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Research Article

Convoluted Neural Networks, CNN, AI Deep Learning Models and their Role in the Diagnosis of Glaucoma

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Abstract

Aim: To review the advancing role of CNNs in the last decade in detecting glaucoma.

Methods: Google Scholar and PubMed were searched for CNN methodology in image detection, the use of CNNs to detect glaucoma and CNNs with 90% or better outcomes in glaucoma diagnosis. MobileNet, ResNet, InceptionV3, ReLU, Sigmoid, Max Pooling, SoftMax, loss function, binary cross-entropy, Stochastic Gradient Descent, and forward and backward pass and "you only look once" (Yolo) were also used as search terms with glaucoma. References obtained were then checked for accuracy metrics; additional references were obtained from papers citing previous CNN glaucoma papers with high accuracy metrics.

Significance: Over the last decade CNN because of its leveraged hierarchical approach to extract salient optic nerve features from color fundus photos and OCT images has become a valuable, non-invasive tool in diagnosing glaucoma with over 90% accuracy.

Keywords: Glaucoma; Optic nerve images: fundus photos and OCT images; CNN; AI Deep Learning Models; Accuracy; Convolutional Layers; Kernels; Activation Functions; Max Pooling; Loss functions; stochastic gradient descent; Forward pass; Backward pass.

Introduction

Glaucoma Epidemiology

The global prevalence of glaucoma in 2020 was approximately 79.6 million individuals affected with open angle and closed angle glaucoma [1]. About 4.5 million individuals worldwide are blinded by glaucoma, such that glaucoma worldwide is the second most common cause of loss of vision [2].

Glaucoma Diagnostics Plus CNN

While intraocular pressure, visual field testing, (especially with the digital field analyzers), and Optical Coherence Tomography, OCT, and gonioscopy are all valuable tools in the diagnosis of glaucoma, the addition of CNN to analyze fundus photo and OCT images of the optic nerve is a valuable, relatively inexpensive, non-invasive, adjunctive technique to gain earlier diagnostic knowledge of individual, familial and population at risk levels in this silent but threatening disease.

The glaucoma diagnostic leverage with the addition of CNN has widespread implications in terms of early: personal care adjustments, community access in underdeveloped areas, and management of lack of sustained glaucoma medication adherence over extended periods.

The CNN optic nerve layers from fundus or OCT images, with their guided deep learning and, forward and backward numeric tensor propagations, can iteratively decipher glaucoma patterns, at close to experienced ophthalmologist level.

CNNs Deep Historical Elements

CNNs historically go back to Hubel and Wiesel who discovered that the visual cortex has "simple cells" that respond to bars and edges and "complex cells" (less position sensitive) responding to bars/slits [3]. Torsten Wiesel's 1981 Nobel Lecture begins with "In the early sixties, having begun to describe the physiology of cells in the adult cat visual cortex, David Hubel and I decided to investigate how the highly specific response properties of cortical cells emerged during postnatal development" [4]. "This modest statement belies the tidal wave of experiments on developmental brain plasticity that was initiated by their publications in 1962, continues to this day, and extends well beyond the occipital lobe to virtually all sensory areas, motor areas, and to "higher centers" involved in learning, memory, and decision making" [5]. This neurophysiological tapestry of simple to more complex sensory responses to visual stimuli morphing into contextually plastic and developmental iterations resulting in motor "learning, memory and decision making" forms the basis of the granular elements of CNN.

Table 1: Some Operational Roles of CNN Layers/Terms in Diagnosing Glaucoma.

Convolutional Layers	Function	Reference Source
Convolutional Layers	Apply filters to the input for edge, texture, and key feature detection at different spots of the image	Yamashita R (2018) [9]
Pooling Layers	Downsample feature maps of Convolutional layers	Sarvamangala DR (2022) [10]
Fully Connected Layers	Collect the features learned from the image and predict spatial info, transforming info into a format for classification	Yamashita R (2018) [9]
Hierarchical Representation	Extract key features of subtle patterns automatically: optic nerve cupping, neuroretinal rim thinning, and retinal nerve fiber layer defects, and distinguish different classes of images e.g. levels of advance in optic nerve damage	Raghavendra DR (2018), Haja SA (2023), Chen J (2021) [11, 12, 13]
VGG 16	16 layers, multiple convolution layers with small filters for greater image classification	Haja SA (2023), Ananda KC (2020) [12, 14]
ResNet	Residual connections allow the network to skip some connections and train with large layers	Haja SA (2023), Alzubaldi L (2021) [12, 15]
GoogleNet	Uses "inception" modules, which are parallel convolution operations to learn discriminative features; high accuracy for glaucoma vs. normals	Haja SA (2023), Ananda KC (2020), Camara (2022) [12, 14, 16]
Automated CNNs; VGG + Resnet	Auto extract relevant features, separating glaucoma features from normals	Haja SA (2023), Chen J (2021), Camara J (2022) [12, 13,16]

CNNs Technical Evolution, Historical Elements

In 1979 and 1980 K Fukushima published the basic CNN architecture of convolutional layers and downsampling layers. (Fukushima first introduced non-linear activation units ReLU, rectified linear units to learn edges and complex patterns [7,6]) in 1969). His network was trained by unsupervised learning rules and was 100x more expensive than in 1989 and a billion times more expensive than today [6,7]. Fukushima made a video in 1986 of a CNN that recognizes handwritten digits [7]. In 1987, Alex Waibel (a German researcher working in Japan) trained supervised learning, weight sharing neural networks with 1-dimensional convolutions by Linnainmaa's 1970 backpropagaton algorithm to recognize speech. A similar proposal by Homma et al. introduced the "convolution" terminology to neural networks. Convolving means taking a small numerical sample of a pattern in an image [7].

Both Wei Zhang and Yann LeCun, et al. (at Bell Labs) independently developed backpropagation-trained CNNs, (Zhang for Chinese letter character recognition and LeCun for zip codes) [7]. Backpropagation generates gradients or derivatives backward from the output layer to correct how much each weight and bias needs to be reduced to minimize the forward propagation overages; thus, using differential calculus to find optimal layers adjustments to fine tune the forward propagation of weights and biases, the back propagation allows for weights to be updated and reduce prediction errors and avoid redundant calculations [7,8].

Table 2: CNN lexicon of terms.

Term	Definition
ADAM	An optimization method that helps neural networks learn by adjusting the learning rates* for each parameter individually. It combines the benefits of two other methods: momentum and Root Mean Square Prop. Example: Imagine you're trying to find the fastest route to work every day. Some days, traffic is heavier, so you adjust your route based on that. ADAM does something similar by adjusting how much it changes the model's parameters based on past experiences.
Accuracy	The ratio of correctly predicted instances to the total instances in a dataset. It is a measure of the overall performance of a model. **AUC or area under the curve, typically AUC-ROC is related to balancing true positive and true negative rates across all thresholds acting as a single measure of a classifier's ability.
Back Propagation	A training algorithm used for neural networks, where the model learns by adjusting weights based on the error from the output layer back through the network.
Biases	Values added to the output of neurons to allow models to fit the data better. They help adjust the output along with the weights.
Confusion Matrix	A table used to evaluate the performance of a classification model by comparing predicted and actual values. It shows true positives, false positives, true negatives, and false negatives.
Convolutional Layer	A layer in a CNN that applies a convolution operation to the input, extracting features from the data through the use of filters (kernels).
Data Loader	A utility that provides an efficient way to load and preprocess data in batches for training or testing a model.
Data Set	A collection of data used for training and evaluating models. It can be divided into training, validation, and test sets.
Dense Layer(s)	Fully connected layers in a neural network where each neuron is connected to every neuron in the previous layer. They are used for classification tasks after feature extraction.
Deep Learning	A subset of machine learning that uses multi-layered neural networks to model complex patterns in large datasets.
Epoch	One complete pass through the entire training dataset during the training process.
EfficiencyNet B3	A family of CNN architectures that optimize both accuracy and efficiency, often used in image classification tasks.
Flattening Layer	A layer that converts multi-dimensional input (like images) into a one-dimensional vector, allowing it to be processed by dense layers. It is used before the dense layers.
F1 Score	A measure of a model's accuracy that considers both precision and recall, calculated as the harmonic mean of the two.
Forward Propagation	The process of passing input data through the network to obtain an output, which is then compared to the actual value to compute the loss.
Inception V3	A deep learning architecture that uses multiple types of convolutions (1x1, 3x3, and 5x5) in parallel within the same layer, allowing the model to capture different aspects of the input data efficiently.
Kernel	A small matrix used to perform convolution operations on the input data, extracting features such as edges and textures.
Kernel Size	The dimensions of the kernel (e.g., 3x3, 5x5) that determine how much of the input the kernel covers during the convolution operation.
Learning Transfer Model	A model that leverages knowledge from previously learned tasks to improve learning efficiency and performance on new tasks.
Linear Activation Function	An activation function where the output is directly proportional to the input. It is defined as $f(x)=x$ and is often used in the output layer for linear regression tasks.
Loss Function	A function that measures the difference between the predicted output and the actual output, guiding the optimization process during training.
Max Pooling	A downsampling technique that reduces the spatial dimensions of the input by taking the maximum value in each patch defined by the kernel.
MobileNet	A lightweight deep learning architecture designed for mobile and embedded vision applications. It uses depth wise separable convolutions to reduce the number of parameters and computation while maintaining performance.
Non-linear Activation Layers	Layers that apply non-linear transformations to the input, enabling the network to learn complex and non-linear patterns. Common examples include ReLU, sigmoid, and tanh.
Optimizer	An algorithm used to adjust the weights of the network based on the gradients computed during backpropagation. Examples include SGD and ADAM.
Padding	The process of adding extra pixels (usually zeros) around the edges of an image before applying a convolution operation. This helps preserve the spatial dimensions of the input and allows the model to capture features at the borders.
Pooling Layers	Layers that reduce the spatial dimensions of the input, helping to decrease computational cost and control overfitting.
Precision	The ratio of true positive predictions to the total positive predictions made by the model.
Recall	The ratio of true positive predictions to the total actual positives in the dataset.

ReLU (Rectified Linear Unit)	A non-linear activation function defined as. It allows CNNs to learn edges and complex patterns by introducing non-linearity, enabling better feature representation.
ResNet	A deep learning architecture that uses skip connections to allow gradients to flow more easily through the network, making it easier to train very deep networks.
Segmentation	The process of partitioning an image into multiple segments to simplify the representation of an image and make it more meaningful for analysis.
Sensitivity	Also known as recall, it measures the proportion of actual positives that are correctly identified by the model.
SGD (Stochastic Gradient Descent)	An optimization algorithm that updates the model's weights incrementally based on a subset of the training data.
SoftMax	An activation function often used in the output layer of a model for multi-class classification. It converts raw scores (logits) into probabilities, ensuring they sum to one.
Specificity	The proportion of actual negatives that are correctly identified by the model.
Strides	The number of pixels by which the kernel moves over the input data during convolution.
Tensor	A multi-dimensional numeric array that can represent data of various dimensions. In the context of neural networks, tensors are the data structures that hold inputs, outputs, and intermediate values (activations) during forward and backward propagation. For example, a tensor can represent a batch of images as a 4D array with dimensions corresponding to batch size, height, width, and color channels.
Training Data* **	The portion of the dataset used to train the model, allowing it to learn patterns and make predictions.
Unet	A CNN architecture designed for image segmentation tasks, characterized by its U-shaped structure that captures context and enables precise localization.
VGG	A deep convolutional network architecture known for its simplicity and depth, using small (3x3) convolutional filters.
You Only Look Once (YOLO)	A real-time object detection system that predicts bounding boxes and class probabilities from full images in one evaluation, making it extremely fast and efficient for detecting objects in images.
Weights	Parameters within the model that are adjusted during training to minimize the loss function, determining the strength of the connection between neurons.
Zip Code	An example of structured data that can be processed by CNNs in tasks like handwriting recognition.

*Learning rate "literally is a hyperparameter that the coder uses to determine the step size the model takes as it adjusts the internal weights during training so as to minimize error. Adam optimizer (Adaptive Movement Estimation) dynamically adjusts the learning rate for each individual parameter of a CNN during training, rather than using a single fixed learning rate for an entire batch being convoluted in the network.

**AUC, area under the curve, is most closely related to balancing Sensitivity (True positive rate) and Specificity (True negative rate) as a single measure of a classifier ability to separate between different classes; Accuracy (True Positives + True Negatives divided by total samples) is a single point at one threshold, often 0.5, and Precision-Rcall focuses on the positive class performance; thus, when Accuracy fails on imbalanced data, Precision-Recall AUC is useful; AUC-ROC (Area under the receiver Operating Characteristic Curve) plots Sensitivity, true positives vs Specificity false positives at various thresholds.

***Training data is the primary data set to learn patterns and relationships from the data by adjusting parameters, such as weights and biases. Validation data is used during the model development to provide an unbiased evaluation of the model's performance on unseen data not used during training; it can help prevent "overfitting" of the training model because it works with different portion of the data set and does not learn from the model the way the training data does; Test data, like the validation data is usually a smaller percentage of the data, e.g. 15%, unlike the 70% for the trained data set, and the test data set, not having been trained, is only used after the model has been fully trained; thus test data set represents the actual outcome and evaluation of the model, its accuracy and its ability to generalize or make predictions about the data.

The Centrality of the optic nerve changes to glaucoma diagnosis; non-AI glaucoma diagnostic accuracy, and false positives that can look like glaucomatous optic atrophy

CNNs, after importing an optic nerve image on a computer, for example, can convert it to a numeric array and then with coded directions through guided neural net layers iteratively identify glaucoma patterns in the optic nerve. These glaucoma associated patterns are learned so well from the CNN models, that their accuracy rivals that of experienced ophthalmologists.

In 2002 a randomized controlled study in ocular hypertension found:

1. Ocular hypertension is a major risk factor in developing primary open angle glaucoma.
2. Treatment of ocular hypertension with pressure lowering medication delayed or prevented glaucoma onset.
3. Over half the patients who developed glaucoma showed optic nerve changes, without early visual field loss, emphasizing the need for optic nerve monitoring alongside ocular pressure checks.

4. Lowering intraocular pressure helps protect the optic nerve and slows down the damage rate.

5. Thinner central corneal thickness is another significant risk factor for glaucoma [17].

Therefore, by using CNN to detect glaucoma optic nerve changes, even before visual field loss, early diagnosis, treatment and patient counseling can be achieved. The latter, of course, contextually demands a critical evaluation of the individual patient: the patient's medical history, physical data, lab data, and clinical and familial background.

That said, over the last decade several papers using CNN on optic nerve images found glaucoma patterns, and their level of identification compared well to that of trained ophthalmologists.

However, to start with, let's examine a non-AI baseline accuracy level in trained eyecare settings, in a "masked performance study" in Scotland. Patients suspected of having glaucoma, within one month, underwent a full ophthalmic assessment in both a newly established community led glaucoma management location, AGO, and a consultant led eye hospital. Agreement between the AGO and the consultant unit in diagnosing glaucoma was 89%. Agreement between trainee ophalmologists and the consultant unit was 83%. The accuracy of optometrists in detecting glaucoma in this population was good with a specificity of .93, but lower for sensitivity at .76. There was no difference in sensitivity between AGO and junior ophthalmologist [18]. The diagnosis of glaucoma in this study rested on optic nerve changes and or visual field abnormalities [18].

The other side of the coin, false positives, may be neuro-ophthalmological conditions that mimic glaucoma and result in misdiagnosis [19]. These include: ischemic optic neuropathy, 25%, compressive optic neuropathy, 18.7%, hereditary optic neuropathy, 18.7%, and congenital optic neuropathy, 2%, from a study of 68 patients enrolled with neuroophthalmological diseases screened from a single Eye Clinic within a 24-month period.

The researchers selected the eyes with pre-defined glaucoma criteria:

Vertical cup-to-disc ratio greater than or equal to 0.6, asymmetric disc ratio greater than 0.2 between the two eyes, presence of localized retinal nerve fiber layer and or neuroretinal rim defects and disc hemorrhages.

The images were mixed randomly and a masked glaucoma expert was asked to distinguish if each patient exam derived from a patient with glaucoma or a neurophthalmological condition. "Based on the analysis of fundus photographs and HVF, (Humphrey Visual Field) tests, 25% of these were misdiagnosed as glaucoma (two ischemic optic neuropathies and two congenital optic disc anomalies). Conversely, 11.9% of the glaucomatous neuropathies were misdiagnosed as neurophthalmological disorders. Overall, the glaucoma specialist correctly diagnosed 84.5% of the eyes" [19].

References 18 and 19 illustrate the need for extensive analysis and for thorough individual patient data review for a glaucoma diagnosis to be made, even in the setting of prima facie, conventional clinical markers of glaucoma.

With that introduction, we can explore the results of CNN glaucoma pattern recognition in about a decade worth of papers, using different CNN deep learning models to detect glaucoma and their relative accuracies.

Results

CNN Layers, Activators, features to develop a Model to test, validate and train optic nerve images for normal/ glaucoma prediction, Procedural Considerations

After downloading a series of "procedural software packages", the initial activity of the CNN neural network coder is to import the image or data set of images. In this setting the image(s) will be either fundus photo(s) or an OCT, Optical Coherent Tomogram, image(s) of an optic nerve with an identifying label.

The programmer can then elect to use an established, well vetted deep learning platform with its parameters or implement a custom platform with additional parameters. In any case, the platform will serve as a base for the CNNs network to import the image data set, convolve it, add weights, adjust it, and optimize it, prior to train, validate, test and predict dynamics. Yet additional modulatory features that the coder wishes to adjust /add called hyperparameters can also be implemented. How different the CNN model is from the actual desired outcome or its loss function as well as and the training model's accuracy will determine just how much adjustment the training model requires.

One or more convolutional neural network layers, each with a specific function, such as feature extraction, segmentation, classification [12, 20], will without the knowledge or assistance of the coder/observer process large amounts of visual data. The CNN layer will capture an extracted kernel of the image (which is a smaller sample of numerical matrix feature) for the character of the item it is detecting and connect it to others of a similar nature. These are joined and either made to relate, or not, to other layers. A hierarchy of layer connections results in optimizing the input and creating an architecture of learning matrices with corresponding numeric outputs called logits that represent complex digital outputs of salient patterns in the image. These logits or quantized outputs can then be used for training, testing, and plotting the image data, and evaluating the data for inference and predictions [12, 20,21,22].

To reduce the large spatial dimensions of the convolutional layers, pooling layers downsize the feature data maps but still preserve the essential data [12,22].

To introduce non-linearity into the CNN model, the ReLU, rectified linear unit, is used; other activation functions are sigmoid and tanh; sigmoid maps from 0 to 1 and tanh maps from -1. to 1; tanh is zero centered which leads to faster image data convergence and better hidden layer performance. Sigmoid, on the other hand, is better for working the output layer in binary classification where you need a probability of 0 to 1 [21].

Connected layers join the learned features of the other layers, combine spatial information and transform it into a format suitable for classification and provide the basis for making relationships and enabling high level decisions [12, 22].

Thus, the CNN architecture provides a learning platform for image pattern recognition, representation, segmentation, classification and automatic aggregation to facilitate identification of normal vs glaucoma, e.g. cupping, neuronal rim thinning, and retinal nerve fiber layer features. This collection of CNN aggregated images can be used to develop, test, and train data sets of new images that can (with a background of good accuracy validation) be used to predict normal from abnormal optic nerves in successive glaucoma test samples [9,11,12,22].

Table 3 illustrates some of the papers with greater than or equal to 90% accuracy in diagnosing glaucoma with various CNN methods. These papers reflect glaucoma detection from fundus photos (from conventional fundus photo units as well as a portable ophthalmoscope combined with a smart phone) as well as glaucoma detection from 3D OCT images of the optic nerve, and recurrent neural network images of sequential video fundus images.

Table 3: Papers with >90% Accuracy Diagnosing Glaucoma with CNN

Reference	CNN used	Accuracy, Sensitivity, Specificity, AUC, F-1
Shoukat A, Auto Dx Gl from retinal images, Diagnostics (Basal)2023	ResNet-50 Architecture	Accuracy: 98.48%
Akbar S, Detection of microscopic GL, fundus photos, deep transfer approach, Micrsc Res Tech, 2022	Fusion of DenseNet and DarkNet	Accuracy: 99.7%
Ataly E, CNN architectures Dx Gl using color photography, Turkish J Ophthalmol, 2022	Deep Residual Networks and Very Deep Neural Networks	Accuracy: 96.2%
Liu H, Dev and Validation DL to detect Gl from fundus photos, JAMA 2019	Glaucoma Diagnosis CNN.	AUC .996
Braganca CP, Det of Gl from fundus images w DL on new image from smart phone and handheld ophthalmoscope, Healthcare (Basel)2022	CNN Ensemble Model: ResNet50V2, ResNet 101, InceptionResnet, Densenet, Mobilnet, InceptionV3, Xception	Accuracy 90%
Maetschke S, feature agnostic glaucoma detection OCT volumes 2018	3D CNN 5 convolutional layers, ReLU Activation; Class Activ Maps, CNN identified neuroretinal rim, cup and lamina cribrosa: glaucoma regions	AUC .94
George Y, Attention-guided 3D-CNN Glaucoma detection and Structure-Functional Assoc using Volume images,2020	End to End attention guidance to 3D DL Model Estimating visual function from retinal structures; same network architecture but with 3 pathways: 1. 3D OCT cube, 2. other 2: 3D gradient class activation heatmaps	AUC 93.8%
Gheisari S, Combined CNN and recurrent neural network for glaucoma detection Sci Rep 2021	Combined CNN and recurrent neural network which extracts temporal features embedded in sequential fundus video images	F-1 96.2%

CNN workflow:

1.Data Download,

2.CNN layers, Activating layers, Pooling Layers

3.Flattening Layers, Hidden Layers, Linear/non-Linear Layers

4.Dense, Condensing Layers, Optimizers Layers,

5.Initial Model Output, Check Loss function and Accuracy, if good,

6.Train, Validate, Test Data Set; make predictions, compare outputs

7.From different CNN methods and platforms, Optimize CNNs and platform, adjust hyperparameters, re-train the model for lower loss function and greater accuracy

8.Re-adjust platform/ parameter(s) and hyperparameters as necessary [21].

Discussion

Exploring the realm of refining CNN choices from the established CNN glaucoma deep learning models requires experienced investigation in not only the basic parameters of the established model, but also the adaptation of hyperparameters by the programmer for the new model. This type of experienced investigation, (at least until agentic modelling in this area can be validated) is definitely one of the drawbacks of the current CNN application to the diagnosis of glaucoma in a given data set, especially if the data set needs adaptation to a particular CNN model that may not have been used with that data set previously.

Collection and transferring images, as was evident in Bragance, et al. (using e.g. portable ophthalmoscope and smart phone) can also be a challenge. However, if functional code programs or agentic programs connect image: intake, preparation for CNN, integration with CNN and development of optimal outputs for glaucoma predictions, then even in an eye clinic setting portable ophthalmoscopes and smart phones may be used in the future.

That said, agentic deep learning is progressing at a nice pace. With the laudable ideal of streamlining CNNs and their linkage to diagnosing glaucomatous optic nerve photos for millions in need, the technology may be short in coming.

Conclusion

From the above work on using CNNs to detect glaucoma from fundus or OCT images of the optic nerves, it would appear that it is only a matter of time for the conventional eye clinic to integrate CNN with tonometry and visual fields for glaucoma detection. As fundus or OCT imaging gains greater bandwidth with CNN integration, in house earlier glaucoma detection can become a reality even in more rural areas.

Conflicts of interest

None.

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