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A Novel Method Using Deep Learning Technique for Automatic Grading and Classification of Interferometry Video Frames for Dry Eye Analysis

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Abstract

Maintaining good ocular health is vital to overall health, wellness and well-being. Dry eye is a syndrome that affects people of all ages if the blink rate is not up to the mark. A normal mean blink rate of up to 22 blinks/min has been observed under relaxed conditions. Tears protect eyes from irritants and infections and keep the eyes wet. A thin layer of tear film is spread across the outer layer of the eye with each blink. Dry eye occurs when eyes do not produce enough tears or good quality of tears. There are several diagnostic techniques available in the market to detect dry eye syndrome. One of the techniques is tear film interferometry, which is based on interferometric patterns developed under extended white light source over outer most layer of tear film, called lipid layer. It is a non-invasive technique used to evaluate the quality of the tear film. Interferometric patterns develop over lipid layer can be classified into five different dry eye grades: grade 1, grade 2, grade 3, grade 4 and grade 5 based on color and distribution of fringes. This work intends to propose a novel method for automatic classification of interferometry video frames to detect the dry eye condition using a combination of computer vision and deep learning technique based on sequential convolutional neural network architecture. The proposed novel technique has achieved an overall accuracy of 86.25% and the results look promising.

***Keywords*: Lipid layer, interferometry, dry eye, convolutional neural network**

1. Introduction

The advancement in technology has brought with it various health concerns along with its advantages. The pandemic era caused a lot of children, youngsters and old people to get more inclined towards electronic gadgets. Disconnection from the outside physical world forced people to excessively rely on gadgets. This excessive exposure to screen time has caused an increase in occurrence of dry eye syndrome in all age groups.

Dry eye syndrome is a condition in which a person doesn't have enough quality of tears. Good quality of tears plays an important role in maintaining healthy eyes. Tear helps to lubricate our eyes and reduces the possibility of infections. The tear film consists of three layers namely lipid layer, aqueous layer and mucin layer. The lipid layer is secreted by meibomian glands which coats the aqueous layer and prevents quick evaporation of tears from the surface of the eye. The aqueous layer is secreted by lacrimal glands. It helps in spreading tears over the surface of the eyes. The mucous is secreted by goblet cells which coat the cornea and helps in even distribution of tears over the surface of eyes. Any imbalance in these layers will lead to dry eyes.

Dry eye is a very prevalent and long-term problem, particularly in an ageing population. People with dry eyes do not produce enough tears or their tears are of a bad quality. The quantity of tears reduces due to several conditions like age, gender, medications, medical conditions like rheumatoid arthritis, diabetes and thyroid problems or due to other environmental conditions. Symptoms of dry eyes include burning sensation in eyes, stingy mucus in and around eyes, sensitivity to light, sensation of having something in the eyes, difficulty in wearing contact lens and difficulty with nighttime driving.

It has been reported that 18.4% to 54.3% [1] in globe are affected by dry eye syndrome. Though the early symptoms of dry eye are perceived to be mild and manageable, the syndrome may progress to a more severe stage like corneal damage. Hence it is extremely important to detect dry eye syndrome in the early stage.

Dry eye can be classified into two different groups, *aqueous-deficient* dry eye syndrome and *evaporative* dry eye syndrome. Aqueous-deficient dry eye syndrome is caused due to reduction in aqueous production from lacrimal glands. Evaporative dry eye syndrome is caused due to deficient tear film lipid layer.

Dry eye syndrome can be detected using several examination techniques like ocular surface staining with fluorescein or lissamine green, tear breakup time with fluorescein, Schirmer test and examination of eyelids, meibomian glands. These techniques are invasive procedures and may cause some discomfort to the subject.

The tear film interferometry under extended while light source is a non-invasive method that analyses interference pattern formed over lipid layer, thickness of which increases with progression of disease. Distribution and color of the interference fringes change with the thickness of the lipid layer. Therefore, a careful investigation of fringe pattern reveals the status of the dry eye.

Many authors [2] [3] presented a relationship between color of the fringes and lipid layer thickness. These methods mapped color of the fringes and lipid layer thickness. These methods mapped color of fringes and lipid layer thickness in microns. In a similar way, N. Yokoi attempted to grade interference patterns into five different classes and mapped them into different stages of progression of disease [4]. The grade of normal eye is 1 in Yokoi grading system, and this number climbs to 5 as severity increases. The detailed description of five grades in Yokoi grading system [4] are given below.

- *Grade 1*: Lack of fringes and uniform coloration
- *Grade 2*: Presence of non-uniformly distributed monotone fringes
- *Grade 3*: Presence of non-uniformly distributed area of colored fringes
- *Grade 4*: Presence of multiple non-uniformly distributed colored fringes
- *Grade 5*: Corneal surface partially exposed

The proposed method used artificial intelligence to categorize lipid layer interferometric patterns into five grades of Yokoi grading system. It starts with capturing video of lipid layer interference pattern using an extended white light source and a digital camera, in this case a fundus camera. Next it extracts frames from video and analyzes. To the best of our knowledge the proposed method for the dry eye analysis is one of the first methods that combines computer vision and deep learning technique to generate accurate and operator independent results.

The rest of the paper is organized as follows: Section 2 provides a brief review of dry eye syndrome and different deep learning architectures used for medical image classification. Section 3 discusses the image processing and deep learning methods used for automatic classification of interferometry video frames. Section 4 provides the experimental result and common performance metrics used for the analysis of classification model. The work concludes with a discussion on possible future work to enhance the performance of the model, in section 5.

2. Related Work

Limited work has been done on automatic dry eye grading using tear film interferometry. A brief overview of dry eye and its conditions and an outline of related work on convolutional neural network is presented below.

Dry Eyes and Its Conditions:

"Dry eye is a multifactorial disease of tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to ocular surface. It is accompanied by increased osmolarity of tear film and inflammation of ocular surface" [5].

[6] explained the importance of tear film and how biochemical composition of tears gets altered in dry eye condition. They have also explained different biophysical measurements of tear film like tear film structure and dynamics, tear film stability, tear osmolarity, tear ferning, Potential of Hydrogen(pH) value of tear and different measurement techniques associated with all these biophysical changes. A complete study has been made to understand how biochemical changes are related to biophysical changes.

[7] explained different types of examinations like examination of eyelid, blink rate, examination of conjunctiva, ocular surface, tear film, tear breakup time and tear osmolarity tests. The author has also described different types of treatments for dry eye disease. The work also explained the importance of educating patients and inferred that dry eye is a chronic disease and the treatment is a long term and slow process.

[8] presented analysis of the performance of the top three popular convolutional neural network (CNN) namely AlexNet, GoogleNet and ResNet50. The performance of all three networks has been tested for both static images and live videos. The accuracy of all three networks has been tested using popular datasets namely CIFAR10 and CIFAR100. The study has been conducted for 10 classes of each dataset. The average accuracy on CIFAR100 dataset of AlexNet is 44.10%, GoogleNet is 64.40% and RestNet50 is 59.82%. Similarly, the average accuracy on CIFAR10 dataset using AlexNet is 36.12%, GoogleNet is 71.67% and RestNet50 is 78.10%. The objective of the work was to find out the performance of different convolutional neural networks on the same datasets.

[9] explained the importance of convolutional neural networks (CNN) in medical image classification and introduction to CNN and its architecture. The authors have considered different convolutional neural networks like GoogleNet, Dynamic CNN, LeNet CNN, Ensemble CNN etc. The survey has been conducted on different papers which include image classification, image segmentation, image detection and localization. The authors have concluded that CNN is an efficient and popular technique and can be used to solve different challenging problems in the medical field.

3. Methodology

The block diagram consists of the overall workflow of the system as depicted in Fig.1. The solution proposed for dry eye analysis progresses in 2 phases. The first phase is based on traditional computer vision-based techniques to extract frames and detect blink from the video captured. The second phase is based on a multi class classification deep learning model for prediction of grade. The result is computed based on the statistical analysis of the grades of frames in each blink.

The basic components of the dry eye detection and grading system given in the block diagram are described below.

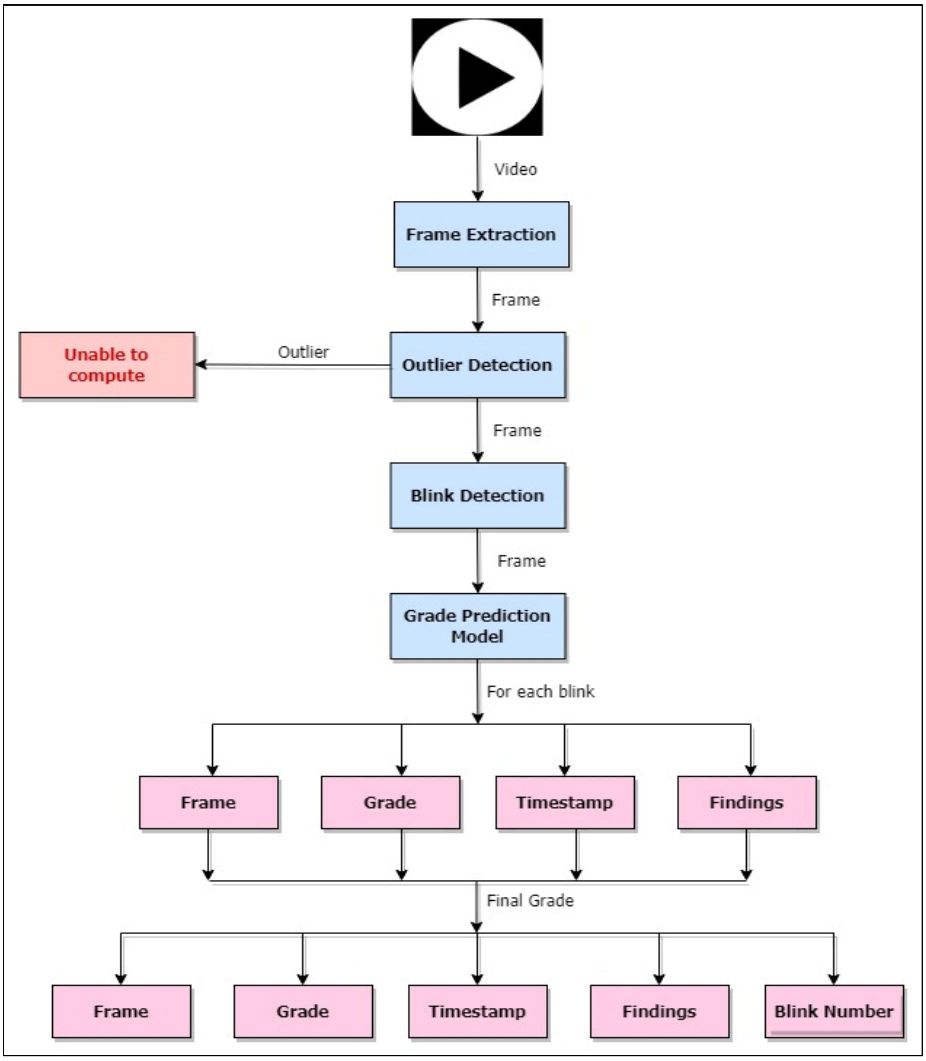
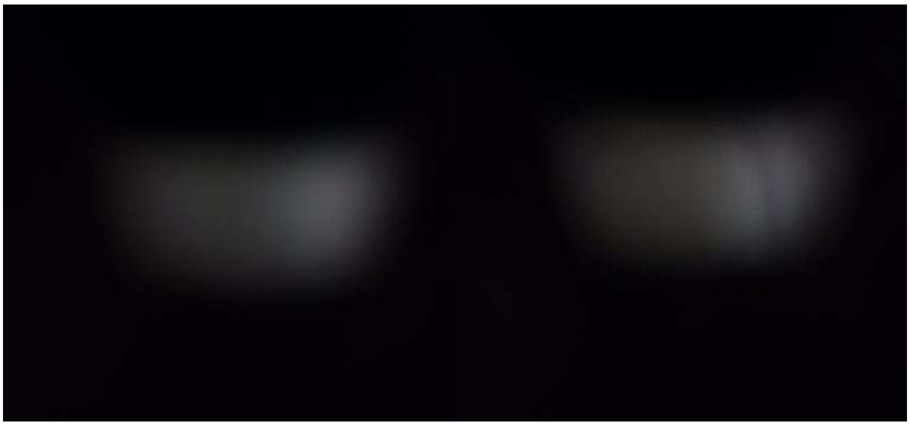


Fig.1. Overall workflow of the system

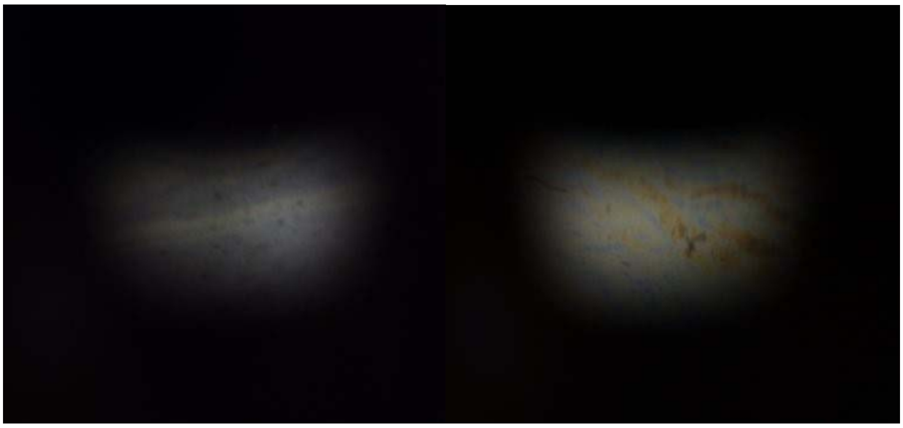
3.1 Frame extraction

Tear film interferometry video is captured and processed frame by frame. All frames from the video are extracted at a frame rate of 10 frames per second and saved in compressed format. The extracted frames are in RGB color space with a resolution of 3088x2076 pixels. Fig.2. shows examples of all four categories A total of 300 frames are selected and divided into 4 categories:

- Grade 1 (lack of fringes) - 70 images
- Grade 2 (monotone fringes) - 73 images
- Grade 3 (few colored fringes) - 75 images
- Grade 4 (colored fringes) - 85 images



(a) Grade 1 frame (b) Grade 2 frame



(c) Grade 3 frame (d) Grade 4 frame

Fig.2. Four categories of interferometry images

3.2 Outlier Detection

The extracted frames are passed on to an outlier detection module which verifies whether the input frames are valid ones or invalid. Only valid frames are sent to the ROI segmentation module.

3.3 Region of Interest (ROI) Segmentation

Selected frames after extraction contain irrelevant information which appear as the external dark area as illustrated in Fig.2**.** The relevant region of interest is located in the center part of the frame which is formed by the anterior surface of the tear film that covers the lower part of the cornea. To avoid the irrelevant region, ROI segmentation process is carried out.

3.4 Blink detection

Normal blinking is necessary to ensure even distribution of tear film and to protect the eyes. Abnormal blinking results in poor distribution of tear film on ocular surface and hence causes damage to the ocular surface. The normal mean blink rate is 22 blinks/min has been reported under relaxed conditions [10]. Various conditions like Parkinson's disease, corneal sensitivity disorder, lighting, temperature, humidity and usage of computer, tablet and smartphones affect the blink rate.

The workflow of blink detection is depicted in Fig.3**.** To identify the frame with blink, average intensity of all the frames is computed after identifying the region of interest. The frame with highest intensity is considered as the blink frame. Frames between two successive blinks form a single group. Multiple such groups are generated based on number of blinks detected.

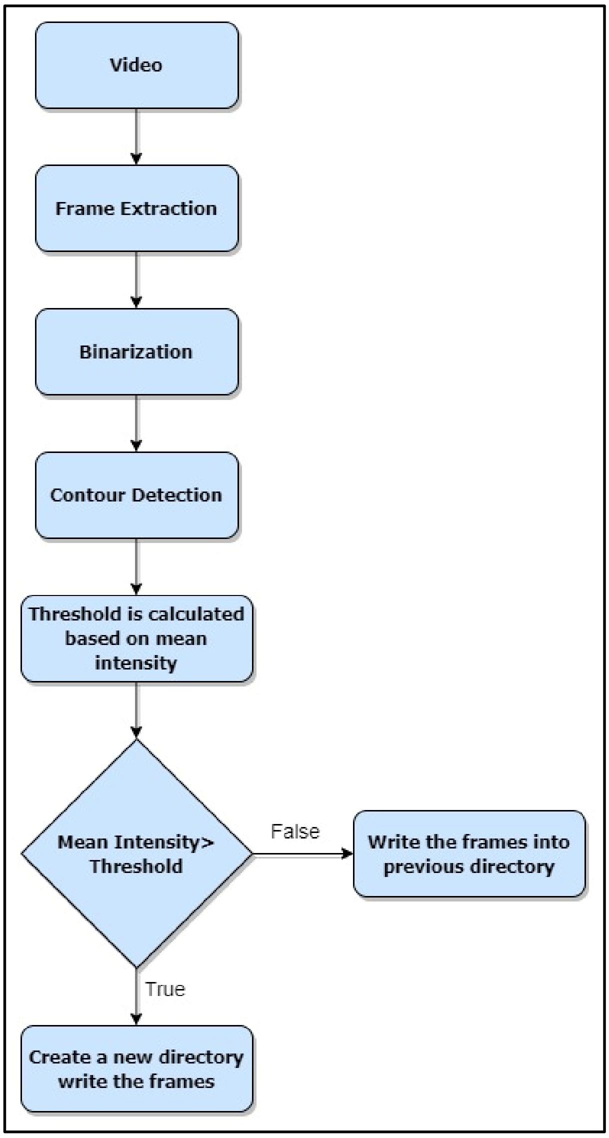


Fig.3. Flow chart for blink detection

3.5 Grade Prediction using Deep Learning Model

Convolutional neural network (CNN) is used for grade prediction. It is computationally efficient. It uses convolution and pooling operation and carries parameter sharing. This feature of CNN allows it to run on any device. The architecture of CNN is shown in Fig.4. CNN is a class of neural networks that concentrate on processing data like images. CNN usually has five layers - an input layer, convolutional layer, activation function, pooling layer and a fully connected layer.

3.5.1 Input Layer

This layer holds image data as it is. Input to this layer would be a three channels RGB image of height 256 pixels, width 256 pixels and depth 3.

3.5.2 Convolutional Layer

The convolutional layer is the foundation of convolutional neural network. It transfers the main part of the network's computational load. The purpose of this layer is to detect a set of features in the input image. Most of the computation is done in convolutional layer. Convolution is where a small array of numbers called kernel is applied across the input image which is called as tensor. Convolution operation is performed between the tensor and a filter of size 'MxM'. By moving the filter over the input tensor, the dot product is taken between part of tensor and filter with respect to the size of the filter. The output of this layer is known as a feature map which provides information about the images. This result is passed on to the next layer as input.

3.5.3 Pooling Layer

The pooling layer is added after the convolutional layer. It receives the feature map and performs pooling operation on them. The main role of the pooling layer is reducing the size of the images while maintaining their important features. Max pooling is used for their pooling operation to select the maximum area of the feature map that is covered by the filter. The output of pooling layer is feature map that contains most important features of the feature map.

3.5.4 Fully Connected Layer

This layer forms the last layer of the neural network. The output of the pooling layer is flattened and passed as input to the fully connected layer.

3.5.5 Activation Function

It is one of the important parameters of the CNN model. By computing weighted sum and adding bias to it, the function decides whether a neuron should be activated or not. It introduces nonlinearity to the output of the neuron. “Rectified linear unit (ReLU) activation function is used in this method which is a piecewise linear function that will output the input directly if it is positive, otherwise, it will output zero” (A Gentle Introduction to the Rectified Linear Unit (ReLU)). The advantage of using ReLU is that it is computationally efficient and improves the convergence of gradient descent towards global minimum of the loss function. The final layer uses SoftMax activation function which gives the probabilities of the input being in a particular class.

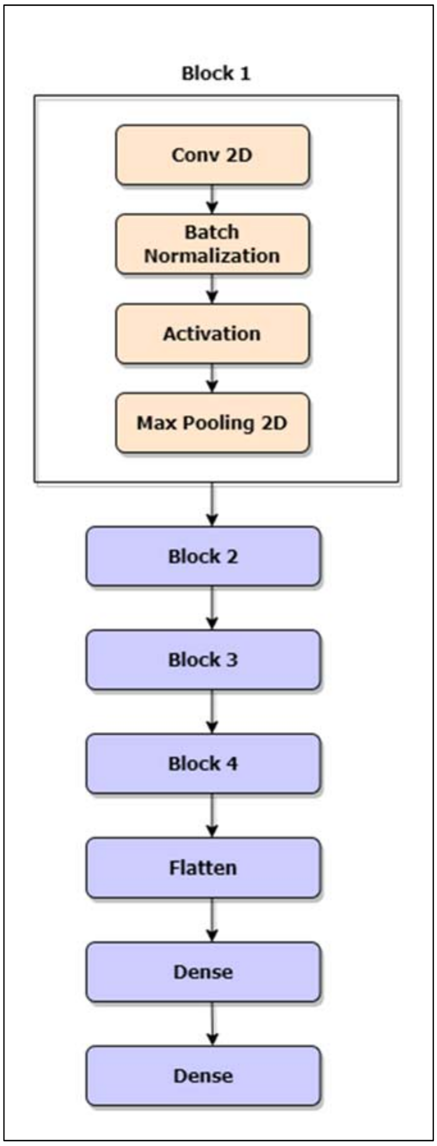


Fig.4. CNN model architecture

3.6 Image Classification and Final Grade Selection

The image classification is done based on the prediction value given by model. Frames are extracted and grouped per blink. The model will generate 4 prediction values for each frame in a blink. It may be noted that the proposed method restricts its prediction to four because of insufficient data for grade 5, and not due to any other inability. Out of four values, the index of highest value is considered as grade for that particular frame. Fig.5. illustrates the distribution of grades for each frame in one group. The grade for the blink is set as the highest grade obtained for a frame in that group. Fig.6. depicts the final grade selection in the analysis video. The final Yokoi grading for the video is computed after analyzing the grade of each blink and selecting the highest occurring grade.

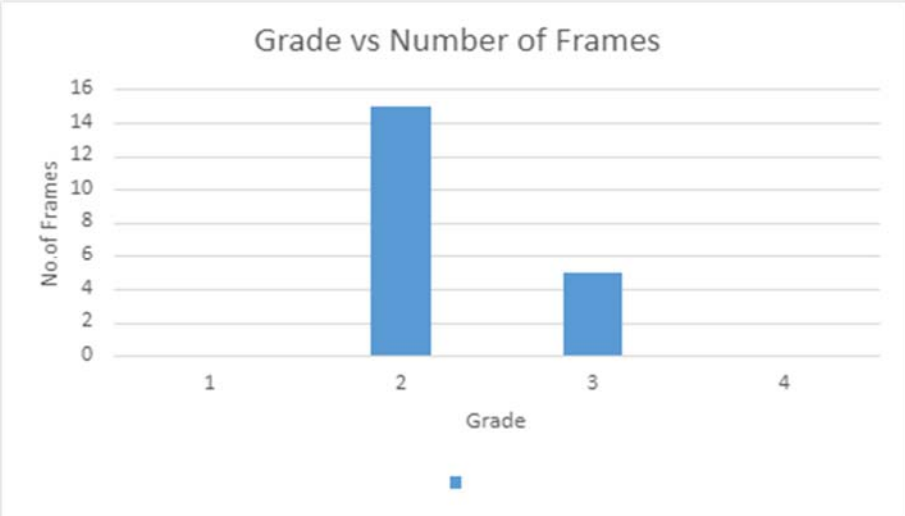


Fig.5. Statistical information of grade with number of frames

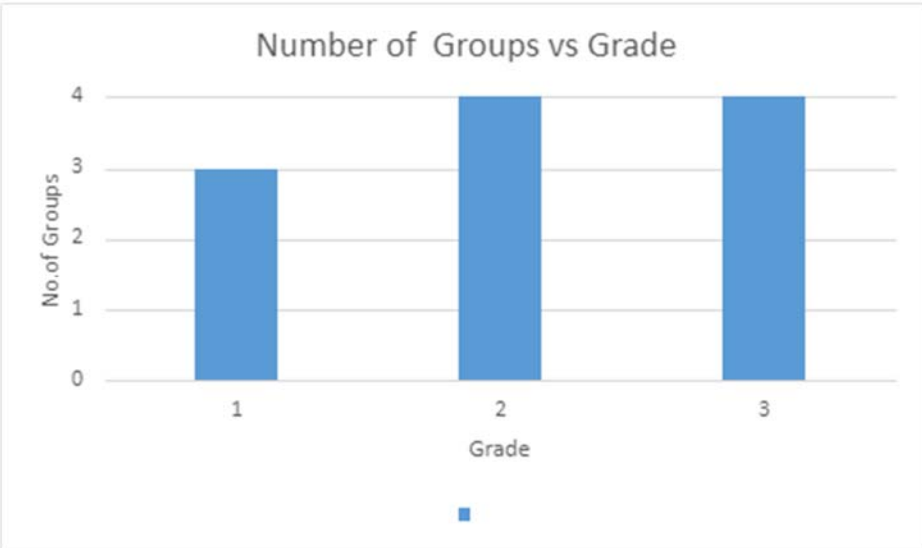


Fig.6. Statistical information of number of groups and grades

4. Experimental Results

4.1 Image Acquisition

The data for this study was acquired from subjects of different age groups using Forus Health 's 3nethra classicHD device [12]. It is a digital fundus camera that captures high resolution images offering various imaging modes such as high dynamic range imaging, red-free imaging in both mydriatic and non-mydriatic modes. The device is also equipped with non-invasive interferometry technology to image the anterior part of the eye. This feature allows the ophthalmologist to visualize and assess the tear lipid layer.

4.2 Datasets

A total of 30 videos were captured and subjects were asked to blink normally while capturing the video. The maximum duration of the video is 60 seconds, and the frame rate of the video is 10 frames per second. All frames from each video are extracted and manually selected for training. To increase the dataset, different augmentation techniques like flipping and rotating were used. The total number of images after augmentation was 2030. Out of these, 500 images were of grade 1, 504 of grade 2, 526 of grade 3 and 500 of grade 4 respectively.

4.3 Evaluation Matrix

Performance analysis of the proposed system against the ground truth is accomplished using quantitative measures namely sensitivity, specificity and accuracy. Sensitivity measures the number of positives that are correctly identified. Specificity measures the number of negatives that are correctly identified, and accuracy is how well the model predicts the different grades.

4.4 Implementation details

The proposed method is implemented using the publicly available Keras library. The classification has been done using basic convolutional neural network. In the training phase Adam optimizer is utilized to optimize the deep learning model. The learning rate was experimented starting from 0.00001 and momentum of 0.1. In addition to this, the same level of preprocessing was used for all the images which includes resizing and normalization of the image.

4.5 Classification performance

This section describes the classification performance of the model. Table 1 shows the true positive (TP), true negative (TN), false positive (FP) and false negative (TP) values of the model. The classification performance of the model can be computed using these values. The metrics sensitivity, specificity and accuracy computation are defined in Eq. (1), (2), (3):

$$Sensitivity = \frac{TP}{TP+FN} \tag{1}$$

$$Specificity = \frac{TN}{TN+FP} \tag{2}$$

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \tag{3}$$

Where TP is the actual value and predicted value are the same. TN is the actual negative predicted as negative. FP is the actual negative is predicted as positive and FN is the actual positive is predicted as positive.

The results given in Table 2 clearly indicate that the CNN model yields overall sensitivity of 86% specificity of 87% and accuracy of 86.25%. The accuracy might significantly improve if the number of training samples are increased.

		Predicted Values			
		Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Actual Values	**Grade 1**	30	6	4	-
	Grade 2	1	33	6	-
	Grade 3	-	3	37	-
	Grade 4	-	-	2	38

Table 1: Confusion matrix

	Sensitivity	Specificity	Accuracy
Grade 1	0.75	0.96	
Grade 2	0.82	0.78	
Grade 3	0.925	0.75	
Grade 4	0.95	1.0	
Overall Performance	**0.86**	**0.87**	**86.25%**

Table 2: Performance of the model

5 Conclusion

This work presents a novel method of determining dry eye condition using interferometry patterns analysis on tear film. The analysis was done after observing the lipid layer interference pattern of lower cornea and it shows that colorful interference pattern is observed only in grade 3 and grade 4 of dry eyes. Similarly grade 1 and grade 2 show without or with gray interference patterns respectively. A deep learning approach-based model for dry eye diagnosis has been developed and proposed in this work. The system classifies the image into 4 different grades - grade 1, 2, 3 and 4 respectively. The system first predicts the number of blinks from the video and extracts all the frames in between the blinks, identifies the interferometry patterns in the images and classifies it into the respective grade.

The primary advantage of this method is it is non-invasive as it analyses the tears instead of the meibomian gland. This might prove to be a very useful tool for early screening and automatic detection of dry eye grades that eliminates operator or user dependency and improves consistency. The work could be further enhanced based on data availability for grade 5. Training the model with a larger data set will improve the performance of the model to a considerable extent. Evolving deep learning architectures may be explored for the multi-class classification of the detected frames for improving the overall accuracy. To the best of our knowledge, the proposed methodology is one of the first techniques in dry eye syndrome analysis that uses artificial intelligence and the results obtained are encouraging.

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Conflict of Interest

"The authors have no conflicts of interest to declare. All coauthors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication."

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Authors' Profiles

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Deepthi K. Prasad received a Ph.D. degree in Computer science engineering from Visveswaraya Technological University in 2019. Her doctoral research focused on developing innovative methodologies for early detection and classification of ophthalmic diseases using image processing and data mining techniques. She has academic experience of over 10 years and overall research experience of over 8 years. Deepthi is currently working as a manager in the Image processing and analysis team, Research and Development at Forus Healthcare Private Limited, Bangalore. Her primary research interest is in developing applications and tools using image processing and deep learning techniques for early detection & classification of various ophthalmic diseases like glaucoma, Diabetic retinopathy, Macular edema and Age-related macular degeneration. She has been a peer reviewer of an international conference and has reviewed over 20 manuscripts. She has published over 11 papers in international SCOPUS indexed journals and conferences and has around 73 citations for her research publications.

Sourav Pal received his PhD in Applied Optics and Photonics from the University of Calcutta in 2012. Concurrently he worked as visiting faculty in multiple colleges for Optometry. He joined Forus Health Pvt. Ltd. in 2013. He works with fundus imaging systems and other optical devices connected to ophthalmology practice. His area of interest includes zoom lens design and optimization, fundus imaging system design, illumination design, and interferometry. He has many publications in international journals in the field of applied optics, and also applied for multiple patents. He is associated with Optica and SPIE as a regular reviewer of journal papers.

Venkatakrishnan S is presently working as chief technology officer (CTO) of Forus Health Pvt. Ltd. He has over 25+ years' experience in various technical responsibilities which include architecting and developing Products, Software, AI solutions, managing large and diverse product domain teams, product and technology roadmap generation, IP generation, conceiving new ideas, many of products/solutions are first of a kind in areas of medical devices, semiconductors and consumer electronics products. He led the team that conceived and developed the world's first affordable ophthalmic fundus camera which can perform anterior, posterior imaging and refraction in a single device. His interests include working on a first of a kind healthcare product.

Meghna Kulkarni is presently working with Forus Health Pvt. Ltd, Bangalore, India. She graduated in Medical Electronics from B.M.S College of Engineering, Bangalore in the year 2019. She has worked on diagnosis of retinal complications associated with young preterm children using various markers as part of academic research. Her interests include clinical research, medical imaging, and applied research on various systemic diseases and eye disorders.

Madhura Prakash M is working as a Technical Specialist with the Research and Development team at Forus Health Private Limited, Bangalore. She is also a Research Scholar at the Research center of Department of Computer Science and Engineering, BNM Institute of Technology, Bangalore. Her research interests include developing Artificial Intelligence backed Computer Vision techniques for extracting insights and scene understanding in medical videos and images.