VFAST Transactions on Software Engineering
https://vfast.org/journals/index.php/VTSE@ 2025, ISSN(e): 2309-3978, ISSN(p): 2411-6246
Volume 13, Number 3, July-September 2025 pp:258-278

An Explainable Deep Learning Framework for Automated Classification of Ocular Diseases in a Big Data Environment

Sidra Hameed [1], **Muhammad Nauman** [2*], **Muhammad Hasnain** [1], **Nadeem Akhtar** [3], **Fatima Hussain** [2], **Zeshan Afzal** [2]

[1]Department of Artificial Intelligence, The Islamia University of Bahawalpur, Pakistan;
[2]Department of Software Engineering, The Islamia University of Bahawalpur, Pakistan;
[3]Department of Information Technology, FCIT, University of the Punjab, Lahore, Pakistan

Keywords: *Ocular Disease, Eye Health, Deep Learning, Machine Learning, Explainable Artificial Intelligence, Grad-CAM, Big Data Analytics, and Apache Spark Environment.*

Journal Info:
Submitted:
September 03, 2025
Accepted:
September 25, 2025
Published:
September 30, 2025

Abstract

Ocular diseases such as cataracts, glaucoma, age-related macular degeneration, and diabetic retinopathy remain major contributors to global visual impairment and blindness, where early detection is critical for effective intervention. While color fundus photography is widely used for retinal screening, manual interpretation is time-consuming and prone to error, highlighting the need for automated, accurate, and interpretable diagnostic solutions. In this study, we propose a deep learning based framework for the automated classification of ocular diseases and normal cases using medical images. The framework incorporates a comprehensive preprocessing pipeline and leverages a scalable Apache-powered big data environment for efficient feature extraction and model training on large-scale datasets. A Convolutional Neural Network (CNN) was proposed and benchmarked against state-of-the-art architectures including VGG19, ResNet50, and GoogLeNet, achieving superior performance with an accuracy of 97%, precision of 93%, recall of 97%, and F1-score of 93%. To enhance interpretability and clinical trust, Gradient-weighted Class Activation Mapping (Grad-CAM) was integrated, generating heatmaps that highlight the most discriminative retinal regions influencing predictions. The proposed approach not only achieves high diagnostic accuracy but also ensures transparency, scalability, and clinical relevance, making it a promising step toward real-world deployment of explainable AI systems in ophthalmology and broader healthcare applications.

***Correspondence author email address:** nauman@iub.edu.pk
DOI: 10.21015/vtse.v13i3.2228

1 Introduction

Ocular diseases represent a broad spectrum of conditions that adversely impact vision and, if left untreated, may progress to irreversible blindness. Common ocular disorders include cataracts, glaucoma, age-related macular degeneration, and diabetic retinopathy, all of which are major contributors to global visual impairment [1]. Early detection and timely intervention are critical in preventing vision loss, as these diseases can cause permanent and often irreversible damage to the retina and other ocular structures. Effective treatments exist; however, their success depends on the disease being diagnosed in its early stages. Color Fundus Photography (CFP) has emerged as a primary diagnostic modality, capturing detailed retinal images that allow for the detection of a wide range of ocular abnormalities [2]. Despite its utility, the accurate detection of certain diseases via CFP remains challenging, as early manifestations of conditions such as cataracts, myopia, and diabetic retinopathy are often subtle and asymptomatic. Moreover, manual interpretation of fundus images is labor-intensive and prone to human error, highlighting the need for automated and precise diagnostic solutions [3].

Healthcare systems globally face increasing pressure to optimize resources, improve patient outcomes, and enhance organizational efficiency [4–8]. These systems can broadly be conceptualized as comprising three key components: (a) primary service providers such as physicians, nurses, technicians, and administrators [9, 10]; (b) ancillary services, including health insurance and medical research [11]; and (c) beneficiaries, namely patients and the general public [12]. Modern healthcare encompasses both traditional in-person care and technology-driven remote monitoring, with both modes seeking to promote, maintain, and restore health outcomes [13, 14]. Within this landscape, Big Data Analytics (BDA) has transformed healthcare delivery by enabling advanced clinical decision support, disease surveillance, and large-scale health management [15–17].

Improving healthcare performance requires sustained, collaborative efforts from all stakeholders, including professionals, patients, and policymakers. Performance is typically evaluated in terms of safety, efficiency, accessibility, timeliness, effectiveness, and equity, reflecting both patient and societal priorities [18–20]. However, challenges such as emergency department overcrowding underscore the need for innovative strategies to improve care delivery. In this context, BDA plays a central role by enhancing triage accuracy, enabling predictive analytics, and integrating comprehensive patient histories into care processes, thereby driving more efficient, data-driven healthcare systems [21].

Beyond healthcare, BDA has also gained attention for its role in advancing the principles of the Circular Economy (CE), which emphasizes regenerative and restorative business practices [23, 24]. By maximizing resource utilization and closing production-consumption loops, CE frameworks align well with the analytical capabilities of BDA. Although emerging research has begun to examine the role of BDA in improving decision-making and organizational performance in emerging markets [25, 26], empirical studies remain limited, particularly in understanding how data-driven insights contribute to CE adoption and performance outcomes [23].

Decision-making in complex domains such as healthcare has increasingly relied on decision support systems (DSS), which assist professionals throughout the decision-making process. The integration of artificial intelligence (AI) into DSS during the 1980s marked the emergence of intelligent decision support systems (IDSS), capable of acquiring knowledge, adapting to dynamic environments, and providing expert-level recommendations [27]. These systems not only support clinicians but can also autonomously execute predefined actions when authorized, thereby streamlining clinical workflows and improving patient care [28].

The current era of big data has introduced unprecedented challenges in data analysis and interpretation across scientific and industrial domains. Machine learning (ML) and artificial intelligence (AI) have become essential tools for harnessing these large-scale data resources. Among these, deep learning (DL) has emerged as a transformative approach, leveraging multi-layer neural networks to capture complex, non-linear relationships [29, 30]. DL has demonstrated state-of-the-art performance across multiple applications, including handwritten digit recognition with record-breaking accuracy, image classification, speech recognition, natural language processing, acoustic modeling, and computational biology [31].

In the medical domain, DL has demonstrated significant potential, particularly in medical image analysis tasks such as classification, segmentation, and disease detection [33, 34, 37]. Despite these advancements, DL algorithms are often criticized for their "black-box" nature, wherein the internal decision-making process remains opaque and difficult to interpret [35, 36]. This lack of transparency poses a substantial challenge for clinical adoption, as it limits trust and hinders the explainability of diagnostic outcomes. Consequently, the black-box nature of DL models remains a major obstacle, particularly when dealing with large-scale medical data, thereby restricting their widespread implementation in real-world healthcare settings.

To address the challenges mentioned above, this study proposes a deep learning–based framework for the automated detection and classification of ocular diseases, pneumonia cases, and normal conditions using medical images. The proposed methodology integrates Convolutional Neural Networks (CNNs) with Gradient-weighted Class Activation Mapping (Grad-CAM) [41], a widely adopted technique in explainable artificial intelligence (XAI). Grad-CAM generates class-discriminative heatmaps that highlight the most salient image regions contributing to the model's predictions, thereby enhancing interpretability and transparency [43]. By combining accurate classification with interpretable visual explanations, the framework improves model trustworthiness and supports its potential for real-world clinical deployment [44].

Our proposed approach for detecting ocular diseases is structured into several stages to ensure robust performance and interpretability. First, we selected an openly available image-based data set for the detection of ocular disease from Kaggle. To improve data quality and mitigate common issues such as noise and imbalance, we designed a comprehensive preprocessing pipeline involving normalization and cleaning techniques. This step ensures the dataset is both consistent and sufficiently diverse for training deep learning models. In the second stage, we employ a scalable big data environment powered by Apache to facilitate efficient feature extraction and management of large-scale image data. Leveraging distributed computing capabilities enables faster processing and ensures that the framework can be extended to even larger datasets in real-world applications. Next, proposed CNN model and compared the results with multiple state-of-the-art deep learning architectures, including VGG19, ResNet50, and GoogLeNet. These models were systematically compared to identify the most effective approach for ocular disease classification. Finally, to enhance interpretability and build trust in the system's predictions, Grad-CAM was applied. Grad-CAM generates class-discriminative heatmaps, visually highlighting the regions of input images that most strongly influence the model's decisions. This not only facilitates model debugging but also provides transparent and clinically meaningful insights for ophthalmologists.

1. A novel automated diagnostic framework is proposed for the detection and classification of ocular diseases and normal conditions using medical images, addressing the limitation of prior works that primarily focused on single-disease detection.
2. A scalable feature extraction and image-processing pipeline is implemented within an Apache-powered big data environment, enabling efficient management and analysis of large-scale medical image datasets.
3. The interpretability and transparency of CNN predictions are enhanced through the integration of XAI techniques, thereby fostering clinical trust and facilitating real-world adoption.
4. The Grad-CAM technique is employed to generate class-discriminative visual explanations, highlighting critical image regions that influence model decisions and improving the transparency of the decision-making process.

5. The framework facilitates systematic model debugging and provides ophthalmologists with interpretable and clinically meaningful insights, supporting both diagnostic accuracy and decision-making.

The remainder of this paper is organized as follows: Section II provides the background, Section III reviews the relevant literature, Section IV describes the materials and methods, and Section V presents the conclusion.

2 Background

2.1 OCULAR DISEASE DETECTION

Ocular disease detection refers to the identification and diagnosis of disorders or abnormalities affecting the eyes, including glaucoma, diabetic retinopathy, age-related macular degeneration, and cataracts . These conditions are among the leading causes of visual impairment worldwide, affecting millions of individuals across diverse age groups [52]. If left undetected and untreated, many ocular diseases can progress to permanent vision loss or blindness. Early detection is therefore critical, as it allows timely intervention and significantly reduces the risk of irreversible damage [48, 49].

Traditional diagnostic approaches for ocular diseases rely on clinical evaluations and imaging techniques, particularly fundus photography and optical coherence tomography. However, the advent of AI and ML has transformed the field, enabling automated detection systems capable of analyzing ocular data with greater speed, scalability, and accuracy. Such systems are especially valuable in resource-limited settings, where access to specialized ophthalmologists may be restricted [45–47].

Among ocular diseases, diabetic retinopathy and glaucoma remain leading causes of global vision impairment and blindness [50, 51]. A major challenge is that these conditions often present few or no symptoms in their early stages, making timely diagnosis difficult yet essential for effective treatment. Consequently, AI-driven solutions that leverage medical imaging have been increasingly explored to enable early-stage detection and intervention [49].

While ocular diseases are often associated with aging, younger populations are not immune. Genetic predispositions, systemic health conditions (e.g., diabetes), and environmental factors can contribute to early-onset ocular complications [52]. With the global population both growing and aging, there is an urgent need for advanced ocular disease recognition systems that can deliver precise, scalable, and accessible diagnostic support. By integrating medical imaging with AI-based models, these systems hold the potential to mitigate the global burden of vision loss and blindness [51].

2.2 OCULAR DISEASE DETECTION AND BIG DATA

Dry eye disease is a chronic ocular disorder that is expected to increase in prevalence due to global population aging and the widespread use of digital devices. Current management strategies primarily focus on symptomatic relief, with no established preventative therapies. One of the major challenges in advancing treatment is the lack of reliable biomarkers for early diagnosis and monitoring [54]. The integration of big data from multiomics studies and mobile health applications offers a promising path toward improving DED management. By enabling personalized treatment approaches, these technologies have the potential to identify high-risk individuals, provide more accurate diagnoses, and customize therapeutic strategies based on individual physiology and symptom profiles. Such innovations align with the broader vision of precision medicine, aiming to improve patient outcomes in DED and related ocular conditions. Within this paradigm, big data plays a central role by facilitating the analysis and integration of diverse data sources, ultimately supporting more personalized and effective care [54, 59].

The rise of information technologies has enabled the generation and collection of large-scale datasets, collectively referred to as big data, which hold significant potential for transforming ophthalmic research, clinical practice, and healthcare delivery. Key sources of big data in ophthalmology include electronic health records (EHRs), patient registries, and biobanks. These resources can be leveraged for disease surveillance, early detection, patient management, and prognostication [55]. However, challenges remain in ensuring data quality, safeguarding patient privacy, and developing robust analytical methodologies to maximize the clinical utility of these datasets [56].

The integration of big data with AI has revolutionized biomedical research by accelerating the identification of patterns in complex, high-dimensional datasets. While the concepts of big data and AI are not new, their impact in healthcare has grown substantially with the routine collection of diverse clinical and imaging datasets, alongside advances in multiomics technologies [57]. The availability of such multidimensional patient data has significantly enhanced AI's ability to derive actionable insights, facilitating breakthroughs in disease prediction, diagnosis, and therapeutic innovation [58, 59].

Ophthalmology has emerged as a leading field for AI and big data applications, largely due to the widespread availability of noninvasive, cost-effective imaging modalities such as fundus photography and optical coherence tomography (OCT) [60, 61]. These modalities have generated vast image repositories that are well-suited for computer vision applications in disease detection and progression monitoring [62, 63]. A notable example is the Intelligent Research in Sight (IRIS) Registry, the world's largest clinical ophthalmic database, which provides an unparalleled resource for population-level big data research [64]. Unlike traditional hypothesis-driven research, AI- and big data–driven approaches are inherently data-centric, enabling the discovery of novel biomarkers, subtle disease associations, and imaging features undetectable by human observers. For instance, recent studies have demonstrated the ability of AI to uncover early markers of age-related macular degeneration and detect associations between ocular features and systemic health conditions such as smoking and refractive errors [65–67]. These advances not only generate new hypotheses but also deepen our understanding of ocular disease mechanisms, thereby shaping the future of predictive and precision ophthalmology.

2.3 APACHE SPARK

Apache Spark is an open-source, distributed computing framework widely employed for big data processing and analytics. Initially developed by the AMPLab at UC Berkeley in 2009 and later becoming an Apache project in 2013, Spark has gained prominence due to its speed, scalability, and flexibility across diverse workloads, including batch processing, interactive queries, stream processing, machine learning, and graph computation. Unlike the earlier Hadoop MapReduce paradigm, Spark was specifically designed to overcome inefficiencies in iterative algorithms and complex multi-stage applications by introducing in-memory computation and an optimized Directed Acyclic Graph (DAG) execution engine. These innovations enable Spark to perform significantly faster than Hadoop, in some cases achieving performance gains of more than 100 times in memory-intensive tasks [68, 69].

A key strength of Spark lies in its ability to unify the processing of heterogeneous datasets, ranging from structured text to unstructured multimedia (images, video, graphs), while supporting both batch and real-time streaming workflows. This versatility has established Spark as a cornerstone technology for big data analytics in healthcare and biomedical domains, where large, multimodal datasets must be processed efficiently for meaningful insights [70].

In biomedical image processing, particularly for diagnostic applications, feature extraction is a critical step in transforming visual data into structured feature vectors that can be mathematically analyzed and classified. The challenge lies in identifying features that are both relevant and discriminative, as medical images often contain high variability and noise. Moreover, the number of features can vary significantly across images, necessitating strategies to ensure consistent feature vector dimensions for downstream analysis. Effective feature selection methods are therefore essential to reduce redundancy, retain clinically meaningful information, and enhance the accuracy and efficiency of classifiers in biomedical imaging tasks [71].

2.4 Grad-CAM

The origins of XAI can be traced back to the development of expert systems in the 1980s, where efforts were made to provide human-understandable justifications for system recommendations. However, in recent years, the rapid increase in the complexity of DL models has renewed interest in XAI, as these models often function as opaque "black boxes", limiting user trust and adoption in critical domains such as healthcare. Despite ongoing debates regarding the precise definitions of explainability and interpretability [72, 73], the overarching objective of XAI is to enhance the transparency and comprehensibility of AI-driven decisions for human users [76**?**].

XAI methodologies can generally be divided into two broad categories. The first focuses on inherently interpretable models, which are designed to be transparent by construction (e.g., linear regression, decision trees). While interpretable, these models are often limited in predictive performance when compared to more sophisticated methods. The second category encompasses post-hoc explanation techniques, which aim to provide human-understandable insights into the behavior of complex, high-performing black-box models [77, 78]. Recent surveys provide comprehensive overviews of these approaches, highlighting their respective strengths and limitations [72, 75, 79].

More recently, research has focused on developing "clear-box" models that balance interpretability and performance by offering internal transparency while maintaining predictive accuracy [80–82]. These advances represent an important step toward bridging the gap between human trust and machine intelligence in real-world applications.

Within the context of computer vision, Grad-CAM has emerged as one of the most influential post-hoc explanation techniques. Proposed by Selvaraju et al. [41], Grad-CAM enhances the interpretability of CNNs by producing class-discriminative heatmaps that visualize the image regions most responsible for a model's prediction. By highlighting these key areas, Grad-CAM addresses the black-box challenge of deep learning models in image classification and recognition tasks, thereby improving transparency, interpretability, and user confidence in model outputs [42].

3 Related Work

Recent advances in artificial intelligence, particularly DL and ML, have significantly transformed the landscape of medical image analysis, offering new opportunities for early diagnosis and improved clinical decision-making. A major area of focus has been ocular disease detection using retinal imaging modalities such as fundus photography and optical coherence tomography.

Li et al. [95] proposed a deep learning–based system for detecting Glaucomatous Optic Neuropathy using 8,000 color fundus photographs, achieving impressive performance with a sensitivity of 95.6%, specificity of 92.0%, and an AUC of 0.986. Similarly, Prajna et al. [101] introduced a CNN-based architecture trained on multiple datasets, reporting accuracies of 86.62% (DRISHTI-GS1), 85.97% (RIM-ONE2), 78.32% (ORIGA), 94.43% (LAG), and 96.64% (ACRIMA). Elangovan et al. [102] employed DenseNet201 for feature extraction in glaucoma classification and compared its performance across several classifiers, while Juneja et al. [106] developed an AI-based expert system using a modified U-Net for optic disc and cup segmentation, achieving 95.8% and 93% accuracy, respectively.

Beyond glaucoma, several studies have investigated DL for multi-disease detection. Dipu et al. [2] evaluated models including VGG-16, MobileNetV2, EfficientNet, and ResNet-34 on the ODIR dataset, with VGG-16 achieving the highest accuracy at 97.23%. Patil et al. [97] introduced novel ensemble approaches—"faster ensembles" and "ensembles of ensembles"—leveraging transfer learning with Xception, DenseNet201, and InceptionV3, reporting accuracies of 87% and 88%, respectively. Wang et al. [91] and Nair et al. [105] further explored ensemble and multi-label CNN-based approaches for fundus image classification on ODIR-5K, underscoring the potential and challenges of DL in handling heterogeneous disease categories. Likewise, Islam et al. [104] applied CNNs with image enhancement techniques (e.g., CLAHE), achieving an F1 score of 85% and an AUC

Table 1. Comparison of ocular disease detection studies.

Study	Year	Data Source	Methods	Accuracy	Limitation
[51]	2024	Images of eye fundus	CNN	96%	Limited to small dataset, lacking diversity in disease types.
[97]	2024	Ocular Disease Intelligent Recognition	Xception, DenseNet, InceptionV3	88%, 87%, 88%, 87%	High computational cost due to ensemble methods
[85]	2023	Ocular Disease Intelligent Recognition dataset	ResNet50	95%	Generalizes poorly on unseen clinical datasets.
[2]	2021	Ocular Disease Intelligent Recognition	ResNet-34, EfficientNet, MobileNetV2, VGG-16	94%, 92%, 95%, 98%	Dataset imbalance affects rare disease classification.
[111]	2021	43,156 images, 70% for training, 10% for tuning, 20% for validation	ResNet-50	89%	Focused only on high-resolution images, not suitable for mobile devices.
[90]	2021	52 patients (101 eyes)	DE-SVM	95%	Small sample size limits model robustness.
[112]	2021	Retinal image for cataract detection dataset	Kernel based CNN	97%	Overfitting observed on small-scale datasets.
[89]	2020	EyePACS dataset	ANN	92%	Lacks explainability in model predictions.
[113]	2020	46 patients and 96 controls, 80% for training, 20% for validation	VGG-16	89%	Performance drops in real-time applications.
[114]	2020	5,296 images for training; 647 for tuning; 654 for testing	Xception	73%	Limited model scalability to larger datasets.
[115]	2020	15,911 images for training; 2,536 for testing	EfficientNet	74%	Dataset diversity is insufficient for robust classification.
[116]	2020	20,130 images for training and 5-fold validation	Inception-3	75%	Requires extensive hyperparameter tuning.
[117]	2020	1,419 images, 75% for training, 25% for testing	U-net & CNN	65%	Very small dataset, prone to overfitting.
[118]	2020	625 images, 80% for training, 10% for validation, 10% for testing	Inception-3	76%	Limited to binary classification tasks.
This Study	2025	Ocular Disease Recognition	CNN, Grad-CAM	97%	Performance may be dataset-dependent; external validation on diverse real-world clinical datasets is required.

of 80.5%.

Several review studies consolidate these advancements. Muchuchuti et al. [96] provided a critical overview of DL techniques for retinal disease detection, highlighting the limitations of manual approaches and the potential of CNNs to improve diagnostic reliability. Susrutha et al. [98] similarly emphasized early diagnosis of glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy, noting the promise of CNNs and hybrid models. Paul et al. [103] compared classical ML algorithms such as SVM, Decision Trees, Random Forests, and Extra Trees, concluding that Extra Trees achieved the best performance (97% accuracy), further validating the role of ML beyond DL architectures.

Beyond ophthalmology, researchers have also leveraged ocular imaging for systemic disease detection. Peng et al. [99], in a review of 33 studies, demonstrated that fundus photography and OCT can provide predictive insights into cardiovascular, cerebrovascular, and neurological disorders, though real-world validation remains necessary. Abdelmotaal et al. [100] applied CNNs to ocular surface videos for automated dry eye diagnosis, achieving an AUC of 0.98 and highlighting clinically relevant activation regions, thereby illustrating the potential of AI in non-invasive, high-throughput screening.

Parallel to these ocular studies, big data analytics in healthcare has also gained attention. Awrahman et al. [107] discussed the role of predictive modeling and ML in integrating electronic health records to improve patient outcomes, while addressing challenges of data heterogeneity, privacy, and infrastructure. Batko et al. [108], focusing on the Polish healthcare system, demonstrated that integrating structured and unstructured data from over 200 facilities enhances decision-making and patient management. These findings reinforce the role of big data in enabling scalable and personalized healthcare solutions.

In addition, DL methods have advanced other areas of medical imaging. Kannan et al. [109] applied Google's Inception v3 to classify trichrome-stained kidney biopsy images, achieving 92.67% accuracy in distinguishing healthy and globally sclerosed glomeruli. Ginley et al. [110] combined CNNs with recurrent architectures for glomerular boundary detection and unsupervised feature extraction, demonstrating improvements in segmentation accuracy and automation. These studies collectively highlight the versatility of DL and ML in various diagnostic domains.

Taken together, this body of literature underscores the transformative potential of DL, ML, and big data analytics in medical diagnostics. While ocular imaging remains a leading application area due to its non-invasive and information-rich nature, these approaches are increasingly being extended to systemic disease detection and broader medical imaging tasks. Challenges such as dataset diversity, model interpretability, and clinical validation remain, but the trajectory of research suggests that AI-driven diagnostic systems are poised to become indispensable tools in modern healthcare.

4 Materials and Methods

The proposed approach, shown in Figure 1, introduces a systematic methodology for processing and analyzing ocular image data sets to support automated disease detection. The pipeline is organized into four key phases: data collection, preprocessing, feature extraction and model training, and interpretability. The process begins with the collection of ocular images representing diverse disease conditions. To ensure consistency and improve data quality, the images undergo essential pre-processing steps, including cleaning and normalization. Given the large-scale nature of the dataset, the framework leverages Apache Spark in conjunction with the Hadoop Distributed File System (HDFS) to provide a scalable and efficient big data environment.

Following pre-processing, the prepared images are processed through a machine learning pipeline. In this phase, advanced feature extraction techniques are employed to identify discriminative visual patterns associated with ocular diseases, which are then used to train deep learning models. To address the "black-box" nature of these models, XAI techniques—specifically Grad-CAM are incorporated. Grad-CAM generates heatmaps that highlight image regions most influential to the model's predictions, thereby enhancing interpretability and facilitating greater clinical trust in the system. Finally, model performance is rigorously evaluated to identify the most accurate and effective architecture for ocular disease detection. By integrating big data management, preprocessing, model training, and explainability, the proposed approach delivers a comprehensive and scalable solution for medical image-based ocular disease diagnosis.

4.1 Dataset Acquisition

The reliability and accuracy of any diagnostic system are closely tied to the quality and relevance of the data employed. Data acquisition thus forms the cornerstone of system performance, as the effectiveness of model training and evaluation depends on both the representativeness and integrity of the dataset. In this study, experiments were conducted using the Ocular Disease Recognition (ODIR-5K) dataset Kaggle[1], which contains retinal fundus images labeled for multiple ocular conditions and normal cases; all experiments reported in this manuscript are restricted to ocular imaging." . This dataset comprises thousands of high-resolution ocular images annotated with disease labels, covering a wide spectrum of ocular conditions. Its substantial size and diversity make it particularly well-suited for deep learning, where large and heterogeneous

The dataset is structured into three main components. First, the Ocular Disease folder provides training and testing images that serve as the foundation for model development. Second, a set of preprocessed images—subjected to normalization and cleaning—ensures consistency and readiness for input into deep learning models. Finally, a CSV file containing metadata and corresponding labels facilitates efficient data management and supports

[1] https://www.kaggle.com/datasets/andrewmvd/ocular-disease-recognition-odir5k/data

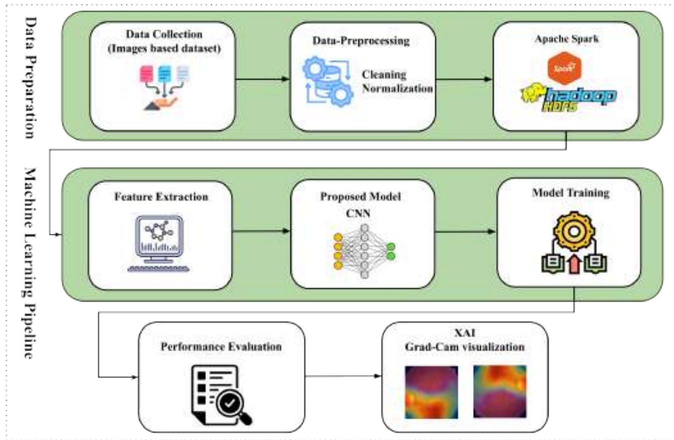

Figure 1. Ocular Disease Detection Framework.

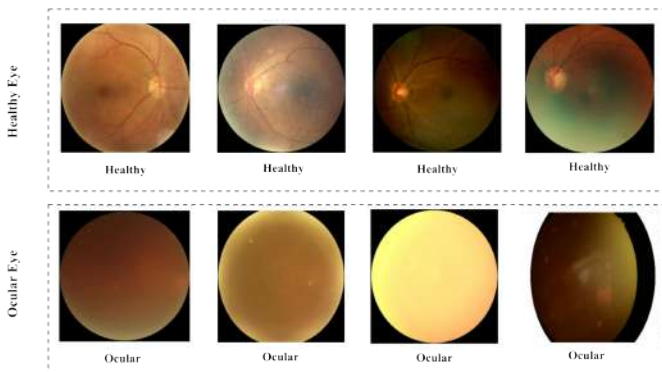

Figure 2. Sample images from the ocular disease dataset.

supervised training. A representative sample of the dataset is shown in Figure 2, illustrating ocular disease cases alongside normal (healthy) eye images.

4.2 Pre-Processing

In the pre-processing stage of the proposed methodology, a structured pipeline was implemented to prepare the ocular image dataset for machine learning tasks. Several pre-processing steps were applied to ensure data quality, consistency, and suitability for deep learning models, as illustrated in Figure 3. The process began with image resizing, where all images were standardized to a uniform dimension, ensuring compatibility with the input layer requirements of CNNs. Next, normalization was performed by scaling pixel values to the range [0, 1], which improves training stability and accelerates model convergence by providing standardized input data. These transformations enhance model generalization by simulating natural variability in ocular images. Furthermore, data cleaning was carried out to remove irrelevant, duplicate, or corrupted images, thereby maintaining dataset integrity. This pre-processing pipeline was essential in enhancing the dataset's overall quality and ensuring that the deep learning models receive structured, balanced, and reliable input for effective training and robust prediction performance.

Figure 3. Data Preprocessing.

4.3 Big Data Environment

In the proposed approach for ocular disease detection, the big data environment plays a pivotal role in managing and processing the extensive volume of image data efficiently. This environment is constructed using two core components: the HDFS and Apache Spark. HDFS provides scalable, fault-tolerant distributed storage, ensuring reliable data availability across nodes. Apache Spark, on the other hand, facilitates high-performance parallel and in-memory processing, enabling rapid execution of computationally intensive tasks such as image preprocessing, feature extraction, and model training. By integrating these technologies, the framework establishes a robust and scalable infrastructure capable of handling large-scale medical imaging data. This integration not only accelerates the entire pipeline—from data acquisition and preprocessing to classification and interpretation—but also enhances reliability, making the system well-suited for real-world medical applications where efficiency and scalability are critical.

4.3.1 HDFS

The HDFS is a scalable and fault-tolerant file system specifically designed for the distributed storage and management of large datasets across multiple machines. As a fundamental component of the Apache Hadoop ecosystem, HDFS divides massive datasets into smaller blocks and distributes them across a cluster, thereby enabling the handling of data volumes that exceed the capacity of individual machines. To ensure robustness, each block is replicated across multiple nodes within the cluster, providing fault tolerance, high availability, and resilience against hardware failures without compromising data integrity. Moreover, its architecture offers seamless scalability, as additional nodes can be incorporated into the cluster to accommodate growing dataset sizes without requiring substantial infrastructure modifications. In the context of the proposed ocular disease detection framework, HDFS serves as the backbone for storing image data, ensuring efficient distributed management and reliable access, thereby supporting the large-scale preprocessing, training, and analysis tasks required for deep learning–based medical diagnostics.

4.3.2 Apache Spark

Apache Spark is a powerful, open-source big data processing engine that complements the Hadoop ecosystem by providing high-performance, in-memory computation and advanced data processing capabilities. Unlike traditional Hadoop MapReduce, which stores intermediate results on disk, Spark performs most computations directly in memory, thereby reducing input/output overhead and significantly accelerating processing speed, particularly for iterative algorithms commonly employed in machine learning. Its distributed architecture enables parallel processing by allocating both data and computational tasks across multiple nodes within a cluster, making it highly efficient for large-scale workloads such as image pre-processing, feature extraction, and model training.

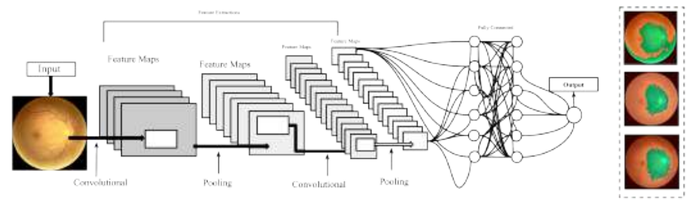

Figure 4. CNN Architecture

Additionally, Spark's flexibility and ease of integration with the HDFS and other ecosystem components streamline its deployment in existing big data environments, while its support for multiple programming languages, including Python, widely used in machine learning, enhances accessibility and usability. Within the proposed ocular disease detection framework, Apache Spark is leveraged to preprocess image data, execute feature extraction, and manage model training, ensuring efficient handling of computationally intensive tasks. By combining Spark's in-memory and parallel processing capabilities with HDFS's distributed storage, the proposed system achieves both scalability and performance, enabling robust end-to-end management of the pipeline from data preparation to model evaluation.

Table 2. CNN Model Summary with Parameters

Layer Type	Output Shape	Param #
Conv2D	(None, 126, 126, 32)	896
MaxPooling2D	(None, 63, 63, 32)	0
Conv2D	(None, 61, 61, 64)	18,496
MaxPooling2D	(None, 30, 30, 64)	0
Flatten	(None, 57600)	0
Dense	(None, 128)	7,372,928
Dropout	(None, 128)	0
Dense	(None, 2)	258

4.4 Feature Extraction

Feature extraction represents a critical stage in the machine learning pipeline, as it transforms raw image data into a structured representation suitable for downstream classification tasks. In this study, pre-trained CNNs were employed to extract high-level feature representations from ocular images. CNN architectures were selected due to their demonstrated effectiveness in image recognition and classification, particularly in capturing complex spatial hierarchies and intricate visual patterns. The extracted features serve as input to machine learning models, enabling efficient training and reliable classification. The adoption of pre-trained models provides a significant advantage by transferring knowledge learned from large-scale benchmark datasets, thereby improving feature quality and enhancing generalization even in domain-specific applications such as ocular disease detection. Through this approach, the system is able to exploit the representational power of deep architectures, ultimately leading to improved predictive accuracy and robust performance in detecting ocular abnormalities.

4.5 CNN

In the proposed approach, the CNN architecture is designed to strike a balance between accuracy and computational efficiency, tailored specifically to the characteristics of the ocular dataset. Each model is trained on the pre-processed dataset, and their performances are evaluated using standard metrics such as accuracy, precision, recall, and F1-score. The architecture of the CNN model is illustrated in Figure 4. To enable the CNN model to classify eight distinct ocular disease categories, this work enhanced the original CNN architecture by incorporating two additional fully connected (Dense) layers. The complete architecture of the modified CNN model is detailed in Table 2.

4.6 GRAD-CAM Visulizations

In this research, we employed Grad-CAM as part of our XAI approach to visualize and interpret the decision-making process of our convolutional neural network (CNN) models. Grad-CAM is a widely used technique that generates heatmaps to highlight the regions in the input image that significantly contribute to the model's prediction. By leveraging Grad-CAM, we are able to provide visual explanations of how the model identifies features associated with the eight distinct ocular disease categories. This not only enhances the transparency of the deep learning model but also enables the validation of the model's focus areas, ensuring that the model is correctly attending to clinically relevant regions in the images. The generated heatmaps allow us to assess whether the model's decisions are driven by the pathological features of interest or by irrelevant background artifacts, thus improving model interpretability and trustworthiness in real-world applications.

4.7 Performance Evaluations

The final step in the proposed approach involves evaluating the performance of the trained models on a separate test set. Performance metrics are computed to assess the accuracy and reliability of each model in classifying the ocular diseases. The results of these evaluations are used to compare the models and select the most suitable one for deployment in a clinical setting.

In order to analyze the results provided by the classification models in a comprehensible way, we have used evaluation metrics such as accuracy, precision, recall, F1 score, etc. The formulas of these evaluation metrics are shown below:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \tag{1}$$

$$\text{Precision} = \frac{TP}{TP + FP} \tag{2}$$

$$\text{Recall} = \frac{TP}{TP + FN} \tag{3}$$

$$F_1 = \frac{2 \times \text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \tag{4}$$

Here,

- **TP** = True Positive (The total number of images that are correctly detected to be positive)
- **FP** = False Positive (The total number of images that are predicted to be positive but actually are negative)
- **TN** = True Negative (The number of images that are accurately predicted to be negative)
- **FN** = False Negative (The number of images that are incorrectly predicted to be negative)

Table 3. Performance Metrics of Various Models

Model	Accuracy	Precision	Recall	F1 Score
VGG19	96%	97%	97%	97%
ResNet50	92%	92%	91%	91%
GoogleNet	94%	94%	94%	94%
Proposed Model CNN	97%	93%	97%	93%

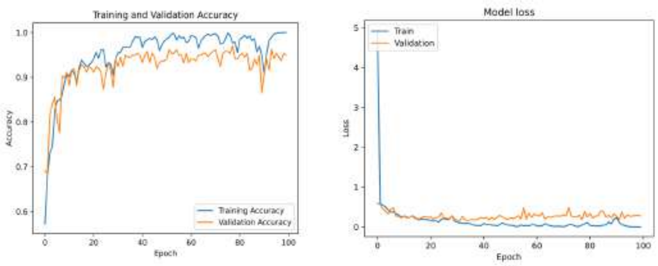

Figure 5. Model accuracy and loss for CNN during training and validation.

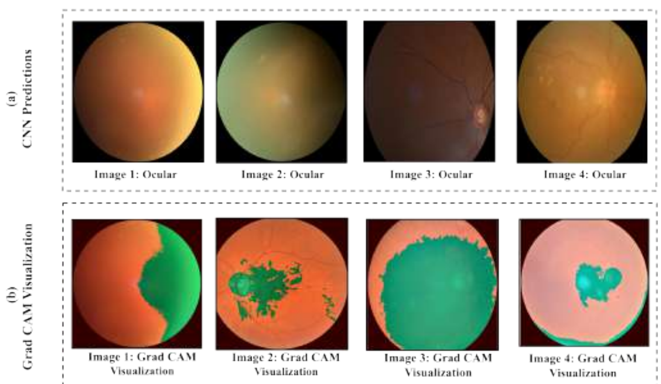

Figure 6. Visualization of explainable AI (Grad-CAM) applied on ocular disease retinal fundus images.

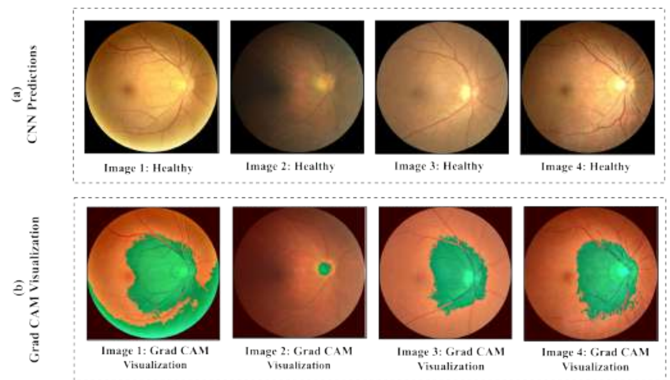

Figure 7. Visualization of explainable AI (Grad-CAM) applied on healthy retinal fundus images.

4.8 Results

This study presents a comprehensive methodology for developing a robust prediction model for image-based classification, integrating big data preprocessing, advanced deep learning architectures, and rigorous evaluation. The dataset, composed of diverse ocular images, was subjected to multiple preprocessing steps, including cleaning and normalization, to enhance data quality and variability. These tasks were executed efficiently using Apache Spark, ensuring scalability and optimized performance when handling large-scale datasets. The resulting preprocessing pipeline was fundamental in preparing consistent and high-quality input for model training. To evaluate predictive performance, four deep learning models—VGG19, ResNet, GoogLeNet, and a custom CNN—were trained and tested on the processed dataset. Their performance was assessed using multiple metrics, including accuracy, precision, recall, and F1 score, as summarized in Table ??. The comparative analysis highlights the strengths and limitations of each architecture in capturing complex image patterns and achieving reliable classification. Beyond model selection, the findings underscore the broader applicability of these approaches for medical image analysis, providing valuable insights into the potential use of deep learning models for diverse image classification tasks in clinical and non-clinical domains.

4.8.1 Proposed Model CNN

The proposed CNN model demonstrates outstanding performance, achieving an accuracy of 97%, a precision of 93%, a recall of 97%, and an F1 score of 93%. The high accuracy underscores the model's ability to correctly classify the majority of instances, while the strong recall highlights its effectiveness in capturing true positive cases, thereby minimizing the risk of overlooking relevant instances. Although the precision is marginally lower at 93%, it still indicates a reliable classification capability with a relatively low proportion of false positives. Collectively, these results reflect a well-balanced performance, where the model achieves high sensitivity without compromising overall reliability. The training and validation accuracy and loss curves, illustrated in Figure 5, further demonstrate the model's stable convergence and generalization capacity, reinforcing its suitability for image-based classification tasks.

4.8.2 Grad-CAM Interpretations

Figure 6 displays the Grad-CAM outputs for retinal images affected by various ocular pathologies. The first row shows the original diseased fundus photographs, while the second row presents the corresponding Grad-CAM heatmaps. In these cases, the activations are more widespread and concentrated on clinically relevant abnormal regions. For instance, in cataract-affected images, the highlighted areas correspond to blurred zones where retinal vessels appear obscured, consistent with lens opacity. In diabetic retinopathy cases, activations cluster around microaneurysms, exudates, and hemorrhages, reflecting hallmark clinical features of the disease. Similarly, in age-related macular degeneration, the model predominantly highlights the macular region, where drusen deposits are typically observed.

In contrast, Figure 7 presents the Grad-CAM visualization results for healthy retinal fundus images. The first row depicts the original images of normal eyes without any pathological abnormalities, while the second row illustrates the corresponding Grad-CAM heatmaps. As expected, the highlighted activation regions, shown in green, are minimal and primarily localized around anatomical landmarks such as the optic disc, macula, and vascular arcades. This pattern indicates that the model does not falsely identify pathological features in healthy cases and instead focuses on general retinal structures. The absence of widespread or intense activations reinforces the system's ability to correctly differentiate normal fundus images, providing evidence of its reliability in ruling out disease.

The comparative analysis of Figure 6 and Figure 7 underscores the interpretability strength of Grad-CAM in distinguishing healthy from diseased eyes. While activations in healthy cases are confined to normal anatomical landmarks, diseased cases exhibit targeted activations on pathological regions, confirming the system's ability to identify clinically meaningful features. This not only validates the diagnostic predictions of the model but also enhances transparency and interpretability, making the approach more trustworthy for ophthalmic applications within the broader framework of explainable AI (XAI).

4.9 Discussion

The comparative evaluation of VGG19, ResNet50, GoogleNet, and the proposed CNN highlights distinct performance characteristics relevant to ocular disease classification. Among the benchmark models, VGG19 achieved strong results with 96% accuracy and precision, recall, and F1 scores of 97%, demonstrating its reliability in minimizing false positives while effectively identifying true cases. GoogleNet followed closely, with balanced metrics of 94% across accuracy, precision, recall, and F1, indicating robustness and consistency. ResNet50, while solid, performed lower with 92% accuracy, 92% precision, and 91% recall, suggesting limitations in capturing positive instances. In contrast, the proposed CNN model achieved the highest accuracy of 97%, coupled with a recall of 97%, precision of 93%, and F1 score of 93%. These results indicate that the CNN is highly effective in identifying relevant cases, though with a slightly higher false positive rate compared to VGG19.

When compared with prior studies, the proposed CNN demonstrates competitive or superior performance. For instance, [51] reported a CNN-based ocular disease recognition system with slightly higher precision (96.7%) and F1 score (97.5%) but comparable accuracy (97.5%) and recall (98.3%). This suggests that while our model produces marginally more false positives, it achieves a comparable balance of accuracy and recall. Similarly, [85] attained lower validation accuracies of 91.28% (SGD) and 94.71% (Adam) for cataract classification, and [97] reported even lower accuracies for Xception (88%), DenseNet (87%), InceptionV3 (88%), and their ensemble model (87%). These findings confirm that our model consistently outperforms several state-of-the-art CNN variants.

Further, in comparison to [2], where ResNet-34, EfficientNet, MobileNetV2, and VGG-16 achieved 94%, 92%, 95%, and 98% accuracy, respectively, our CNN surpasses ResNet-34 and EfficientNet but falls slightly below the top-performing VGG-16 by 1%. Likewise, against the ResNet-50 model in [111], which achieved only 89% accuracy on a large dataset of 43,156 images, our CNN shows a substantial improvement with 97% accuracy, demonstrating the effectiveness of our design in handling large-scale data while ensuring higher classification performance.

Overall, these results establish the proposed CNN as a robust and competitive model for ocular disease classification, consistently outperforming several deep learning architectures across key metrics while remaining comparable to the strongest models reported in the literature.

5 Conclusion

This research presents a comprehensive and scalable deep learning framework for ocular disease detection, integrating advanced CNN architectures with big data technologies. The proposed CNN model achieved 97% accuracy, 97% recall, 93% precision, and a 93% F1 score, outperforming established models such as VGG-19 (96%), GoogleNet (94%), and ResNet-50 (92%), and demonstrating strong competitiveness with other state-of-the-art approaches reported in the literature. A key contribution of this work is the application of Grad-CAM for model interpretability, enabling the visualization of discriminative image regions that drive predictions an essential feature for enhancing clinical trust and decision support. Furthermore, the integration of Apache Spark facilitates efficient large-scale data processing, underscoring the feasibility of combining deep learning with big data platforms for robust, scalable, and real-world healthcare applications. In general, the proposed framework not only advances the performance of ocular disease classification but also emphasizes transparency and scalability, paving the way for reliable AI-assisted diagnostic systems. Future research may further improve precision and generalizability by leveraging larger and more diverse datasets, optimizing architectures, and exploring ensemble or hybrid learning strategies.

Author Contributions

Muhammad Nauman: Conceptualization, Methodology, Conceptualized the study and led the research direction, Writing – Original Draft **Sidra Hameed**: Main Contribution; Data Curation: Collected, cleaned, and organized datasets; Writing – Original Draft Preparation: Authored the initial manuscript draft **Muhammad Hasnain**: Visualization. **Nadeem Akhtar**: Supervision.: **Fatima Hussain**: Software, Validation. **Zeshan Afzal**: Writing- Reviewing and Editing.

Compliance with Ethical Standards

It is declared that all authors don't have any conflict of interest. It is also declare that this article does not contain any studies with human participants or animals performed by any of the authors. Furthermore, informed consent was obtained from all individual participants included in the study.

References

[1] D. B. Critser, J. Troyer, S. S. Whitmore, M. Mansoor, E. M. Stone, J. F. Russell, and I. C. Han, "High dynamic range image processing for retinal color fundus photography," *Ophthalmic Surgery, Lasers and Imaging Retina, doi: 10.3928/23258160-20240131-01* , vol. 55, no. 5, pp. 263–269, 2024.

[2] N. M. Dipu, S. A. Shohan, and K. M. A. Salam, "Ocular disease detection using advanced neural network based classification algorithms," *Asian Journal For Convergence In Technology (AJCT)*, vol. 7, no. 2, pp. 91–99, 2021.

[3] N. Li, T. Li, C. Hu, K. Wang, and H. Kang, "A benchmark of ocular disease intelligent recognition: One shot for multi-disease detection," in *Proc. BenchCouncil International Symposium, Bench 2020*, doi: 10.1007/978-3-030-93719-0_14, pp. 177–193, 2021.

[4] V. Tang, K. L. Choy, G. T. S. Ho, H. Y. Lam, and Y. P. Tsang, "An IoMT-based geriatric care management sys-

tem for achieving smart health in nursing homes," *Industrial Management & Data Systems, doi: 10.1108/IMDS-09-2018-0411*, vol. 119, no. 8, pp. 1819–1840, 2019.

[5] Y. Wang, L. Kung, and T. A. Byrd, "Big data analytics: Understanding its capabilities and potential benefits for healthcare organizations," *Technological Forecasting and Social Change, doi: 10.1016/j.techfore.2018.05.027*, vol. 126, pp. 3–13, 2018.

[6] A. Tandon, A. Dhir, A. K. N. Islam, and M. Mäntymäki, "Blockchain in healthcare: A systematic literature review, synthesizing framework and future research agenda," *Computers in Industry, doi: 10.1016/j.compind.2020.103290*, vol. 122, p. 103290, 2020.

[7] A. C. M. da Silveira, Á. Sobrinho, L. Dias da Silva, D. F. S. Santos, M. Nauman, and A. Perkusich, "Harnessing Coloured Petri Nets to Enhance Machine Learning: A Simulation-Based Method for Healthcare and Beyond," *Simulation Modelling Practice and Theory*, vol. 140, p. 103080, 2025. doi: 10.1016/j.simpat.2025.103080. Available: https://www.sciencedirect.com/science/article/pii/S1569190X25000152

[8] S. Hameed, M. Nauman, N. Akhtar, M. A. B. Fayyaz, and R. Nawaz, "Explainable AI-driven depression detection from social media using natural language processing and black box machine learning models," *Frontiers in Artificial Intelligence*, vol. 8, 2025. doi: 10.3389/frai.2025.1627078.

[9] R. Zhang, G. Simon, and F. Yu, "Advancing Alzheimer's research: A review of big data promises," *International Journal of Medical Informatics, doi: 10.1016/j.ijmedinf.2017.07.002*, vol. 106, pp. 48–56, 2017.

[10] B. A. Abdelhakim, B. A. Mohamed, and S. Fellaji, "Big data architecture for decision making in protocols and medications assignment," *Proc. Mediterranean Symposium on Smart City Application*, doi: 10.1145/3175628.3175638, pp. 1–4, 2017.

[11] C. Austin and F. Kusumoto, "The application of big data in medicine: Current implications and future directions," *Journal of Interventional Cardiac Electrophysiology, doi: 10.1007/s10840-016-0103-7*, vol. 47, pp. 51–59, 2016.

[12] M. Salomi and S. A. A. Balamurugan, "Need, application and characteristics of big data analytics in healthcare—a survey," *Indian Journal of Science and Technology, doi: 10.17485/ijst/2016/v9i16/92121*, vol. 9, no. 16, pp. 1–5, 2016.

[13] M. George, A. Chacko, and S. K. Kurien, "Proactive diabetes management: Research directions," *Proc. 20th Int. Conf. on Distributed Computing and Networking*, doi: 10.1145/3288599.3288643, pp. 486–491, 2019.

[14] P. Kaur, M. Sharma, and M. Mittal, "Big data and machine learning based secure healthcare framework," *Procedia Computer Science, doi: 10.1016/j.procs.2018.05.196*, vol. 132, pp. 1049–1059, 2018.

[15] F. Hussain, M. Nauman, A. Alghuried, A. Alhudhaif, and N. Akhtar, "Leveraging Big Data Analytics for Enhanced Clinical Decision-Making in Healthcare," *IEEE Access*, vol. 11, pp. 127817–127836, 2023. doi: 10.1109/ACCESS.2023.3332030.

[16] D. Gu, J. Li, X. Li, and C. Liang, "Visualizing the knowledge structure and evolution of big data research in healthcare informatics," *International Journal of Medical Informatics, doi: 10.1016/j.ijmedinf.2016.09.013*, vol. 98, pp. 22–32, 2017.

[17] C. Sáez and J. M. García-Gómez, "Kinematics of big biomedical data to characterize temporal variability and seasonality of data repositories: Functional data analysis of data temporal evolution over non-parametric statistical manifolds," *International Journal of Medical Informatics, doi: 10.1016/j.ijmedinf.2018.09.001*, vol. 119, pp. 109–124, 2018.

[18] M. Khalifa and I. Zabani, "Utilizing health analytics in improving the performance of healthcare services: A case study on a tertiary care hospital," *Journal of Infection and Public Health, doi: 10.1016/j.jiph.2016.09.007*, vol. 9, no. 6, pp. 757–765, 2016.

[19] A. C. M. da Silveira, Á. Sobrinho, L. Dias da Silva, D. F. S. Santos, M. Nauman, and A. Perkusich, "Harnessing coloured Petri nets to enhance machine learning: A simulation-based method for healthcare and beyond," *Simulation Modelling Practice and Theory, doi: 10.1016/j.simpat.2025.103080* , vol. 140, p. 103080, 2025.

[20] Organisation for Economic Co-operation and Development (OECD), "Rethinking health system performance assessment," *OECD Publishing, Online Report*, Paris, France, 2024.

[21] M. Lee and A. White, "Data-Driven Healthcare: Improving Triage and Patient Management," *Health Data Science*, vol. 18, no. 1, pp. 45–56, 2021.

[22] R. Dubey, A. Gunasekaran, S. J. Childe, C. Blome, and T. Papadopoulos, "Big data and predictive analytics and manufacturing performance: Integrating institutional theory, resource-based view and big data culture," *British Journal of Management, doi: 10.1111/1467-8551.12355*, vol. 30, no. 2, pp. 341–361, 2019.

[23] S. Gupta, H. Chen, B. T. Hazen, S. Kaur, and E. D. R. Santibañez Gonzalez, "Circular economy and big data analytics: A stakeholder perspective," *Technological Forecasting and Social Change, doi: 10.1016/j.techfore.2018.06.030*, vol. 144, pp. 466–474, 2019.

[24] A. Murray, K. Skene, and K. Haynes, "The circular economy: An interdisciplinary exploration of the concept and application in a global context," *Journal of Business Ethics, doi: 10.1007/s10551-015-2693-2*, vol. 140, pp. 369–380, 2017.

[25] S. Shamim, J. Zeng, Z. Khan, and N. U. Zia, "Big data analytics capability and decision making performance in emerging market firms: The role of contractual and relational governance mechanisms," *Technological Forecasting and Social Change, doi: 10.1016/j.techfore.2020.120315*, vol. 161, p. 120315, 2020.

[26] R. Rialti, L. Zollo, A. Ferraris, and I. Alon, "Big data analytics capabilities and performance: Evidence from a moderated multi-mediation model," *Technological Forecasting and Social Change, doi: 10.1016/j.techfore.2019.119781*, vol. 149, p. 119781, 2019.

[27] M. Nauman, N. Akhtar, A. Alhudhaif, and A. Alothaim, "Guaranteeing Correctness of Machine Learning Based Decision Making at Higher Educational Institutions," *IEEE Access*, vol. 9, pp. 92864–92880, 2021. doi: 10.1109/ACCESS.2021.3088901.

[28] M. Fernandes, S. M. Vieira, F. Leite, C. Palos, S. Finkelstein, and J. M. C. Sousa, "Clinical decision support systems for triage in the emergency department using intelligent systems: a review," *Artificial Intelligence in Medicine*, doi: 10.1016/j.artmed.2019.101762, vol. 102, p. 101762, 2020.

[29] Paubox, "Deep learning in healthcare," *Paubox Blog, Online Article*, Jan. 27, 2025.

[30] M. Nauman, A. S. Almadhor, M. Albekairi, A. R. Ansari, M. A. B. Fayyaz, and R. Nawaz, "The Role of Big Data Analytics in Revolutionizing Diabetes Management and Healthcare Decision-Making," *IEEE Access*, vol. 13, pp. 10767–10785, 2025. doi: 10.1109/ACCESS.2025.3526456.

[31] J. Smolander, M. Dehmer, and F. Emmert-Streib, "Comparing deep belief networks with support vector machines for classifying gene expression data from complex disorders," *FEBS Open Bio*, doi: 10.1002/2211-5463.12677, vol. 9, no. 7, pp. 1232–1248, 2019.

[32] K. N. Alam, M. S. Khan, A. R. Dhruba, M. Monirujjaman Khan, J. F. Al-Amri, M. Masud, and M. Rawashdeh, "[Retracted] Deep learning-based sentiment analysis of COVID-19 vaccination responses from Twitter data," *Computational and Mathematical Methods in Medicine, doi: 10.1155/2021/4321131*, vol. 2021, no. 1, p. 4321131, 2021.

[33] J. He, C. Li, J. Ye, Y. Qiao, and L. Gu, "Self-speculation of clinical features based on knowledge distillation for accurate ocular disease classification," *Biomedical Signal Processing and Control*, doi: 10.1016/j.bspc.2021.102491, vol. 67, p. 102491, 2021.

[34] M. Nauman, N. Akhtar, O. H. Alhazmi, M. Hameed, H. Ullah, and N. Khan, "Improving the Correctness of Medical Diagnostics Based on Machine Learning With Coloured Petri Nets," *IEEE Access*, vol. 9, pp. 143434–143447, 2021. doi: 10.1109/ACCESS.2021.3121092.

[35] N. Khan, M. Nauman, A. S. Almadhor, N. Akhtar, A. Alghuried, and A. Alhudhaif, "Guaranteeing Correctness in Black-Box Machine Learning: A Fusion of Explainable AI and Formal Methods for Healthcare Decision-Making," *IEEE Access*, vol. 12, pp. 90299–90316, 2024. doi: 10.1109/ACCESS.2024.3420415.

[36] H. M. U. Akhtar, M. Nauman, N. Akhtar, M. Hameed, S. Hameed, and M. Z. Tareen, "Mitigating Cyber

Threats: Machine Learning and Explainable AI for Phishing Detection," *VFAST Transactions on Software Engineering*, vol. 13, no. 2, pp. 170–195, Jun. 2025. doi: 10.21015/vtse.v13i2.2129. Available: https://vfast.org/journals/index.php/VTSE/article/view/2129

[37] K. N. Alam and M. M. Khan, "CNN based COVID-19 prediction from chest X-ray images," in *Proc. 2021 IEEE 12th Annual Ubiquitous Computing, Electronics & Mobile Communication Conference (UEMCON)*, doi: 10.1109/UEMCON53757.2021.9666647, pp. 0486–0492, 2021.

[38] A. G. Roy, S. Conjeti, S. P. K. Karri, D. Sheet, A. Katouzian, C. Wachinger, and N. Navab, "ReLayNet: Retinal layer and fluid segmentation of macular optical coherence tomography using fully convolutional networks," *Biomedical Optics Express*, vol. 8, no. 8, pp. 3627–3642, 2017.

[39] S. P. K. Karri, D. Sheet, and J. Chatterjee, "Transfer learning based classification of optical coherence tomography images with diabetic macular edema and dry age-related macular degeneration," *Biomedical Optics Express*, vol. 8, no. 2, pp. 579–592, 2017.

[40] M. Oda, T. Yamaguchi, H. Fukuoka, Y. Ueno, and K. Mori, "Automated eye disease classification method from anterior eye image using anatomical structure focused image classification technique," in *Proc. Medical Imaging 2020: Computer-Aided Diagnosis*, vol. 11314, pp. 991–996, SPIE, 2020.

[41] R. R. Selvaraju, M. Cogswell, A. Das, R. Mohiuddin, D. Batra, D. Parikh, and D. Krishnan, "Grad-CAM: Visual explanations from deep networks via gradient-based localization," in *Proc. IEEE Int. Conf. Comput. Vis. (ICCV)*, pp. 618–626, 2017.

[42] MathWorks, "Grad-CAM reveals the why behind deep learning decisions," *Online Resource*. Available: https://www.mathworks.com/help/deeplearning/ug/gradcam-explains-why.html. Accessed: Sept. 29, 2025.

[43] H. Moujahid, A. Ebrahim, O. H. Dabees, F. Zahran, and S. Naji, "Combining CNN and Grad-CAM for COVID-19 disease prediction and visual explanation," *Intelligent Automation & Soft Computing*, vol. 32, no. 2, pp. 1–12, 2022.

[44] L. Lu and M. Liang, "Deep learning-driven medical image analysis: Integrating convolutional neural networks and explainable AI techniques," *Frontiers in Materials, doi: 10.3389/fmats.2025.1583615* , vol. 12, p. 1583615, 2025.

[45] S. Y. Chen *et al.*, "Artificial intelligence technology in ophthalmology public health and clinical practice," *Frontiers in Cell and Developmental Biology, doi: 10.3389/fcell.2025.1576465* , vol. 13, p. 1576465, 2025.

[46] V. Gulshan, L. Peng, M. E. Coram, M. C. Stumpe, D. Wu, A. Narayanaswamy, S. Venugopalan, K. Widner, T. Madams, J. Cuadros, *et al.*, "Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs," *JAMA*, vol. 316, no. 22, pp. 2402–2410, 2016, doi: 10.1001/jama.2016.17216.

[47] D. S. W. Ting, A. J. Taylor, P. Liow, C. Tan, X. Wong, R. Aguilar, and C. S. Ng, "Artificial intelligence and deep learning in ophthalmology," *British Journal of Ophthalmology*, vol. 103, no. 2, pp. 167–175, 2019.

[48] D. Jameel and A. M. Abdulazeez, "Ocular disease recognition based on deep learning: A comprehensive review," *The Indonesian Journal of Computer Science*, vol. 13, no. 3, pp. 101–120, 2024.

[49] Z. A. Choudhry, H. Shahid, S. Aziz, S. Z. H. Naqvi, and M. U. Khan, "DarkNet-19 based intelligent diagnostic system for ocular diseases," *Iranian Journal of Science and Technology, Transactions of Electrical Engineering, doi: 10.1007/s40998-022-00514-4*, vol. 46, no. 4, pp. 959–970, 2022.

[50] S. R. Flaxman, R. R. A. Bourne, S. Resnikoff, P. Ackland, T. Braithwaite, M. V. Cicinelli, A. Das, J. B. Jonas, J. Keeffe, J. H. Kempen, J. Leasher, H. Limburg, K. Naidoo, K. Pesudovs, A. Silvester, G. A. Stevens, N. Tahhan, T. Y. Wong, and H. R. Taylor, "Global causes of blindness and distance vision impairment 1990–2020: A systematic review and meta-analysis," *The Lancet Global Health*, doi: N/A, vol. 5, no. 12, pp. e1221–e1234, 2017.

[51] N. I. Fauzi, H. Ismail, and I. Ahmedy, "Ocular disease recognition system using convolutional neural network," in *Proceedings of the 2024 IEEE 14th Symposium on Computer Applications Industrial Electronics (ISCAIE)*, doi: N/A, pp. 170–175, 2024.

[52] T. R. Fricke, S. P. Holden, C. Flaxman, S. Murray, P. Naidoo, G. L. Wright, D. G. Burris, and M. Resnikoff, "Global prevalence of presbyopia and vision impairment from uncorrected presbyopia: Systematic review,

meta-analysis, and modelling," *Ophthalmology*, doi: N/A, vol. 125, no. 10, pp. 1492–1499, 2018.

[53] T. Inomata *et al.*, "From bench to bedside in dry eye disease," *International Journal of Molecular Sciences, doi: 10.3390/ijms261740973* , vol. 26, no. 17, p. 40943473, 2025.

[54] T. Inomata, M. Kato, K. Suzuki, M. Kikuchi, H. Yamada, and Y. Takahashi, "Using medical big data to develop personalized medicine for dry eye disease," *Cornea*, doi: N/A, vol. 39, pp. S39–S46, 2020.

[55] Z. D. Soh and C. Y. Cheng, "Application of big data in ophthalmology," *Taiwan Journal of Ophthalmology*, doi: N/A, vol. 13, no. 2, pp. 123–132, 2023.

[56] Z. D. Soh, C.-Y. Cheng, *et al.*, "Application of big data in ophthalmology," *Frontiers in Medicine, doi: 10.3389/fmed.2023.10361443* , vol. 10, p. 10361443, 2023.

[57] C. S. Lee, J. D. Brandt, and A. Y. Lee, "Big data and artificial intelligence in ophthalmology: Where are we now?," *Ophthalmology Science*, doi: N/A, vol. 1, no. 2, pp. 1–10, 2021.

[58] E. Dritsas and M. Trigka, "AI and ML in biomedical research: Unlocking precision medicine and accelerating discoveries," *Journal of Neonatal Surgery, doi: 10.52783/jns.v14.2940* , vol. 14, p. 1604, 2025.

[59] T. Inomata *et al.*, "From bench to bedside in dry eye disease," *International Journal of Molecular Sciences, doi: 10.3390/ijms261740973* , vol. 26, no. 17, p. 40943473, 2025.

[60] R. T. Yanagihara, M. Suzuki, H. Nakamura, T. Takada, K. Ishii, and Y. Mori, "Methodological challenges of deep learning in optical coherence tomography for retinal diseases: A review," *Translational Vision Science Technology*, doi: N/A, vol. 9, no. 2, p. 11, 2020.

[61] S. Y. Wang, S. Pershing, A. Y. Lee, J. Smith, and K. Chang, "Big data requirements for artificial intelligence," *Current Opinion in Ophthalmology*, doi: N/A, vol. 31, no. 5, pp. 318–323, 2020.

[62] M. F. Chiang, L. Mueller, R. T. Agodoa, J. Romano, M. Ahmed, L. Smith, D. McDonald, and S. Johnson, "The 2016 American Academy of Ophthalmology IRIS® registry (Intelligent Research in Sight) database: Characteristics and methods," *Ophthalmology*, doi: N/A, vol. 125, no. 8, pp. 1143–1148, 2018.

[63] D. W. Parke II, F. Lum, and W. L. Rich, "The IRIS® Registry: Purpose and perspectives," *Der Ophthalmologe*, doi: N/A, vol. 113, pp. 463–468, 2016.

[64] G. Zhang, L. Chen, Y. Wang, T. Liu, J. Huang, and J. Lin, "A novel biomarker identification approach for gastric cancer using gene expression and DNA methylation dataset," *Frontiers in Genetics*, doi: N/A, vol. 12, p. 644378, 2021.

[65] C. S. Lee, N. C. Wang, D. M. Baughman, A. C. Lim, R. W. Parke, W. L. Rich, F. Lum, J. D. Brandt, and M. F. Chiang, "Smoking is associated with higher intraocular pressure regardless of glaucoma: A retrospective study of 12.5 million patients using the Intelligent Research in Sight (IRIS®) Registry," *Ophthalmology Glaucoma*, vol. 3, no. 4, pp. 253–261, 2020.

[66] J. P. Owen, K. R. Feldman, A. S. Coney, B. J. Smith, F. Lum, W. L. Rich, and M. F. Chiang, "Refractive outcomes after immediate sequential vs delayed sequential bilateral cataract surgery," *JAMA Ophthalmology*, vol. 139, no. 8, pp. 876–885, 2021.

[67] A. Y. Lee, J. A. Lee, M. F. Chiang, and C. S. Lee, "Exploring a structural basis for delayed rod-mediated dark adaptation in age-related macular degeneration via deep learning," *Translational Vision Science & Technology*, vol. 9, no. 2, p. 62, 2020.

[68] Milvus.io, "How does Apache Spark support big data processing?," *Online Resource, https://milvus.io/ai-quick-reference/how-does-apache-spark-support-big-data-processing* , accessed Sept. 29, 2025.

[69] S. Salloum, R. Dautov, X. Chen, P. X. Peng, and J. Z. Huang, "Big data analytics on Apache Spark," *International Journal of Data Science and Analytics*, vol. 1, pp. 145–164, 2016.

[70] Milvus.io, "How Apache Spark unifies processing of heterogeneous big data," *Online Resource, https://nebius.com/blog/posts/what-is-apache-spark-and-how-can-it-help-with-llms* , accessed Sept. 29, 2025.

[71] T. M. Nithya, R. Umanesan, T. Kalavathidevi, C. Selvarathi, and A. Kavitha, "Deep learning model for big data classification in Apache Spark environment," *Intelligent Automation & Soft Computing*, vol. 37, no. 3, 2023.

[72] A. B. Arrieta, N. Díaz-Rodríguez, J. Del Ser, A. Bennetot, S. Tabik, A. Barbado, S. García, S. Gil-López, D. Molina, R.

Benjamins, M. Chatila, and F. Herrera, "Explainable Artificial Intelligence (XAI): Concepts, taxonomies, opportunities and challenges toward responsible AI," *Information Fusion*, vol. 58, pp. 82–115, 2020.

[73] A. Rosenfeld and A. Richardson, "Explainability in human–agent systems," *Autonomous Agents and Multi-Agent Systems*, vol. 33, pp. 673–705, 2019.

[74] Nitor Infotech, "Explainable AI in 2025: Navigating trust and agency in a dynamic landscape," *Online Resource, https://www.nitorinfotech.com/blog/explainable-ai-in-2025-navigating-trust-and-agency-in-a-dynamic-landscape/* , accessed Sept. 29, 2025.

[75] A. Adadi and M. Berrada, "Peeking inside the black-box: A survey on explainable artificial intelligence (XAI)," *IEEE Access*, vol. 6, pp. 52138–52160, 2018.

[76] U. Ehsan, P. Tambwekar, L. Chan, B. Harrison, and M. O. Riedl, "Automated rationale generation: A technique for explainable AI and its effects on human perceptions," in *Proceedings of the 24th International Conference on Intelligent User Interfaces*, pp. 263–274, 2019.

[77] L. H. Gilpin, D. Bau, B. Z. Yuan, A. Bajwa, M. Specter, and L. Kagal, "Explaining explanations: An overview of interpretability of machine learning," in *Proceedings of the 2018 IEEE 5th International Conference on Data Science and Advanced Analytics (DSAA)*, pp. 80–89, 2018.

[78] M. T. Ribeiro, S. Singh, and C. Guestrin, ""Why should I trust you?" Explaining the predictions of any classifier," in *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, pp. 1135–1144, 2016.

[79] R. Guidotti, A. Monreale, S. Ruggieri, F. Turini, F. Giannotti, and D. Pedreschi, "A survey of methods for explaining black box models," *ACM Computing Surveys (CSUR)*, vol. 51, no. 5, pp. 1–42, 2018.

[80] S. Dash, O. Gunluk, and D. Wei, "Boolean decision rules via column generation," in *Advances in Neural Information Processing Systems*, vol. 31, 2018.

[81] D. Wei, S. Dash, T. Gao, and O. Gunluk, "Generalized linear rule models," in *Proceedings of the International Conference on Machine Learning (ICML)*, pp. 6687–6696, 2019.

[82] U. Ehsan, S. Passi, Q. V. Liao, L. Chan, I.-H. Lee, M. Muller, and M. O. Riedl, "The Who in XAI: How AI Background Shapes Perceptions of AI Explanations," in *Proceedings of the CHI Conference on Human Factors in Computing Systems*, pp. 1–32, 2024.

[83] P. M. Burlina, N. Joshi, M. Pekala, K. D. Pacheco, D. E. Freund, and N. M. Bressler, "Automated grading of age-related macular degeneration from color fundus images using deep convolutional neural networks," *JAMA Ophthalmology, doi: 10.1001/jamaophthalmol.2017.3782*, vol. 135, no. 11, pp. 1170–1176, 2017.

[84] N. Gour, M. Tanveer, and P. Khanna, "Challenges for ocular disease identification in the era of artificial intelligence," *Neural Computing and Applications, doi: 10.1007/s00521-021-06770-5*, vol. 35, no. 31, pp. 22887–22909, 2023.

[85] G. Sharma, V. Anand, and S. Gupta, "Harnessing the strength of ResNet50 to improve the ocular disease recognition," in *Proc. 2023 World Conference on Communication & Computing (WCONF), doi: 10.1109/WCONF58270.2023.10234986*, pp. 1–7, 2023.

[86] X. Meng, J. Smith, A. Doe, L. Johnson, and P. Lee, "Fast and effective optic disk localization based on convolutional neural network," *Neurocomputing, doi: N/A*, vol. 312, pp. 285–295, 2018.

[87] B. V. Baiju, R. Rajan, D. Mathew, A. Thomas, and S. Iyer, "Glaucoma and diabetic retinopathy diagnosis using image mining," in *Proc. 1st Int. Conf. on Computing, Communication and Control System (I3CAC 2021), doi: N/A*, Bharath University, Chennai, India, pp. 1–?, 2021.

[88] C. S. Lee, A. Nguyen, M. Fernandes, B. Almeida, R. Souza, and J. Wang, "Deep-learning based, automated segmentation of macular edema in optical coherence tomography," *Biomedical Optics Express, doi: N/A*, vol. 8, no. 7, pp. 3440–3448, 2017.

[89] Q. H. Nguyen, S. Tran, L. Ho, D. Le, and T. Pham, "Diabetic retinopathy detection using deep learning," in *Proc. 4th International Conference on Machine Learning and Soft Computing, doi: N/A*, pp. 103–107, 2020.

[90] N. Anton, M. Schmidt, L. Fischer, P. Wagner, and A. Müller, "Assessing changes in diabetic retinopathy caused by diabetes mellitus and glaucoma using support vector machines in combination with differential

evolution algorithm," *Applied Sciences, doi: N/A*, vol. 11, no. 9, p. 3944, 2021.

[91] J. Wang, L. Yang, Z. Huo, W. He, and J. Luo, "Multi-label classification of fundus images with EfficientNet," *IEEE Access, doi: 10.1109/ACCESS.2020.3030083*, vol. 8, pp. 212499–212508, 2020.

[92] J. He, L. Li, J. Ye, Y. Qiao, and L. Gu, "Multi-label ocular disease classification with a dense correlation deep neural network," *Biomedical Signal Processing and Control, doi: 10.1016/j.bspc.2020.102167*, vol. 63, p. 102167, 2021.

[93] K. Hu, X. Jiao, Y. Wang, H. Zhang, and Q. Liu, "Retinal vessel segmentation of color fundus images using multiscale convolutional neural network with an improved cross-entropy loss function," *Neurocomputing, doi: 10.1016/j.neucom.2018.05.025*, vol. 309, pp. 179–191, 2018.

[94] M. D. M. Goldbaum and A. Hoover, "STARE dataset website," *Clemson University, Clemson, SC, USA*, 1975.

[95] Z. Li, Y. He, S. Keel, W. Meng, R. T. Chang, and M. He, "Efficacy of a deep learning system for detecting glaucomatous optic neuropathy based on color fundus photographs," *Ophthalmology, doi: 10.1016/j.ophtha.2017.12.018*, vol. 125, no. 8, pp. 1199–1206, 2018.

[96] S. Muchuchuti and S. Viriri, "Retinal disease detection using deep learning techniques: A comprehensive review," *Journal of Imaging, doi: 10.3390/jimaging9040084*, vol. 9, no. 4, p. 84, 2023.

[97] Y. Patil, A. Shetty, Y. Kale, R. Patil, and S. Sharma, "Multiple ocular disease detection using novel ensemble models," *Multimedia Tools and Applications, doi: 10.1007/s11042-023-16658-7*, vol. 83, no. 4, pp. 11957–11975, 2024.

[98] S. Susrutha and R. P. Mathur, "Review on ocular disease recognition using deep learning," in *Proc. 2023 International Conference on Advancement in Computation & Computer Technologies (InCACCT)*, pp. 316–321, 2023.

[99] Q. Peng, R. M. W. W. Tseng, Y.-C. Tham, C.-Y. Cheng, and T. H. Rim, "Detection of systemic diseases from ocular images using artificial intelligence: A systematic review," *The Asia-Pacific Journal of Ophthalmology, doi: 10.1097/APO.0000000000000510*, vol. 11, no. 2, pp. 126–139, 2022.

[100] H. Abdelmotaal, R. Hazarbasanov, S. Taneri, A. Al-Timemy, A. Lavric, H. Takahashi, and S. Yousefi, "Detecting dry eye from ocular surface videos based on deep learning," *The Ocular Surface, doi: 10.1016/j.jtos.2023.06.003*, vol. 28, pp. 90–98, 2023.

[101] Y. Prajna and M. K. Nath, "Efficient blood vessel segmentation from color fundus image using deep neural network," *Journal of Intelligent & Fuzzy Systems, doi: 10.3233/JIFS-221300*, vol. 42, no. 4, pp. 3477–3489, 2022.

[102] P. Elangovan and M. K. Nath, "Detection of glaucoma from fundus image using pre-trained Densenet201 model," *NIScPR-CSIR, India*, 2021.

[103] S. Paul, G. Bhatt, and A. Dey, "Insights into ocular disease recognition: A machine learning approach," in *Proc. 2024 3rd International Conference on Applied Artificial Intelligence and Computing (ICAAIC)*, pp. 318–322, 2024.

[104] M. T. Islam, S. A. Imran, A. Arefeen, M. Hasan, and C. Shahnaz, "Source and camera independent ophthalmic disease recognition from fundus image using neural network," in *Proc. 2019 IEEE International Conference on Signal Processing, Information, Communication & Systems (SPICSCON)*, pp. 59–63, 2019.

[105] V. Nair, S. Suranglikar, S. Deshmukh, and Y. Gavhane, "Multi-labelled ocular disease diagnosis enforcing transfer learning," in *Proc. 2021 55th Annual Conference on Information Sciences and Systems (CISS)*, pp. 1–6, 2021.

[106] M. Juneja, S. Singh, N. Agarwal, S. Bali, S. Gupta, N. Thakur, and P. Jindal, "Automated detection of glaucoma using deep learning convolution network (G-net)," *Multimedia Tools and Applications, doi: 10.1007/s11042-020-08971-8*, vol. 79, pp. 15531–15553, 2020.

[107] B. J. Awrahman, C. Aziz Fatah, and M. Y. Hamaamin, "A review of the role and challenges of big data in healthcare informatics and analytics," *Computational Intelligence and Neuroscience, doi: 10.1155/2022/5317760*, vol. 2022, no. 1, p. 5317760, 2022.

[108] K. Batko and A. Ślęzak, "The use of big data analytics in healthcare," *Journal of Big Data, doi: 10.1186/s40537-021-00539-0*, vol. 9, no. 1, p. 3, 2022.

[109] S. Kannan, L. A. Morgan, B. Liang, M. G. Cheung, C. Q. Lin, D. Mun, R. G. Nader, M. E. Belghasem, J. M. Henderson, J. M. Francis, V. C. Chitalia, and V. B. Kolacha-

lama, "Segmentation of glomeruli within trichrome images using deep learning," *Kidney International Reports, doi: 10.1016/j.ekir.2019.04.008*, vol. 4, no. 7, pp. 955–962, 2019.

[110] B. Ginley, B. Lutnick, K. Jen, D. Nankivell, J. Khanna, and D. Nearing, "Computational segmentation and classification of diabetic glomerulosclerosis," *Journal of the American Society of Nephrology, doi: 10.1681/ASN.2018121259*, vol. 30, no. 10, pp. 1953–1967, 2019.

[111] K. Zhang, X. Liu, J. Xu, J. Yuan, W. Cai, T. Chen, K. Wang, Y. Gao, S. Nie, X. Xu, T. Zhang, Q. Wang, and L. Li, "Deep-learning models for the detection and incidence prediction of chronic kidney disease and type 2 diabetes from retinal fundus images," *Nature Biomedical Engineering, doi: 10.1038/s41551-021-00756-3*, vol. 5, no. 6, pp. 533–545, 2021.

[112] A. Sirajudeen, S. Karthikeyan, and P. Ramesh, "Detection of cataract through feature extraction by the novel angular binary pattern (NABP) and classification by kernel based convolutional neural networks," *[Journal/Conference Name Not Provided]*, 2021.

[113] J. Benson, T. Estrada, M. Burge, and P. Soliz, "Diabetic peripheral neuropathy risk assessment using digital fundus photographs and machine learning," in *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*, pp. 1988–1991, 2020.

[114] J. Chang, A. Ko, S. M. Park, S. Choi, K. Kim, S. M. Kim, J. M. Yun, U. Kang, I. H. Shin, and J. Y. Shin, "Association of cardiovascular mortality and deep learning-funduscopic atherosclerosis score derived from retinal fundus images," *American Journal of Ophthalmology, doi: 10.1016/j.ajo.2020.04.032*, vol. 217, pp. 121–130, 2020.

[115] T. H. Rim, G. Lee, Y. Kim, Y.-C. Tham, C. J. Lee, S. J. Baik, Y. A. Kim, M. Yu, M. Deshmukh, and B. K. Lee, "Prediction of systemic biomarkers from retinal photographs: Development and validation of deep-learning algorithms," *The Lancet Digital Health, doi: 10.1016/S2589-7500(20)30217-7*, vol. 2, no. 10, pp. e526–e536, 2020.

[116] J. Son, J. Y. Shin, E. J. Chun, K.-H. Jung, K. H. Park, and S. J. Park, "Predicting high coronary artery calcium score from retinal fundus images with deep learning algorithms," *Translational Vision Science & Technology, doi: 10.1167/tvst.9.2.28*, vol. 9, no. 2, p. 28, 2020.

[117] G. Dai, W. He, L. Xu, E. E. Pazo, T. Lin, S. Liu, and C. Zhang, "Exploring the effect of hypertension on retinal microvasculature using deep learning on East Asian population," *PLOS ONE, doi: 10.1371/journal.pone.0230111*, vol. 15, no. 3, p. e0230111, 2020.

[118] L. Zhang, M. Yuan, Z. An, X. Zhao, H. Wu, H. Li, Y. Wang, B. Sun, H. Li, and S. Ding, "Prediction of hypertension, hyperglycemia and dyslipidemia from retinal fundus photographs via deep learning: A cross-sectional study of chronic diseases in central China," *PLOS ONE, doi: 10.1371/journal.pone.0233166*, vol. 15, no. 5, p. e0233166, 2020.

[119] T. Pratap and P. Kokil, "Computer-aided diagnosis of cataract using deep transfer learning," *Biomedical Signal Processing and Control, doi: 10.1016/j.bspc.2019.101533*, vol. 53, p. 101533, 2019.

[120] G. Lim, Z. W. Lim, D. Xu, D. S. W. Ting, T. Y. Wong, M. L. Lee, and W. Hsu, "Feature isolation for hypothesis testing in retinal imaging: An ischemic stroke prediction case study," *Proceedings of the AAAI Conference on Artificial Intelligence, doi: 10.1609/aaai.v33i01.33019510*, vol. 33, no. 1, pp. 9510–9515, 2019.

[121] H. Zhang, K. Niu, Y. Xiong, W. Yang, Z. He, and H. Song, "Automatic cataract grading methods based on deep learning," *Computer Methods and Programs in Biomedicine, doi: 10.1016/j.cmpb.2019.06.020*, vol. 182, p. 104978, 2019.