Algorithm for Fundus Image Analysis through Segmentation and Object Classification of Tracing Retina Blood Vessel

C. Ahalya[1], M. Jayalakshmi[2], K. Prasad Babu[3]
Email: ahalyatdp@gmail.com, Associate Professor, Department of ECE, Ravindra College of Engineering for Women, Kurnool, A.P, 518002
Email: associatedean@recw.ac.in Associate Professor, Department of ECE, Ravindra College of Engineering for Women, Kurnool, A.P, 518002
Email:kprasadbabuece433@gmail.com, Associate Professor, Department of ECE, Ashoka Womens Engineering College, Kurnool, A.P, 518218

Article Info
Page Number: 155 - 166
Publication Issue:
Vol 71 No. 1 (2022)

Article History
***Article Received**: 02 February 2022*
***Revised**: 10 March 2022*
***Accepted**: 25 March 2022*
***Publication**: 15 April 2022*

Abstract

Fundus imaging is complicated by the fact that the illumination and imaging beams cannot overlap because that results in corneal and lenticular reflections diminishing or eliminating image contrast. Consequently, separate paths are used in the pupillary plane, resulting in optical apertures on the order of only a few millimeters. Fundus imaging is the most established way of retinal imaging. Until recently, fundus image analysis was the only source of quantitative indices reflecting retinal morphology. The major limitation of fundus photography is that it obtains a 2-D representation of the 3-D semi-transparent retinal tissues projected onto the imaging plane. The initial approach to depict the 3-D shape of the retina was stereo fundus photography The proposed algorithm was verified by using two online databases, DRIVE and HRF to validate the performance measures. Hence, proposed method is capable to extract the retina blood vessel and give the accuracy of 0.7917, the sensitivity of 0.9077 and the specificity of 0.7215. In conclusion, the extraction of the blood vessels is highly recommended as the early screening stage for the eye diseases beneficially.

Keywords: Retinal image,Kirschs template, Accuaracy, Sensitivity, Specificity

I. Introduction

Retina is a thin layer of tissue that lines at the back of the eye on the inside and it purpose is to send signals to the brain for visual recognition. Retina blood vessel consist of arteries and veins which help to transport the blood throughout the eyes. It is one of the important elements in the eyes. But there can be a situation where the disorder in blood vessels can lead to diseases. Some of the examples that can arise from retina blood vessel disorders are retinal vein occlusion, hypertensive retinopathy, central retinal artery occlusion, wet macular degeneration, diabetic retinopathy, ocular ischemic syndrome and others. There are about one hundred and three patients were diagnosed with central retinal artery occlusion between January 2009 and December 2017. All this disease can lead to loss of vision blindness, and even stroke. An early detection of subclinical diabetic retinopathy could contribute to the management and timely recognition for the patients before it gets worse. Researchers from engineering, medical and others that related to the fields have studied and researched about the various symptoms and diseases that can arise from the retina. Thus, because of its architecture—dictated by its function—both diseases of the eye, as well as diseases that affect the circulation and the brain can manifest themselves in the retina. A number of systemic diseases also affect the retina. Complications of such systemic diseases include diabetic retinopathy from diabetes, the second most common cause of blindness in the developed world, hypertensive retinopathy from cardiovascular disease, and multiple sclerosis. Thus, on the one hand, the retina is vulnerable to organ-specific and systemic diseases, while on the other hand, imaging the retina allows diseases of the eye proper, as well as complications of diabetes, hypertension and other cardiovascular diseases, to be detected, diagnosed and managed. Here, the fundus image from the online database is used as the element of the work. The online databases that will be evaluated are DRIVE and HRF databases.

This work is about to propose a method for retina blood vessel extraction to help the specialists in analyses, diagnose and give treatment to the patient with various retinal diseases. To achieve this purpose, the extraction method needs to be accurate and reliable. The proposed method uses the Kirsch template as the method for extracting the blood vessel. The Kirsch template is one of the various techniques that can be used to extract the retinal blood vessel. The previous research shows that plenty of researcher also used this method to segment the blood vessel. This method also can be applied to detect the optic disk edges. Research on the tracing of retina blood vessel have been widely utilized with various methods of segmentation being used. Some of the various methods are supervised and unsupervised learning. This method divides the data into groups based on their similarity measure such as the ‗non-vessel' and ‗vessel' group. Next, the matched filtering (MF) approach propose by Kolar et. Al. The 2D MF make use of the 2D masks and connection of local image areas. Five 2D filters were modelled according to typical blood vessel cross-sectional intensity profiles while another five different blood vessel widths were considered (thinnest to thickest). The image obtained from the preprocessing part is convolved with each of the five kernels, then is rotated to 12 orientations. The locally maximum response is selected for each pixel by the fused of resulting parametric images. Then, the image is threshold to acquire the binary map of the blood vessel tree. The origin of this method is proposed by Nguyen et al, but is being improved in the pre-processing phase. This is because the previous method generates strong false vessel detection, and mostly in the area of the optic disk. Thus, with the improved method, it is designed to produce an enhanced input image that provides more blood vessels information and reduce false vessel response at the optic disk area. This method is also used by Yanqi Hou which propose the improved multiscale line detector to yield the blood vessel response. In addition, there also others method using the adaptive thresholding technique, Bar-selective Combination of Shifted Filter Response (B-COSFIRE), Kirsch method and others. The research is able to reduce the time for the ophthalmologist to analyses and diagnose the result of the fundus image of patient. This research is important because eyes disease can lead to a loss of vision, thus it need to be detected and treated early before it gets worse. Biomedical image processing has experienced dramatic expansion, and has been an interdisciplinary research field attracting expertise from applied mathematics, computer sciences, engineering, statistics, physics, biology and medicine. Computer-aided diagnostic processing has already become an important part of clinical routine. Accompanied by a rush of new development of high technology and use of various imaging modalities, more challenges arise; for example, how to process and analyze a significant volume of images so that high quality information can be produced for disease diagnoses and treatment. The principal objectives of this course are to provide an introduction to basic concepts and techniques for medical image processing and to promote interests for further study and research in medical imaging processing. We will introduce the Medical Image Processing and summarize related research work in this area and describe recent state-of-the-art techniques. The development in communication infrastructure in the global scale has made possible the concepts like telemedicine and robotic assisted surgery. These developments have rendered the role of image processing more critical and essential.

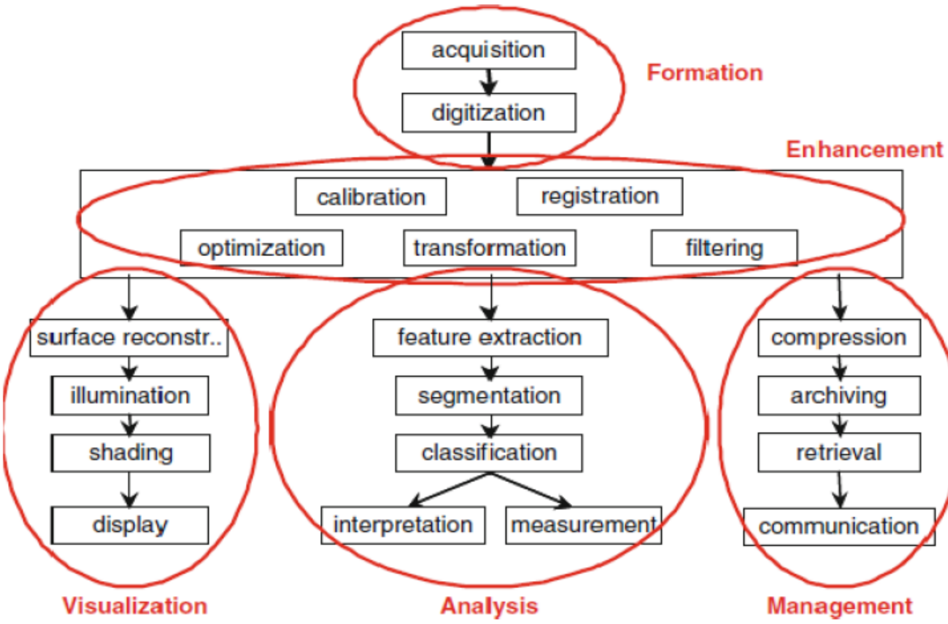


Fig 1: Modules of Image Processing

The following modalities/techniques all belong to the broad category of fundus imaging:

1. Fundus photography (including so-called red-free photography)—image intensities represent the amount of reflected light of a specific waveband.

2. Color fundus photography—image intensities represent the amount of reflected R, G, and B wavebands, as determined by the spectral sensitivity of the sensor.

3. Stereo fundus photography—image intensities represent the amount of reflected light from two or more different view angles for depth resolution.

4. Hyperspectral imaging—image intensities represent the amount of reflected light of multiple specific wavelength bands.

5. Scanning laser ophthalmoscopy (SLO)—image intensities represent the amount of reflected single wavelength laser light obtained in a time sequence.

6. Adaptive optics SLO—image intensities represent the amount of reflected laser light optically corrected by modeling the aberrations in its wavefront.

7. Fluorescein angiography and indocyanine angiography—image intensities represent the amounts of emitted photons from the fluorescein or indocyanine green fluorophore that was injected into the subject‘s circulation.

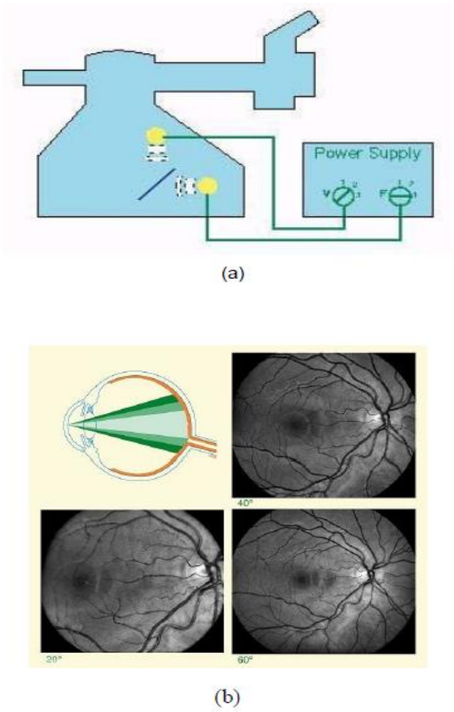


Fig 2. Fundus photography overview

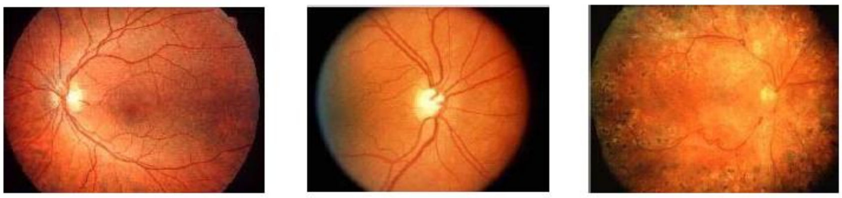


Fig 3. Retinal Fundus Image.

DRIVE and HRF datasets

The Digital Retinal Images for Vessel Extraction (DRIVE) dataset is a dataset for retinal vessel segmentation. It consists of a total of JPEG 40 color fundus images; including 7 abnormal pathology cases. The images were obtained from a diabetic retinopathy screening program in the Netherlands. The images were acquired using Canon CR5 non-mydriatic 3CCD camera with FOV equals to 45 degrees. Each image resolution is 584*565 pixels with eight bits per color channel (3 channels). The set of 40 images was equally divided into 20 images for the training set and 20 images for the testing set. Inside both sets, for each image, there is circular field of view (FOV) mask of diameter that is approximately 540 pixels. Inside training set, for each image, one manual segmentation by an ophthalmological expert has been applied. Inside testing set, for each image, two manual segmentations have been applied by two different observers, where the first observer segmentation is accepted as the ground-truth for performance evaluation. The HRF dataset is a dataset for retinal vessel segmentation which comprises 45 images and is organized as 15 subsets. Each subset contains one healthy fundus image, one image of patient with diabetic retinopathy and one glaucoma image. The image sizes are 3,304 x 2,336, with a training/testing image split of 22/23.

II. Literature Survey

Retina vessel segmentation methods are generally divided into filter-based methods, machine learning algorithms, and deep learning methods. The filter-based technology (Annunziata et al., 2016) is almost consistent with image processing methods, using the filter window to process fundus images. Peter et al. (2012) used a wavelet transform to quickly detect blood vessels and calculated vascular profiles to determine blood vessel boundaries. Fraz et al. (2012) employed the Gabor filter and top-hat transformations of morphological operations for feature extraction and vessel segmentation. Nguyen et al. (2013) performed vessel segmentations by linear operators of different scales. Salazar-Gonzalez et al. (2014) used graph cut technology for vessel segmentation. In addition, machine learning (Roychowdhury et al., 2014) models usually extract feature vectors and then construct a classifier to label pixels. Orlando and Blaschko (2014) used a conditional random field (CRF) with a fully connected model to segment the fundus retina vessels. Gu and Cheng (2014) proposed an iterative two-step learning-based method to boost the segmentation performance by existing basic segmenters. Lupascu et al. (2010) constructed a 41-D vector for each pixel in the image to encode the alignment information, and then classified pixels using the AdaBoost classifier. With the rapid development of deep learning in recent years, convolutional neural network (CNN) performs well on classification and regression tasks because it can hierarchically abstract representations using local operations. It is very suitable for computer vision–related applications. Especially, since the advent of U-net (Ronneberger et al., 2015) in 2015, it brought great progress to medical image segmentation tasks. It is an encoder–decoder structure, and skip connections inspired many subsequent studies. For example, M2UNet by Laibacher et al. (2018) and LadderNet by Zhuang (2018) obtained excellent results in the fundus retina vessel segmentation. They both are inspired by U-net. In addition, Melinscak et al. (2015) developed a 10-layer CNN for a binary classification based on the patch-wise method. Fu et al. (2016) constructed a deeply integrated network consisting of a convolutional neural network (CNN) and a conditional random field (CRF). In detail, multi-scale and multilevel CNNs were used to extract features, and a CRF was used to model the pixel interaction. In the recent years, many researchers made great progress. CS-Net (Mou et al., 2019) adds two attention mechanisms: spatial attention and channel attention, to the encoder and decoder to better capture the local and global features of images, thereby improving the segmentation results. DUnet (Jin et al., 2019) integrated the deformable convolution into U-net so that it can adaptively adjust the receptive field of the filter during the feature extraction process to extract features of different scales. Vessel-Net (Wu et al., 2019) embedded the inception-residual convolution block into U-net to improve the feature extraction ability of the encoder, and then used multiple supervision paths to train the network to obtain more refined segmentation. Wang et al. (2020) separately trained the “easy” and “hard” parts in the encoder stage to perform targeted vascular segmentation, and added an attention mechanism to the “hard” part for more effective segmentation. NFN+ (Wu et al., 2020) used two networks to achieve more refined segmentation. It exploited the front network to obtain a basic prediction probability map, and then used the followed network for post-processing. In addition, the author applied inter-network skip connections to unite the two networks to make better use of multi-scale features. SCS-Net (Wu et al., 2021) first used a scale-aware feature aggregation (SFA) module to extract multi-scale features, then employed the adaptive feature fusion (AFF) module to fuse different levels of features to obtain richer semantic information, and finally used the multilevel semantic supervision (MSS) module to obtain more refined segmentation results. RV-GAN (Kamran et al., 2021) used a generative network to perform blood vessel segmentation. It employed two generators and two multi-scale discriminators for microvessel segmentation. In addition, it replaced the original adversarial loss with a new weighted loss. However, the abovementioned methods are more focused on obtaining accurate prediction probability maps rather than binary segmentation features. But only increasing the accuracy of probability maps is very limited for the ability to improve the accuracy of segmentation. In addition, existing methods do not predict thick and thin vessels separately although they have different characteristics, which also leads to the relative neglect of improving accuracy on thin blood vessel segmentation. Therefore, we propose a specific method to skillfully fuse prediction results from original, thick, and thin vessels.

III. Implementation

The previous research shows that plenty of researcher also used this method to segment the blood vessels. Over the years many developments, many approaches to automated retinal blood vessel segmentation were suggested. Some of the various methods are supervised and unsupervised learning. This method divides the data into groups based on their similarity measure such as the ‗non-vessel' and ‗vessel' group. Analysis on the retina blood vessels from fundus images have been widely used in the medical community to detect the disorder condition in the blood vessels. An automated tracing of retina blood vessel can help to provide valuable computer-assisted diagnosis for the ophthalmic disorders. Thus, it helps to reduce the time for the ophthalmologist to analyses and diagnose the result of the fundus image of patient. The purpose of this research is to build an algorithm to trace the retina blood vessels.

PROPOSED METHODOLOGY

The steps followed in proposed method are:

STEP 1: Input fundus image

The first stage is data acquisition stage which starts with taking a collection of images from Dataset. We have to give fundus image as input. The fundus images are obtained from the DRIVE and HRF databases.

i. The DRIVE database contains the data that has been conducted to enable comparative studies on segmentation of blood vessels in retinal images. It contains forty images of half training and half test set. Images were taken so that Field of View is circular with a diameter of approximately 540 pixels.

ii. High Resolution Fundus (HRF) database was organized by a collaborative research group to support comparative studies on automatic segmentation algorithms on retinal fundus images.it Contains 45 images in total, with Image sizes of 3304 x 2336. Sets were divided as training and testing images as 22/23.

First a fundus image is applied for a preprocessing stage and next extraction is done by using a Kirsch's template method. We define fundus imaging as the process whereby reflected light is used to obtain a two-dimensional (2D) representation of the 3D, semitransparent, retinal tissues projected on to the imaging plane. Thus, any process that results in a 2D image where the image intensities represent the amount of a reflected quantity of light is fundus imaging. Consequently, OCT imaging is not fundus imaging, while the following modalities/techniques all belong to the broad category of fundus imaging.

STEP 2: Preprocessing

Color images usually have a lot of noise. In the case of the retinal fundus image the noise may come from the moment of capturing or when there are symptoms of diseases in the retina image of the patient. Hence, the pre-processing process is important to be conducted to remove the noise, or any unwanted artifacts and enhance the retina fundus image before undergoing further analysis stage.

i. Unsharp method: The unsharp masking method is carry out to sharpen the image. The concept of this method is to blur the actual image and the next step is to subtract the blurred image from the actual image. It focused on enhancing the edges andtiny details of the image.

ii. CLAHE: The Contrast Limited Adaptive Histogram Equalization (CLAHE) to enhance the contrast of the image as in Figure. This method is used to improve the contrast and to reduce the noise amplification.

iii. Gaussian filtering: The final stage is the Gaussian filtering. The fig shown is the image after Gaussian filtering is conducted to eliminate the noise.

STEP 3: Extraction using Kirsch's template slide

After the noise has been removed by the filtering process in the earlier pre-processing, the blood vesselthen can be extracted. Use of Kirsch‘s template of size 3x3 is done in this proposed method. This process is to identify the pixel values in the image. The output of this method is the production of image consist of grey level pixels of value 0 and 255. The 0-pixel value indicate the black pixel while the 255-pixel value indicate the white pixel. The brightness level of the neighboring pixels determined the edge information for the targeted pixel. The possibility to detect the edge in the image is based on the brightness levels difference present in the image. If there are no difference, so there is no edge detected.

STEP 4: Morphological closing slide

The method of morphological closing is conducted after the edges have been detected. It is needed to close the holes or empty space within the retina blood vessel and the result is displays in Figure. The morphological closing operation is a process of dilation followed by an erosion, using the same structuring element for both operations. Operation of dilation thickens the retina blood vessels in the binary image.

STEP 5: Object classification

The method is conducted to remove the small object, or noise that is created during the edge detection and morphological closing method. The function removes all the connected components (objects) present in the binary image that have fewer than threshold pixel and producing another binary image. This operation is known as an area opening. By using bwareaopen in the image processing toolbox in MATLAB, the noises and the unwanted small object is successfully removed. The proposed method to be used in this research consist of two parts which are the pre- processing part and the feature extraction by using the Kirsch‘s template. Combining the pre- processing at theearly stage and feature extraction at the next stage is applied to extract the edges of the blood vessels. The proposed algorithm was verified by using two online databases, DRIVE and HRF to validate the performance measures. Hence, proposed method is capable to extract the retina blood vessel and give the accuracy of 0.7917, the sensitivity of 0.9077 and the specificity of 0.7215. In conclusion, the extraction of the blood vessels is highly recommended as the early screening stage for the eye diseases beneficially.

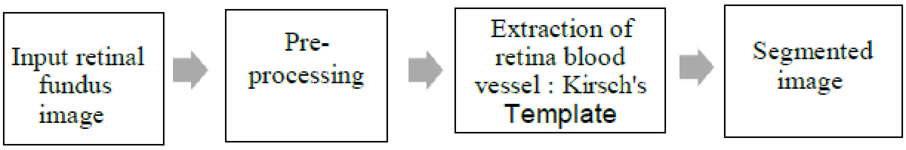


Fig 4. Block diagram for the proposed method

The method of morphological closing is conducted after the edges have been detected. It is needed to close the holes or empty space within the retina blood vessel [9] and the result is displays in Figure 5 (b). The morphological closing operation is a process of dilation followed by an erosion, using the same structuring element for both operations. Operation of dilation thickens the retina blood vessels in the binary image. The thickening happens because of the controlling shape referred as the structuring element. It is a means of interpret the start of the structuring element all through the domain of the image and see whether it overlaps with 1- valued pixels. While, erosion is an operation of shrinks or thins in a binary image. It also, controlled by the structuring element as in dilation. The result of structuring element overlaps only 1-valued pixels in the binary image happen when the output of erosion consists of value 1 at each location of the structuring element origin. Mathematically, the morphological closing of A and B is denoted by A • B, where:

$A \bullet B = (A \oplus B)\ B$

Geometrically,

A • B is the complement of the union of all translations of B that do not overlap with A.

The process is continued with the object classification. The method is conducted to remove the smallobject, or noise that is created during the edge detection and morphological closing method. By using bwareaopen, in the image processing toolbox in MATLAB, the noises and the unwanted small object is successfully removed. Figure 5 (c) display the image result of successfully removing the noise and unnecessaryobjects present in the previous image. The function removes all the connected components (objects) present in the binary image that have fewer than threshold pixel and producing another binary image. This operation is known as an area opening. The threshold is the area of unwanted object that need to be removed. It can be set to get the exact result that the user wants. Figure 4 (d) and (e) is the result image of method used by S. Badsha et al and the ground truths of the input image respectively.

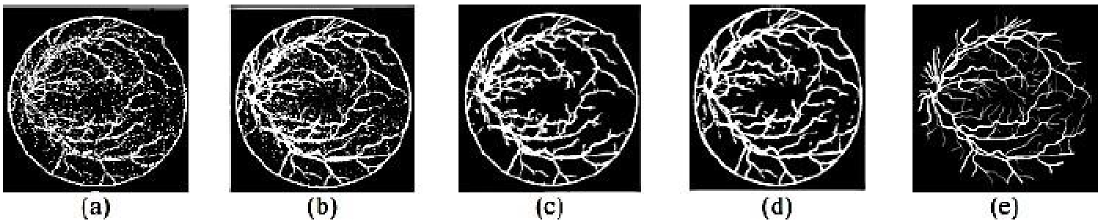


Fig 5 Feature Extraction (a) Blood vessel extraction image using Kirsch's template (b) morphologicalclosing image (c) After object classification image (d) Blood vessel extraction image using Kirsch's template (e) groundtruth image.

Table 1 shows the list of formula to calculate the performance measures. The measure of sensitivity is to determine the ability of the proposed method to successfully detect the vessel pixels. While, the specificityis to compute the proposed method ability to detect the non-vessel pixels. For the accuracy, the ratio between the sum of correctly detected vessels and non-vessels pixels with the total number of pixels is calculated. The total number of false positive (FP), false negative (FN), true positive (TP), and true negative (TN) pixels are used as the parameter for the formula to quantify the extraction performance. The comparison of the images will be between the ground truth image and the segmented image.

Measure	Description
Sensitivity	$\frac{TP}{(TP+FN)}$
Specificity	$\frac{TN}{(FP+TN)}$
Accuracy	$\frac{TP+TN}{(TP+TN+FP+FN)}$

Table 1. The Performance Measures for Retina Blood Vessel Segmentation

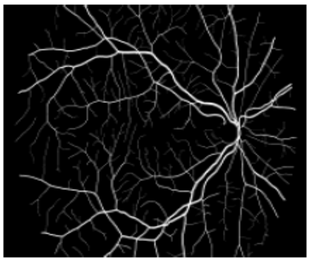
IV. RESULTS

Table 2 shows the result of the MSE and PSNR for the pre-processing part. The closer the value of MSE to zero, the better the result. While, for the PSNR the higher the value, the better the quality of the image. The calculation is conducted to measure the effectiveness of the method used. The results are evaluated on ten images from each database, which 5 of the images is the healthy retina images and another five are the unhealthy retina image shows that the method has minimum error and the image quality is suitable to continue with further method. The result is not only being compared based on the visuality between the segmented image and the groundtruth image, it also evaluates on the performance of the proposed method statistically. Figure 6 displays the result of the proposed method evaluated on the two databases and the method used by S. Badsha et al comparing with the ground truth image. While, Table 3 indicates the results of the performance measures evaluated on the two online databases in terms of the accuracy, sensitivity and the specificity. The results evaluated on the DRIVE database gives the accuracy of 0.7597, sensitivity of 0.7767 and the specificity of 0.7215. While HRF databases achieves the accuracy of 0.7917, the sensitivity of 0.9077 and the specificity of 0.5832. The results show that HRF database can detect the vessel and non-vessel pixel more accurately than the DRIVE database. Generally, HRF have more higher image quality that the DRIVE database, which make the image clearer

DRIVE			HRF		
Image	MSE	PSNR	Image	MSE	PSNR
Healthy retina images					
Image 1	0.0123	67.2227	Image 1	0.0181	65.5563
Image 2	0.0161	66.0642	Image 2	0.0165	65.9465
Image 3	0.0240	64.3362	Image 3	0.0280	63.6662
Image 4	0.0313	63.1781	Image 4	0.0352	62.6604
Image 5	0.0232	64.4801	Image 5	0.0369	62.4656
Unhealthy retina images					
Image 6	0.0187	65.4220	Image 6	0.0267	63.8667
Image 7	0.0239	64.3517	Image 7	0.0242	64.3013
Image 8	0.0267	63.8686	Image 8	0.0258	64.0223
Image 9	0.0260	63.9750	Image 9	0.0253	64.1022
Image 10	0.0289	63.5222	Image 10	0.0279	63.6737

Table 2. The Result of the MSE and PSNR for the Online Databases

Proposed method



Ground truth

Fig 6 outputs obtained

Database	Accuracy	Sensitivity	Specificity
DRIVE	0.7597	0.7767	0.7215
HRF	0.7917	0.9077	0.5832

Table 3. The Performance Measure of DRIVE and HRF Databases

V. CONCLUSION

Retina blood vessel extraction helps specialists in analyses, diagnose and give treatment to the patient with various retinal diseases. The proposed method of this project uses the Kirsch template method for extracting the blood vessels present in the retina and to enhance the edge of the blood vessels and to identify the pixel values in the image. The research is able to reduce the time for the ophthalmologist to analyses and diagnose the result of the fundus image of patient. It is important because eyes disease can lead to a loss of vision, thus it needed to be detected and treated early before it gets worse. In this project the proposed method is evaluated on two online databases which are the DRIVE and HRF. The performance of the method applied is measured in terms of sensitivity, specificity and accuracy between the image and the ground truth image to see the effectiveness of the applied method.

References

[1]Peter, B., Norman, S. C., Graham, M. J., M., C. T., and Teresa, S.-G. (2012). Fast Retinal Vessel Detection and Measurement Using Wavelets and Edge Location Refinement. Plos One 7, e32435. doi:10.1371/journal.pone.0049632

[2] Fraz, M. M., Remagnino, P., Hoppe, A., Uyyanonvara, B., Rudnicka, A. R., Owen, C. G., et al. (2012). An Ensemble Classification-Based Approach Applied to Retinal Blood Vessel Segmentation. IEEE Trans. Biomed. Eng. 59, 2538–2548. doi:10.1109/tbme.2012.2205687

[3] Nguyen, U. T. V., Bhuiyan, A., Park, L. A. F., and Ramamohanarao, K. (2013). An Effective Retinal Blood Vessel Segmentation Method Using Multi-Scale Line Detection. Pattern Recognition 46, 703–715. doi:10.1016/j.patcog.2012.08.009

[4] Orlando, J. I., and Blaschko, M. (2014). “Learning Fully-Connected Crfs for Blood Vessel Segmentation in Retinal Images,” in Medical Image Computing and Computer-Assisted Intervention – MICCAI 2014. Editors P. Golland, N. Hata, C. Barillot, J. Hornegger, and R. Howe (Cham: Springer International Publishing), 634–641. doi:10.1007/978-3-319-10404-1_79

[5] Salazar-Gonzalez, A., Kaba, D., Yongmin Li, Y., and Xiaohui Liu, X. (2014). Segmentation of the Blood Vessels and Optic Disk in Retinal Images. IEEE J. Biomed. Health Inform. 18, 1874–1886. doi:10.1109/jbhi.2014.2302749.

[6] Ronneberger, O., Fischer, P., and Brox, T. (2015). “U-net: Convolutional Networks for Biomedical Image Segmentation,” in Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015. Editors N. Navab, J. Hornegger, W. M. Wells, and A. F. Frangi (Cham: Springer International Publishing), 234–241. doi:10.1007/978-3-319-24574-4_28.

[7] Fu, H., Xu, Y., Lin, S., Kee Wong, D. W., and Liu, J. (2016). “Deepvessel: Retinal Vessel Segmentation via Deep Learning and Conditional Random Field,” in Medical Image Computing and Computer-Assisted Intervention – MICCAI 2016. Editors S. Ourselin, L. Joskowicz, M. R. Sabuncu, G. Unal, and W. Wells (Cham: Springer International Publishing), 132–139. doi:10.1007/ 978-3-319-46723-8_16

[8] Laibacher, T., Weyde, T., and Jalali, S. (2018). M2u-net: Effective and efficient retinal vessel segmentation for real-world applications. 2019 IEEE/CVF Conference on Computer Vision and Pattern Recognition Workshops (CVPRW), 115–124

[9] Jin, Q., Meng, Z., Pham, T. D., Chen, Q., Wei, L., and Su, R. (2019). Dunet: A Deformable Network for Retinal Vessel Segmentation. Knowledge-Based Syst. 178, 149–162. doi:10.1016/j.knosys.2019.04.025

[10] Wang, D., Haytham, A., Pottenburgh, J., Saeedi, O., and Tao, Y. (2020). Hard Attention Net for Automatic Retinal Vessel Segmentation. IEEE J. Biomed. Health Inform. 24, 3384–3396. doi:10.1109/JBHI.2020.3002985

[11] Wu, Y., Xia, Y., Song, Y., Zhang, Y., and Cai, W. (2020). NFN+: A Novel Network Followed Network for Retinal Vessel Segmentation. Neural Networks 126, 153–162. doi:10.1016/j.neunet.2020.02.018

[12] Wu, H., Wang, W., Zhong, J., Lei, B., Wen, Z., and Qin, J. (2021). Scs-net: A Scale and Context Sensitive Network for Retinal Vessel Segmentation. Med. Image Anal. 70, 102025. doi:10.1016/j.media.2021.102025

[13] Kamran, S. A., Hossain, K. F., Tavakkoli, A., Zuckerbrod, S. L., Sanders, K. M., and Baker, S. A. (2021). Rv-gan: Segmenting Retinal Vascular Structure in Fundus Photographs Using a Novel Multi-Scale Generative Adversarial Network.