Preliminary study on differentiation between glaucomatous and non-glaucomatous eyes on stereo fundus images using cup gradient models

Chisako Muramatsu[a], Yuji Hatanaka[b], Kyoko Ishida[c], Akira Sawada[c], Tetsuya Yamamoto[c], Hiroshi Fujita[a]

[a]Department of Intelligent Image Information, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan

[b]Department of Electronic Systems engineering, School of Engineering, The University of Shiga Prefecture, 2500 Hassaka-cho, Hikone, Shiga 522-8533, Japan

[c]Department of Ophthalmology, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan

ABSTRACT

Glaucoma is one of the leading causes of blindness in Japan and the US. One of the indices for diagnosis of glaucoma is the cup-to-disc ratio (CDR). We have been developing a computerized method for measuring CDR on stereo fundus photographs. Although our previous study indicated that the method may be useful, cup determination was not always successful, especially for the normal eyes. In this study, we investigated a new method to quantify the likelihood of glaucomatous disc based on the similarity scores to the glaucoma and non-glaucoma models. Eighty-seven images, including 40 glaucomatous eyes, were used in this study. Only one eye from each patient was used. Using a stereo fundus camera, two images were captured from different angles, and the depth image was created by finding the local corresponding points. One of the characteristics of a glaucomatous disc can be not only that the cup is enlarged but it has an acute slope. On the other hand, a non-glaucomatous cup generally has a gentle slope. Therefore, our models were constructed by averaging the depth gradient images. In order to account for disc size, disc outline was automatically detected, and all images were registered by warping the disc outline to a circle with a predetermined diameter using thin plate splines. Similarity scores were determined by multiplying a test case with both models. At the sensitivity of 90.0%, the specificity was improved from 83.0% using the CDR to 97.9% by the model-based method. The proposed method may be useful for differentiation of glaucomatous eyes.

Keywords: Glaucoma, retinal fundus images, differentiation, cup-to-disc ratio, cup models

1. INTRODUCTION

Glaucoma is the second leading cause of blindness worldwide, and the number of affected patients is expected to be about 80 million in 2010. [1] It has been found in a population-based prevalence survey of glaucoma in Tajimi, Japan, that 93% of the patients diagnosed with primary open-angle glaucoma were previously undiagnosed.[2, 3] This is likely due to the slow progressive nature of this disease and the lack of symptom in those with early-stage glaucoma. Once ganglion cells are damaged, they cannot be restored. Therefore, early detection and treatment are considered the best way to minimize the likelihood of significant visual impairment.

Retinal fundus photography is frequently obtained for diagnosis and record in ophthalmology visit and sometimes in internal medicine examination. It is relatively inexpensive and easy to perform; therefore, it may be effectively used for screening purposes. One of the signs of glaucoma that can be found on retinal fundus images is enlargement of optic cup, called cupping. For the assessment of cupping, a cup-to-disc ratio (CDR), which is measured by the ratio of the largest vertical diameters of optic cup and disc, is often used as the clinical guide. However, it is rarely quantitatively measured in routine clinical practice, but visually assessed in general. Even if it is measured, the measurement includes intra- and inter-reader variations. The studies have reported that these variations would not be negligible, making the consistent diagnosis difficult.[4, 5]

Medical Imaging 2014: Computer-Aided Diagnosis, edited by Stephen Aylward, Lubomir M. Hadjiiski,
Proc. of SPIE Vol. 9035, 903533 · © 2014 SPIE · CCC code: 1605-7422/14/$18 · doi: 10.1117/12.2043409

For improving diagnostic efficiency and assisting consistent diagnosis, several groups have studied the computerized measurement of CDR[6-10]. We have also investigated the methods to automatically measure the CDRs on stereo and plain retinal fundus images.[12, 13] In our previous study with stereo images,[12] optic disc margin was determined by use of an active contour model based on the edge information.[13] The depth image was produced from a pair of stereo images by finding the corresponding points at local regions.[14] The depth image was transformed to polar coordinate system with respect to the deepest point, and the cup boarder was determined by dynamic programming. When the method was applied to the test cases, the result indicated the usefulness of the method in determination of CDRs and in distinction between glaucomatous and control eyes. However, cup determination was not always successful, especially for normal cases. One of the reasons was the lack of clear edge between cup and rim in normal eyes.

While attempting to improve our scheme for determination of CDR, we are also investigating a new method to supplement CDR in classifying glaucomatous and non-glaucomatous eyes. In this study, we investigated a new method to quantify the likelihood of glaucomatous-like disc based on the similarity scores to the glaucomatous and non-glaucomatous cup gradient models.

2. MATERIALS AND METHODS

2.1 Database

The retinal fundus images used in this study were obtained at Gifu University Hospital with a stereo fundus camera (WX-1; Kowa Company, Ltd., Nagoya, Japan). The images were different from ones used in the previous study.[11] Unlike ones in the previous study, a stereo image pair in this study was saved as a single image with 2144 x 1424 pixels in a JPEG format. These images were obtained almost simultaneously from two directions with a field angle of 20 x 27 degrees centered on the optic disc. The clinical information and the results of perimetry, if tested as a routine diagnostic work-up, were retrospectively collected. An ophthalmologist reviewed one of the stereo pairs in a 2D monitor and provided the diagnosis without knowing clinical information. In this preliminary investigation, the cases in which visual field test results and ophthalmologists' assessment on images agreed were included. The database consisted of 87 cases, including 40 glaucomatous eyes and 47 non-glaucomatous eyes. Only one eye from each patient was used in this study. This study was approved by our institutional review board.

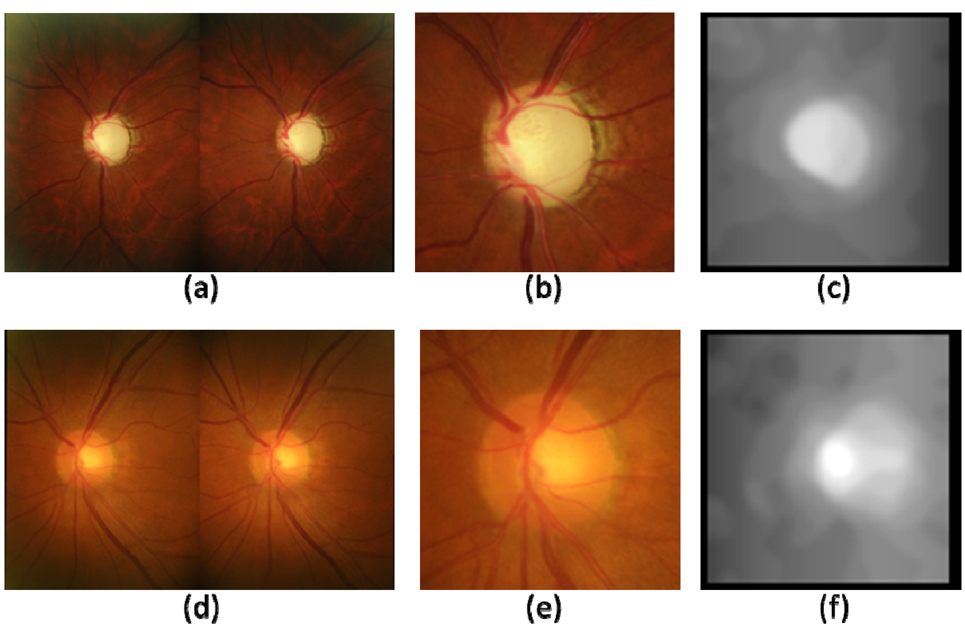

Figure 1. Depth images of a glaucomatous eye (top row) and non-glaucomatous eye (bottom row). (a), (d) Original stereo pair images, (b), (e) ROIs of the discs, and (c), (f) depth images.

2.2 Disc Localization and Segmentation

After a stereo pair was separated in the middle into two images, one was used for localization and segmentation of optic disc. The methods for the localization and segmentation have been described in detail elsewhere.[11, 13] In brief, for the localization of disc, bright regions were detected using red and green planes with the p-tile thresholding method. Subsequently, a region of interest with 600 x 600 pixels centered at the detected location was extracted and used for precise segmentation. The potential disc boarder was detected by the Canny edge detector. Using it as an initial model, the final boarder was determined by an active contour model.

2.3 Reconstruction of Depth Map

The depth image was reconstructed by searching the corresponding points between two views of a stereo image pair.[11, 14] For every four pixels, the corresponding points on the other view were searched by matching the local regions of interest with 21 x 21 pixels on the basis of the cross correlation. The lateral distance between the corresponding points were converted to the depth. If the correlation value was lower than the prespecified threshold value, it was considered that the corresponding point was not found. After all points were searched, the missing points were interpolated from surrounding pixels. Subsequently, the depth map was smoothed to reduce noise. Figure 1 shows original stereo pair images, ROIs of the discs, and depth images of a glaucomatous eye and a non-glaucomatous eye.

2.4 Construction of Cup Gradient Models

The characteristics of the glaucomatous disc include the enlarged cup and the steepness of the cup shape. On the other hand, it was observed that the depth of the cup gradually changes in the non-glaucomatous eyes. Therefore, we attempted to use the statistics of cup gradient for the differentiation of glaucomatous discs from normal discs. First, magnitude of the depth gradient was determined for each pixel inside the disc region using a Sobel-like filter with a 5 x 5 kernel. In order to account for the size variation of discs, the gradient images were warped by registering the sample points on the disc margin to a circle using thin plate splines with bicubic interpolation. The number of sample points was set to 72 points, i.e., every 5 degrees, and the diameter of the circle was set to 340 pixels. Two models were constructed by averaging the warped gradient images of the glaucomatous cases and control cases. Figure 2 shows the depth gradient images of the glaucoma and non-glaucoma cases in Fig. 1 and the examples of two models created by 39 glaucoma and 47 non-glaucoma cases excluding a glaucoma test case.

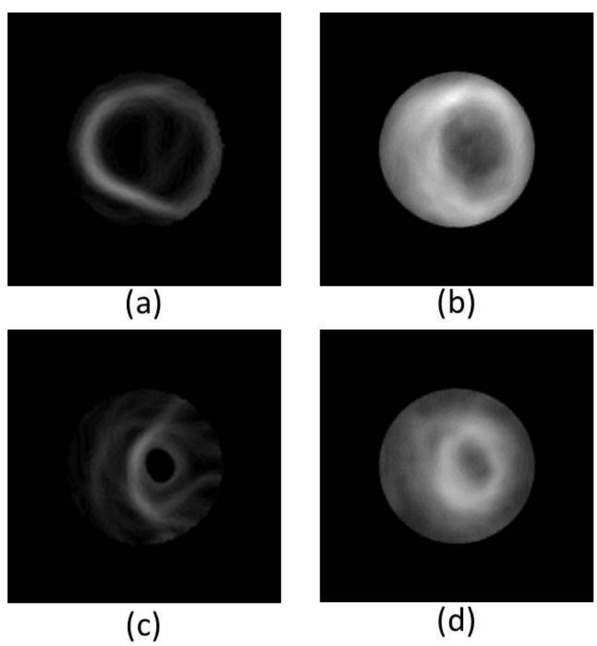

Figure 2. The depth gradient images. (a), (c) The gradient images of Fig.1 (c) and (f); and (b), (d) examples of glaucoma and non-glaucoma cup gradient models.

2.5 Determination of Similarity Scores and Classification

Similarity scores were determined by multiplying the gradient image of a test case with the two models. Because the number of cases in this study was not very large, training and testing were performed by a leave-one-out cross validation method, in which two models were constructed using all cases but a test case. The difference in similarity scores to the glaucoma model and the non-glaucoma model was used for evaluation by the receiver operating characteristic (ROC) analysis (PROPROC software; the University of Chicago).

3. RESULTS

Using the CDR determined by the previous method, the classification accuracy for the glaucomatous and non-glaucomatous eyes was relatively high, with the sensitivity of 90.0% and the specificity of 83.0%. By using the proposed method, the specificity was 97.9% at the same sensitivity level. At the sensitivity of 95.0%, the specificities for the CDR and the proposed method were 72.3% and 78.7%, respectively. Based on the ROC analysis, the area under the curves (AUC) was slightly improved from 0.952 to 0.960. Figure 3 shows the ROC curves for the CDR and the similarity score by the model-based method. Note that the difference between two curves appears smaller because of the curve fitting.

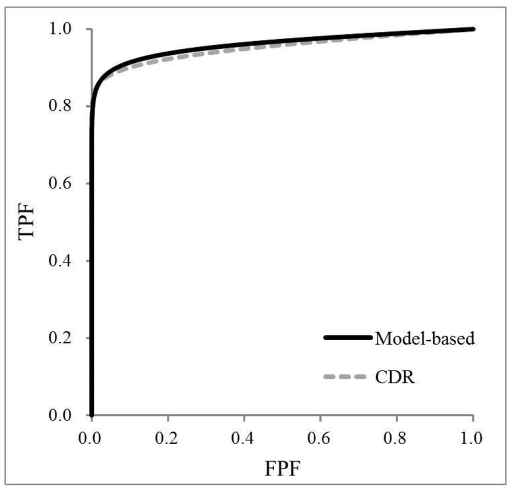

Figure 3. ROC curves for differentiation of glaucomatous eyes from non-glaucomatous eyes using the CDR and the similarity score by the model-based method.

4. DISCUSSION AND CONCLUSION

In our previous study, cup and disc borders were determined using the active contour model and dynamic programming. Based on the segmentation results, CDRs were determined and used for differentiation of glaucomatous eyes from non-glaucomatous eyes. The method was applied to a new database, and relatively good result in terms of classification accuracy was obtained. However, in some cases, CDRs were not determined correctly when the depth images include some noise and do not include strong edges at cup margin. In this study, we investigated a new method that does not require segmentation of cup but utilizes the cup curvature information for differentiation of glaucomatous eyes from non-glaucomatous ones. Figure 4 shows a case in which strong edges in the depth image were absent, and it was difficult to segment the cup. The CDR was relatively high for the non-glaucomatous case, but the similarity score with the non-glaucoma model was higher than that with the glaucoma model. On the other hand, when disc is tilted, and the large gradient was observed near the center of the disc, a glaucoma case may be incorrectly classified as non-glaucoma by the model-based method, as shown in Fig. 4. In this case, CDR was high because the vertical diameter of the segmented cup was large.

Overall, the classification accuracy was slightly improved by the proposed model-based method in terms of AUC. However, CDR has some value because it is a quantitative measure and in accordance with the clinical practice. The result of this study indicates that two methods could supplement each other for distinction between glaucomatous and non-glaucomatous eyes. Further improvement is needed for both methods.

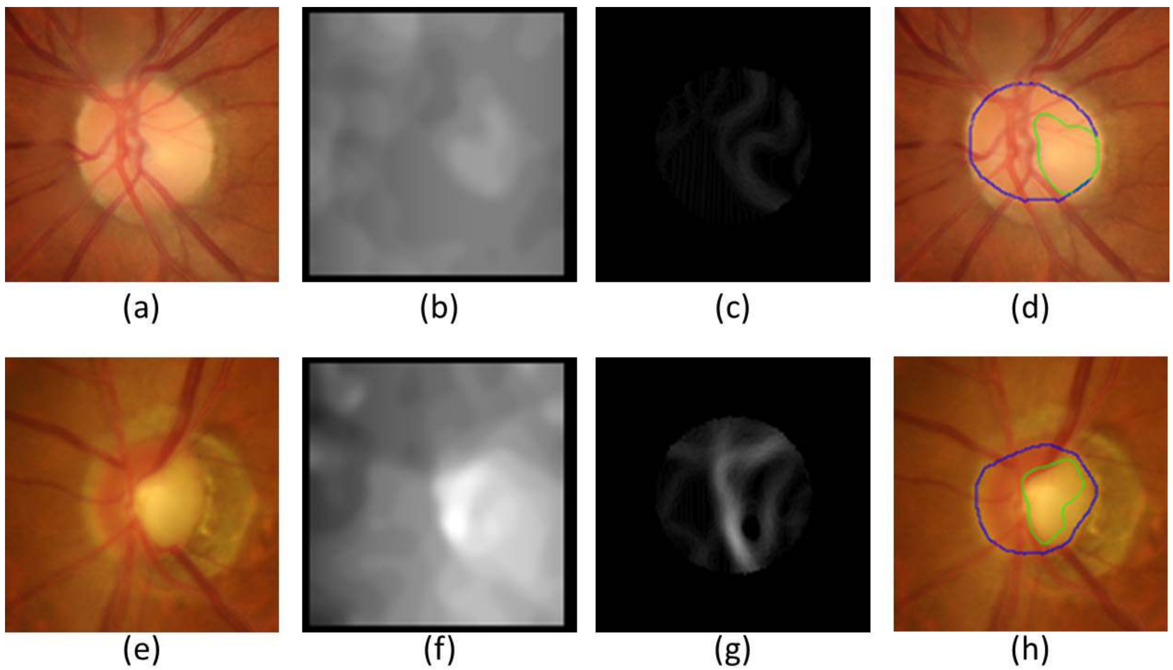

Figure 4. Examples of results by both methods. (a) Non-glaucomatous eye and (e) glaucomatous eye; (b), (f) the depth images of (a) and (e); (c), (g) the gradient images; and (d), (h) cup and disc outlines determined by the previous method.[11]

ACKNOWLEGEMENTS

This study was partly supported by a Grant-in-Aid for Scientific Research on Innovative Areas (21103004), Ministry of Education, Culture, Sports, Science and Technology, Japan and a research grant by Tateishi Science and Technology Foundation.

REFERENCES

[1] Quigley, H. A. and Broman, A. T., “The number of people with glaucoma worldwide in 2010 and 2020,” Br. J. Ophthalmol. 90, 262-267 (2006).

[2] Iwase, A., Suzuki, Y., Araie, M., Yamamoto, T., Abe, H., Shirato, S., Kuwayama, Y., Mishima, H. K., Shimizu, H., Tomita, G., Inoue, Y. and Kitazata, Y., “The prevalence of primary open-angle glaucoma in Japanese: The Tajimi Study,” Ophthalmol. 111(9), 1641-1648 (2004).

[3] Yamamoto, T., Iwase, A., Araie, M., Suzuki, Y., Abe, H., Shirato, S., Kuwayama, Y., Mishima, H. K., Shimizu, H., Tomita, G., Inoue, Y. and Kitazawa, Y., “The Tajimi Study report 2: prevalence of primary angle closure and secondary glaucoma in a Japanese population,” Ophthalmol. 112(19), 1661-1669 (2005).

[4] Varma, R., Spaeth, G. L., Steinmann, W. C. and Katz, L. J., “Agreement between clinicians and an image analyzer in estimating cup-to-disc ratios,” Arch. Ophthalmol. 107(4), 526-529 (1989).

[5] Tielsch, J. M., Katz, J., Quigley, H. A., Miller, N. R. and Sommer, A., "Intraobserver and interobserver agreement in measurement of optic disc characteristics," Ophthalmol. 95(3), 350-356 (1988).

[6] Corona, E., Mitra, S., Wilson, M., Krile, T., Kwon, Y. H. and Soliz, P., "Digital stero image analyzer for generating automated 3-D measures of optic disc deformation in glaucoma," IEEE Trans. Med. Imaging 21(10), 1244-1253 (2002).

[7] Abramoff, M. D., Alward, W. L. M., Greenlee, E. C., Shuba, L., Kim, C. Y., Fingert, J. H. and Kwon, Y. H., "Automated segmentation of the optic disc from stereo color photographs using physiologically plausible features," Invest. Ophtalmol. Vis. Sci. 48(4), 1665-1673 (2007).

[8] Xu, J., Ishikawa, H., Wollstein, G., Bilonick, R. A., Sung, K. R., Kagemann, K, Townsend, K. A. and Schuman, J. S., "Automated assessment of the optic nerve head on stereo disc photographs," Invest. Ophthalmol. Vis. Sci. 49(69, 2512-2517 (2008).

[9] Nayak, J., Acharya, R. U., Bhat, P. S., Shetty, N. and Lim, T. C., "Automated diagnosis of glaucoma using digital fundus image," J. Med. Syst. 33, 337-346 (2009).

[10] Cheng, J., Liu, J., Tao, D., Yin, F., Wong, D. W. K., Xu, Y., Wong, T. Y., "Superpixel classification based optic cup segmentation," Mori, K., et al (Eds.) MICCAI 2013, LNCS 8151, 421-428 (2013).

[11] Muramatsu, C., Nakagawa, T., Sawada, A., Hatanaka, Y., Yamamoto, T. and Fujita, H., "Automated determination of cup-to-disc ratio for classification of glaucomatous and normal eyes on stereo retinal fundus images," J. Biomed. Opt. 16, 096009-1-8 (2011).

[12] Hatanaka, Y., Noudo, A., Muramatsu, C., Sawada, A., Hara, T., Yamamoto, T. and Fujita, H., "Automatic measurement of cup to disc radio based on line profile analysis in retinal images," Proc. IEEE Eng. Med. Bio. Sci. 2011, 3387-3390 (2011).

[13] Muramatsu, C., Nakagawa, T., Sawada, A., Hatanaka, Y., Hara, T., Yamamoto T. and Fujita, H., "Automated segmentation of optic disc region on retinal fundus photographs: Comparison of contour modeling and pixel classification methods," Comput. Methods Programs Biomed. 101, 23-32 (2011).

[14] Nakagawa, T., Suzuki, T., Hayashi, T., Mizukusa, Y., Hatanaka, Y., Ishida, K., Hara, T., Fujita, H. and Yamamoto, T., "Quantitative depth analysis of optic nerve head using stereo retinal fundus image pair," J. Biomed. Opt. 13(6), 064026 (2008).