

## **GlaucoScreen: A Novel Deep Learning-Based System for Glaucoma Detection and Progression Monitoring**

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### **ABSTRACT**

*Glaucoma, an eye disease that causes damage to the optic nerve, is the second-leading cause of blindness worldwide. Swift diagnosis and treatment of glaucoma is crucial to prevent any glaucoma-induced vision loss; however, this is not usually achievable in developing countries due to their lack of medical personnel and resources. This research aims to solve this through GlaucoScreen, an inexpensive, accessible system for both reliable glaucoma detection and accurate real-time progression monitoring. The first component of the GlaucoScreen system is the smartphone attachment. This attachment allows for the cheap and precise capture of a retinal fundus. The retinal fundus image (RFI) is then uploaded onto the mobile application to be processed by three different deep learning models. First, in order to reduce the computation needed by subsequent models and emphasize diagnostic features, the optic disk region of the RFI is localized and segmented out by the optic disk segmentation model. This model, employing the U-Net architecture, has an intersection-over-union score of 95.11%. The segmented optic disk image is then analyzed by the glaucoma detection model, which has an accuracy of 98.68%, and finally the progression categorization model, which has an accuracy of 95.88%. The glaucoma detection model utilizes a novel convolutional neural network architecture, while the progression categorization model utilizes the InceptionV3 architecture. GlaucoScreen is unique in that it monitors the progression state of glaucoma, which is crucial for its treatment, while also providing a cost-effective method of retrieving RFIs. Through GlaucoScreen, anyone from anywhere around the world will have access to quality glaucoma care.*

### **Introduction**

Glaucoma, an eye disease that causes damage to the optic nerve, is the second leading cause of blindness worldwide with around 5.9 million people having some sort of glaucoma related vision loss in 2020 (Susanna, et al, 2015). Glaucoma occurs when fluid is not drained out the eye

properly, resulting in the pressure within the eye, also known as intraocular pressure (IOP), to rise. This increase in IOP leads to the death of nerve fibers within the optic nerve and the impairment of the visual field (VF) (Boyd, 2019). This vision loss and eventual blindness due to glaucoma can have detrimental consequences on a patient's quality of life. This includes making every day tasks more difficult, leading to an increase in anxiety and even depression (Skalicky, 2008). Treatment for glaucoma in its early stages can mitigate and even prevent any damage to the VF, so swift diagnosis of glaucoma is crucial. However, due to its asymptomatic nature, glaucoma goes commonly undetected in its critical early stages and is not found until extensive VF loss already develops (Chua, et al, 2015). Another factor that goes into the treatment of glaucoma and is just as important as the actual diagnosis is progression monitoring (Brusini, 2008). Knowing how a treatment being used on a patient is affecting the glaucoma progression status is vital to planning out how the treatment will continue. For instance, after a follow-up examination for glaucoma, if the glaucoma is continuing to progress then a more harsh treatment may be in order (stronger medications or surgery), but if the condition of the glaucoma is stable then the current treatment may be continued or even stopped. The current screening process for glaucoma includes an eye angle exam, corneal thickness measurement, dilated eye exam, IOP check, optic nerve imaging, and a VF test. All of this must be done by an experienced ophthalmologist in order for the diagnosis to be accurate (Cleveland Clinic, 2022). This process for early glaucoma detection is problematic, though, as it is expensive, time-consuming, and requires an experienced professional. Even though yearly screenings would reduce the chance of being undiagnosed with glaucoma by up to 23 percent, its expensive and time-consuming nature deters most from doing so (Allison, et al, 2021). These problems are even more prevalent in developing countries where glaucoma screening isn't accessible. In India, for example, around 90 percent of people who have glaucoma are undiagnosed (Rewri, 2023). This is mainly due to the cost of the equipment for a glaucoma examination being too high and also a lack of professionals to accurately carry out the examination. This lack of medical resources leaves people living in developing countries with only two real options for glaucoma screening: either be examined by an local unqualified optometrist with faulty equipment or travel to the nearest eye clinic that houses an experienced ophthalmologist and has the tools needed to give an accurate diagnosis. Both options are not feasible as the first would be very prone to misdiagnosis and improper progression monitoring while the second would be a high-cost, long process which many cannot afford to do. Thus, this study aims to develop a low-cost, quick, accurate, and accessible deep learning system that can be used by under qualified professionals to diagnose glaucoma and categorize its progression, mitigating blindness rates due to glaucoma worldwide.

The proposed system will analyze retinal fundus images (RFIs) using a deep learning (DL) model to make its predictions. DL is a specialized branch of machine learning (ML) that works by extracting features from raw data by using multiple layers for identifying different aspects

relevant to input data (Mishra, et al, 2021). The specific deep learning architecture that will be used is a convolutional neural network (CNN). CNNs are primarily used to solve image-driven pattern recognition tasks, which is perfect as RFIs will be evaluated by the model (O'shea, et al, 2015). An RFI is an image of the back side of the eye and captures the following parts: retina, optic disk (OD), macula, retinal blood vessels, choroid, and the vitreous. Ophthalmologists actually commonly examine RFIs to diagnose glaucoma and categorize its progression along with the other methods that were mentioned earlier (Madhumalini, et al, 2022). The aspects of an RFI that are usually examined for a diagnosis include cup to disk ratio, occurrence of parapapillary atrophy, and OD dilation. CNNs have trouble processing the indicators above and in turn have difficulty classifying a whole RFI, leading to a diminished diagnostic accuracy. However there is another indicator for glaucoma that can be isolated for and the model could use as a basis for accurate diagnosis: loss of nerve fibers in the optic nerve. This loss changes the appearance of the OD, so the OD must be segmented from the RFI in order for accurate diagnosis and categorization by the model. This means a model for OD segmentation must also be developed.

Currently there exists a plethora of models for OD segmentation and glaucoma diagnosis, however there does not exist a model that also classifies the progression of the glaucoma using the glaucoma real-world appraisal progression ensemble (GRAPE) dataset. Additionally, currently available models are inaccessible to people living in developing areas as the tools to acquire an RFI are too expensive and there is no large, open source application that can be used to evaluate the RFI if it is acquired. That is why in addition to the DL model for OD segmentation, glaucoma diagnosis, and classification the system will include a cheap, functional smartphone attachment that can obtain clear RFIs and will also include a mobile application where an individual can directly upload a RFI and analyze it with the DL model through the app from anywhere around the world.

## **Methodology**

### **Data Collection**

For the development of the GlaucoScreen system, three different DL models were needed. One for OD segmentation, one for glaucoma detection, and one for glaucoma progression categorization. This also means that three datasets were used to train each of the models. The OD segmentation model was trained on the Indian Diabetic Retinopathy Image Dataset (IDRiD) (Porwal et al., 2018). This dataset was split into three folders labeled as Segmentation, Disease Grading, and Localization respectively. For our purposes the only folder that was used was the segmentation folder. This folder contains 81 RFIs each with a corresponding ground truth for the OD. These images were obtained from an eye clinic located in Nanded, India using a non-

invasive fundus camera, and the ground truths were marked up by a master's and PhD student. The glaucoma detection model was trained on a variety of datasets. This includes the EYEPAC, G1020, and SMDG-19 datasets. 2,500 glaucomatous images from EYEPAC were used, 284 glaucomatous and 757 normal images were used from G1020, and 6,656 glaucomatous and 10,586 normal images were used from SMDG-19. This is a total of 21,414 RFIs used for the training of the glaucoma detection model. Lastly, the glaucoma progression categorization model was trained using the GRAPE dataset (Huang et al., 2023). This dataset contains an ensemble of 265 different glaucomatous RFIs each labeled as progressing or non-progressing. Three different methods were used to determine the state of progression: PLR2, PLR3, and MD. For the pointwise linear regression (PLR) method an eye is defined as progressing if the number of test points with a significant negative regression slope is greater than or equal to two (PLR2) or three (PLR3). The median deviation (MD) method considers an eye to be progressing if the slope of MD is presented with negative linear regression and a P value less than 0.05. If any of these methods deemed an RFI as progressing then it was categorized as progressing during the training of the model.

### **Data Preprocessing and Augmentation**

Both the datasets used to train the glaucoma detection model and the GRAPE dataset, which was used to train the glaucoma progression monitoring model, were augmented during the training of their respective models. Data augmentation enlarges the dataset and increases the training time, leading to a higher diagnostic accuracy. Images in the EYEPAC, G1020, and SMDG-19 datasets were transformed in various ways including parallel shifting, changing their horizontal orientation, and manipulating the magnification of the image. This procedure was very effective as the OD has a sort of symmetry that can allow for augmented images to be similar to the actual images. The approach for data augmentation in the GRAPE dataset was different. Originally, it had 522 glaucomatous RFIs classified as progressing and 109 glaucomatous RFIs classified as non-progressing. This disparity in the amount of data in each class would lead to non representative training and poor prediction accuracy. To remedy this, only the images in the progressing class were augmented at first to reduce the difference between the two classes and then an overall augmentation was applied. The first augmentations applied to the progressing class include changes made to magnification, horizontal and vertical orientation, angle, width and height, and brightness. These changes increased the amount of RFIs in the progression class to 422, decreasing the disparity between classes. This decrease in disparity led to a more generalizable, accurate model. Then the same augmentation operation that was done to the ACRIMA dataset was done to the whole of the GRAPE dataset, being effective for the same reasons. Apart from the augmentation, both datasets were also processed so that the scale of the pixels for each image goes from 0 to 1 instead of 1 to 255. This normalization was done to bring

all features to a similar scale, preventing certain features from dominating the training, and to ensure that the values are within a stable range for computation.

### **Three-Part Glaucoma Monitoring System**

In order to get precise predictions, GlaucoScreen will be a three part system each with a separate task. The first part of the system uses the biomedical image segmentation CNN U-Net to localize the OD from an RFI. This is done to remove any unnecessary areas of analysis from the RFI so that the other two models can more accurately make their prediction. Then in the second part of the system, a custom CNN is used to diagnose a segmented OD as with or without glaucoma. If the OD does come back as glaucomatous then InceptionV3 is used again to categorize the progression of the glaucoma in the third part of the system. A smartphone attachment and mobile application were also developed so that this system can be accessible anywhere in the world.

### **Optic Disk Segmentation Model**

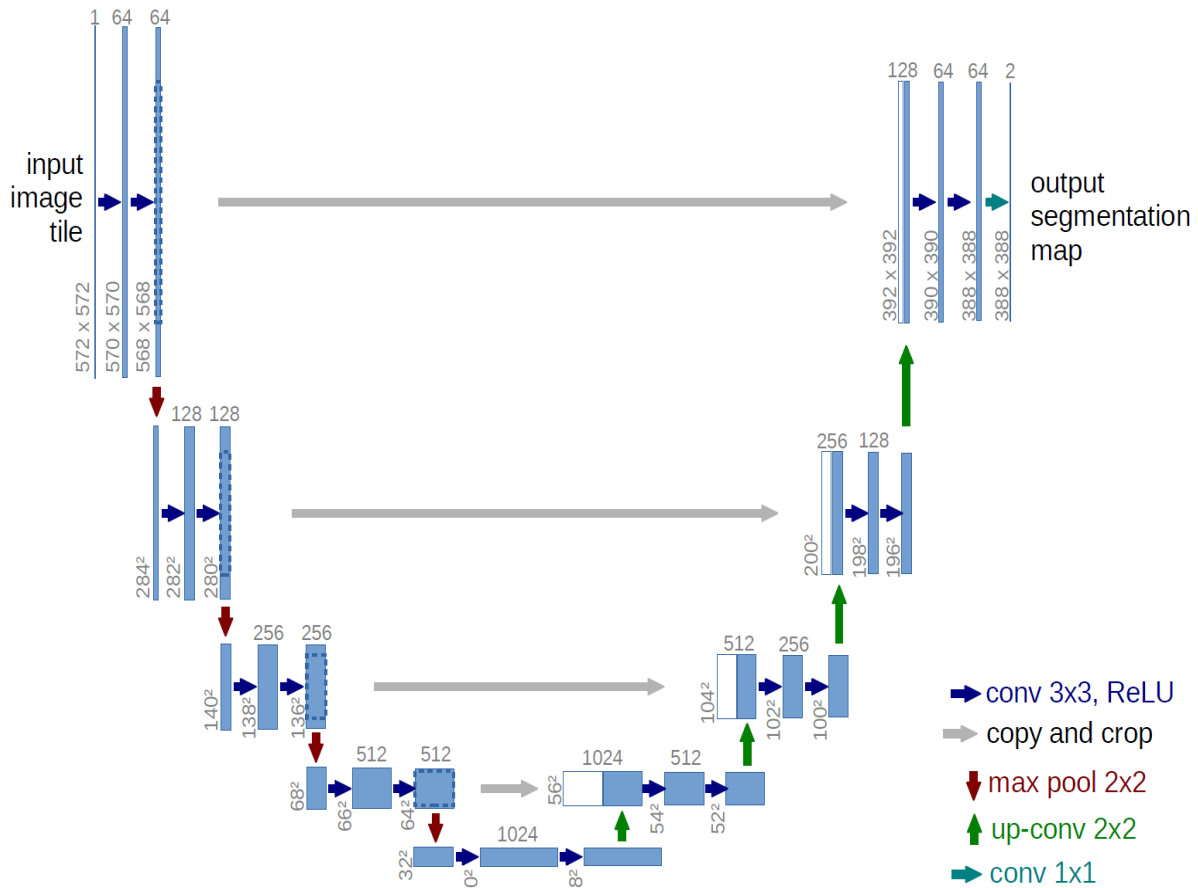
The OD segmentation model works by first predicting for the mask of an OD on a given RFI. The predicted mask is then applied back to the RFI where it and a surrounding area of 50 pixels are segmented out while all other areas of the RFI are removed. Now the image is ready for classification by the other two models. U-Net, the CNN architecture used for the segmentation model, was first designed in 2015 to process biomedical images, more specifically for object detection (Zhang, 2019). Because of this principle, U-Net was able to effectively segment the OD from the rest of the retina. The backbone, which is used to extract features from the input data, that was used for this model was EfficientNetB4 (Megha, 2023). Because of EfficientNetB4's high resource efficiency and ability to improve segmentation performance, it is the perfect architecture to use alongside U-Net. Callbacks such as 'reduce lr on plateau' and 'early stopping' were also used to reduce the learning rate when the intersection over union (IOU) plateaued and to stop training early if the IOU score stopped having significant improvement. The framework used for this model was Keras and the specific hyperparameters are listed on Table 1.

**Table 1: Optic Disk Segmentation Model Hyperparameters**

<b>Hyperparameter</b>	<b>Value</b>
Optimizer	Adam
Learning Rate	0.001
Number of Epochs	75



**Figure 1: U-Net Architecture (Uni-freiburg.de, 2015)**



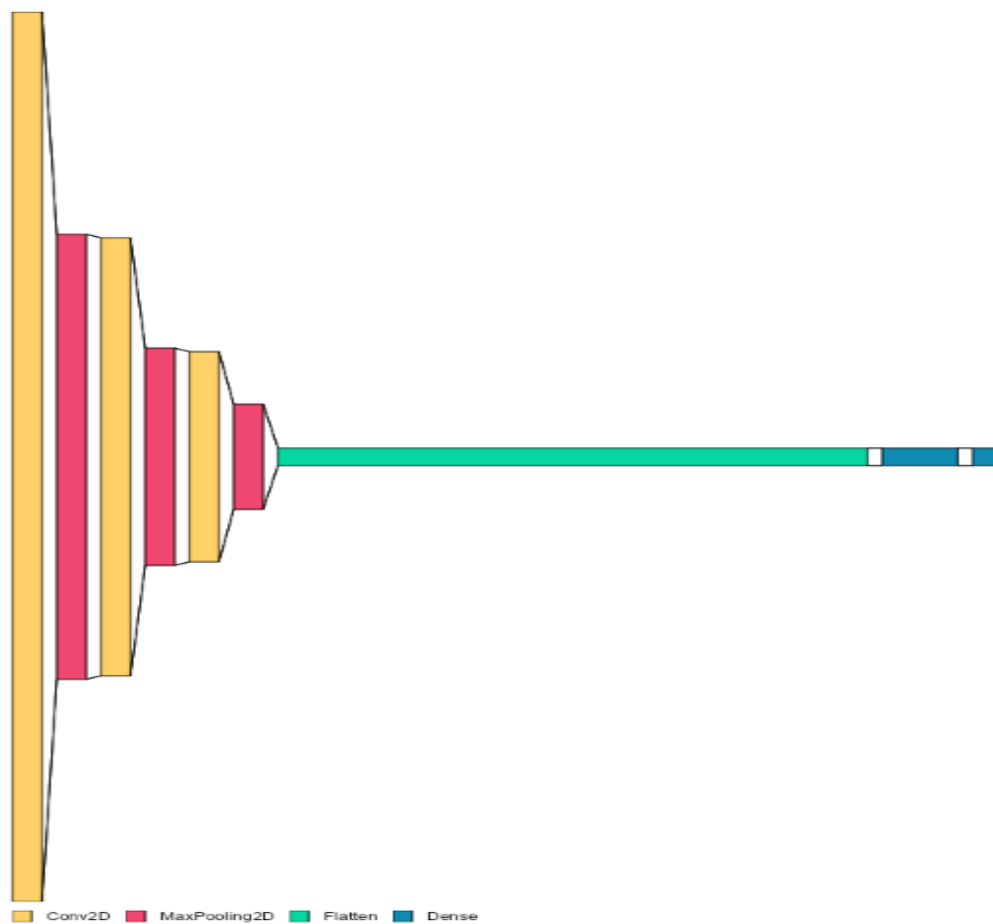
### Glaucoma Detection Model

The glaucoma detection model used a custom CNN. It features a sequence of convolutional and max pooling layers that extract and downsample features from input images. The architecture includes a total of three convolutional layers with depths increasing from 64 to 128 filters, followed by corresponding max pooling layers. The network's high-level reasoning is handled by a dense layer with 512 units, leading to a final dense layer with a single unit for binary classification. Overall, the model has 59,206,657 trainable parameters, which allow it to perform complex pattern recognition in detailed image analysis tasks. The framework used for this model was Keras and the specific hyperparameters are listed on Table 2.

**Table 2: Glaucoma Detection Model Hyperparameters**

Hyperparameter	Value
Optimizer	Adam
Learning Rate	0.01
Number of Epochs	150
Dropout Rate	0.5
Loss Function	Focal

**Figure 2: Custom CNN Architecture**



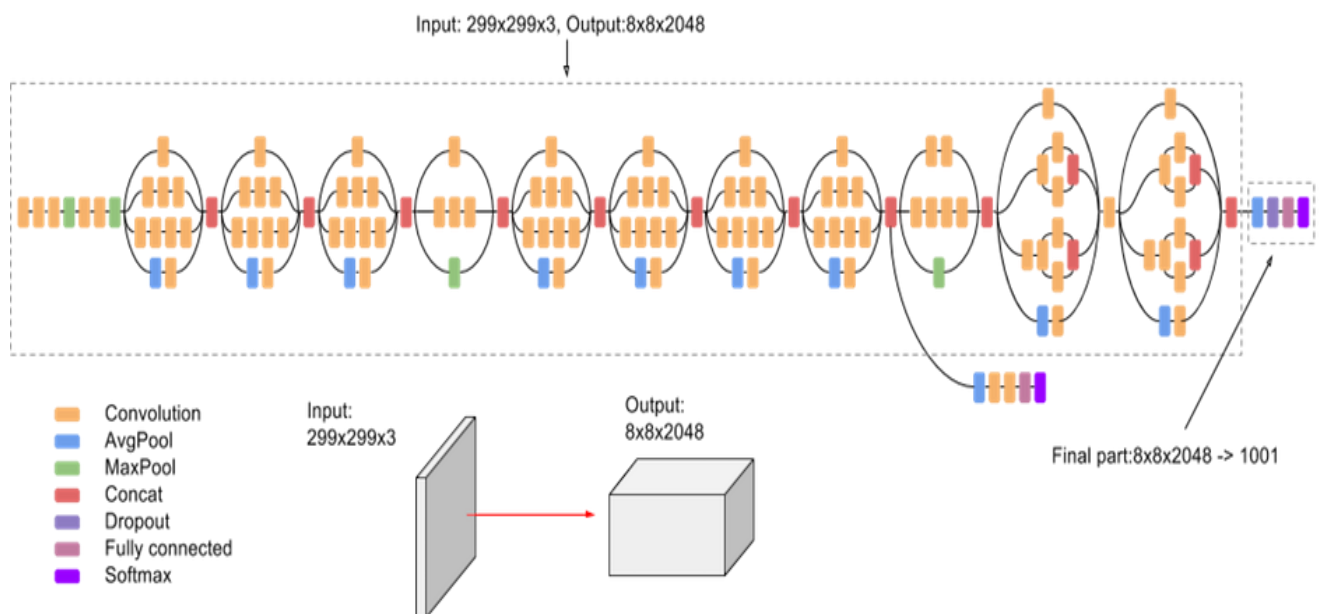
### Glaucoma Progression Categorization Model

InceptionV3, Google’s pretrained image classification architecture, was used to evaluate whether glaucoma in an RFI is stable or progressing (Google Cloud, 2019). The extra layers used in this model were the same as the ones in the glaucoma detection model, and the hyperparameters used were very similar as can be seen in Table 3. The framework used for this model was Keras.

**Table 3: Glaucoma Progression Model Hyperparameters**

Hyperparameter	Value
Optimizer	Adam
Learning Rate	0.001
Number of Epochs	300
Dropout Rate	0.5
Loss Function	Binary Crossentropy

**Figure 3: InceptionV3 Architecture (Google Cloud, 2019)**





## Results

### Loss Functions

Loss functions are mathematical methods used to evaluate how good a model does at predicting the expected outcome. In this paper, two different loss functions were used to evaluate the three models. For the OD segmentation model dice loss was calculated. Dice loss is commonly used for segmentation tasks and denotes the difference between the predicted segmentation mask and the ground truth segmentation mask. The formula used to calculate for dice is shown in the figure below. The dice value is then subtracted from one to get dice loss.

**Figure 4: Dice Derivation**

$$\mathbf{Dice} = \frac{2|X \cap Y|}{|X| + |Y|}$$

Since progression monitoring is a binary categorization model, binary cross entropy was the loss function used to evaluate the model since it is commonly used for binary classification tasks. Its formula is shown in the figure below.

**Figure 5: Binary Cross Entropy Derivation**

$$L = -\frac{1}{m} \sum_{i=1}^m y_i \cdot \log(\hat{y}_i)$$

Focal loss was used for the glaucoma detection model as it allows for the model to focus on RFIs that were harder to classify, yielding better results. Because of this focal loss is also currently being tested with the progression categorization model. The formula for focal loss is shown below.

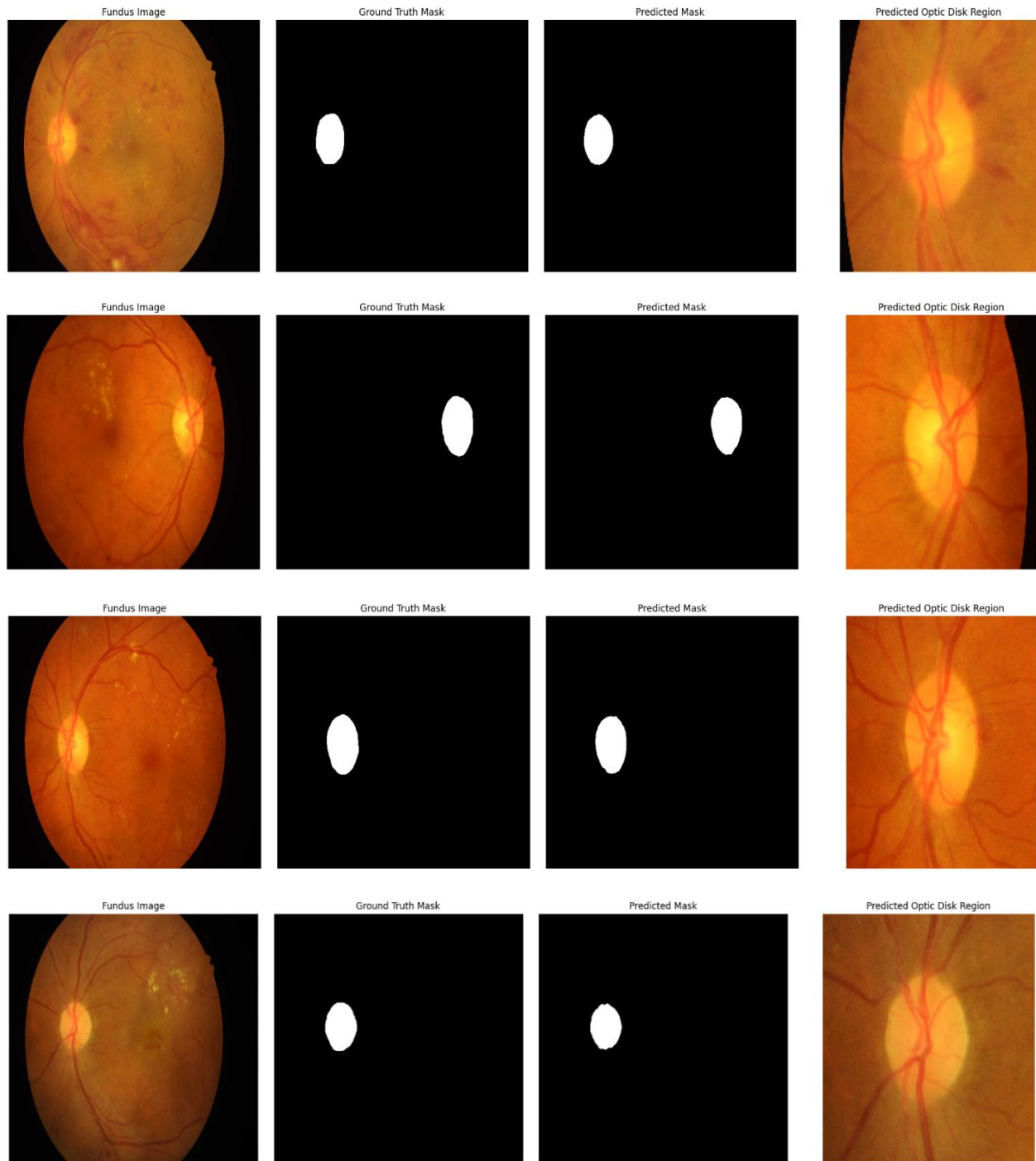
**Figure 6: Focal Loss Derivation**

$$FL = -(1 - P_t)^\gamma \log(P_t)$$

### Optic Disk Segmentation Model Evaluation

IOU score was the main metric used to measure the effectiveness of the OD segmentation model. The final IOU score for the model was 91% and for every inputted RFI a correctly predicted OD region was outputted. Examples of input images, ground truth masks, predicted masks, and predicted OD regions are shown below.

**Figure 7: Optic Disk Segmentation Visualization**



### Glaucoma Detection Model Evaluation

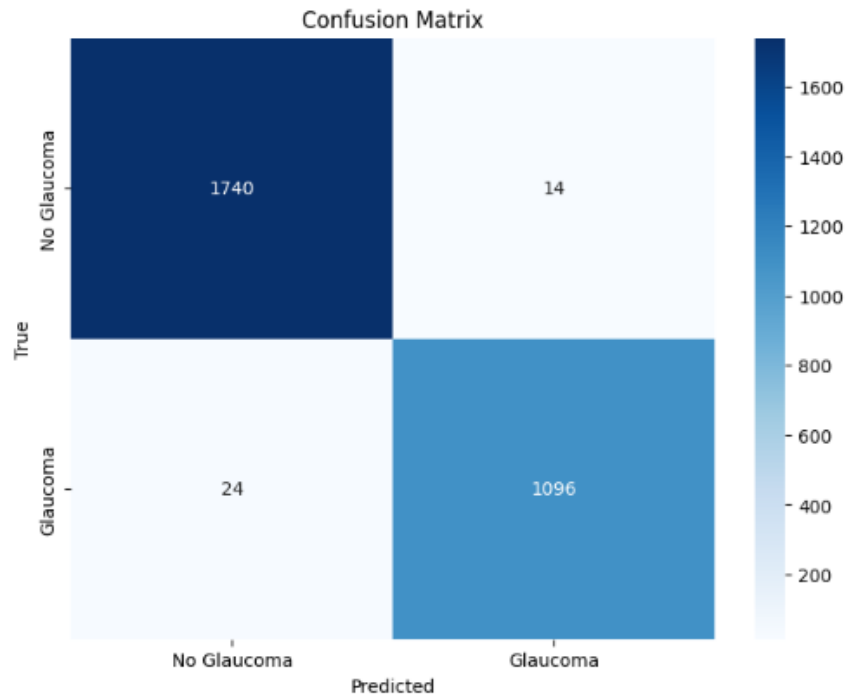
The main metric used to evaluate the performance of the glaucoma detection model was prediction accuracy on the test set of RFIs. The model yielded an excellent accuracy of 98.68% while also being generalizable because of the large size of the dataset. Figure 6 shows a comparison of training accuracy to validation accuracy and training loss to validation loss as the model training occurred.

**Figure 8: Training Accuracy vs. Validation Accuracy and Training Loss vs. Validation Loss in the Glaucoma Detection Model**



A confusion matrix can give much more insight on the effectiveness of a model by providing a much easier way to visualize and calculate a multitude of performance metrics. A confusion matrix along with a table of secondary metrics are depicted below.

**Figure 9: Confusion Matrix for the Glaucoma Detection Model**



**Table 4: Secondary Performance Metrics for the Glaucoma Detection Model**

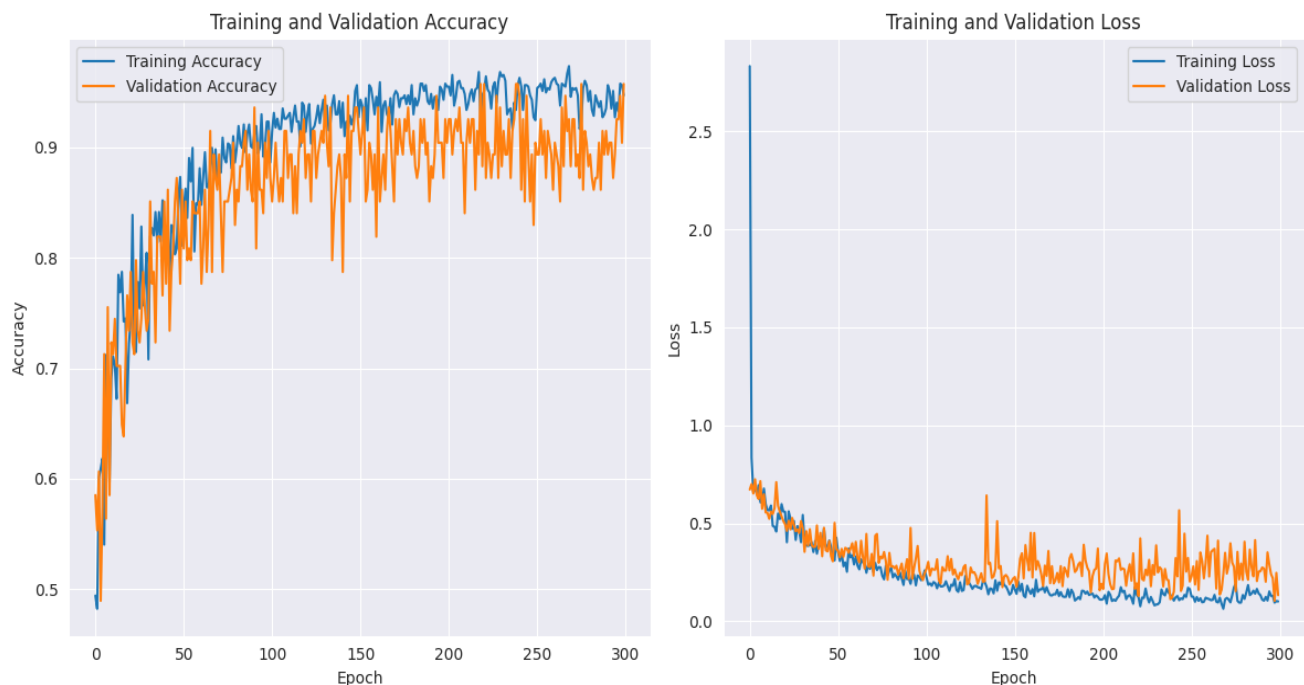
Metric	Value	Calculation
Sensitivity	0.9786	$TP / ( TP + FN )$
Specificity	0.9920	$TN / ( TN + FP )$
Precision	0.9874	$TP / ( TP + FP )$
Negative Predicted Value	0.9864	$TN / ( TN + FN )$
False Positive Rate	0.0080	$FP / ( FP + TN )$
False Discovery Rate	0.0126	$FP / ( FP + TP )$
False Negative Rate	0.0214	$FN / ( FN + TP )$

Matthews Correlation Coefficient	0.9722	$(TP * TN - FP * FN) / \sqrt{((TP + FP) * (TP + FN) * (TN + FP) * (TN + FN))}$
F1 Score	0.9830	$2TP / ( 2TP + FP + FN )$

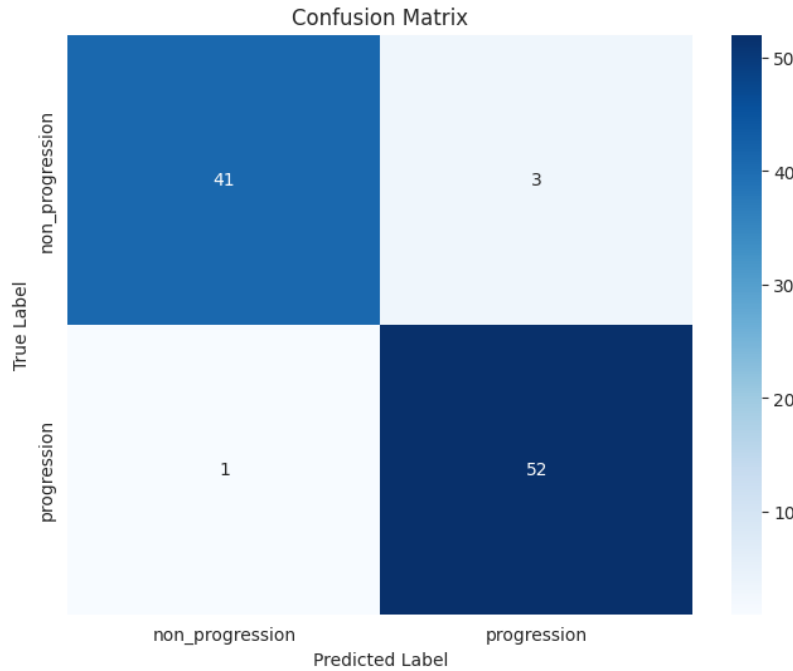
**Glaucoma Progression Categorization Model Evaluation**

The final model to be evaluated is the glaucoma progression classification model. Accuracy was used as the primary indicator for effectiveness of the model. Its final accuracy was a high 95.88%, making it a strong option for glaucoma monitoring especially in areas where there aren't qualified personnel to do the monitoring. Figure 8 shows the comparison of training accuracy to validation accuracy and training loss to validation loss as the model training occurred. Figure 9 shows a confusion matrix for the model, and Table 5 shows secondary performance metrics of the model based on the confusion matrix. For the secondary metrics, progressing was considered a positive diagnosis and non-progressing was considered a negative diagnosis.

**Figure 10: Training Accuracy vs. Validation Accuracy and Training Loss vs. Validation Loss in the Glaucoma Progression Categorization Model**



**Figure 11: Confusion Matrix for the Glaucoma Progression Categorization Model**



**Table 5: Secondary Performance Metric for the Glaucoma Progression Categorization Model**

Metric	Value	Calculation
Sensitivity	0.9811	$TP / ( TP + FN )$
Specificity	0.9318	$TN / ( TN + FP )$
Precision	0.9455	$TP / ( TP + FP )$
Negative Predicted Value	0.9762	$TN / ( TN + FN )$
False Positive Rate	0.0682	$FP / ( FP + TN )$
False Discovery Rate	0.0545	$FP / ( FP + TP )$
False Negative Rate	0.0189	$FN / ( FN + TP )$
Matthews Correlation Coefficient	0.9173	$(TP * TN - FP * FN) / \sqrt{(TP + FP) * (TP + FN) * (TN + FP) * (TN + FN)}$

<b>Metric</b>	<b>Value</b>	<b>Calculation</b>
Sensitivity	0.9811	$TP / ( TP + FN )$
Specificity	0.9318	$TN / ( TN + FP)$
Precision	0.9455	$TP / ( TP + FP)$
Negative Predicted Value	0.9762	$TN / ( TN + FN )$
False Positive Rate	0.0682	$FP / ( FP + TN )$
False Discovery Rate	0.0545	$FP / ( FP + TP )$
False Negative Rate	0.0189	$FN / ( FN + TP )$
Matthews Correlation Coefficient	0.9173	$(TP * TN - FP * FN) / \text{sqrt}((TP + FP) * (TP + FN) * (TN + FP) * (TN + FN))$
F1 Score	0.9630	$2TP / ( 2TP + FP + FN )$

**Conclusion**

The system proposed in this paper has the potential to transform the glaucoma diagnosis and treatment landscape in developing countries. Glaucoma is the second leading cause of blindness worldwide even though potential vision loss from it can be completely prevented if it is caught in its early stages. This is due to its asymptomatic nature which leads people to neglect glaucoma screenings until it's too late. Although yearly screenings for glaucoma could effectively decrease the amount of people with glaucoma induced vision loss, it is simply not feasible in developing countries. These areas traditionally don't have proper access to health care workers that can give a glaucoma diagnosis while also monitoring its state progression, leading to people in these areas commonly living with glaucoma unknowingly. However, with the introduction of GlaucoScreen into these areas, this can change. Anyone can utilize GlaucoScreen to properly diagnose glaucoma with an accuracy of 98.68% and monitor its progression with an accuracy of 95.88%.

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