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Automated Detection System for Diabetic Retinopathy Using Two Field Fundus Photography

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Abstract

Diabetic retinopathy (DR) is a leading cause of vision loss, caused by damage to the retina from complications of diabetes. Analysis of the retinal photographs for key characteristics of DR can result in early diagnosis and better management of DR. This paper presents a method for automated analysis and classification of the retina as DR or non-DR using two-field mydriatic fundus photography. The optic disc region is located by multi-level wavelet decomposition and recursive region growing from an automatically identified seed point. Blood vessels are extracted by applying histogram analysis on the two median filtered images. Red lesions are detected using three stage intensity transformation and white lesions from multi-level histogram analysis. The final classification of the retina as DR or non-DR is based on an aggregate of the lesions extracted from each image. The proposed method has been validated against diagnosis by a panel of expert ophthalmologists on images from 368 patients. The observed sensitivity and specificity were 80% and 50% respectively. The results show that automated screening based on two-field photography can be applied in routine screening

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Keywords: diabetic retinopathy; automatic detection; fundus images; red lesions; white lesions; microaneurysms; hemorrhages; exudates; cotton-wool spots

1. Introduction

Diabetic Retinopathy (DR) is the disease affecting blood vessels in the retina where capillary vessels in particular are vulnerable to high glucose levels caused by diabetes. DR is the most common complication of diabetes and the leading cause of blindness. The most significant predictor of the prevalence of DR is the duration of the diabetes[1].

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DR is divided into various stages. The earliest signs of DR are microaneurysms (MA), dot & blot hemorrhages (HE), cotton-wool spots and exudates that result from abnormal permeability and non-perfusion of capillaries. These early signs are known as non-proliferative DR (NPDR). Fluid leaking from retinal capillaries indicates a further progression of the disease. This may lead to sight threatening diabetic retinopathy, if the leakage is located in the area of most acute vision, the macula. Advanced stage of DR, proliferative DR (PDR), develops from occluded capillaries that lead to retinal ischemia and formation of new vessels on the surface of the retina either near optic disc (OD) or in the retinal periphery[2]. Other complications of PDR include detachment of the retina due to scar tissue formation and new blood vessels bleeding into vitreous chamber giving rise to vitreous hemorrhage[3].

In India, there are approximately 31.7 million diabetes patients and every year 1.7 million new patients get added to this[4]. Of these approximately 5.6 million patients are thought to suffer from DR. Symptoms of disease will only surface during the advanced stages of the disease either by the development of macular edema or PDR where treatment will be aimed at preventing further vision loss than restoring lost vision. Asymptomatic nature of the disease during the early stage mandates systematic and periodic screening of apparently healthy person for the risk of DR that can be prevented by medical intervention[2]. Studies by Kristinsson et al.[5] and Singer et al.[6] points that systematic screening and timely treatment significantly reduces vision loss and costs to the society.

Although there are numerous methods for the detection of DR like direct or indirect ophthalmology, Optical Coherence Tomography (OCT), retinal imaging using digital fundus camera has been widely used for screening and diagnosis of DR. Seven standard field stereoscopic color photography as defined by the ETDRS is the gold standard for detecting and classifying DR[7]. Even then practicing this standard for DR screening is quite impractical as it requires highly skilled photographer and longer time for each patient imaging and increased patient co-operation, in addition to the logistics of storing and handling large number of images. Grading for DR and assessing the need for referral treatment from remote diagnosis of has been reliably executed in telemedicine applications8. From the studies, it has been identified that a single field photography including macula may be sufficient[9]. In this study, we follow the two field fundus photography. One image with macula as centre covering majority of temporal retina and smaller part of nasal retina; while the second image field with optic disc as the center further increases the coverage of nasal retina. Thus by combining the two fields, sufficiently good coverage of retina is obtained.

In India, patient to ophthalmologist ratio is 100,000:1[10], with such an enormous disparity in ratios an ophthalmologist will have no time for blindness preventive surgeries but will be instead flooded with general eye-check-ups. Computer Aided Detection (CAD) can play a pivotal role in addressing prevention of avoidable blindness by automated detection of retinal pathologies and can thus alleviate the burden of screening from ophthalmologists. It also needs to be understood that 80% of diabetics will have will have no sign of DR[4]. Hence with automated screening, only those patients with likely pathology need to be referred, thereby reducing the workload of ophthalmologists. The method described in this paper is intended to be a first step towards automated DR screening system.

Similar work has been done by Keith Goatman et al.[11-14] where primary focus was microaneurysm detection. In this paper, we use alternate techniques for detection of red lesions like microaneurysm, dot, blot and flame hemorrhages. Additionally, detection of white lesions like exudates and cotton wool spots which have received lesser attention among researchers is also included in this work. The techniques described in this paper are following the previous work of Sharath Kumar et al.[18, 20] and applied on a larger number of retinal images and finally giving the decision of diagnosis screening compared to clinical evaluation.

This paper presents the implementation of the screening system as a four stage process. In the first step, the retinal images are normalized via bi-cubic interpolation, local contrast enhancement and background subtraction. The second step is to automatically locate optic disc and blood vessels regions. The third step is to recognize signs of DR, namely red and white lesions. Finally, the information from both fields are accumulated and the retina is classified as DR or non-DR.

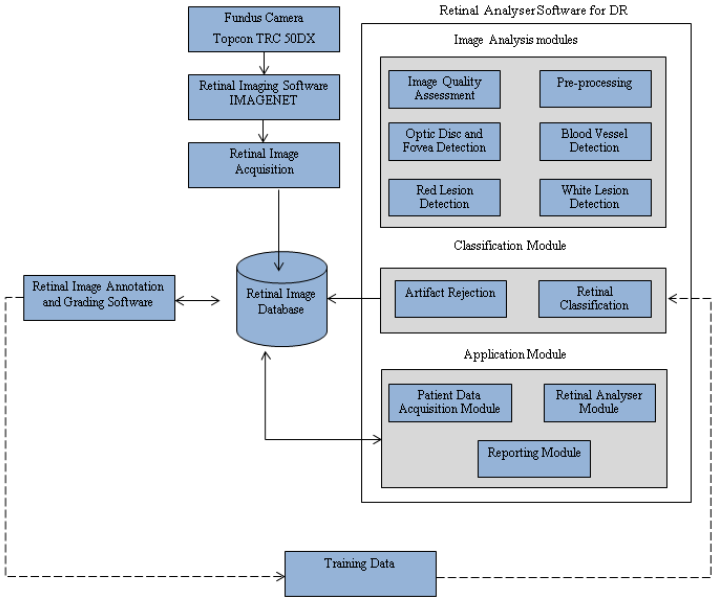

Fig. 1. Architecture diagram of the proposed method

2. Materials

2.1. Data Collection

A dataset of 1344 retinal images from 715 retinas of 368 diabetic patients were obtained from the DR diagnosis program at the Regional Institute of Ophthalmology (RIO), Thiruvananthapuram. The retinas were imaged with a field-of-view of 50º using Topcon TRC-50DX mydriatic fundus camera with Nikon D90 DSLR camera. Images were captured as lossless TIFF format with a resolution of 2144 X 1424 pixels. All patients underwent routine mydriasis with Tropicamide 1% and two image fields per eye were captured, one fovea centric and the other disc centric.

2.2. Manual Grading of the Retina for Ground Truth

Images from all the patients were annotated and independently graded by a team of two ophthalmologists at RIO according to the Early Treatment Diabetic Retinopathy Study (ETDRS)[15]. Using the Retinal Image Annotation and Grading Software (RIAG) developed by the authors, the ophthalmologists marked lesions, assessed image quality and graded the images. The grade for each eye was a combined assessment of the fovea and optic disc fields and the highest grade of the two fields was assigned to that eye.

3. Methods

Architecture diagram of the proposed DR detection method is as shown in Fig. 1. The captured images were analyzed for symptoms of DR using the proposed multistage method as described below.

3.1. Preprocessing of Retinal Images

For computation efficiency, the scale of the image was first standardized to 640 X 480 pixels using bi-cubic interpolation.

3.2. Optic Disc Detection

Optic disc appear as a bright yellowish region in the retinal image. The optic disc detection algorithm relies on three known facts. The first pertains to the image acquisition. Since acquisition of fundus images follows a fixed protocol, some information about the retina and its structures can be exploited. The practitioner knows which eye (left/right) is being imaged and whether the image is centered on the macula or the optic disc (OD). This a priori information is exploited in order to guide the search for the OD in a specific portion of the image. The second comes from observations that the OD represents a bright region (not necessarily the brightest) in a fundus image of good quality. The third relates to the form of the OD, which always appears approximately circular. Work by Lalonde et al.[16] and Mallat et al.[17] is being incorporated which are detailed in the flowchart (see Fig. 3.a).

3.3. Blood Vessels Detection

Due to the external light, retinal fundus image will suffer from an uneven illumination causing atypical change in the color of the fundus images. To negate this and to obtain uniform brightness in the fundus image, we applied a scheme of brightness correction using hue saturation value (HSV) space[18,19]. The process is detailed in the flow chart (see Fig. 3.b).

3.4. White Lesions Detection

Presence of white lesions such as exudates (also called as hard exudates) and cotton-wool spots are the symptoms of moderate DR. Of these, the detection of exudates is one of the key features in the early diagnosis of DR. Exudates are fatty deposits on the retina which appear as yellowish regions in fundus image. Fundus images show considerable variation in brightness which makes automatic detection of exudates difficult. We made use of the work presented by Sharath Kumar et al.[18] which describes a new method for preprocessing and false positive elimination towards the reliable detection of exudates and is detailed in the flowchart (see Fig. 3.c).

Here, the brightness of the fundus image was changed by the nonlinear curve with brightness values of the hue saturation value (HSV) space. To enhance brighter yellow regions (exudates), gamma correction was performed on each red and green components of the image. Subsequently, the histograms of each red and green component were extended. After that, the exudates candidates were detected using histogram analysis. Finally, false positives were removed by using multi-channel histogram analysis.

Cotton-wool spots appear as white fluffy patches in the fundus image. Compared to exudates, these are blurred regions which need more attention in the process of detection. Here, we modified the method[18] as follows. Firstly, shading correction was applied on the green channel of standardized RGB color image. Here, background was estimated by choosing kernel size of 25 x 25 pixels and preprocessed image was obtained by suppressing red lesions by considering only positive intensity values from the shade corrected image. Next, to emphasize cotton-wool spots, gamma correction was performed on the preprocessed image. Subsequently, the histogram of the resulting image was extended. Finally, binary thresholding was performed to detect cotton-wool spots. The threshold value chosen was automatically extracted from the histogram analysis.

3.5. Red Lesions Detection

Signs of DR include red lesions such as microaneurysms (MAs) and hemorrhages (Dot, blot and flame). A modified red lesion detection method presented by Sharath Kumar et al.[20] has been incorporated. In this paper, they have addressed the problem of detecting red-lesions in two phases by integrating the three stage fine extraction of red-lesions and three stage false positive elimination.

In the extraction phase, scale of the image was first standardized to 640 X 480 pixels using Bi-cubic interpolation. As red lesions have the highest contrast with the background in the green plane image[21], information from red and blue plane images were not used. To separate retinal features from the background, shading correction was performed on the green plane image by estimating the background image. The resulting shade corrected image contained red and white lesions which comprised pixels with negative and positive values respectively. The

preprocessed image was then obtained by suppressing the white lesions by setting pixels with positive values to zero. To distinguish between objects representing red-lesions and blood vessels, a morphological top-hat transform was used. This operation is based on morphologically opening the preprocessed image with a linear structuring element at different orientations. A total of twelve rotated structuring elements were used with a radial resolution of 15^0. The length of the structuring element was experimentally set to 9 pixels. A vascular image was obtained by taking maximum response at each pixel by comparing all the twelve images. This vascular image is then subtracted from the preprocessed image to obtain an image containing actual red lesions and red lesion like objects. In the final stage, a 2D Gaussian matched filter is employed for accurate detection of red lesions. This matched filtered image is then thresholded to obtain binary image consisting of red lesions.

In the elimination phase, falsely detected red-lesions elsewhere in the retinal image were first removed by comparing the object average intensity with neighboring pixel intensities; next, red lesions findings on the blood vessel were removed by using blood vessels detection; and finally, optic disc extraction by Sharath Kumar et al.[18] was employed to eliminate false findings in the optic disc region. To take advantage of prior works and to enable comparisons between our method and previous approaches, the work by Spencer et al.[22] together with the extensions to this work proposed by Frame et al.[23] was taken as our starting point.

As flame hemorrhages appear as brighter than MAs and elongated in shape compared to dot and blot hemorrhages, the method[20] failed to detect flame hemorrhages because of limitation on size and shape of the detection algorithm. This has been taken care with the additional algorithm based on CLAHE (Contrast Limited Adaptive Histogram Equalization) which is independent of size. Here, green plane of RGB color image whose intensity values are distributed uniformly using CLAHE. Next, the threshold values of the window are obtained from the histogram of the corrected image. Finally, binary thresholding was performed on the corrected image to locate flame hemorrhages. Flow chart of the red lesion detection is detailed in Fig. 3.d.

3.6. Classification

Classification module consolidates results of red and white lesion detection algorithms from optic disc and fovea centric images and classifies a retina as either Non-DR or suspicious of DR which needs ophthalmologist's review. A 'waterfall model' based classification approach was followed in this work to optimize the algorithm execution and keeps the average retinal processing time under check.

Detection of white lesions like hard exudates and cotton-wool-spots is an indication that the disease has progressed beyond DR grade of Mild NPDR in which case regardless of presence of red lesion the patient need to be referred to an ophthalmologist. Similarly, in red lesion detection as explained in Section 3.5 three algorithms were used to detect presence of lesions with varying size. If any algorithms detected a lesion the classifier would not proceed to next level and classifies the retina as suspicious of DR needing ophthalmologist review. Both optic disc and fovea centric image were analyzed and if either shows presence of any of lesions, the retina is classified as suspicious for DR. Only if both images return negative, the retina will be classified as non-DR. Approach is represented diagrammatically in the Fig. 4

4. Results

A data set of 1344 images obtained from 368 patients from the Regional Institute of Ophthalmology, Thiruvananthapuram was used for this study. Here, two images (disc centered and fovea centered) were acquired per eye. Each image was then graded along with lesion markings by a panel of ophthalmologists. Ophthalmologists graded 902 images as having some stage of DR, 352 images as Non-DR. Another 90 images were marked as insufficient evidence to be graded. The same set of images was analyzed using the automated method proposed here and compared with the ground truth provided by the ophthalmologists. Accuracy of the proposed method was measured using Sensitivity (Sn) and Specificity (Sp) which are defined by equation (1) & (2). Sn and Sp of the proposed method were 80% and 50% respectively.

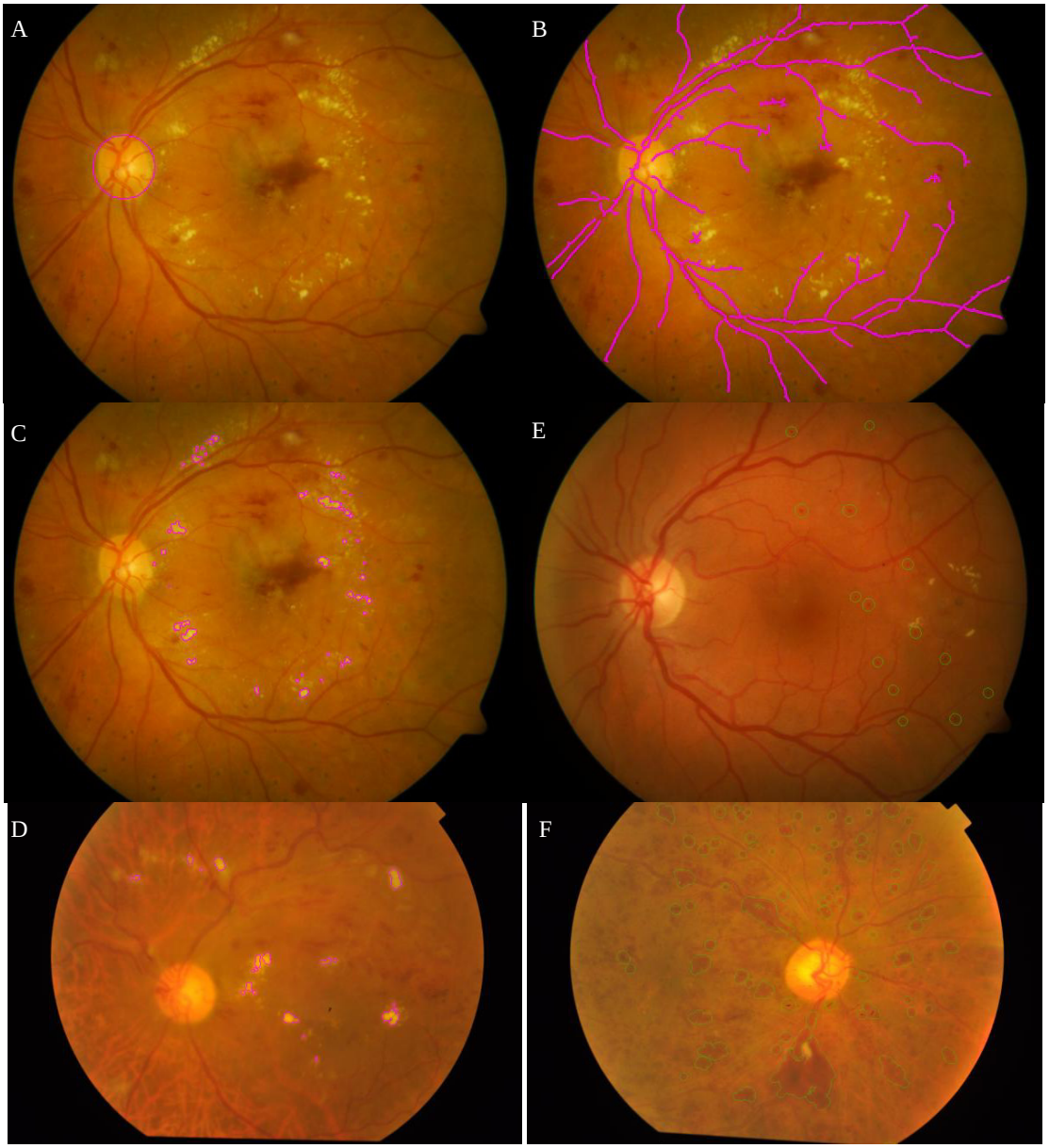

Fig. 2. Automated detection outputs. (A) Optic disc. (B) Blood vessels. (C) Hard exudates. (D) Cotton-wool spots. (E) Microaneurysms. (F) Hemorrhages (Dot, blot and flame).

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

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

Where, TP = No. of True Positive Retinas; FN = No. of False Negative Retinas; TN = No. of True Negative Retinas; FP = No. of False Positive Retinas

Table I shows the accuracy of the proposed method for different grades of DR defined by ophthalmologists as per ETDRS standard. Here, accuracy is presented as Sn for DR cases and Sp for Non-DR cases

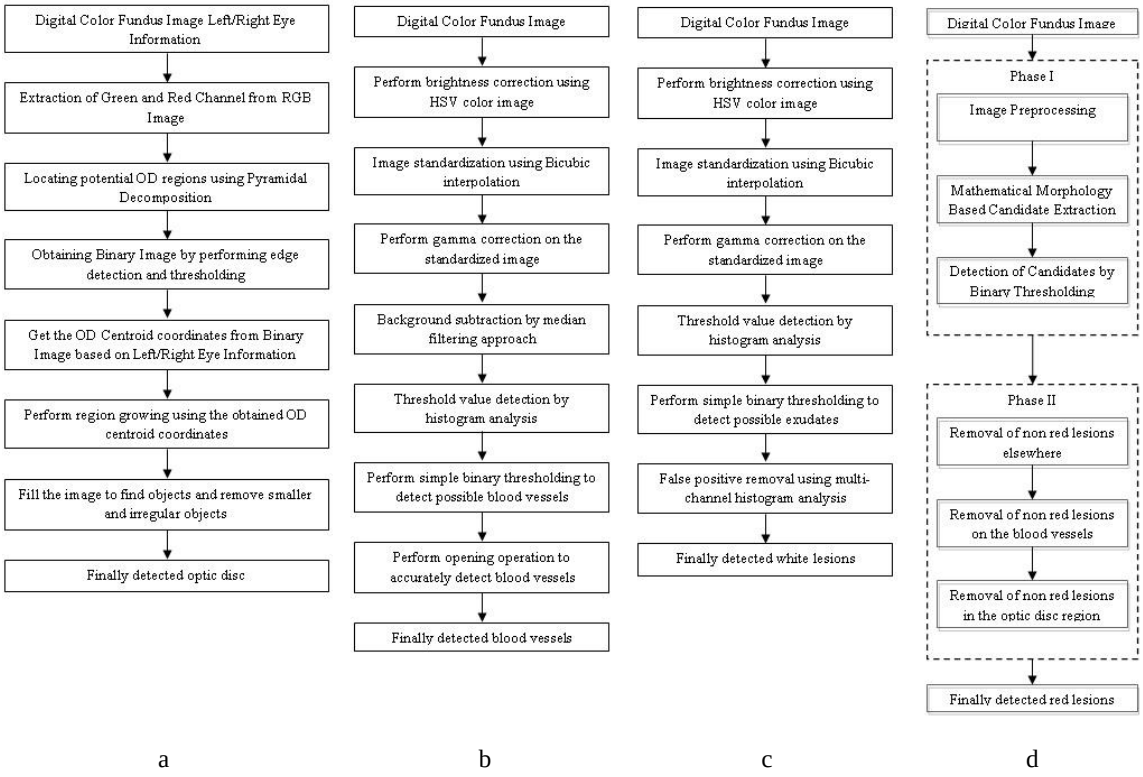

Fig. 3. Flow Chart of (a) Optic Disc Detection (b) Blood Vessel Detection (c) White Lesion Detection (d) Red Lesion Detection

Table 1: Accuracy of proposed method for different grades of DR

Diagnosis	No. of Retinas	Accuracy (%)
Very Mild	4	50
Mild	65	62
Moderate	105	84
Severe	75	93
Very Severe	93	96
Regressed PDR	3	100
Non High Risk PDR	21	81
High Risk PDR	77	82
ADED	40	67
Non DR	192	50
Insufficient Evidence	40	NA

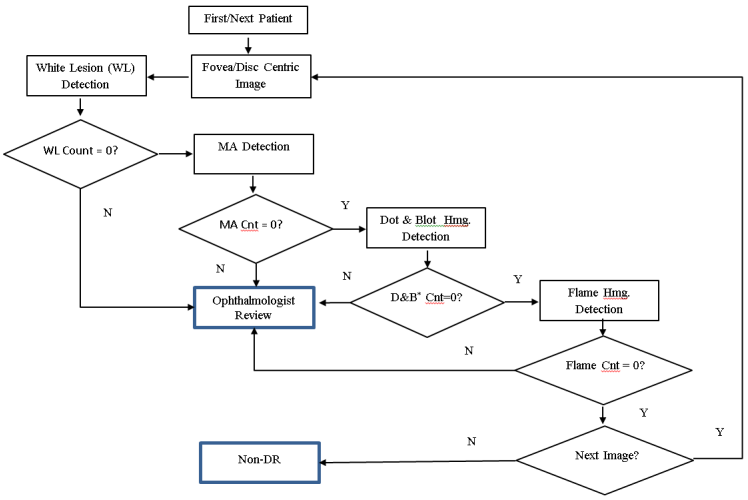

Fig. 4. Classification flow chart

5. Conclusion

In this study, detection methodologies for the automatic diagnosis of retinal images using two-field fundus photography were presented. The proposed method was validated against expert ophthalmologist's evaluation of the fundus images. The proposed method returned an overall sensitivity of 80% and specificity of 50%.

Considering that 80% of the diabetic populations don't have any symptoms of DR[4], Sp of 50% will reduce the ophthalmologist's workload by approximately 41% which is a huge advantage as the ratio of ophthalmologist to patients is in the range of 1:100,000[10]. The proposed method can be developed into a screening system and operated by a person without the diagnostic ophthalmology skills which eases the adoption of the system in the peripheral healthcare centers where there is scarcity of qualified ophthalmologists. The results from Table I show that the proposed method is able to screen out half of the Non-DR cases and detect DR cases with high sensitivity, especially on higher grades of DR where severe and very severe retinas were detected with an accuracy of 93% & 96% respectively. Due to image quality issues, our system could not correctly classify 28% of the retinal images; which can be addressed with proper care while capturing images.

The method employed in our study will help in improving diagnostic accuracy as well as in improving the workflow efficiency of the DR screening at peripheral healthcare centres and diabetic clinics. Further, we plan to improve the detection rate of mild NPDR cases by analyzing specific characteristics which will further increase Sn of the system. Similarly, Sp of the system can be improved by devising an algorithm for quantifying the image quality and that information can be used for dynamic selection of the red lesion detection algorithm. To facilitate an easier usage of the system and to better organize the patient details we plan to develop an application module also.

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