BIA report: development of pyScan

Introduction

Glaucoma is the leading cause of irreversible vision loss worldwide. It is characterized by progressive degeneration of retinal ganglion cells. The damage is often caused by abnormally high intraocular pressure. Degeneration of these cells often leads to cupping, a morphological change in optic disk, characterized by atrophy of the neuroretinal rim area, an increase in the absolute size of the optic cup and in the cup-to-disc ratio, vertical elongation of the optic cup, and asymmetry of these features between the two eyes. In some cases, the intraocular pressure is relatively low, but glaucoma could be also induced by diabetic-retinopathy, characterized by retinal ischemia and sometimes proliferation of new vessels in iris and retina (Havens and Gulati, 2016).

Since glaucoma is often asymptomatic, around 50% patients do not know they had the disease. Thus, population screening might be helpful for early diagnosis and treatment for the disease. Nowadays, diagnosis of glaucoma is largely dependent on trained physicians. For underdeveloped regions where such physicians are limited, diagnosis of glaucoma may be difficult. To measure features of optic disk, optic cup and retinal vessels, physicians need to manually segment these regions, which is time-consuming and highly subjective.

To assist the diagnosis of glaucoma, we developed pyScan, a software that can automatically perform segmentation of optic disk, optical cup and retinal vessels on user-input retina image, classify the image to glaucoma positive and glaucoma negative, as well as measure glaucoma related properties such as cup-to-disc ratio (CDR) and (possibly neovascular glaucoma related) total vessel length.

Literature Review and Algorithm Implementation

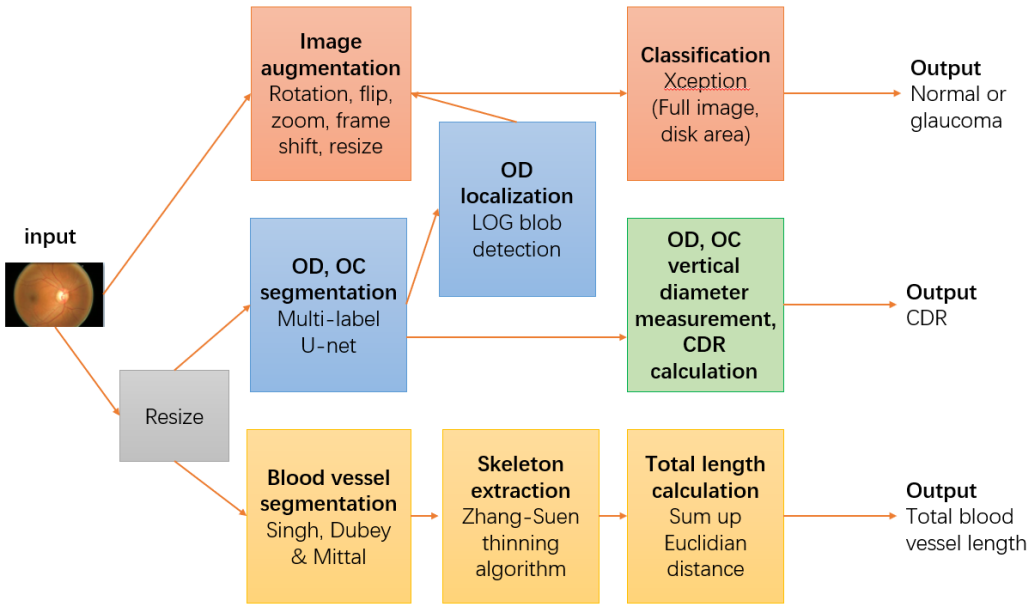

Figure 1. The overall workflow of pyScan development

1. Glaucoma detection

   One possible approach to detect glaucoma is to segment anatomical structures in

a fundus image and then perform clinical measurement and calculation. For example, Yu et al. (2019) used a modified U-net architecture to segment and measure CDR. In the first phase, they built a single-label model to segment and localize the optic disk. In the second phase, they cropped the region around the disk as region of interest and built a multi-label model to segment OD and OC. Finally, CDR is calculated by dividing the vertical disk diameter (VDD) by the vertical cup diameter (VCD). However, these measurement-based methods largely depend on the accuracy of segmentation and require an expert to interpret the measured results.

Thus, it is necessary to develop a model that can directly classify glaucoma fundus from normal ones. Diaz-Pinto and colleagues (2019) had compared 5 different CNN architectures (VGG16, VGG19, InceptionV3, ResNet50 and Xception) for glaucoma detection. As a result, Xception architecture was the most effective with an average AUC of 0.9605.

In 2018, Fu et al. developed Disc-Aware Ensemble Network. The model segments and localizes OD with U-net, and the disk region is cropped for further analysis. The final glaucoma screening result integrates the full fundus image model, segmentation guided network, disk region model and polar transformed disk region model. DENet was trained on ORIGA dataset, and was tested on SCES and SINDI datasets, with AUC of 0.9183 and 0.8173. It is also mentioned that the combined model has the highest AUC, while AUC of disk region model is higher than full image model.

Our glaucoma detection model (Fig.1, blue and red part) first segmented and localized the OD and OC with a multi-label U-net. The segmented OD, OC and the ground truth OD, OC had mean Intersection over Union (IoU) of 0.88 and 0.71. The location of OD was detected with LOG blob detection algorithm. The output x, y and radius were used to crop the disk region. Two Xception models were trained separately on the full fundus image and the cropped disk region. The combined model output was an average of full image model and disk region model prediction. As a result, the full image model has an AUC of 0.64, the disk region model has a much higher AUC of 0.79, and the combined model has the highest AUC of 0.84, which is consistent with the findings of Fu et al.

We also computed CDR as a reference for glaucoma detection. We obtained VDD and VCD by measuring the maximal length of OD and OC on y axis. However, the predicted CDR and the true CDR had a standard deviation of 0.11, which is not very accurate.

2. Blood vessel analysis

At first, we tried ridge detection to segment blood vessels, but this method is sensitive to the edge of the optical disk and the largest vessels often seem tubular. We referred to a method proposed by Singh, Dubey & Mittal in 2017 on GitHub. They first performed CLAHE to the fundus image to increase contrast. Subsequently, they applied Alternate Sequential Filtering, which is a series of morphological opening and closing transformations, to the image to filter the darker vessel structures form the fundus. Then, they subtract this image from output of CLAHE to remove the optical disk and other structures. At last, they binarized the image and removed blobs of unwanted bigger structures. We implemented this algorithm, and the result image

clearly segmented the small vessels and excluded other structures (Fig.2A).

To measure the length of blood vessels, it is necessary to extract the skeleton of the segmented vessels. We first tried morphological skeletonization, which can be considered as a controlled erosion process (Abecassis, 2011). However, it is very sensitive to noise on the edges and small branches may form during the erosion process (Fig.2B). Finally, we employed Zhang-Suen Thinning Algorithm, which is a controlled process of iteratively removing pixels from the edge until it is thinned down to a skeleton of unitary thickness. It consists of two sub iterations: one aimed at deleting the south-east boundary points and the north-west corner points while the other one is aimed at deleting the north-west boundary points and the south-east corner points (Zhang and Suen, 1984). This algorithm preserves end points and pixel connectivity, and the result is strictly one-pixel wide skeleton.

Finally, we traversed all points on the skeleton to sum up the Euclidian distance between all neighboring points as the total length of vessels. Length obtained by this method might be slightly larger than actual value (Fig.2C). We also detected vessel bifurcation/crossover by drawing a circle at every point of the skeleton and counted the hit of the circle with the vessels. More than 2 hits indicate the point is on a bifurcation/crossover. We later counted the number of bifurcations and crossings (Fig.2D). But since this number is not highly clinical meaningful, we did not present the value on GUI. In the end, we divided vessel skeleton to non-bifurcating segments for measuring arc length of each segment for future improvement (Fig.2E).

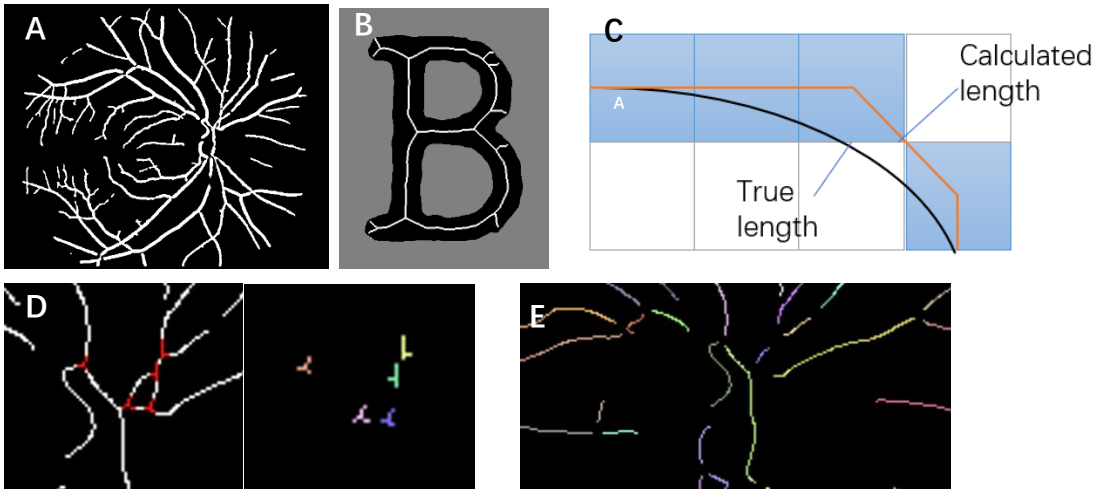

Figure 2. Blood vessel segmentation and relative feature measurement

Group work reflection

We divided our project to several parts: 1. segmentation and localization of OD and OC; 2. classification of normal and glaucoma images; 3. segmentation of blood vessels; 4. measuring features of blood vessels; 5. combining group members' code and develop a GUI for the software. I was responsible for 1, 3 and 4 parts of the work. I compared between different methods and obtained generally satisfactory result. But there are still some drawbacks. I tried to set the keras evaluation metrics to mean IoU when training the OD and OC segmentation model, but several errors occurred. At last, I set the metrics to accuracy.

As a group, we meet regularly used google colab to share our code. However, our

cooperation would be smoother if some group members communicate more with others. We should also write more comments for our code so other members could understand our code more easily. We could improve the GUI of our software by embedding output figure of segmented results.

Future improvement

1. Improve OD, OC segmentation accuracy

Currently, segmented OD, OC and the ground truth had a mean IoU of 0.88 and 0.71. An IoU of 0.88 might be enough to localize OD for analysis of disk region model, but can result in inaccurate CDR. This could be improved by setting evaluation metrics of the U-net model to mean IoU. We can also perform figure augmentation before training as we did in the classification process. Employing method proposed by Yu et al. might also be effective - we could first localize the disk region and then use this region to segment OD and OC.

2. Improve classification accuracy

Since glaucoma is often related to asymmetry of features between two eyes, we could develop a new model that takes image of both eyes as input. But this requires us to find a suitable dataset. Also, we could train a new Xception model on polar transformed disk region image to see if the AUC increase, as the DENet model did.

3. Improve measurement of blood vessel feature

Since the Euclidian distance of neighboring points may be larger than the true length of vessels, it might be better to measure the arc length of each non-bifurcating segments with cv2.arcLength(). With arc length divided by chord length, we can easily calculate tortuosity. We can also measure other features, such as vessel density in macula and peripapillary region, the decrease of which is related to glaucoma.

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