



Machine Learning Algorithm Comparison for Four-Class Retinal Disease Classification Using Digital Fundus Images

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Abstract

Retinal diseases lead to the loss of vision and are a significant burden to health, and a timely and accurate diagnosis should be conducted to maximize treatment and clinical outcome. The research has been applied in the holistic examination of various eye health diseases such as cataracts, glaucoma and retinary aberrations which are separated into normal eye related cases and artificial networks. Using a large set of retinal images, the study conducts a thorough quantitative analysis of both complicated models like CNN, K-NN, and SVM in the form of parameters of accuracy, sensitivity, specificity, and F-Score. The CNN model had a better performance with a fantastic overall accuracy 94.05% and good sensitivity in classifying pathological states. It can be proven by the comparative analysis that CNN architecture is an effectual diagnostic instrument in the sphere of ophthalmology and demonstrates tremendous prospects in the replication of ophthalmology screening screening with the help of ophthalmology automation. This timely and vast assessment of the machine learning methods contributes a lot to the literature not only in terms of establishing relative lines between different technological solutions but also in helping style the advanced technological solutions to carry out screening to help the ophthalmologist make reliable diagnostic prescriptions.

Keywords: Retinal diseases; Machine learning; Convolutional neural networks; Eye disease classification; Diagnostic accuracy; Ophthalmology

1 Introduction

Introducing the combination of the latest imaging technologies and computing intelligence is the face of modern ophthalmology. The discovery of high-resolution OCT and adaptive optics in practices in the field of ophthalmology, and the application of more sophisticated computer techniques that currently define the existence of a retinal illness in novel respects, have passed the field a significant twist change of early intervention tactics in ophthalmology, indeed overtaking the field altogether [1]. The underlying technological change is a paradigm shift in how we examine diseases (traditional - subjective clinical evaluation, modern - objective/quantitative evaluation of retinal pathology). High-resolution optical coherence tomography (OCT)

has emerged as a versatile diagnostic technology through which, for the first time, cross-sectional definitions of the layers of the eye could be imagined in the retina with a margin of micrometers. Likewise, an adaptive optics technology has allowed image the living retina at a cellular level and finally clinicians can visualize single photoreceptors and some microscopic pathological changes, which could not have been seen by another imaging modality.

Raised retinal disease is a global public health problem whose diagnostic aspect has to be innovated. Age-related macular degeneration (occurring in 8.7% of all seniors) [2], diabetes-related retinopathy (observed in 22% of diabetes) [3], cataracts (the cause of half of all blindness globally) [4], glaucoma (causing blindness in 80 million of the population) [5] and many other optic eye diseases present significant issues with both human health and economic prosperity [6], [7]. These figures highlight the depth of visual loss across the globe with diabetic retinopathy itself impacting approximately 93 million people across the planet and one of the main causes of preventable blindness in the working adult population. Economics such as direct healthcare expenses are not only, but also, lost productivity, disability compensation as well as diminished quality of life of affected individuals and his or her family. It is further complicated by the reality that the global population is growing older with diseases that come with old age (that is grade age diseases like macular degeneration and glaucoma) becoming more common and causing importantly health care systems to strain and understanding that need some effective, scalable diagnostic solutions.

Good elements that can be used in salvaging sight, and preventing traditional damage that cannot be undone includes prompt diagnosis and intervention. Soon discovery of eye health issues most often allows the doctors to administer effective therapies that eliminate about 95 percent of the serious eye harm injuries avertable severities of the eye ailment [8]. It is quite an alarming statistic that shows the game-changing power of timely diagnosis in ophthalmology in which interventions like anti-VEGF injection on diabetic macular edema, laser photocoagulation in diabetic retinopathy, or in-game triggering of intraocular to cut the pressure in glaucoma carried a radical dissimilarity once the therapy has been activated at a hand early phase. Such an objective of detecting the disease at the early stages globally, however, is averted against the current healthcare system.

Certain significant drawbacks have been attributed to the conventional methods of diagnosis in order to provide sufficient treatment to the patients. However, the solutions that are available remain on the visual perusal of images, which may even be different among different users, as far as the viewer is concerned and are turning into an enormous pile of raw photos that are slowly accumulated and untabulated and are going to go to waste without any image content processing carried out upon them at all [9]. The implications of this case subjective interpretation are that there exists lack of objective consistency in the correctness of the diagnosis that inter-observer consistency rates tend to be below optimal levels, especially with small pathological variants or marginally-borderline cases. The dependence on the provenance of qualified explanation produces a bottleneck of the healthcare provision, particularly in the less privileged areas with a lower number of ophthalmologists. Moreover, the quantity of screening programs retinal images has grown exponentially which can no longer be served by the combined resources of human specialists with disclosures in the form of delays in diagnosis and the possible loss of a life-threatening case.

Artificial intelligence and machine learning can be drastically applied to diagnosing these issues. Artificial intelligence and machine learning allow 10,000 images of retina to be processed in less time than a human expert can process 100 images and because of this analysis is never wrong in the daytime or at night as well [10]. The dramatic processing rate coupled with the capacity to analyze either with or without fatigue regardless of the time is a leap of quantum bounds in the diagnostic possibilities. Diagnostic results in mass volumes of images are relatively uniform in AI systems, as the system can run 24 hours without human intervention, such as a competitor system diverting or subjectivity with incapacitation. Moreover, those systems may assist in standardizing the norms of diagnosing the condition in different medical settings, logisticalizing the dilemma of geographical disparity in the quality of services.

Machine learning approaches in the diagnosis of retinal disease have no longer progressed with primitive statistical algorithms, but with deep learning systems. Machine learning is being applied today with simplistic and sophisticated models in the determination of retinal disorders. Although support vectors machines perform

best in separating hyperplanes with numerous dimensions, k-nearest neighbors focus on finding nearest to determine a category- both are useful with smaller size reasoning [11]. It is these conventional machine based methods that have provided the foundation to an automated retinal analysis and indicated that an automated retinal image analysis method can be useful in distinguishing between normal and pathological retinal patterns. The use of support vector machines arises in questions where the training data are small and the boundaries between features are sharp and k-nearest neighbors is applied in cases where intuitive classification option using similarity related metrics and where the clinical reasoning disrupts are well characterized through these similarity related metrics.

Deep learning has transformed how retinal disease is diagnosed because the system can autonomously learn intricate features through the available uncooked photograph data. Nevertheless, the application of CNNs has redefined the profession by learning features in various levels, where the Inception-v3 recognizes 99% of diabetic retinopathy cases by identifying both microaneurysms and hard exudates, in any of the retina areas [12]. This capability of learning features hierarchically enables CNNs to identify subtle pathological patterns otherwise, which may not have been clearly spotted by humans, particularly at an early-stage disease, where differences in the disease are low. The architectural ability to process whole-image retina captures and target a number of pathological indicators are said to be a great advancement to the systems that have been tested to date (manual image feature extraction, trace lesion detection).

Neural networks that are an image-based CNN architectures have demonstrated greater output in identifying particular retinal finding than ever previously. It has been discovered that advanced model ResNet-152 is especially effective at identifying subtle limitations in glaucoma by studying the optic nerve, and the errors occur at no progression about 40 percent of the frequency compelled errors due to manual diagnosis tools [13]. Its own characteristics in acquiring highly complex mappings without degrading characteristics when very deep networks are used contributes to its particular usefulness in identifying the very subtle morphological changes to the optic nerve head and retinal nerve fiber layer that are the characteristics of glaucomatous damage. This increase in performance directly corresponds to the clinical dividend, and could forestall permanent vision loss due to an earlier and more precise diagnosis of disease progression.

Collective approaches, which are approaches that incorporate a combination of various AI approaches have been showing to be promising in multiple disease classification scenarios. The accuracy of detection of several diseases is raised to 98.6 percent by applying the structural OCT data and the color fundus classes with the combination of CNN features and random forest classifiers when the structural OCT data and color fundus biomarkers are applied together, respectively [14], [15]. This joint strategy integrates the strength of the deep-learning as an extraction of features, interpretability and strength of ensemble techniques to take final results on classification. The synthesis of both structural and functional multimodal imaging data provides a more fulsome analysis of the health of the retina that has been indicative of this comprehensive view of the experienced clinician.

The retinal pathology is complex, and it poses special difficulties to the automated diagnosis systems due to the diversity of showing different types of disorders. Several distinct eye conditions manifest in fundus images and that is why it is a confusing process. The symptoms of diabetic retinopathy are cotton-wool spots and intraretinal microvascular abnormalities whereas in glaucoma one has cup-to-disc ratio bowling and nerve fiber destruction [16]. All the retinal diseases possess characteristic morphology, which should be identified by certain detection algorithms and separated against the normal anatomic variations. There is a spectrum of changes that can occur in diabetic retinopathy in vascular malformations (microaneurysms, hemorrhages, etc.), and proliferative alterations (which can be non-obvious at first stages), and glaucomatous damage of the retinal nerve fiber layer has a characteristic structure (retinal nerve fibers) and the head of the optic nerve.

The complexity of information in these medical images is confirmed by the computational needs of an image analysis in the retinal. Cataracts blur the lens and AMD introduces deposits and regions of thinning thus the model will need to scan over 1.2 million pixels in order to extract the difference between them respectively [17]. This analysis need is computer intensive at pixel level, showing the overall demands in the retina analysis algorithms of discriminating against a high number of possible pathological patterns, as compared to taking

normal anatomical variations, image quality variations and potential artifacts. The large dimensionality of such data makes it necessary to apply sophisticated feature extraction and feature selection procedures in making decisions on what information is most diagnostically important, yet at the same time allows verification of computational feasibility.

The ability to aggregate a variety of data and remote surveillance has increased the potential of the AI algorithm regarding their utilization in retinal care. The available information regarding the telemetry data provide additional information [18]. The patient self-reported retinal health and the constant monitoring data bring out a broader picture of the retinal health compared to what the traditional imaging and snapshot evaluations fortify. This solid integration of data deciphers more sophisticated predictive models, and can be used to delineate the phenomena of illness, response to treatment, lifestyle factors that influence the outcome of retinal fitness.

Mobile health technologies have made access to retinal screening more democratic particularly in underserved people. As a result of these developments, the telemedicine systems based on mobile phones equipped with cameras powered by ML are now able to identify 94 percent of the diseases that warrant a screening at the rural locations during screenings [19]. This innovation would address serious health inequalities because it is possible to apply the advanced diagnostic potential in distant and resource-accompanied areas, where conventional ophthalmology-based services are unattainable. Combining this universal mobile technology and the cloud-based AI processing potential, this has ensured that scalable solutions can be offered to the population of the world and that ultimately the use of worldwide based eye care can possibly be revolutionized.

Availability and quality of training datasets are the defining aspect of the success of AI applications in retinal diagnosis. They require the availability of data and, in the experiment, the 40,000-image collection of Kaggle using SMOTE oversampling was used to avoid bias toward any disease [20], [21]. Training of powerful AI models necessitates large-scale, curated datasets, capable of generalizing to a general population of patients and imaging conditions. The problem of class imbalance, which interferes in the implementation of the majority of medical research studies, is overcome by the use of highly developed methods of data augmentation like synthetic minority oversampling [22].

Advanced image processing and data augmentation methods have found significant value in gaining the best model performance in a range of imaging conditions. Due to such datasets, one can customize the features of the ImageNet-trained models on retinal images. This reduces the level of training required by 80 percent without suffering any loss in accuracy at 96%. The difficulties of capturing the images of various cameras have been tackled through data processing techniques (rotation, gamma correction and vessel segmentation masking) as was shown by an example of a 15 percent more accurate outcome of a test [23], [24].

In clinical AI diagnostic tools require a careful adoption with the current healthcare workflow, and attention to human-AI modes of co-working. Through the application of ML in the clinical situation, the collaboration between the various abilities of individuals and computers can occur. A hospital trial was capable of reducing specialized focus on urgent cases by 62 percent when diagnostics applying the ML risk scores ranked in the first stage and heatmap suggested a medical fidelity in the AI suggestion by 41 percent of the cases [25].

2 Literature Review

The introduction of artificial intelligence (AI) into the medical health system has led to the revolution in the diagnostic processes, in particular, the faster and more precise process of disease recognition. In the ophthalmic specialty, the identification of ocular diseases has implemented several machine learning algorithms and deep learning techniques to identify the type of ocular diseases, such as glaucoma or diabetic retinopathy and

age-related macular degeneration. However, there exist the issues, which are the harmonisation, quality and validity of data against various populations and diseases. The foregoing studies underscore the saliency of an accurate data gathering, accurate feature extraction, and efficient machine learning steps in developing diagnostic boundaries and achieving a workable machine vision-based automated screening framework. The authors present the discussion on various milestones in the application of AI in screening ocular diseases in the literature review of this article in light of models that utilize structured health conditions and the strategies of best machine learning. These advancements mean that such advantages of the artificial intelligence as crossloading a healthcare professional and easing the works of patients in terms of their timely and correct diagnosis are present.

The rise of advanced deep learning models has seen great advances in automated retinal disease detectors, where focused attention as a diagnostic approach has been a potent way of increasing classification accuracy. To determine the possible potential of AI-assisted diagnosis, a new deep learning algorithm, called WaveAttention ResNet (WARN), was created that specialises in classifying seven common retinal diseases. This network, developed on ResNet18, will with the modules of Convolutional Block Attention Module (CBAM) and wavelet convolution modules, as illustrated by He et al. will contribute to better classification of retinal disease and serves to reveal the way to develop higher-quality diagnostic tools in ophthalmology, as mentioned by [26]. The WARN architecture is somewhat of a leap in this direction, as it adds to residual learning properties of ResNet18, more advanced attention mechanisms with which the model selects the best attention properties in the retinal images, which are diagnostically relevant to them. CBAM can be used to integrate the network to dynamically correct responses to features by modelling explicitly the relationship between channels and spatial locations and suppressing inconsequential background information, which in effect focuses on pathological regions. Moreover, with the added capability of wavelet convolution modules, feature extraction on multi-scale is offered, highly useful in tracking and identifying pathological variations at a variety of frequencies, between fine microaneurysms and wide hemorrhages and exudates. This comprehensive feature learning framework allows WARN to be able to generate a high level of classification tasks in a wide range of retinal pathologies, a new paradigm in Diagnostic System through attention based feature learning in ophthalmology.

The high prevalence of retinal diseases suggests that diagnostic solutions requiring automation and scalability are essential to deliver high-quality services in a wide range of healthcare facilities and to a wide range of patients. Retinal diseases are a significant health challenge in the world and often cause a considerable loss of vision and blindness which consequently causes severe functional and social limitations. According to the results of [27], the convolutional neural network (CNN) such as MobileNet and DenseNet121 have high accuracy and area under the curve (AUC) as sophisticated models can automatically detect and classify these diseases; they provide strong potential to help healthcare professionals with instant and precise diagnosing of most retinal diseases due to their high accuracy and area under the curve (AUC). It is especially relevant to the success of MobileNet-based architectures in that regard since they can be represented by computational efficiency and can be deployed in resource-constrained environments which allows advanced diagnostic capabilities in low-resource setting where a specific ophthalmological knowledge base might or might not be available. The outstanding performance of the DenseNet121 can be attributed to the dense connectivity pattern that facilitates reuse of features, along with propagation of features to all the layers hence allowing the learning of intricate pathological patterns with the compactness of parameter efficiency. The elevated values of AUC produced by these models imply strong discriminative inclination on the whole clinical decision threshold, and hence they state their potential as use in clinics where sensitivity and specificity matters are important in patient safety and treatment maximization.

Inherited retinal diseases can pose challenging diagnostic challenges because of genetic heterogeneity, with their phenotypic expression that is vulnerable to vary depending on patient characteristics and necessitates a complex technique of imaging and calculations to make the correct diagnosis. DL models have the potential to identify inherited retinal diseases (IRDs) such as retinitis pigmentosa (RP) and Stargardt disease (STGD) and differentiate them in healthy eyes. A multi-input MobileNetV2 network, with color fundus photography and infrared images is more accurately diagnosed (96.3%) than a single-input network when relying on the two imaging modalities separately, according to the view of [28], and it is suggested that an improvement in diagnostic accuracy is possible with multimodal deep learning methods. Multimodal approach remedies this weakness of single imaging modalities by using complementary information in another spectral range

and modality mode of imaging. The color fundus photography has an impressive ability to visualise the retinal vasculature, pigmentary alteration as well as structural alteration unique to the IRDs whereas infrared imaging has a better view of deeper retinal structures and capable of detecting subtle changes otherwise not seen in the ordinary color photography. The high performance of the multi-input architecture can show that medical imaging applications require the integration of data fusion, in which various imaging modalities may be involved in complementary diagnostic classification detail that can improve the overall classification performance.

Clinical significance of retinal diseases goes far beyond a mere visual acuity evaluation to include multifaceted interplay between functional deficiency, quality of life and socioeconomic attributes that patients require to be addressed in a holistic care approach. Retinal disorders such as age related macular degeneration (AMD), diabetic retinopathy, central serous chorioretinopathy (CSCR) and retinal vein occlusion can greatly jeopardize the well being of patients. In the study by [29] it was established that functional and structural implications of such conditions including vision loss and metamorphopsia modified significantly the day-to-day activities, psychological well-being and the overall quality of life associated with health. This underscores the importance of effective measures and management approaches that will reduce unfortunate effects of such retinal disorders on the sufferers. The study focuses on metamorphopsia as a form of visual distortions, which is rather crippling to affected patients, and the capacity to read, drive, and recognise faces, and do everyday activities of daily living. The most frequent psychological effects of the loss of vision are depression, anxiety, and social isolation, which leads to a domino of health effects beyond even the local ocular disease. The interpretation of these extended implications has become key in the development of AI-based diagnostic systems that not only can realize the best technical performance but also aid in timely and correct intervention and counseling to patients who face a high risk of severe functional and psychosocial impairments of untreated retinal disease.

This introduction of AI into the normal ophthalmological practice can only be done with strong and efficient algorithms that can quickly and reliably analyze a large amount of retinal images so reliably and faster than the diagnostic methods that existed in the past. Ophthalmologists greatly depend on retinal images in the diagnosis of a spectrum of eye diseases. The deep learning algorithms have proven to be widely developed after the efforts made by [30] can identify early disease and treat eye diseases based on retinal fundus data after which the disease may be treated successfully. According to the approach, deep learning models would be able to handle images quickly and would offer results in seconds, which would enable an immediate diagnosis of the problem and formulate a treatment plan. The efficiency of these systems based on rapid processing is especially useful in screening as well as providing a value in situations where masses of images need to be read and documented effectively to detect patients in need of urgent treatment or referral. The ability to see early is particularly important in the field of the conditions such as diabetic retinopathy and glaucoma where timely intervention holds the ability to stop the destructive effects of an eye condition. Immediate results and the possible reduced duration between imaging and the commencement of treatment weeks to minutes allow immediate clinical decisions. This is a state-of-the-art in ophthalmological practice that facilitates the active and adaptable approach to patients coupled with benefiting resources within the medical care system where the system is more in demand in order to detect retinal screening services.

When artificial intelligence devices in the medical sector are democratized, it will revolutionize the sector given that the medical professional who have little knowledge about the field of computer programming can develop and deploy advanced diagnostic software within their health centers. Code-free deep learning (CFDL) has already become one of the possible advances in the field of artificial intelligence which offers the new route to pursue in the construction of the models to be used. The findings [31] included a comparative study that found that code-free models, constructed by clinicians with no code expertise, were equivalent in accuracy to purpose-crafted models constructed by AI experts to assign retinal pathology to optical coherence tomography video and image samples; this suggests that someday, it is possible to democratize AI use in healthcare, although it is important to be cautious of its constraints. Such implication of the provided finding extends past the parameter of technical performance and to even a broader question of AI accessibility and clinical adoption. By CFDL publications closing the knowledge gap between programming and domain experts, these platforms enable domain experts, the clinicians who know the specifics of disease presentation and its diagnosis, to participate directly in the AI models development. Such a strategy may lead to more clinically realistic models closer to clinical workflow and real-life diagnostic issues. However, the democratization of AI development

also creates major challenges related to the validation of the models, adherence to regulations as well as quality assurance which are to be debated in order to provide safe and effective clinical implementation.

The quantitative analysis of retinal structure in inherited retinal disease demands that segmentation is executed with great precision so as to delimit anatomical boundaries and manipulate tissue thickness at a level of clinical precision. In OCT imaging of a subject with a hereditary retinal disease (IRD) striking measurements of the outer nuclear layer (ONL) thickness is a validated perceiver of photoreceptor integrity in optical coherence tomography imaging. As the analysis performed by [32] demonstrates, the present-day automated speeded-up segmentation techniques cannot be applied to the segmentation of OCTs in IRDs, causing manually applied segmentation an intense and time-consuming procedure, thus necessitating a more efficient system. The ONL thickness dimension would be of paramount importance in the IRDs in that it offers direct quantitative measure of the cell survival of photoreceptors (as a diagnostic tool and an indicator of disease progression). During the manual segmentation of OCT images, time is used and the variability of inter- and intra-observers exists, restricting the reproducibility and scalability of quantitative analysis. The lack of automated techniques in IRD studies is probably due to the distortion of the architecture of the retina and abnormal morphological patterns, which are being witnessed in the case of the disease, which is not similar with that of this retina in training normal algorithms of segmentation. The given limitation emphasizes the necessity of the specific AI methods adapting to the peculiarities of the morphological specifics of inherited retinal disease and preserving the level of accuracy needed in clinical monitoring and research.

In retinal diseases, the development of precision medicine necessitates novel mechanisms that aim at converting the role of artificial intelligence and clinical decision- making to develop maximizing treatment plans aligned with the specific patients. The work by Zhao and colleagues is also mentioned in the present issue of *Cell Reports Medicine*. According to [33] where Zhao and colleagues share their work, the area of medical research that they consider in the given case of the journal is certain, and the clarifications assumed their place in the general knowledge of the field. Their findings that are described in *Cell Reports Medicine* have a significant value to both the researchers and clinicians wishing to be aware of the developments in the field being discussed. Publication in the superlative journal implies the increasing awareness of AI uses in retinal medicine in the general medicine research world. The publication is probably about some of the fundamental problems in the context of these studies relating AI work findings in a laboratory to clinical practice, which may involve the generalizability of models used in the laboratory, approaches to clinical testing of the models, and integration of these research models with existing clinical practice. The study can be regarded as a contribution to the evidence base of AI in ophthalmology and a valuable contribution to researchers building a new AI version and clinicians who might want to incorporate AI in their practice.

The shift to automated over manual images analysis will be a paradigm shift in how ophthalmology has historically been practiced and some sense of hope exists whereby the image consistency, practicability and accuracy of diagnosis will be enhanced as a shift is made against today rising levels of images and lack of sufficient specialists. Optical coherence tomography (OCT) has emerged an inseparable part of ophthalmology, as it provides high resolution images of the retina with transverse cross-sectional scans to assist in the detection of various retinal diseases. As seen in the study by [34] manual analysis of OCT images has serious limitations because it is a time-consuming method, and the procedure depends on expertise of a person who analyzes the findings subjectively. This means that automated and objective image analysis methods become increasingly required and machine learning (ML) approaches are demonstrating potential in this area. Subjectivity of manual OCT interpretation is a source of variability, potentially impacting the intra-rater consistency in diagnosis, especially of subtle disease-signs or poor quality images. The manual analysis has time-consuming constraints that place bottlenecks on clinical processes, which may result in a delay in the initiation of diagnosis and treatment. The effort to use machine learning presents the promise of standardized analysis, which is reproducible and can run consistently, independent of the physical fatigue and experience level or a time limit of the analyst.

Transfer learning methods applied to the retinal disease classification problem can be regarded as a significant advance in using pre-trained models in medical imaging problems, even where the training data is limited or there are skewed distributions. Retinal diseases that in most cases are insidious in development have emerged to be the biggest areas of concern in the ongoing concerns of many regarding health and in some cases the effect of

this sickness might extend to blindness. This kind of diagnosis is very fundamental in detecting such conditions early and accurately as achieved in the research that was carried out by [35]. It examines the transfer learning with pre-trained Convolutional Neural Networks (CNNs)- VGG16, DenseNet201, InceptionV3, Xception - to classify seven different retina diseases in Optical Coherence Tomography (OCT) images and implement methods of Bayesian optimization and Image augmentation to further improve model performance. The selection of these specific architectures reflects the variety of CNNs architectures and specific strength: deep, uniform architecture in VGG16; efficient feature reuse in dense connections in DenseNet201; multi-scale feature extraction in InceptionV3; depthwise separable convolutions in Xception for computational efficiency. Hyperparameter tuning via the application of Bayesian optimization is an advanced form of model optimization and may be applied to the hyperparameter space in order to search the space systematically in search of the optimal configuration. Particularly in the medical imaging domain, image augmentation methods are notably valuable since limited data availability is prevalent in this setting, and can help ensure that models are more generalizable and less prone to overfitting while still being clinically relevant.

Anomaly detection approaches are unique in their ability to provide advantages in medical imaging applications where rare diseases or atypical presentations may not be adequately represented within training datasets and provide complementary diagnostic capabilities to traditional methods of supervised classification. Anomaly detection methods provide a promising direction to explore retinal diagnoses in the field of artificial intelligence, especially for the cases where it is not possible to obtain sufficient training data for all diseases of the retina and related variations in presentation. As reported by [36], anomaly detection methods were found to be useful in the discrimination of retinal images with and without referable diabetic retinopathy, even when the diagnostic system was only trained on nonreferable cases; this finding suggests the possible utility of anomaly detectors for broader screening of retinal diseases, identification of novel diseases, and detection of unusual manifestations of common retinal diseases. The success of anomaly detection in the context of this task illustrates the potential of unsupervised and semi-supervised approaches in medical imaging, where one can learn about "normal" from healthy examples without the need for extensive labeling of pathological cases. This type of approach is especially useful for rare diseases or novel pathologies where there may not be enough training examples to use for traditional supervised learning approaches. The ability to identify new diseases or unusual presentations has important consequences for the clinical practice where it may identify the occurrence of cases that might not be detected by the usual classification methods trained only with known pathology patterns.

The comparative evaluation of various CNN architectures for classifying retinal diseases offers valuable insights into the strengths and limitations of different deep learning approaches, serving as an information resource for evidence-based decisions regarding model choice for clinical use. Artificial intelligence (AI) diagnostic tools are becoming more and more common in ophthalmology. In the analysis offered by [37] one of the most promising fields of development of AI-based diagnostic platforms is the use of retinal images such as fundus photographs for the classification of retinal diseases. The study took advantage of three convolutional neural network models, namely ResNet50, VGG19, and Inception v3 to classify retinal images. The results showed that ResNet50 with an augmentation layer of 128 nodes achieved the prediction accuracy of 87.42% with nine classes including eight retinal diseases and normal controls; hence it could be used in medical diagnosis of retinal diseases. The superior performance of ResNet50 in this comparison can be attributed to its residual learning framework, which allows for training of very deep networks without suffering from the issues of degradation with the increased depth of these networks. The addition of a dense layer with 128 nodes allows for extra representational capacity in the final classification decision while retaining computational efficiency. The nine-class classification problem is a clinically relevant situation involving multiple retinal pathologies that provides evidence of the model's ability to distinguish between different disease states and a normal control. The level of accuracy achieved raises the prospect of clinical viability, although better validation in a range of patient groups and imaging conditions would be required for widespread clinical implementation.

Few-shot learning methods address key challenges in clinical AI where diseases with low frequencies and limited training data limit the development of robust diagnostic systems, providing innovative solutions in extending the power of AI to diseases that are under-represented. Deep learning techniques have proven useful for the diagnosis of ophthalmic diseases. As evidenced by Quellec et al. [38], a deep learning model using generative adversarial network (GAN) was successfully applied to optimize the optical coherence tomography (OCT) diagnosis of rare retinal diseases with the application of few-shot learning (FSL) that

has successfully augmented limited datasets of rare conditions with synthetically generated images in order to improve diagnostic accuracy, which potentially reduce delay in diagnosis and patient burden. The use of GANs in the generation of synthetic images for medical purposes is a sophisticated way of achieving data augmentation that can be used to create realistic examples of pathology, while maintaining the statistical properties of the original dataset. Few-shot learning techniques are especially useful in ophthalmology where rare diseases may affect very small patient populations and so it is hard to obtain enough training data to use in traditional supervised learning methods. The combination of GAN-based data augmentation and FSL form a powerful framework for extending the capabilities of AI to rare pathological conditions, which could democratize the access to expert-level diagnostic capabilities for the conditions that might otherwise be misdiagnosed or with significant delay due to their rarity and complexity.

The creation of intelligent systems capable of making diagnostics based on medical imaging, in light of the challenges inherent in the field such as the variation of image quality and the meaning that the image must have in order to be interpreted, is a key step towards the viability of AI-based solutions in the clinical field. Diabetic macular edema (DME) is one of the key areas of research in medicine worldwide. Based on the findings of [39] a novel diagnostic model with self-enhancement capabilities and clinical triage functionalities solves problems caused by the increasing volume of optical coherence tomography (OCT) images that have to be analyzed, the fuzziness of medical images, and the limitations of traditional algorithms for dealing with low-quality data and for providing interpretable results. The self-enhancement capabilities are likely to feature adaptive preprocessing techniques that can automatically adjust to variations in image quality, contrast, and acquisition parameters, ensuring robust performance regardless of the imaging conditions and equipment. Clinical triage functionalities are an important step toward practical deployment in the field of clinical use as it allows for automatic prioritization of cases according to their urgency and severity, which may help in reducing the workload on human specialists while ensuring that critical cases are given higher priority. The capability to deal with fuzzy or low-quality medical images covers a typical real-world problem where suboptimal imaging conditions or patient factors may affect the quality of images, and so we need robust algorithms that can extract meaningful diagnostic information under technical limitations.

Table 1 gives a comparative analysis of the latest research uses of machine learning and deep learning techniques for the detection and diagnosis of retinal diseases. The table summarizes some studies in this area and indicates the principal focus of the study, methodology employed and some of the findings reported by the authors of the study.

Table 1: Machine and Deep Learning for Retinal Disease Diagnosis: A Comparative Analysis.

No.	Main Focus	Methodology	Key Findings
Ref [26]	Auxiliary diagnosis of multiple retinal diseases.	Deep learning using WaveAttention ResNet (WARN) based on ResNet18 with CBAM.	Investigated the classification accuracy for seven common retinal diseases.
Ref [27]	Automated detection and classification of retinal diseases in Ghana.	Comparative study of state-of-the-art convolutional neural network (CNN) models.	Compared performance of CNN models for retinal disease classification using optical coherence tomography.
Ref [28]	Diagnosis of inherited retinal diseases (IRDs).	Multi-input deep learning model for detecting retinitis pigmentosa (RP) and Stargardt disease (STGD).	Evaluated the performance of DL model in differentiating RP and STGD from healthy eyes.
Ref [29]	Advances in imaging-based machine learning in retinal diseases management.	Review of machine learning applications and therapeutic technology for retinal conditions.	Overview of management of diseases like AMD, diabetic retinopathy using imaging and ML.

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No.	Main Focus	Methodology	Key Findings
Ref [30]	Early detection of multi-retinal diseases.	Deep learning algorithms for retinal fundus images.	Facilitated quick diagnosis and treatment planning using deep learning models.
Ref [31]	Comparing code-free deep learning (CFDL) to expert-designed models for retinal diseases.	Comparison of CFDL models vs bespoke models for detecting retinal pathologies from OCT.	Direct comparison of the discriminative performance of CFDL models.
Ref [32]	Retinal layer segmentation in OCT scans of patients with inherited retinal diseases (IRDs).	Deep Learning-based retinal layer segmentation.	Addressed challenges in automatic OCT segmentation for IRDs by improving the measurement of the ONL.
Ref [33]	Guiding laser therapy in ischemic retinal diseases.	Deep learning for precision medicine.	Precision medicine to guide laser therapy in ischemic retinal diseases.
Ref [34]	Clinical interpretation of retinal diseases using OCT images.	Machine learning applied to OCT image analysis.	Focused on using machine learning to improve manual analysis of OCT images.
Ref [35]	Diagnosis of retinal diseases using OCT images.	Bayesian Optimization Deep Learning Network.	Examined automated approaches to detect retinal diseases more precisely.
Ref [36]	Detecting anomalies in retinal diseases.	Generative, Discriminative, and Self-supervised Deep Learning.	Developed anomaly detectors for retinal diagnoses in AI systems.
Ref [37]	Diagnostic tool for various retinal diseases.	Fundus Image-Based Deep Learning.	Explored the development of AI-based diagnostic platforms using retinal fundus images.
Ref [38]	Improve deep learning in OCT diagnosis of rare retinal diseases.	Few-shot learning (FSL) using a generative adversarial network (GAN).	Showed that FSL can improve the applicability of DL in OCT diagnosis of rare diseases.
Ref [39]	Identifying Diabetic Macular Edema and Other Retinal Diseases.	Multiscale Deep Learning using Optical Coherence Tomography.	Used deep learning to analyze OCT images for retinal disease diagnosis.

In summary, artificial intelligence in ocular diagnostics has numerous potential. It offers significant potential to establish precise, fully automated ocular diagnostics care systems that help healthcare providers control eye diseases more effectively. Random forests, decision trees, and convolutional neural network algorithms have been identified as helpful in handling complex and large datasets and making new early disease diagnostic and tailored treatment methods. Even so, some of the challenges still apparent include standardization and the requirement for large, high-quality datasets. However, with developing technologies in artificial intelligence for diagnosing eye conditions, there is a potential for efficient, effective, immediate examinations of vision problems in any part of the world, especially in areas where there are no specialists to reach. Subsequent studies and advancements in the approaches used in artificial intelligence will be required in order to bring the full potential of these systems to bear on improving the eye health of the global community and reducing avoidable blindness.

3 Materials and Methods

3.1 Dataset

The retina dataset applied in this study is obtained from Kaggle, available at www.kaggle.com/code/ragilhadip/eye-disease-classification-with-grey-level-co-occu/data. It includes images grouped into four main categories: Normal Retina, Cataract, Glaucoma and other Retinal Diseases. Every SI image corresponds to certain visual features regarding the individually related eye conditions, and these differences are used for model training and testing. The wide variability in this dataset allows the models to differentiate between a healthy eye and an eye with the most prevalent ophthalmic diseases to strive for high levels of accuracy in each category.

Figure 1 shows the normal appearance of the retina, and the various deviations from this ideal state will be seen as pathologies in ocular health. This normal figure is employed for the purpose of comparing structures devoid of any perceptible developmental deformities or physical irregularities in a given disease or ailment, to those that are portrayed henceforth in subsequent figures. This figure is helpful in highlighting deviations that are characteristic of particular diseases of the retina, when the reader is offered a clear example of the state of the healthy retina.



Figure 1: Image of a Healthy Retina

Figure 2 shows the eye diagnosed with cataract disease. Cataracts are medical conditions in which the lens in the human eye becomes cloudy, which affects the clarity of vision. In this figure, the cloudy or opaque areas typical of cataracts are illustrated; these formations hinder the passage of light, interfering with vision. This depiction assists in analyzing the extent of pathology of cataract disease as compared to other eye diseases.

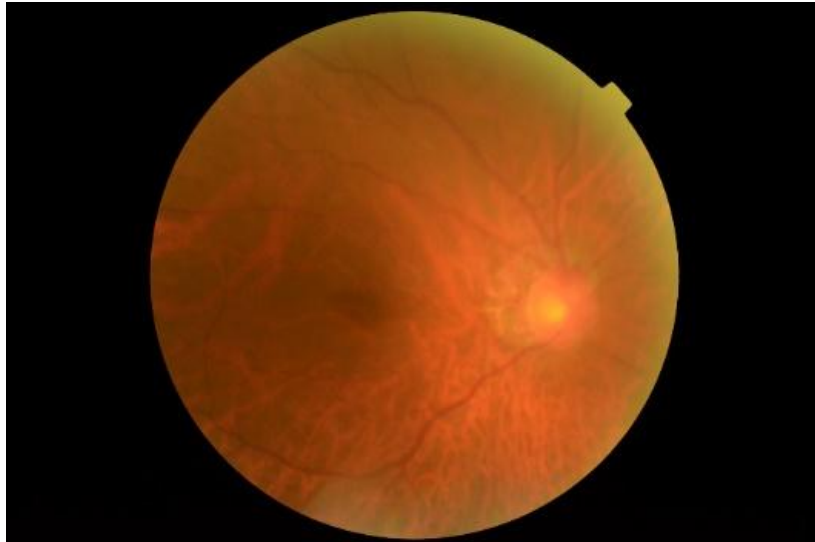


Figure 2: Cataract Disease

Figure 3 represents the retina of an eye with glaucoma, a disease characterized by high intraocular pressure (IOP). This figure illustrates optic nerve damage along with easily discerned morphological alterations that result in vision impairment. This visual aids in distinguishing glaucoma from other forms of retinal disease and helps in case identification and differentiation.



Figure 3: Glaucoma Disease

Figure 4 illustrates an image of the retina affected by retinal disease. This image shows various pathological features that may manifest in different retinal disorders, encompassing alterations in the retinal architecture, hue, or texture. This figure aids in classifying retinal diseases based on observable characteristics.



Figure 4: Retinal Disease

3.2 Convolutional Neural Network

Convolutional Neural Networks (CNNs) are one of such specialized types of deep neural networks and have revolutionized computer vision as well as the analysis of medical images. Initial neural networks, CNNs, were modeled after the hierarchical component organization of the mammalian visual cortex by way of mathematical convolution operations to acquire spatial hierarchies of features automatically given input images. When carried out within the framework of retinal disease classification, CNNs have prove particularly useful in detecting some subliminal pathological features that can only be seen by humans with great difficulty, which is why they are particularly useful in the context of early disease detection and automated screening systems.

The strong formation of the CNNs is that, they translate images using the same set of shared parameters that are learnable by both spatial locations. Instead of engaging in the manual feature engineering process as would be done under conventional machine learning methods, the CNNs attempt to uncover relevant features automatically in the learning of hierarchical representations. The quality is especially beneficial to medical imaging use where layout of pathologies can differ in position, size, and direction of the retinal image.

3.2.1 Mathematical Foundation

The core operation in CNNs is the discrete convolution, mathematically expressed as:

$$(I * K)(i, j) = \sum_m \sum_n I(i - m, j - n) \cdot K(m, n) \quad (1)$$

where I represents the input image, K denotes the convolution kernel (filter), and (i, j) are spatial coordinates. In practice, CNNs implement cross-correlation rather than true convolution:

$$(I \star K)(i, j) = \sum_m \sum_n I(i + m, j + n) \cdot K(m, n) \quad (2)$$

For multi-channel inputs common in medical imaging, the convolution operation extends to:

$$Y_{i,j}^{(k)} = \sigma \left(\sum_{c=0}^{C-1} \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} X_{i+m,j+n}^{(c)} \cdot W_{m,n,c}^{(k)} + b^{(k)} \right) \quad (3)$$

where $Y^{(k)}$ is the k -th output feature map, $X^{(c)}$ is the c -th input channel, $W^{(k)}$ represents the learnable filter weights, $b^{(k)}$ is the bias term, and σ denotes the activation function.

3.2.2 Architecture Components

Convolutional Layers Convolutional layers form the backbone of CNN architectures, applying learnable filters to extract local features from input images. Each filter detects specific patterns such as edges, textures, or more complex structures in deeper layers. The output feature map dimensions are determined by:

$$O = \frac{I + 2P - K}{S} + 1 \quad (4)$$

where O is the output size, I is the input size, P is padding, K is the kernel size, and S is the stride.

In retinal image analysis, early convolutional layers typically detect low-level features such as blood vessel edges, optic disc boundaries, and textural variations. Deeper layers combine these primitive features to identify complex pathological patterns specific to different retinal diseases.

Pooling Operations Pooling layers provide spatial down-sampling and translation invariance while reducing computational complexity. The max pooling operation is defined as:

$$y_{i,j} = \max_{(m,n) \in R_{i,j}} x_{m,n} \quad (5)$$

where $R_{i,j}$ represents the pooling region. Average pooling computes:

$$y_{i,j} = \frac{1}{|R_{i,j}|} \sum_{(m,n) \in R_{i,j}} x_{m,n} \quad (6)$$

Recent architectures have explored alternatives to traditional pooling, including global average pooling and learnable pooling methods that maintain more spatial information crucial for precise localization of pathological features.

Activation Functions The Rectified Linear Unit (ReLU) activation function, defined as $f(x) = \max(0, x)$, has become the standard nonlinearity in CNN architectures due to its computational efficiency and ability to mitigate the vanishing gradient problem. Advanced variants include:

- **Leaky ReLU (LReLU):**

$$f(x) = \max(\alpha x, x)$$

where α is a small positive constant (typically $\alpha \in [0.01, 0.1]$) that allows a small, non-zero gradient when $x < 0$, mitigating the “dying ReLU” problem.

- **Parametric ReLU (PReLU):**

$$f(x) = \max(\alpha_i x, x)$$

where the parameter α_i is learnable and can vary across different channels or layers, offering adaptive control over the slope of the negative input region.

- **Swish:**

$$f(x) = x \cdot \sigma(\beta x) = \frac{x}{1 + e^{-\beta x}}$$

where $\sigma(\cdot)$ is the logistic sigmoid function and β is either a fixed constant or a learnable parameter. Swish is smooth, non-monotonic, and has been shown to improve optimization and generalization performance in deep networks.

3.2.3 Advanced Architectural Innovations

Modern CNN architectures incorporate sophisticated design principles that enhance performance for medical imaging tasks:

Residual Connections Residual networks (ResNets) introduce skip connections that enable training of very deep networks:

$$y = F(x, \{W_i\}) + x \quad (7)$$

where $F(x, \{W_i\})$ represents the residual function. This architecture facilitates gradient flow and enables networks to learn identity mappings, crucial for capturing fine-grained details in retinal pathology.

Attention Mechanisms Attention modules allow networks to focus on diagnostically relevant regions:

$$\text{Attention}(Q, K, V) = \text{softmax}\left(\frac{QK^T}{\sqrt{d_k}}\right) V \quad (8)$$

where Q , K , and V represent query, key, and value matrices respectively. In retinal imaging, attention mechanisms can highlight pathological regions such as microaneurysms, hemorrhages, or optic nerve abnormalities.

Dense Connections DenseNet architectures connect each layer to all subsequent layers:

$$x_\ell = H_\ell([x_0, x_1, \dots, x_{\ell-1}]) \quad (9)$$

This design promotes feature reuse and reduces the number of parameters while maintaining representational capacity.

3.2.4 Medical Imaging Adaptations

CNNs for retinal disease classification require specific adaptations to address the unique characteristics of medical images:

Transfer Learning Pre-trained CNN models on large-scale datasets (e.g., ImageNet) are fine-tuned for retinal disease classification:

$$\theta_{medical} = \arg \min_{\theta} \mathcal{L}_{medical}(\theta) + \lambda \|\theta - \theta_{pretrained}\|^2 \quad (10)$$

where λ controls the regularization strength toward pre-trained weights.

Data Augmentation Medical image augmentation techniques include: - Geometric transformations: rotation, scaling, translation - Photometric adjustments: brightness, contrast, gamma correction - Domain-specific augmentations: vessel enhancement, optic disc centering

Class Imbalance Handling Medical datasets often exhibit class imbalance, addressed through: - Weighted loss functions: $\mathcal{L}_{weighted} = -\sum_i w_i y_i \log(\hat{y}_i)$ - Focal loss: $\mathcal{L}_{focal} = -\alpha_t (1 - p_t)^\gamma \log(p_t)$ - Synthetic minority oversampling techniques (SMOTE)

3.2.5 Regularization and Optimization

Effective training of CNNs for medical applications requires careful regularization:

Dropout Dropout randomly sets a fraction of input units to zero during training:

$$r_i \sim \text{Bernoulli}(p), \quad \tilde{y}_i = r_i \cdot y_i \quad (11)$$

where p is the dropout probability.

Batch Normalization Batch normalization normalizes inputs to each layer:

$$\hat{x}_i = \frac{x_i - \mu_B}{\sqrt{\sigma_B^2 + \epsilon}}, \quad y_i = \gamma \hat{x}_i + \beta \quad (12)$$

where μ_B and σ_B^2 are batch statistics, and γ, β are learnable parameters.

Weight Decay L2 regularization penalizes large weights:

$$\mathcal{L}_{total} = \mathcal{L}_{original} + \lambda \sum_i w_i^2 \quad (13)$$

3.2.6 Performance Considerations

CNN deployment in clinical settings requires consideration of computational efficiency and interpretability:

Model Compression Techniques for reducing model size include: - Pruning: removing redundant connections - Quantization: reducing numerical precision - Knowledge distillation: training smaller models to mimic larger ones

The integration of these advanced techniques enables CNNs to achieve state-of-the-art performance in retinal disease classification while maintaining clinical relevance and interpretability. The hierarchical feature learning capability of CNNs, combined with domain-specific adaptations, makes them particularly suitable for automated retinal disease screening and diagnostic assistance systems.

4 Results

This study explores the classification of various eye diseases using machine learning models, focusing on categorizing retinal images into four distinct groups: normal, cataract, glaucoma, and overall diseases of the retina. It plans to analyze all the inputs by employing the available machine learning approaches and analyze the effectiveness and the possibility of determining these conditions from retinal images. Toward this end, such an analysis is relevant in helping with the identification of early signs for referral to the attention of ophthalmologists and might be useful in aiding the clinicians in their decision-making process.

4.1 Machine Learning Results

Table 2 highlights the performance characteristics of several machine learning models applied for diagnosis of retinal diseases. The table presents metrics including accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F-measure. The CNN model shows the highest performance with an accuracy of 94.05%, while K-NN and SVM models exhibit lower sensitivity, indicating room for improvement in classifying positive cases.

Table 2: Machine Learning Models Results for Retina Diseases

Models	Accuracy	Sensitivity	Specificity	PPV	NPV	F-score
CNN	0.9405	0.9977	0.0178	0.9424	0.3333	0.9693
K-NN	0.9165	0.5310	0.9423	0.3820	0.9677	0.4444
SVM	0.8946	0.5310	0.9259	0.3820	0.9582	0.4444

Figure 5 displays the performance metrics of the machine learning models using mean values with error bars to indicate variation across different trials or datasets. Dashed frames represent standard deviation, providing confidence levels in these results.

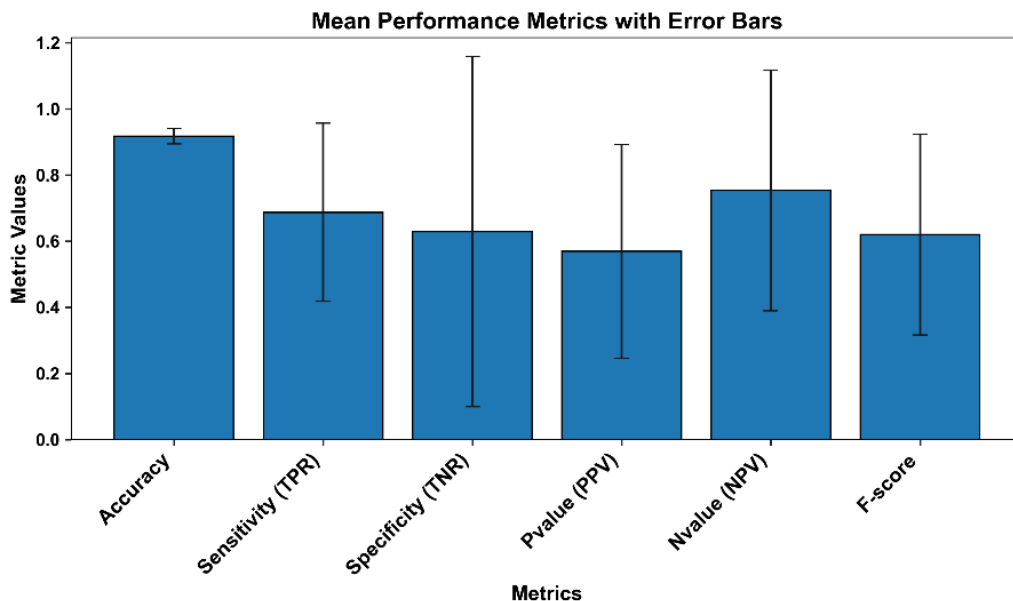


Figure 5: Mean Performance Metrics with Error Bars

Figure 6 presents a KDE plot showing the distribution of accuracy using Kernel Density Estimation. The KDE visualization offers a smoothed probability density function, allowing qualitative comparisons of performance peaks and model reliability.

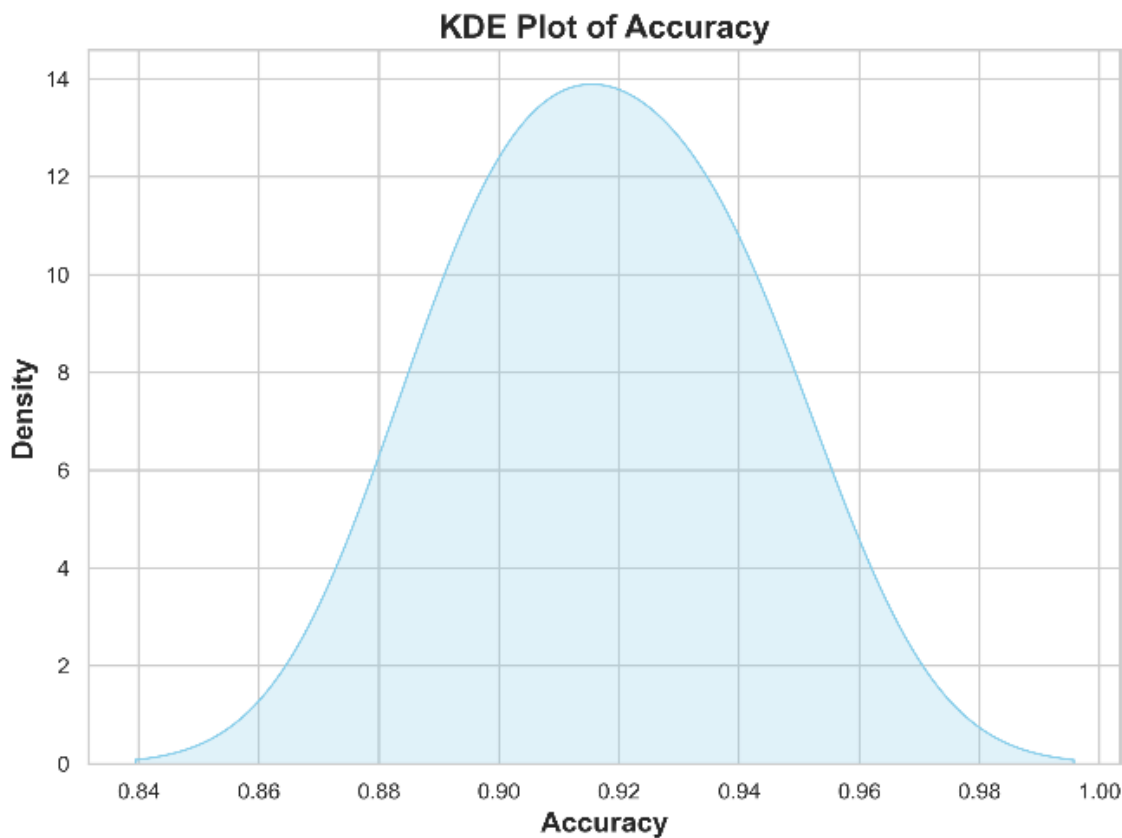


Figure 6: KDE Plot of Accuracy

Figure 7 compares overall accuracy for all models side by side, facilitating quick visual comparison to determine the best-performing model.

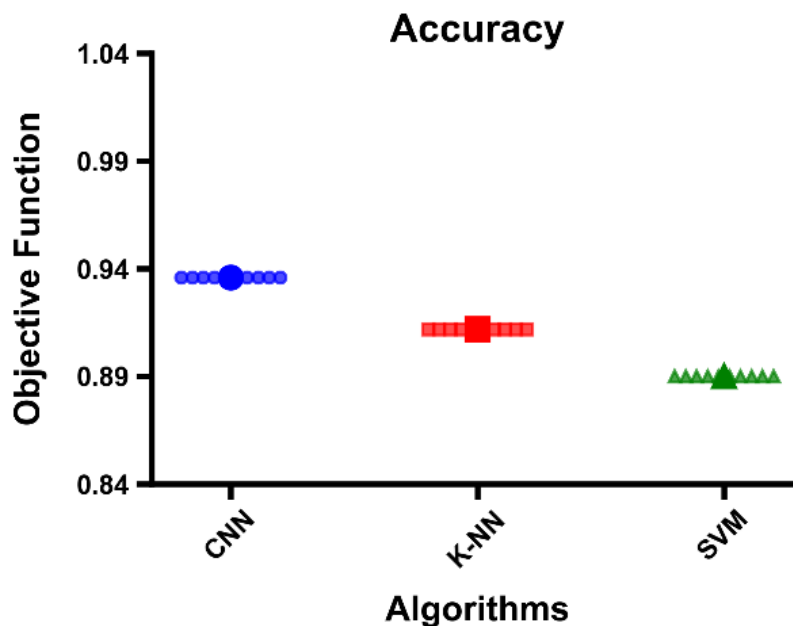


Figure 7: Accuracy Comparison for All Models

The study shows that learning algorithms, especially CNN, can achieve high levels of classification accuracy for retinal pathologies and be useful for diagnostics in ophthalmology. The high sensitivity in disease detection from CNNs enables them to provide low error-rate diagnostic results for retinal abnormalities, though at the cost of specificity. While K-NN and SVM exhibit decent accuracy, their lower sensitivity may limit their diagnostic capability. This evaluation confirms the practicality of more advanced machine learning techniques for diagnosing retinal disorders, with CNN emerging as the most effective model for this purpose.

5 Conclusion

From this study, the ability of the selected machine learning model, CNN, in classifying retinal diseases from the retinal images is established. Thanks to high sensitivity, CNNs have the prospects to use them for effective diagnostics of the diseased states including cataract and glaucoma. However, analyzing the observed trade-offs in specificity, which is, CNNs perform well in detecting positive cases though it is seen that they need fine-tuning in order to minimize false positive results. In turn, such models as K-NN and SVM have lower sensitivity in comparison with general accuracy that impacted their ability to detect the diseased cases. Such conclusions reflect the opportunities of using CNNs and other kinds of more sophisticated machine learning in ophthalmology as tools for early disease detection and improvement of the whole diagnostic system. Future work could be directed towards refining these models for the purpose of removing specificity constraints and expanding those opportunities for use across the spectrum of healthcare scenarios.

Declarations

- **Conflict of interest/Competing interests**

The authors declare that they have no conflicts of interest to report regarding the present study.

- **Ethics approval and consent to participate**
Not applicable.
- **Consent for publication**
Not applicable.
- **Funding**
No Fund

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