Computer Based Early Diagnosis of Glaucoma in Biomedical Data Using Image Processing and Automated Early Nerve Fiber Layer Defects Detection using Feature Extraction in Retinal Colored Stereo Fundus Images

Jyotika Pruthi, Dr.Saurabh Mukherjee
Email : jyotika0507@gmail.com,mukherjee.saurabh@rediffmail.com

Abstract— Glaucoma, an eye disorder is one of the supreme causes of blindness. The inception of Glaucoma causes devastation of these indispensable nerves and eventual vision loss. Hence it calls for a need to have an early detection of the disease and espy the degeneration of nerve in a non-invasive mode through the Retinal Fundus images. In particular, Anisotropic Diffusion Filter for noise removal, Otsu Thresholding, Canny edge map and Image Inpainting for extraction of retinal blood vessels, K means Clustering, Multi-thresholding, Active Contour Method, Artificial Neural Network, Fuzzy C Means Clustering, Morphological Operations have been used and compared using average measures for detection of boundary of optic disc and cup, modeled as elliptical objects. Adaptive Neuro Fuzzy Inference System, Support Vector Machine and Back Propagation Network classifies batch of 20 images obtained from Vitreo Retina Unit, AIIMS, New Delhi,India and Optos, Scotland, UK as normal and abnormal samples. Quantitative analysis and comparison of classifiers is performed by computing Classification Accuracy, Sensitivity and Specificity. Conclusively, Cup-to-Disc Ratio is computed and values are compared with truths obtained from Heidelberg Retina Tomograph and ophthalmologists for clinical validation, bring forth a model to get perception of progressive degeneration of optic nerve and the impact of glaucoma on Retinal Nerve Fiber Layer. This automatic retinal image analysis contributes to the field of ophthalmology by providing a screening tool for the early detection of Glaucoma.

Index Terms— Active Contour Method, Cup-to-Disc, Optic Nerve, Optic Disc, Optic Cup

1 INTRODUCTION

Glaucoma, a silent thief of sight (as described by Eduard Jaeger in 1854) is the second leading cause of blindness worldwide with 75 to 105 million people affected (WHO) and its pervasiveness is likely to increase [1, 2]. Glaucoma is a pathological condition that leads to progressive and irrevocable damage to the optic nerve and causes vision loss. The preeminent reason behind the devastation of optic nerve due to glaucoma is the pressure elevation within the eye, coined as Intra Ocular Pressure (IOP).There are various existing clinical ophthalmic instruments like Heidelberg Retina Tomograph (HRT) and Optical Coherence Tomography (OCT) that provide a colorless 3-D visualization but the identification of optic cup and optic disc is not automatic and demands clinician's supervision [3]. Therefore there is a need to develop an automated fundus image analyzing and diagnosing system that would act as an aid to ophthalmologists in detecting glaucoma before vision loss. This paper proposes a computer aided system for an automated detection of disease at an earliest for effective treatment through the usage of retinal color fundus photographs. A section of optic nerve that is apparent in the retinal fundus image is called the Optic Disc (OD) or Optic Nerve Head (ONH).OD is the brightest feature, orange-pink in color with a pale centre known as Cup. Blood vessels and the optic nerve fibers are radiated out of the OD. The neuro retinal rim consists of the nerve fibers and the pale center is free from the nerve fibers. The normal optic disc consists of approximately 1.5 million nerve fibers but in glaucoma the pressure within the eye reduces the blood supply and consequently there is lack of nourishment in the retina resulting in death of the nerve fibers [4].Thus, thinning of the neuroretinal rim along with the enlargement of cup (Cupping) takes place (Figure 1).Evaluation of the size of the cup can be made with respect to the size of the disc as a whole and can be termed as a Cup-to-Disc Ratio. The Cup-to-Disc Ratio (CDR) expresses the proportion of the disc occupied by the cup and it is widely accepted as an index for the appraisal of glaucoma [5]. For normal eye, CDR value is found to be 0.1 to 0.3 [6]. As the optic nerve degenerates, the said ratio increases. Calculation of cup- to-disc ratio (C/D) helps in classifying the extent of differentiation among the normal and the glaucomatous cases. The rest of this paper is organized as follows. Section II introduces Proposed Methodology. Section III presents the Experimental results. Section IV presents the conclusions.

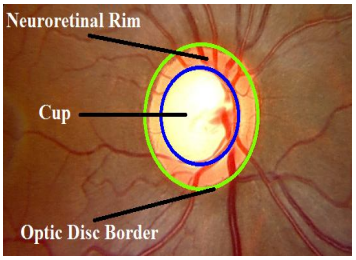


Fig 1.Optic Disc Structure

2 RESEARCH METHODOLOGY

The proposed system is composed of six different stages: Preprocessing, Region of Interest (ROI) Extraction, Feature Extraction stage, Calculation of CDR, Classification and Performance Analysis stage. All the stages are shown in flow chart (Figure 2).

Fig 2. Flow Chart of Proposed Methodology

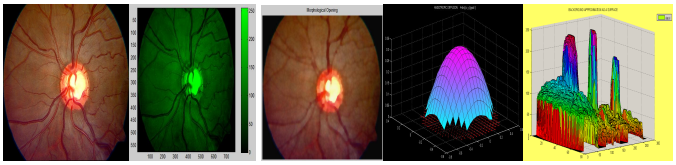
2.1 Preprocessing

2.1.1 Illumination Correction and Intensity Inhomogenity

The RGB retinal images are pre-processed using anisotropic diffusion filter to remove noise. Formally let $\Omega \subset R^2$ denote a subset of the plane and $I(.,t):\Omega \to R$ be the family of gray scale images, then anisotropic diffusion is given by Eq. 1 and Figure 3(d).

$$\frac{\partial I}{\partial t} = div(c(x,y,t)\nabla I = \nabla c.\nabla I + c(x,y,t)\Delta I \quad (1)$$

where Δ denotes ∇ Laplacian, denotes the gradient, div (…) is the divergence operator and c(x,y,t) is the diffusion coefficient. The red channel of the fundus image is usually oversaturated and blue channel is very noisy, thus green channel has been used for processing (Figure 3(b)). It displays the highest contrast between the blood vessels and the background and provides better visualization for the analysis of the optic nerve head. During image acquisition, different visual angles of patients cause bright speckles to spread over the image i.e. inhomogeneous background (Figure 3(e)). So it affects the illumination of ONH making it difficult to bring statistical analysis. Homogeneity can be achieved by subtracting the estimated background from the original image. In this work, Morphological opening is used for achieving homogeneity (Figure 3(c)).



(a) (b) (c) (d) (e)

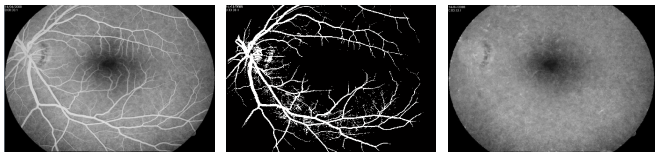
Fig 3: (a) Original Fundus Image, (b) Green Channel of Image, (c) Morphological Opening Operation (d) 3D Plot of Anisotropic Diffusion (e) Plot of Background Approximation

2.1.2 Blood Vessel Removal

Blood vessels that evolve out of ONH are minimally affected by glaucoma and unnecessarily interfere with the analysis of ONH .Hence it is needed to remove the vessels in the fundus image. To remove the vessels Grayscale image is used (Figure 4(a)) as it provides a higher magnitude of contrast then segmentation and Inpainting of vessel tree is carried out. Various segmentation techniques are reported in the literature but we use Otsu Thresholding to separate foreground from background (Figure 4(b)). The information from this binary image is combined with Canny edge map [7] to create and filter a vessel mask. Image Inpainting [8] of mask is done to replace blood vessels with a plausible background (Figure 4(c)). A directional model for retinal vessels requires the definition on the whole image of a function given by Eq. 2 that represents preferential direction in any retinal image of a vessel at point (x, y).

$$\theta^{mod}(x,y;p) \qquad -\frac{\pi}{2} \leq \theta^{mod} \leq \frac{\pi}{2} \quad (2)$$

Vector p is the set of parameters defining the model and its positioning including OD coordinates.

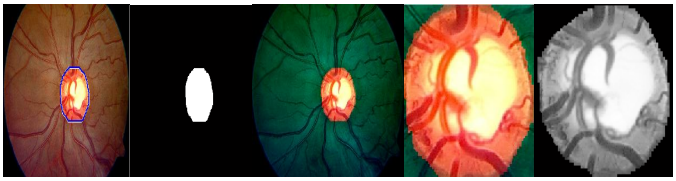


(a) (b) (c)

Fig 4. (a) Grayscale Fundus Image (b) Extracted Blood Vessels (c) Inpainted Image

2.2 Region of Interest Extraction

As optic disc is the portion whose analysis helps to detect glaucoma, the approximate region around the brightest portion has to be selected as ROI. After the analysis of entire image, a small square of size 360 X 360 pixels around the brightest region along with a small portion of other regions is considered as ROI. The G plane is considered for the extraction of optic disc by creating a binary mask (Figure 5).



(a) (b) (c) (d) (e)

Fig 5. ROI Extraction (a) ROI selected (b) Binary Mask created (c) G Channel with Mask (d) ROI extracted in G channel (e) ROI in grayscale image

2.3 Feature Extraction

Transforming images into its set of features is known as feature extraction. Features used in this work are the ones extracted from optic disc and optic cup. Diameter of cup and optic disc for calculating Cup to disc ratio are extracted from the segmented optic disc and cup.

2.3.1 K means Clustering

K-means clustering is an iterative unsupervised learning algorithm that is used to partition the ROI image into K clusters .The ROI covers mainly the entire optic disc, optic cup and a small portion of other regions of the image. Hence the K value is chosen as 3.The procedure follows a simple way to classify a given data set through a certain number of clusters (k clusters) fixed a priori. The main idea is to define k centroids, one for each cluster. The next step is to take each point belonging to a given data set and associate it to the nearest centroid. At this point k new centroids are calculated as the mean of the clusters resulting from the previous step. As a result of repetitive application of these two steps, the k centroids change their location step by step until no more changes take place. In other words centroids do not move any more (Figure 6(a~b)).From the three clusters the optic disc cluster has to be identified and removed for the extraction of optic disc and optic cup as well.

2.3.2 Optic Disc and Optic Cup Extraction

In this work the boundary and area of the cup and OD is determined by Multi Thresholding, Active Contour Method [9], Fuzzy C means Clustering (Figure 6(c~e)) and Artificial Neural Network. Finally, the morphological operation is performed to fill the holes and small region inside optic disc and cup clusters (Figure 7(b), 7(c)).The comparison results on the basis of disc region agreement of method with that of ophthalmologist for the dataset using three methods are shown in Table I and it is clear that better results are obtained with Active Contour Method.

TABLE 1

DETERMINATION OF DISC USING THREE METHODS

	ACM Disc Region Agreement	FCM Disc Region Agreement	ANN Disc Region Agreement
GLAUCOMA	0.899	0.712	0.788
NORMAL	0.888	0.800	0.646

ACM: Active Contour Method, FCM: Fuzzy C Means, ANN: Artificial Neural Network

FCM is based on minimization of the following objective function given by Eq. 3:

$$J_m = \sum_{i=1}^{N} \sum_{j=1}^{C} u_{ij}^{m} \| x_i - c_j \|^2 \quad 1 \leq m < \infty \tag{3}$$

where m is any real no. greater than 1, u_{ij} is degree of membership of x_i in the cluster j, x_i is the ith of d-dimensional measured data, c_j is the d-dimension center of the cluster and $\|*\|$ is any norm expressing similarity between any measured data and the center. Fuzzy portioning is carried out through an iterative optimization of the objective function shown above, with the update of membership u_{ij} and the c_j cluster centers by Eq. 4.

$$u_{ij} = \frac{1}{\sum_{k=1}^{C} \frac{\|x_i - c_j\|^{\frac{2}{m-1}}}{\|x_i - c_k\|}} \qquad C_j = \frac{\sum_{i=1}^{N} u_{ij}^{m} \cdot x_i}{\sum_{i=1}^{N} u_{ij}^{m}} \tag{4}$$

This iteration will stop when $max_{ij}\{|u_{ij}^{(k+1)} - u_{ij}^{(k)}|\} < \varepsilon$ where ε is a termination criterion between 0 and 1, whereas k is the iteration steps. From the three clusters the optic disc cluster has to be identified and removed for the extraction of optic disc and optic cup as well. To perform the image segmentation we start with the initial curve and evolve its shape by minimization of energy function that is represented by level set function. The evolution of curve has to stop at the image boundaries where the energy becomes minimum. The contour is represented by zero level set function $\emptyset$ and energy function is iteratively minimized to find out the object boundary as given by Eq.5:

$$F_{\emptyset, r_1, r_2} = E_{\emptyset, r_1, r_2} + lP(\emptyset) + vL(\emptyset) \tag{5}$$

where $E_{\emptyset, r_1, r_2}$ is the external energy function, $\emptyset$ is the zero level set representing contour C in the image domain , r_1 and r_2 are two values that fit the image inside and outside of contour. P($\emptyset$) is the distance regularizing term used to penalize the deviation of level set $\emptyset$ from a signed distance function. It is given by Eq.6:

$$P(\emptyset) = \int_{\Omega} \frac{1}{2}(|\nabla\emptyset(x)| - 1)^2 dx \quad (6)$$

$L(\emptyset)$ is the length of zero level curve of $\emptyset$ used to regularize the contour. It is given by Eq.7:

$$L(\emptyset) = \int_{\Omega} \delta(\phi(x))|\nabla\emptyset| dx \quad (7)$$

l and v are positive constants, δ is the smoothing function called dirac function. The energy function is to be minimized to find optic disc boundary. The gradient descent method proposed by Li *et al.*, 2007 is used to minimize the energy function and is given by Eq. 8:

$$\frac{\partial\phi}{\partial t} = -\delta(\phi)(\alpha_1 e_1 - \alpha_2 e_2) + v\delta(\phi) div\left(\frac{\nabla\phi}{|\nabla\phi|}\right) + l(\nabla^2\phi - div\left(\frac{\nabla\phi}{|\nabla\phi|}\right)) \quad (8)$$

$$e_1(x) = \int_{\Omega} k_\sigma(y-x)|I(x) - r_1(y)|^2 dy \quad (9)$$

$$e_2(x) = \int_{\Omega} k_\sigma(y-x)|I(x) - r_2(y)|^2 dy \quad (10)$$

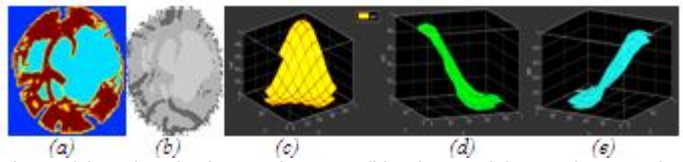


Fig 6: (a) Colored Clustered Image (b) Clustered image in gray (c~e) Membership Function Plots for three clusters

2.3.3 Ellipse Fitting

The presence of blood vessels across the boundary of the disc makes the detected contour uneven. Therefore the direct ellipse fitting method proposed by Fitzgibbon [10] is used to mark the optic disc and cup boundary (Figure 7(d~g)).

(a) (b) (c) (d) (e) (f) (g)

Fig 7. (a)Fundus Image (b)Extracted Optic Disc (c)Extracted Optic Cup (d~e) Ellipse fitted boundary of optic cup (f~g) Ellipse fitted boundary of optic disc

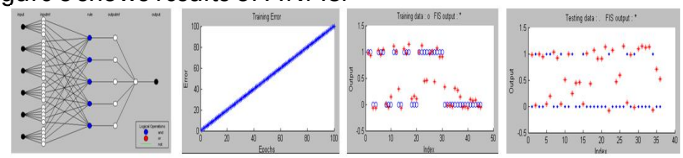
2.4 Cup-to-Disc Ratio Calculation

The area of the optic disc and cup is the area of the ellipse calculated by using Eqn.11 where a, b are major axis length and minor axis length respectively.CDR which is the ratio between the area of the optic cup and the area of the optic disc is computed. Figure 9(b~c) shows surface plot and contour of CDR with disc and cup.

$$Area = \pi ab \quad (11)$$

2.5 Classification

Classifiers namely ANFIS, SVM and Back Propagation Neural Network are used to classify between normal and abnormal cases of glaucoma. Parameters that are used for generating Fuzzy Inference System (FIS) are shown in Table II. ANFIS integrates the learning capabilities of neural networks with approximate reasoning of fuzzy inference algorithms [11]. Figure 8 shows results of ANFIS.

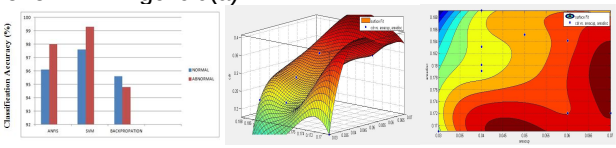


(a) (b) (c) (d)

Fig 8. (a)ANFIS Structure (b)Training Error (c)Training data vs FIS Output (d) Testing data versus FIS output

2.6 Performance Measure of Classifiers

The system is trained and tested for a dataset shown in Table III. Classification accuracy is the ratio of the total number of correctly classified images to total number of misclassified images [11]. Table IV shows the Classification Accuracy of the classifiers that shows that the proposed method has the highest classification rate with SVM as classifier. The classification accuracy achieved by ANFIS, SVM and Back Propagation is also shown in Figure 9(a).



(a) (b) (c)

Fig 9. (a) Classification Accuracy (b~c) Surface, Contour Plot of CDR, area of disc, cup

TABLE 2

PARAMETERS FOR FIS GENERATION

Range of Influence	0.5
Squash Factor	1.25
Accept Ratio	0.5
Reject Ratio	0.15

TABLE 3

DATASET FOR TRAINING AND TESTING

Category	**No of training images**	**No of Testing images**
Normal	10	10
Abnormal	10	10

TABLE 4

CLASSIFICATION ACCURACY OF CLASSIFIERS

Category	No. of Test Images	ANFIS			SVM			Back Propagation		
		CCI	MI	CA (%)	CCI	MI	CA (%)	CCI	MI	CA (%)
Normal	10	5	5	96.1	7	3	97.6	3	7	95.6
Abnormal	10	7	3	98	9	1	99.3	2	8	94.8

CCI=Correctly Classified Images, MI=Misclassified Images, CA=Classification Accuracy

2.6.1 Calculation of Accuracy of Automated Segmentation Technique

Sensitivity refers to proportion of true positives or proportion of pixels classified as lying within the optic cup / disc that are also part of the optic cup / disc drawn by the ophthalmologist (Eq.12) [12]. Specificity refers to the proportion of true negatives or proportion of pixels not classified as lying within the optic cup / disc that are also not part of the ophthalmologist's optic cup / disc (Eq. 12) [12]. Table VIII shows the results of sensitivity and specificity analysis on the cup as well as the disc segmentation. Figure 10 shows the sensitivity and specificity plots for optic cup and disc.

$$\text{Sensitivity} = TP/TP+FN \quad \text{and Specificity} = TN/TN+FP \qquad (12)$$

Performance of each classifier is also measured on basis of sensitivity, specificity and accuracy. Accuracy determines correctly classified results. Table V shows the performance measure of the classifiers.

TABLE 5

PERFORMANCE MEASURE OF THE CLASSIFIERS

CLASSIFIER	SPECIFICITY (%)	SENSITIVITY (%)	ACCURACY (%)
ANFIS	96.45	97.11	97.77
SVM	97.61	99.23	98.12
BACKPROPAGATION	96.32	96.57	97.35

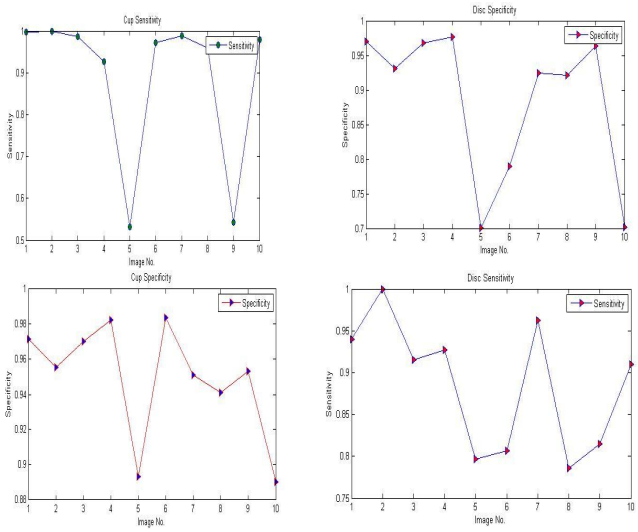


Fig 10. Sensitivity and Specificity plots for Optic Cup and Optic Disc (Ref: Eq.12)

3 RESULTS AND DISCUSSIONS

CDR values are calculated for 10 colored Normal and Abnormal fundus images in jpeg format using MATLAB 7.9 (R2009B) and ImageJ 1.47f and obtained results are compared with HRT and results obtained by ophthalmologists (Table VI, Fig. 11,12(a~b)). For normal eye, CDR value is 0.1 to 0.3. As the optic nerve degenerates, the ratio increases. Correlations of results with ground truth are calculated and are found to be 0.54 for proposed method and 0.51 for HRT implying that proposed method gives results near to those of HRT. Receiving Operating Characteristics (ROC) has also been plotted showing the compared results in Figure 12(c).

TABLE 6

COMPARISON OF RESULTS WITH HRT AND OPTHALMOLOGISTS (NORMAL)

IMAGE NO.	CALCULATED CDR	HRT	OPTHALMOLOGIST
Normal 1	0.2114	0.3123	0.2004
Normal 2	0.3381	0.3512	0.3781
Normal 3	0.2341	0.3353	0.2441
Normal 4	0.2742	0.2112	0.3042
Normal 5	0.22943	0.2001	0.25943
Normal 6	0.38865	0.3555	0.39865
Normal 7	0.22866	0.3000	0.19866
Normal 8	0.28457	0.3000	0.29457
Normal 9	0.20477	0.3532	0.19477
Normal 10	0.39071	0.36712	0.30071

TABLE 7

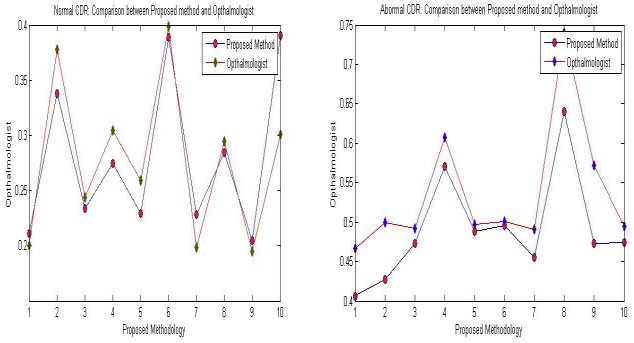
COMPARISON OF RESULTS WITH HRT AND OPTHALMOLOGISTS (ABNORMAL)

IMAGE NO.	CALCULATED CDR	HRT	OPTHALMOLOGIST
Abnormal 1	0.40631	0.5523	0.46631
Abnormal 2	0.42789	0.4511	0.50000
Abnormal 3	0.47254	0.5513	0.49254
Abnormal 4	0.57097	0.5612	0.60797
Abnormal 5	0.48756	0.5612	0.49756
Abnormal 6	0.49513	0.4533	0.50023
Abnormal 7	0.45532	0.4812	0.49032
Abnormal 8	0.6405	0.6552	0.7405
Abnormal 9	0.47243	0.5423	0.57243
Abnormal 10	0.6211	0.5713	0.7145

TABLE 8

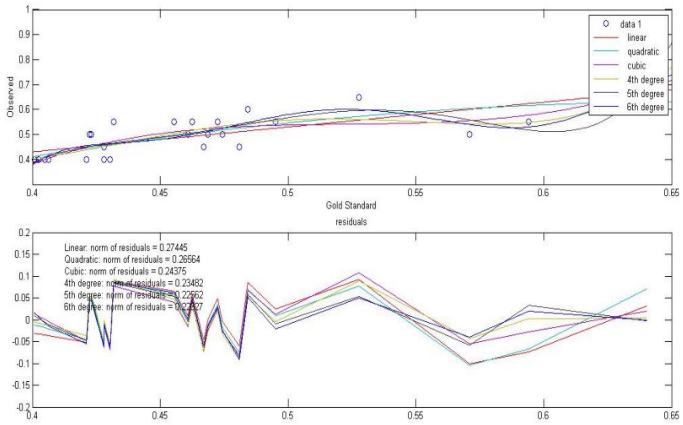
SENSITIVITY AND SPECIFICITY ANALYSIS

Disc		Cup	
Sensitivity	*Sensitivity*	*Sensitivity*	*Specificity*
0.9402	0.9704	0.9975	0.9717
1	0.9312	0.9991	0.9553
0.9155	0.9684	0.9859	0.9701
0.9272	0.9766	0.9267	0.9825
0.7963	0.7002	0.5324	0.8932
0.8065	0.7892	0.9722	0.9837
0.9626	0.9240	0.9883	0.9512
0.7862	0.9211	0.9600	0.9411
0.8151	0.9640	0.5433	0.9533
0.9100	0.7012	0.9800	0.8900

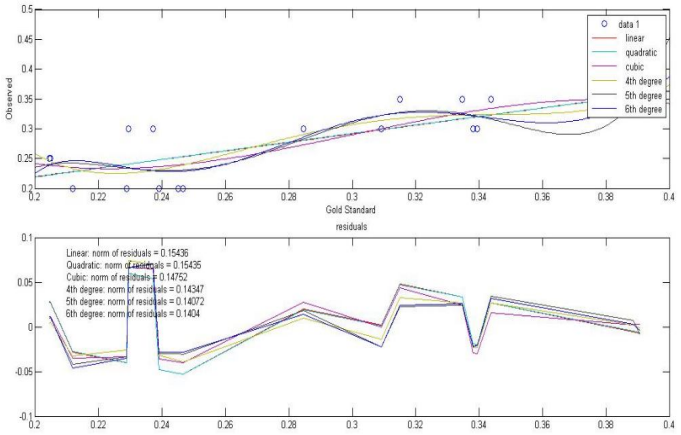


(a) (b)

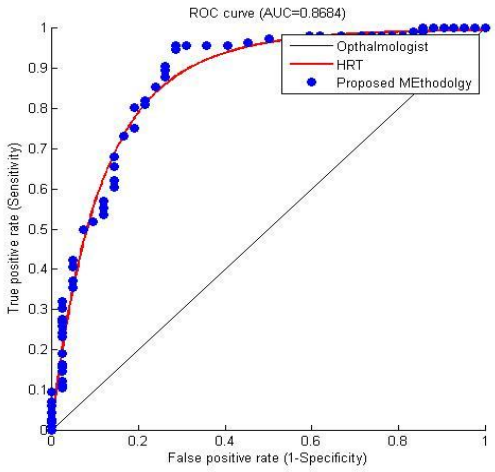
Fig 11. Comparison between Proposed method and Opthalmologist (a) Normal (b) Abnormal



(a)



(b)



(c)

Fig 12 (a~b) Comparison of proposed method with HRT results till 6th degree polynomial along with their residuals (Abnormal, Normal) (c) ROC of three techniques

4 CONCLUSION

CDR is an important indicator of the presence of glaucoma in an individual. The method fails for some images as other pathologies are present. Automated analysis of optic disc can be a valuable diagnostic resource for clinicians. The computed C/D values show good compatibility and nearness when compared with results from HRT and ophthalmologists. If the proposed approach is combined with existing ophthalmologist's technique, it can prove to be a breakthrough in field of ophthalmology. Simulation shows promising results. Further the research would be carried to bring out improvements.

ACKNOWLEDGMENT

The satisfaction and euphoria that accompany the successful completion of any task is incomplete without the mention of the people who made it possible and crowned our efforts with success. We can't forget to give a note of thanks to Dr. Lalit Verma , Professor, Vitreo Retina Unit, R.P Centre AIIMS, Dr. Fiona Howie, Marketing Coordinator ,Optos ,Scotland UK who helped in all the ways needed to carry out this research initiative. We hope to refine and carry this work further.

REFERENCES

[1] S.Resnikoff, D.Pascolini,d.Etya'ale, L.Kocur, R.Pararajasegaram, G.P Pokharrel, S.Mariotti, "Global data on visual impairment in the year 2002,Bull",WHO 82 844-851,2004.

[2] H.A Quigley,A.T Broman,"The number of people with glaucoma worldwide in 2010 and 2020 , Br. J.Opthalmol.90",262-267,2006.

[3] J Xu, et al ,"Optic Disc feature extraction via modified deformable model technique for glaucoma analysis", The Journal of the Pattern Recognition Society,10.1016/j.patcog.2006.10.015,2006.

[4] C.Radhika , "A morphological approach for discrimination between Glaucomatous and Non glaucomatous Eyes by Optic Disc Localization", ISSN:2278-1323

[5] http://www.optic-disc.org

[6] R.Bock,J.Meier,L.G Nyl,J.Hornegger and G.Michelson, "Glaucoma Risk Index : Automated glaucoma detection from color fundus images" , Medical Image Analysis, vol. 14,pp. 471-481,2010

[7] Canny, J.F , "A computational approach to edge detection", IEEE Trans Pattern Anal Mach Intell, 8(6) (1986) 679698,1986.

[8] A.Criminisi, P.Prez and K.Toyama , "Region Filling and object removal by exemplar-based image impainting" IEEE Transactions on Image Processing,Vol.13, pp. 1200-1212,2004.

[9] T.F.Chan and L.A Vase,Active Contours without edges. IEEE Transactions on Image Processing, Vol. 10, pp. 266-277,2001.

[10] Fitzgibbon, A, Pilu, M, Fisher, R.B ,Direct least square fitting of ellipses. IEEE T. Pattern Anal.21, 476-480,1999.

[11] S.Kavitha, K.Duraiswamy ,An Efficient Decision Support System for Detection of Glaucoma in Fundus Images Using ANFIS. International Journal of Advances in Engineering and Technology, ISSN: 2231-1963,2012.

[12] Archie Sharma,Automated Depth Analysis of Optic Nerve Head from Stereo Fundus Images. Thesis in Electrical Engineering, Texas Tech University,2006.