

# Analysis of Foveal Avascular Zone in Color Fundus Image for Grading of Diabetic Retinopathy

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**Abstract**—An enlargement of foveal avascular zone (FAZ) is usually found in eyes with diabetic retinopathy (DR) resulting from a loss of capillaries in the perifoveal capillary network. Currently it is difficult to discern the FAZ area and to measure FAZ enlargement in an objective manner based on raw color fundus images. Instead, ophthalmologists observe and record the occurrences of DR pathologies for the grading of DR severity. Fundus image analysis presents several challenges such as high image variability, improper illumination and artifacts due to presence of pathologies for different patients and differing imaging conditions for the same patient. A new approach for grading the severity of DR by analyzing the FAZ enlargement in color fundus image has been developed. It is based on the binary map of retinal vasculature where the vessel ends and pathologies surrounding FAZ are derived for accurate determination of the FAZ area. The paper discusses image analysis of FAZ area for grading of DR. Results obtained show that FAZ area ranges are highly correlated to the severity of DR. The mean accuracy and standard deviation of ranges obtained are 92.2% and 3.22, respectively. This new approach is found reliable, accurate and fast compared to the current method based on DR pathologies. It has the potential to be used for mass screening of DR enabling early detection and intervention to prevent the progression of the disease and blindness.

**Index Terms**— biomedical image processing, color fundus image, foveal avascular zone, diabetic retinopathy grading

## I. INTRODUCTION

Finest blood vessels linking arteries to veins that are called retinal capillaries (thin/ micro vessels), tend to be damaged by changes of chemical due to diabetes. This progressive damage is called diabetic retinopathy (DR) and occurs due to a combination of micro-vascular leakage and micro-vascular occlusion [1].

DR can be classified into two main forms based on presence of pathologies; non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). NPDR can further be divided into 3 level of severity namely mild, moderate and severe NPDR. According to National Eye Database 2007, among 10,856 Malaysian populations with diabetes, 36.8% has any form of DR, of which 7.1% has proliferative diabetic retinopathy [2]. In 2008, Singapore Malay Eye Study on 3261 persons with diabetes found 35.3% prevalence of

any retinopathy, of which 6.8% had proliferative diabetic retinopathy [3].

NPDR is the earliest form of DR caused by micro-vascular leakage away from the macula [4]. At this stage, there are often no obvious warning signs and patients suffering from the disease are unaware until it advanced into more severe levels. Treatment of the disease at this stage may prevent future complications and towards blindness. The Early Treatment Diabetic Retinopathy Study (ETDRS) identified multiple retinal haemorrhages, venous caliber (width) changes and IRMA as main indicator of risk of advancement to proliferative DR (PDR) [5].

Several methods have been studied to automatically detect the presence of DR pathologies [6, 7]. Other develop methods have been focused on detection of retinal anatomy such as optic disk, fovea and retinal vessels [8-10]. An extensive review of image analysis and intelligent systems for automated diabetic retinopathy ocular screening has been well summarized in [11]. However, most of the systems developed involved invasive retinal fluorescein angiograms procedure. Moreover, the above mentioned efforts focus on the detection of retinal anatomy and retinal abnormalities to determine whether a patient is suffering diabetic retinopathy rather than to monitor and grade DR severity level.

In this research work, the correlation of foveal avascular zone (FAZ) enlargement with DR progression in color fundus images is investigated. It is known that the FAZ enlarges in diabetic retinopathy (DR) resulting from a loss of capillaries in the perifoveal capillary network [1, 12]. This is often observed in early DR such as NPDR and also in PDR [13]. Previous studies have been conducted to measure FAZ in fundus fluorescein angiography [14]. Currently it is difficult to discern FAZ and thus impossible to measure FAZ enlargement based on color fundus images. This research work aims to develop a new DR grading system based on FAZ enlargement and analysis. Early detection of FAZ enlargement at NPDR stage may prevent the progress of the disease to PDR stage and towards visual loss.

## II. APPROACH

The FAZ is the fovea devoid of capillaries in the macula [15]. FAZ varies in size for healthy subjects but usually has a diameter around 500  $\mu\text{m}$  [16] and size of about 0.4  $\text{mm}^2$ . FAZ is the most accurate vision zone on the retina. An enlargement of the zone is usually found in eyes with DR resulting from a loss of capillaries in the perifoveal capillary network [13]. This condition appears early in the development of the disease. The defect of the perifoveal area can lead to a rapid loss in visual acuity [15].

A flowchart of FAZ analysis is shown in Fig. 1. In order to analyze FAZ, the binary retinal vasculature map of a fundus image is firstly obtained as shown in Fig. 2(a). Previous work has been conducted to detect and reconstruct certain retinal pathologies in addition to the retinal vasculature map [18]. The detection and reconstruction algorithm reported by Fadzil *et al* [18] is applied to fundus images to detect and reconstruct certain retinal pathologies in addition to the retinal vasculature map. In this algorithm, for vessel detection, the fundus image is firstly enhanced using a mean filter followed by Contrast Limited Adaptive Histogram Equalization (CLAHE) and bottom-hat morphological transformation to extract retinal vasculature (blood vessels). A sum of bottom-hat with 12 linear structuring elements of size 15 and at  $0^\circ - 180^\circ$  (incremental at  $15^\circ$ ) is performed to ensure all blood vessels are extracted. Background noise removal is then carried out to reduce unwanted linear features at the background being enhanced during bottom-hat. Further enhancement of vessels is then carried out using contrast stretching. For vessel reconstruction, a gradient-based region growing based on first-order Gaussian derivative (GRG) is performed on the extracted retinal vasculature. GRG incorporates both gradient magnitude change and average intensity as the homogeneity criteria that enable the process to adapt to intensity changes and intensity spread over the vasculature region.

The resultant images for each process involved are shown in Fig. 2 with vessels inside the rectangle representing the detected perifoveal capillary network and pathologies. As shown in Fig. 2, morphological operations including thinning, spurring are performed on

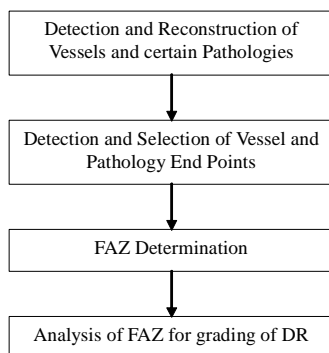


Fig. 1. A flowchart of FAZ analysis.

the binary image with reconstructed vessel lines and pathology regions to obtain end points on the perifoveal

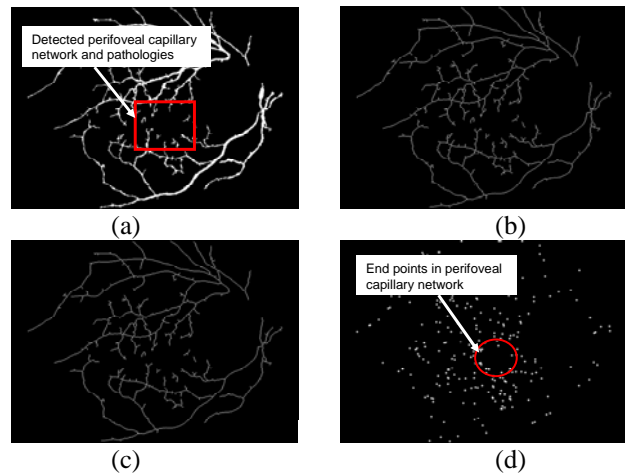


Fig. 2. End points detection process using image with mild NPDR: (a) Reconstructed retinal vasculature, (b) Image after thinning, (c) Image after removal of end points, (d) End points after dilation.

capillary network that will be used to determine FAZ as shown in Fig. 3(a). The selected points are then connected to each other for FAZ analysis as shown in Fig. 3(b). The measured area is used in grading of DR that will be discussed in the next section. The area of the determined FAZ region is computed as below.

$$A(S) = \sum_{i=0}^{i=\max} \sum_{j=0}^{j=\max} I(x_i, y_j) \quad (1)$$

$I(x,y)$  is 1 if the pixel is within the shape,  $(x,y) \in S$ , and 0 otherwise.

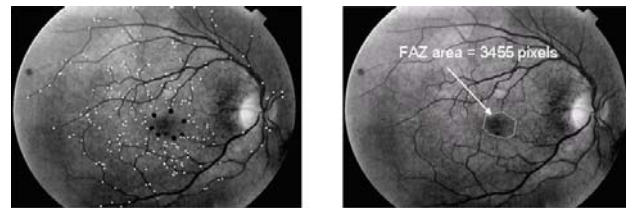


Fig. 3. Process of FAZ determinations: (a) End points superimposed on CLAHE applied image, (b) Selection of points to determine FAZ.

In grading of DR, the FAZ area is measured for several known DR related fundus images to obtain FAZ area ranges corresponding to the severity of DR. The FAZ area ranges that overlap show progression of the disease from a DR stage to the next. The categorization of each range used in this work is as follows:

- Range 1 – No DR stage
- Range 2 – Progression range from No DR to mild NPDR
- Range 3 – Non-proliferative DR (NPDR) stage
- Range 4 – Progression range from NPDR to severe NPDR / proliferative DR (PDR)

## III. RESULTS AND DISCUSSION

In this work, 26 fundus images are used as dataset: 8 images of normal retina (No DR), 11 images of NPDR and 7 images with PDR. These images are obtained from a medical website of School of Medicine of the University of Birmingham [19] and from General Hospital of Kuala Lumpur. The size of these images is  $640 \times 480$  pixels, 8 bits per color channel in JPEG

format.

The distribution of the FAZ areas is then plotted as shown in Fig. 4 to form the above mentioned ranges. Overlapping of FAZ areas between two stages indicates the progression of the disease. Non-overlapping areas indicate DR stages. This is further illustrated in Fig. 5. The FAZ areas obtained by the developed for Range 1 (Normal or No DR stage), Range 2 (progression from normal to mild NPDR), Range 3 (NPDR stage), Range 4 (progression from NPDR to severe NPDR / PDR) and Range 5 (severe NPDR / PDR stage) are shown in Table I. Note that the values of the upper and lower bounds for each range are obtained by rounding the identified FAZ area to the nearest hundredth.

TABLE I  
FAZ AREA RANGES FOR DR STAGES AND PROGRESSION FOR GIVEN DATASET USING THE DEVELOPED ALGORITHM

Name	DR Stages and Progressions	Area Range (pixels)
Range 1	Normal stage	< 3300
Range 2	Progression from Normal to Mild NPDR	3300 – 3400
Range 3	NPDR stage	3400 – 6500
Range 4	Progression from NPDR to severe NPDR/PDR	6500 – 6600
Range 5	Severe NPDR / PDR stage	> 6600

From Fig. 4 and Fig. 5, it is observed that the FAZ area for patient Norm 8 which is the maximum FAZ area for normal eyes exceeds the minimum FAZ area of eyes with mild NPDR (patient NPDR1). This shows that overlapping of FAZ area between two DR stages has occurred. Range 2 would be an early indicator for progression of normal to mild NPDR. The detection of Range 2 cases create awareness to both ophthalmologists and DR patients so that suitable treatment can be taken to prevent progression to mild NPDR stage, which is the earliest stage of DR.

Range 1, which is the range for normal FAZ area, would therefore be below the lower bound of Range 2 that is < 3300 pixels while the upper bound of Range 2 becomes the lower bound of Range 3 that indicates the next stage of DR that is the mild NPDR stage. Range of FAZ area for the mild NPDR stage is called Range 3. To identify the upper bound of Range 3, the range showing progression from mild NPDR to severe NPDR/ PDR is firstly investigated. The maximum FAZ area of eyes with mild NPDR (patient NPDR 6) has found to overlap the minimum FAZ area of eyes with severe NPDR/ PDR (patient Pre-PDR 1) as shown in Fig. 5. Thus, these 2 FAZ areas are used to obtain Range 4 which is the range showing progression from mild to severe NPDR/ PDR. Taking the round of the FAZ areas to the nearest hundredth, Range 4 is found to be from 6500 pixels to 6600 pixels. Ophthalmologist can be more attentive in findings other retinal changes associated in the fundus image that falls in this range to be more assured of the stages. The lower bound of Range 4 is then taken as the upper bound of the previous range which is Range 3 (range for mild NPDR). Therefore, Range 3 is from 3400 pixels to 6500 pixels.

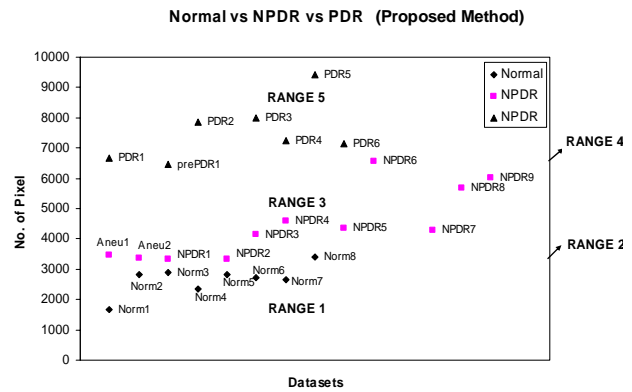


Fig. 4. Distribution of FAZ area for dataset showing DR ranges using the developed algorithm.

The FAZ areas above the upper bound of Range 4 (> 6600 pixels) indicate the severe NPDR / PDR stage. Usually severe NPDR is diagnosed when few microaneurysms (MAs), dot and blot haemorrhages (DBHs), and exudates (Exs) can be found in all 4 quadrants of a fundus image and at least one of the following signs; cotton wool spot, venous beading in 2 or more quadrants and IRMA (Intraretinal microvascular abnormalities) in one or more quadrants [13].

In order to determine the accuracies, a comparison is made between FAZ area ranges obtained from the develop algorithm and that of the Manual CLAHE which is used as the reference shown in Table . The accuracy of each bound obtained by the developed algorithm is calculated as follows:

$$\text{Accuracy for Algorithm-Ranges} = \left( 1 - \left( \frac{|\text{Manual-CLAHE} - \text{Algorithm}|}{\text{Manual-CLAHE}} \right) \times 100 \right) \% \quad (3)$$

From Table II, it can be observed that the accuracy

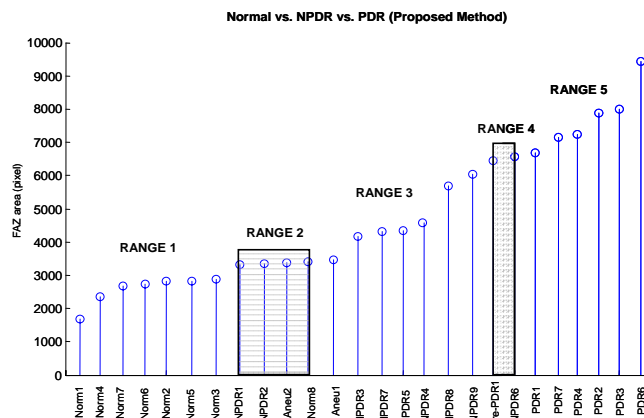


Fig. 5. FAZ area ranges for dataset showing DR stages (ranges 1, 3 and 5) and progression ranges of DR (ranges 2 and 4) using the developed algorithm.

obtained for the lower bounds and the upper bounds of the ranges for DR grading using the developed algorithm is between 90.2% - 96.9%. The mean accuracy is about 92.2% and the standard deviation is about 3.22.

TABLE II  
THE LOWER AND UPPER BOUNDS OF EACH RANGE FOR THE RESULTS  
OBTAINED BY THE PROPOSED METHOD AND MANUAL-CLAEHE WITH  
THE ACCURACIES FOR DR

	Lower bound (pixels)			Upper bound (pixels)		
	Algo-rithm	Manual CLA HE	Accura cy (%)	Algo rithm	Manual CLA HE	Accu racy (%)
R 1	-	-	-	3300	3000	90.0
R 2	3300	3000	90.0	3400	3300	96.9
R 3	3400	3300	96.9	6500	6000	91.7
R 4	6500	6000	91.7	6600	6010	90.2
R 5	6600	6010	90.2	-	-	-

The proposed method for determination of FAZ is a semi-automated approach where human intervention is necessary during determination of FAZ. A manual FAZ determination using enhanced fundus image by CLAHE is used as a reference. This type of manual segmentation is chosen as the user can select points interactively without any limitations (without using detected end points). In a CLAHE enhanced fundus image, the fine vessels in the macula region are clearly visible and thus make FAZ determination more accurate as long as large DR pathologies are not affecting the region.

#### IV. CONCLUSIONS

The paper has shown that FAZ area has a potential to be used for grading of DR (no DR to severe NPDR/ PDR) with good accuracy based on its correlation with the severity of DR. The most important objective of the DR grading based on FAZ area is to obtain FAZ area ranges indicating the stage and progression of the disease. In grading of DR, the mean accuracy and standard deviation of ranges obtained using the proposed method is 92.2% and 3.22, respectively for both lower and upper bounds. If an FAZ area lies within the progression ranges obtained, actions could be taken to prevent the progression of the disease and towards blindness. This new approach is found reliable to determine and analyze FAZ with good and better accuracy compared to the current method of making diagnosis by ophthalmologists. By using the developed approach, early onset of DR can be detected as enlargement of FAZ is usually observed in early DR stages.

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