Mobile-based Risk Assessment of Diabetic Retinopathy using a Smartphone and Adapted Ophtalmoscope

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Abstract: The large prevalence of diabetes in the global population is associated with an increasing number of Diabetic Retinopathy cases. This disease is associated with a progressive risk of blindness, due to physiological changes that affect the retina. Since most of the progression is asymptomatic and late stage damage is often irreversible, there is a large incentive to implement effective methodologies that allow large scale screening of the diabetic population. In this work, a research study of a mobile approach for the assessment of Diabetic Retinopathy was conducted, by analyzing 80 patients already being followed for ophthalmological care. A smartphone-based fundus imaging system was used to acquire images of the retina during the normal clinical workflow in a Central Hospital in Portugal. Relevant images were automatically analyzed by a Decision Support System (DSS) based on computer vision methods. The results were obtained for ground-truth correlation as well as time impact of this novel system. Our conclusions support that the DSS is highly sensitive in detecting pathological information on images, after a dedicated quality image filtering, and the acquisition procedure has minimal adverse impact in the clinical setting.

1 INTRODUCTION

The increasing prevalence of diabetes in the population is associated with several health issues, one of which is the development of Diabetic Retinopathy. This disease causes several cumulative lesions to the patient retina through microvascular changes and, if left untreated, may lead to blindness.

Diabetic retinopathy affects a large proportion of the diabetic population: around 40% of all the people with type 2 diabetes in the United States suffer from some stage of the disease (Cheung et al., 2010), and a particularly problematic aspect is that its progression is mostly asymptomatic until the later stages, often already associated with some degree of vision loss.

Even though effective treatment is possible in early stages of the disease, vision loss is often irreversible, motivating the need for implementation of screening programs. In these screening programs, images of the patient retinas are acquired by trained personnel and analyzed by experts in opthalmology, but this requires the use of expensive equipment to perform retinal image acquisition as well as the manual time-consuming analysis of those images.

In order to tackle the limitations associated with traditional retinal imaging equipment, several mobile solutions have been proposed. Volk inView is a recent development which allows low cost acquisition of retinal images with iPhone devices, but it is not suitable for non-mydriatic acquisition, thus requiring the administration of pharmacological agents for enabling mydriasis.

More recently, a solution for telemedicine screening was developed to detect retina diseases with a portable non-mydriatic fundus camera. However, it only performs image acquisition and the camera is incorporated into the device. By having an embedded camera, these kind of approaches do not take advantage of the widely available and expansible smartphones with increasingly enhanced cameras (Jin et al., 2017). Besides reducing the cost for retinal image acquisition, the use of smartphone exploits the considerable computing power of these devices to perform automatic analysis of the acquired retinal images. Other solutions are the Volk Pictor and Pictor Plus cameras, which allow non-mydriatic acquisition but at very high costs (Zhang et al., 2015).

In a previous research work by (Costa et al., 2016), it was proposed a methodology for mobile-based computer-aided detection of Diabetic Retinopa-

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thy signs in retinal images. This approach was tested using images from tabletop fundus cameras while achieving a sensitivity of 87% in the detection of Diabetic Retinopathy, running in smartphones with relatively low computational requirements and fast processing.

In this work, we introduce a smartphone compatible system for acquisition of retinal images which, by building upon the work of (Costa et al., 2016), allows an end-to-end low cost solution for Diabetic Retinopathy screening and detection, without requiring pupil dilation. The main goal is to evaluate automatically the quality of the acquired images obtained during the normal clinical workflow and, at the same time, measure the performance of a Decision Support System (DSS) on the previously filtered images.

2 METHODOLOGY

2.1 Retinal Image Acquisition Device

In order to acquire retinal images without using cumbersome equipment, a mobile prototype was developed, based in the commercial Welch Allyn PanOptic ophthalmoscope, which provides a relatively large Field of View of 25°. The ophthalmoscope enables easy access to the patient retina without requiring pupil dilation, which is of major importance in a screening setting, even if not necessarily so in specialized ophthalmological care.

Welch Allyn commercializes a mechanical adapter for the iPhone 4/4s smartphone, but the Android ecosystem was preferred for our work, due to the higher flexibility offered. As such, we developed a 3D printed mechanical case (see Figure 1) for the Samsung S6 smartphone, which aligns the optical axis of the ophthalmoscope with the smartphone camera.

The unmodified ophthalmoscope uses a standard halogen lamp for illumination of the retina, whose intensity is manually adjusted through a rheostat. Since the retina has low light reflectance, it is generally desirable to use a relatively high light intensity in order to obtain images with good quality. However, this makes the examination process extremely uncomfortable for the patient, since he needs to withstand this light for one or two minutes while the operator aligns and acquires the retinal images. This also hinders the operator, since alignment is more difficult due to the inevitable blinking of the patient and pupil constriction (or myosis). Our preliminary experiments revealed that it was very difficult to achieve a satisfying trade-off between image quality and patient comfort/operator ease of use and so an alternative was researched.

The alignment of the ophthalmoscope with the patient retina is crucial for obtaining meaningful images for analysis, but image quality is not a priority for this task. As such, it is possible to improve patient comfort by using a very low light intensity, offsetted by using a high camera sensor sensitivity (ISO). Since image acquisition is very brief, taking less than 50 milliseconds, we can minimize exposure of the patient to the high light intensity (see Figure 2 and 3).

However, the process of using different light intensities for alignment and acquisition is not feasible with the manual light intensity adjustment through the rheostat. As such, we developed a Custom Light Controller hardware module, directly powered and controlled by the smartphone through USB On-The-Go (OTG). The Custom Light Controller adjusts the light output of a white high powered LED, at the command of a Android smartphone application. This application manages the process of acquiring the retinal images, by accommodating several camera parameters such as focus, sensor exposure time, sensitivity, etc. The applications sets the light output extremely low while the user is aligning the ophthalmoscope, and, when the user presses a physical button associated with the Custom Light Controller, an order to acquire an image is triggered, and the application synchronizes the camera shutter with a high intensity light pulse, similar to a flash.

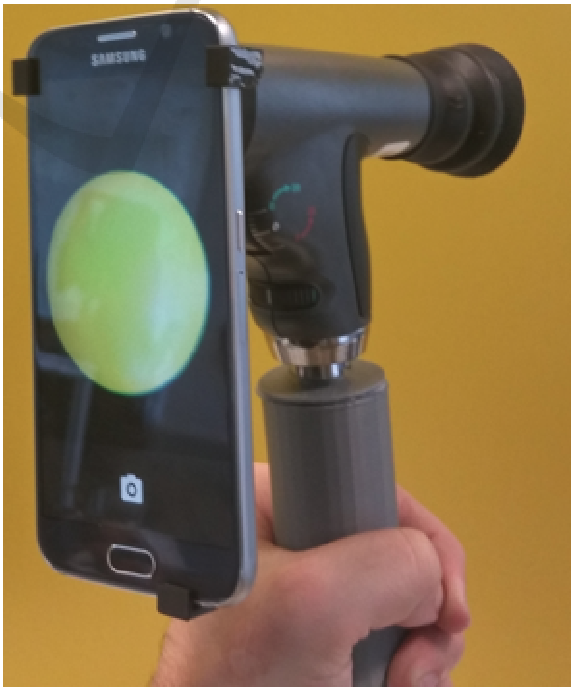

Figure 1: Assembled EyeFundusScope prototype.

Figure 2: Example of an EyeFundusScope acquisition procedure.

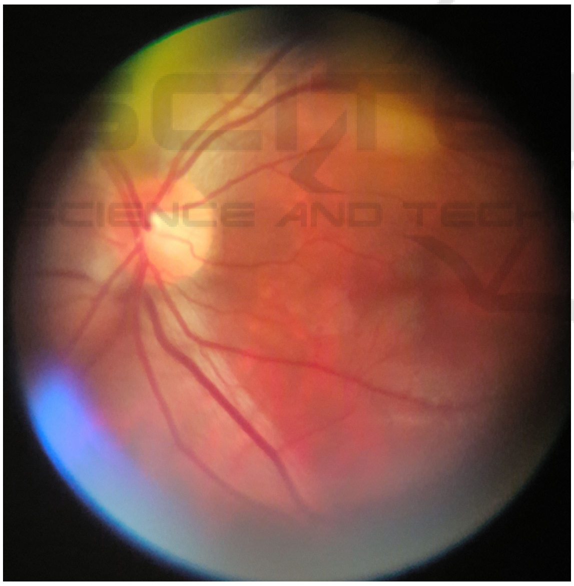

Figure 3: Example of an acquired image.

2.2 Quality Image Algorithm

The quality of the acquired retinal image is the main focus of mobile image acquisition systems (Jin et al., 2017) for ocular diseases. Therefore, it is important to verify if the EyeFundusScope prototype acquires an image with enough quality and details about the presence of Diabetic Retinopathy. In order to evaluate the images collected in this study, a Quality Image Algorithm was implemented with the goal of selecting images with good quality for further processing, as shown in Figure 4. This algorithm is not only based on image luminosity and color, but also in entropy and most relevantly in the tissue area. If the area is higher than a predefined minimum value, the current image is further analyzed by the next stages of quality evaluation. The minimum area value is an absolute value and it was calculated using the dimensions of the full image capture. To determine the tissue area, the algorithm calculates the median filter of the image using the red channel and applies a region threshold on the median filtered image. All these transformations are done with downsized images, with the objective of reducing computational costs.

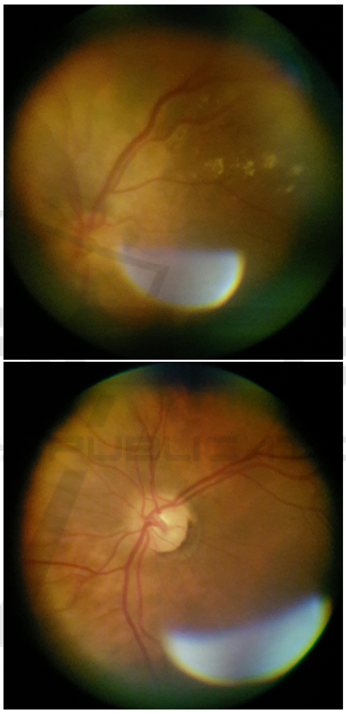

Figure 4: Images with good quality, according to the Quality Image Algorithm, despite minor reflections.

2.3 Panoramic Image

To increase the field-of-view obtained by the proposed acquisition system using the commercial ophthalmoscope, which can be a problem for clinical use when compared with the gold standard of tabletop fundus cameras, the EyeFundusScope software application performs stitching of the acquired images. There are two main steps when generating a panoramic image, one of which is to extract the blood vessels from the green channel and use them for image registration. The other step aims to create the mosaic image with the original images and the registration calculated with the blood vessels. This allows the stitching of various images from different quadrants of the eye to get a greater field-of-view. The objective is to provide to the prototype operator the most complete and easy to use information from the acquisition that is performed, as shown in Figure 5.

Figure 5: Example of a stitched image, as a result of merging two overlapping retinal images.

2.4 Decision-Support System

After the first phases of image acquisition and quality filtering, the Decision-Support System is executed, aiming at the separation between pathology-free and positive cases. When Diabetic Retinopathy is detected earlier, the success of the treatment will increase. Therefore, in early stages, an automated computer-aided tool may increase the success of the diagnosis, particularly in remote scenarios. The Decision-Support System receives as input the results from microaneurysms detection and from the decision-tree that classifies the exudates, based on the approaches developed in (Costa et al., 2016) and (Felgueiras et al., 2016). Having this information, the DSS outputs if the image is pathology-free or not.

2.4.1 Microaneurysms Detection

Microaneurysms formation is the first evident (and visible) sign of Diabetic Retinopathy. Histologically, microaneurysms present a loss of capillary cells (the perycites) on its walls. This leads to acellular capillaries, thus enabling the pouching of these capillaries, which originate the microaneurysms. The mechanisms that causes the decellularization are not well understood, but they include release of a vasoproliferative factor and an increase in capillary pressure (Adal et al., 2014).

Automated microaneurysm detection on the acquired retinal images follows a similar approach to (Costa et al., 2016). This approach uses the characteristics of microaneurysms, such as small size and low grayscale intensity to extract them from the rest of the image. An example of detected microaneurysms is shown in Figure 6.

Template matching using an inverted 2D Gaussian kernel is applied to the green channel of the image and the result is thresholded, with each component in the resulting binary image constituting a detected microaneurysm. In order to account for variation in microaneurysm size, several σ values are used for the Gaussian kernel.

Since retinal vessels are a common source of false positives, the microaneurysm extraction method also relies on the segmentation of vessels in the image, in order to exclude microaneurysms located on those regions. As a first step, the green channel of the original image is subtracted to its median filtered version, which is followed by a top hat transform. The result of this operation is thresholded, and small connected components are discarded as noise.

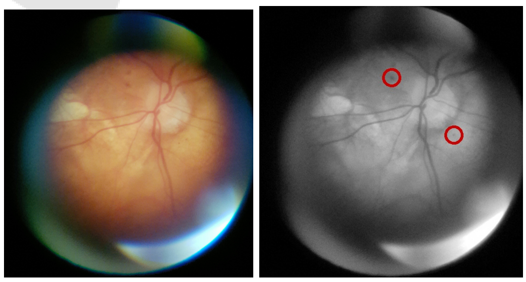

Figure 6: Retinal image with microaneurysms.

2.4.2 Exudate Detection

There are two types of exudates, the soft exudates, also known as cotton wool spots, and the hard exudates. Soft exudates are accumulations of axioplasm and hard exudates accumulations of lipid and protein in the retina (Ravishankar et al., 2009). Their typical characteristics are bright, reflective, white or cream colored lesions found in the retina (Ravishankar et al., 2009). These lesions indicate increased vessel permeability and an associated risk of retinal edema. If they appear close to the macula center, they are considered as sight threatening lesions. Exudates are often associated with microaneurysms.

EyeFundusScope performs automatic detection of soft and hard exudates based on the work of (Felgueiras et al., 2016) comprising image pre-processing, feature extraction and candidate classification.

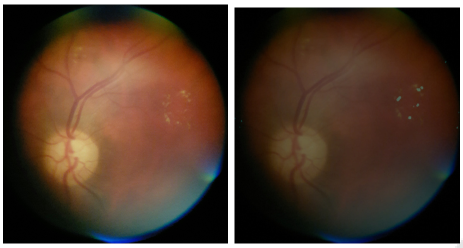

Figure 7: Retinal image with exudates. Right image highlights the area where the exudates are located.

3 STUDY SETUP

The ophthalmology department at Hospital Santo António, Centro Hospitalar do Porto, Portugal, hosted this study with patients in a real scenario. Written informed consents were obtained from the patients as well as the approval from the institution's research ethics committee. The main objective of the study was the validation of the mobile acquisition in diabetic patients without intrusive procedures. In the sense, the acquisition was planned for the duration of 2 minutes per eye. Some patient data had to be registered: age, type and duration of diabetes, and presence of Diabetic Retinopathy according to a previous diagnosis.

An Android application was developed to allow the enhanced hardware control of the camera. Additionally, the application was responsible for the anonymization of the data by generating a unique randomized key for each patient. The images acquired are divided in two groups, images from the left and the right eye. A form to insert information about the patient status was part of the acquisition workflow.

To perform image acquisition the room should comply with some basic guidelines. The luminosity should be low and a chair for the patient should be available. The acquisition should also follow a protocol. The patient should sit on the chair, remove the glasses if necessary, and look to a fixed point. While acquiring images the operator will try to obtain images around the macula region. After performing this action on both eyes the acquisition is ended.

The acquisitions took place after the ophthalmologist appointment and the specialist rated the acquired images in terms of quality and gave a diagnosis about Diabetic Retinopathy.

4 RESULTS

A total of 80 patients were analyzed, 68 of which suffer from Diabetic Retinopathy. Diabetes type 2 is the predominant condition, and there is no information about 4 patients. The acquired database includes 16 patients with pharmacologic dilation of the pupil. Based on clinical expert analysis, no cases were found with the presence of soft exudates. Only 4 cases do not have been analyzed by the Doctor on both eyes, due to physical conditions of the patients. The youngest patient acquired was 43 years old and the oldest was 85 years old. The longest acquisition with EyeFundusScope took 9 minutes and the fastest one 4 minutes, being the average 5 minutes per case.

Photocoagulation treatment was already applied to 30 patients, 12 of which had visible marks that are noticeable in the acquired images. Analysing these acquisitions, 7 exams have hard exudates and 4 present microaneurysms. From these photocoagulation cases, 10 have good quality and no presence of lesions on the acquired quadrants of the eye.

From the complete dataset, 31 acquisitions presented bad quality, 23 due to acquisition conditions and 8 due to wrong prototype configuration. The database has 13 exams where the acquisition difficulties were originated from various patient conditions. Problems like cataracts, retinal detachment, strabismus and intermittent eyelids movement have a negative impact on the acquisition process.

The quality image algorithm evaluated the acquired images from all acquisitions, resulting in a total of 277 good quality images for classification purposes using the DSS.

As expected, the images considered as having bad quality by the Quality Image Algorithm were automatically excluded. Figure 8 represents the number of cases with medical diagnosis for which at least one image was selected after quality filtering. The class of Other Problems is related with other eye problems presented on patient eyes, as already mentioned above.

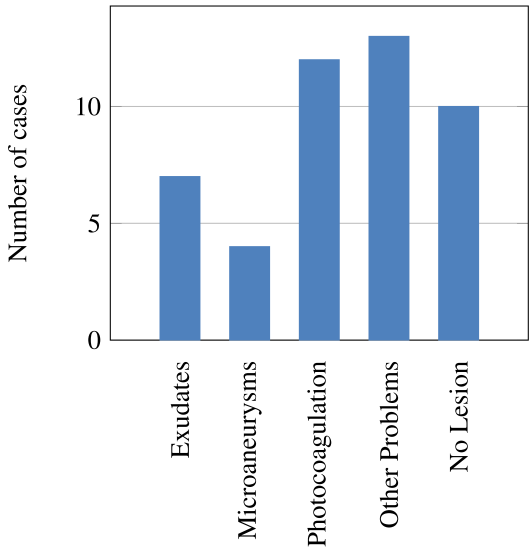

Figure 8: Medical diagnosis for the patients from which the images were selected after quality filtering.

4.1 Quality of the Acquisitions

From a specialist perspective, a good image should always contain retinal tissue with minimal reflections, vessels, macula and optic disc. However, during the analysis of the exams, some images were found containing hard exudates and vessels, but without macula or optic disc. For this reason, the quality metric that provided the best results was the tissue area. The other group of metrics already mentioned in section 2.2, ensures that the acquired image has relevant structures to be detected, as shown in Figure 9.

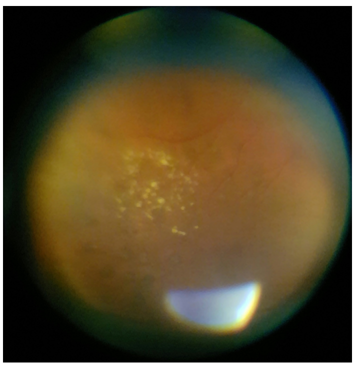

Figure 9: Image with vessels and hard exudates only.

4.2 Performance of the Detection Algorithms

The exudates detection was tested on the selected images by the quality image algorithm and a classification accuracy of 91% was achieved using the DSS (see Table 1).

Table 1: Exudates classification obtained.

	Predicted Exudates	Predicted No Exudates
Exudates	31	11
No Exudates	12	223

From the quality image algorithm analysis, 277 images were considered adequate, 235 of which without the presence of lesions. A Sensitivity of 74% and a Specificity of 95% was achieved by the proposed system on a per image-based analysis, as shown in Table 2. Without considering the 16 images acquired with a dilated pupil (removing mydriatic cases) as part of the dataset, the Specificity is 95% and the Sensitivity is reduced to 67%. Therefore, it is relevant to state that the performance of EyeFundusScope is naturally affected in non-mydriatic cases, due to the reduced pupil size which complicates pupil and ophtalmoscope alignment. However, the results show no variance in the high values of Specifity performance which is relevant for screening use cases. The system has the advantage of acquiring multiple images and the Quality Image Algorithm works as a filter to achieve the best images. For this reason, it is feasible to acquire images with relevant information without pupil dilation.

Table 2: Classification Performance.

	Full dataset	Non-mydriatic dataset
Sensitivity	74%	67%
Specificity	95%	95%

Before this study, the EyeFundusScope automated screening algorithms were tested with Messidor and E-Ophta databases. Knowing if the analyzed eye is the left or the right, we can predict if the macula is to the right or left of the optic disc, since anatomically it is located temporally. In order to detect the optic disc, EyeFundusScope uses a template matching algorithm, using a circular shape as a kernel. Since the macula is usually located at a distance of approximately 2.5 times the diameter of the optic disc, and knowing the macula direction, it is possible to locate the macular region. If the acquired image contains the temporal quadrants of the retina and the optic disc is visible, the developed methodology is then able to find the location of the macula, as shown in Figure 10.

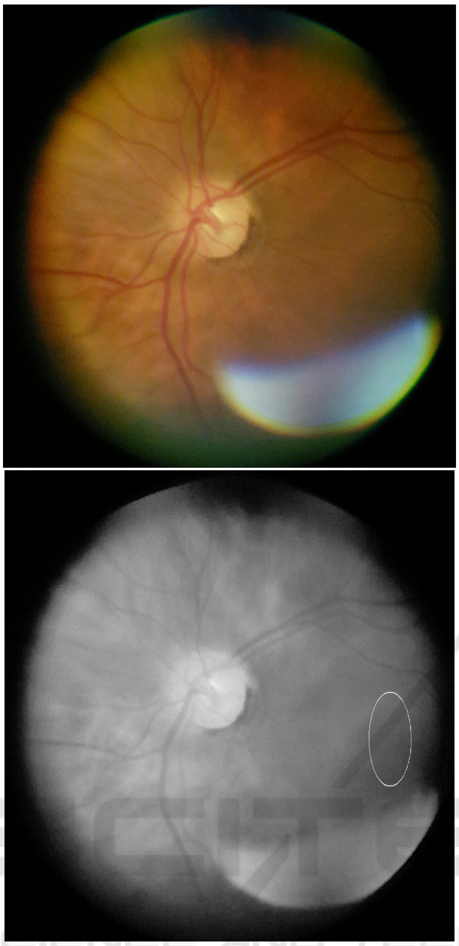

Figure 10: The probabilistic risk zone near to the macula.

4.3 Clinical Impact

As found in this study, the adverse impact of integrating the retinal image acquisition with the EyeFundusScope prototype is minimal. The appointment generally last from 10 to 15 minutes per patient and the EyeFundusScope acquisition has an average duration of 5 minutes, but without requiring specialist time.

The obtained images have enough information to provide feedback about Diabetic Retinopathy. However, sometimes it is complicated to provide feedback about all quadrants of the eye. Regarding this aspect, the solution needs to be improved in order to cover all the retinal regions.

The pupil dilation improves the quality and the area acquired in each image, but the objective of the solution is to avoid requiring this procedure. To enable a similar result without performing dilation will allow more flexibility for the retinal image acquisition, since the patient will have full visual capabilities after the examination, being able to walk without assistance and even drive on its own.

5 CONCLUSIONS

In this paper, a mobile approach is evaluated for fundus image acquisition, together with quality and pathology assessment, by software suitable for running in smartphone devices. The time taken for the proposed acquisition procedure in clinical context was very low, even facing old adults with severe optical conditions, which fits the use case of a mobile system in remote places with operation by non-experts in opthalmology.

The Quality Image Algorithm works as a filter and ensures each exam performed has acceptable images, so that the detection algorithms are able to extract valuable information.

The classification results has shown that the usage of EyeFundusScope may contribute for the reduction of the time-consuming task of image interpretation by specialists.

This study provided valuable data to improve the research in the scope of the EyeFundusScope software, hardware and trigger new acquisition perspectives and use cases.

In the future, the authors intend to improve the classification performance by employing state-of-art Deep Learning approaches to the problem of Diabetic Retinopathy risk assessment, considering the specificities of smartphone-based image acquisition. Moreover, improving the usability of operation with minimal training of the health professional is expected by leveraging real-time quality image assurance to provide feedback to the prototype operator, improving human-machine interaction.

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REFERENCES

Adal, K. M., Sidib, D., Ali, S., Chaum, E., Karnowski, T. P., and Mriaudeau, F. (2014). Automated detection of microaneurysms using scale-adapted blob analysis and semi-supervised learning. *Computer Methods and Programs in Biomedicine*, 114(1):1–10.

Cheung, N., Mitchell, P., and Wong, T. Y. (2010). Diabetic retinopathy. *The Lancet*, 376(9735):124 – 136.

Costa, J., Sousa, I., and Soares, F. (2016). Smartphone-based decision support system for elimination of pathology-free cases in diabetic retinopathy screening.

Felgueiras, S., Costa, J., Soares, F., and Monteiro, M. P. (2016). Cotton wool spots in eye fundus scope.

Jin, K., Lu, H., Su, Z., Cheng, C., Ye, J., and Qian, D. (2017). Telemedicine screening of retinal diseases with a handheld portable non-mydriatic fundus camera. *BMC Ophthalmology*, 17.

Ravishankar, S., Jain, A., and Mittal, A. (2009). Automated feature extraction for early detection of diabetic retinopathy in fundus images. In *IEEE Conference on Computer Vision and Pattern Recognition, 2009. CVPR 2009*, pages 210–217.

Zhang, W., Nicholas, P., Schuman, S., Allingham, M., Faridi, A., Tushar, S., Cousins, S. W., and Prakalapakorn, S. G. (2015). Screening for diabetic retinopathy using the hand-held pictor camera. *Investigative Ophthalmology & Visual Science*, 56(7):1426–1426.