Original Article

Evaluating the Generalizability of Machine Learning Models for Glaucoma Detection

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Abstract

Objective: The proposed research aims to develop a novel deep learning method based on a 2D Convolutional Neural Network (CNN), which would successfully merge information from two essential ocular imaging techniques, including fundus photography and optical coherence tomography.

Methods: The proposed CNN model achieved both high diagnostic precision and generalization capability through its use of the RMSprop optimizer and categorical cross-entropy loss function. Multiple publicly available datasets were used to evaluate the proposed method, including RIM-ONE, Drishti-GS, ORIGA-light, HRF, and ACRIMA (fundus images), as well as a specialized clinical OCT dataset. The proposed method was tested using standard performance metrics against previous notable studies.

Results: The proposed CNN model produced AUC scores of 0.97 for OCT images and 0.96 for fundus images, which outperformed previous results. The OCT images delivered vital information about the optic nerve head structure, which fundus images confirmed through their display of essential clinical indicators for glaucoma diagnosis.

Conclusion: The research shows that the proposed deep learning method can perform real-time glaucoma detection during medical procedures. The proposed model produced exceptional diagnostic results for subclinical glaucoma suspects through its dual imaging system, which improved the ability to protect vision quality and reduce the impact on life quality.

Keywords: Glaucoma, Fundus Oculi, Diagnostic Imaging, Computer-Aided Diagnosis, OCT.

Introduction

Glaucoma exists as a long-term eye condition that causes the optic nerve fibers that carry visual information from the retina to the visual cortex to experience continuous deterioration. The damage to these fibers becomes permanent, which results in complete visual loss and eventually blindness when the condition reaches its most severe stage.[1] The medical field recognizes two main types of glaucoma, which are open-angle glaucoma and closed-angle glaucoma. The development of open-angle glaucoma occurs slowly without any warning signs, but closed-angle glaucoma causes sudden eye pressure spikes, which bring intense eye discomfort and light sensitivity.[1] The main cause of glaucomatous optic neuropathy development stems from different disease mechanisms, but elevated intraocular pressure (IOP) remains the primary factor. The pressure inside the eye becomes higher when the body fails to drain aqueous humor properly or when it produces too much of this fluid, which results in decreased eye blood flow and damaged optic nerve fiber transport.[2] Research has identified multiple factors that increase the risk of developing glaucoma, including older age, genetic background, racial heritage, eye shape, and steroid medication use, as well as specific medical conditions. Owing to its largely asymptomatic onset, glaucoma is often referred to as the “silent thief of sight”.[3] The diagnosis of this condition requires healthcare providers to perform three main tests, which include visual field assessment, optic nerve imaging, and intraocular pressure measurement.[4] The available treatments, which include topical anti-glaucoma medications, laser therapy, and surgical procedures, help glaucoma patients, but the disease requires ongoing management because it has no permanent solution. The process of early detection helps doctors make better treatment choices, which results in enhanced visual results for patients.[5]

The proposed research investigates deep learning methods for glaucoma diagnosis through a single two-dimensional Convolutional Neural Network (CNN), which processes fundus photographs and optical coherence tomography (OCT) images.[6] The research provides a reproducible method to evaluate diagnostic accuracy between imaging modalities through its use of one model structure for both types of data.[7] The proposed method enables doctors to detect glaucoma at an earlier stage, allowing them to start treatment right away and reducing the number of people who become blind from glaucoma worldwide.[8]

Reports on glaucoma detection have emphasized the use of a 2D CNN model rather than a 3D model. Mehta et al. created an integrated model that unites medical information with ocular data.[1] Their scheme developed a 2D CNN architecture with a DenseNet201 backbone to analyze each B-scan from OCT volumes in the UK Biobank dataset. The proposed model achieved an AUC of 0.950 by combining both input modalities. Rasel et al. developed a scheme based on a 2D CNN model that gathered information from wide-angle swept-source OCT of the retinal nerve fibre layer.[2] The researchers used wide-angle imaging to achieve better diagnostic results than traditional medical tests, which evaluated peripapillary retinal nerve fiber layer thickness and standard perimetric tests for glaucoma detection. Glaucoma exists in different stages, which start with suspected cases followed by early stages and then progress to moderate and finally advanced stages. The research by García et al. investigates stage-specific diagnosis as a solution to this problem. The authors created a hybrid system that used human-extracted features together with a two-dimensional convolutional neural network. The combination of residual connections with attention mechanisms produced major performance improvements for classification tasks according to.[3]

Research studies have employed deep learning techniques to assess glaucoma through analysis of fundus photography images that contain color information. Akter et al. developed a diagnostic model that used various analytical features to enhance its ability to make accurate predictions.[11] The research conducted by Li et al. assessed how well an artificial intelligence system performed in detecting glaucomatous optic nerve damage, showing positive diagnostic outcomes.[10] Additionally, to accurately classify glaucoma stage, Velverde et al. used a CNN and transfer learning.[12] In another approach, Maetschke et al. studied a three-dimensional CNN scheme that utilized unsegmented OCT images of the optic nerve head,[4] to grade healthy and glaucomatous optic nerves, managed to yield a significant AUC of 0.940. Yasmeen et al. also worked on a 3D deep learning model to diagnose glaucoma.[5] Their model employed three pathways with similar architectures and different inputs, yielding an AUC of 0.983 and demonstrating superior efficacy compared to traditional models. However, previous studies have compared 2D and 3D CNN models. Comparison yielded superior efficacy and practicality of 2D CNN models.

Alghamdi et al.[6] developed a method that was unique in using two CNNs: one to label different areas of the disc, and the second to classify them as normal, suspect, or abnormal. The proposed method was evaluated on publicly available datasets like Drive, Messi-Dor, and Stare. The major weakness was that these datasets were not suitable for glaucoma; later, it was tested on a private dataset, and its reproducibility was difficult.

Another noteworthy study by Abbas,[7] was based on an unsupervised CNN architecture, named Glaucoma-Deep. It automatically retrieved salient glaucoma features from colored fundus images. To extract the features most relevant to glaucoma, a deep-belief network (DBN) was used. Later, it was applied to four different datasets, one private and three public. Their results showed a specificity of 98.01% and a sensitivity of 84.50%, but they failed to provide information on its architecture or how it is applied.

Similarly, Orlando et al,[8] conducted a study using two different networks, OverFeat and VGG-S. They identified salient features of glaucoma in fundus images and later analyzed them using Contrast-Limited Adaptive Histogram Equalization (CLAHE) and vessel-deletion techniques. The conclusion highlighted that the performance of CNNs can be influenced by different preprocessing approaches. 2D CNNs have superiority over 3D CNNs primarily due to the availability of numerous pre-trained models, mainly for smaller data sets. Also, transfer learning is efficient with 2D as it works for the augmentation of dimensions. On the other hand, 3D CNNs have fewer pre-trained models and datasets and also require more thoroughly annotated datasets for optimal performance, which compromises their generalizability. Moreover, although macular and ONH OCT provide volumetric data, the computational demands of 3D-CNNs often outweigh the benefits, particularly when large, well-annotated datasets are not available. Another study, conducted in 2024 by Rasel et al., compared the efficacy of 2D and 3D CNNs on OCT images for glaucoma detection.[2] The AUC scores achieved by 2D were 0.96 and 0.943 for macular and ONH OCT images, which were far better than those of the 3D CNN model. This conclusion, once again, proves that 2D CNNs are more efficient, particularly when working with small datasets in clinical settings.

Latif et al proposed a scheme titled ODGNet, which was unique in a way that it utilized both visual saliency features and transfer learning to identify optic disc and aid glaucoma diagnosis,[9] at a mass level, as it generated an accuracy of 95.75% across five datasets. Mangipudi et al. developed a model with the potential to localize and segment the optic

disc and cup using modified intersection/union measures, but low-contrast images compromised its effectiveness.[13] Additionally, Hemelings et al. worked to improve the color contrast of fundus images for better feature extraction, but did not account for varying disease stages or changes in myopia.[14]
Another study on CAD systems was conducted by Afreen et al. and used a CNN. This study used architectures such as U-Net and LeNet and demonstrated potential as an accurate tool for glaucoma detection.[15] But their efficiency is yet to be tested on complicated cases among a variety of glaucoma cases. Similarly, Hamid et al developed a two-branch deep learning network, TWEEC, which gained an accuracy of 98.78%, it showed great potential but is less likely to generalize due to the unavailability of a large amount of training data.[17] Other noteworthy studies on glaucoma detection include those by Surya et al,[18] and Shinde et al.[16]
In summary, both 2D and 3D CNN models have shown potential for glaucoma diagnosis and classification. However, 2D CNNs are currently more practical in many clinical settings. They are easier to train and implement. They also require fewer computational resources. This makes them more suitable when the available dataset is limited. In our study, the same CNN architecture was applied to both OCT and fundus images for glaucoma detection. This provides a consistent framework for evaluating both imaging modalities. In addition, transfer learning and data augmentation further improved the suitability of the 2D approach.

Materials And Methods

The proposed CNN architecture was designed to ensure clarity and reproducibility of the model. Each input image is first resized to 64×64 grayscale resolution and then passed through a sequence of convolutional blocks for hierarchical feature extraction. The first block consists of a Conv2D layer with 32 filters and a 3×3 kernel, followed by batch normalization and ReLU activation, enabling the model to capture basic spatial patterns such as edges and local intensity variations. Three subsequent convolutional blocks employ 64 filters with 3×3 kernels, which allow the network to learn more complex structural features associated with glaucomatous changes in the optic nerve region. Max-pooling layers with a 2×2 window are applied after selected convolutional layers to reduce spatial dimensionality while preserving the most informative features. The resulting feature maps are then processed using global average pooling, which helps reduce overfitting by minimizing the number of trainable parameters. Finally, the extracted features are passed to a fully connected dense layer with a SoftMax activation function to classify the images into normal and glaucomatous categories. An extensive evaluation has been done of the proposed system using publicly available notable datasets such as RIM-ONE, Drishti-GS, ACRIMA, ORIGA-light, and HRF, which ensure the model learns varied patterns effectively. By combining OCT with fundus images through this approach, performance in glaucoma detection improves noticeably. Instead of relying on standard methods, a 2D Convolutional Neural Network (CNN) is applied here for task-specific analysis. Publicly available fundus images are combined with an optical coherence tomography (OCT) dataset to train the model. The next section comprises a detailed description of the datasets and our proposed framework, followed by a discussion of different augmentation strategies.

A. ***Fundus Images Dataset***

Our study used five publicly available datasets. (RIM-ONE, Drishti-GS, ORIGA-light, HRF, and ACRIMA). Details are mentioned in Table 1. Data from these sources was used, keeping in view the source policies and recommendations, and none of the patients' personal information was revealed or disclosed. Our study followed the ethical guidelines of the Declaration of Helsinki, and the participating institution's review board permitted our study design and layout.

- **RIM-ONE:** Rim one dataset,[20] is publicly available and was made from three sources: Hospital Universitario de Canarias, Hospital Cl´ınico San Carlos, and Hospital Universitario Miguel Servet. All these institutions are Spanish. This database contains 455 retinal images, of which 261 are healthy, and 194 are glaucomatous.
- **DRISHTI-GS:** DRISHTI-GS,[21] data set has a total of 101 images, out of which 70 are glaucomatous, and the rest are normal. This dataset is used for diagnosing multiple ophthalmic disorders.
- **ORIGA-light:** ORIGA-LIGHT,[22] is a publicly available dataset consisting of 650 retinal images, of which 168 images are glaucomatous, and 482 are normal. The dataset is intended for research into ocular diseases such as glaucoma and diabetic retinopathy.
- **HRF**: HRF,[23] consists of 45 retinal images, 27 being glaucomatous and the rest being normal.

- **ACRIMA:** The ACRIMA dataset,[24] is also a bank of retinal images taken when the pupil is dilated, has 705 images out of which 309 are normal, and the rest are glaucomatous.

OCT SCANS:

- 2D OCT scans required for our study were obtained from a publicly available dataset.[19] One important aspect of this dataset is that the class distribution is symmetrical and evenly distributed. This feature helped to reduce the workload and did not require further complex processing. Details are shown in Table 1.

Table 1: Distribution of Glaucoma and Normal Cases in Datasets

Dataset	Glaucoma	Normal	Total
	Fundus		
DRISHTI-GS [21]	70	31	101
ORIGA-light[22]	168	482	650
HRF [23]	27	18	45
RIM-ONE [20]	194	261	455
ACRIMA[24]	396	309	705
Total (Fundus)	**855**	**1101**	**1956**
	OCT		
2D Scans [19]	1052	847	1899

B. *Data Augmentation*

Since the OCT scan dataset had a balanced class distribution, extensive data augmentation was not required for this; however, data augmentation was done due to an uneven number of normal and glaucomatous images. Steps included in data augmentation were flipping, rotation, occlusion, and translation in order to achieve balanced class distribution. Importantly, the dataset was first divided into training, validation, and testing subsets, and augmentation was performed only on the training data. This ensured that augmented samples originating from the same image did not appear in multiple subsets, thereby preventing data leakage. The validation and test datasets were kept unaltered to provide an unbiased evaluation of the model's performance. After these steps, each dataset contained 3000 normal and 3000 glaucomatous images, resulting in a cumulative dataset size of 30,000 (15,000 normal and 15,000 glaucomatous). Assessment was made on both individual and collective datasets to analyze the influence of data augmentation.

C. *Proposed Framework*

Our proposed method utilizes a convolutional neural network (CNN), specifically designed to aid in the clinical diagnosis of glaucoma and to further stratify patients into different glaucoma stages. The proposed framework is shown in Figure 1. There are multiple layers through which input has to be processed. The first layer receives input as a standardized 64×64-pixel grayscale image. CNN comprises 3 blocks: the first has 32 filters with a 3×3 kernel; its primary role is to derive simple local spatial features. Batch normalization and ReLU activation are also used to stabilize training. The second and third layers of the designed network have 64 3×3 filters, which further augment the retrieval of glaucoma-specific features, again using batch normalization and ReLU activation. After each convolutional block, images pass through 2×2 max pooling, which helps reduce computational load while maintaining the integrity of the extracted features. Next comes global average pooling (GAP), which minimizes spatial features to a great extent and reduces overfitting. Then comes the classification stage, which uses the Softmax function, and is comprised of a fully connected dense layer. This stage effectively stratifies images into normal or glaucomatous. The RMSprop optimizer works with categorical cross-entropy loss to create a stable training system that handles complex data structures. The optimization process for models uses organized validation methods instead of arbitrary assumptions to protect the best-performing model parameters through checkpointing and model freezing methods. The training system provides both strong system stability and a wide application range, which leads to dependable results during different experimental tests.

I. EXPERIMENTS

The following sections explain the experimental design and evaluation methods that were used to compare the proposed method with other notable studies.

A. Experimental Setup

An extensive evaluation was done to analyze the efficacy of the proposed model. The dataset was divided into a 60-20-20 split for training, validation, and testing purposes. Model implementation was carried out using TensorFlow, and training was performed for 100 epochs on a single NVIDIA Quadro P5000 GPU equipped with 12 GB of memory. Learning rate of 0.0001 was used with a categorical cross-entropy loss function. Figure 2 shows learning curves on both the fundus and the OCT image datasets.

B. Evaluation Metrics

Accuracy: Measures the overall correctness of a model's predictions. It is calculated as the ratio of correctly classified instances to the total number of instances.

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

Where *TP* = True Positives, *TN* = True Negatives, *FP* = False Positives, and *FN* = False Negatives. **Precision:** Focuses on the accuracy of positive predictions. It measures the proportion of true positive predictions among all positive predictions made by the model.

$$Precision = \frac{TP}{TP + FP}$$

Recall (Sensitivity): Measures the model's ability to identify all actual positive instances. It is the proportion of true positives among all actual positive instances.

$$Recall = \frac{TP}{TP + FN}$$

Area Under the Curve (AUC): The ROC curve demonstrates the relationship between true positive rate (TPR) and false positive rate (FPR), which occurs when different classification thresholds are used. The performance of a model becomes better when its AUC value increases

Results

1) ***Fundus Dataset Results:*** The proposed model achieved a 0.96 AUC on the fundus dataset, which included all images. The detailed results have been summarized in Table 2. The results showed consistent and reliable outcomes throughout all datasets because the method achieved 96% accuracy on the Drishti-GS1 dataset despite having more glaucomatous images. The model produced a mean accuracy of 0.914 while achieving an AUC of 0.96, a precision of 0.916, and a recall of 0.958, which proved its ability to detect glaucomatous cases effectively. The confusion matrix in Figure 2 displays negligible false negatives and false positives. The HRF and DRISHTI-GS1 datasets produced no errors because they achieved 100% classification accuracy. The ORIGA-LIGHT dataset, with its limited size, produced results that were 88% accurate. The model's performance on different datasets makes it a strong candidate for real-time clinical deployment for screening purposes and validates its generalizability across different datasets.

Table 2: Performance analysis for Both Datasets

Dataset	Accuracy	Precision	Recall	AUC
Rim-One	0.94	0.886	1.0	0.98
ORIGA-LIGHT	0.88	0.919	0.830	0.96
HRF	0.97	1.0	1.0	0.99
Drishti-GS1	0.96	1.0	1.0	0.97
ACRIMA	0.84	0.773	0.962	0.95
Combined	0.914	0.916	0.958	0.96
OCT Data	0.96	0.94	0.98	0.97

OCT Dataset Results**:** The model produced an AUC value of 0.97 when it processed OCT datasets, as shown in Table 2. The confusion matrix in Figure 4 demonstrates how well the model performs in distinguishing normal cases from glaucomatous cases, especially for POAG (Primary Open-Angle Glaucoma). POAG develops insidiously, with the patient unaware of the slowly developing vision loss. Doctors need to diagnose eye problems correctly and begin treatment immediately to achieve successful vision protection. The proposed model shows promise for medical practice because it accurately identifies these cases through its high detection rates.

Discussion

The results of this study indicate that a 2D CNN model can efficiently identify and help in the early diagnosis of glaucoma by utilizing both OCT and fundus images. However, the system's accuracy fluctuates between the two imaging modalities. The OCT dataset produced better results, which proved that retinal nerve fibre layer thickness serves as a vital diagnostic factor for detecting initial glaucomatous conditions. The OCT system demonstrates superior sensitivity through its 98.0% detection rate and AUC value of 0.97, which allows it to identify glaucoma damage during its initial development. The research shows that OCT scans function as vital diagnostic instruments that help doctors identify glaucoma during its first stages of development. The fundus image analysis produced results with 91.4% accuracy and 95.8% sensitivity. Despite being less sensitive than OCT scans, fundus images have significance as structural changes in the optic nerve head can be picked up, such as optic disc size and cup to disc ratio, which are key in early glaucoma detection.

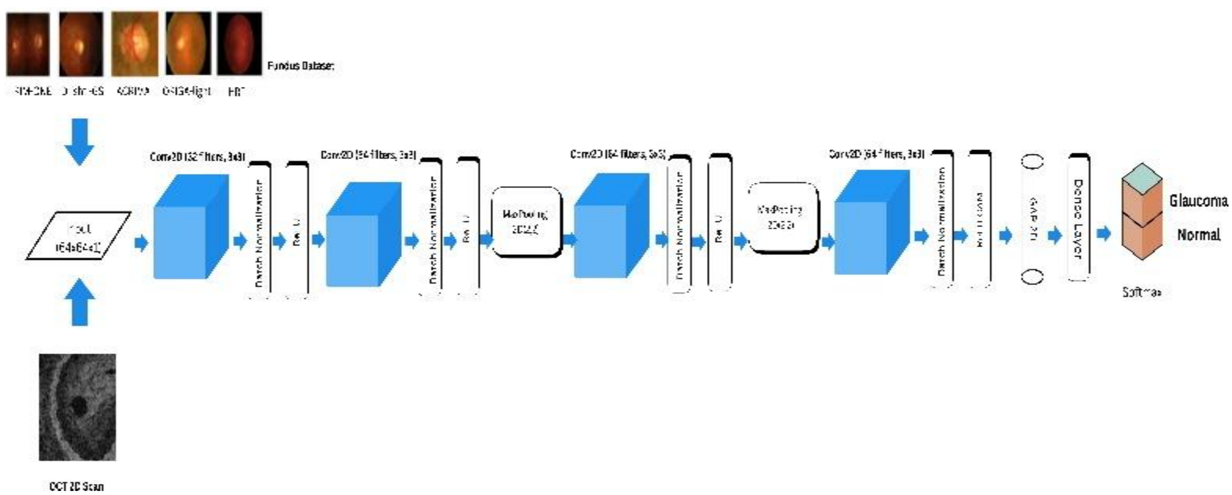

Figure 1: Block Diagram of Our Proposed Framework for Glaucoma Detection

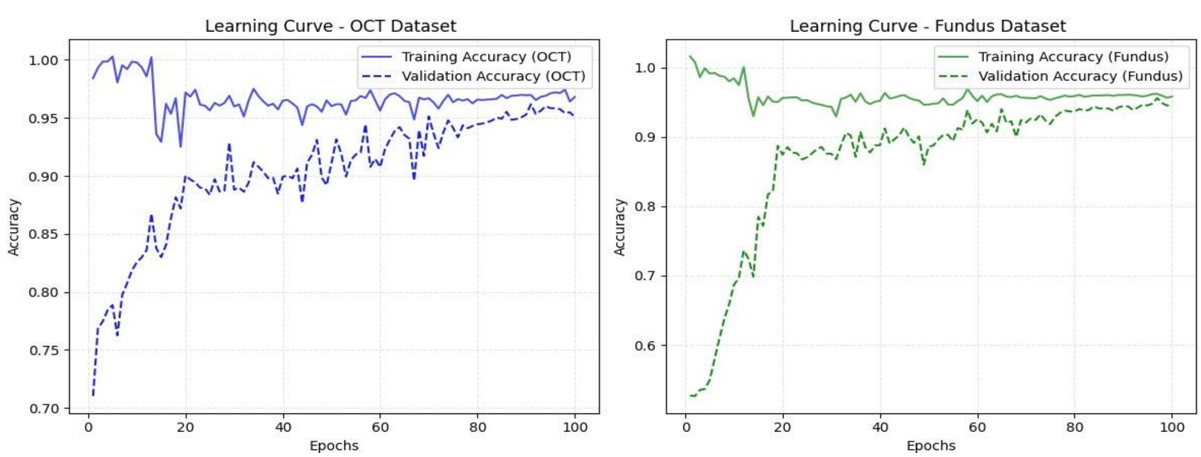

Figure 2: Learning Curves for OCT & Fundus

Because it is challenging to detect subtle changes in the optic nerve head at this stage, the accuracy was lower for early-stage glaucoma (91.4%). This demonstrates how difficult it is to identify glaucoma in its early stages using fundus images alone and implies that additional imaging modalities, like OCT, are frequently required for a thorough evaluation. The use of the same model for both datasets ensured that model variations did not influence the performance differences between the two modalities. The model learned distinct features from each modality, but the higher sensitivity and specificity for OCT scans reflect the advantages of structural imaging in glaucoma detection. The results demonstrate that OCT provides superior diagnostic capabilities for glaucoma detection and monitoring because it detects early-stage changes that fundus images cannot detect. To determine whether the observed difference in diagnostic performance between the fundus and OCT-based CNN models was statistically significant, a McNemar's test was performed using their paired classification outcomes. The test produced a p-value that was less than 0.001 to show that the prediction performance results were statistically different from each other. This result confirms that the OCT-based CNN model significantly outperformed the fundus-based model in distinguishing glaucomatous eyes from normal ones.

Lastly, the performance of the proposed model was compared with previously reported deep learning approaches for glaucoma detection. For instance, Li et al.,[10] reported an AUC of 0.986 using a deep learning system trained on a large-scale fundus photograph dataset. Similarly, Gómez-Valverde et al,[12] achieved an AUC of 0.94 using a transfer learning-based CNN evaluated on fundus image datasets including ESPERANZA, DRISHTI-GS, and RIM-ONE. In another study, Maetschke et al,[4] reported an AUC of 0.94 using deep learning applied to OCT volumes. More recently, Rasel et al,[2] reported that a 2D-CNN achieved AUCs of 0.960 and 0.943 on macular and ONH OCT test images, respectively. In comparison, the proposed model achieved AUC values of 0.96 for fundus images and 0.97 for OCT scans, demonstrating competitive performance while maintaining a relatively simple and reproducible architecture.

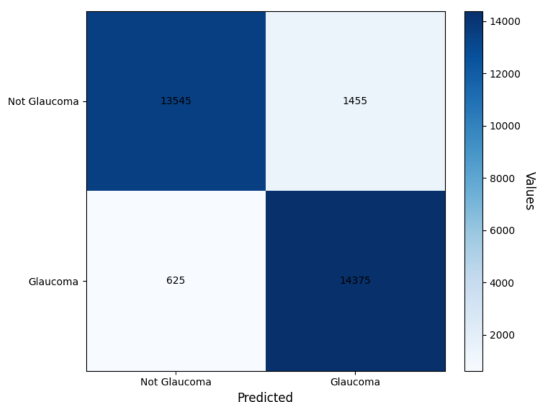

Figure 3: Fundus Confusion Matrix

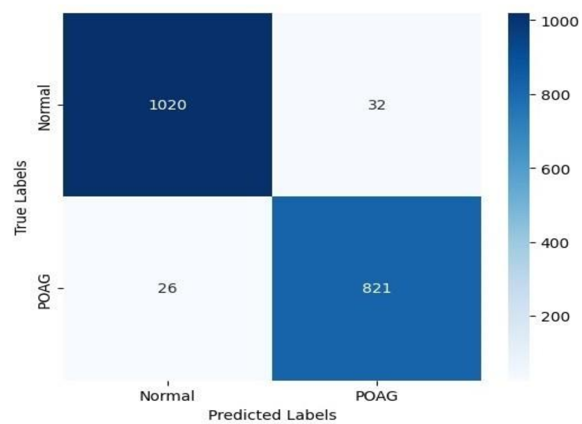

Figure 4: OCT Confusion Matrix

Conclusions

The research results show that two-dimensional convolutional neural networks (2D CNNs) work well for glaucoma detection through their application to fundus photographs and optical coherence tomography (OCT) images. The proposed model outperformed all current OCT-based assessment techniques because it provided better accuracy, sensitivity, and specificity, and complete structural data, which enables glaucoma diagnosis. The analysis of fundus images showed that these images continue to provide clinical value, but they do not perform well in detecting glaucoma during its initial development. The study results demonstrate that OCT serves as a fundamental diagnostic tool that helps doctors identify glaucoma at its initial stages, while fundus imaging offers additional data that doctors use to make treatment choices. The model requires future research to improve its ability to detect fundus images through data enhancement techniques and interface design improvements, which will allow medical staff to use this system during their professional activities. The model achieved successful results when processing both fundus and OCT images, but it needs additional development work. The fundus image model requires improved sensitivity through research into various CNN structures and data enhancement methods, which would enhance its ability to detect glaucoma at its initial stages. The model needs evaluation of its ability to predict different population groups through the inclusion of various demographic data, which should represent people from different age groups and cultural backgrounds. Medical imaging needs deep learning models to reach their maximum potential because their ability to be interpreted remains essential. The model should make decisions through Grad-CAM (Gradient-weighted Class Activation Mapping), which reveals to clinicians which parts of the images produce the model's prediction results. The system should require complete transparency to build trust in automated diagnostic systems, so that medical staff can understand the decision-making process of their predictions. The model needs to show its ability to work with different populations through the addition of various demographic information, which should include people from different age ranges and cultural backgrounds. Future work will focus on testing the framework on an entirely unseen multi-center clinical dataset collected using different imaging devices and protocols.

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