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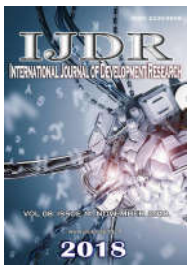

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

SCREENING DIABETIC RETINOPATHY USING STATISTICAL METHODS

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ABSTRACT

An analysis has been made to the recent digital image processing algorithms in diabetic retinopathy. Diabetic Retinopathy is the common cause of blindness and vision defects in the developing countries. Several algorithms have been developed to pre-process the retinal image and defect the hard exudates in the retinal image. Different digital image processing techniques such as digital image enhancement digital image filter, digital image segmentation, morphology techniques, colour processing, image classification, etc. have been used in diabetic retinopathy. Several fully automatic image processing algorithms have been envolved to diagnose the diabetic retinopathy digital images. A classification of retinal images based on statistical algorithm has proposed. The experimental results show that the proposed algorithm classifies the retinal images with minimum error and faster compared to other existing algorithms.

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INTRODUCTION

The population of diabetic patients has been increasing against the total world population. Uncontrolled and prolonged diabetes can damage the microvasculature of the vital organs of the body such as eyes and kidneys. The damage caused to the tiny blood vessels in the retina of the human eye, is known as Diabetic Retinopathy. Due to elevated amounts of glucose circulating through the body, the walls of blood vessels become damaged and several anomalies such as Microaneurysms, hemorrhages, Hard Exudates, Cotton wool spots start developing at various phases of retinopathy. The patient affected by Diabetic Retinopathy may not experience visual impairment until the disease has progressed to a severe stage, when the treatment is less effective. Therefore the early detection and the regular follow-ups is necessary to treat diabetic retinopathy. The earliest symptoms of Retinopathy are the Micro aneurysms, which occur due to dilatations of the blood capillaries and they appear as dark red spots on the retina. Hemorrhages occur when the microaneurysms burst. Bright-yellow colored Lesions such as hard exudates occur as a result of fluid leaking into the retinal surface from the capillaries or from Microaneurysms. Another bright white colored lesions, called the soft Exudates or cotton wool spots occur occlusions of the nerve fibre layer.

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Diabetic Retinopathy is a progressive disease. The first stage of retinopathy is known as Non-Proliferative Retinopathy, during which the retinal lesions appear and increase as the disease progresses. Initially, at least one micro aneurysm is seen. With the progression of the disease, the blood vessels become blocked and are short of blood supply. In an attempt to create new paths for blood supply, abnormal and fragile new blood vessels are formed on the surface of retina in the stage of Proliferative Retinopathy that might leak blood into retina causing permanent blindness. The various lesions associated with diabetic retinopathy are as shown in the figure below. Diabetes retinopathy (DR) is a severe eye disease that affects many diabetic patients. Diabetic retinopathy is the most common cause of blindness which a complication of diabetes mellitus, so it is necessary to diagnosed early. The eye, a vital organ of the human body, gives us the sense of color, shape and state of physical objects. But if Abnormalities occurs in the eye because of diseases such as Conjunctivitis, Fungal Keratitis, glaucoma, diabetic retinopathy, fungal infection, diabetes then eye may be damaged (http://www.sightsavers. net/our_work/ around_the_world/asia/india/9817). The complicated images obtained from infected eye will be processed using digital Image Processing (DIP) technique, which manipulates the image for the purpose of either extracting information from the image or produces an alternative representation of the image. Thus screening is the most effective method to detect early signs of diabetic retinopathy (Preethi and Vanithaman, 2012 and Fraz *et al.,* 2012).

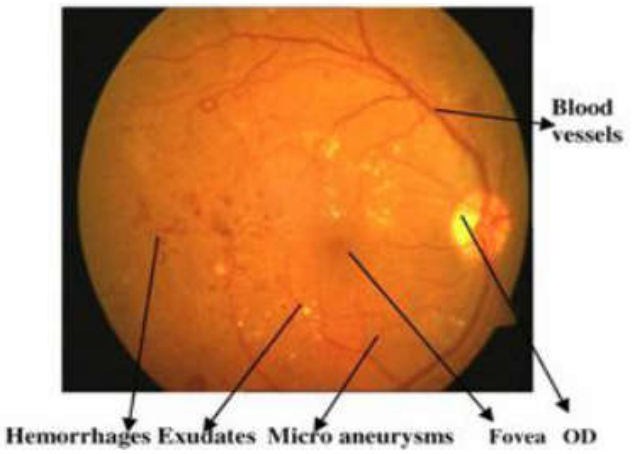

Fig 1. Retinal lesions associated with diabetic retinopathy

Using screening method big blood clots called hemorrhages, Hard exudates, The bright circular region from the blood vessels called optic disk, The fovea defines the center of the retina, and is the region of highest visual acuity, exudates and microaneurysms, irregular shaped, and found in the posterior pole of the fundus can be detected. Ma et al. (Fraz *et al.,* 2012) defined a quality descriptor according to three classes, namely, out-of-focus images, motion blurred images and severely occluded images of eyelids and eyelashes. Zhu *et al.* (Nekovei and Ying, 1995) proposed a quantitative quality measure using discrete wavelet decomposition. Analyzing and interpreting retinal images have become a necessary and important diagnostic procedure in ophthalmology. We are interested in vessel segmentation in color images for screening of diabetic retinopathy. Thus to remove noise, enhance objects of interest - blood vessels, damaged areas, Changes in the blood Vessel Structure we can use Sobel algorithm, and Laplacian of Gaussian operator, which detects the edges of blood vessels (Leandro *et al.,* 2006). Micro aneurysms (tiny dilations of the blood vessels) are the first apparent sign of diabetic retinopathy so that their detection in fund us images through photography might be detect the disease in an early stage.

Diabetes is a disease which occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. This disease affects slowly the circulatory system including that of the retina. As diabetes progresses, the vision of a patient may start to deteriorate and lead to diabetic retinopathy. In this study on different stages of diabetic retinopathy, 124 retinal photographs were analyzed. As a result, four groups were identified, viz., normal retina, moderate non-proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy. Automated computer techniques of digital image processing offer a fast, objective and repeatable method for identifying diabetic retinopathy. There are several algorithms available in the literature to identify diabetic retinopathy using image processing techniques. The algorithms use different image processing techniques such as localization, normalization, shade correction, histogram equalization, enhancement, segmentation, filtering, classification, etc. These image processing techniques assists the physical to make correct decision

Literature Review

Diabetic retinopathy (DR) is a major cause of blindness in the developed countries. A mass screening of the vision can be successful to detect diabetic retinopathy for people who are at the risk of this eye disease. Manual extraction of the blood vessels is very time consuming in fundus images and its accuracy will definitely depend on the skill of the user. So, automatic detection of the retinal blood vessels is of utmost importance. Retinal blood vessel segmentation techniques can be divided into five different classes according to (3): (1) Matched filtering, (2) Pattern recognition, (3) Mathematical morphology, (4) Vessel tracking, (5) Multi scale approaches. In each category, several methods have been described in (3).Pattern recognition techniques can be divided into two main methods: supervised and unsupervised. An approach based on back-propagation neural network is described for the blood vessels segmentation in angiography in (Nekovei and Ying, 1995). 2D Gabor wavelet with supervised classification are used for the segmentation of the retinal vessels in (Leandro *et al.,* 2006). The intensity of the pixels and 2DGabor wavelet coefficients forms the feature vectors. A technique based on feeding 7D features consisting of gray level with invariant based features to a supervised neural network is described in (Marin *et al.,* 2011). The approach in (Chaudhuri *et al.,* 1989, Gang *et al.,* 2002 and Yao and Chen, 2009), can be considered as matched filter methods. A 2D kernel with Gaussian is described for the vessel detection in (Chaudhuri *et al.,* 1989). Because a vessel can occur in any angles, the kernel is rotated in 12 different directions and maximum response in each pixel is retained. The amplitude modified second order Gaussian filter has been proposed for segmentation of the blood vessel of the retina in (Gang *et al.,* 2002). Also a 2D Gaussian matched filter is used for enhancement of the vessels and then a neural network is applied for the vessel detection in (Fraz *et al.,* 2012 and Yao and Chen, 2009). Tracking method with the Kalman and Gaussian filters combination for segmentation of the vessels in the fund us images is proposed in (Fraz *et al.,* 2012 and Chutatape *et al.,* 1998).

The second order matched filter is used for centre line estimation and after that the track process is started, i.e., the location of the next blood vessel is estimated by the application of the Kalman filter. A supervised method for segmentation of the retinal vessels is proposed in Fraz *et al.,* 2012 and Anzalone *et al.,* 2008), where using scale space theory, the image background is normalized for non-uniform intensity variations and an optimization technique is applied to decide the optimal scale (Fraz *et al.,* 2012). Several scientists have been working in the diabetic retinopathy and published many research papers and articles. Some of the works are discussed below to have a basis idea about diabetic retinopathy in the digital image processing domain. C. Heneghen presented a general technique for segmenting out vascular structures in retinal images and characterized the segmented blood vessels (Nekovei and Ying, 1995). The segmentation technique consists of several steps. Morphological preprocessing has used to emphasize linear structures such as vessels. A second derivative operator has used to emphasize thin vascular structures, and is followed by a final morphological filtering stage. Thresholding of this image has used to provide a segmented vascular mask.

Skeletonisation of this mask allowed identification of points in the image where vessels cross (bifurcations and crossing points) and allows the width and tortuosity of vessel segments were calculated. The accuracy of the segmentation stage is quite dependent on the parameters used, particularly at the thresholding stage. However, reliable measurements of vessel

width and tortuosity were shown using test images. Using these tools, a set of images drawn from 23 subjects being screened for the presence of threshold ROP disease is considered. Of these subjects, 11 subsequently required treatment for ROP, 9 had no evidence of ROP, and 3 had spontaneously regressed ROP. The average vessel width and tortuosity for the treated subjects was 96.8 mm and 1.125. The corresponding figures for the non-treated cohort were 86.4 mm and 1.097. These differences were statistically significant at the 99% and 95% significance level, respectively.

Subjects who progressed to threshold disease during the course of screening showed an average increase in vessel width of 9.6 mm and in tortuosity of 10.008. Only the change in width was statistically significant. Appling a simple retrospective screening paradigm based solely on vessel width and tortuosity yields a screening test with a sensitivity and specificity of 82% and 75%. They have shown that segmentation of the vascular structure in retinal images is possible by use of a combination of morphological and linear filtering. Rawi *et al.* proposed better matched filter parameters (Leandro *et al.,* 2006). Comparisons with other approaches show that matched filter that uses the newly found parameters outperforms the matched filter that uses the classical filter parameters as well as some vessel detection techniques. A technique is also discussed to find the best threshold value for the continuous matched filter output image and hence the best segmented vessel image. S'anchez *et al.* proposed an automatic image processing algorithm to detect hard exudates (HE) (Marin *et al.,* 2011).

HEs detection is composed of four main stages: (1) image preprocessing and enhancement, (2) feature extraction (3) classification, and (4) post processing. In the first stage, the image is enhanced to obtain adequate illumination normalization and contrast. Following this step, the algorithm extracts dynamical training sets from each image. Next, the algorithm classifies the pixels using a Fisher's linear discriminate. Finally, a post processing technique is applied to distinguish HEs from cotton wool spots (CWs) and other artifacts. Sopharak *et al.* proposed proposes a set of optimally adjusted morphological operators to be used for exudates detection on diabetic retinopathy patients' non-dilated pupil and low-contrast images (Chaudhuri *et al.,* 1989). The red, green, and blue (RGB) space of the original image was transformed to Hue, saturation and intensity (HSI) space because HIS color space is more appropriate since it allows the intensity component to be separated from the other two color components. A median filtering operation was then applied on I band to reduce noise before a contrast-limited adaptive histogram equalization (CLAHE) was applied on I band to reduce noise before a contrast-limited adaptive histogram equalization (CLAHE) was applied for contrast enhancement (http://www.vision2020india.org/dr_manual.pdf). CLAHE operates on small regions in the image. The contrast of each small region is enhanced with histogram equalization.

After performing the equalization, the neighboring small regions were then combined by using bilinear interpolation. T. Walter et al. proposed a new algorithm (Gang *et al.,* 2002). The algorithm can be divided into four steps. The first step consists in image enhancement, shade correction and image normalization of the green channel. The second step aims at detecting candidates, i.e. all patterns possibly corresponding to MA, which is achieved by diameter closing and an automatic threshold scheme. Then, features are extracted, which are used in the last step to automatically classify candidates into real MA and other objects; the classification relies on kernel density estimation with variable bandwidth. C. Kose et al. developed automatic method for segmenting the ARMD in retinal funds image (Yao and Chen, 2009). A simple inverse segmentation method is proposed to exploit the homogeneity of healthy areas of the macule rather than unhealthy areas. This method first extracts healthy areas of the macule by employing a simple region growing method. Then, blood vessels are also extracted and classified as healthy regions.

In order to produce the final segmented image, the inverse image of the segmented image is generated as unhealthy region of the macule. The performance of the method is examined on various qualities of retinal fundus images. The segmentation method without any user involvement provides over 90% segmentation accuracy. Direct segmentation techniques are more complex and costly than our inverse method. W. L. Yun completed study on different stages of diabetic retinopathy, 124 retinal photographs were analyzed (10). As a result, four groups were identified, viz., normal retina, moderate non-proliferative diabetic retinopathy, severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy. Classification of the four eye diseases was achieved using a three-layer feed forward neural network. The features are extracted from the raw images using the image processing techniques and fed to the classifier for classification. We demonstrate a sensitivity of more than 90% for the classifier with the specificity of 100%. A. Haddouche et al. dealt with the segmentation of the Foveal Avascular Zone (FAZ) in digital retinal angiograms (11). Retinal angiography is used for detection and progression in some eye pathologies. The proposed method consists of two-stages: Singular Value Decomposition (SVD) and FAZ segmentation using Markov Random Fields (MRF). The obtained results decomposition that the method is encouraging as a first approach for location and evolution of FAZ in retinal images.

THE METHODS OF DETECTION

The Methodology

Detection of vessels, exudates, and hemorrhages, blood clots, Hard exudates, optic disk is possible using Sobel method. Edge detection is the process of localizing pixel intensity transitions. The Sobel operator is an algorithm for edge detection in images discovers the boundaries between regions also it determine and separate objects from background in an image. It's an important part of detecting features and objects in an image (Marin *et al.,* 2011). The Sobel method finds edges using the Sobel approximation to the derivative. It returns edges at those points where the gradient of I is maximum. Where the gradient of the considered image is maximum. The horizontal and vertical gradient matrices whose dimensions are 3 × 3 for the Sobel method has been generally used in the edge detection operations (Chaudhuri *et al.,* 1989). If we define A as the source image, and Gx and Gy are two images which at each point contain the horizontal and vertical derivative approximations, the computations are as follows.

$$G_x = \begin{bmatrix} -1 & 0 & +1 \\ -2 & 0 & +2 \\ -1 & 0 & +1 \end{bmatrix} * A \qquad \ldots\ldots(1)$$

$$G_y = \begin{bmatrix} -1 & -2 & -1 \\ 0 & 0 & 0 \\ +1 & +2 & +1 \end{bmatrix} * A \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

$$G = \sqrt{Gx + Gy} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$|G| = |G_x| + |G_y| \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

G_x==$(W_7+2W_8+W_9)-(W_1+2W_2+W_3)$

G_y==$(W_3+2W_6+W_9)-(W_1+2W_4+W_7)$

Where, W1 to w9 are pixcels values in a sub image (Chaudhuri *et al.,* 1989). These filters estimate the gradients in the horizontal (x) and vertical (y) directions and the magnitude of the gradient is simply the sum of these 2 gradients. Using this information, we can also calculate the gradient's direction (Gang and Krishnan, 2002).Where, for example, Θ is 0 for a vertical edge which is darker on the right side.

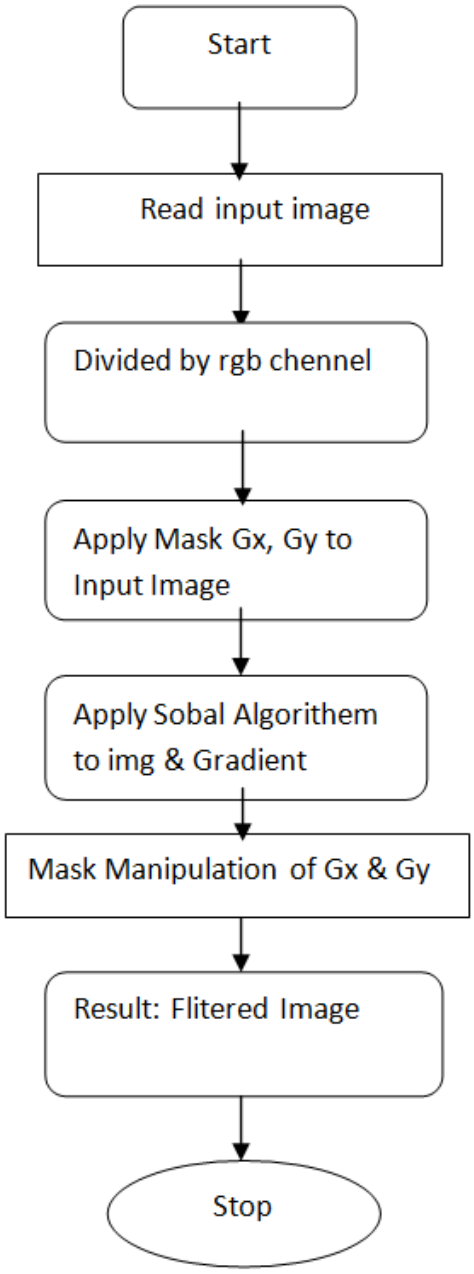

Fig. 2. Flowchart for Sobel Method

RESULTS EVALUATION

A colour photographic angiogram covering the patient's retina is taken with a conventional fundus imaging camera. The image colour depth is twenty four bit. It is observed that the existing algorithms are time consuming and resource consuming due to complicated computations. It is planned to work on a simple solution using statistical algorithm. The medical expert has classified the retinal images into normal, mild and severe as shown in the following Figure 1. We have selected totally ninety images, thirty images from each category normal, mild, and severe. The categorization is based on the number of micro aneurysms, small intra retinal dot hemorrhages, larger blot hemorrhages, whitish lesions, and cotton wool spots in the retinal image (http://www.worlddiabetesfoundation.org/composite-35.htm, 2011). The proposed algorithm applies Sobel operator to each Red and Green Channel to identify the dots present in the retinal image. This detects the hard exudates present in the Red, Green and Blue channels. Then, Variance value of red channel and variance value of Green Channel are calculated. The blue channel is noisy and may contain small and false information. Therefore, the Red and Green channels are considered for variance calculation and blue channel is ignored. Finally, difference of variance values between Red and Green channel is calculated. From the value obtained from the difference between the Red and Green channel values the retinal image could be classified into normal, mild and severe. The different steps in the proposed algorithm are represented in the following flowchart.

Formula of SD and VAR :

$$\text{SD} = S = \sqrt{\frac{\sum(X-M)^2}{n-1}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (5)$$

M = mean, n = number of element.

$$Variance = S^2 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

It is observed form Table 1 and figure 4 that the 0% to 40 % difference for normal category retinal images with 0.13 errors, 40% to 95% difference for mild category retinal images with 0.6 errors and 95% to 100% difference for severe category retinal images with 0.10 errors. The experiment results show that the statistical algorithm is simple and fast in processing. Also, the statistical algorithm is less in error. On an average the error is close to 0.12. It is noted the normal category of retinal images are low in difference in between red and green channel variance values, whereas the severe category of retinal images are in the higher difference variance values and the mild images are in between the normal and severe categories of the retinal images.

Evaluation of the Performance of Classifire

Several parameters such as True Positive (TP), True Negative (TN), False Positive (FP) and False Negative (FN) are calculated. These parameters are calculated by comparing the classifier outcome with the number of normal and abnormal images from the database. For an abnormal image, the result is true positive if the outcome of classification is abnormal and the result is False Negative (FN) if the classifier output is normal. For normal image, the result is True Negative (TN), if the classifier output is normal and False Positive (FP) if the classification outcome is abnormal.

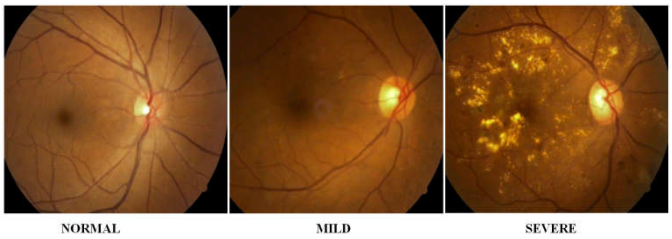

Fig. 3 Retinal image of Normal, Mild and Severe

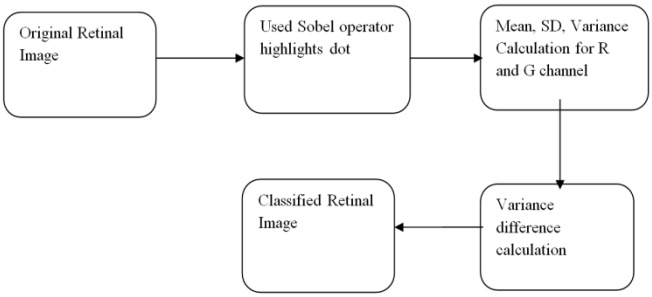

Fig. 4. Different steps in Proposed Algorithm

Table 1. Normal Image Green Channel

Image	Tot mean	Tot median	Tot var.	Tot STD
Image1	87.7360	0	343	18.520259
Image2	87.9929	0	532	23.065125
Image3	87.1700	0	780	27.928480
Image4	88.1747	0	520	22.803508
Image5	86.6433	0	156	12.489996

Table 2. Normal Image red Channel

Image	Tot mean	Tot median	Tot var.	Tot STD
Image1	86.5908	0	314	17.720045
Image2	86.5780	0	417	20.420577
Image3	86.5765	0	514	22.671568
Image4	86.6166	0	318	17.832554
Image5	86.5794	0	346	18.601075

Table 3. Mild Image Green channel

Image	Tot mean	Tot median	Tot var.	Tot STD
Image1	112.0927	2	517	22.737634
Image2	117.2858	7	686	26.134268
Image3	118.4639	7	535	23.130067
Image4	110.8993	0	636	25.219040
Image5	117.2919	7	861	29.342801

Table 4. Mild Image Red channel

Image	Tot mean	Tot median	Tot var.	Tot STD
Image1	86.5782	3	324	18
Image2	86.5975	8	368	19.183326
Image3	86.7316	9	432	20.784609
Image4	86.9724	0	382	19.544820
Image5	86.6461	7	513	22.649503

Table 5. Severe Image Green channel

Image	Tot mean	Tot median	Tot var.	Tot STD
Image1	87.4940	4	493	22.203603
Image2	88.6474	13	448	21.166010
Image3	88.2667	8	406	20.149441
Image4	87.5741	4	302	17.378147
Image5	88.3960	9	546	23.366642

In a given image dataset, these parameters, TP,TN, FP, FN are used in the calculation of the accuracy, Sensitivity (SN) and specificity (SP). Performance of the classifier can be measured in terms of sensitivity, specificity and accuracy.

- Sensitivity = TP / (TP+FN)
- Sensitivity is measure of the percentage of abnormal images classified as abnormal.
- Specificity = TN / (TN+FP)
- Specificity gives the measure of normal images that are classified correctly as normal.
- Accuracy = (TP+TN)/ (TP+FN+TN+FP)
- It is the measure of total number of well classified normal and abnormal images.

Table 6. Severe Image Red channel

Image	Tot mean	Tot median	Tot var	Tot STV
Image1	87.2704	3	258	16.062378
Image2	86.5687	6	292	17.088007
Image3	86.6487	7	315	17.748239
Image4	86.6442	7	432	20.784609
Image5	86.5872	6	618	24.859605

Table 7 .Variance value of Red, Green Channel of Normal Images

No.	Green Channel	Red Channel
1.	343	314
2.	532	417
3.	780	514
4.	520	318
5.	156	346

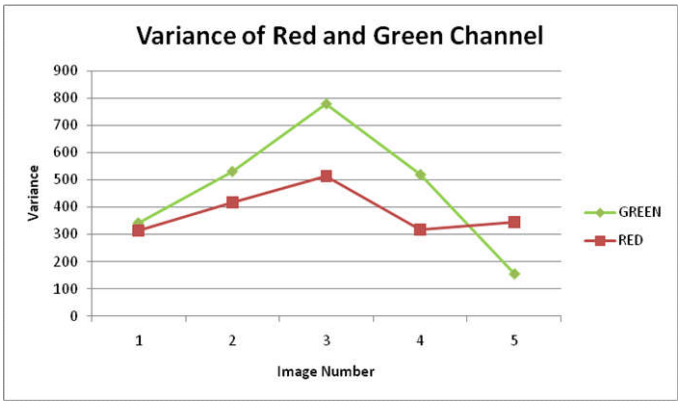

Fig. 5. Variance of Red and Green Channel of Normal Images

Table. 8 Variance value of Red, Green Channel of Mild Images

No.	Green Channel	Red Channel
1.	517	324
2.	686	368
3.	535	432
4.	636	382
5.	861	513

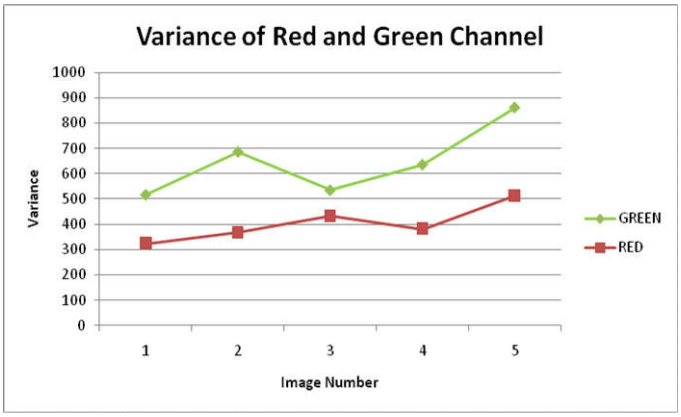

Fig. 6. Variance of Red and Green Channel ofMild Images

Table 9. Variance value of Red, Green Channel of Severe Images

No.	Green Channel	Red Channel
1.	493	258
2.	448	292
3.	406	315
4.	302	432
5.	546	618

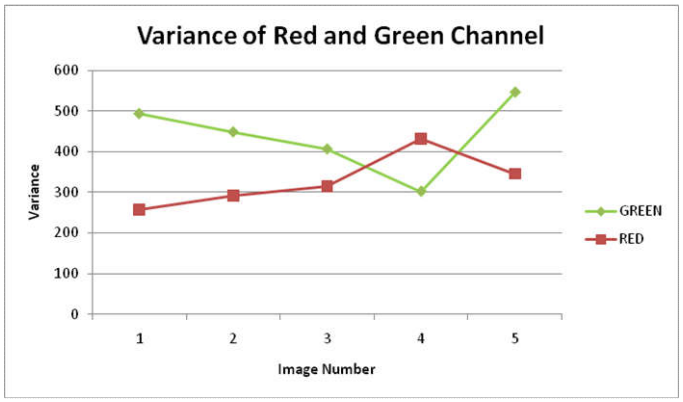

Fig. 7. Variance of Red and Green Channel ofSevere Images

Table 10. Experiment result of normal, mild and severe retinal images

No.	Normal			Mild			Severe		
	Red	Green	Difference	Red	Green	Difference	Red	Green	Difference
1	314	343	29	324	517	193	258	493	235
2	417	532	115	368	686	318	292	448	156
3	514	780	266	432	535	103	315	406	91
4	318	520	202	382	636	254	432	302	180
5	346	156	190	513	861	348	618	546	72
6	378	498	120	431	860	429	475	513	38
7	410	641	231	389	776	387	370	325	45
8	510	209	301	412	822	410	506	473	33
9	321	602	281	365	752	387	283	473	190
10	415	535	120	379	539	160	294	550	256
11	385	528	143	445	790	345	334	619	285
12	456	758	302	456	869	413	424	715	291
13	511	326	185	469	603	134	523	282	241
14	473	290	183	473	822	349	483	300	183

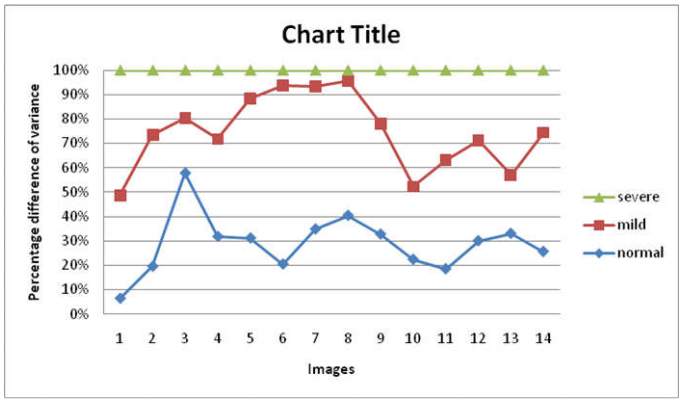

Fig. 8. Difference between red and green channel of different retinal images

Conclusion

We proposed an efficient method based on Sobel method which differentiates between original diabetic image & processed image. Sobel method can show separates parts of the edges of nerves from whole image. This paper has demonstrated an automated system which is able to distinguish normal and abnormal vasculature on the optic disc. The main focus of this work is on segmenting the diabetic retinopathy image and classifies the Exudates, micro aneurysms and hemorrhages. These methods give almost good results. Thus Image processing techniques can reduce the work of ophthalmologists and the tools used automatically locate the exudates. The proposed algorithm consists of two basic operations, one is Sobel operator and another one is variance calculation of Red and Green channel of the retinal image. The Sobel operator is used to identify the dots in the Red and Green channel of the retinal images. The difference between the variance values of Red and Green channel categorises the retinal image into normal, mild and severe. The experimental results show that the algorithm works faster because of simple computation and categorises the retinal images with minimum amount of error compared to the presently available algorithms.

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