Explainable Retinal Image Analysis for Early Detection of Systemic and Ocular Diseases

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***Abstract*— Fundus imaging of the retina has been popularized due to its usage as a non-invasive method for analyzing blood vessels in the retina to aid in the diagnosis of diseases. Nevertheless, there are numerous existing Computer Aided Diagnosis (CAD) systems that have black box models as their core architecture; thus, it is difficult to trust such methods. To solve this problem, we present an interpretable method to diagnose various diseases using Retinal Fundus Images. We do this by incorporating a fractal- based feature extraction along with the Explainable Machine Learning models to perform the task of diagnosing diseases using the image of blood vessels. Fractal analysis has been incorporated into our algorithm to capture structural complexities of the blood vessels and extract the relevant features to detect disease related alterations. Finally, we use these features to perform classification via machine learning as well as deep learning algorithms and estimate the likelihood of various diseases like diabetic retinopathy, glaucoma, hypertension among others.**

Keywords*— *Retinal Fundus Images, Fractal Features, Explainable Machine Learning, Multi-Disease Detection, Medical Image Analysis.

I. INTRODUCTION

The ability to non-invasively identify both ocular and systemic disease through the analysis of structural and vascular characteristics in retinal fundus images have establish this imaging modality as an effective method for obtaining this type of information. The visibility of blood vessels in retinal images has become an important pathway for detecting the presence of various diseases early, such as diabetic retinopathy, glaucoma, and hypertension; therefore, the increasing prevalence of these diseases has created the need for more automated and scalable diagnostic solutions to provide clinical support when early screening and/or decision-making occurs.

Recent advancements in artificial intelligence have greatly improved the diagnostic capabilities of these non-invasive methods of diagnosis through the use of retinal images. In recent studies, deep-learning model performance, particularly with the use of convolutional neural networks, have proven very effective for the identification of retinal disease at a high level of accuracy [1], [3], [12]. Furthermore, many of the publicly available datasets that are used to support these efforts have been introduced in order to assist with the development of robust learning models, including the FIVES database [2]. Several researchers have examined image enhancement techniques for the purpose of improving the quality of fundus images, as well as the ability to extract features from fundus images to achieve better diagnostic performance [5].

Several studies have shown that increasing the accuracy of classifying images can be obtained by combining deep learning algorithms, called meta-classifiers or ensemble methods [6], whereas other researchers have used machine-learning algorithms to identify the features of diseases that may predict the presence of high myopia by analyzing the structure of the retina [7]. Advanced architectures such as Vision Transformers have also demonstrated potential through their application to the diagnosis of retinal diseases, together with the use of visualization techniques like Grad-CAM, which allow for the identification of key areas in images [9].

While improvements in classification have occurred, many models are classified as black boxes with very little information provided about their decision processes. Therefore, new ways to improve the interpretability of medical diagnoses have been explored using explainable artificial intelligence (XAI) approaches [10][15]. XAI visually and/or feature-based explanation techniques enable the investigation of how models are made, allowing doctors to have a better understanding of how models generate predictions. However, even when an XAI approach is used, the model features may not provide clinically significant information because they do not address the interpretation of models prior to their application.

The use of fractal analysis as a method of quantifying the irregularity of retinal blood vessels has also been shown to quantify vascular irregularities due to disease through measurement of fractal dimensions. However, these methods suffer from limitations regarding their scope and thus have not yet been incorporated into current machine learning paradigms and explainable frameworks for providing comprehensive detection of diseases.

In addition, most existing systems only support single disease classifications and do not include the ability to detect multiple diseases simultaneously. Furthermore, a vast majority of the published literature on this subject only focuses on developing models with no provision for an integrated, end-to-end framework that encompasses preprocessing, prediction, explanation, and reporting as essential components in order to support the use of these technologies in actual healthcare settings.

An Explainable AI based detection system for multiple diseases using retinal fundus images, offering probabilities of disease presence and severity levels along with suitable explanations for medical screening. It also provides a complete pipeline for real life clinical use from preprocessing through prediction, visualization, and automated reporting.

II. Literature Review

A. Deep Learning-Based Retinal Disease Detection

Deep learning approaches, especially convolutional neural networks, have been used extensively as part of recent research into retinal images to detect various disorders such as diabetic retinopathy and glaucoma, etc., e.g., [1], [3], and [12]. Although deep learning models have performed very well with high degrees of accuracy in detecting many retinopathy and glaucoma disorders, they tend to function as black boxes and therefore do not provide much insight into the predictions being made. Unfortunately, the inability of deep learning models to provide interpretability limits their usefulness in clinical environments where there is usually a strong emphasis on transparent and interpretable processes.

B. Retinal Image Datasets and Preprocessing Techniques

The effectiveness of automated diagnosis systems is contingent on sufficient high-quality datasets and pre-processing techniques. In the FIVES dataset published by Jin et al. [2] to perform vessel segmentation, retinal structures are extracted accurately using computer vision methods. Additionally, Lee et al. [5] introduced an image enhancement technique that enhances the quality of fundus images; however, while these two advancements will help provide better-quality data and make features visible, they do not provide an entire diagnostic system (i.e., they are limited to pre-processing).

C. Advanced Machine Learning and Multi-Model Approaches

Various advanced architectures and ensemble learning methodologies have been researched to improve classification performance. Hemal and Saha [6] developed a multiple-model/multiple-classifier meta-classifier to perform multi-label classifications using combinations of various deep learning algorithms and hybrid machine learning algorithms. Also, Zou et al. [7] developed separate model-based machine learning algorithms to detect different structural characteristics associated with certain patient conditions (i.e., high myopia). Though these approaches improve the accuracy of the predictions/ classifications, they usually have increased computational complexity and limitations with regard to the types of diseases that can be detected, as they generally provide diagnostic capabilities only for a specific type of disease rather than collectively classifying multiple diseases.

D. Explainable Artificial Intelligence in Medical Imaging

The emergence of Explainable AI aims to fill the gap of explainable deep learning models. Bhuiyan et al. [9] used Grad-CAM to provide visual explanations about how their model arrived at its prediction, while Bhatt et al. [10] and Belle and Papantonis [15] stressed that interpretability is a necessity within the healthcare domain. Muduli et al. [11] additionally worked on developing explainable models for glaucoma diagnosis. However, the majority of current solutions implement explainability as a post-process without ensuring that the original features used in training are clinically relevant.

E. Fractal Analysis of Retinal Vasculature

Fractal analysis is a method being investigated to quantify the complexity and irregularity of blood vessels in the retina. Venkataramani et al. [4] have shown the ability of fractal dimension to quantify the changes in vessels that occur due to disease, but most of the existing methods are based on feature extraction only and therefore lack integration with contemporary machine learning and explainable frameworks which limits the extent of their practical use.

F. Medical Imaging Advancements Beyond Retinal Analysis

The progression of research in other areas of the medical imaging field has led to advances in disease diagnostics. For instance, Nicolaou and colleagues [8] used quantitative MRI analysis to evaluate patients with neurological disorders; Song and colleagues [14] developed deep learning models to create new imaging modalities from retinal images developed with advanced imaging technologies. Despite these two examples providing evidence that there is promise for AI applications within the medical field in general, neither of these studies provides an integrated, explainable framework for detecting retinal diseases.

III. Proposed Methodology Architecture

The combination of Artificial Intelligence, Deep Learning, and a Web Application has created a full Retinal Diagnostic Platform utilizing performance to acquire Retinal Fundus Images and patient records over a remote maintenance procedure. Preprocessing steps are taken in order to make sure the resulting images are consistent through processes such as resizing, noise reduction, contrast enhancement, and normalization before image analysis via Convolutional Neural Networks (CNNs) is conducted to extract features from the images to classify multiple retinal disease(s) with a probability score assigned to each individual disease instead of obtaining a single output/classification. Thus, providing much more detailed and accurate diagnosis results.

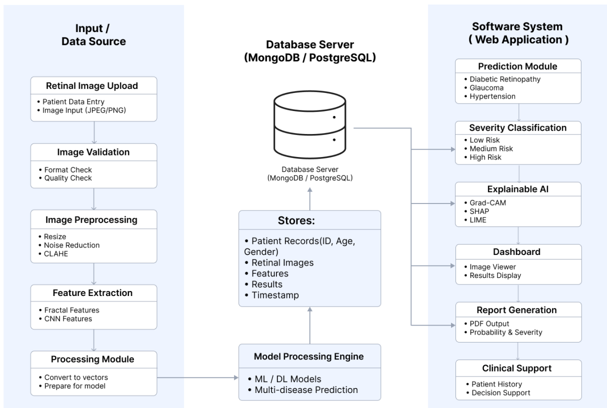

Fig. 1. Architecture for Retinal Disease Diagnosis

A. Acquisition Of Retinal Images/Initialization Of Patient Session

A simple interface facilitates secure upload of retinal fundus images. The system accepts retinal fundus images in standard formats (i.e., JPEG, PNG, TIFF). In conjunction with uploaded images, patient demographic information will be

captured, including automatically generated patient ID, name, age, and gender.
Key Functions:
1. Upload images through drag-and-drop or browse method.
2. Validate and check each uploaded image for standard parameters (format and resolution).
3. Automatically generate a unique patient ID
4. Create time-stamped entries.
This module is designed to establish and maintain data integrity and to provide traceability for the data maintained by the system, as well as provide a defined methodology to enter data into the system that will support all future activities based on this data.

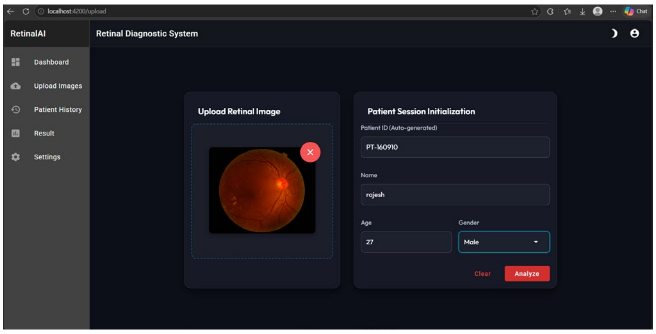

Fig. 2. Retinal fundus image acquisition, secure upload, and patient session initialization in the proposed diagnostic system

B. *Automated Image Enhancement and Diagnostic Standardization*

Once a retinal fundus image has been uploaded, it will be automatically enhanced so that its quality will remain constant even though the conditions used to obtain the images may differ (e.g., due to lighting differences). Such differences have the potential to negatively impact the accuracy of any subsequent deep learning models. So, image preprocessing is performed to "standardize" images prior to using them as input to deep learning models. The enhancement process will include resizing the image, reducing noise levels, increasing contrast, and normalizing pixel intensity values. Pixel intensity normalization will be performed by transforming all pixel intensity values into a common range using the following formula:

$$I_{norm}(x, y) = \frac{I(x, y) - \min(I)}{\max(I) - \min(I)}$$

To assist with visualizing retinal structures such as blood vessels and lesions, Contrast-Limited Adaptive Histogram Equalization (CLAHE) is applied to the images to enhance local contrast, but will not enhance noise. Furthermore, the automation provides users with an interactive interface, allowing users to see a variety of different image views - e.g., normal, red-free, inverted, and contrast-enhanced image views. A deep learning algorithm will then analyze and classify each image based on the processed image provided as input.

Fig. 3. Retinal image enhancement process breakdown

C. *Disease Probability Estimation and Severity Stratification*

The finished image of the retina is then analyzed using a diagnostic decision support system, generating an estimated probability score for ocular and systemic diseases. The system produces risk values based on the estimated probability score of the diseases as opposed to the traditional classification model, allowing for more valuable information provided as part of the clinical input used to find and track the diseases. The risk value is assigned to the respective disease by mapping the probability score to the appropriate medical risk range. The finished image of the retina will then be analyzed/determined through a decision support system analysis to calculate the probability that a specific disease(s) exists based on the analysis, using the pre-defined clinical thresholds. The Probability of the disease is based on the following equation:

$$P(d_i \mid x) = \frac{1}{(1 + e^{-z})}$$

where z is the model score. The outcomes are presented through the use of color-coded severity identifiers and probability statements

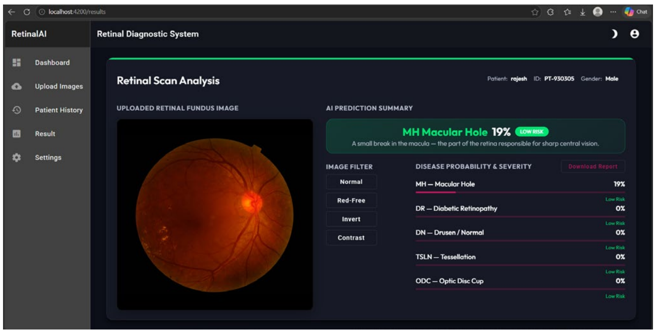

Fig. 4. Disease Probability Estimation and Severity Stratification

D. *Explainable Diagnostic Visualization and Clinical Inter- pretability*

A system has been created that will help improve the confidence and transparency of clinical diagnosis through an explainable ai module that shows the regions of the retinal image contributing to the prediction made by the model. This contrasts with current black box models, allowing users to see how the model produced its prediction and as such, help users trust clinicians, creating a more interpretable model. Furthermore, the areas highlighted will include clinically relevant areas (optic disc, blood vessels, and lesions) to ensure the region identified correlates with the medical significance of the area. The explainability is completed using Grad-CAM that generates a visual heat map defining the region of interest in the retinal image. The representation of the Grad-CAM is defined as:

$$L_{\text{Grad}-\text{CAM}} = \text{ReLU}\left(\text{k}\sum \alpha\text{k}A\text{k}\right)$$

Where Ak is the kth feature map and αk is the weight associated with the kth feature map. The heat map produced by the Grad-CAM is then overlaid onto the original retinal image to produce a visual representation of what has contributed to the model's prediction. In addition, the system also provides an interactive visualization letting users explore the architecture of the retina using various enhancement techniques (contrast and red-free filtering) as well as through image inversion; overall, all of these pieces combined provide a complete explainable solution.

E. Secure Patient Data Storage and Longitudinal Case Management

Metadata includes an explanation of each individual record type and a timestamp. The patient record is structured according to defined rules as follows:

PatientRecord = {ID, ImageRef, Pi, Severityi, Time}

where ID is the unique identifier for an anonymous patient, ImageRef is the reference number of the retinal image that has been saved, Pi is the probability of the disease that has been assessed, Severityi is the severity of the disease, and Time is the date and time when the assessment was performed. These are the various features that are offered by the user interface (UI) as a means of supporting practical applications of patient records within a clinical environment such as patient history dashboards, retrieving and comparing cases, and visualizing disease progression through timelines. This phase of the project will enable the hospital to provide practical clinical services such as follow-up screening, longitudinal monitoring, and evaluating outcomes. Good data management is provided through secure storage methods and will allow the system to be used for many years to come, creating a sustainable solution for many hospitals.

F. Automated Diagnostic Report Generation

A fully automated diagnostic report is generated by the automated retinal analysis system that presents the results of the retinal analysis in a clear manner and with clinical significance. The report contains the percentage of the patient at risk for developing any of the diseases, how severe the diseases may be, what visual outputs would be expected, and a risk index that provides a measure of the patient's overall risk. The report also supports consistent and efficient evaluations, and can be printed as a PDF or exported for further analysis. The report will assist Clinician in their clinical decision making, but is not intended to supplant or replace a Clinician's professional judgement.

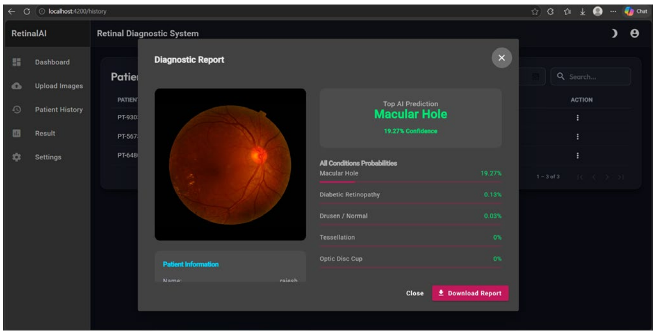

Fig. 5. Automated Patient Report Generation and Clinical Documentation

IV. Technologies Used

A. Angular for User Interface Development

The intent of this report was to create an easy-to-use, real time diagnostic application through which users would be able to obtain a better understanding of their disease predictions. The application uses Angular built in data binding to allow the user instantaneous updates for probability scores, along with user-friendly step-by-step directions for how those scores were calculated. The user is also able to upload medical imaging data, and is presented with an interactive dashboard displaying an organized set of viewable, easy-to-understand health-related data (many different types). In addition, to create a visually appealing and user-friendly design, we utilized Angular Material, which has pre-designed components (i.e. card, table, dialog, progress-bar, etc.) to organize and present crucial information regarding a predicted disease's probability, severity and representation of data in a graphical way such that a user can readily understand it. Ultimately, the design of this application enables the healthcare provider and the user to reach more timely, accurate decisions about their results compared to older traditional AI systems.

B. Python for Backend Development

The central backend technology being employed in this system is from Python because of the power of its flexibility and degree of molecular support given to the discipline of medical image analysis and machine learning. Python has a role beyond the basic technical aspects; it also enables fractal based feature calculation/estimation and implements Explainable AI (XAI) or Probabilistic XAI. The system uses Python to perform analytical and interpretive functions, which will enhance the development of an intelligent, clinically relevant, and superior alternative to traditional systems that are only predictive.

C. RESTful API using Python (Flask/FastAPI)

The RESTful API built in FastAPI or Flask framework allows smooth communication between the frontend and the backend of the project. The RESTful API executes some critical operations such as secure image uploading, predicting model, fetching output, and creating comprehensive diagnostic reports. Instead of building the application in a monolithic fashion whereby all the modules of the software interact directly with one another, this project is designed using a modular architecture to allow separate services to run independently and scale effectively. Apart from facilitating efficiency and ease of maintenance, the modular architecture will make the process of integrating the application with existing healthcare IT tools such as hospital information systems and telehealth applications simple.

D. Image Processing Libraries (OpenCV and scikit-image)

Libraries like OpenCV and scikit-image are widely used in order to conduct a detailed preprocessing of retinal fundus images to ensure quality input data for the following analyses. Preprocessing includes rescaling images into a single resolution, normalization of pixel values, noise reduction by means of applying filtering algorithms, as well as enhancing contrast. All these actions help to emphasize fine details of retinal vessels that play an important role in the diagnosis of certain pathological states. Moreover, blood vessels can be isolated and segmented through the application of advanced image processing algorithms provided by these libraries, as a result of which clinicians receive information about such features of blood vessels as thickness, branching and their overall density. Finally, after all the mentioned actions fractal analysis of retinal vessels can be carried out. It allows revealing clinical biomarkers of various diseases.

E. *Machine Learning and Deep Learning Frameworks*

Models for disease prediction could be developed by using Python libraries, such as scikit-learn, along with popular deep learning frameworks, such as TensorFlow and PyTorch. The traditional approach is based on predicting a specific disease by applying either binary or multi-class classification. It has limited clinical utility due to the inability to provide a detailed examination of health problems. In the suggested solution, a model will use the multi-disease prediction approach, when a certain number of diseases will be predicted from a single set of inputs simultaneously. Besides, the suggested model will also identify the severity level of each disease that could help clinicians prioritize treatment options. Unlike the conventional models that produce separate results for each disease, this method will be able to deliver a detailed health analysis.

F. *Explainable AI Libraries (Grad-CAM, SHAP, LIME)*

The XAI libraries like Grad-CAM, SHAP, and LIME are instrumental in achieving the transparency and reliability of the proposed model. For instance, Grad-CAM is utilized in generating heat maps to pinpoint the vital regions within a retinal image for a particular prediction by the model so that the decision-making process can be visualized by the clinicians. SHAP, on the other hand, assigns contribution values to each of the features in the input to come up with a comprehensive understanding of how certain features impact the prediction made by the model. Likewise, LIME generates a local approximation of the predictions made by the black box model to enhance its interpretability. Contrary to traditional models that make optional use of interpretability or do so after making the predictions, the current proposed model integrates interpretability into the very process of predictions.

G. *Database Management System (MongoDB / PostgreSQL)*

This database is designed to accommodate a variety of patient data ranging from medical records to retinal images, prediction results, and other relevant information regarding explainability. For this purpose, a hybrid storage method has been considered for its benefits in accommodating the flexibility of the data while also structuring it into logical schemas that can be easily queried. For this purpose, the retinal images and their associated data, which may be unstructured, are stored on a MongoDB platform that allows for flexible schema design, making it possible to handle a variety of data types and images. In contrast, patient-related data that is structured, such as demographic data, unique identifiers, and visit history, is stored on a PostgreSQL database, where there is consistency and integrity of data due to a relational model.

H. *Deployment and Integration Environment*

The system is based on cloud computing technology, which allows for scalable software development and deployment of an application that can be used from any location. Cloud computing ensures that the system is highly available, flexible, and capable of handling substantial volumes of medical data and user interactions. The system's front end is implemented using a responsive web application, which enables health professionals to easily load retinal images, receive predictions, and retrieve patient information using conventional web browsers. The back-end services run on cloud servers and perform tasks such as processing medical images, performing model inference, and storing medical data. The use of application programming interfaces provides modularity in the design, ensuring that the application is seamlessly integrated with current telemedicine solutions and hospital information systems. In practical settings, particularly in underdeveloped regions, the system is advantageous because of its accessibility.

V. RESULT AND DISCUSSION

The implementation of a web-based deep learning model for analyzing fundus images has resulted in the development of a retinal diagnostic system that utilizes predictions with probability scores on a number of different diseases. The way of reporting these results by the model can be seen in Figure 6. The use of probability bars, confidence values and labels makes interpretation simple. The model labels the disease class of highest probability as the dominant disease class based upon effective classification; this demonstrates both the ability of the model to accurately extract features and its ability to make reliable disease predictions.

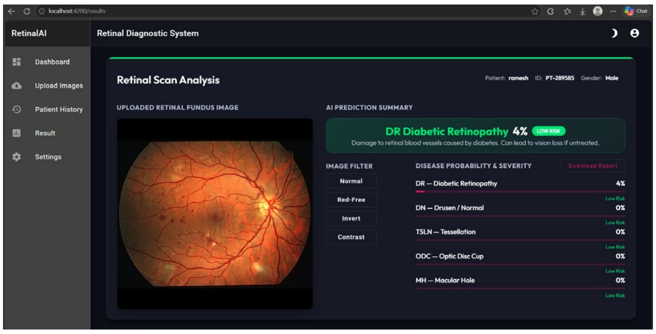

Fig. 6. Retinal Disease Prediction Output with Probability Scores

The System Dashboard contains an integrated interface that lets you monitor Diagnostic Activity and the performance of your system (see Fig. 7). The System Dashboard includes important statistics such as the Number of Completed Scans, Number of High-Risk Results, and Average Confidence Level as well as various graphical visualizations of your, scans by disease; as well as the historical trends of your scan activity. These graphical representations can help you to visualize usage patterns and identify critical results. The System Dashboard will enhance your system's usability and provide you with the tools you need for large-scale screening and monitoring applications.

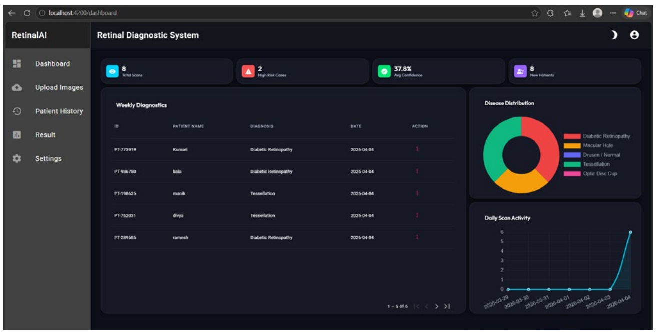

Fig. 7. System Dashboard Showing Scan Statistics and Disease Distribution

The patient history module, along with database integration, allows for the quick and easy access and storage of diagnostic records as shown in Figure 8. Patient information including details about each patient, predictions made about their disease, probability of having a disease and timestamped entries into records are kept in a structured format as shown in the Figure 9. Additionally, reports can be exported to either a clinical or telemedicine application. The entire system is designed with reliability, scalability and ease of use for the user to be an automated method to detect retinal disease and to support decision making.

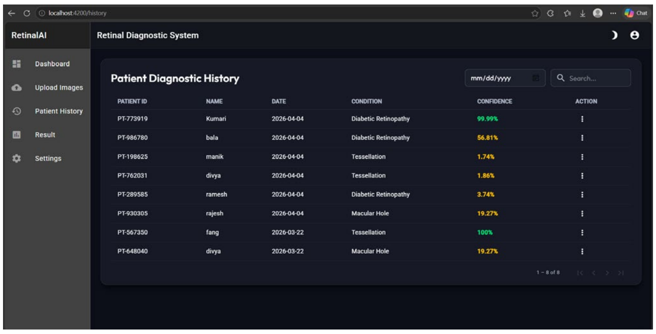

Fig. 8. Patient History and Stored Diagnostic Records

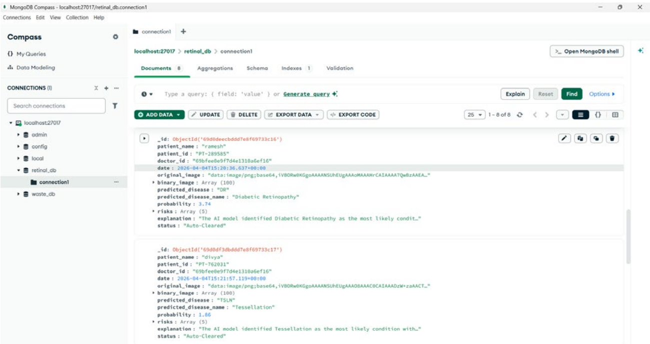

Fig. 9. Patient History and Stored Diagnostic Records

CONCLUSION

The proposed guidebook offers an innovative, unified, and simplified way to diagnose retinal disorders through the use of fractal analysis in conjunction with machine learning techniques using retinal fundus images. This approach extracts biologically significant features from areas of complexity in both structure and fractal qualities from a patient's blood vessels and then utilizes those features to generate more accurate and interpretable results to support decision-making. Being able to simultaneously predict multiple disease outcomes from the retina to systemic disease and also identify predicted severity provides a valuable tool for large-scale screening programs. Another distinguishing feature of this method is the use of various explainable artificial intelligence techniques, such as Grad-CAM, SHAP, and LIME, that allow medical professionals to see clear visual and feature-based reasons for specific prediction results in order to establish clinical confidence and trust in the predictive capabilities of the model.

The data-driven process for patient analysis includes all phases of analysis: image acquisition and preparation; feature extraction and classification; prediction of disease outcomes and severity, explanation of results; and automated report generation into an all-in-one. By combining superior predictive accuracy with meaningful interpretability in a single solution, the end-to-end data-driven process model overcomes the limitations of uncoordinated data-driven methodologies and offers clinicians a scalable, high-quality, reliable, and clinically applicable decision support tool for the early identification and ongoing management of retinal and systemic ailments.

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