Automatic Characterization of Choroidal Neovascularization Lesions in Fluorescein Angiograms using Parametric Modeling

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ABSTRACT
In many older adults, it is very common to observe Age related Macular degeneration which ultimately results in a medical condition called Choroidal Neo-Vascularization (CNV). It is characterized by having loss of linearity in the retinal image, fusiform thickening, and disruption of blood vessels in Retinal Pigment Epithelium (RPE) layer and thus results in vision loss. The images obtained from fluorescein angiography are further processed using digital image processing techniques and the results are obtained stating whether the person is suffering from the disease or not. Using parametric modeling of the intensity variation, the factors such as peak amount of the fluorescein that accumulates in the early stage, middle stage and late stage of the images are obtained. The end result which are the parameters obtained from the images, are fed to a Neural classifier. It classifies the quantized image parameters into occult CNV and classical CNV. This will tend to show whether the particular disease is dangerous and in the final stage or in the starting stage.

Keywords
Age related Macular Degeneration (AMD, Fluorescein Angiography (FA), Choroidal Neo-Vascularization (CNV), Image Registration, Neural classifier.

1. INTRODUCTION
Choroidal Neo Vascularization [1] is a disease condition in adults (50 years and above) which results in severe vision loss. It is mostly due to Age related macular degeneration, in which there is formation of new blood vessels and simultaneous disruption of the vessels due to cell damage resulting in sight loss. It is found out that more than 30 billion humans are suffering from this type of medical condition. In CNV, the cells in the center of vision(macula) gets disrupted and break their cellular material into the space in the eye and get mixed up with proteins and other lipids and get accumulated in the RPE layer called the drusen. The standard method for visualizing and evaluating CNV is Fluorescein Angiography (FA). FA is an essential tool in diagnosing and mapping CNV. In FA, a fluorescent dye is injected into the systemic circulation, and then an angiogram is obtained by photographing the retina using a fundus camera. The intensity of the acquired images reflects the amount of fluorescein leaks into the retinal and choroidal areas. Typically, two types of CNV lesions can be identified in FA images depending on their pattern of fluorescence – classic CNV or occult CNV. Identifying the lesion type is important for picking the proper treatment methodology.

2. IMAGE PROCESSING STRATEGY
This work consists of four main processing steps followed by the image acquisition. First sequence of the images is preprocessed to get the clear information about CNV lesions. To compensate the effect of eye movement, the images are aligned after estimating the translation and rotation between each consecutive pair of images. After alignment a set of images $I(x,y,t_i)$ are obtained where the location (x,y) in any image represent the same location in the retina. Two contours enclosing a normal retinal region and an AMD region are drawn manually and the average intensity within each region is calculated at the different times. The difference in the time-intensity signals between the diseased and normal retinal areas are due to an implicit transfer function whose parameters can be used to characterize the retina.

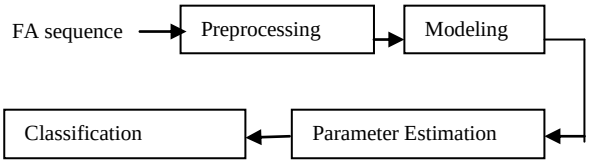

Fig 1: Flow chart of the proposed method

2.1 Image Acquisition
The standard method for visualizing and evaluating CNV is Fluorescein Angiography (FA).The Fluorescent angiography is a technique for examining the circulation of the retina and choroid using a fluorescent dye and a specialized camera. The purpose of fluorescent dye is to highlight retinal and choroidal circulation, detect the early vascular pathologies and confirm diagnosis. The Eye Images of CNV patients are collected from Vasan Eye Care Hospital, Chennai, Tamilnadu. The images are taken for the CNV patient in time frames spanning time intervals from 0 to 8 minutes. The image time difference from first image to next image is five seconds. Datasets for eight patients are used to test the proposed method. Patients, with known CNV lesions, were injected with 50 ml fluorescein. Images were acquired with a fundus camera integrated with a digital acquisition system. The acquired images (for sample image see Figure 1) are taken for data pre-processing such as green channel enhancement, contrast enhancement, image registration.

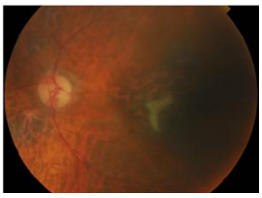

Fig 2: Eye affected by CNV

2.2 Green Channel Enhancement

The images are pre-processed with green channel enhancement .Using this red and blue components in the image are eliminated. The CNV lesions appear bright in green channel compared to red and blue channels in RGB image (see Figure 3). Hence green channel is used for further processing by neglecting other two components.

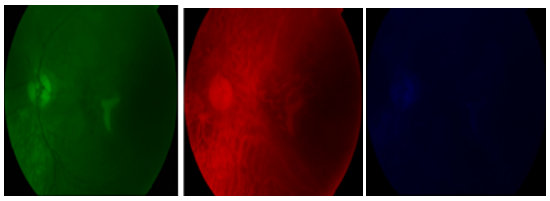

Fig 3: Green, Red and Blue channels of image

2.3 Contrast Enhancement

The appearance of the CNV lesions is further improved (see Figure 4) by increasing its contrast after green channel enhancement. The contrast enhancement can be done only with the grayscale images. Hence the green channel enhanced image is first converted to gray scale image before increasing its contrast.

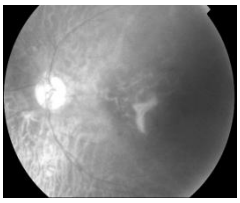

Fig 4: Image after contrast enhancement

2.4 Image Registration

Image registration is the process of aligning two or more images of the same scene. Typically, one image, called the base image or reference image, is considered the reference to which the other images, called input images, are compared. The object of image registration is to bring the input image into alignment with the base image by applying a spatial transformation to the input image. The differences between the input image and the output image might have occurred as a result of terrain relief and other changes in perspective when imaging the same scene from different viewpoints. Lens and other internal sensor distortions, or differences between sensors and sensor types, can also cause distortion.

The image processing techniques provide tools to support point mapping to determine the parameters of the transformation required to bring an image into alignment with another image. In point mapping, pick points or control points (see Figure 5) in a pair of images are used to identify the same feature or landmark in the CNV images. Then, a spatial mapping is inferred from the positions of these control points. Image registration using point mapping is to specify the control point pairs in the CNV images and to save the control point pairs. Finely tuning the control points using cross-correlation and specify the type of transformation to be used and infer its parameters from the control point pairs. Then transform the unregistered image to bring it into alignment.

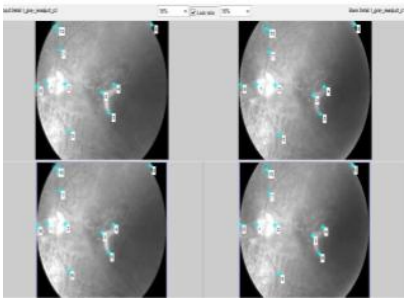

Fig. 5 Control Point mapping

2.5 Region of Interest

A region of interest (ROI) is a portion of an image that you want to filter or perform some other operation on. For image analysis, we want to investigate more closely a specific area within an image. Region of Interest (ROI) requires operations that modify the spatial coordinates of the image. To reduce the computation time, all processing steps are confined to a region-of-interest drawn manually around the macula. The manually drawn around the macula region is cropped separately (see Figure 6). That is the region where the algorithm is to be applied.

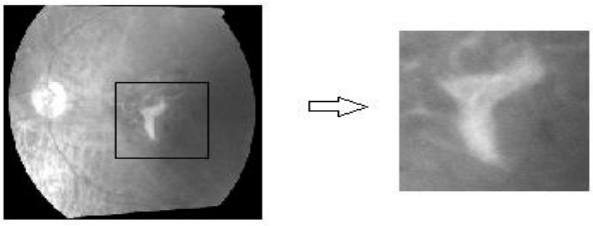

Fig 6: Region of Interest (ROI) of Aligned Grey Image

2.6 Modeling of Image Intensity

After alignment a set of images $I(x,y,t_i)$ are obtained where the location (x,y) in any image represent the same location in the retina. Two contours enclosing a normal retinal region and an AMD region are drawn manually and the average intensity within each region is calculated at the different times. This gives two time-intensity signals: $I_{norm}(t)$ and $I_{AMD}(t)$.

A simple input/output linear time-invariant model to study the leakage dynamics at the different areas of the retina is given by the following convolution operation,

$$I_{out}(x,y;t) = h(x,y;t) * I_{in}(x,y;t) \quad (1)$$

The input of the model is the concentration of the fluorescein at the upstream. The fluorescein concentration arriving at the retinal circulation can be modeled by a gamma function according to the gamma-variate relationship for tracer dilution curves introduced by Robertson Davenport[10].Hence, the input to the model at any given retinal location, $I_{in}(t)$, is given by,

$$I_{in}(t) = A(t^{\alpha_{in}} . e^{\frac{t}{\beta_{in}}}) \quad (2)$$

Where α_{in} and β_{in} are respectively the shape and scale parameters of the gamma function. The image intensity of normal retinal areas at the different timeframes, $I_{norm}(t)$, can be used as a good approximation of the input function $I_{in}(t)$ .At the diseased area, the output function, $I_{out}(t)$, is just the observed image intensity at the AMD lesion areas, i.e., $I_{out}(t) = I_{AMD}(t)$. The temporal variation of image intensity during the early phase can be modeled by a gamma function is given by (3)

$$I_{out}(t) = C(t^{\alpha_{out}} . e^{\frac{t}{\beta_{out}}}) \quad (3)$$

The sampled image intensities at the AMD lesions is used to estimate α_{out} and β_{out} .The transfer function model h(t) using a gamma function from the input and output functions is

$$h(t) = B(t^{\alpha_{TF}} . e^{\frac{t}{\beta_{TF}}}) \quad (4)$$

The parameters *A*, *B* and *C* are represent the peak amount of the fluorescein that accumulates in the early, mid, and late phases respectively. The parameter t is the time delay of the fluorescein to recirculate in the body and flushes again in the choroid. The parameters *A*, *B* and *C* are estimated using curve fitting method which is capturing the trend in the data by assigning a single function across the entire range. The parameters are estimated for 8 patients and the estimated parameters for three patients are given in Table 1.

Table 1.Estimated Parameters for Three Patients

Parameters (A,B,C) in pixels	Patient 1	Patient 2	Patient 3
Peak Amount of the Fluorescein that accumulates in the early stage (A)	161.31	367.3	372.13
Peak Amount of the Fluorescein that accumulates in the middle stage (B)	258.46	431.1	415.2
Peak Amount of the Fluorescein that accumulates in the late stage (C)	368.61	477.5	492.83

2.7 Classification

The parameters extracted are the main elements keeping which the image classification has to be done. In addition to function fitting, neural networks are also good at recognizing patterns. Hence, a feed-forward back propagation neural network is effectively used to classify the type of CNV (see Figure 7).The three parameters A, B and C are the inputs to the NN classifier .After training, the NN classifier suggests whether the appropriate image describes a diseased macula with occult CNV or classical CNV.

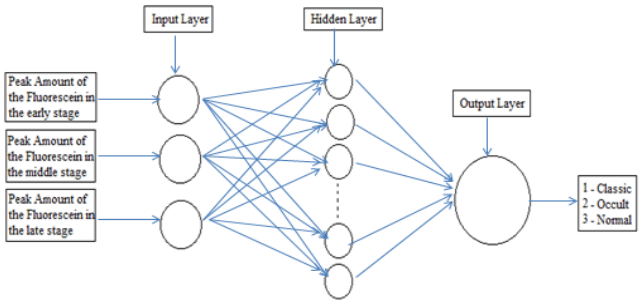

Fig 7: Back propagation neural network

The feed-forward back propagation network does not have feedback connections, but the errors are back propagated during training. Back propagation learning consists of two passes through the different layers of the network: a forward pass and backward pass. During the forward pass the synaptic weights of the network are all fixed. During the backward pass, the synaptic weights are all adjusted in accordance with an error correction rule. The actual response of the network is subtracted from a desired (target) response to produce an error signal. This error signal is then back propagated through the network, against the direction of synaptic connection.

The classification process starts by obtaining a dataset (input–output data pairs) and dividing it into a training set and validation dataset. The feed-forward neural network was trained with **8** dataset and validated and tested with 30% of datasets. The confusion matrix (see Figure 8) shows the various types of errors that occurred for the final trained network.

Fig 8: Confusion Matrix

The diagonal cells show the number of cases that were correctly classified, and the off-diagonal cells show the misclassified cases. The blue cell in the bottom right shows the total percent of correctly classified cases (in green) and the total percent of misclassified cases (in red). The results show very good recognition. For accurate results, we could try any of the following approaches:

- Reset the initial network weights and biases to new values and train again.
- Increase the number of hidden neurons.
- Increase the number of training vectors.
- Increase the number of input values, if more relevant information is available.
- Try a different training algorithm.

The classification done in this work using the NN classifier efficiently did the classification with 100 % efficiency. The observation made was such that, out of 8 patients, 4 patients had Classical type CNV, 3 had occult type CNV, and one was having a normal macula without any affected part. The all confusion matrix summarizes all the above said points in a matrix format. This classifier was thus an effective way of classification regarding this work.

3. CONCLUSION

This work is based on a parametric model of the temporal intensity variation during early, mid and late phases of the FA image sequence. The parameters of the transfer function representing the lesion response to the flow of the injected eye are used to classify the type of CNV are determined by using Curve Fitting method. The Neural Network classifier is used to automatically achieve the classification process with 100 % efficiency. Thus, it is possible to differentiate between the image of the normal macula and the diseased macula based on the estimated parameters and this method can be used as a diagnostic technique in medical fields to detect the presence of Choroidal Neo- vascularization. If the technique considers only images acquired during the early phase then the examination time can be reduced.

4. ACKNOWLEDGMENTS

Our sincere thanks to Vasan Eye Care hospitals,Tamilnadu who provided CNV datasets required for our work .

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