QUANTIFICATION OF PROGRESSION OF RETINAL NERVE FIBER LAYER ATROPHY IN FUNDUS PHOTOGRAPH

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Abstract: Measuring the retinal nerve fiber layer atrophy and its progression is important in the early detection and the management of glaucoma. On the fundus image, the center of optic disc and the fovea are localized and used to acquire the intensity profile around the optic disc. To quantify the progression of RNFL atrophy, the registration of intensity profiles taken at different times is performed using the blood vessel information acquired by multi-layer perception. After negating the artifact caused by the difference in overall luminescence among two or more fundus images, the progression of RNFL atrophy is calculated quantitatively

Introduction

Glaucoma is a group of diseases caused by the damage of the optic nerve, resulting in visual field loss and blindness. Because the loss of vision in glaucoma is irrevocable, early diagnosis and treatment are important. Measuring the retinal nerve fiber layer (RNFL) atrophy and its progression are critical in the early detection and the management of glaucoma. For the quantitative analysis of the RNFL atrophy, several methods were suggested [1][2]. However, they are not completely quantitative and automatic. Especially they has not yet mentioned about progression of RNFL atrophy.

To quantify the RNFL atrophy and its progression, the novel method based on image processing and learning technique are proposed in this paper. On fundus photograph, the region with RNFL atrophy shows lower intensity value compared to normal region. Thus, the intensity profile of the pixels on the circle around the optic disc was analyzed after automatic recognition of the optic disc and the macula. To detect the progression of RNFL atrophy, the registration method utilizing blood vessel information was devised for fundas images taken at different times.

Material and method

A. Subjects and Photography

For the 11 patients attending a glaucoma screening service at Seoul National University Hospital, RNFL photographs were acquired by digital fundus camera system (CF-60UD / D60, Canon Inc., Tokyo, Japan) where the green filter was inserted in order to enhance the RNFL on the photograph in the course of the acquisition. Acquisition angle was 60° and the image was stored in 1600x1216 pixel DICOM format and transferred for further analysis.
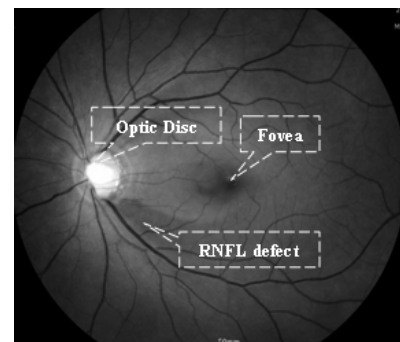

Figure 1: Optic disc, fovea, RNFL defect on the digital fundus image

B. Preprocessing of Retinal Images

The captured DICOM images are converted to JPEG format and the images are quantized in 8 bit depth and gray-scaled using luminescence channel information, which is equal to green channel information since the green filter was already used during the acquisition.

To remove the speckle noises without reducing the sharpness of the image, median filtering is performed on the image.

C. Localization of Optic Disc

As shown in figure 1, the background illumination is brighter in the center of the image than the outer region because of the spherical configuration of the eye and the optic system of the fundus camera. For the further

image processing, the correction of the non-uniform illumination is needed, and the local contrast enhancement is suitable rather than global enhancement on the entire image.

To enhance the contrast locally, contrast-limited adaptive histogram equalization (CLAHE) is used [4]. At first, the image is divided into small regions called tiles. In this study 50x50 pixel tiles are used. For each region, histogram equalization is performed, so that the histogram of the output region approximately matches a uniform distribution. After that operation, neighboring tiles are combined using bilinear interpolation to eliminate artificially induced boundaries. To avoid amplifying any noise that might be present in homogeneous areas, the contrast is limited to the specific level.
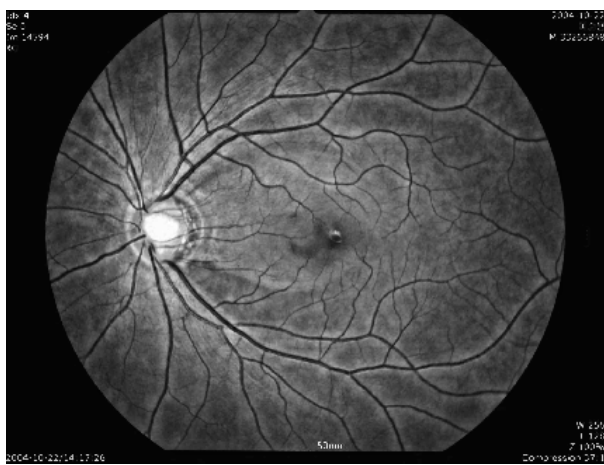

Figure 2: Fundus image after contrast-limited adaptive histogram equalization on Figure 1.

On the fundus image, the optic disc (also called optic nerve head) is the circular area where the optic nerve fibers and retinal blood vessels converge. Since dark blood vessels and bright optic nerve fibers are simultaneously located on the optic disc, the fluctuation of intensity in that region is relatively wilder than other places on the image. Thus the local standard deviation of the image is used as a feature for the localization of optic disc. The standard deviation image is acquired by sliding neighborhood operation and each output pixel is contains the standard deviation of the disk-shaped neighborhood around the corresponding pixel in the input image, where the radius of the disk is 90 pixels in this study. And the averaging filter having the filter size of 180 is applied into the standard deviation image to smooth the sharpness inherent by previous procedure. Finally, the center of the optic disc is taken as the brightest point in the smoothed version of standard deviation image. Figure 2 and figure 3 show the overall process of the localization of optic disc.
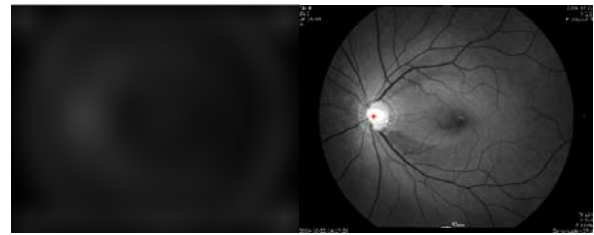

Figure 3: Smoothed version of standard deviation image of Figure 2 (left) and the location of the optic disc (right)

D. Localization of Fovea

The macula is a small and highly sensitive part of the retina responsible for detailed central vision and is located roughly in the center of the retina. The fovea is the very center of the macula and the darkest region in the fundus image. To find the center point of the fovea, template matching approach is used. Based on several fundus images, the template of macula is made like Figure 4, not two dimensional Gaussian distribution. Even though the fovea is the darkest point of the retina in the real view, there is a bright point on the fovea or around the fovea usually, because of the reflex of the retina to the ring flash of the fundus camera and the aberration of the optic system of the fundus camera. The point having maximum cross-correlation value between preprocessed fundus image and the template of the fovea is selected as a vicinity point of the fovea. After CLAHE is performed, the darkest point within neighborhood of the vicinity point is selected as the center point of the fovea. The detected center point of fovea is shown in figure 5.
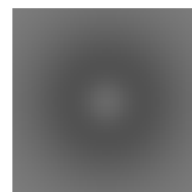

Figure 4: Template of macula in fundus image

E. Intensity Profiling Around Optic Disc

The set of intensity values is taken from the points along the circle line around optic disc in the preprocessed fundus image. The center of the circular line is the center of the optic disc. And the radius of the circle is determined by the specific fraction of the line segment between the center of the optic disc and the fovea. And intensity values are acquired counterclockwisely from the intersection point of the circle and the line segment. For the figure 5, the fraction is 0.5 and the intensity profile is shown at figure 6.
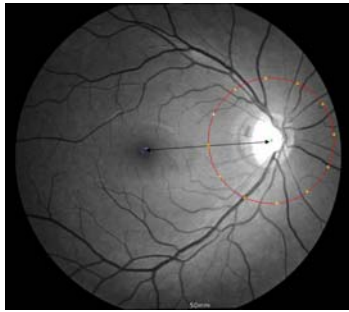
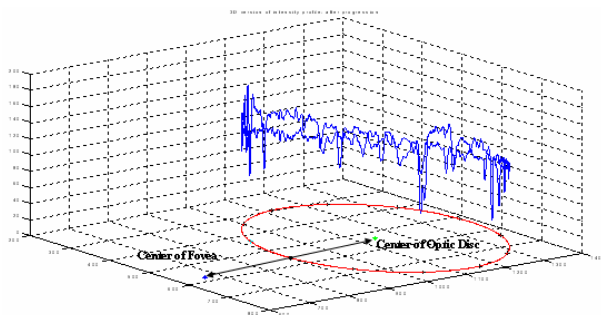Figure 5: Determination of the investigation line for intensity profiling around optic disc

Figure 6: Example of 3-dimensinal version of intensity profile (blue) for Figure 5.

F. Registration of Intensity Profiles

There can be a little spatial transformation among fundus images taken at different times for several reasons, which are the cyclotorsion and duction of the eye, difference of photographic situation, and so forth. In order to detect and quantify the progression of RNFL atrophy for a person, the process of aligning two or more intensity profiles from such fundus images should be preceded. Because the retinal vessels do not change their positions in the fundus images in the same person, the locations of blood vessels on the intensity profile are utilized to register two or more intensity profiles.

Preliminarily the detection of vessel locations is accomplished by following procedure. To determine each pixel on the intensity profile either as blood vessel or as non-vessel, supervised learning scheme is used. Intensity, max-min difference, standard deviation, entropy, the first derivative and the second derivative values in small window on the intensity profiles are selected as input features for the multi-layer perceptron (MLP) classifier which has three layers with six input nodes, three hidden nodes and one output node. As training dataset, 100 vessel segments and 100 non-vessel segments having specific window size are used and learning of the MLP is performed by backpropagation algorithm. After training, each pixel on the intensity profile in testing dataset is classified into vessel point or non-vessel point by the MLP.
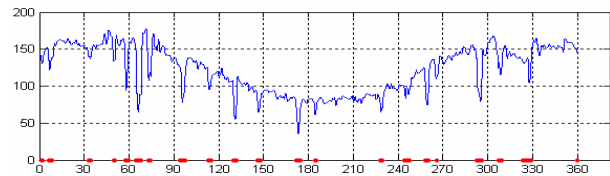

Figure 7: Example of 2-dimentional version of intensity profile (blue) and detected locations of blood vessels (red segment) for Figure 5.

For the registration, the locations of blood vessel on the intensity profile of the image taken after 6 months of follow-up are aligned onto those of the baseline image. And non-vessel points between adjacent vessels on the intensity profile of the follow-up photograph are interpolated by bicubic interpolation method [5] so as to have the same number of non-vessel points between adjacent vessels on the baseline intensity profile. Figure 8 shows the result of the registration of two profiles taken at six months before and after.
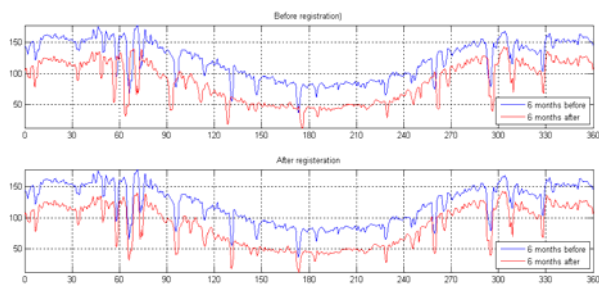

Figure 8: Example of before (upper) and after (lower) registration of two intensity profiles taken at different times.

G. Detection of Progression of RNFL Defect

Because of the difference in the intraocular illumination during the image acquisition and the fixation point of the eye, there also can be differences in overall luminescence among two or more fundus images taken at different times as shown in figure 8. In order to compensate for this effect, the trend line is calculated from the intensity profile by robust version of local weighted scatter plot smoothing (LOWESS) method [6], where the size of sliding window is specified as 20% of the total number of data point on the intensity profile.
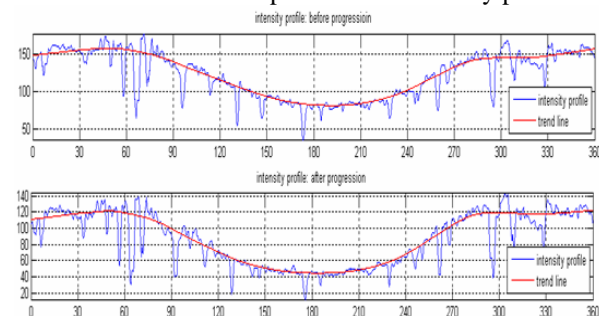

Figure 9: Example of intensity profiles and its trend lines for fundus images taken at different times.

Because the RNFL defect between 270° and 90° on the intensity profile is clinically important and the RNFL defect is rare in the rest, blood vessels between 90° and 270° are used as the reference vessels. On trend-subtracted intensity profile, RNFL atrophy regions should have wider width than average width of reference blood vessel and have y-axis values lower than -5. And the progression of RNFL atrophy is quantitatively calculated by the ratio between the baseline and the follow-up photograph.
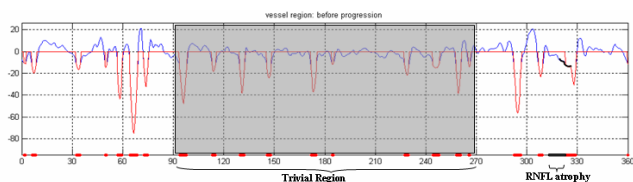

Figure 10: Blood vessel (red segment) and RNFL atrophy (black segment) on trend-subtracted intensity profile detected by the proposed methods

Results

Figure 11 is the sample of the RNFL photograph taken with the 6 months of time interval. On the review by the experts, the progression of the RNFL atrophy was not definite. On the analysis proposed in this paper, RNFL atrophy around the 310° region revealed its progression, showing 50% increment of width compared to the baseline (figure 12).
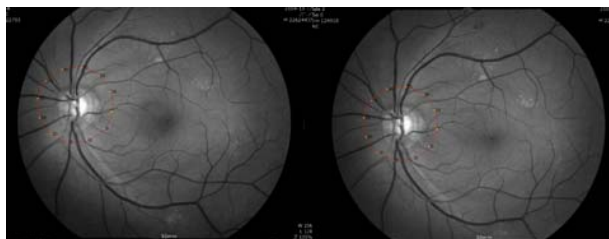

Figure 11: Baseline RNFL photograph (right) and 6 months follow-up photograph.

Figure 12: intensity profiles (upper) and its trend-subtracted version (lower) for Figure 11.

In figure 13, there are two peaks located around 70° and 300° on the intensity profile, about 30° width. This finding coincides that the RNFL is most densely distributed along the vascular arcades, shown in figure 11.
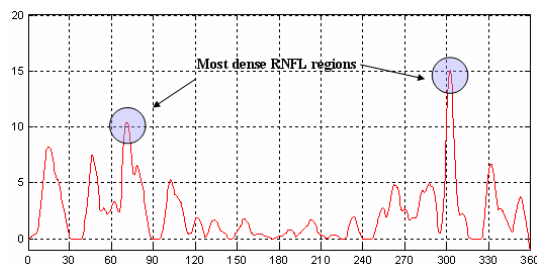

Figure 13: Two peaks in the trend-subtracted intensity profile.

Discussion

Using trend-subtracted intensity profile, the retinal artery and vein can be differentiated by our novel method. But pseudo-split peak of veins can mimic the real split peak of artery.

Until now, the proposed method have not solved the difficult points such that the skewed blood vessel along the circle line can be misinterpreted as RNFL atrophy and this method may be sensitive to the result of fovea localization.

Conclusions

The degree and the progression of RNFL defect in the serially taken digital RNFL photographs were successfully calculated by our novel approach based on image processing and learning technique.

Acknowledgement

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