVD(S-6mm), and FAZA(S) are four sensitive traits that may be used to distinguish between healthy, NPDR, and SCR individuals. Scatter plot analysis demonstrates strong discrimination between the three groups of participants (healthy controls, DR, and SCR). Finally, it indicated a sensitivity of 95.01% for DR against SCR, a sensitivity of 92.18% for NPDR staging, and a sensitivity of 93.19% for SCR staging.

A CNN and SVM-based DR diagnostic paradigm was presented by Zaylaa et al. [32]. Where required, they downsized the OCTA images and converted them to binary or grayscale. CNN was used to identify features, which were then fed into the SVM algorithm. Their method for identifying and categorizing DR cases was 88.88% sensitive and 95.55% specific. Using multifractal geometry, Abdelsalam and Zahran [33] suggest a new method for early identification of DR. They used macular OCTA analysis to detect NPR in its earliest stages of NPDR. Moreover, the SVM algorithm, a supervised ML technique, was used to implement automation into the diagnostic process and boost accuracy. Their method of categorization was 98.5 percent accurate. Extracting texture information from OCTA photos has been the focus of work by Liu et al. [34], who used a DWT. To classify wavelet features into distinct categories, four diverse machine learning models were utilized: LR, LR-EN, SVM, and XGBoost. The best DR detection results were obtained with LR-EN and LR, with diagnostic precision of 82%, and AUCs of 84%, Sensitivity of 84% and specificity of 80%.

Another recent work [35] employed SVM classifiers developed by a genetic evolutionary method to categorize 148 samples from 78 diabetic retinopathy patients with PDR and NPDR using OCTA vascular density maps at SCP, DCP, and total retina (R) levels. In three independent models, their algorithm diagnosed PDR and NPDR in all three layers of vascular density maps with up to 85% accuracy. The extensive tissue of the retinal level blood vessel volume maps executed the best, distinguishing PDR and NPDR with 90% accuracy. Table 1 summarizes some of the work in ML for autonomously segmenting or diagnosing DR from OCTA images. According to Abtahi et al. [37], differential CLV analysis promotes the classification of diabetic retinopathy using OCTA. The use of an SVM-based classifier using features taken from the whole image and from specific regions in the retina for CLV analysis enhanced binary classification accuracy from 77.45% to 89.26% and multiclass accuracy from 78.68% to 86.23%, highlighting the role of the capillary changes in the DR development. Machine learning algorithms such as random forest and gradient boosting machine were used by Li et al.[39] to classify DR using clinical data and parameters of 203 patients from OCTA. The predicted accuracy of AUC values is high on multiple classifications of DR.

TABLE I
SUMMARY OF RESEARCH WORKS ON AUTOMATING DR DIAGNOSIS IN THE STATE-OF-THE-ART USING MACHINE LEARNING METHODS

Author and Year	**Database**	**Method**	**Results (Best)**
Sandhu et al. 2018 [25]	DM Type 2 Eyes: 106 DM without DR: 23 Mild NPDR Eyes: 83	Features: BVD, BVC, and the size of the FAZ Classification: SVM	Accuracy = 94.3% Sensitivity= 97.9% Specificity=87.0% AUC = 92.4% DSC = 95.8%.
Eladawi, 2018 [26]	OCTA images, University of Louisville, USA	Vessel segmentation, Local feature extraction, SVM	Accuracy=97.3% Sensitivity=97.9% Specificity=96.4% AUC=0.97
Eladawi et al. 2018 [27]	Healthy Eyes: 23 DR Eyes: 82	Features: VD, BVC, and Width of the FAZ Classification: SVM with RBF kernel	Accuracy = 94.3% Sensitivity = 97.9% Specificity =87.0% AUC = 92.4%,

			DSC = 95.8%.
Alam et al. 2019 [28]	Healthy Eyes: 40 Mild NPDR Eyes: 20 Med. NPDR Eyes: 20 Severe NPDR Eyes: 20	categorizes: BVC, BVT,FAZ-A , BVD, FAZ-CI, and VPI Classification: SVM	Sensitivity = 94.84%
Aslam et al. 2020 [29]	Healthy Eyes: 49 DM without DR Eyes: 50 DR Eyes:53	Features: FAZ Circularity, Area of Ischemic Zones Around FAZ, Average Percentage of SkeletonizedCapillary Vessels, Mean Capillary Intensity, Mean Vessel Intensity Classification: NB, DT, LR, RF, and XGBoost	AUC = 0.91
Sandhu et al. 2020 [30]	DM w/o DR Eyes 36 Mild NPDR Eyes: 53 Moderate NPDR Eyes: 22	Features: FAZ-A, BVD, BVC, and bifurcation points Classification: Multistep RF	Accuracy = 96.0% Sensitivity =100.0% Specificity 94.0%, AUC = 0.96
Alam et al. 2021 [31]	Healthy Eyes: 40 Mild NPDR Eyes: 20 Moderate NPDR: 20 Severe NPDR: 20 PDR Eyes: 100	Features: VCI, FD, and BVT Classification: Multivariate regression	Accuracy = 94.75%
Zaylaa et al. 2021 [32]	91 participants	Features: CNN Classification: SVM	Sensitivity = 88.88% Specificity = 95.55%
Abdelsalam and Zahran 2021 [33]	Healthy Eyes: 90 DR Eyes: 80	Features: Multifractal Analysis Classification: SVM	Accuracy=98.5% Sensitivity=100% Specificity=97.3%
Liu et al. 2021 [34]	Healthy Eyes: 132 DR Eyes: 114	Features Wavelet Classification: LR, LR-EN, SVM and XGBoost	Accuracy = 82%
Khaliliet al. 2022 [35]	NPDR Eyes: 103 PDR Eyes: 45	Features: VD maps at SCP, DCP, and total retina (R) Classification: SVM with GA	Accuracy = 90%
Khalili Pour, E et al. 2023 [36]	45 PDR, 103 NPDR	Features Superficial Capillary Plexus (SCP) , Deep Capillary Plexus (DCP), Total Retina (R) Support Vector Machine (SVM) classifier optimized by Genetic Evolutionary Algorithm	Accuracy: - SCP: 85% - DCP: 90% (Best performance) - Total Retina (R): 85%
Abtahi et al.2024 [37]	212 OCTA images from National Taiwan University Hospital	SVM-based differential CLV analysis	Binary Accuracy=89.26%, Multiclass Accuracy=86.23%.
Meng, Z et al. 2024 [38]	13 eyes from 82 patients with diabetic macular edema (DME)	Logistic Regression, Support Vector Machine (SVM), Backpropagation Neural Network (BPNN)	Logistic: Sensitivity = 0.904, Specificity = 0.741, F1 Score = 0.887, AUC = 0.910 - SVM: Sensitivity = 0.923, Specificity = 0.667, F1 Score = 0.881, AUC = 0.897 - BPNN: Sensitivity = 0.962, Specificity = 0.926, F1 Score = 0.962, AUC = 0.982

2. Deep learning in optical coherence tomography angiography for DR detection and classification

Ophthalmologists are interested in deep learning-based technologies because of their many OCTA applications, including OCTA reconstruction, OCTA denoising, and division of various regions of interest including vasculature, FAZ, and others. According to current studies and the use of quantitative OCTA characteristics for ML categorization, OCTA images include the essential data to recognize various retinopathies and stages of illness. Theoretically, CNN can automatically extract and classify features, eliminating the need for detailed feature engineering. Also, there could be factors that have not yet been looked at; by sending the image straight to CNN, CNN might be able to use a variety of data for early sickness detection. Millions of images would be required to optimize the millions of network parameters to teach a CNN system for an individual categorization activity. Because OCTA is a novel imaging modality with few datasets, investigating DL for OCTA classification is challenging.

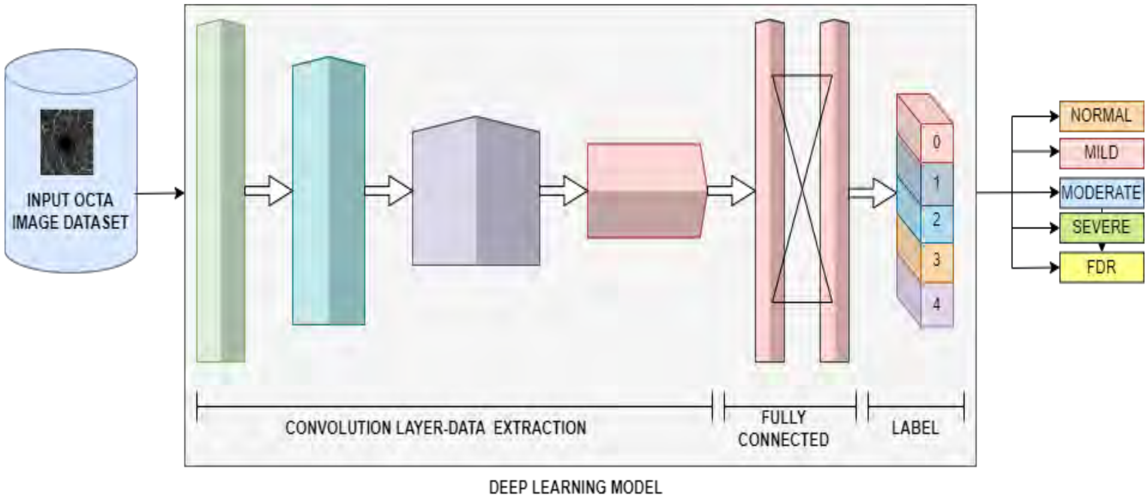

Fig. 5.Deep learning-based DR detection and classification using OCTA images.

An automatic AI-based diagnostic system that identified DR in a crucial analysis by Abramoff et al. [40] has now been approved by the Food and Drug Administration for use by healthcare professionals to identify mild DR and DMO. Islam [41] used the Kermani OCT dataset to evaluate the performance of DenseNet-201 for medical image classification. This model achieved an outstanding accuracy of 98.6%, with sensitivity at 98.6% and specificity at 99.5%, clearly showing its potential for finding vital patterns in OCT images. Such results emphasize the working ability of DenseNet-201 for accurate and automated diagnosis in medical imaging.

Heisler et al. [42] trained DenseNet, ResNet50, and VGG19 architectures before utilizing them to fine-tune neural network components built using single data types. They co-registered OCT samples of the retinal layers and investigated the function of ensemble DL in categorizing DR from OCTA images. This study validates CNN's capacity to detect DR in OCTA properly, although it does have certain limitations, such as the need to train many networks when utilizing ensemble learning techniques, which significantly raises computing costs. Le et al. [43] employed transfer learning in their work to automate OCTA categorization, utilizing a DL CNN architecture and VGG16. Their teaching and cross-validation involved databases of 131 images, comprising 75 images of diabetic retinopathy (DR), 24 images of diabetic patients without DR (non-DR), and 32 images of good individuals. By retraining the final nine layers of the CNN's design, significant improvements were observed. The categorizer achieved enhanced cross-validation specificity, sensitivity, and accuracy, measuring 90.820%, 83.70%, and 87.270%, respectively, in distinguishing mid of diabetic retinopathy, non-diabetic retinopathy, and healthy eyes. A doctor won't know how the CNN came to that prognosis, even though the CNN can make one. As a result, one of the shortcomings of this study is its interpretability. Abdelsalam [44] suggested that OCTA images be pre-processed in ways like resolving and contrast better and re-building and reconnecting the blood vessels. They took seven features from the OCTA images.

This included measurements such as the mean of inter-capillary areas for the top 10 and 20 selected regions, with or without the FAZ, the FAZ perimeter, the circularity index, and vascular density. These particular features were used to train an ANN to differentiate between diabetics who did not have DR and diabetics who had mild to moderate proliferative NPDR. Cano Jennifer et al. [45] used ordinary least squares modeling on OCTA images to differentiate advanced and early diabetic retinopathy from non-diabetics. 200 people were surveyed. The approach detected early and advanced diabetic retinopathy with 91% accuracy. The study also identified substantial changes in microvascular architecture between diabetic and non-diabetic participants, revealing the pathophysiology of diabetic retinopathy. Nevertheless, a small sample size and lack of external validation necessitated more research to confirm the findings. This work shows promise for OCTA-based diabetic retinopathy diagnosis and categorization.

Kim et al. [46] developed a wide-field SS-OCTA and utilized it to create a semi-automated diagnostic system focusing on microvascular parameters for assessing the severity of DR from multiple perspectives. In their study, 235 diabetic eyes were categorized into five groups: PDR, severe NPDR, moderate NPDR, mild NPDR, and diabetes without any non-diabetic retinopathy. The assessment encompassed VD, capillary NPA, and FAZ parameters. The NPA cutoff values to differentiate between severe NPDR and PDR, moderate NPDR and severe NPDR, mild NPDR, and moderate NPDR, and non-DR were AUC:90%, AUC: 94%, AUC:94%, and AUC: 91% respectively. The primary drawback of this investigation is that normal microvasculature may get obscured by projection artifacts brought on by bleeding or vitreous opacity, obscuring the NPA. Ryu et al. [47] evolved a completely automated categorization technique to diagnose DR by integrating OCTA images with a CNN model. They employed the ResNet101 model, which engaged in processing images through 101 layers of residual blocks.

Subsequently, it summarized the source and exit map data of the layer of convolution in every case using batch normalization, batch ReLU function activation, and maximum pooling. Post the residual blocks, the probability for every stage was computed using an FC layer employing a softmax function, while each feature map underwent averaging in the GAP layer. To visualize regions significantly associated with the task at hand, CAM was constructed from the GAP layer by aggregating the characteristics maps with the weights derived from the preceding layer. It is unimportant that the network's beginning parameters, except for the first and last layer parameters, were obtained from the ImageNet dataset's pre-trained parameters. Finally, using our OCTA dataset, all parameters were retrained and optimized using the cross-entropy loss with an AO and a learning rate of 0.0001. Their classifier was 91-98% accurate, 86-97% sensitive, 94-99% specific, and had an area under the curve of 0.919-0.976. Zang et al. proposed DcardNet[48], which is a CNN-based model capable of carrying out multi-level DR classification using en face OCT and OCTA data. Adaptive rate dropout and label normalization were applied to their model to minimize overfitting. The model's overall accuracy on referable DR, through 10-fold cross-validation, was 95.7%, while it achieved 85.0% for NPDR and PDR, and 71.0% for finer DR stage classification. C. H. Hua et al. [49] proposed TFA-Net given an efficient classifier for medical images from KHUMC and Messidor datasets. The model obtained 90.2%-Quadratic Weighted Kappa, 94.8%-accuracy, and 99.4%-area under the receiver operating characteristic curve, proving its high performance and reliability in classifying medical images.

Li et al. [50] suggested a deep learning architecture for OCTA image fusion that merges multilayer information. Initially, an OCTA picture was labeled with the borders of major retinal arteries and the FAZ using a U-Net-based segmentation model. The researchers subsequently created a separate ICB framework to gather and combine data from the raw OCTA samples and division findings at various levels of a blend. Using their suggested classification model, they achieved a DR diagnostic Acc of 88.10% and an AUC of 0.920.Hou et al. [51] give three components of their methodology: segmentation, image quality evaluation, and DR rating. They employed UNet and UNet++ networks with pre-trained encoders for DR lesion segmentation. Using specialized methodologies, three unique lesions, IRMA, NPA, and NV, were employed to train the segmentation models. For IRMA segmentation, they developed a learning rate sequence and a color jittering augmentation. They did not, however, employ it to increase the division quality of NPAs and NV lesions. They also employed the example aggregate technique to forecast IRMA and NPA segmented masks. To solve the overtraining issue caused by limited sample numbers, they pre-trained their system using the large OCTA-25K-IQA-SEG dataset for assessing image quality. For the DRAC dataset, the model was then updated using a hybrid MixUp and CutMix approach. They integrated three models into one: Inception-V3, SE-ResNeXt, and ViT. Finally, for DR grading, they used a ViT model, which takes an OCTA picture as input and generates the assessment. The area under the curve of 0.919-0.976.

Lyu et al. [52] proposed the AADG method, to automatically augment data and generalize it to continue learning separate domains and minimize domain-shift affect in a training-testing dat-set. For this purpose, they used both OCTA-500 and ROSE (OCTA).Yuan et al. [53] used deep learning-based high-resolution angiogram reconstruction with a generative adversarial network (SAR-GAN) to improve enface OCTA image quality, utilizing 50 OCTAs from healthy volunteers. Qiaoyu Li et al.'s [54] approach could classify various patterns in the OCT angiography images of the OCTA-500 dataset into background, vessels, and foveal a vascular zones. They observed an accuracy of 93.2% for the background, 93.8% for vessels, and 92.3% for the FAZ, thus demonstrating a reliable model for OCTA image analysis. According to Yuhan Zheng, Fuping Wu, and Bartlomiej W. Papie˙z [55], the ensemble method integrating ResNet, DenseNet, EfficientNet, and VGG could enhance the accuracy of OCTA data classification on the DRAC 2022 UW-OCTA dataset. The cross-validated QWK and AUC scores were reported at 0.9346 and 0.9766, respectively, reiterating the power of ensemble techniques on medical imaging tasks.

The methodology developed by Fei Ma et al. [56] achieved classification of diabetic retinopathy (DR) using the Road dataset, with an accuracy of 87.5%, thus exemplifying progressive development in DR detection while acknowledging the constant challenge of improving accuracy in this domain. According to S. F. Rabbi et al. [57], use of a CBAM-augmented model could classify a custom OCT dataset with 10,000 images with very high accuracy. The model achieved values of 96% accuracy, F1 score, precision, and recall, indicating very strong performance in OCT image analysis. Matten et al. [58] proposed a multiple instance learning-based network for classification of diabetic retinopathy using OCTA images, named MIL-ResNet. The model was trained on a dataset collected with a diagnostic ultra-wide field swept-source OCT device without requiring pixel-level annotations. State of the art ResNet and VGG16 were outdone by MIL-ResNet with impressive accuracy and robustness against adversarial attacks while being focused on clinically relevant biomarkers. Hatode and Edinburgh [59] introduced a method for diabetic retinopathy classification by generating synthetic OCTA images with Wasserstein Generative Adversarial Nets for data augmentation, overcoming limitations of small datasets. The synthetic images were classified into DR stages (PDR, severe NPDR, moderate NPDR, mild NPDR) using a fine-tuned ResNet50 model, achieving 99.95% accuracy, surpassing previous studies

Bidwai et al. [60] developed a deep learning approach for the detection of diabetic retinopathy among aged subjects using specially created OCTA datasets containing 262 high-resolution images taken from Natasha Eye Center, Pune. Their protocol classified DR into different severity levels through training CNN models (Inception V3, ResNet-50, DenseNet121, EfficientNetV2B0), which were aimed at assisting the doctors in providing timely diagnosis and interventions of unadulterated ocular diseases prevalent among the aged.

TABLE II
SUMMARYOF RESEARCH WORKS ON AUTOMATING DR DIAGNOSIS IN THE STATE-OF-THE-ART USING DEEP LEARNING METHODS

Author and Year	Database	Method	Results (Best)
Abràmoff et al. 2018 [40]	900 OCTA Images	Classification: Multilayer CNN	AUC=0.980
Islam, 2019 [41]	Kermani OCT dataset	DCNN: DenseNet 201	Accuracy=98.6 % Sensitivity=0.986% Specificity 0.995%
Heisler et al. 2020 [42]	No DR Eyes: 224 DR Eyes: 156	Features: Axis Ratio Index, Area, Perimeter, Diameter, Circularity, Maximum Eccentricity and Minimum of the FAZ Classification: Ensemble method including VGG19, ResNet50, and DenseNet	Accuracy = 90.71% Sensitivity=93.32% Specificity = 87.74%
Le et al. 2020 [43]	Healthy Eyes: 32 DM w/o DR Eyes:24 DR Eyes: 75 eyes	Classification: Transfer learning using CNN and VGG16	Accuracy = 87.27% Sensitivity = 83.76%, Specificity = 90.82% AUC=0.97
Abdel salam 2020 [44]	Healthy Eyes: 40 DM w/o DR: 30 Mild to moderate NPDR Eyes: 30	Categories: Mean of the inter-capillary, FAZ perimeter, circularity index, and vascular density Classification: ANN	Accuracy = 97%
Cano Jennifer et al. 2020[45]	33 no DR, 26 mild NPDR, 13 PDR, 22 normal from private eye hospital	Classification: Normal minimal squares demonstrating the technique	PDR Accuracy = 94% Mild NPDR vs. healthy Accuracy = 91%
Kim et al. 2021 [46]	DR Eyes: 235	Features: FAZ,VD, and the NPA	AUC = 0.922
Ryu et al. 2021 [47]	Healthy Eyes: 51 DM w/o DR: 51 Mild NPDR Eyes: 53 Moderate NPDR: 49 Severe NPDR: 48	CNN classifier	Accuracy = 95.4%
Zang et al.2021 [48]	En face OCT and OCTA	DcardNet (CNN-based) with adaptive dropout and label normalization	95.7% (referable DR), 85.0% (NPDR, PDR), 71.0% (finer stages).
C. H. Hua et al. 2021[49]	KHUMC, Messidor	TFA-Net	KHUMC - Quadratic Weighted Kappa= 90.2% Accuracy=94.8 % Area Under ROC=99.4%
Li et al. 2022 [50]	ROSE dataset Healthy Eyes: 244 DR Eyes: 57	Segmentation: U-Net Classification-ResNet 50	Segmentation Accuracy = 93.1% Classification Accuracy=87.8 %
Hou et al. 2022 [51]	DRAC dataset	Features: IRMA, NPA, and NV Classification: UNet and	AUC = 0.9083

		UNet++	
Lyu et al. 2022[52]	OCTA-500, ROSE (OCTA)	AADG method for data augmentation and domain shift minimization	Improved generalizability across domains.
Yuan et al. 2022[53]	50 OCTA images	SAR-GAN for high-resolution angiogram reconstruction	Enhanced OCTA image quality.
Qiaoyu Li et al 2022 [54]	OCTA-500	ResNet50	Accuracy =93.2% for the background, 93.8% for vessels, 92.3% for the FAZ
YuhanZheng, et al. 2023[55]	DRAC 2022 UW-OCTA Dataset	Ensemble method +ResNet, DenseNet, EfficientNet, and VGG;	QWK=0.9346, AUC= 0.9766
Fei Ma et al 2023 [56]	ROAD dataset	PACNet	Accuracy = 87.5% for DR
S. F. Rabbi et al. 2023 [57]	Custom OCT Dataset -10,000 images	Custom OCT Dataset +CBAM	Accuracy =96% F1 Score=96% Precision=95% Recall=96%
Matten et al.2023 [58]	Ultra-wide-field OCTA	MIL-ResNet for DR classification	Superior accuracy and robustness compared to ResNet and GG16.
Hatode and Edinburgh2024 [59]	Synthetic OCTA images	Wasserstein GAN + fine-tuned ResNet50	99.95% accuracy for DR stage classification.
Bidwai et al.2024 [60]	Natasha Eye Center, Pune (262 images)	CNN models (Inception V3, ResNet-50, DenseNet121, EfficientNetV2 B0)	DR severity classification in aged subjects.

IV. DATASETS

From the literature we have analyzed, we understand that there is a lack of a benchmark OCTA database for diabetic retinopathy diagnosis. Most of the researchers have gathered their databases from different ophthalmology clinics for diagnosis purposes.

The four recently released OCTA datasets are ROSE [66], for which an application email with the necessary form must be sent to [61], OCTA-500 [65], which is freely accessible from [65], OCTA-SS [46], which is downloadable from [47],DRAC 22[55] and OCTA-500 [65]. The OCTA-500 provides entire estimate images of various depths as well as 3D OCTA data from 500 eyes. OCTA-SS provides the most comprehensive vessel commenting, which is utilized for numerical assessment and comparison. It gave 55 slices of the area that was fascinating derived from 3mm3mm FOV images of 11 people with and without a family history of dementia, rather than the entire field of view (FOV) images. ROSE is divided into two distinct datasets, ROSE-1 and ROSE-2. ROSE-1 [70] consists of 117 OCTA images from 39 people, 39 with and 39 without Alzheimer's disease. The ROSE-2[70] subgroup comprises 112 OCTA samples from 112 eyes with various macula abnormalities. The DRAC dataset, introduced as part of the Diabetic Retinopathy Analysis Challenge (DRAC) at the 25th MICCAI Conference in 2022, is a comprehensive ultra-wide Optical Coherence Tomography Angiography (UW-OCTA) dataset comprising 1,103 high-resolution images. It was designed to address three critical clinical tasks in diabetic retinopathy (DR) management: lesion segmentation, image quality assessment, and DR grading. By focusing on UW-OCTA imaging, the dataset provides detailed retinal vascular information over a wide field of view, enabling more precise analysis compared to traditional imaging methods.

The primary focus among the four mentioned datasets is the OCTA-500, specifically tailored for diabetic retinopathy. Curated by Li et al. [39], the OCTA-500 database comprises 500studies, encompassing two variations of FOV with both OCT and OCTA data. This dataset involves six projection types, four text labels, and two pixel-level labels. One subset, OCTA 6M, consists of 300 subjects with a 6mm x 6mm field of view, while the other subset, OCTA 3M, includes 200 subjects with a 3mm x 3mm FOV. The data was gathered using a commercial 70 kHz spectral-domain OCT system, operating at a center wavelength of 840 nm. The OCTA 6M subset is derived from images captured at Jiangsu Province Hospital between March 2018 and September 2019, where only one image per eye study is included to ensure unique and non-repetitive data.

V.DISCUSSION AND INFERENCES FROM THE REVIEW OF DR CLASSIFICATION MODELS AND DATASETS

The field of automated diabetic retinopathy (DR) classification has significantly advanced due to the advent of machine learning (ML) and deep learning (DL). The present review endeavors to provide a brief account of developments right from the initial ML-based approaches towards sophisticated deep learning approaches enabling improved accuracy. Earlier, machines learned using handcrafted features like size of the foveal a vascular zone (FAZ), vascular density, bifurcation points, etc., for DR detection using various machine learning algorithms, primarily Support Vector Machines (SVM). These frameworks showed reasonable accuracy; however, they could not scale to diverse datasets as intended and thus had a problem with generalization. Figure 6 show cases the accuracy levels of different ML models used in

OCTA-based DR studies, together with the pros and cons of early ML techniques.

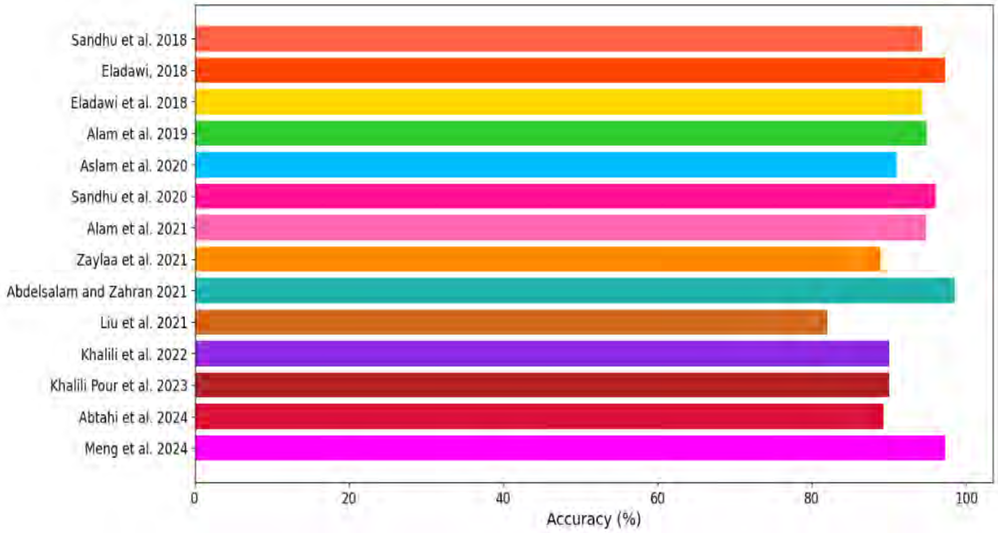

Fig. 6.Accuracy of Machine Learning Models in OCTA-Based DR Studies.

With the rise of deep learning, several advancements have been made in DR classification. CNN-based architectures such as DenseNet, ResNet, and VGGNet were revolutionary by being able to learn features directly from raw data more competently. Fig. 8 shows a comparative study on the different accuracies attained by these deep learning models in OCTA-based DR studies, which is far superior in feature extraction than the classical ML models. The combination of transfer learning and ensemble method enhances model robustness, and multimodal techniques which combined OCTA with fundus imaging have added diagnostic value, as demonstrated in Fig. 7, illustrating the distributions of OCT/OCTA datasets utilized in DR studies.

As the field continues to develop, the diversity and size of datasets become key aspects for the construction of powerful models. Fig. 7 emphasizes the need for varied OCT/OCTA datasets for training machine learning and deep learning models, with an increasing number of studies concerning this area. However, issues such as domain shifts, dataset augmentation, and clinical validation remain in the realm of concerns needing additional progress in order to ensure the models' generalization and usability in real clinical scenarios.

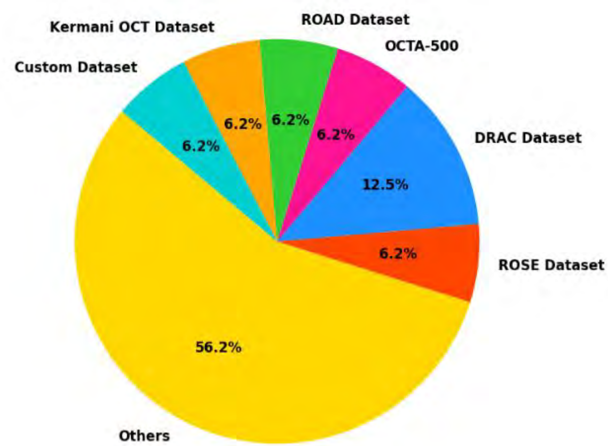

Fig.7.Distribution of OCT/OCTA Datasets Used in Diabetic Retinopathy Studies.

Fig. 8 depicts the various DL models used in research studies dealing with Optical Coherence Tomography Angiography technology for detection and classification of Diabetic Retinopathy. The performances may have been indicated through different classification accuracies climbed within the domain of either convolutional neural networks or another of the deep learning architectures or models. The x-axis might represent the studies or categories of models, while the y-axis might show the percentage accuracies used for detection of DR from OCTA images. This figure highlights the efficacies of DL models applied in this domain, showing high accuracies in DR diagnosis that are critical for early detection and treatment planning. Besides, it underlines the expanding role of deep learning in the development of medical image analysis in diabetic retinopathy detection.

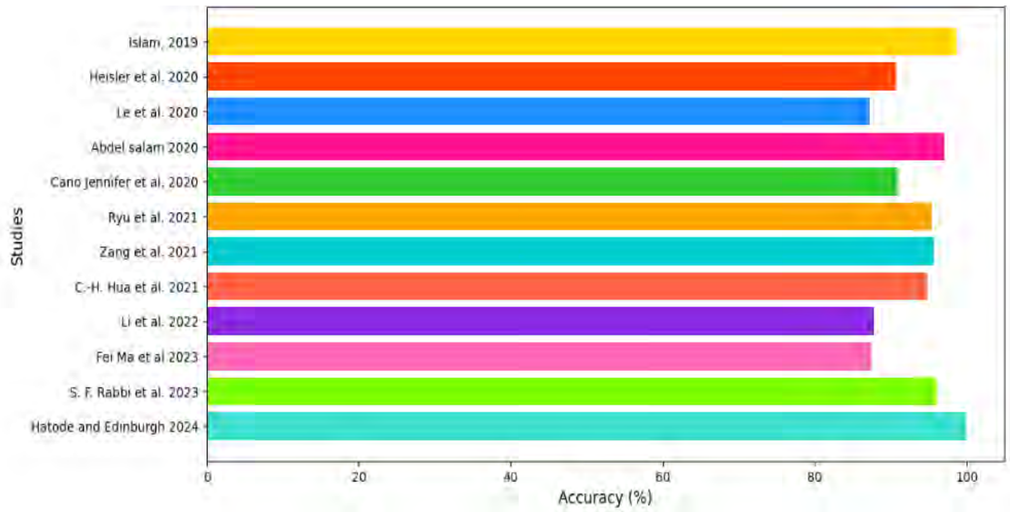

Fig.8.Accuracy of Deep Learning Models in OCTA-Based DR Studies.

Fig. 9 summarizes the AUC and dataset sizes for various machine learning models used in DR classification. It shows that the AUC score, which gives a measurement to the ability of the model to differentiate between different stages of DR, increases as the size of the dataset is larger. Traditional ML models such as SVM and Random Forest performed well and attained a level of plateau in performance as the dataset size becomes larger. The focus of this figure is on how the size of the dataset should be viewed as important in increasing diagnostic accuracy in ML models.

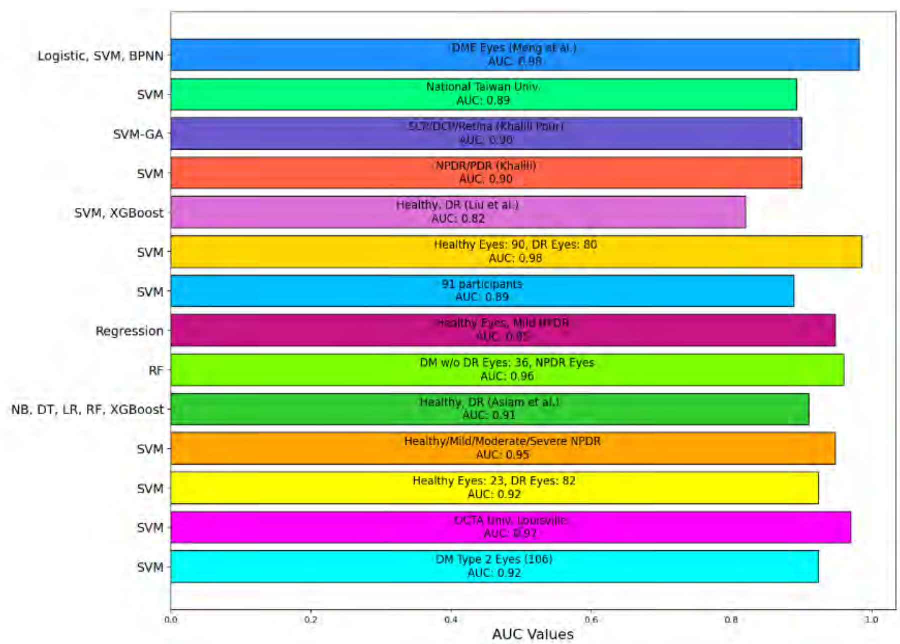

Fig. 9.AUC and Datasets of Machine learning Models in OCTA-Based DR Studies.

On the other hand, Fig. 10 depicts the comparison between the AUC performance of deep learning models in OCTA-based DR classification. The figure depicts that as the dataset size increases, deep learning models such as DenseNet, ResNet, and EfficientNet have higher AUC scores, meaning that they can more easily distinguish different stages of DR. This also points out deep learning models are better in handling larger datasets, from which they can extract more complex features and thus can achieve greater accuracy in DR detection.

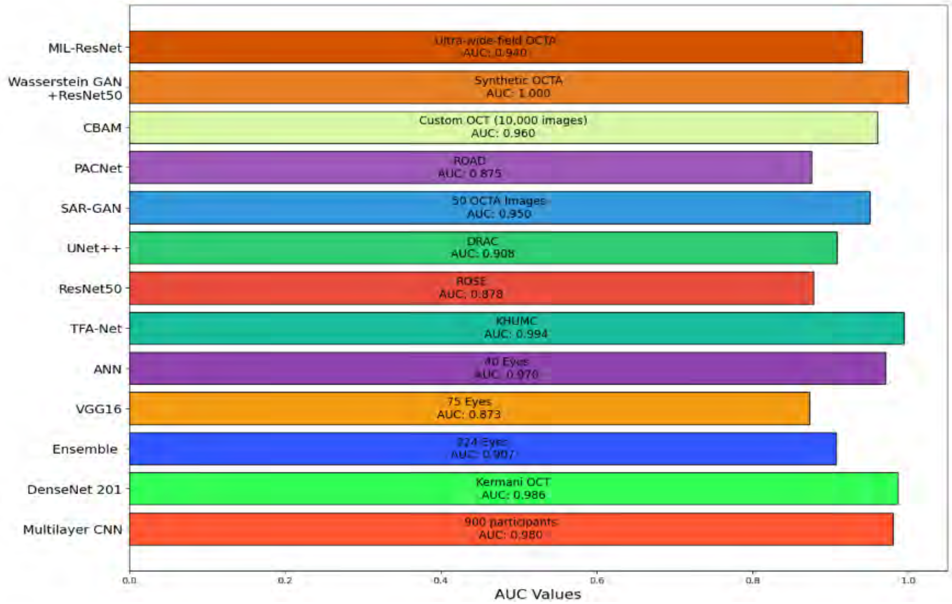

Fig. 10.AUC and Datasets of Deep Learning Models in OCTA-Based DR Studies.

Fig. 11 shows the number of studies utilizing Machine Learning and Deep Learning techniques for classification of Diabetic Retinopathy using Optical Coherence Tomography Angiography over time. The figure indicates how research in this area has evolved, with increasing interest being shown towards ML and DL methods of analyzing OCTA images in detection and monitoring of DR. The trend may reflect a cultural change substituting an early generation of conventional machine learning methods for second-generation deep learning techniques into practice, pointing towards the advancements of AI and its growing role in medical imaging. Such advancement is suggestive of the ever-increasing role to be played by AI in increasing DR classification capacity and efficiency.

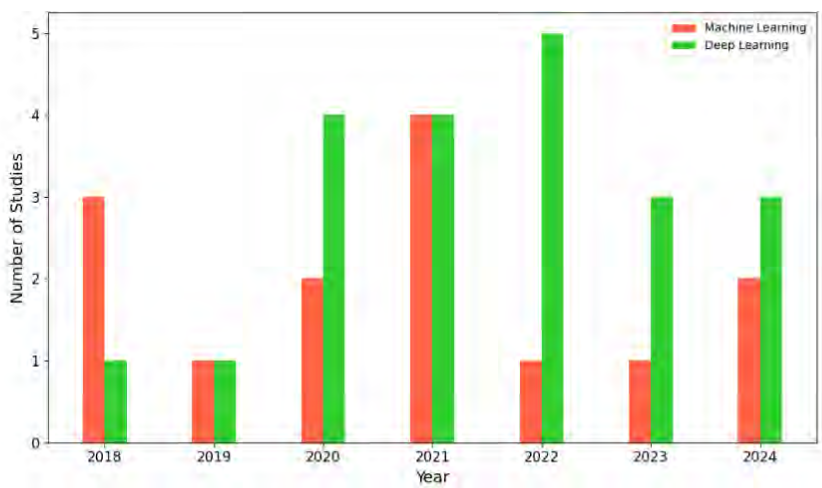

Fig.11.Number of ML and DL Studies in OCTA for Diabetic Retinopathy Classification.

In recent years, Diabetic Retinopathy detection has really changed. DR detection started out in 2018 with basic machine learning methods, with SVM, Random Forest, and Logistic Regression. These methods were very basic in nature; nevertheless, they opened up the realm of automated DR detection through retinal images. Beginning in 2019, deep learning, especially CNN, surged to the fore due to its superior performance in image-related works, giving a big boost in terms of high accuracy levels. By 2020, focus diverted towards more advanced DL architectures like DenseNet, VGGNet, and ResNet that could extract features and classify better. Researchers also utilized multimodal approaches by fusing OCTA and fundus images to increase the robustness of DR classification.

These advances continued in the years through 2021, when ensemble methods and transfer training became the topic of discussion, leading to the development of models with greater accuracy and generalizability. 2022 saw the introduction of EfficientNet, among high-performance models based on transformer networks to introduce computational efficiency and accuracy. By 2023 hybrid models encompassing all-inclusive methods became popular, enabling classification of DR into different stages. In 2024, generative adversarial networks played an indispensable role in generating synthetic retinal images for dataset augmentation to enhance generative performance of the models, especially OCTA images, thus boosting their application between domains. These developments demonstrate the continuous evolution of DR detection from basic ML models to sophisticated hybrid systems incorporating DL innovations.

The following figure depicts these progresses, which are visions of essential inventions made year by year through ML and DL on Diabetic Retinopathy detection.

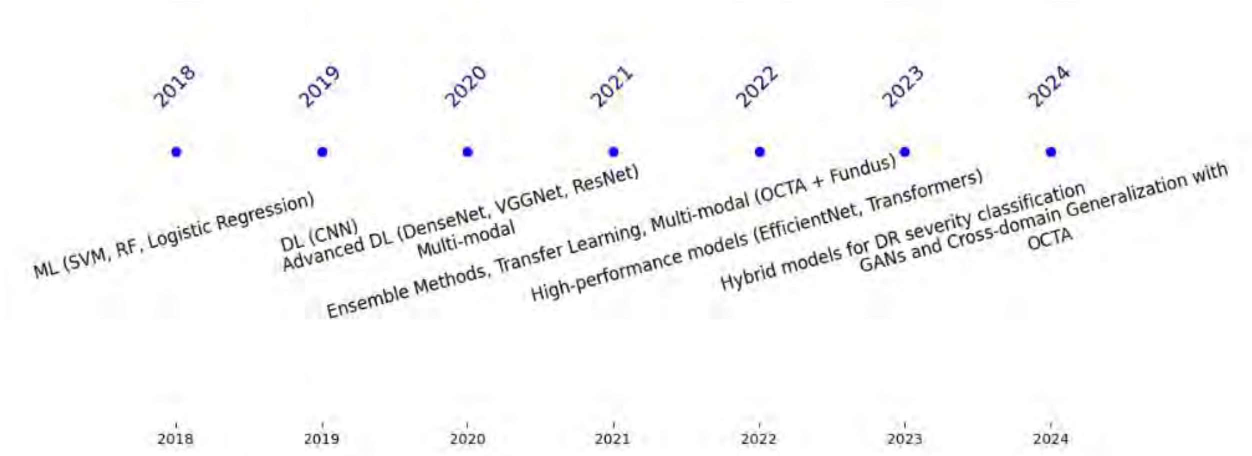

Fig.12.Timeline of Research Progress in DR Detection.

VI. RESEARCH GAPS

Multiple research gaps must be filled to automate the system, even though a significant quantity of research yields experienced methods for the detection of DR. Here is how the research gap has been described.

A. Applicability of Machine Learning

Further research in healthcare environments is required to determine the applicability of ML , and automated screening procedures should be used to detect disease early on .

B. OCTA selection for DR screening

OCT and OCTA with DR have just recently been adopted for screening purposes. In terms of several performance measures, however, improving the automatic DR categorization yields better outcomes .

C. Insights for storing clinical data

Many ophthalmology practices provide smart healthcare solutions. However, using medical data that has been extensively stored electronically can enhance decision-making

D. Research in artificial intelligence conducted in DR led to the development of an efficient system of automated grading

Ophthalmology DR Research faces difficulties. So, the grading of DR occurs automatically as a result of executing an AI program using DR. However, the prediction is more accurate with more training images. Retinal structure and alterations can be covered by a single technique using the identification of OD, blood vessels, etc. The peripheral lesions are not primarily captured by the different imaging modalities. It is necessary to increase DR detection and categorization to improve the results.

E. The algorithm's applicability should be narrowed down.

Because of the insufficient dataset, the training dataset's effectiveness decreases. Additionally, generalizability should be performed on a diverse demographic sample. The method should be created in a way that prevents broad applicability. A revised definition of success and a deeper comprehension of medically applicable information in digital imaging will be included in the program's rapid development into a clinical environment during the following five years.

F. Getting rid of the differences that exist between several fields of study such as computer science and medical science.

AI research is a challenging area of study. It can develop a variety of scientific disciplines, including computer and medical science. The related research is narrowly targeted and relevant to a specific field. To lessen the variability between the areas, future studies will concentrate on combining the two fields.

G. Affordability of disease diagnosis for cost-efficient treatment

DR comes with a variety of difficulties. The advancement in DR screening is one such obstacle, though. After that, time-saving remedies are required to automate the procedure by removing the diseases that manifest on the retinal surface. The issue of acquiring cost-effective, high-quality retinal images is expected to be solved by the growth of community-specific retina scanning methods, including cell phone technology to m-Health.

VII. PROPOSED METHODOLOGY

The proposed methodology for classifying DR with OCTA images includes crucial steps to achieve more accurate diagnosis and develop improved clinical care. Systematic collection of OCTA images of the retina begins this process by providing the input images necessary to detect the abnormality in the retina. After capture, the images undergo pre-processing. This is a critical phase in which certain operations are aimed at improving the image quality in detecting noise and artifice and making it suitable for better analysis. The next step is data expansion, further expansions are applied to our preprocessed images to expand the data set. This includes transformation processes through rotating, mirroring and zooming to simulate different conditions under which images might later be captured. By expanding the training data, the model generalizes better and is more resilient to variations that the model may encounter in the real world. In addition to image data, data derived from other demographic variables considered in this model include, but are not limited to, age and gender. These provide additional training context as these parameters can influence susceptibility and onset of DR, which in turn allows the model to consider classification based on these factors. The next step is to split the dataset into three different subsets: training, validation and testing data. The training data gives the model general discriminative patterns and features for diabetic retinopathy. The validation data is then used to fine-tune the parameters so that overfitting of the training data does not occur and the model is preserved unlike the training data. Finally, test data uses a different evaluation platform to provide an objective assessment of model performance and measure its effectiveness for clinical purposes. Model training uses advanced techniques, particularly convolutional neural networks (CNNs). CNNs process the data across many levels, which can focus on increasingly abstract representations. Architectures like VGG or ResNet could be useful in this case as they are associated with superior performance in image recognition. This training phase allows the model to optimally learn the parameters to reduce the number of classification errors. This method concludes with the classification phase, where the trained model looks at the test data and classifies the images into two large groups: normal and diabetic retinopathy, divided into NPDR and PDR. This approach is very systematic and structured and aims to improve diagnostic accuracy and support clinical decision making, ultimately leading to better patient outcomes in diabetic eye diseases.

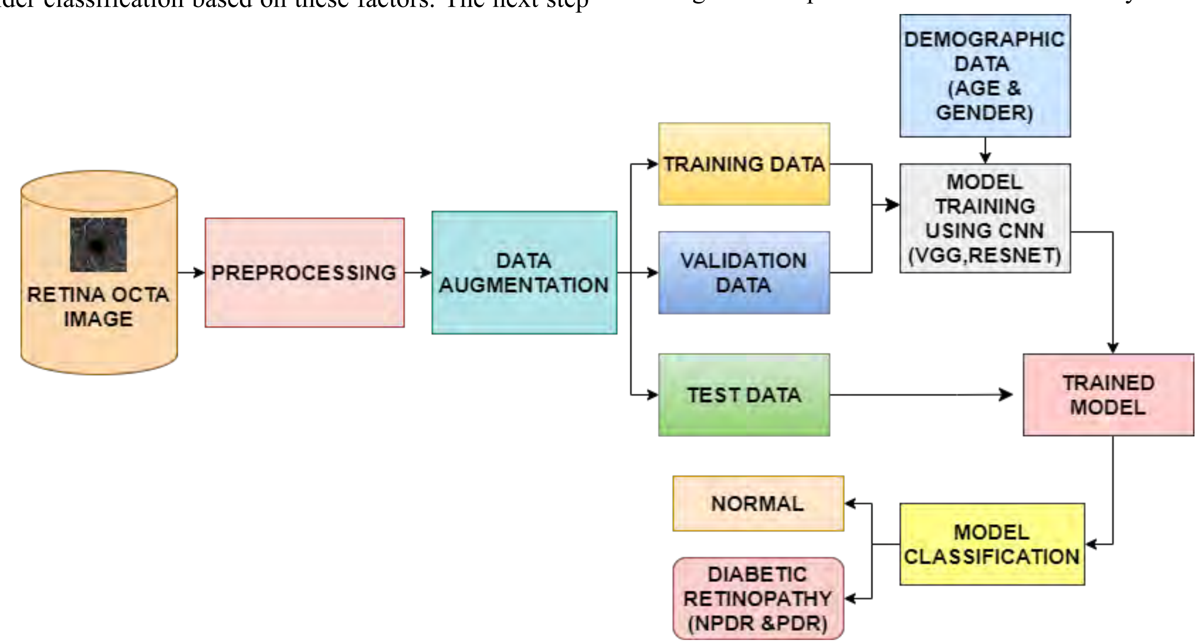

Fig. 13. Proposed block diagram of DR detection and Classification Using Deep learning from OCTA images.

VIII. PERFORMANCE MEASURES

The confusion matrix is a way to show how well a classification model works. The confusion matrix's measures have been calculated according to the assumptions and the reality of the scenario. Based on these measurements, other specific metrics like Specificity, Precision, F1 score, Sensitivity, Accuracy, and Cohen's Kappa are defined. Also, the ROC[77,78] curve shows how well a classifier works by plotting the classifier's Sensitivity against its Specificity at different threshold settings based on the outcome of the classification (i.e. at which probability a given sample is considered as a positive or negative outcome). Last, AUC figures out the AU-ROC curve. This gives an overall measure of performance across all criteria for categorization.

$$\text{Precision}=TP/(TP+FP) \quad (6.1)$$

$$\text{Sensitivity/Recall}=TP/(TP+FN) \quad (6.2)$$

$$\text{Specificity}=TN/(TN+FP) \quad (6.3)$$

$$\text{F1-score}=2*(\text{precision}*\text{recall})/(\text{precision}+\text{recall}) \quad (6.4)$$

$$\text{Accuracy}=(TP+TN)/(TP+TN+FP+FN) \quad (6.5)$$

IX. CHALLENGES AND FUTURE SCOPE

Despite significant developments over the past several years, reliable clinical diagnostics still face several challenges that must be overcome and continually enhanced to effectively treat new illnesses and diseases. At the moment, even doctors do not fully rely on AI-based methods because they are unsure of their capacity to foresee illnesses and their related symptoms. It takes a lot of work to train AI-based systems so that they can anticipate disease diagnosis techniques with greater accuracy. Therefore, in the future, research on AI should be undertaken while taking the problem noted before into account to create a partnership between AI and doctors that is mutually beneficial. Moreover, employing a decentralized federated learning model is crucial to create a unified training model for disease databases located remotely, enhancing early detection of illnesses.

The majority of studies concentrate on fundus imaging methods, and scholars have devised several innovative methods that employ CNN and image processing techniques, DL, or hybrid[79] models that also deliver very accurate findings. All of this leads to the conclusion that OCTA images should be used through the identification of DR since they are crucial for understanding the severity patterns of the retina layer by layer as well as for neovascularization and changes in retinal blood vessel width that have not gotten much attention from researchers.

The majority of studies have achieved the greatest success rates either when they have focused on a specific kind of irregularity or lesion in DR detection or when they have not taken into consideration all class grading of illness, which indirectly affects the usefulness of research. Strong color model algorithms need to be developed because the primary challenge in lesion identification is how the image is collected or under which settings such as values of the brightness or intensity of pixels can confuse the detection of normal retinal features. This means that the most important step in this process is determining the appropriate settings.

Due to its established significance, DL algorithms[79,80] constitute the foundation of the majority of current image and video processing applications. However, several potential directions must be handled, making the robust DL network required. In reality, DL-based models are also used to improve DR detection systems automatically. There are many DL models in the literature that, to predict the DR from retinal images, mostly use CNN methods for creating deep multi-layer architectures. Ophthalmologists are required for this image annotation, even though it is a time- and money-consuming task. Therefore, in order to improve learning from an image collection, DL-based models must be created. Usually, when automatic clarification for DR images is implemented, there may be a problem with class imbalance. Therefore, it is crucial to examine the class imbalance issue in order to improve the DL-based models by taking a specific class learning bias into account.

As there are many photographs acquired[81,82] under various situations, they must go through a lot of preprocessing and augmentation, which may cause some elements of the image to be lost. As a result, techniques should be utilized that not only maintain all the little critical information but can also successfully do pre-processing. Additionally, more than two photographs should be provided for each patient. This will increase the likelihood that the images will be accurately classified because more information can be acquired.

X. CONCLUSION

An OCTA-based automated approach for the early identification and categorization of diabetic retinopathy can significantly transform the realm of diagnosis by allowing high-fidelity and precise documentation of the disease; thus, it can elevate the standard of medical practice. Early detection of DR allows for timely intervention to-enable the prevention of visual-nerve damage and vision loss. While any imaging has diagnostic ability, OCTA captures reliable and high-resolution three-dimensional vascular detail superior to fundus imaging and invaluable for DR analysis.

Our systematic review highlights the future promise of OCTA in predicting DR progression and analyzing its diagnostic feedback. Prospects of using it in detecting DR remain scant and limited by the absence of publicly available datasets and specialized methodologies for its analytics. Most incorporated techniques are based on fundus images, thus not being directly applicable to OCTA due to the intricate 3D nature of OCTA data; a much-needed factor for further study and development in this field. By marrying OCTA biomarkers with modern deep learning methods, there is an opportunity to integrate DR detection into routine clinical practice by fully automating the grading process.

Recent developments in DL algorithms, notably Convolutional Neural Networks (CNNs) and transfer learning, posses high potential for the application of analyzing OCTA images through automated feature extraction from complex retinal patterns. Such methods could increase the accuracy, efficiency, and scalability of DR diagnosis, especially for patients who do not have access to skilled ophthalmologists. Conventional machine learning techniques, such as support vector machines and random forests, have demonstrated the potential, but would struggle with the complexity of three-dimensional OCTA data.

To fully leverage OCTA's potential, future efforts must stand or fall on optimizing the biomarkers, enlarging high-quality datasets, and developing strong algorithms that would generalize in diverse outpatient populations. Ideally merging OCTA biomarkers with novel deep-learning algorithms will set a new standard in DR diagnosis, classification, and its timely detection. Together we will be able to integrate against timely intervention and vision loss in diabetic patients. This will, in turn, allow us to seek greater availability and accuracy of DR screening through OCTA, bridging the gap in accessibility and patient outcomes.

- OCT and OCTA represent groundbreaking advancements in retinal imaging, capable of extracting significantly more retinal information compared to traditional fundus images.
- When compared to traditional fundus photography and OCT, DL in OCTA categorization hasn't been explored yet because there aren't enough public datasets.

- One of the major limitations of retinal fundus images is their inability to capture depth, as they are restricted to two-dimensional representations. OCT, in contrast, provides depth measurement, offering a more comprehensive analysis of retinal structure.
- This review highlights the potential of OCTA imaging as a powerful tool for diabetic retinopathy detection, offering detailed visualization of retinal microvasculature changes that are critical for early and accurate diagnosis.
- DL models have demonstrated promising performance in analyzing OCTA images, leveraging their ability to process complex vascular patterns and subtle pathological changes.
- Despite the advancements, the adoption of DL for OCTA-based DR detection is limited by the scarcity of publicly available, large-scale, annotated datasets, which hampers the development and validation of robust models.
- Collaborative efforts are essential to create and share diverse, high-quality datasets and to develop innovative DL architectures tailored to the unique characteristics of OCTA imaging.
- Continued research focusing on improving model generalizability, addressing class imbalance, and integrating multimodal data could pave the way for more accurate, reliable, and clinically applicable solutions for DR detection using OCTA.
- Combining OCTA biomarkers with advanced DL techniques could establish a new standard for the early identification, diagnosis, and classification of DR, enabling timely interventions and reducing the risk of vision loss in diabetic patients.
- Future studies should prioritize optimizing OCTA biomarkers, enhancing dataset quality and size, and developing robust algorithms that generalize across diverse patient populations.

Abbreviation	Description
PDR	Proliferative diabetic retinopathy
NPDR	Non-Proliferative diabetic retinopathy
FA	Fluorescein Angiography
OCTA	Optical Coherence Tomography Angiography
DR	Diabetic Retinopathy
CNN	Convolutional neural network
ICP	Intermediate capillary Plexuses
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
DL	Deep Learning
ML	Machine Learning
SVMs	Support Vector Machines
FAZ	Foveal avascular zone
BVB	Blood vessel density
VCI	Vessal complexity index
FAZA	Foveal avascular zone area
FD	Foveal density
CAD	Computer-aided diagnostic
ReLU	Rectified linear unit
GAP	Global Average Pooling
ViT	Vision transformer
AO	Adam optimizer
VD	Vessel Density
CNV	Choroial Neovascularization
FOV	Field of view
AUC	Area Under the Curve
DWT	Discrete Wavelet Transform
LR-EN	Logistic Regression with Elastic Net Regularization
SS-OCTA	Swept-Source OCTA
VD	Vascular density
NPA	NON-perfusion area
ICP	Isolated Concatenated Block
CAM	Class Activation Maps
VLD	Vessel Length Density
DNN	Deep Neural networks
XGBoost	gradient boosting tree
3D	three- Dimensional
ROV	Receiver Operating Characteristic

AUTHOR CONTRIBUTION

Author 1: **Abini M.A:** Conceptualization, Investigation, Methodology, Validation, Writing- original draft, review &Editing.

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Not applicable

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The authors declare that we have no conflict of interest. On behalf of all authors, the corresponding author states that there is no conflict of interest.

DATA AVAILABILITYSTATEMENT

All the data is collected from the simulation reports of the software and tools used by the authors. Authors are working on implementing the same using real world data with appropriate permissions.

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REFERENCES

[1] "The cost of diabetes," Diabetes.org.[Online].Available: https://diabetes.org/about-us/statistics/cost-diabetes.[Accessed: 13-Sep-2022].

[2] K. Ogurtsova, et al., "IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040," *Diabetes Res. Clin. Pract.*, vol. 128, pp. 40–50, 2017.

[3] C. Agurto, et al., "Multiscale AM-FM methods for diabetic retinopathy lesion detection," *IEEE Trans. Med. Imaging*, vol. 29, no. 2, pp. 502–512, 2010.

[4] GBD 2019 Blindness and Vision Impairment Collaborators and Vision Loss Expert Group of the Global Burden of Disease Study, "Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study," *Lancet Glob. Health*, vol. 9, no. 2, pp. e144–e160, 2021.

[5] T. Y. Wong, C. M. G. Cheung, M. Larsen, S. Sharma, and R. Simó, "Diabetic retinopathy," *Nat. Rev. Dis. Primers*, vol. 2, pp. 16012, 2016.

[6] "Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. Early Treatment Diabetic Retinopathy Study Research Group," *Ophthalmology*, vol. 98, no. 5 Suppl., pp. 823–833, 1991.

[7] C. P. Wilkinson, et al., "Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales," *Ophthalmology*, vol. 110, no. 9, pp. 1677–1682, 2003.

[8] D. Ellis, P. I. Burgess, and P. Kayange, "Management of diabetic retinopathy," *Malawi Med. J.*, vol. 25, no. 4, pp. 116–120, 2013.

[9] J. K. H. Goh, C. Y. Cheung, S. S. Sim, P. C. Tan, G. S. W. Tan, and T. Y. Wong, "Retinal imaging techniques for diabetic retinopathy screening," *J. Diabetes Sci. Technol.*, vol. 10, no. 2, pp. 282–294, 2016.

[10] E. Stefánsson, T. Bek, M. Porta, N. Larsen, J. K. Kristinsson, and E. Agardh, "Screening and prevention of diabetic blindness," *ActaOphthalmol.Scand.*, vol. 78, no. 4, pp. 374–385, 2000.

[11] B. J. Fenner, R. L. M. Wong, W.-C. Lam, G. S. W. Tan, and G. C. M. Cheung, "Advances in retinal imaging and applications in diabetic retinopathy screening: A review," *Ophthalmol. Ther.*, vol. 7, no. 2, pp. 333–346, 2018.

[12] W. Fan et al., "Retinal vascular bed area on ultra-wide field fluorescein angiography indicates the severity of diabetic retinopathy," *Br. J. Ophthalmol.*, vol. 106, no. 8, pp. 1126–1131, 2022.

[13] Z. Gao et al., "End-to-end diabetic retinopathy grading based on fundus fluorescein angiography images using deep learning," *Arbeitsphysiologie*, vol. 260, no. 5, pp. 1663–1673, 2022.

[14] M. C. Savastano et al., "Fluorescein angiography versus optical coherence tomography angiography: FA vs OCTA Italian Study," *Eur. J. Ophthalmol.*, vol. 31, no. 2, pp. 514–520, 2021.

[15] A. S. L. Kwan, C. Barry, I. L. McAllister, and I. Constable, "Fluorescein angiography and adverse drug reactions revisited: the Lions Eye experience," *Clin. Experiment.Ophthalmol.*, vol. 34, no. 1, pp. 33–38, 2006.

[16] R. F. Spaide, J. G. Fujimoto, N. K. Waheed, S. R. Sadda, and G. Staurenghi, "Optical coherence tomography angiography," *Prog. Retin. Eye Res.*, vol. 64, pp. 1–55, 2018.

[17] H. R. Novotny and D. L. Alvis, "A method of photographing fluorescence in circulating blood in the human retina," *Circulation*, vol. 24, no. 1, pp. 82–86, 1961.

[18] R. F. Spaide, "Optical coherence tomography angiography signs of vascular abnormalization with antiangiogenic therapy for choroidal neovascularization," *Am. J. Ophthalmol.*, vol. 160, no. 1, pp. 6–16, 2015.

[19] R. F. Spaide, J. M. KlancnikJr, and M. J. Cooney, "Retinal vascular layers imaged by fluorescein angiography and optical coherence tomography angiography," *JAMA Ophthalmol.*, vol. 133, no. 1, pp. 45–50, 2015.

[20] R. S. Weinhaus, J. M. Burke, F. C. Delori, and D. M. Snodderly, "Comparison of fluorescein angiography with microvascular anatomy of macaque retinas," *Exp. Eye Res.*, vol. 61, no. 1, pp. 1–16, 1995.

[21] K. R. Mendis, et al., "Correlation of histologic and clinical images to determine the diagnostic value of fluorescein angiography for studying retinal capillary detail," *Invest. Ophthalmol. Vis. Sci.*, vol. 51, no. 11, pp. 5864–5869, 2010.

[22] R. N. Johnson, et al., "Fluorescein Angiography," in *Retina*, Elsevier, 2013, pp. 2-50.e1.

[23] H. Ishibazawa, et al., "Optical coherence tomography angiography in diabetic retinopathy: A prospective pilot study," *Am. J. Ophthalmol.*, vol. 160, no. 1, pp. 35–44.e1, 2015.

[24] D. Moher, et al., "Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement," *Syst. Rev.*, vol. 4, no. 1, p. 1, 2015.

[25] H. S. Sandhu, et al., "Automated diabetic retinopathy detection using optical coherence tomography angiography: a pilot study," *Br. J. Ophthalmol.*, vol. 102, no. 11, pp. 1564–1569, 2018.

[26] N. Eladawi, et al., "Early diabetic retinopathy diagnosis based on local retinal blood vessel analysis in optical coherence tomography angiography (OCTA) images," *Med. Phys.*, vol. 45, no. 3, pp. 1148–1159, 2018.

[27] N. Eladawi, et al., "Early diagnosis of diabetic retinopathy in OCTA images based on local analysis of retinal blood vessels and foveal avascular zone," in *Proc. 24th Int. Conf. Pattern Recognition (ICPR)*, Beijing, China, 2018, pp. 3886–3891.

[28] M. Alam, D. Le, J. I. Lim, R. V. P. Chan, and X. Yao, "Supervised machine learning based multi-task artificial intelligence classification of retinopathies," *J. Clin. Med.*, vol. 8, no. 6, p. 872, 2019.

[29] T. M. Aslam, D. C. Hoyle, V. Puri, and G. Bento, "Differentiation of diabetic status using statistical and machine learning techniques on optical coherence

tomography angiography images," *Transl. Vis. Sci. Technol.*, vol. 9, no. 4, p. 2, 2020.
[30] H. S. Sandhu, et al., "Automated diagnosis of diabetic retinopathy using clinical biomarkers, optical coherence tomography, and optical coherence tomography angiography," *Am. J. Ophthalmol.*, vol. 216, pp. 201–206, 2020.
[31] M. Alam, D. Le, J. I. Lim, and X. Yao, "Vascular complexity analysis in optical coherence tomography angiography of diabetic retinopathy," *Retina*, vol. 41, no. 3, pp. 538–545, 2021.
[32] A. J. Zaylaa, G. I. Wehbe, and A. M. Ouahabi, "Bringing AI to automatic diagnosis of diabetic retinopathy from optical coherence tomography angiography," in *2021 Sixth International Conference on Advances in Biomedical Engineering (ICABME)*, 2021.
[33] M. M. Abdelsalam, and M. A. Zahran, "A novel approach of diabetic retinopathy early detection based on multifractal geometry analysis for OCTA macular images using support vector machine," *IEEE Access*, vol. 9, pp. 22844–22858, 2021.
[34] Z. Liu, C. Wang, X. Cai, H. Jiang, and J. Wang, "Discrimination of diabetic retinopathy from optical coherence tomography angiography images using machine learning methods," *IEEE Access*, vol. 9, pp. 51689–51694, 2021.
[35] E. Khalili Pour, et al., "Automated machine learning-based classification of proliferative and non-proliferative diabetic retinopathy using optical coherence tomography angiography vascular density maps," *Arbeitsphysiologie*, 2022.
[36] E. Khalili Pour, K. Rezaee, H. Azimi, et al., "Automated machine learning-based classification of proliferative and non-proliferative diabetic retinopathy using optical coherence tomography angiography vascular density maps," *Graefes Arch. Clin. Exp. Ophthalmol.*, vol. 261, pp. 391–399, 2023.
[37] M. Abtahi, D. Le, B. Ebrahimi, A. K. Dadzie, M. Rahimi, Y. T. Hsieh, M. J. Heiferman, J. I. Lim, and X. Yao, "Differential artery-vein analysis improves the OCTA classification of diabetic retinopathy," *Biomed. Opt. Express*, vol. 15, pp. 3889–3899, 2024.
[38] Z. Meng, Y. Chen, H. Li, Y. Zhang, X. Yao, Y. Meng, W. Shi, Y. Liang, Y. Hu, D. Liu, M. Xie, B. Yan, and J. Luo, "Machine learning and optical coherence tomography-derived radiomics analysis to predict persistent diabetic macular edema in patients undergoing anti-VEGF intravitreal therapy," *J. Transl. Med.*, vol. 22, no. 1, pp. 358, 2024.
[39] M. Li, Y. Chen, W. Zhang, and Q. Chen, "Image magnification network for vessel segmentation in OCTA images," *2021*.
[40] M. D. Abràmoff, P. T. Lavin, M. Birch, N. Shah, and J. C. Folk, "Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices," *NPJ Digit. Med.*, vol. 1, no. 1, p. 39, 2018.
[41] K. T. Islam, S. Wijewickrema, and S. O'Leary, "Identifying diabetic retinopathy from OCT images using deep transfer learning with artificial neural networks," in *2019 IEEE 32nd International Symposium on Computer-Based Medical Systems (CBMS)*, Cordoba, Spain, 5–7 June 2019, pp. 281–286, doi: 10.1109/cbms.2019.00066.
[42] M. Heisler, et al., "Ensemble deep learning for diabetic retinopathy detection using optical coherence tomography angiography," *Transl. Vis. Sci. Technol.*, vol. 9, no. 2, pp. 20, 2020.
[43] D. Le, et al., "Transfer learning for automated OCTA detection of diabetic retinopathy," *Transl. Vis. Sci. Technol.*, vol. 9, no. 2, pp. 35, 2020.
[44] M. M. Abdelsalam, "Effective blood vessels reconstruction methodology for early detection and classification of diabetic retinopathy using OCTA images by artificial neural network," *Inform. Med. Unlocked*, vol. 20, pp. 100390, 2020.
[45] J. Cano, W. D. O'Neill, R. D. Penn, N. P. Blair, A. H. Kashani, C. L. Kaloostian, M. Shahidi, "Classification of advanced and early stages of diabetic retinopathy from non-diabetic subjects by an ordinary least squares modeling method applied to OCTA images," *Biomed. Opt. Express*, vol. 11, pp. 4666–4678, 2020.
[46] K. Kim, J. I. You, J. R. Park, E. S. Kim, W. Y. Oh, and S. Y. Yu, "Quantification of retinal microvascular parameters by severity of diabetic retinopathy using wide-field swept-source optical coherence tomography angiography," *Arbeitsphysiologie*, vol. 259, no. 8, pp. 2103–2111, 2021.
[47] G. Ryu, K. Lee, D. Park, S. H. Park, and M. Sagong, "A deep learning model for identifying diabetic retinopathy using optical coherence tomography angiography," *Sci. Rep.*, vol. 11, no. 1, pp. 23024, 2021.
[48] P. Zang, L. Gao, T. T. Hormel, J. Wang, Q. You, T. S. Hwang, Y. Jia, "DcardNet: Diabetic Retinopathy Classification at Multiple Levels Based on Structural and Angiographic Optical Coherence Tomography," *IEEE Trans. Biomed. Eng.*, vol. 68, pp. 1859–1870, 2021.
[49] C. H. Hua, et al., "Convolutional network with twofold feature augmentation for diabetic retinopathy recognition from multi-modal images," *IEEE J. Biomed. Health Inform.*, vol. 25, no. 7, pp. 2686–2697, Jul. 2021.doi: 10.1109/JBHI.2020.3041848.
[50] Q. Li, X. R. Zhu, G. M. Sun, L. Zhang, M. Zhu, T. Tian, C. Guo, S. Mazhar, J. K. Yang, and Y. Li, "Diagnosing diabetic retinopathy in OCTA images based on multilevel information fusion using a deep learning framework," *Comput. Math.Methods Med.*, vol. 2022, pp. 4316507, 2022.
[51] J. Hou, F. Xiao, J. Xu, Y. Zhang, H. Zou, and R. Feng, "Deep-OCTA: Ensemble deep learning approaches for diabetic retinopathy analysis on OCTA images," *arXiv: 2203.09713* [eess.IV], 2022.
[52] J. Lyu, Y. Zhang, Y. Huang, L. Lin, P. Cheng, and X. Tang, "AADG: Automatic augmentation for domain generalization on retinal image segmentation," *IEEE Trans. Med. Imaging*, vol. 41, no. 12, pp. 3699–3711, 2022.
[53] X. Yuan, et al., "Image enhancement of wide-field retinal optical coherence tomography angiography by super-resolution angiogram reconstruction generative adversarial network," *Biomed. Signal Process. Control*, vol. 78, pp. 103957, 2022.

[54] Q. Li, X. R. Zhu, G.-m. Sun, L. Zhang, M. Zhu, T. Tian, C. Guo, S. Mazhar, J. K. Yang, and Y. Li, "Diagnosing diabetic retinopathy in OCTA images based on multilevel information fusion using a deep learning framework," *Comput. Math.Methods Med.*, vol. 2022, pp. 4316507, 2022.

[55] Y. Zheng, F. Wu, and B. W. Papież, "An ensemble method to automatically grade diabetic retinopathy with optical coherence tomography angiography images," in *Mitosis Domain Generalization and Diabetic Retinopathy Analysis*, B. Sheng and M. Aubreville, Eds., vol. 13597, *Lecture Notes in Comput. Sci.*, Springer, pp. 198–210, 2023.

[56] F. Ma, S. Wang, C. Dai, F. Qi, and J. Meng, "A new retinal OCT-angiography diabetic retinopathy dataset for segmentation and DR grading," *J. Biophotonics*, vol. 16, no. 11, pp. e202300052, 2023.

[57] S. F. Rabbi, M. A. Mamun, M. F. Faruk, S. M. MahedyHasan, and A. Y. Srizon, "A multi-branch and attention based CNN architecture for the classification of retinal diseases from OCT images," in *2023 International Conference on Information and Communication Technology for Sustainable Development (ICICT4SD)*, Dhaka, Bangladesh, pp. 36–40, 2023.doi: 10.1109/ICICT4SD59951.2023.10303384.

[58] P. Matten, J. Scherer, T. Schlegl, et al., "Multiple instance learning based classification of diabetic retinopathy in weakly-labeledwidefield OCTA en face images," *Sci. Rep.*, vol. 13, pp. 8713, 2023.

[59] P. P. Hatode, and M. Edinburgh, "Optical coherence tomography angiography image classification and analysis of diabetic retinopathy, using Wasserstein generative adversarial network augmentation," *Int. J. Electr.Comput.Eng.*, vol. 14, no. 6, pp. 7046–7056, 2024.

[60] P. Bidwai, S. Gite, B. Pradhan, H. Gupta, and A. Alamri, "Harnessing deep learning for detection of diabetic retinopathy in geriatric group using optical coherence tomography angiography-OCTA: A promising approach," *MethodsX*, vol. 13, pp. 102910, 2024.

[61] P. L. Nesper, et al., "Quantifying microvascular abnormalities with increasing severity of diabetic retinopathy using optical coherence tomography angiography," *Invest. Ophthalmol. Vis. Sci.,* vol. 58, no. 6, pp. BIO307–BIO315, 2017.

[62] Y. Guo, A. Camino, J. Wang, D. Huang, T. S. Hwang, and Y. Jia, "MEDnet, a neural network for automated detection of avascular area in OCT angiography," *Biomed. Opt. Express*, vol. 9, no. 11, pp. 5147–5158, 2018.

[63] Y. Guo, et al., "Development and validation of a deep learning algorithm for distinguishing the nonperfusion area from signal reduction artifacts on OCT angiography," *Biomed. Opt. Express*, vol. 10, no. 7, pp. 3257–3268, 2019.

[64] D. Gildea, "The diagnostic value of optical coherence tomography angiography in diabetic retinopathy: a systematic review," *Int. Ophthalmol*., vol. 39, no. 10, pp. 2413–2433, 2019.

[65] M. Li, et al., "IPN-V2 and OCTA-500: Methodology and Dataset for Retinal Image Segmentation," 2020.

[66] Y. Ma, H. Hao, J. Xie, et al., "ROSE: a retinal OCT-angiography vessel segmentation dataset and new model," *IEEE Transactions on Medical Imaging,* vol. 40, no. 3, pp. 928–939, 2021.

[67] N. S.Keskar, and Socher R. "Improving generalization performance by switching from adam to sgd."arXiv preprint arXiv:1712.07628. 2017, Dec 20.

[68] M. Li, et al., "Image projection network: 3D to 2D image segmentation in OCTA images," *IEEE Trans. Med. Imaging*, vol. 39, no. 11, pp. 3343–3354, 2020.

[69] "Optical Coherence Tomography Angiography retinal scans and segmentations." *University of Edinburgh.Medical School,* 20-Dec-2019.

[70] "ROSE1&2," Nimte.ac.cn.[Online].Available: https://imed.nimte.ac.cn/dataofrose.html.[Accessed: 28-Sep-2022].

[71] J. Chaki, S. Thillai Ganesh, S. K. Cidham, and S. AnandaTheertan, ''Machine learning and artificial intelligence based Diabetes Mellitus detection and self-management: A systematic review," *J. King Saud Univ. - Comput. Inf. Sci.,* no. xxxx, 2020. 10.1016/j.jksuci.2020.06.013.

[72] T.Bek, "Fine structure in diabetic retinopathy lesions as observed by adaptive optics imaging,"*A qualitative study. ActaOphthalmol.*,vol. 92, no. 8, pp. 753–758,2014.

[73] M. Kouroupis, N. Korfiatis, and J. Cornford, "Artificial intelligence À assisted detection of diabetic retinopathy on digital fundus images: concepts and applications in the National Health Service," Elsevier Inc., 2020.

[74] K. Ghosh, and B. C. Capell,"The senescence-associated secretory phenotype: critical effector in skin cancer and aging,"*J. Invest. Dermatol.,*vol. 136, no. 11, pp. 2133–2139,2016.

[75] S. Joshi, and P. T. Karule, ''Biomedicine & Pharmacotherapy A review on exudates detection methods for diabetic retinopathy," *Biomed.Pharmacother.,* vol. 97, no. October 2017, pp. 1454–1460, 2018. 10.1016/j.biopha.2017.11.009.

[76] D. T.Hogarty, D. A.Mackey, and A. W.Hewitt, "Current state and future prospects of artificial intelligence in ophthalmology: A review,"*Clin. Exp. Ophthalmol*.,vol. 47, no. 1, pp. 128–139,2019.

[77] K. C.Jordan, M.Menolotto, N. M. Bolster, I.A. T.Livingstone, and M. E.Giardini, "A review of feature-based retinal image analysis,"*Expert Rev. Ophthalmol*.,vol. 12, no. 3, pp. 207–220,2017.

[78] P.A. Pattanaik, and T. Swarnkar, ''Vision-based malaria parasite image analysis: a systematic review,"*International Journal of Bioinformatics Research and Applications*, vol. 15, no. 1, pp.1-32, 2019. doi.org/10.1504/IJBRA.2019.097987

[79] P. A.Pattanaik, Z.Wang, andP.Horain, "Deep CNN frameworks comparison for malaria diagnosis,"2019.arXiv preprint arXiv:1909.02829.

[80] S. Mascarenhas, and M. Agarwal, "A comparison between VGG16, VGG19 and ResNet50 architecture frameworks for Image Classification," *in 2021 International Conference on Disruptive Technologies for Multi-Disciplinary Research and Applications (CENTCON),* 2021.

[81] X. Li, X. Wen, X. Shang, J. Liu, L. Zhang, Y. Cui, X. Luo, G. Zhang, J. Xie, T. Huang, Z. Chen, Z. Lyu, X. Wu, Y. Lan, and Q. Meng, “Identification of diabetic retinopathy classification using machine learning algorithms on clinical data and optical coherence tomography angiography,” *Eye (London, England),*vol. 38, no. 14, pp. 2813–2821, 2024.

[82] Y. Guo, T. T. Hormel, M. Gao, Q. You, J. Wang, C. J. Flaxel, S. T. Bailey, T. S. Hwang, and Y. Jia,“Multi-Plexus Nonperfusion Area Segmentation in Widefield OCT Angiography Using a Deep Convolutional Neural Network,” *Translational vision science & technology*, vol. 13, no. 7, pp. 15,2024.

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