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

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Abstract—This paper proposes 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 fiber layer defect detection [7, 8]. But, it is difficult to diagnosis glaucoma in an early stage by 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 NFL’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 thickness 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.

\[
thickness(A) = thick(A)
\]
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.

C. Classification Method

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

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

\[
X_t^{(C)} = [x_{i1}, \ldots, x_{iK}]^T (t = 1, \ldots, T^{(C)})
\]

\[
A^{(C)} = \frac{1}{T^{(C)}} \sum_{t=1}^{T^{(C)}} X_t^{(C)}
\]

\[
S^{(C)} = \begin{bmatrix} S_{11}^{(C)} & \cdots & S_{1K}^{(C)} \\ \vdots & \ddots & \vdots \\ S_{K1}^{(C)} & \cdots & S_{KK}^{(C)} \end{bmatrix}
\]

\[
S_{ij}^{(C)} = \frac{1}{T^{(C)}} \sum_{t=1}^{T^{(C)}} (x_{ij} - A_{ij}^{(C)}) (x_{ij} - A_{ij}^{(C)})
\]

Mahalanobis’ generalized distance \( d_{m}^{(C)} \) for each class is obtained by the following equation.

\[
d_{m}^{(C)} = \left( x - A^{(C)} \right)^T (S^{(C)})^{-1} (x - A^{(C)})
\]

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.

\[
L^{(C)} = \frac{1}{(2\pi)^{K/2}|S^{(C)}|^2} \exp \left( -\frac{1}{2} (x - A^{(C)})^T (S^{(C)})^{-1} (x - A^{(C)}) \right)
\]
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 evaluateation 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.

\[
\begin{align*}
\text{minimize} & \quad L(w, \zeta) = \frac{1}{2} \| w \|^2 + \gamma \sum_{a=1}^{K} (\zeta_a) \\
\text{subject to} & \quad \zeta_a \geq 0, \zeta_a \left( w^T X_t^{(C)} a + b \right) \geq 1 - \zeta_a \\
& \quad (a = 1, \cdots, K)
\end{align*}
\]

(10)

\( w \) and \( b \) are parameters called a weight vector and a bias respectively. \( \gamma \) is the penalty parameter of the error term. \( \zeta_a \) 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 15x11. 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.

\[
K(x_1, x_2) = \exp \left( -\frac{\| x_1 - x_2 \|^2}{\sigma^2} \right)
\]

(12)

\( \sigma \) is the kernel parameter. \( \gamma \) in (10) and \( \sigma \) 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.

\[
\begin{align*}
\text{TPrate} &= TP/(TP + FN) \\
\text{FPrate} &= FP/(FP + TN) \\
d &= FPrate^2 + (1 - TPrate)^2
\end{align*}
\]

(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 segments

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.

\[
\begin{align*}
\text{Recall} &= TP/(TP + FN) \\
\text{Precision} &= TP/(TP + FP) \\
\text{Accuracy} &= (TP + TN)/(TP + FP + TN + FN)
\end{align*}
\]

(14) (15) (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

<table>
<thead>
<tr>
<th>Thickness</th>
<th>Asymmetry</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>log(γ)</td>
<td>-7</td>
<td>1</td>
</tr>
<tr>
<td>log(σ)</td>
<td>16</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Thick_SD</th>
<th>Thickness &amp; Asymmetry</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>log(γ)</td>
<td>-2</td>
<td>-9</td>
</tr>
<tr>
<td>log(σ)</td>
<td>21</td>
<td>19</td>
</tr>
</tbody>
</table>

### TABLE II.  EXPERIMENTAL RESULTS[%]

<table>
<thead>
<tr>
<th>Disease condition</th>
<th>Evaluation value</th>
<th>Glaucoma</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahalanobis</td>
<td>Ave_thick</td>
<td>71.5</td>
<td>39.0</td>
</tr>
<tr>
<td></td>
<td>Ave_asym</td>
<td>58.3</td>
<td>37.7</td>
</tr>
<tr>
<td></td>
<td>Ave_diff</td>
<td>43.1</td>
<td>24.8</td>
</tr>
<tr>
<td></td>
<td>Ave_SD</td>
<td>59.7</td>
<td>21.0</td>
</tr>
<tr>
<td></td>
<td>Ave_thick &amp; Ave_asym</td>
<td>58.3</td>
<td>36.2</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>47.2</td>
<td>41.7</td>
</tr>
<tr>
<td>MLE</td>
<td>Ave_thick</td>
<td>68.1</td>
<td>38.1</td>
</tr>
<tr>
<td></td>
<td>Ave_asym</td>
<td>52.1</td>
<td>40.1</td>
</tr>
<tr>
<td></td>
<td>Ave_diff</td>
<td>57.6</td>
<td>25.3</td>
</tr>
<tr>
<td></td>
<td>Ave_SD</td>
<td>34.7</td>
<td>19.7</td>
</tr>
<tr>
<td></td>
<td>Ave_thick &amp; Ave_asym</td>
<td>54.2</td>
<td>37.7</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>46.5</td>
<td>42.1</td>
</tr>
<tr>
<td>NN</td>
<td>Ave_thick</td>
<td>66.0</td>
<td>37.0</td>
</tr>
<tr>
<td></td>
<td>Ave_asym</td>
<td>41.0</td>
<td>46.1</td>
</tr>
<tr>
<td></td>
<td>Ave_diff</td>
<td>29.9</td>
<td>26.2</td>
</tr>
<tr>
<td></td>
<td>Ave_SD</td>
<td>25.7</td>
<td>22.2</td>
</tr>
<tr>
<td></td>
<td>Ave_thick &amp; Ave_asym</td>
<td>52.1</td>
<td>43.1</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>51.4</td>
<td>43.3</td>
</tr>
<tr>
<td>SVM</td>
<td>Ave_thick</td>
<td>68.1</td>
<td>40.8</td>
</tr>
<tr>
<td></td>
<td>Ave_asym</td>
<td>36.8</td>
<td>42.7</td>
</tr>
<tr>
<td></td>
<td>Ave_diff</td>
<td>36.8</td>
<td>29.3</td>
</tr>
<tr>
<td></td>
<td>Ave_SD</td>
<td>28.5</td>
<td>26.6</td>
</tr>
<tr>
<td></td>
<td>Ave_thick &amp; Ave_asym</td>
<td>64.6</td>
<td>30.6</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>70.1</td>
<td>31.1</td>
</tr>
</tbody>
</table>

**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.

### 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


