Segmentation of Foveal Avascular Zone in Colour Fundus Images Based on Retinal Capillary Endpoints Detection

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***Abstract*—Diabetic retinopathy (DR) is one of the diabetes complications affecting the retina. It can be detected by investigating foveal avascular zone (FAZ) since there is a correlation between enlargement of FAZ and DR progression. In this research work, a method of FAZ detection is developed. Firstly, pre-processing is conducted to enhance and improve image quality. Afterwards, segmentation of FAZ is conducted using matched filter and local entropy thresholding to extract retinal vessels. FAZ area segmentation is done based on retinal capillary endpoints detection. This work is validated using retinal fundus images from Messidor and DRIVE databases. The result of FAZ segmentation has been verified by measuring the correlation coefficient of determined FAZ areas between the capillary endpoints of the proposed method and that of detected by ophthalmologists. The correlation values achieved are 0.912 and 0.802 for two aforementioned databases, respectively. These results indicate that the proposed method has successfully detected and segmented FAZ area, due to the highly significant correlation coefficient obtained between the proposed FAZ and that of the ophthalmologists.**

***Index Terms*—Foveal Avascular Zone; Local Entropy Thresholding; Matched Filter; Retinal Capillary.**

I. INTRODUCTION

Diabetes mellitus (DM) is a chronic degenerative disease commonly causing high morbidity and mortality in the world. As reported by International Diabetes Federation (IDF) [1], around 10 million cases of diabetes occurred in Indonesia by 2015. This number was predicted by World Health Organisation (WHO) to reach 21.3 million in 2030 [2]. Diabetic retinopathy (DR) as a microvascular complication of DM that is the primary cause of blindness in adult people [3, 4].

Epidemiological studies in the United States, Australia, Europe and Asia reported that the number of DR patients was predicted to increase from 100.8 million in 2010 to 154.9 million in 2030 and 30% of them were associated with blindness [5]. The Diabcare Asia 2008 Study involving 1785 patients with DM at 18 primary and secondary health centres in Indonesia reported that 42% of diabetic patients underwent proliferative diabetic retinopathy (PDR) complication [6].

The risk of DR has increased in line with the period of someone suffered from DM. Other risk factors of DR is the dependence of insulin in people with type II diabetes, nephropathy and hypertension [7, 8]. Blindness due to DR leads to many other problems, such as quality of life and productivity degradation and may be inducing social burden. The main problem in the treatment of DR is that the disease cannot be easily detected in the early stages [7, 9].

DR is indicated by the presence of some pathologies, such as hard and soft exudates, haemorrhages and the growth of new blood vessels [10]. In addition, FAZ can be also used to indicate DR since there is a correlation between enlargement of FAZ and DR progression [11-13]. FAZ as the most accurate sight area in the human visual system is located at the very centre of foveal and does not contain any retinal capillaries. Hence, the foveal is very dependent on blood supply from the choriocapillaris. The exact area of FAZ can be delineated accurately only by fluorescence angiography in which retinal vessels from the temporal retina surround the central foveal [14].

Various studies of detection and segmentation of FAZ using colour retinal fundus images and fluorescence angiographies have been conducted. Simo *et al*. [15] studied detection of FAZ area using eye fundus angiographies and Bayesian statistical algorithm, iterated conditional modes (ICM) and simulated annealing (SA). The authors stated that ICM algorithm was more robust and faster than SA. Although FAZ contour obtained was only a little larger than that obtained by ophthalmologists, this method needed very high computation time.

Conrath *et al*. [16] proposed detection of FAZ using fundus angiographies. The result from proposed method was evaluated using the U-Test of Mann-Whitney or Kruskal-Wallis test and Spearmann correlations test. Correlation test showed a strong correlation between perimeters versus FAZ measurements.

Haddouch *et al*. [17] investigated the method of FAZ detection using fundus angiographies. This proposed method used singular value decomposition (SVD) and Bayesian Markov random field (MRF) as the pre-processing and segmentation algorithms, respectively. Segmentation was done based on the contour of foveal. The proposed method can detect the smaller FAZ area than that of ophthalmologists.

In another hand, FAZ detection and segmentation using colour retinal fundus images has been conducted by Fadzil *et al*. [18]. The authors proposed several pre-processing techniques and morphological bottom-hat operator for vessel extraction and gradient region growing (GRG) for vessel reconstruction. Then, FAZ segmentation was done using binary retinal vessel endpoints. The achieved accuracy ranged from 66.67% to 98.69%.

Hajeb *et al*. [19] detected FAZ using colour retinal fundus images. The proposed method based on curvelet transform was to enhance colour fundus images. Segmentation of FAZ was also based on the detected vessel endpoints. The obtained results were 93% of sensitivity and 86% of specificity of for DR grading on normal and abnormal cases. The results indicated that the proposed method successfully detected and segmented the FAZ area.

Based on the aforementioned literature, FAZ can be well detected in FFA images. It is because FFA images have higher contrast than retinal fundus images do. Hence, FAZ detection tends to be more easily conducted in FFA images than in colour retinal fundus images. However, FFA images are acquired through invasive method due to the injection of contrast agent into blood vessels causing physiological problems in some patients. Therefore, this work proposes an algorithm of FAZ detection in colour fundus images which can be categorised as a non-invasive approach.

The objective of this work is to segment FAZ area in the colour retinal fundus images from Messidor and DRIVE databases. FAZ segmentation in a computer-based image processing is a challenging problem due to its difficulty to be recognised in low contrast image. The proposed method in this work has several steps, i.e. pre-processing, retinal vessels extraction and FAZ segmentation. The obtained results are analysed using correlation test. Pre-processing is conducted based on a combination of top-hat transformation and contrast stretching to enhance the quality of the image. Segmentation of retinal vessels is performed using a matched filter and local entropy thresholding since the matched filter is proved to have the suited shape to the blood vessels as reported by Chanwamiluang *et al*. [20]. Thereafter, local entropy thresholding is conducted by taking into account the spatial distribution of grey levels. Local entropy thresholding can well preserve spatial structures in the binary or thresholded image. Then, the results are analysed by measuring the correlation between detected FAZ area by the proposed method and that of the ophthalmologists. A correlation test of determined FAZ area between the connected capillary endpoints of the proposed method and that detected by ophthalmologists using Messidor and DRIVE databases is conducted for validation purpose.

II. APPROACH

The approach of this work is presented as follows. Colour retinal images are taken from Messidor and DRIVE databases. Then, FAZ determination is started by choosing the initial points of FAZ in the macular area by the user. Having estimated the macular region, the next process is green channel extraction. Greyscale is associated with the green channel, while red and blue components are zeroed. Image enhancement technique is subsequently applied. This step is needed in order to produce a brighter image than before, particularly in the macular region. Since the location of the FAZ is difficult to see in plain view, FAZ detection is conducted based on retinal vessel endpoints connection. Therefore, segmentation blood vessel is needed in order to find the endpoints of retinal vessels. Retinal vessels segmentation is performed using a matched filter and local entropy thresholding. FAZ is detected by connecting the retinal capillary endpoints. FAZ area is obtained in the form of unit pixels area. Afterward, detected FAZ is compared to that of the ophthalmologist for validation. The flowchart of the approach is depicted in Figure 1.

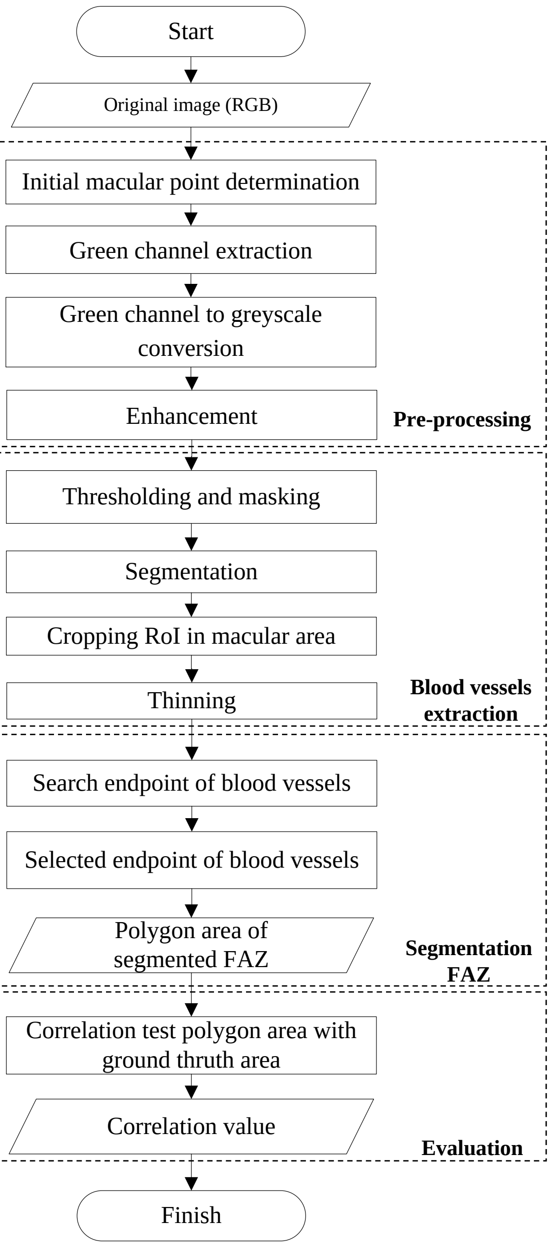


Figure 1: Flowchart of the approach

A. *Pre-processing*

Image enhancement is the initial stage of the retinal vessels segmentation process. This stage is needed because the success of the segmentation process depends on the results of pre-processing stage. Pre-processing stage aims to produce an enhanced image with better quality for segmentation process. Pre-processing phase begins from user determine a starting point in the macular area. Macular area is the darkest area in colour fundus retinal image. The next step is green channel extraction by adopting the technique in [21]. The green channel is activated while red and blue components are zeroed. This new composition of the digital colour image is converted to greyscale. After that, the top-hat transformation is used to extract bright areas in the dark areas. It is then followed by contrast stretching to enhance the contrast of thin blood vessels or capillaries and to improve the poor image contrast.

In contrast stretching, the increased brightness is achieved by adding a constant to the whole pixel values. For example,

$f(y, x)$ expresses the pixel values in the grey scale image at coordinates (y, x). Then a new image increases the brightness value of all pixel intensities on the image of the original large $\beta f(y, x)$. If β is a number of negative, brightness will decrease or become darker. The formula of contrast stretching is expressed in Equation (1).

$$g(y,x) = f(y,x) + \beta \tag{1}$$

The bright vessels on the background of higher intensity level are then extracted by applying morphological filter called top-hat expressed as follows:

$$TTH\ (A,B) = A - (A^{\circ}gB) \tag{2}$$

In the above formula, A and B represent the image and element structure, respectively. Symbol g shows that the operation applies to the greyscale image.

B. Retinal Vessels Extraction

Retinal vessels segmentation procedures are subsequently conducted to identify the FAZ area correctly. Segmentation of retinal vessels is conducted using a matched filter and local entropy thresholding. The matched filter is a template-matching algorithm that is extensively used in retinal vessels detection and other applications as well. The matched filter is started by taking a number of samples of retinal blood vessels cross-section. The Gaussian function is used to approximate the grey level profile achieved [22].

The matched filter kernel is determined by the following equation (see [23] for details):

$$K(x,y) = -exp\left(\frac{x^2}{2\sigma^2}\right), \leq -L/2 \tag{3}$$

Here L is the length of the segmented vessels in a constant orientation while σ is the standard deviation of the Gaussian function. The main is oriented along the y-axis in order to detect blood vessels at different orientation angles. In this work, 16 × 15 kernels and incremental rotation angle of 15 are used. Hence, 12 different kernels are needed to span all possible orientations. All matched filter kernels are convoluted with the original images and only take the maximum response of each pixel of all kernels as the output image.

Entropy thresholding is then applied to the matched filter image with a size of MxN for separating the segmented retinal vessels and the background. Let $f(x, y)$ be the original grey value of the pixel at the point (x, y), $x = 1, 2, \ldots, M$ and $y = 1, 2, \ldots, N$. Then, the probability distribution $0 \leq p_i \leq 255$ calculated. Next P_A, P_B are calculated by using Equation (4) and Equation (5).

$$P_A = \sum_{i=0}^{s}\sum_{j=0}^{s} p_{ij} \tag{4}$$

$$P_B = \sum_{i=s+1}^{L-1}\sum_{j=s+1}^{L-1} p_{ij} \tag{5}$$

To generate a probability equal to 1, it is necessary to normalise the probability of each quadrant. The result of the local entropy is the sum total entropy of the background and entropy of the object as expressed in Equation (6).

$$H_T^{(2)}(s) = H_A^{(2)}(s) + H_c^{(2)}(s) \tag{6}$$

C. Segmentation of FAZ

In this work, FAZ detection is started by detecting retinal vessels or capillary endpoint candidates. Afterwards, the distance between macula centre point and those endpoint candidates are measured. Four endpoints with the shortest distance that represent four quadrants of the circle are then selected. Finally, the endpoints are connected to obtain detected FAZ in a polygon shape. Ground truth of FAZ area in DRIVE database is formed in the same polygon shape in which its radius is determined as the shortest distance between centre point and the four selected endpoints. Moreover, ophthalmologist's FAZ area in Messidor is formed in a circular shape in which its radius is determined as the longest distance between the centre point and the four selected endpoints. The measured FAZ area is computed in Equation (7).

$$A(S) = \sum_{i=0}^{i=i_{max}} \sum_{j=0}^{j=j_{max}} I(x_i, y_j) \tag{7}$$

D. Correlation test

Pearson's correlation application in detection of FAZ produced high correlation value as shown by Shin *et al*. [22]. Pearson's method shows the degree of relationship between two variables or more. Correlation is a statistical analysis technique that is widely used to measure the magnitude and direction of the linear relationship between two random variables. The level of the relationship between two or more variables can be found by determining the magnitude of correlation, which is called as the correlation coefficient.

III. Result and Discussion

In this research work, 59 colour retinal fundus images in TIF format with the resolution of 2240x1488 pixels taken from Messidor database are used [23]. The images consist of four grades, i.e. grade 0, grade 1, grade 2 and grade 3. Grade 1 and grade 2 are combined; so that the image is only divided into three grades namely grade 0, grade (1, 2) and grade 3. The colour fundus image of Messidor database was captured with a 45-degree field of view (FoV) using a colour video 3CCD camera on a Topcon TRC NW6 non-mydriatic retinograph. Three kinds of resolution of images are 1440×960, 2240×1488 and 2304×1536 pixels in TIFF format. The acquisition process was conducted by ophthalmologists from three ophthalmology departments, so there are 3 packages image which every package consists of 400 images.

In this work, DRIVE image database obtained from screening program in the Netherland is also used [24]. This retinal image database consists of 40 images with a resolution of 786 x 584 pixels in JPEG format. The early sign of diabetic retinopathy was found in 7 images while 33 images were no any sign. These images were captured using a Canon CR5 non-mydriatic 3CCD camera with a 45-degree field of view (FoV) and 8 bits per colour plane. For this database, masking images that represent the FoV is provided for each image. These 40 images are divided into two sets, i.e. training and testing sets. Each set contains 20 images. A single manual segmentation of vasculature is available for training set images while for the testing ones, there are available two manual segmentations; one is a gold standard and the other one is used to compare the segmented vasculature result by computer with manually segmented result of independent observation that has been trained by ophthalmologists. Having considered the presence of macular area in the centre of the images, only 33 images of DRIVE database are used in this work.

Colour retinal images with the activated green channel are converted into greyscale to visualise of retinal vessels more clearly and to remove other objects appeared in the centre of the macular area. Afterwards, the greyscale image is enhanced by using top-hat transformation followed by contrast stretching. Stretched image shows that macular area as the dark area can be seen more clearly. The results of enhancement process are from Image 02_tes.tif as shown in Figure 2.

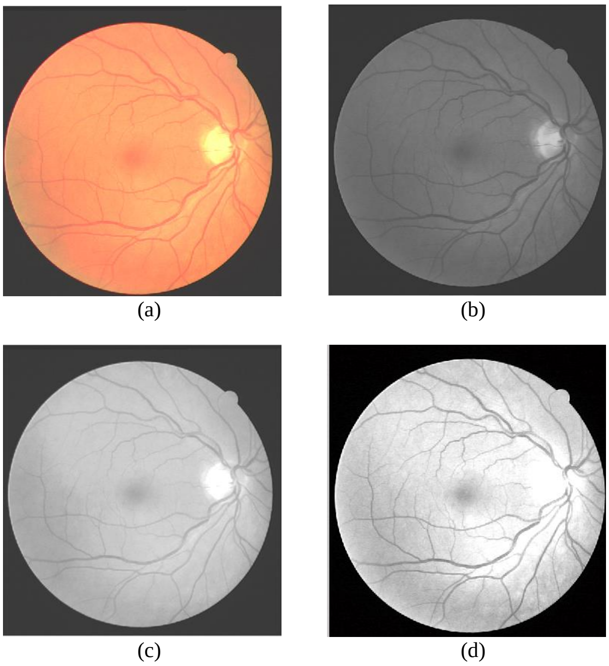


Figure 2: The result of the enhancement method (a) Original image, (b) Greyscale from green channel=1, red and blue=0, (c) Top hat transformation and (d) Contrast stretching

The stretched image is filtered using a matched filter to facilitate extraction process of retinal vessels. These retinal vessels are then separated from the background. Thresholding and masking operations are applied to obtain extracted retinal vessels. The results of these processes are depicted in Figure 3.

Figure 3 (a) shows filtered image produced by the matched filter. Figure 3 (b) shows the initial process of retinal vessels extraction on filtered image followed by inverting the image. Inverted image aims to obtain the output based on inverse information of input image. If the binary image input is 1 then the output will be 0. Moreover, if the input value is 0, it will produce output 1. In the inversed image (Figure 3 (c)), a lot of noises are still present. The morphological operation is used to remove these noises and to extract retinal vessels clearly. Figure 3 (d) shows the extracted retinal vessels in which the candidate of FAZ area is marked as a region of interest (RoI). Figure 4 shows the results of segmentation of FAZ.

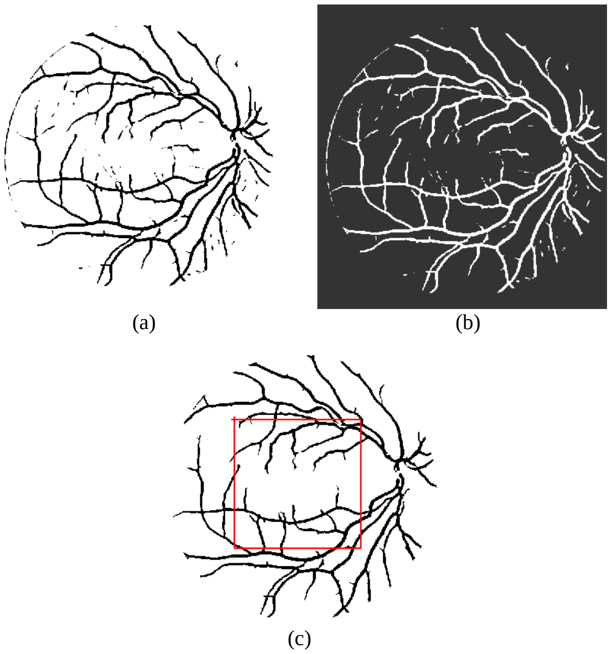


Figure 3: The result of the retinal vessels extraction method (a) The retinal vessels and the background separation (b) Inverse image and (c) Extracted retinal vessels

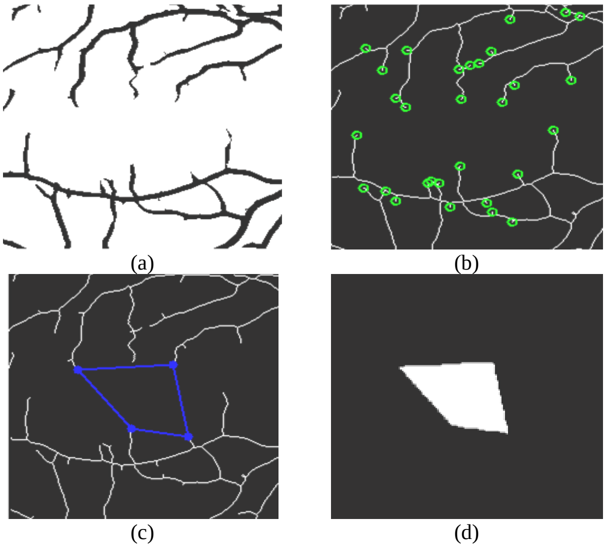


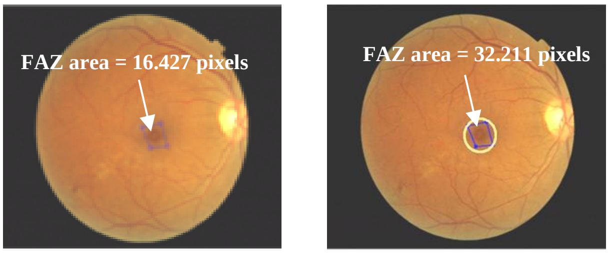
Figure 4: The result of FAZ segmentation (a) RoI (b) Endpoints of retinal vessels (c) Detected FAZ (d) Segmented FAZ

Detection of FAZ is conducted after the stage of extraction of retinal vessels because FAZ is obtained by connecting endpoints of retinal vessels. Endpoints are selected from four quadrants, i.e. 0º-90º is the first quadrant, the second quadrant is 90º-180º, the third quadrant is 180º-270º and the fourth quadrant is 270º-360º. Afterwards, the closest endpoints to the centre of the macula in each quadrant are selected. Four selected endpoints are then connected as presented in Figure 4 (c). Segmented FAZ is expressed in binary scale as shown in Figure 4 (d). Comparison segmented FAZ resulted by the proposed method and ground truth image is shown in Figure 5.

(a) (b)

Figure 5: (a) Segmented FAZ by ground truth (b) Segmented FAZ by proposed method

As shown in Figure 5, the ground truth area has an area of 2144 pixels, which have a size smaller than the area by the proposed method. As for the proposed method has an area of FAZ 4500 pixels. The FAZ area of the proposed method is larger than the area of ground truth as shown in Figure 6.



(a) (b)

Figure 6: (a) Detected FAZ by the proposed method (b) Detected FAZ of ophthalmologist

Polygon area of the proposed method has the size inside area of the circular shape FAZ area by ophthalmologists. Table 1 shows the comparison of FAZ area obtained by the proposed method and ground truth (pixels).

Table 1
Comparison of FAZ Area by Proposed Method and Ground Truth

Image	Ground truth (pixels)	Proposed method (pixels)
Image 01_ tes.tif	1753	3886
Image 02_ tes.tif	2144	4500
Image 03_ tes.tif	1953	4036
Image 05_ tes.tif	951	2640
Image 06_ tes.tif	2271	5262
Image 07_ tes.tif	1769	5032
Image 09_ tes.tif	1394	3035
Image 10_ tes.tif	2000	7808
Image 11_ tes.tif	869	2146
Image 12_ tes.tif	1796	4643
Image 13_ tes.tif	1323	2822
Image 14_ tes.tif	1927	4077
Image 16_ tes.tif	1113	2514
Image 17_ tes.tif	2773	5642
Image 18_ tes.tif	1207	3087
Image 19_ tes.tif	1384	3993
Image 20_ tes.tif	2779	7042
Image 21_ training.tif	2300	6238
Image 22_ training.tif	1320	3132
Image 24_ training.tif	1107	4931
Image 25_ training.tif	1738	4348
Image 26_ training.tif	1533	4449
Image 27_ training.tif	1703	3594
Image 28_ training.tif	2496	5557
Image 29_ training.tif	1982	4983
Image 30_ training.tif	1557	4530
Image 32_ training.tif	1861	5025
Image 35_ training.tif	1213	1791
Image 36_ training.tif	1092	2337
Image 37_ training.tif	2409	6163
Image 38_ training.tif	2027	4155
Image 39_ training.tif	1243	3439
Image 40_ training.tif	1679	3409

As shown in Table 1, all of FAZ areas of the proposed method are larger than the FAZ area defined by ground truth.

The real endpoints of retinal capillaries cannot be properly detected by a proposed method due to the low contrast of retinal capillaries. Using DRIVE database, the reference of endpoints obtained from the ground truth the correlation of FAZ areas between the proposed method and ground truth can be analysed. The result of correlation analysis between Messidor and DRIVE can be seen from the Table 2.

Table 2
Validation FAZ Area toward Grading

	Messidor	DRIVE
Correlation coefficient	0.912	0.802

Statistically, Table 2 shows that correlation coefficient between polygon area and ophthalmologist area from Messidor database is 0.912 at 0.01 of significant level [25]. It indicates that there is a significantly high correlation between polygon area and ophthalmologist area while in DRIVE database shows that correlation value is 0.802

IV. CONCLUSION

Segmentation of FAZ is very important because FAZ is the sharpest vision zone in the retina. The proposed method successfully detects enlargement of FAZ area in colour retinal fundus images. Separating extracted retinal vessels from the background can facilitate the detection of FAZ. The proposed method was applied to two retinal image databases and obtained high correlation coefficient with the significant level at 0.01. In Messidor database, the correlation coefficient between FAZ in polygon shape by the proposed method and FAZ in a circular shape as defined by ophthalmologists achieves 0.912. In DRIVE database, the correlation coefficient between detected FAZ and ground truth FAZ achieves 0.802. These results indicate that the proposed method can assist ophthalmologists in the grading of DR by analysing retinal colour fundus images and have potential to reduce the use of FFA images, which are invasive.

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