Detection of Affected Segments of Glaucoma Using Features of Nerve Fiber Layer

Kiyoshi Takita
Course of Precision Engineering
Chuo University
1-13-27 Kasuga, Bunkyo-ku, Tokyo 112-8551, Japan
takita@sensor.mech.chuo-u.ac.jp

Kazunori Umeda
Dept. Precision Mechanics
Chuo University
1-13-27 Kasuga, Bunkyo-ku, Tokyo 112-8551, Japan
umeda@mech.chuo-u.ac.jp

Kenji Terabayashi
Dept. Mechanical Engineering
Shizuoka University
3-5-1 Johoku, Hamamatsu Naka-ku, Shizuoka 432-8561, Japan
tera@eng.shizuoka.ac.jp

Atsuo Tomidokoro
Tomidokoro Eye Clinic
5-1-1 Higashinakano, Nakano-ku, Tokyo 164-0003, Japan
Tomidokoro-tky@umin.ac.jp

***Abstract*—This paper propose a method of detecting affected segments from glaucoma using features of nerve fiber layers. These days, a method to help doctors by making a color map of nerve fiber layer thickness is established as computer-aided diagnosis (CAD) for glaucoma. However, it is difficult to help doctors using the color map in incipience cases because change of disease condition cannot be monitored. Comparison of detected area and identified area as affected segments by a doctor is performed to demonstrate the effectiveness of the proposed method.**

Keywords— glaucoma; computer-aided diagnosis; nerve fiber layer

I. INTRODUCTION

Amongst Japan's aging population, there have been concerns with extending healthy life expectancy as people become more health conscious. Because of these factors, number of people or frequency of checkup examination has continued to rise. This is expected to continue, and increasing pressure on doctors is a critical problem. Work is proceeding with Computer-aided diagnosis (CAD) for the reduction of this problem. CAD for breast cancer [1] or subarachnoid bleeding [2] is more common, however, there are also CAD for glaucoma. Epidemiological study in Tajimi City, Gifu Prefecture indicates that glaucoma is suffered one-in-twenty people aged forty or over [3, 4] and the number of glaucoma patients is estimated to reach into eighty million worldwide by 2020 [5]. Glaucoma is a disease that is very close to home. Some CAD for glaucoma has already been proposed, for example, cup-to-disc ratio [6], thelorrhagia and retinal nerve fiver layer defect detection [7, 8]. But, it is difficult to diagnosis glaucoma in an early stage using these CAD. And so it has been shown that it is possible to indicate possibility of glaucoma even at early stage by assessing asymmetry of nerve fiber layer (NFL) when a straight line passing through papilla and macula is defined as symmetric line focusing on features of eye and glaucoma [9]. However, when doctors examine patients, the important part is not just to make a judgment of disease condition but to detect affected segments. A prior study detects affected segments focusing on thickness of NFL and its asymmetry. But the results are insufficient for CAD. This study proposes a detection method of affected segments using a number of different methods, considering not only NFL thickness and its asymmetry but also its difference and dispersion. Moreover, the usefulness of the proposed method is discussed through evaluation experiments.

II. ACQUISITION OF EVALUATION VALUES

Four evaluation values expressing NFL's thickness, asymmetry, difference and dispersion are obtained. A straight line passing through papilla and macula is obtained as line-symmetric axis to define evaluation values expressing asymmetry as shown in Fig.1. We use NFL's thickness that can be obtained from optical coherence tomography (OCT) image (Fig.2). Let S be the region of scan range, $N(S)$ be the amount of data within S, (x, y) be the position A within S, and $thick(A)$ be the NEL's thickness at A. Two points at line-symmetric positions need to be within scan range to calculate asymmetry. Let S' be the region of range where there is each line-symmetric position and B be the line-symmetric position of A. We calculate NFL's difference in the range of $U \times V$ mainly around A. The evaluation value *thickness* expressing thickness, *asymmetry* expressing asymmetry and *difference* expressing difference are obtained by the following equations.

$$thickness(A) = thick(A) \tag{1}$$

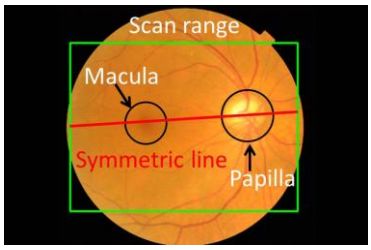

Fig. 1. Fundus image

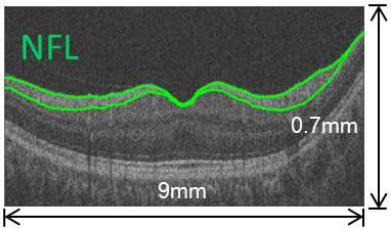

Fig. 2. OCT image

$$asymmetry(A) = \frac{thick(A) - thick(B)}{\{thic(A) + thick(B)\}/2} \tag{2}$$

$$difference(A) = \frac{1}{(U \times V) - 1} \sum_{u=1}^{U} \sum_{v=1}^{V} \left| thick(x,y) - thick\left(x - \frac{U+1}{2} + u, y - \frac{V+1}{2} + v\right) \right| \tag{3}$$

Also standard deviations of rows and columns within scan range, *row_SD* and *column_SD*, are calculated to define evaluation value *thick_SD* expressing dispersion. Using *row_SD* and *column_SD*, *thick_SD* is obtained by the following equation.

$$thick\_SD(A) = \frac{column\_SD(A)}{row\_SD(A)} \tag{4}$$

III. Detection Method of Affected Segments

After acquisition of evaluation values, the scan range is segmented and averages of each evaluation value are calculated using them within each segmented region. We make 2 classes, Normal and Glaucoma, for each segmented region with training data and detect affected segments using the classes.

A. Calculaton of Average

For the system to detect affected segments, the scan range is segmented into M×N parallel and perpendicular to a line passing through papilla and macula, and the base point is set on the midpoint of papilla and macula as shown in Fig.3. Then, averages of evaluation values, *Ave_thick(m, n)*, *Ave_asym(m, n)*, *Ave_dif(m, n)* and *Ave_SD(m, n)* ($m=1,\cdots,M$ $n=1,\cdots,N$), are calculated using evaluation values within the segmented region of the $(m,n)^{th}$ region.

B. Making Classes

We make 2 classes, Normal and Glaucoma, for each segmented region. Classes are made using data within all segmented regions in the case of Normal class. Classes are made using data within segmented regions in which the ratio of affected segments is more than adequate threshold in the case of Glaucoma class. An eye doctor determined whether each segment is affected segment.

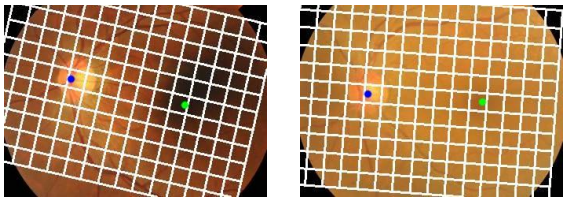

Fig. 3. Results of area segmentation

C. Classification Method

Classification methods explained below are applied to 2 constructed classes to detect affected segments.

1) Mahalanobis' generalized distance method : Let $\boldsymbol{X}^{(C)}$ be the training vector of evaluation values in class C, K be the dimension of $\boldsymbol{X}^{(C)}$ and $T^{(C)}$ be the number of data to make class C. The mean vector $\boldsymbol{A}^{(C)}$ and the covariance matrix $S^{(C)}$ are obtained by the following equations.

$$\boldsymbol{X}_t^{(C)} = \left[x_{t1}, \cdots, x_{tK}\right]^T (t = 1, \cdots, T^{(C)}) \tag{5}$$

$$\boldsymbol{A}^{(C)} = \frac{1}{T^{(C)}} \sum_{t=1}^{T^{(C)}} \boldsymbol{X}_t^{(C)} \tag{6}$$

$$S^{(C)} = \begin{bmatrix} S_{11}^{(C)} & \cdots & S_{1K}^{(C)} \\ \vdots & \ddots & \vdots \\ S_{K1}^{(C)} & \cdots & S_{KK}^{(C)} \end{bmatrix}$$
$$S_{ij}^{(C)} = \frac{1}{T^{(C)}} \sum_{t=1}^{T^{(C)}} \left(x_{ti} - \boldsymbol{A}_i^{(C)}\right)\left(x_{tj} - \boldsymbol{A}_j^{(C)}\right) \tag{7}$$

Mahalanobis' generalized distance $d_m^{(C)}$ for each class is obtained by the following equation.

$$d_m{}^{(C)2} = \left(x - \boldsymbol{A}^{(C)}\right)^T \left(S^{(C)}\right)^{-1} \left(x - \boldsymbol{A}^{(C)}\right) \tag{8}$$

If the distance for Glaucoma class is less than that for Normal class, the segmented region is classified to affected segment in each segmented region.

2) Maximum likelihood estimation method (MLE) : Likelihood $L^{(C)}$ for each class is obtained by the following equation.

$$L^{(C)} = \frac{1}{(2\pi)^{\frac{K}{2}} \left|S^{(C)}\right|^{\frac{1}{2}}} \exp\left(-\frac{1}{2}\left(x - \boldsymbol{A}^{(C)}\right)^T \left(S^{(C)}\right)^{-1} \left(x - \boldsymbol{A}^{(C)}\right)\right) \tag{9}$$

If the likelihood for Glaucoma class is larger than that for Normal class, the segmented region is classified to affected segment in each segmented region.

3) Nearest Neighbor Distance Method (NN) : Euclidean distance is calculated for all training vectors, and a training vector with the minimum distance is obtained. When the training vector belongs to Glaucoma class, the segmented region is classified to affected segment in each segmented region.

4) Support Vector Machine (SVM) : The problem of affected segments detecting results in the binary classification. Then, it is possible to apply SVM. In the case of the problem of affected segments detecting, training vector of evaluateion values cannot be separated by a linear separating hyperplane. An SVM creates a soft margin that permits some misclassifications. A hyperplane, which separates the feature space, is determined by the solution of the following optimization problem.

$$\text{minimize} \quad \boldsymbol{L}(\boldsymbol{w},\varsigma) = \frac{1}{2}\|\boldsymbol{w}\|^2 + \gamma\sum_{a=1}^{K}(\varsigma_a) \tag{10}$$

$$\text{subject to} \quad \varsigma_a \geq 0, s_a\left(\boldsymbol{w}^T \boldsymbol{X_t}^{(C)}{}_{\boldsymbol{a}} + b\right) \geq 1-\varsigma_a \quad (a=1,\cdots,K) \tag{11}$$

$\boldsymbol{w}$ and b are parameters called a weight vector and a bias respectively. γ is the penalty parameter of the error term. ζ_a is a slack variable. Furthermore, the SVM used in our method applies the kernel function [10]. Each segmented region is determined as an affected segment or not.

IV. EXPERIMENT

To verify the usefulness of the constructed detection system of affected segments, we conducted experiments.

A. Experimental conditions and parameters

We set U and V used to obtain *difference* as 1 and 3 respectively.

The scan range was segmented into 15×11. We used 13 normal cases to make Normal class and 14 glaucoma cases to make Glaucoma class. As Glaucoma class, we used only affected segments identified by a doctor.

The threshold used to determine affected segment when Glaucoma class was made was set to 0.15.

When applying SVM to the proposed method, the radial basis function (RBF) shown in the following equation was utilized.

$$\boldsymbol{K}(x_1,x_2) = \exp\left(-\frac{\|x_1-x_2\|^2}{\sigma^2}\right) \tag{12}$$

σ is the kernel parameter. γ in (10) and σ in (12) were decided by Grid-search, which selects the pair of parameters that have highest performance. This selection is carried out by changing the parameters thoroughly and optimizing an evaluation function. As the index to express performance, d is obtained by the following equations using the result of leave-one-out cross-validation for training data.

$$\begin{aligned} TPrate &= TP/(TP+FN) \\ FPrate &= FP/(FP+TN) \\ d &= FPrate^2 + (1-TPrate)^2 \end{aligned} \tag{13}$$

TP, *FP*, *TN* and *FN* represent true positive, false positive, true negative and false negative. Table 1 presents the parameters.

B. Experiments of detecting affected segmets

We conducted experiments with 14 cases whose affected segments are identified by a doctor and 13 normal cases. *Recall*, *Precision* and *Accuracy* were obtained by the following equations to evaluate the performance.

$$Recall = TP/(TP+FN) \tag{14}$$

$$Precision = TP/(TP+FP) \tag{15}$$

$$Accuracy = (TP+TN)/(TP+FP+TN+FN) \tag{16}$$

Recall is the ratio of classifying disease group as positive. *Precision* is the ratio of proper positive. *Accuracy* is the ratio of properly classifying. *Recall*, *Precision* and *Accuracy* of experiments in each detection method are presented in Table 2. Fig.4 shows detection of affected segments. The results with combination of four evaluated values are given as *All*. We used leave-one-out cross validation for all experiments.

On referring to *Recall* involving glaucoma, the highest result, 71.5%, was obtained when using the Mahalanobis' generalized distance method with *Ave_thick*, and the second highest result, 70.1%, was obtained when using the SVM with *All*. On referring to *Precision* involving glaucoma, the highest result, 46.1%, was obtained when using the nearest neighbor distance method with *Ave_asym*. However, *Recall* using the same method was low, 41.0%. On referring to *Accuracy* involving glaucoma, we saw that the higher results of *Precision*, the higher results of *Accuracy*. The results of each evaluation value show that *Recall* with *Ave_thick* is high in each method. This is because disease condition of all cases of glaucoma using experiments is middle stage or over and thus NFL's thickness reduction is definite. If disease condition is in initial stage, it is known that *Ave_asym* respond more sensitive than *Ave_thick* [9]. However, *Recall* with *Ave_asym* is not high. This is because *Ave_asym* is evaluation value expressing thickness's difference at symmetrical position and thus thickness's difference becomes smaller as affected segments spread. Therefore, the reason why *Recall* with *Ave_thick* & *Ave_asym* and that with *All* are low is that *Ave_asym* is combined. If we conduct the experiment using initial stage of glaucoma, we can expect that *Recall* with *Ave_asym* becomes higher than *Ave_thick*. In contrast, *Precision* with *Ave_asym* is high in each method. This is because *Ave_asym* could respond features of glaucoma by examining asymmetry. *Precision* with

TABLE I. PARAMETER FOR SVM

	Thickness	*Asymmetry*	*Difference*
log(γ)	-7	1	3
log(σ)	16	15	20
	Thick_SD	***Thickness & Asymmetry***	***All***
log(γ)	-2	-9	-14
log(σ)	21	19	19

TABLE II. EXPERIMENTAL RESULTS[%]

Disease condition		**Glaucoma**			**Normal**
Metod	***Evaluation vallue***	***Rec.***	***Prec.***	***Acc.***	***Acc.***
Mahalanobis	*Ave_thick*	71.5	39.0	91.3	97.0
	Ave_asym	58.3	37.7	91.4	93.7
	Ave_dif	43.1	24.8	88.3	93.7
	Ave_SD	59.7	21.0	83.5	85.1
	Ave_thick & Ave_asym	58.3	36.2	91.0	97.4
	All	47.2	41.7	92.6	99.2
MLE	*Ave_thick*	68.1	38.1	91.1	96.6
	Ave_asym	52.1	40.1	92.2	93.6
	Ave_dif	57.6	25.3	86.8	89.7
	Ave_SD	34.7	19.7	87.1	93.6
	Ave_thick & Ave_asym	54.2	37.7	91.6	97.5
	All	46.5	42.1	92.7	99.3
NN	*Ave_thick*	66.0	37.0	90.9	97.4
	Ave_asym	41.0	46.1	93.3	96.2
	Ave_dif	29.9	26.2	90.4	95.2
	Ave_SD	25.7	22.2	89.7	95.3
	Ave_thick & Ave_asym	52.1	43.1	92.7	97.6
	All	51.4	43.3	92.8	97.8
SVM	*Ave_thick*	68.1	40.8	91.9	99.5
	Ave_asym	36.8	42.7	93.0	99.5
	Ave_dif	36.8	29.3	90.5	99.5
	Ave_SD	28.5	26.6	90.6	99.8
	Ave_thick & Ave_asym	64.6	30.6	88.7	99.8
	All	70.1	31.1	88.4	99.8

Ave_thick was lower than that with *Ave_asym* because thickness is different for each person and thus if thickness of normal part is low as compared to others, *Ave_thick* responds.

On referring to *accuracy* involving normal, high results, over 99%, were obtained in many detection methods. Among them, high results over 99.5% are obtained, when using the SVM with regardless of evaluation values.

This indicates that the proposed method can detect affected segments. An obvious superiority was not seen in each detection methods. Comparatively good results were obtained when using the Mahalanobis' generalized distance method and SVM with *Ave_thick*. The results of *Recall* and *Precision* are not enough so far, partly because the number of samples is not enough. However, we could build a fundamental system to detect affected segments.

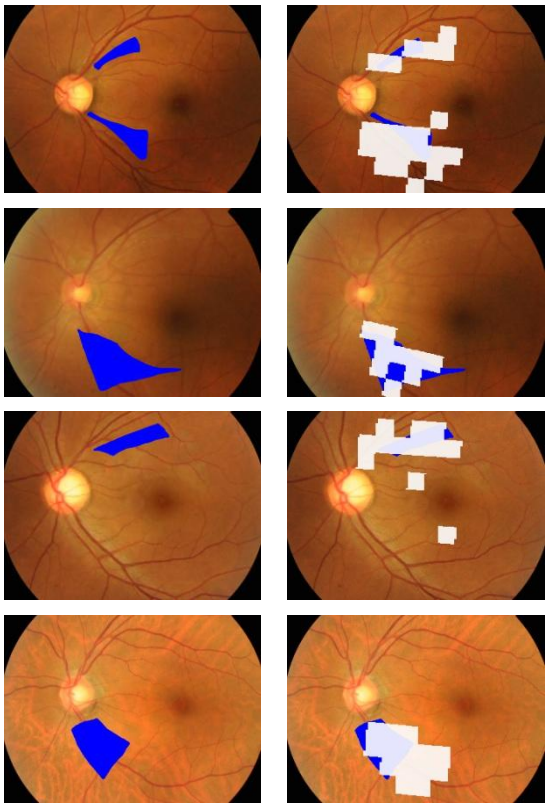

Fig. 4. Results of detection (Area colored blue were identified affected segments by a doctor. Area colored white were result of detection.)

V. CONCLUSION

This study has proposed a method to detect affected segments of glaucoma. With the proposed method, 4 evaluation values expressing NFL's thickness, asymmetry, difference and dispersion are obtained, and then the scan range is segmented, and finally averages of each evaluation value are calculated using evaluation values within the segmented regions. We made 2 classes, Normal and Glaucoma, for each segmented region and classified affected segments using classification algorithms: Mahalanobis' generalized distance method, maximum-likelihood method, nearest neighbor distance method and support vector machine.

The usefulness of the proposed method has been verified through experiments. From the results, an obvious superiority was not seen in each detection method. But, the experiments indicate that the detection system we have built can detect affected segments.

In the future, studies will include improve method of efficiency of classification. Therefore, we intend to build a system that achieves high performance by boosting amount of data for creating class and combining different detection methods.

REFERENCES

[1] H.P. Chan, K. Doi, S. Galhotra, C.J. Vyborny, H. MacMahon, and P.M. Jokich, "Image feature analysis and computer-aided diagnosis in digital

radiography. I. Automated detection of microcalcications in mammography," Medical Physics, 14(4), pp.538-548, 1987.

[2] N. Hayashi, Y. Matsutani, T. Matumoto, H. Mori, A. Kunimatsu, O. Abe, S. Aoki, K. Ohtomo, N. Takano, and K. Matsumoto, "Feasibility of a curvature-based enhanced display system for detecting cerebral aneurysms in MR angiography," Magnetic Resonance in Medical Scienece, 2, pp.29-36, 2003.

[3] A. Iwase, Y. Suzuki, M. Araie, and T. Yamamoto, "The prevalence of primary open-angle glaucoma in Japanese: The Tajimi sutudy," Ophthalmology, 111(9), pp1641-1648, 2004.

[4] T. Yamamoto, A. Iwase, M.Araie, Y. Suzuki, H. Abe, S. Shirato, Y. Kuwayama, H. Mishima, H. Shimizu, H. Shimizu, G. Tomita, Y. Inoue, and Y. Kitazawa, "The Tajimi study report 2 prevalence of primary angle closure and secondary glaucoma in a Japanese population," Ophthalmology, 112(10), pp1661-1669, 2005.

[5] H. Quigley, and A. Broman, "The number of people with glaucoma worldwide in 2010 and 2020," Br J Ophthalmology, 90(3), pp.262-267, 2006.

[6] D.W.K Wong, J. Liu, J.H. Lim, H. Li, and T.Y. Wong, "Automated detection of kinks from blood vessels for optic cup segmentation in retinal images," Proc.of SPIE Medical Imaging 2009, 7260, pp.72601J-1-72601j-8, 2009.

[7] Y. Hayashi, T. Nakagawa, Y. Hatanaka, A. Aoyama, M. Kakogawa, T. Hara, H. Fujita, and T. Yamamoto, "Detection of retinal nerve fiber layer defects in retinal fundus images using Gabor filtering," in Proc. SPIE Medical Imaging 2007: Computer-aided Diagnosis, San Diego, 6514, pp.65142 Z-1-65142 Z-8, 2007.

[8] R. Sihota, P. Sony, V. Gupta, T. dada, and R. Singh, "Diagnostic capability of optical coherence tomography in evaluating the degree of glaucomatous retinal nerve fiber damage," Invest Ophthalmol Vis Sci 2006, 47(5), pp.2009-2010, 2006.

[9] K. Takita, Y. Nishi, K. Terabayashi, K. Umeda, and A. Tomidokoro, "Diagnostic aid of glaucoma using thickness of layers extracted from OCT images," The 18th symposium on sensing via image information, IS1-11, 2012 (in Japanese).

[10] N. Cristianini and J. Shawe-Taylor, "An Introduction to Support Vector Machines and Other Kernel-based Learning Methods", Cambridge University Press, 2000.