Automatic Detection of Diabetic Retinopathy in Non-dilated RGB Retinal Fundus Images

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ABSTRACT
In this paper, a method for automatic detection of microaneurysms in digital eye fundus image is described. To develop an automated diabetic retinopathy screening system, a detection of dark lesions in digital fundus photographs is needed. Microaneurysms are the first clinical sign of diabetic retinopathy and they appear small red dots on retinal fundus images. The number of microaneurysms is used to indicate the severity of the disease. Early microaneurysm detection can help reduce the incidence of blindness. Here, we have discussed a method for the automatic detection of Diabetic Retinopathy (ADDR) in color fundus images. Different preprocessing, feature extraction and classification algorithms are used. The performance of the automated system is assessed based on Sensitivity and Specificity. The Sensitivity and Specificity of this approach are 94.44 % and 87.5 %, respectively.

General Terms
True Positive, True Negative, False Positive, False Negative

Keywords
Diabetic Retinopathy, Microaneurysms, Fundus Image, Sensitivity, Specificity.

1. INTRODUCTION
Diabetic Retinopathy (DR) is an eye disease that can lead to partial or even complete loss of visual capacity, if left undiagnosed at the initial stage. Retinal lesions associated with diabetes are used to evaluate different stages and the severity of this disease. Microaneurysms are among the earliest signs of diabetic retinopathy they arise due to high sugar levels in the blood. According to WHO (World Health Organisation) there will be 79 million people with diabetes by 2030, making the India Diabetic capital of the world [26]. Among the patients below the age of 30 years, when first diagnosed with diabetes, the prevalence of retinopathy is 17% during the first 5 years. This increases to 97% after 15 years of diabetes. Amongst the patients above the age of 30 years, 20% have showed signs of retinopathy immediately after diagnosed and this increased to 78% after 15 years of diabetes. The ratio of ophthalmologists to the number of Diabetic patients is very low. Ophthalmologists in India are insufficient to support the growing Diabetic population. India has 1 Ophthalmologists per 1,00,000 patients and this ratio is even smaller for rural settings. Today Diabetic Retinopathy is the 3th cause of blindness in India.

Medical imaging allows scientists and physicians to understand potential life-saving information using less invasive techniques. This automated algorithm indicates places in the image that require extra attention from the physician because they could be
abnormal. These technologies are called Computer Aided Diagnosis (CAD).

This paper describes components of an automatic system that can aid in the detection of diabetic retinopathy. As the number of diabetes affected people is increasing worldwide, the need for automated detection methods of diabetic retinopathy will increase as well. To automatically detect diabetic retinopathy, a computer has to interpret and analyze digital images of the retina.

The Fundus Image Analysis system described in this paper is developed to assist ophthalmologist's diagnosis by providing second opinion and also functions as an automatic tool for the mass screening of diabetic retinopathy. Colour fundus images are used by ophthalmologists to study eye diseases like diabetic retinopathy, age related macular degeneration (AMD) and Retinopathy of pre-maturity (ROP). Extraction of the normal features like optic disk, fovea and blood vessels and abnormal features like exudates, cottonwool spots, microaneurysms (MA) and hemorrhages from colour fundus images are used in fundus image analysis system for comprehensive analysis and grading of diabetic retinopathy.

Microaneurysms are the first clinically observable lesions indicating diabetic retinopathy, their detection is critical for a diabetic retinopathy screening system.

There have been an increase in the use of digital image processing techniques for the screening of DR after it was recommended as one of the method for screening DR at the conference on DR held in Liverpool UK in 2005. This increases more work have been done to improve some of the existing screening methods, while new methods have also been introduced in order to really increase the accuracy of this method.

Giri Babu Kande [1] proposed a method of polynomial contrast enhancement and dark lesion detection based on Mathematical Morphology. In this method Morphological top-hat transformation is used to segment candidate MAs from blood vessels. A.M. Mendonça et al. [2] used mean filter to the original image, obtaining an normalized image and scaling as preprocessing techniques. To discriminate microaneurysms from blood vessels "top-hat" transform and a gaussian shaped matched filter is used. Abhir Bhalerao et al. [3] used median filter for contrast normalization and contrast enhancement as preprocessing techniques. Orientation matched filter was used to differentiate microaneurysms from blood vessels. Thresholding on the output of orientation matched filter is done to obtain a set of potential candidates (MAs). Eigen image analysis applied to the potential candidate regions and a second threshold applied on the eigen-space projection of the candidate regions eliminated certain noise artifacts. Iqbal, M.I et al. [6] used Color Space Conversion, Edge Zero Padding, Median Filtering and Adaptive Histogram Equalization as pre-processing techniques and they used segmentation to group the image into regions with same property or characteristics. Methods of image segmentation include simple thresholding, K-means Algorithm and Fuzzy C-means.

Akara Sopharak et al. [8] used median filtering, contrast enhancement by Contrast Limited Adaptive Histogram Equalization and shade correction as pre-processing steps and he used Extended-minima transform for feature extraction. Priya R et al. [9] used pre-processing techniques like Gray scale Conversion, Adaptive Histogram Equalisation, Matched Filter Response and proposed a method for feature extraction based on Area of on pixels, Mean and Standard Deviation. A Shaeidi [14] used Dynamic Thresholding to identify whether a pixel is MA or not, based on color, size, shape and intensity features.

In this paper we concentrate on MA detection as the earliest clinical sign of diabetic retinopathy. Their detection can be used to grade the DR into four stages i.e. no DR, mild DR, moderate DR, and severe DR. This paper consists of four sections, section II consists of anatomy of eye, in section III we have discussed Diabetic Retinopathy, section IV consists of proposed method, section V consists of results and discussion and section VI is the conclusion.

2. DIABETIC RETINOPATHY

Diabetic retinopathy is the prime cause of vision loss amongst the working age population of the developing and the developed countries. Diabetic patients are 25 times more probable to become blind than non-diabetic patients. Diabetic retinopathy is a complication of diabetes to the retina and to the blood vessels.

Blood vessels are continuous patterns with little curvature, originated from optic disc and have a tree shape branching. The mean diameter of the vessels is about 100 μm, i,e 1/40 of retina diameter. Optic disk or optic nerve head is the bright yellowish disk, from which, blood vessels and optic nerve fibres emerge. Optic disk transmits electrical impulses from the retina to the brain. It measures 1.5 to 2 mm in diameter. Macula is the central area of the retina, temporal to the optic disk. It is responsible to have fine central vision and colour vision. The center of macula is called fovea as shown in fig 1. This region of the retina is the most sensitive region. The diameter of the macula is about 4 to 5 mm.

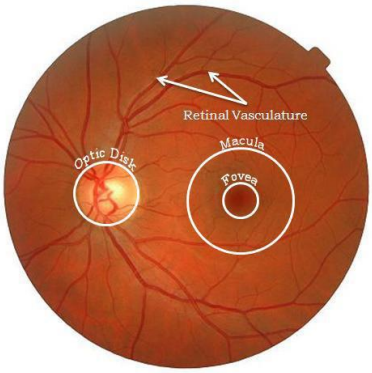
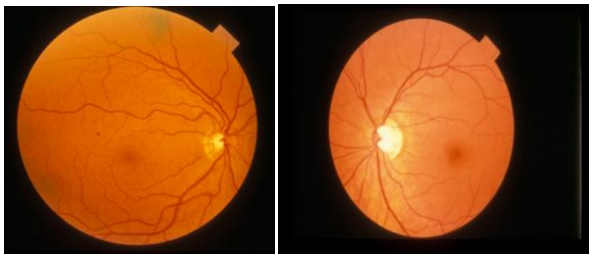


Fig 1: Anatomy of eye

Diabetic retinopathy is caused by both the forms of diabetes i.e. diabetes mellitus and diabetes insepidous. It is a very asymptomatic disease in the early stages and it could lead to permanent vision loss if untreated for long time. The problem here is the patients may not know about it until it reaches advanced stages. Once it reaches advanced stages vision loss becomes inevitable. As diabetic retinopathy is the third major cause of blindness particularly in India, there is an immediate requirement to develop efficient diagnosis method. The main stages of diabetic retinopathy are non proliferative diabetic retinopathy (NPDR) and proliferative retinopathy (PDR).

NPDR is the early stage of Diabetic retinopathy. Nonproliferative diabetic retinopathy (NPDR) is a microvascular complication of diabetes mellitus that can lead to irreversible visual loss. In this case, at least one microaneurysm with or without the presence of retinal haemorrhages, hard exudates, cotton wool spots, or venous loops is present. Microaneurysms are the first clinical abnormality to be noticed in the eye. They may appear in isolation or in clusters as tiny, dark red spots or looking like tiny haemorrhages within the light sensitive retina as shown in fig 3. Their sizes ranges from 10-100 microns i.e. less than 1/12th the diameter of an average optics disc and are circular in shape, at this stage, the disease is not eye threatening. In NPDR, depending on the presence and extent of the features such as hemmorrages, hard exudates, microaneurysms or cotton wools spots due to leakage of fluid and blood from the blood vessels, NPDR can be classified into i) mild, ii) moderate and iii) severe. In mild NPDR, microaneurysms are small areas of balloon-like swellings in the retina's tiny blood vessels as shown in fig 2(b). As the disease progresses, some blood vessels that nourish the retina are blocked and this stage is called Moderate NPDR as shown in fig 2(c)**.** The next stage is Severe NPDR during which many more blood vessels are blocked as shown in fig 2(d).



(a) (b)

(c) (d)

Fig 2: (a)Healthy image (b)Mild DR (c)Moderate DR (d)Severe DR

PDR is the advanced stage whereby signals are not sent by the retina to the brain for the lack of blood supply and this triggers the growth of new blood vessels. In PDR number of Hemmorrages are more. Hemmorrhages occurs in the deeper layers of the retina and are often called ‘blot’ haemorrhages because of their irregular shape. As the disease progresses, microaneurysms will be ruptured. This results in retinal hemorrhages either superficially or in deeper layers of the retina.

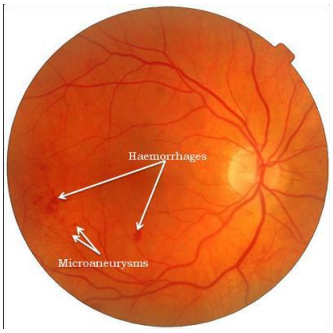


Fig 3: Retinal image having some Microaneurysms and Hemmorrages

3. AUTOMATIC DETECTION OF DIABETIC RETINOPATHY

Automatic detection of Diabetic Retinopathy (ADDR) is a fully automated system for detection of Diabetic Retinopathy (DR). Fig 4 shows the block diagram of ADDR. Input to this system is a fundus image which is part of human eye that can be seen through the pupil. Fundus image is the interior surface of the eye, opposite the lens, and includes the retina, optic disc, macula, Blood vessels and fovea. As the quality of the image is not satisfactory because of noise, bad contrast, uneven illumination etc. pre-processing is used to get better results. The proposed method is made up of three fundamental parts, (1) pre-processing, which involves obtaining an gray image from green channel, background normalization, contrast enhancement and image binarization (2) feature extraction of the microaneurysms based on circularity, area and other features and (3) Classification based on count, thereby we can grade the severity. The detailed procedure for microaneurysms detection is shown in fig 5.

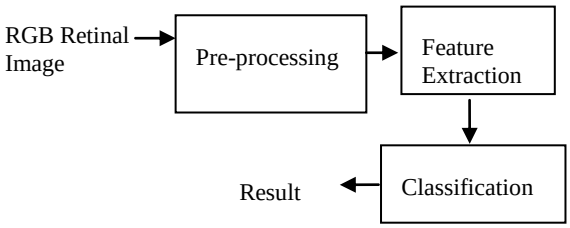


Fig 4: Basic system level block diagram

3.1 Pre-processing

The aim of pre-processing is to attenuate the noise, to improve the contrast and to correct the non-uniform illumination. In the RGB images (fig 6(a)), the green channel exhibits the best contrast between the vessels and background while the red and blue ones tend to be more noise. Hence green channel is used for further processing.

The next step is conversion of green channel image into an gray scale image, as the retinal blood vessels appear darker in the gray image, shown in fig 6 (b). All the features like blood vessels, MAs etc are hidden in the background and are not clearly visible. Thus Normalization and contrast enhancement is performed to improve the image quality. Normalization is performed by subtracting an approximate background from the gray image. A 30x30 median filter is applied to the gray image shown in fig 6(c) and the result image is subtracted from green

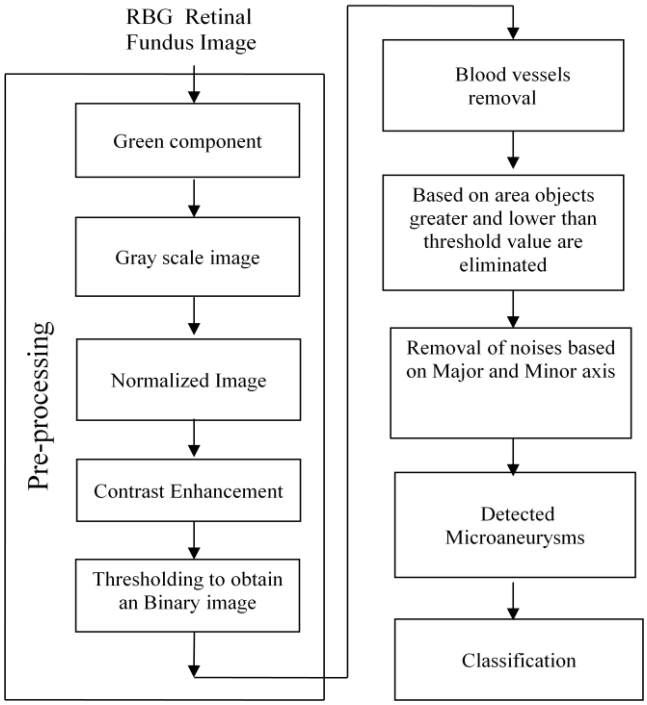


Fig 5: procedure for microaneurysms detection

plane to get normalized image as shown in fig 6(d). Adaptive Histogram Equalization is applied for contrast enhancement. A dark region including vessels, MAs and noise are dominant after contrast enhancement shown in fig 6(e). The gray threshold is selected to determine the vessels and Microaneurysms.

The last step in the pre-processing stage is binarization. The candidate vessels and MAs are then binarized by multi level thresholding as shown in fig 6(f). A correct threshold value is crucial, because smaller threshold value induces more noise and higher threshold value causes loss of some fine vessels. Now the output image is ready for feature extraction.

3.2 Feature Extraction

Objective of Feature Extraction is to select all Microaneurysms present in the pre-processed image. Microaneurysms appear as isolated patterns and are disconnected from the vessels. The features of microaneurysms can be extracted based on shape, size and intensity level. Microaneurysms are dark reddish in colour, they appear as small red dots of 10 to 100 microns diameter and are circular in shape. After the image is pre-processed, the candidate microaneurysms are segmented by separating them from the blood vessels. MA and vessels both appear in a reddish color and MAs cannot occur on vessels. Blood vessels are large in area and are connected component, thus can be identified from MA based on area. Threshold value is decided by experimentation. To remove blood vessels, objects having area greater than threshold value are eliminated as shown in fig 6(g). The result image may include microaneurysms and some noise which are unconnected vessels and other particles in fundus image.

MAs are 10-100 microns diameter in size, thus MAs can be identified from noise based on area. Two threshold values are decided by experimentation to remove noise objects having

area greater and lower than MAs. The resulting image having objects which have the same area and some of them are microaneurysms.

As MAs are circular in shape, they can be identified from noise which is irregular in shape. Based on the major and minor axis, we can eliminate the noise having same area as microaneurysms but is elongated in shape. The result is shown in fig 6(h).

Finally, microaneurysms are detected based on perimeter and circularity. Canny edge detection is performed on the resulting image from the previous section. Each object's area and perimeter is calculated and these results are used to form a simple metric indicating the roundness of an object. The perimeter is calculated by finding the length of the boundary pixels of the candidate. In calculating perimeter, the x and y coordinates are counted as one and diagonal neighbours are counted √2 times.

delta = diff(boundary).^2;

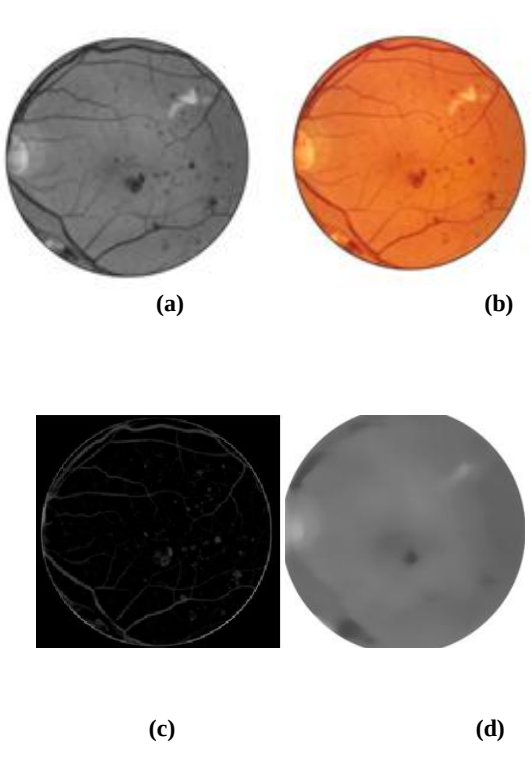
perimeter =sum($\sqrt{sum(delta, 2)}$)

$$metric = \frac{4 * \pi * area}{Perimeter^2}$$

This metric is equal to one for a circle and it is less than one for any other shape. The discrimination process can be controlled by setting an appropriate threshold α.

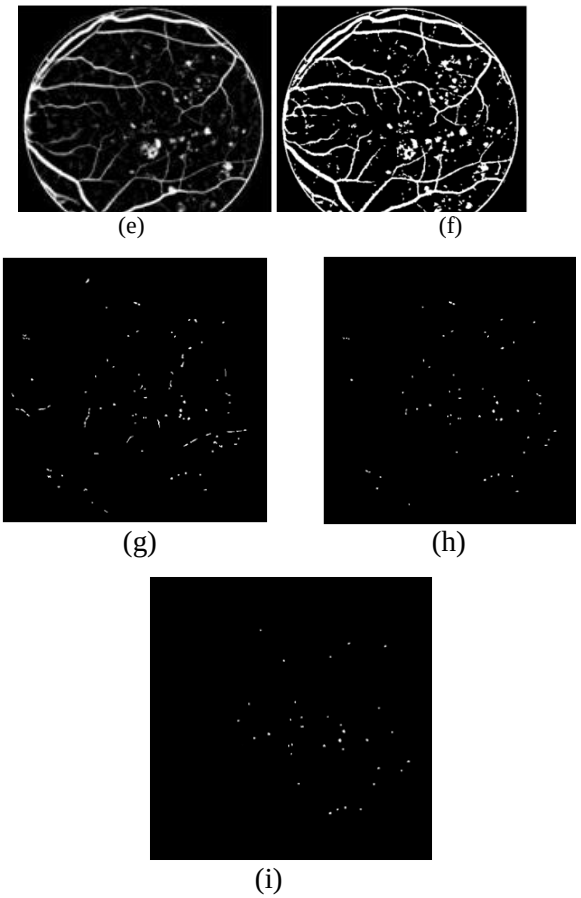
α = {0.94, 0.95, 0.96, 0.97, 0.98, 0.99, 1.00, 1.01, 1.02}

Metric closer to one indicates the microaneurysms shown in fig 6(i).



(a) **(b)**

(c) **(d)**



(e) (f)

(g) (h)

(i)

Fig 6: Various stages of ADDR for detection of MAs (a)Original image (b)Gray image from Green channel (c) Image after median filter (d) Subtracted or normalized image (e) Image after scaling (f) Thresholded image (g) Image after removal of vessels (h)Objects having same area as microaneruysms (i)Detected microaneurysms.

3.3 Classification

After the detection of Microaneurysms, classification groups the eye images as either diseased or normal depending on the count of detected microaneurysms. Classification can be used to grade the DR into four stages as no DR, mild DR, moderate DR, and severe DR as shown in Table 1.

Table 1. Grading of Diabetic Retinopathy

DR Stage	
Grade 0 (No DR)	MA=0
Grade 1 (Mild)	1<MA<5
Grade 2 (Moderate)	5<MA<15
Grade 3 (Severe)	MA>15

MA=Microaneurysms

4. RESULTS AND DISCUSSION

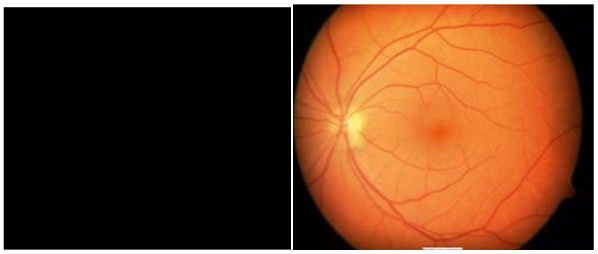
For the purpose of evaluation, four datasets were considered namely, the DIARETDB1 [28], DRIVE [29], ROC [30] datasets and form the University of LINCOLN [31]. Out of these datasets, 100 images were taken for the evaluation. These images are tested on an Intel i3 2.27 GHz PC using the MATLAB program. For hardware implementation, MATLAB, Simulink and System Generator software components are used. MATLAB stands for "MATrix LABoratory". It is developed by MathWorks®. It is a high-

level technical computing language and interactive environment for algorithm development, data visualization, data analysis, and numeric computation. Simulink (Simulation and Link) is a graphical extension to MATLAB for modeling and simulation of the systems. In Simulink, systems are drawn on screen as block diagrams. System Generator is a design tool from Xilinx that enables the use of The Mathworks model-based design environment Simulink for the FPGA design. It converts a Simulink model of Xilinx blocks into an efficient hardware implementation.

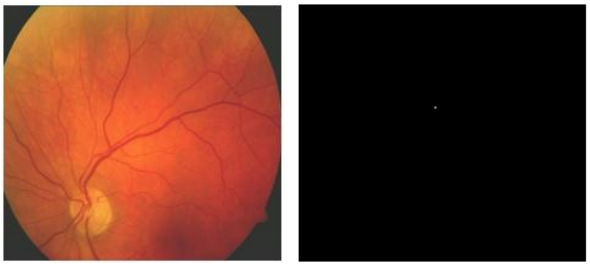
The image size considered here is 512 x 512 pixels with 24 bits per pixel. The proposed algorithm takes twelve seconds for execution. For experimentation, from the data set, twenty six healthy images, twenty four mild images, eighteen moderate images and thirty two severe are taken. Table 2 shows the microaneurysms detected by the algorithm and the actual microaneurysms present in the images and grading is done based on count of detected microaneurysms. Fig 7 shows the four grades of Diabetic Retinopathy.

Table 2. Comparison between automated and manual detection of MA's

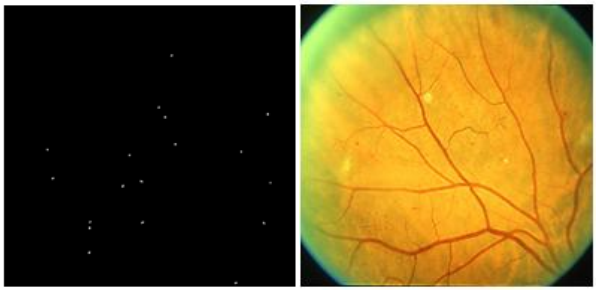
Images	MA's Detected by algorithm	Actual MA's present in image	Grade
Image1	11	12	Moderate
Image2	1	2	Mild
Image3	12	14	Moderate
Image4	10	5	Severe
Image5	1	0	No DR
Image6	23	20	Severe
Image7	2	1	Mild
Image8	30	35	Severe
Image9	2	3	Mild
Image10	5	6	Mild
Image11	0	0	No DR
Image12	12	15	Severe
Image13	6	5	Mild
Image14	6	10	Moderate
Image15	20	15	Severe
Image16	11	20	Moderate
Image17	10	5	Moderate
Image18	9	7	Moderate
Image19	3	1	Mild
Image20	5	8	Mild



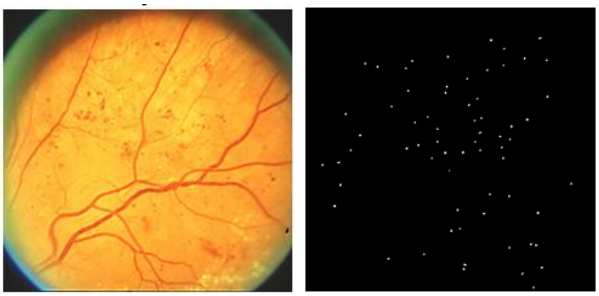
Original image Detected Microaneurysms
Number of Microaneurysms=0
Grade=0



Original image Detected Microaneurysms
Number of Microaneurysms=1
Grade=1



Original image Detected Microaneurysms
Number of Microaneurysms=14
Grade=2



Original image Detected Microaneurysms
Number of Microaneurysms=66
Grade=3

Fig 7: Different grades of images with microaneurysms detected by algorithm

Detected MAs are compared with the ophthalmologists' for verification. For Mild, Moderate and sever it is giving best results. It is clear from the results that for some of the healthy images, algorithm detectes it as mild because of the noise present in the images.

Sensitivity and specificity are the important parameters used to measure the accuracy of the algorithms. The accuracy can be calculated based on four values, namely the true positive (TP) rate, the false positive (FP) rate, the false negative (FN) rate, and the true negative (TN) rate.

True Positive is when an 'abnormal' image is correctly identified as 'abnormal'. False Negative is when an 'abnormal' image is incorrectly identified as 'normal'. True Negative is when an 'normal' image is correctly identified as 'normal' and False Positive is defined as 'normal' image is incorrectly identified as 'abnormal'. These values are also defined in Table 3. Sensitivity is the percentage of the actual MA pixels that are detected, and specificity is the percentage of non-MA pixels that are correctly classified as non-MA pixels. Ideally Sensitivity and Specificity is 100% but because of presense of noise and artifacts in the image it is difficult to achieve 100% results.

Table 3. Performance Evaluation

Test Result	Present	Absent
Positive	True Positive (TP)	False Positive (FP)
Negative	False Negative (FN)	True Negative (TN)

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

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

Table 4 shows the sensitivity and specificity of various grades of images from the dataset images and the results are also compared with the expert opinion. Out of 32 sever images all 32 is detected as sever, out of 18 moderate images all 18 are detected as moderate, out of 24 mild images, 3 images were detected as healthy and out of 26 healthy images 3 images are detected as mild. Figure 8 shows the graph of Sensitivity and Specificity of Grade 0, Grade1, Grade 2 and Grade 3 images from the dataset.

The average sensitivity and specificity for the proposed ADDR is 94.44% and 87.5% respectively. Table 5 shows the comparison results with the other papers.

Table 4
Grading of fundus image analysis system on the Dataset

DR Grade	Number of images	Sensitivity	Specificity
Grade 0	26	89.65%	100%
Grade 1	24	100%	88.88%
Grade 2	18	100%	100%
Grade 3	32	100%	100%

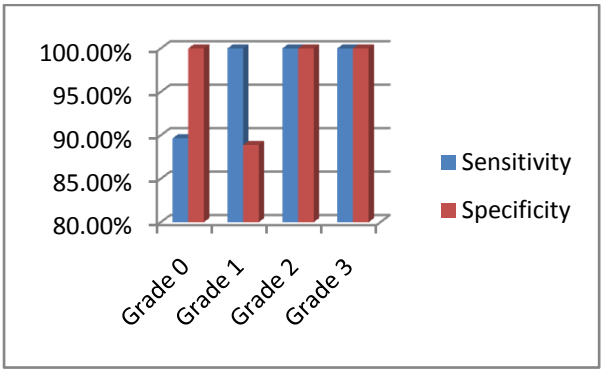


Fig 8: Graph of Sensitivity and Specificity for Grade 0- Grade 3 images

Table 5. Comparison of results with other papers

Author	Sensitvity	Specificity
Proposed algorithm	**94.44%**	**87.5%**
Giri Babu Kande [1]	**100%**	**87.5%**
Abhir Bhalerao et al. [3]	**82.6%**	**80.2%**
Iqbal, M.I et al. [6]	**98 %**	**61%**
Akara Sopharak et al. [8]	**81.61%**	**99.9%**
Rumano A et al. [10]	**85.4%**	**83.1%**

5. CONCLUSION

Our work concentrates on microaneurysm detection in non-dilated digital images from diabetic retinopathy patients. The system intends to help the ophthalmologists in the diabetic retinopathy screening process to detect symptoms faster and more easily. The proposed algorithm could detect MAs on very poor quality images. The average sensitivity and specificity is 94.44% and 87.5% respectively. There are some incorrect MA detections which are caused by the too small MA, too blurred MA, faint blood vessels which cannot detected and removed. There are some missing MAs located next to or nearby blood vessels which are removed as wrongly detected as blood vessels. They are also faint blood vessels which are not removed in vessel detection step, MA could be wrongly detected on those vessels. Faint blood vessels can be incorrectly detected as MA. The results of MA detection depend on the success of vessel detection. A main weakness of the algorithm arises from the fact that the algorithm depends on vessel detection. This indicates the further necessity of improving the robustness of this task. Hemorrhages detection could be also added to the system in order to increase its ability to verify the degree of diabetic retinopathy.

6. ACKNOWLEDGMENTS

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