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# Combining Information from Three Anatomic Regions in the Diagnosis of Glaucoma with Time-Domain Optical Coherence Tomography

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## Abstract

**Purpose—**To improve the diagnosis of glaucoma by combining time-domain optical coherence tomography (TD-OCT) measurements of the optic disc, circumpapillary retinal nerve fiber layer (RNFL), and macular retinal thickness.

**Patients and Methods—**Ninety-six age-matched normal and 96 perimetric glaucoma participants were included in this observational, cross-sectional study. Or-logic, support vector machine (SVM), relevance vector machine (RVM), and linear discrimination function (LDF) were used to analyze the performances of combined TD-OCT diagnostic variables.

**Results—**The area under the receiver operating curve (AROC) was used to evaluate the diagnostic accuracy and to compare the diagnostic performance of single and combined anatomic variables. The best RNFL thickness variables were the inferior (AROC=0.900), overall (AROC=0.892), and superior quadrants (AROC=0.850). The best optic disc variables were horizontal integrated rim width (AROC=0.909), vertical integrated rim area (AROC=0.908), and cup/disc vertical ratio (AROC=0.890). All macular retinal thickness variables had AROCs of 0.829 or less. Combining the top 3 RNFL and optic disc variables in optimizing glaucoma diagnosis, SVM had the highest AROC, 0.954, followed by or-logic (AROC=0.946), LDF (AROC=0.946), and RVM (AROC=0.943). All combination diagnostic variables had significantly

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larger AROCs than any single diagnostic variable. There are no significant differences among the combination diagnostic indices.

**Conclusions—**With TD-OCT, RNFL and optic disc variables had better diagnostic accuracy than macular retinal variables. Combining top RNFL and optic disc variables significantly improved diagnostic performance. Clinically, or-logic classification was the most practical analytical tool with sufficient accuracy to diagnose early glaucoma.

### Keywords

optical coherence tomography; glaucoma; imaging; image processing

In glaucoma, between 30% and 50% of the ganglion cells may be lost before abnormalities appear in perimetric testing.[1, 2] Glaucomatous changes in the optic disc and retinal nerve fiber layer (RNFL) take place over time. Since less than optimal agreement has been reported in subjective assessment of optic disc photographs performed by different observers and even among glaucoma specialists,[3] objective, quantitative measurement of ocular structures implicated in glaucoma is valuable.[4] Optical coherence tomography (OCT) is a commonly used posterior segment imaging technology that has sufficient resolution to measure macular retinal thickness, RNFL thickness, and optic disc dimensions.[5] Many studies have demonstrated the value of measuring these anatomic regions with OCT for the diagnosis and monitoring of glaucoma.[6–9]

Methodologies are still being refined to enhance the sensitivity and specificity for the detection of glaucomatous changes by OCT.[10–15] With data from age-matched participants enrolled in the Advanced Imaging for Glaucoma Study (AIGS), we found that in distinguishing normal eyes from glaucomatous eyes the sensitivity and specificity were optimized with an “or-logic” combination of the 3 best RNFL variables.[16] Using the area under the receiver operating curve (AROC) and linear discriminant function (LDF), Medeiros et al demonstrated that a combination of optic disc and RNFL variables obtained by OCT improved the diagnostic accuracy for glaucoma detection.[17]

In the present study, we used available AIGS data to explore the relative strengths of or-logic combination, support vector machine (SVM),[18, 19] relevance vector machine (RVM),[20, 21] and LDF approaches in analyzing OCT diagnostic variables.[0] Measurements from three anatomical regions, the peripapillary RNFL, optic disc, and macular retina, were combined to increase the diagnostic accuracy of time domain OCT (TD-OCT) in detecting early glaucomatous change. To the best of our knowledge, this is the first time in a single study that various statistical processing strategies have been tested in such an application.

## Methods and Materials

### Study Population and Database

The AIGS is a multi-center bioengineering partnership and clinical study sponsored by the National Eye Institute. The designs and goals of AIGS were described previously.[16, 22] A more detailed description of the study protocols can be found in the AIGS Manual of Procedures, which can be downloaded from the website www.AIGStudy.net.

All study procedures adhered to the principles outlined in the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all participants. Institutional review board and ethics committee approval was obtained in all participating institutions. Study participants are classified into normal (N) and perimetric glaucoma (PG) groups, according to criteria described previously.[16,22] Only age-matched N and PG participants are used in this study. The ages of all participants were between 40 and

79 years at baseline. We performed age-matching selection, as previously described,[16] to prevent bias from age differences between the N and PG groups.

One aim of the AIGS is to evaluate glaucoma diagnostic accuracy using quantitative imaging instruments. The diagnostic variables evaluated in this paper were fast peripapillary RNFL thickness, optic disc variables (described below), and macular retinal thickness obtained by TD-OCT (Stratus OCT system; software version 4.0; Carl Zeiss Meditec, Inc., Dublin, CA, USA). Fast Stratus OCT scans of the optic disc and macular retina were generated from six 6-mm linear scans in a spoke-like radial configuration, each of which were 30 degrees apart. Optic disc data were generated from the automated determination of the disc margin as defined by the Stratus OCT software, which included horizontal integrated rim width (HIRW), vertical integrated rim area (VIRA), vertical cup/disc ratio (VCDR), horizontal cup/disc ratio, rim area, cup/disc area ratio, and cup area. By convention of the Stratus OCT software, the central 6-mm diameter macular region (20.8°) was divided into four quadrants: superior, inferior, nasal, and temporal. Each quadrant was further subdivided into inner and outer regions by a circumferential demarcation line 1.5 mm from the center of the macula. The mean macular retinal thickness was calculated as the weighted average of the sectoral macular thickness measurements given automatically by the Stratus. Performance of peripapillary RNFL thickness scans was as described previously.[16]

The fast scans of peripapillary RNFL thickness, optic disc, and macular retinal thickness were performed twice on the same day and the resulting measurements averaged. The photographers operating the Stratus OCT system were instructed to obtain all scans with signal strength scores of greater than 7 if possible. Scans with signal strength less than 6 were excluded from analysis. Data from both eyes were used. Right and left eye clock-hour data were analyzed together based on the assumption of mirror-image symmetry.

## Statistical Classification Analysis

We sought to combine diagnostic variables across anatomic regions to boost the diagnostic power by two types of classifiers: or-logic and machine learning classifiers. Both eyes of participants were used in the analysis while the inter-eye correlation was appropriately handled using available statistical approaches as we previously reported.[16] In brief, the t-tests were adjusted by the generalized estimating equation (GEE) approach,[23] and estimates of AROC, sensitivity, and variance were incorporated with robust variance-covariance estimates (Huber-White sandwich estimator).[24, 25]

The data were analyzed to characterize the participants and assess the diagnostic power of OCT single and combined variables. Participant characteristics were compared between the N and PG groups using two-tailed t-tests for continuous variables and $\chi^2$ tests for categorical variables. The performance of OCT variables was assessed by AROC for all variables along with sensitivity at 95% specificity for combined variables. Estimates and comparisons of AROC were computed based on the Obuchowski method[26] accounting for inter-eye correlation. This method is a generalization of the Delong method that has generally been used in other eye studies.[27] For comparison of sensitivities, we used a generalized McNemar's test to account for inter-eye correlation in estimation.[28]

**Or-Logic Classifier—**A diagnosis of glaucoma was made if any of the component variables was abnormal based on or-logic classification. In our previous study we derived a composite score based on the minimum standardized deviate values to construct the AROC for or-logic classification.[16] Since this method is only valid for Gaussian-distributed variables, we had to generalize our approach so that it could be applied to any distribution. The generalization was done by transforming the value of each variable into the cumulative

density function (CDF) based on the distribution of the N eyes. Thus, the composite score was formulated by the minimum CDF rather than the minimum standardized deviate. For example, overall, inferior, and superior RNFL thicknesses fit Gaussian distributions. If the composite score (based on previous derivation) of a particular eye had standardized deviate values of −1.75, −1.65, and −1.55 from the N group, then the CDF values would be 0.04, 0.05 and 0.06 respectively. The minimum 0.04 was used as the or-logic classifier to construct the AROC, and the eye would be diagnosed as a PG eye at the level of 95% specificity. The CDF calculation is valid for any parametric distribution and is more straightforward to classify an eye for any given cutoff value. Each OCT diagnostic variable was identified with well-known statistical distributions such as Gaussian, gamma, beta and others to construct the CDF in or-logic classifier.

**Machine Learning Classifiers—**As they have been widely used in other eye studies,[17, 29–31] we selected three machine learning classifiers, LDF, SVM, and RVM, to classify N and PG eyes. To assess the performance of each approach, we used sixteen-fold cross-validation to train and test all classifiers. In *k*-fold cross-validation, each fold was tested by the model trained by the other (*k*-1) fold and the entire procedure was repeated *k* times. This way, the composite score of each eye was generated by the model constructed from independent observations to yield unbiased assessment. Such cross-validation was not necessary for or-logic classifier since it does not involve any optimized procedure.

In the LDF approach, several diagnostic variables were multiplied by different weight coefficients and then formulated through a linear combination. The weights were computed so that the summed variable was optimized for discrimination between N and PG groups. To allow nonlinear combination, SVM and RVM with a Gaussian kernel were used in this study. SVM sought to draw a boundary to maximize the “separation” of diagnostic variables between N and PG eyes and searched supporting vectors located on the boundary for model fitting. Even in relaxing the constraint of linear relationship, it is common to observe non-separable data in high dimensional data. In this case, SVM assigns a parameter (generally denoted by *C*) to penalize the errors. Regarding the penalty for outliers and the relaxation of linear relationship, this approach yields more advantages over LDF. RVM employed a model of identical functional form used under the SVM along with Bayesian framework to identify relevance vectors rather than the supporting vectors. The classifier generated a 0 to 1 composite score reflecting glaucoma probability, which would render to clinicians a more intuitive interpretation for glaucoma diagnosis. In addition, the Bayesian machine learning classifier has been used in the HRT3 scanning laser tomography (SLT) machine to generate a glaucoma probability score.[32, 33]

To account for the inter-eye correlation, the LDF was generalized with robust variance-covariance estimates.[16] One eye was randomly selected from each participant in the training process of cross-validation under the SVM and RVM approaches as they required independent eyes to generate the support and relevance vectors respectively. Then the vectors were applied to both eyes of participants to generate the composite scores in the test process. A set of predictors was selected for classification analysis based on the set finalized in the or-logic classification since our previous study successfully selected a sufficient set of variables in combining the RNFL variables.

Statistical significance was accepted at $P < 0.05$. All analyses were done in SAS 9.1 and MATLAB 7.0. The MATLAB codes were freely available from http://asi.insa-rouen.fr/enseignants/~arakotom/toolbox/index.html for SVM and from http://www.miketipping.com/index.php?page=rvm">http://www.miketipping.com/index.php?page=rvm for RVM.

## Results

Analyses were performed on 96 N (184 eyes) and 96 PG (139 eyes) age-matched participants that were selected from a database of 111 N (214 eyes) and 130 PG (188 eyes) participants. There were no significant differences between the N and PG groups in terms of age and sex; however, there were more Caucasians in the N group (Table 1). In the PG group, 95 eyes (68.4%) had a mean deviation (MD) ≥ −6.0 dB (early glaucoma), 31 eyes (22.3%) had a MD between −6.01 and −12.0 dB (moderate glaucoma), and 13 eyes (9.3 %) had a MD ≤ −12 dB (advanced glaucoma).

All of the diagnostic variables were significantly different between N and PG groups (Table 2). All *P*-values determined by the GEE t-tests were < 0.0001 except two macular scans that had *P*-values ≤ 0.01.

We analyzed AROCs for diagnostic variables from optic disc, peripapillary RNFL, and macular retina (Table 3). We included only RNFL variables from the superior quadrant, inferior quadrant, and overall average RNFL thickness because the nasal and temporal quadrants have low diagnostic accuracy.[16] The 5 best diagnostic variables are optic disc HIRW, optic disc VIRA, inferior quadrant RNFL thickness, overall average RNFL thickness, and optic disc VCDR. The differences of AROCs between the top 5 variables were small and not significant. All macular retinal variables had relatively poor diagnostic accuracy. Among them, even the inferior outer macular thickness, which has the highest AROC value, performed significantly worse than the top four variables (P ≤ 0.01) from optic disc and RNFL thickness.

To evaluate the diagnostic performance of or-logic classifier, we chose the top 3 RNFL variables (superior quadrant, inferior quadrant, and overall average) and the top 3 optic disc variables (HIRW, VIRA, and VCDR). The highest AROC values were obtained when applying or-logic combination to all of the top 6 variables (AROC = 0.946, Table 4). That is, an eye would be diagnosed as having glaucoma if any of the 6 variables were abnormal. Such or-logic combination has a higher AROC than applying the same classifier to the top 3 RNFL variables (AROC = 0.928, *P* = 0.04) or the top 3 optic disc variables (AROC = 0.916, *P* = 0.07). The or-logic combinations that required any 2 variables to be abnormal for an abnormal classification did not perform as well as or-logic that required only 1 variable to be abnormal, although the difference was not statistically significant. Requiring more component variables to be abnormal further decreased AROC values (not listed in table).

Table 5 lists AROC values along with sensitivity at 95% specificity for the best combinations of optic disc and RNFL diagnostic variables. Machine learning classifiers and or-logic classification were employed to compare with the single diagnostic variable HIRW that had the highest AROC. To compute the sensitivity of the or-logic, we fixed the specificity for each of the 6 variables at 99.3% to reach an overall 95% specificity. Compared to the best single variable HIRW, combining diagnostic variables achieved a significantly higher glaucoma diagnostic accuracy as measured by the AROC. Indeed, all of the 19 single variables (Table 3) had significantly (*P* < 0.05) worse AROCs than any of the combination variables (Table 5). The diagnostic sensitivity of the best single variable, HIRW, was 0.648, significantly lower (*P* < 0.02) than the combination variables (Table 5), which all achieved sensitivities greater than 0.73. Although SVM achieved the highest diagnostic power, there were no statistically significant differences among the machine learning and or-logic classifiers.

Or-logic analysis was also performed on the subgroup of PG subject with early glaucoma (MD > −6 dB). We obtained an AROC (SE) of 0.927(0.017), with sensitivity (SE) of 0.642(0.053) at 95% specificity.

## Discussion

With inherently faster acquisition time and better image resolution and repeatability,[34–37] Fourier-domain OCT (FD-OCT) is rapidly replacing TD-OCT in both clinical and research settings. However, TD-OCT machines are still widely used clinically. Although comparative studies have demonstrated good correlation between measurements obtained from TD-OCT and FD-OCT, systemic differences in the two generations of instruments do not allow their output to be used interchangeably.[38–42] TD-OCT is capable of obtaining objective, quantitative, and reproducible measurements of certain anatomic regions of the eye, including RNFL thickness, optic disc topography, and macular retinal thickness.[43–46] Many studies have shown that there are no statistically significant differences between FD-OCT and TD-OCT in discriminating normal from glaucomatous eyes.[35, 41, 47–50] Thus it is still worthwhile to find the best way to clinically utilize the diagnostic information obtained from TD-OCT by using the large dataset accumulated in the AIGS. The AIGS also utilizes FD-OCT systems, and that data will be presented separately.

The AIGS previously found that a simple or-logic combination of the three best RNFL thickness variables (overall, superior quadrant, inferior quadrant) worked significantly better than single variable, and provided a simple practical approach to improving glaucoma diagnosis.[16] Using an LDF approach, Medeiros et al[17] demonstrated that a combination of selected optic disc and RNFL variables, when applied to an independent sample group, resulted in an AROC of 0.97 for glaucoma detection using the Stratus OCT. Bowd et al obtained enhanced differentiation of healthy from glaucomatous eyes by using RVM and SVM classifiers trained on RNFL thickness measurements obtained by scanning laser polarimetry.[29] In this article, we used a larger dataset and considered optic disc variables in addition to the RNFL variables. In addition, we employed more sophisticated machine-learning classifiers to evaluate the diagnostic power of combining various OCT-based diagnostic variables. The selection of variables was based on a post hoc approach in addition to information obtained from our previous study.[16]

We found that optic disc variables had the highest diagnostic power (AROCs) for discriminating glaucomatous from healthy eyes, followed by RNFL and macular retinal thickness variables. For our combined diagnostic variables, we chose as components the single variables with AROCs greater than 0.85, with the exception of cup/disc area ratio. We excluded that particular ratio because it was highly collinear with the VCDR. Highly collinear variables work poorly in LDF and other discriminant function approaches.[51] Because of low AROCs, all macular variables were excluded in the combination. For FD-OCT, such combination would have likely been different because macular ganglion cell complex mapping with FD-OCT achieves high diagnostic accuracy.[52]

Similar to previous articles, we found that combining multiple diagnostic variables significantly improved diagnostic accuracy over any single variable. The most surprising finding of the present study is that simple or-logic worked as well as the much more sophisticated machine learning and statistical classifiers, even in a relatively large combination of 6 variables from both the disc and RNFL regions. The fact that or-logic worked so well reflects the heterogeneous patterns of anatomic damage in glaucoma, some having more damage superiorly, some inferiorly, and some in a diffuse global pattern. This finding has great practical implication. In contrast to SVM, RVM, and LDF approaches, the or-logic approach does not require special software, does not require large training and

evaluation datasets for validation, and does not require additional Food and Drug Administration approval for such software and datasets. Using the or-logic approach, the practicing physician can identify at risk or glaucomatous eyes by simply looking at the most important anatomic variables measured by OCT. In the present study, the or-logic combination increased the AROC value by 0.037 and diagnostic sensitivity by 9%, compared to the best single variable, HIRW ($P = 0.03$). When applying or-logic to the group with early glaucoma, we obtained an excellent AROC value (0.927), suggesting that this approach is robust and applicable to the early diagnosis of glaucoma.

We have advocated for the use of or-logic combinations in a previous article that studied only RNFL variables.[16] The addition of 3 disc variables to the or-logic combination significantly improved AROC, showing that combining more variables reduced specificity only slightly but greatly increased the sensitivity of glaucoma detection. This worked particularly well with the diagnostic threshold of the component variables set near the 1$^{st}$ percentile level. Thus we recommend a practical diagnostic approach where glaucoma is suspected when any one of the 3 disc variables (HIRW, VIRA, VCDR) or RNFL thickness variables (overall, inferior, superior quadrant averages) is abnormal at the 1st percentile level. Of course, clinicians should not solely rely on an OCT printout to make the diagnosis of glaucoma given the limitations of OCT and the wealth of other historical and clinical information that need to be considered in glaucoma evaluation. The clinician should also assess the reliability of OCT variables by looking at the signal strength, RNFL and disc boundary detection by automated software, and the correlation of anatomic loss patterns with visual fields.

In summary, our present study demonstrated that the use of TD-OCT diagnostic information can be improved by combining the top diagnostic variables from the optic disc and peripapillary RNFL regions. Simple or-logic classification worked equally well as more sophisticated machine learning and statistical classifier approaches, and deserves further study in other advanced imaging modalities.

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**Table 1**

Characteristics of the Study Populations

| Parameter | N | PG | *P*-value |
|---|---|---|---|
| Subjects, n | 96 | 96 | |
| Eyes, n | 184 | 139 | |
| Age, year | 56.6 ± 9.5 | 58.2 ± 7.2 | 0.2 |
| % Female | 64.6% | 60.4% | 0.6 |
| % Caucasian | 89.6% | 70.8% | 0.001 |
| Mean Deviation, dB | −0.08± 0.95 | −4.74± 4.28 | <0.0001 |
| Pattern Standard Deviation, dB | 1.5± 0.3 | 6.0± 4.2 | <0.0001 |

N, Normal group; PG, Perimetric glaucoma group; Values are means ± standard deviations; *P*-values based on comparison of N and PG groups; dB, decibel.

## Table 2

Comparison Stratus OCT Variables in Normal and Perimetric Glaucoma Groups

| | N | PG | *P*-value |
|---|---|---|---|
| **RNFL Scan (μm)** | | | |
| Overall | 99.9±9.6 (74.6, 131.4) | 78±15.5 (35.3, 127.5) | <0.0001 |
| Inferior quadrant | 129.1±15.0 (93.5, 173.0) | 91.7±25.1 (42.0, 193.0) | <0.0001 |
| Superior quadrant | 121.3±14.9 (81.5, 159.5) | 92.7±23.1 (35.0, 146.5) | <0.0001 |
| **Optic Disc Scan** | | | |
| HIRW, $mm^2$ | 0.48±0.33 (0.14, 3.06) | 0.16±0.13 (0.01, 0.81) | <0.0001 |
| VIRA, $mm^3$ | 1.74±0.23 (1.14, 2.55) | 1.28±0.27 (0.65, 2.06) | <0.0001 |
| Cup Area, $mm^2$ | 0.70±0.48 (0.07, 2.58) | 1.38±0.61 (0.08, 3.69) | <0.0001 |
| Rim Area, $mm^2$ | 1.62±0.38 (0.00, 2.58) | 1.03±0.39 (0.23, 2.53) | <0.0001 |
| Cup/Disk Area Ratio | 0.29±0.17 (0.03, 1.00) | 0.56±0.17 (0.05, 0.90) | <0.0001 |
| Horizontal Cup/Disk Ratio | 0.54±0.17 (0.16, 1.00) | 0.76±0.14 (0.23, 0.97) | <0.0001 |
| Vertical Cup/Disk Ratio | 0.49±0.15 (0.15, 1.00) | 0.72±0.13 (0.20, 0.97) | <0.0001 |
| **Macula Scan (μm)** | | | |
| Inferior inner macula | 267.9±17.0 (213.5, 310.5) | 249.3±21.3 (201.0, 322.0) | <0.0001 |
| Superior inner macula | 269.7±17.8 (216.0, 309.5) | 256.8±20.3 (194.0, 309.0) | <0.0001 |
| Nasal inner macula | 270.5±19.2 (224.5, 331.0) | 259.4±21.0 (201.5, 322.0) | 0.0005 |
| Temporal inner macula | 258.0±17.5 (204.0, 297.5) | 241.3±19.0 (189.5, 324.5) | <0.0001 |
| Inferior outer macula | 224.7±16.5 (177.0, 273.5) | 201.2±18.6 (159.0, 257.0) | <0.0001 |
| Superior outer macula | 235.1±17.1 (175.0, 275.5) | 217.0±16.8 (163.5, 258.5) | <0.0001 |
| Nasal outer macula | 249.6±18.4 (198.0, 296.0) | 234.3±19.9 (179.5, 292.0) | <0.0001 |
| Temporal outer macula | 217.1±16.2 (159.0, 253.5) | 199.7±14.6 (168.5, 251.0) | 0.01 |

N, Normal group; PG, Perimetric glaucoma group; RNFL, peripapillary retina nerve fiber layer; HIRW, horizontal integrated rim width; VIRA, vertical integrated rim area; *P*-values based on comparison of N and PG groups. Values are means ± standard deviations. Values in parentheses are ranges.

## Table 3

Areas under the Receiver Operating Characteristic Curve Analysis for Single Stratus OCT Variables

| Rank | Scan | Variable | AROC (SE) |
|---|---|---|---|
| 1 | Optic Disc | Horizontal Integrated Rim Width | 0.909 (0.019) |
| 2 | Optic Disc | Vertical Integrated Rim Area | 0.908 (0.019) |
| 3 | RNFL | Inferior quadrant | 0.900 (0.019) |
| 4 | RNFL | Overall RNFL average | 0.892 (0.023) |
| 5 | Optic Disc | Vertical Cup/Disk Ratio | 0.89 (0.021) |
| 6 | Optic Disc | Rim Area | 0.878 (0.023) |
| 7 | Optic Disc | Cup/Disk Area Ratio | 0.871 (0.023) |
| 8 | RNFL | Superior quadrant | 0.850 (0.026) |
| 9 | Optic Disc | Horizontal Cup/Disk Ratio | 0.837 (0.027) |
| 10 | Macular | Inferior outer macula | 0.829 (0.028) |
| 11 | Optic Disc | Cup Area | 0.823 (0.028) |
| 12 | Macular | Temporal outer macula | 0.790 (0.031) |
| 13 | Macular | Superior outer macula | 0.769 (0.033) |
| 14 | Macular | Inferior inner macula | 0.760 (0.034) |
| 15 | Macular | Temporal inner macula | 0.758 (0.034) |
| 16 | Macular | Nasal outer macula | 0.721 (0.035) |
| 17 | Macular | Superior inner macula | 0.685 (0.038) |
| 18 | Macular | Nasal inner macula | 0.641 (0.039) |
| 19 | Macular | Fovea | 0.619 (0.041) |

AROC, area under receiver operating characteristic curve; RNFL, peripapillary retina nerve fiber layer; SE, standard error.

## Table 4

Area under Receiving Operator Characteristic Curve for Combined Stratus OCT Variables using the Or-Logic Classifier

| Rank | Variables | AROC (SE) |
|---|---|---|
| 1 | Any one of 6 diagnostic variables* | 0.946 (0.013) |
| 2 | Any 2 of 6 diagnostic variables* | 0.937 (0.015) |
| 3 | Any one of 3 RNFL diagnostic variables† | 0.928 (0.017) |
| 4 | Any one of 3 Optic Disc diagnostic variables‡ | 0.916 (0.018) |

*Six diagnostic variables: three variables were from optic disc scan (horizontal integrated rim width, vertical integrated rim area, and cup/disk vertical ratio) and the other three were from RNFL scan (overall average, inferior and superior quadrant RNFL thicknesses).

†Three RNFL diagnostic variables: overall average, inferior and superior quadrant RNFL thicknesses.

‡Three optic disc diagnostic variables: horizontal integrated rim width, vertical integrated rim area, and cup/disk vertical ratio. SE, standard error.

## Table 5

Area under Receiving Operator Characteristic Curve Sensitivity and Specificity Analyses for Combined Stratus OCT Variables

| Classifiers | AROC (SE) | *P*–value* | Sensitivity at 95% specificity (SE)† |
|---|---|---|---|
| Or-logic‡ | 0.946 (0.013) | 0.03 | 0.734 (0.042) |
| SVM‡ | 0.954 (0.012) | 0.002 | 0.777 (0.039) |
| RVM‡ | 0.943 (0.015) | 0.03 | 0.748 (0.042) |
| LDF‡ | 0.946 (0.013) | 0.03 | 0.755 (0.044) |

**P*-values were calculated in comparison to optic disc horizontal integrated rim width, the single scan with the highest AROC value.

†There were no significance differences among the combined variables.

‡Classification of the six diagnostic variables included three variables from optic disc scan (horizontal integrated rim width, vertical integrated rim area, and vertical cup/disk ratio) and the other three from peripapillary RNFL scan (overall average, inferior and superior quadrant RNFL thicknesses). SE, standard error.