Early Detection of Diabetic Retinopathy (DR) by Smartphone App

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This report has been endorsed and verified by our supervisors.

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Abstract

This document will include a detailed explanation about the background and overview of this project. There are some reasons why the current screening of Diabetic Retinopathy is not suitable for practical deployment in remote areas of developing country. The discussion of this background will be written in the introduction part of this document.

The following section will display the design, workflow, and implementation of the project. There are several aspects which have constructed the solution, and each will be explained in this section. Lastly, the paper will list the conclusion drawn from this project and possible enhancement for future use.

1. Introduction

Human eyes have an integral role in providing humans with the ability to perform many crucial tasks in their daily life. However, its health condition is threatened by various factors and Diabetic retinopathy (DR) is one of the biggest threats that people face today in the area of ophthalmology, which attacks people who has a diabetes. Since the number of diabetic people keeps increasing every year [1] and DR victims tend to be unaware of the disease onset, the disease has become the leading cause of blindness for the working age generation, especially in developing countries.

The problem is worsened in developing countries, where there is usually a shortage of qualified ophthalmologists and expensive ophthalmological equipment [2]. Despite these intimidating facts, research indicates that early and proper detection which is supported by vigilant treatment and monitoring is able to prevent the impact or at least minimize adverse outcomes from this disease. However, it is not always easy to detect the presence of DR, as subtle and tiny indications in the retina are easily overlooked, thus hindering the observation process of the victim.

Indonesia, on the other hand, is the fourth most populated country in the world...
where diabetes and its complications are among the prominent health problems in all regions of this country. The problem is amplified by the geographical condition of Indonesia, as many of villages are difficult to reach. This accessibility issue has become an obstacle to fight Diabetic Retinopathy, as ordinary fundus camera is large in size and hard to mobilize. Providing every remote areas with its own fundus camera is also not a good solution since it is extremely costly especially for Indonesian government to purchase.

In real example, the current preliminary screening method which is conducted on primary health clinic, must borrow the fundus camera from main hospital in each provinces. The fundus camera itself is utilised for the main hospital daily operation, which lead to the restriction to borrow this equipment. In case at Jakarta, the capital of Indonesia, each district in this province will only be allowed to borrow this camera for a day in the whole week. Approximately each district could only do 1 - 2 screenings a year, based on this condition. It is still possible to get worsened by the availability of an opthamologist which must present to manually analysed the images from the screening.

To overcome these problems, we decide to present a compact and automated solution of Diabetic Retinopathy which will simplify the preliminary screening of Diabetic Retinopathy in Indonesia. The solution consists of portable fundus camera (Horus by Miis), an Android application, and a server for image analysis. We choose to develop the solution in Android platform as statistics data show that in every four Indonesian people that uses smartphone, three of them choose Android as their mobile platform [3]. The application itself is designed to provide a faster and more flexible solution than the current system and procedure in Indonesia. Furthermore, in order to take reliable retinal images from the patients, we would like to utilise Horus fundus camera by Miis, which have been proven accurate in capturing the retinal images. Next, the application is connected through internet to the server where those images are being analysed by an automated algorithm based on certain attributes from the medical perspectives. Finally, the server returns back a result whether the patient needs to be referred to an eye doctor or not.
2. Project Description

2.1. Overall Design

Our proposed solution consists of three major parts; the Horus fundus camera, the Android application and, the integrated Matlab server and its detection algorithm.

![Overall workflow diagram]

As shown in the figure 1 above, the overall workflow of this application starts when the operator / medical staff takes the patient’s retinal image using Horus fundus camera (type DEC100). The staff is required to take images of both left and right eyes of the patient. Next, the staff uses a provided Android device which has our Android client to select and send the images to the server. To allow the Android client to get the images from the camera, we proposed to use a WiFi microSD, which is installed in the fundus camera. This WiFi microSD card connects our application and the camera’s memory, which let the client to browse all retinal images including those that just taken from the patient. Alternatively, the Android phone could be connected to Horus portable camera using cable. The staff will then be prompted to select both right and left retinal images from the patient. These images are sent to the matlab server by pressing “submit” button.
After receiving these images, the server will run the algorithm to perform a certain detection and produce a result based on medical criteria. Finally, this result could be stored in a storage server, while also being sent back to the client so the operator / medical staff are able to inform the patient about his / her condition for next action.

2.2. Matlab Server

The Matlab Server is designed to retrieve the images from the client, run the algorithm with these images, and store / send back the result back to the client. In order to accommodate these communication, the server and the client utilise socket connection using TCP / IP protocols. In the deployment, the server will stand by and accept the connection until it is turned off. We are also planning to add some security measurement in order to protect the server, possibly using some password authentication mechanism which will only be distributed to the authenticated staffs.

To avoid multiple-connection error in this early stage of the development, as we focused more to increase the detection accuracy as high as possible, our server is developed to consider only one connection at one time (non-multi-threaded). When one client has connected with the server, other request will be postponed. Once the connection finished, the server will back to standby mode and ready to receive any postponed request.

Regarding the analysis output, the server is also expected to store the result for each of distinct patient. However, the current development will only return back the result to the client without storing them in server database. The storing feature is currently pending until there is a decision from our partner SIGHT. Therefore, in this project scope, the server is developed with a simple storage mechanism for easier implementation in the future, such as writing the information on txt file.

2.3. Android Development

The Android application is working as the middleware between client and server. It is developed in Android Studio with a communication mechanism that allows connection to the Matlab server. Since it is built in the smartphone, the application
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will be able to access the picture library where retinal images from Horus Scope are stored.

In general, the app mainly consist of three main pages, login page, input page, and response page. The main function of the login page is to limit the subjects who can login and use this application (e.g. medical staff, non-specialist doctor). It consist of an username textbox, a password textbox, and a login button.

After the user has login successfully, the input page will appear as the place to put the patient’s data including name, age, gender, and retinal images. The proceed button in the end of the page will send the data into the server, trigger the detection algorithm, and bring the user into response page. In the response page, the result from detection algorithm in the server will be displayed with “refer” or “not refer” conclusion. In case there is an error occurred, the application will show the error message from the server that explain in which stage the detection fails. The user is allowed to override the error result by choosing “refer” or “not refer” button, while also allowed to retry the process. In the end of both outcomes, there is a return button to start over.

2.4. Detection Algorithm

In order to produce the suggestion for patient’s referral based on its retinal image, the algorithm is developed to meet the specification from the eye specialist in Indonesia. The exact criteria will be displayed below.

The algorithm is designed to identify some objects in retinal images, which some are being the major symptoms of Diabetic Retinopathy disease. There are 5 main objects
that we are trying to identify in each of the screening, and each corresponds to its own characteristics and purpose. The 5 main objects consist of Optic Disc, Fovea (Center of vision), Exudates, Microaneurysm, and Hemorrhage, which is circled in red below respectively.

The object (3) to (5) in the images above will not be found in normal eye retinal image. The appearance of these objects means that the patient has Diabetic Retinopathy, even in the lowest level. Therefore, the main focus of the detection algorithm is to locate and identify these five objects from input image.

Based on our discussion with eye specialist in Indonesia, the existence of these objects alone are not enough to send the patient for referral. The eye specialist mentioned that the spread / location of these objects are more important to know the severity of the disease. The spread will be graded relative to the Fovea position from the retinal image.

Beside is the chart of Detection algorithm’s flow, and below is detailed explanation on method to segment each of these objects.

2.4.1. Optic Disc Segmentation

First, the algorithm reads the patient’s retinal image as an input and a healthy eye image as a template reference. This retinal template image has a function as a reference for the color normalization process. Later, histogram specification is
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performed with aims to transform the image color to be invariant with respect to the changes in the illumination without losing the ability to differentiate the object of interest. This histogram specification technique will transform the red, green, and blue histogram of the patient's retinal images to match the specific template reference of a healthy eye. To determine the reference image, we need help from an expert ophthalmologist to determine a normal eye with a good coloration and contrast.

Next, red channel is extracted from the previous result and since OD region is fragmented into multiple regions by blood vessel, a morphological closing operation is performed by using octagon Structuring Element (SE) of radius 15 pixels in order to obtain a constant region. The resulting image is inverted and applied extended minima transform with an empirically computed h to suppress all the minima whose intensity less or equal than h threshold. This extended minima transform will result in an image that will enhance high intensity region that are more than a h threshold and suppress low intensity to almost zero. Finally morphological opening operation using disk SE with radius 30 pixels is performed to remove wrongly calculated region.

2.4.2. Fovea Detection

The algorithm to detect Fovea is following the steps from paper [4]. This paper has shown that previous researches has proven a fixed relation between position of OD's
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center and Fovea. Therefore, the Optic Disc should be found in the earlier process in order to reach this step.

The algorithm starts with calculating the Optic Disc's diameter and its center's location, which has been segmented on the previous step. The algorithm then uses mathematics formula of finding the area of a circle to calculate the diameter of the Optic Disc. Center of Optic Disc is identified by using Matlab functions 'regionprops' with properties 'centroid', which will find the center of white region within the picture.

In order to successfully segment Fovea, the algorithm extracts the green channel from the image source. Green channel is more sensitive to dark spots, as Fovea characteristics is a dark circular object near the Optic Disc. To have a better image reading, the algorithm enhances the contrast by applying Contrast Limited Adaptive Histogram Equalization (CLAHE) technique on the green channel. As we only required to process the low intensity area (dark spots), the image is processed with Alternating Sequential Filtering (ASF) technique. ASF will eliminate high intensity structure in the image by subtracting the result of this process with the result of CLAHE step, and eventually will enhance the low intensity objects (result in image beside).

As there are a lot of objects that share a similar characteristic to Fovea, the algorithm needs to create a Region of Interest (ROI) to limit the segmentation process only to the relevant area. The algorithm will then invert the ROI color, to enable the segmentation using extended minima transform. The extended minima transform produces a contrasting area between Fovea and non Fovea area within the ROI, which later is binarized using 'imbinarize' operation in Matlab. The result of these steps is an image within ROI area with Fovea area marked as white pixels and
non Fovea area marked with black pixels. The algorithm will calculate the center of Fovea and finally attach the ROI back to the Optic Disc mask to create OD and Fovea masks.

Create and crop Region of Interest

2.4.3. Detection of Hemorrhages and Microaneurysm

The detection of Hemorrhage and microaneurysm is following the detection steps on this paper [5]. Our solution tries to enhance the performance accuracy as we found out that direct implementation of the references' steps will only work for a very healthy eye's image, while those with several disease have unacceptable accuracy. Therefore, the solution we developed combine both of these steps with other steps that we identify to be very helpful. The diagram of this algorithm is provided beside.

First, the algorithm extracts the green channel from the retinal images followed by a histogram equalization technique using CLAHE. In this process, CLAHE will improve the contrast between high and low intensity structures, as we are required to focus on low intensity structures. The extraction of low intensity structures is acquired
after the algorithm applies ASF to the result of CLAHE and subtract the ASF result with the subsequent process' result (similar to processing Fovea's ROI above).

![Fig 11. Red spots - ASF result subtracted by CLAHE processed image](image)

At this moment, the image being processed contains a low intensity objects such as red lesions (microaneurysm + hemorrhage), Fovea, and blood vessels. The elimination of high intensity objects process has also inverted the low contrast objects' intensity, giving them a high contrast in the resulting image. In order to segment these objects, a H minima transform is being applied to the image, which remove regions of low contrast with contrast less than a predefined threshold.

![Detected Red Lesion](image)

In the final result of Hemorrhage and Microaneurysm detection, the blood vessel and Fovea need to be removed from the current image. As we have already segmented Fovea from the previous process, the elimination of Fovea could be done easily. However, the process to remove blood vessel is much more complicated. To start collecting the blood vessel area, we create an initial detection technique which follows the blood vessel segmentation process in our reference. The technique uses the morphological opening of previous steps result with multi scale structuring.
elements. The morphological opening is performed 12 times using 12 different angles linear structuring element, from 15 degrees to 165 degrees for each SE (0, 15, and so on up to 165). The length of the SE is set to 40 pixels, to prevent the structuring element to identify red lesions as blood vessel. All of the results from performing this morphological opening operation are added up to create a single image containing the approximation of the blood vessel.

We produce another technique using another ASF which will help the algorithm to perfecting the approximation. The ASF used on this step is different from ASF process in Fovea detection and hemorrhage initial detection, as this operation only uses one iteration process. The ASF technique used in the previous two processes uses three times iteration, which will still detect the Fovea and red lesions from the input image.

This technique alone will produce another approximation of blood vessel. However, the blood vessel being detected is not perfect as well, which drive us to combine both this technique with the preceding technique we mentioned before. These two techniques complement each other to produce a much better approximation of blood vessel. Finally, the result from the steps prior to blood vessel detection is subtracted by the blood vessel marker. The resulting image will contain red lesions and Fovea region, which could be subtracted with the previous findings.
2.4.4. Detection of Yellow Exudates

In order to segment the exudates from the retinal image, we follow another paper [6]. According to this paper, the first step to detect yellow exudates is by extracting the green channel of the retinal image. After that, Butterworth highpass filter is applied to suppress all of the frequency below the specified threshold (in this case 120) which we have obtained empirically.

Next, the resulting filtered image contrast is enhanced using CLAHE to redistribute the lightness of the retinal image. Later the retinal image is converted into a binary value after the optic disc is eliminated using previously found variable from this retinal image to remove the redundancy between the high intensity of the exudates and optic disc.

The final result of the image will contain the candidate of yellow exudates that is being superimpose to the original image.

2.4.5. Post Processing Techniques

After all pre-processing and processing steps have been done, the algorithm will divide the fundus image into 4 quadrants. By referring to the Fovea location as the center of the quadrants, a horizontal line with 0 degree will be drawn that passess through the middle point of the Fovea and later a perpendicular line will be drawn from the middle point of this horizontal line. If there are more than or equal 2 quadrants that have either exudates or hemorrhages, the patient will be referred to an eye doctor for further diagnosis.
2.5. Testing & Evaluation

During the development phase, individual testing was applied to test each individual detection algorithm. Each time a new feature was added to the application, we conducted regression testing to ensure that previously developed features still work after a new feature has been added. Finally after all features have been created and combined into one single application, we are going to perform integration testing to ensure all of the Diabetic Retinopathy Features detection algorithm works correctly.

2.5.1. Testing the accuracy of the detection of Retinal Image objects

To test the accuracy of detection algorithm, we run the algorithm on sample images. We did qualitative and quantitative analysis towards the algorithm result to see the accuracy of the detection. This algorithm test the detection of the five objects as mentioned above.

The left and right retinal images sample that we have collected consists of around 20 images from Horus portable camera and 2000 fundus images from Kowa Nonmyd 7 Retinal Camera, which we obtained from our partner in Indonesia. We randomly select 10 images as a part of the sample to test the algorithm, and compare the result between actual referral notice and result from the algorithm. The testing was conducted as the quantitative analysis of the performance to determine the number of correct cases and miss detection cases. As the table presented in the figure below, currently our algorithm has around 50% accuracy at the moment, which we will improve in the due course.

<table>
<thead>
<tr>
<th></th>
<th>True Positives</th>
<th>False Negatives</th>
<th>False Positives</th>
<th>True Negatives</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
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Precision = \( \frac{TP}{TP + FP} = 57\% \)
Recall = \( \frac{TP}{TP + FN} = 67\% \)
Accuracy = \( \frac{TP + TN}{TP + FN + FP + TN} = 50\% \)
The qualitative analysis was done by analysing any miss detection of the algorithm on the resulting images and what pattern that usually trigger this miss detection.

2.5.2. Testing of the integration between the android mobile application and the Matlab server

The test of the integration between the Android mobile application (the client) and the Matlab Server (the server) is designed to make sure that the client is able to connect and communicate flawlessly with the server. The server has been designed to accept socket connection (through TCP), and we use this test to ensure the connection and communication through TCP will work in the actual deployment. As the server is also intended to communicate back to the client, we would also like to test whether the Android Application will accept the connection from the server as well.

The test was done by sending some images to the server through the Android client. We then took a look on the server performance and how the images were received. In this case, the server performance that we would like to test is whether there would be any delay between the reception and how long the server could be run without being stopped. Quantitatively, we will measure how much is the transfer rate for the images.

2.5.3. Evaluation on the reliability of Horus portable Camera

We have also had a chance to test the proposed Horus portable Camera on our field testing at Yogyakarta, a city in Indonesia, during the winter break. Based on our trip last January, we took some sample images using the Horus portable camera. According to the expert ophthalmologist and also based from our own experience, there is a moderate difference between using the Horus and the Kowa nonmyd 7 retinal camera. Horus portable camera produces an image with a 1920 x 1080 resolution whilst Kowa nonmyd 7 retinal camera has 4288 x 2848 image resolution. However, when the images are tested using our detection algorithm, it has...
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Successfully identified the objects that we would like to find. Below, we include the images taken from Horus camera.

![Results from Horus Portable Camera](image)

Fig 22. Results from Horus Portable Camera

Unfortunately, due to the fact that majority of the patients being screened were elderly, there have been some problems with the images that we have taken using Horus camera. There are some blockage in the lower part of the images, which mostly contributed to the eyelids of the elderly patients. Our partner in Indonesia has also identified this problem, and they said normally they would ask another staff to hold the eyelids during the process.

In conclusion, although there are moderate differences between the quality of the image using Horus and nonmyd 7 camera, the Horus camera still produces an acceptable result that is still has a feasible quality to be detected using our detection algorithm.

3. Discussion

3.1. Detection algorithm behavior

The detection algorithm has a nearly 80% accuracy when it is being run through 10 sample images of a healthy eye. However, since the algorithm is more focused towards providing a solution to an unhealthy eye of a patient that has already several different eye complication apart from Diabetic Retinopathy, it produces a
lower accuracy (50% ~ 60%). This condition happened because the Diabetic Retinopathy characteristics (hemorrhage and microaneurysms) share a same appearance with blood vessel. The problem occurs when the reconstruction blood vessel of the retinal images is subtracted from the original images, it tends to produce some left-overs and our detection algorithm misclassify it as microaneurysm or hemorrhages. The extraction of blood vessel in the hemorrhage and microaneurysms detection, as explained above, is still on improvement.

Shapes of the structuring element and the different size of it also plays an important role in subtracting the blood vessel from the original image. Because of that, one possible solution that we implement is to use two different reconstruction algorithm that we have mentioned above. It is mentioned before that the first method is to use the line structuring element followed by an iteration of alternating sequence filtering with different sizes and shapes of a structuring element. This approach moderately reduce previous given problem, but the error rate of the detection algorithm must still be minimized.

3.2. Comparison between the current and proposed preliminary screening method

In terms of mobilization, the proposed preliminary screening method has significant advantage over the current method. The current fundus camera is 5 to 6 times larger in terms of size, which hindering the mobilization of this camera to remote areas. The current fundus camera requires a transportation vehicle in order to move from one place to another place, which is not a matter of concern using our proposed screening method.

In terms of availability, the proposed preliminary screening also increased the possibility of preliminary screening for a couple times compared to current method. As the price of the whole environment is 3 to 4 times cheaper, the proposed method will enlarge the possibility of doing the screening to 3 to 4 times as well. Meanwhile, the screening will not be restrained to the availability of an ophthalmologist in order to
3.3. Further Development to improve the accuracy

Although our detection algorithm may have over detect false positive cases, it is suggested that this project could implement a machine learning algorithm to minimize the errors. According to this paper [7], using a supervised machine learning algorithm can increase the accuracy by first, learning all the signatures of the features and later, analyse these patterns by itself to determine the classification rule.

After the rule from the supervised learning has successfully been obtained, this rule is going to be useful for the K-means clustering algorithm to classify the case whether it is referred or not. Since the centroid of each class is known, it will successfully classify the images to each of the corresponding classes. As machine learning is also has a high overhead, it needs parallel programming concept to boost the speed of running the machine learning program.

Furthermore, the detection algorithm can be further developed to run natively on the Android device. This will greatly eliminate the need to use any internet broadband and the budget of subscribing to the internet service provider can be allocated to purchase more of the hardware.

3.4. Extension for other areas

This detection algorithm can be further developed to cover more features of different eye diseases, such as cataract, glaucoma, etc. By using machine learning algorithm to learn all of the corresponding characteristics, we can create a database of images as a reference to store the characteristics of each diseases. As the algorithm takes more input images, it can learn from the database and study it and give a high accuracy classification (whether the patient had one or more eye diseases) based on the reference of the database.
4. References


