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Estimating Lead Time Gained by Optical Coherence Tomography in Detecting Glaucoma before Development of Visual Field Defects

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Purpose: To estimate the diagnostic accuracy and lead time gained by retinal nerve fiber layer (RNFL) thickness measurements from optical coherence tomography (OCT) for detecting glaucoma before the development of visual field defects.

Design: Observational cohort study.

Participants: The study group included 75 eyes of 75 patients suspected of having glaucoma. These eyes had normal standard automated perimetry (SAP) at baseline and demonstrated repeatable (3 consecutive) abnormal tests during a median follow-up of 6.3 years. A control group of 75 eyes of 75 healthy subjects matched by age and number of OCT tests during follow-up was included.

Methods: The RNFL thickness measurements were obtained at the time of development of the earliest SAP defect (time 0) and also at times −1, −2, −3, and so forth, corresponding to 1 year, 2 years, 3 years, and so forth, before the development of field loss. The OCT measurements at corresponding intervals were analyzed for controls. Time-dependent receiver operating characteristic (ROC) curves were used to evaluate diagnostic accuracy of OCT.

Main Outcome Measures: Areas and sensitivities of ROC curve at fixed specificities at different times before development of field loss.

Results: At the date of conversion to the earliest visual field defect (time 0), mean ± standard deviation average RNFL thickness was 75.0±9.8 μm in glaucomatous eyes and 90.6±8.0 μm for controls ($P < 0.001$). Significant differences were seen up to 8 years before development of visual field defects (86.3±8.2 μm vs. 91.4±7.6 μm, respectively; $P = 0.021$). The ROC curve areas decreased with increasing times before detection of field defects. At times 0, −4, and −8 years, ROC curve areas were 0.87, 0.77, and 0.65, respectively. At 95% specificity, up to 35% of eyes had abnormal average RNFL thickness 4 years before development of visual field loss and 19% of eyes had abnormal results 8 years before field loss.

Conclusions: Assessment of RNFL thickness with OCT was able to detect glaucomatous damage before the appearance of visual field defects on SAP. In many subjects, significantly large lead times were seen when applying OCT as an ancillary diagnostic tool. *Ophthalmology 2015;122:2002-2009 © 2015 by the American Academy of Ophthalmology.*

Glaucoma is an optic neuropathy characterized by progressive neuroretinal rim thinning and excavation of the optic nerve head.[1] The loss of neural tissue may result in functional deficits, which are usually assessed by standard automated perimetry (SAP). Although the disease may remain asymptomatic until late stages, the diagnosis of moderate and severe cases is usually straightforward and can be confirmed based on the presence of typical visual field defects on SAP, such as arcuate defects, nasal step, or paracentral losses, associated with corresponding signs of glaucomatous optic nerve damage.

Glaucoma may occur in many patients before visual field defects are detectable on SAP, but the diagnosis can be challenging in this circumstance.[2,3] Because of the wide variability in the appearance of the optic nerve head, funduscopic examination at a single visit generally is insufficient to confirm the diagnosis.[3] Several imaging technologies have been used as ancillary diagnostic tests in this situation. The use of imaging devices may assist the clinician in identifying glaucomatous damage by providing objective quantification of the integrity of neural structures that may be affected by the disease, such as the neuroretinal rim and retinal nerve fiber layer (RNFL).[4−15] One of these technologies, optical coherence tomography (OCT), has been used widely for this purpose.[4−12]

Several previous studies have evaluated the diagnostic accuracy of OCT in glaucoma.[4−11,16] However, most of these studies have evaluated patients with clearly defined

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visual field defects, frequently showing moderate or even severe damage. Even in studies that have proposed to evaluate diagnostic accuracy in patients with early glaucoma, all cases had well-defined visual field defects that would be clearly diagnostic by themselves. When detecting the presence of disease, it should be obvious that an ancillary diagnostic test would not be necessary in cases where the diagnosis can be confirmed clearly by the presence of repeatable visual field defects. In this situation, one is most often interested in applying OCT to detect damage in cases with questionable field losses or where visual field defects cannot yet be demonstrated.

A longitudinal study involving a cohort of glaucoma suspects provides an optimum design to evaluate the diagnostic performance of OCT at the earliest stages of the disease. By following suspects until the first evidence of repeatable SAP defects develops, one can assess whether OCT is able to detect structural damage at the point of earliest confirmed functional loss. In addition, one can analyze the historical data and evaluate how far back in the past OCT started to show the earliest signs of damage before the appearance of visual field defects. Such design would provide information about the lead time that is gained by applying OCT as an ancillary test before patients demonstrate confirmed visual field loss.

In this study, we evaluated imaging results obtained with OCT in a cohort of glaucoma suspects followed up over time who demonstrated the earliest repeatable visual field defects. We evaluated OCT data that was available for several years before the development of visual field defects to estimate the lead time that could be gained by applying OCT for diagnosing the disease before the development of field defects.

Methods

This was an observational study. Participants from this study were included in a prospective longitudinal study designed to evaluate optic nerve structure and visual function in glaucoma (the Diagnostic Innovations in Glaucoma Study) conducted at the Hamilton Glaucoma Center at the Department of Ophthalmology, University of California, San Diego. The institutional review board approved the study methodology, which adhered to the tenets of the Declaration of Helsinki and to the Health Insurance Portability and Accountability Act.

At each visit during follow-up, subjects underwent a comprehensive ophthalmologic examination including review of medical history, best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure measurement, gonioscopy, dilated funduscopic examination, stereoscopic optic disc photography, and automated perimetry using the Swedish interactive threshold algorithm (standard 24-2). Only subjects with open angles on gonioscopy were included. Subjects were excluded if they had best-corrected visual acuity of less than 20/40, spherical refraction outside ±5.0 diopters (D), cylinder correction outside 3.0 D, or a combination thereof, or any other ocular or systemic disease that could affect the optic nerve or the visual field.

Participants

The study group (cases) consisted of 75 eyes of 75 patients suspected of having glaucoma who were followed as part of the Diagnostic Innovations in Glaucoma Study cohort and demonstrated repeatable abnormal visual fields during follow-up, that is, converted to glaucoma. The initial diagnosis as glaucoma suspect was based on the suspicious appearance of the optic disc or elevated intraocular pressure (>21 mmHg), but normal standard automated perimetry results at baseline. Normal visual fields were defined based on mean deviation (MD) and pattern standard deviation within 95% confidence limits and glaucoma hemifield test results within normal limits. These eyes had a median follow-up of 6.3 years (first quartile, 4.1 years; third quartile, 8.9 years) until the development of repeatable abnormal SAP defects. Repeatable abnormal SAP results were defined based on the presence of a sequence of 3 consecutive abnormal SAP results with pattern standard deviation with $P < 0.05$ or glaucoma hemifield test results outside normal limits. Imaging assessment of the RNFL with OCT was performed at the time (within ±3 months) of the first visual field of the sequence of 3 repeatable abnormal fields. In addition, OCT data also were available and analyzed for the period of follow-up before development of the earliest visual field defect (details on data analysis are described below).

A control group matched by age and number of OCT tests during follow-up was included in the study consisting of 75 eyes from 75 healthy participants. These subjects were recruited from the general population and were required to have normal ophthalmologic examination results and intraocular pressure of less than 22 mmHg in both eyes. In addition, they had normal SAP visual field test results during follow-up. Healthy eyes were chosen as the control group because we were interested in evaluating the amount of neural loss associated with early visual field defects or before these defects, compared with normal expected age-matched results. Although a group of glaucoma suspects who did not demonstrate visual field loss initially could be considered a control group, these eyes could have sustained structural damage before functional losses, and therefore, would not constitute a suitable control group for the purposes of this study. Our design best replicates the common clinical practice situation of comparing the results of a test acquired in a patient suspected of glaucoma with a normative age-matched database.

Visual Field Testing

All patients underwent SAP testing using Swedish interactive threshold algorithm standard 24-2 strategy during follow-up. All visual fields were evaluated by the University of California, San Diego, Visual Field Assessment Center.[17] Visual fields with more than 33% fixation losses or more than 15% false-positive errors were excluded. Visual fields exhibiting a learning effect (i.e., initial tests showing consistent improvement on visual field indices) also were excluded. Visual fields were reviewed further for the following artifacts: lid and rim artifacts, fatigue effects, inappropriate fixation, evidence that the visual field results were the result of a disease other than glaucoma (such as homonymous hemianopia), and inattention. The Visual Field Assessment Center requested repeats of unreliable visual field test results, and these were obtained whenever possible.

Optical Coherence Tomography Testing

To maximize the amount of OCT data available during follow-up, we analyzed tests from both time-domain OCT (Stratus OCT; Carl-Zeiss Meditec, Dublin, CA), as well as spectral-domain (SD) OCT (Cirrus HDOCT; Carl Zeiss Meditec). The principles of operation of these instruments have been described in detail elsewhere.[4,5] The RNFL thickness measurements were acquired at a peripapillary 3.46-mm diameter circular scan (10 870-μm length) placed around the optic

disc. To be included, all images were reviewed for noncentered scans and had to have signal strength of more than 6, absence of major movement artifacts, and good centering on the optic disc. The parameter investigated in this study was the global average thickness, corresponding to the average of RNFL thickness measurements obtained in the 360° peripapillary circle. This parameter was chosen because it has been reported as having one of the best, if not the best, diagnostic accuracy in previous studies with OCT.[4,6,12,18,19] Also, this parameter has shown the best reproducibility in previous studies with longitudinal OCT data.[20–22]

As the result of change in OCT technology over time, Stratus OCT images were acquired from 2002 through 2009 and images with Cirrus HDOCT were acquired from 2009 until 2014. Because measurements from these 2 instruments are not directly interchangeable, a conversion factor was obtained from a subgroup of 63 eyes of 63 subjects who had testing with both Stratus OCT and Cirrus HDOCT on the same day during the transition period. The following conversion formula was used by applying a Passing-Bablock regression[23]:

Cirrus HD average thickness = 8.121 + 0.837 × Stratus OCT average thickness.

Data Analysis

For the purposes of this study, time 0 was defined as the date of conversion to the earliest visual field defect for cases. The conversion date was considered the date of the first of the 3 repeatable abnormal visual fields. The OCT examinations that were obtained within 3 months of the conversion date and also before the date of conversion were analyzed for cases. We report OCT measurements obtained at time −1, −2, −3, and so forth, corresponding to 1 year, 2 years, 3 years, and so forth, before the development of visual field defects. The OCT measurements at corresponding intervals also were analyzed for the controls, where time 0 then was determined to be the last available OCT during follow-up.

One would expect that as time t becomes more negative, that is, further before the date of conversion, the ability of OCT to detect the presence of glaucomatous damage would decrease. To evaluate the effect of time before visual field loss on diagnostic accuracy of OCT, we used time-dependent receiver operating characteristic (ROC) curves obtained from an ROC regression model. Application of ROC regression to the ophthalmic literature has been described in detail previously by Medeiros et al and other investigators.[18,24–26] In brief, this model allows the investigation of the effect of covariates on the ROC curve by modeling these curves using a generalized linear regression model. In the current application, time was included as a disease-related covariate, allowing one to obtain estimates of diagnostic accuracy at specific points in time.[27,28] Parameters were estimated using probit regression. To obtain confidence intervals for regression parameters, a bootstrap (with case-control sampling) procedure was used (n = 1000 resamples).[29] The area under the ROC curve was used to summarize the diagnostic accuracy. The ROC curve area ranged from 0.5 to 1.0, with 1.0 indicating perfect discrimination between cases and controls and 0.5 indicating chance discrimination.

All statistical analyses were performed with commercially available software (STATA version 13; Stata Corp, LP, College Station, TX). The α level (type I error) was set at 0.05.

Results

Table 1 shows demographic and clinical characteristics of included subjects at the date of development of the earliest visual field defect for glaucoma patients and at the closest corresponding date for controls. Mean age was 68.3±11.2 years and 65.4±9.0 years for glaucomatous and control subjects, respectively ($P = 0.082$). The median number of OCT tests was 5 (first quartile, 3; third quartile, 7) for both groups ($P = 0.879$). At the date of visual field conversion, average MD and pattern standard deviation of glaucomatous eyes were −1.97±2.1 dB and 2.7±1.1 dB, respectively.

Table 1. Demographic and Clinical Variables for Glaucoma Cases and Controls

	Glaucoma (n = 75)	Controls (n = 75)	P Value
Age (yrs)	68.3±11.2	65.4±9.0	0.082
Female gender (%)	61	61	1.000
Race, no. (%)			
White	48 (64)	53 (71)	0.506
Black	26 (35)	20 (27)	
Asian	1 (1)	2 (2)	
SAP MD at baseline (dB)	−0.84±1.31	−0.47±1.17	0.068
SAP PSD at baseline (dB)	1.64±0.32	1.54±0.24	0.092
SAP MD at time 0* (dB)	−1.97±2.07	−0.02±1.37	<0.001
SAP PSD at time 0* (dB)	2.65±1.15	1.65±0.35	<0.001
No. of OCT tests during follow-up, median (first quartile, third quartile)	5 (3, 7)	5 (3, 7)	0.879
Total follow-up time (yrs)	6.4±3.3	6.6±3.6	0.739

MD = mean deviation; OCT = optical coherence tomography; PSD = pattern standard deviation; SAP = standard automated perimetry.
Data are mean ± standard deviation unless otherwise indicated.
*Time 0 corresponds to the date of conversion to the earliest detectable visual field defect in glaucoma cases and the last follow-up date for controls.

Table 2 shows average RNFL thickness measurements at the date of conversion for glaucomatous eyes and at the corresponding time for controls. At conversion, mean ± standard deviation average RNFL thickness was 75.0±9.8 μm in glaucomatous eyes and 90.6±8.0 μm for controls ($P < 0.001$). Mean values are also shown for different periods before the date of conversion. For example, at $t = -4$ years, corresponding to 4 years before conversion, mean average RNFL thickness was

Table 2. Retinal Nerve Fiber Layer Thickness Measurements Obtained by Optical Coherence Tomography at Different Times during Follow-up

Time (yrs)	No.*	Glaucoma	Controls	P Value
0†	150	75.0±9.8	90.6±8.0	<0.001
−2	136	79.7±9.0	90.4±7.8	<0.001
−4	108	81.3±9.9	91.0±8.0	<0.001
−6	90	83.6±8.0	91.2±7.6	0.002
−8	52	86.3±8.2	91.4±7.6	0.021

Data are mean ± standard deviation in micrometers unless otherwise indicated.
*Total sample size (matched cases and controls) available at each time point.
†Time 0 corresponds to the date of conversion to the earliest detectable visual field defect in glaucoma cases and last follow-up date for controls. Negative time values correspond to years before time 0.

Table 3. Areas under the Receiver Operating Characteristic Curves with Sensitivities at Fixed Specificities for Discriminating Glaucomatous from Control Eyes at Different Times during Follow-up*

Time (yrs)	Receiver Operating Characteristic Curve Area	Sensitivity at Specificity = 95%	Sensitivity at Specificity = 80%
0*	0.87 (0.82–0.92)	53% (40%–67%)	77% (68%–87%)
−2	0.82 (0.77–0.88)	44% (31%–56%)	69% (60%–79%)
−4	0.77 (0.70–0.84)	35% (21%–48%)	61% (49%–72%)
−6	0.71 (0.62–0.81)	26% (12%–40%)	51% (36%–66%)
−8	0.65 (0.52–0.78)	19% (5%–33%)	42% (23%–60%)

*Corresponds to the date of conversion to the earliest detectable visual field defect in glaucoma cases and last follow-up date for controls. Negative time values correspond to years before time 0.

81.3±9.9 μm and 91.0±8.0 μm for glaucoma patients and controls, respectively ($P < 0.001$). Significant differences between glaucomatous and healthy eyes were still seen even at 8 years before the date of visual field conversion ($t = -8$ years), with mean RNFL thicknesses of 86.3±8.2 μm and 91.4±7.6 μm, respectively ($P = 0.021$).

Table 3 shows ROC curve areas for discriminating between glaucomatous and control eyes. Figure 1 shows the corresponding ROC curves. At the date of conversion to the earliest visual field defect, the ROC curve area was 0.87 (95% confidence interval, 0.82–0.92). As expected, ROC curve areas decreased with increasingly longer times before detection of the earliest field defect. For example, at 4 years before field losses were detected, the ROC curve area was 0.77 (95% confidence interval, 0.70–0.84). Although a significant decrease in ROC curve areas was seen, a statistically significant ROC curve area (i.e., discrimination better than chance) was seen up to 8 years before development of visual field defect (ROC curve area, 0.65; 95% confidence interval, 0.52–0.78). Sensitivities for fixed specificities at 95% and 80% also are shown on Table 3. Figure 2 illustrates a case from the study.

Discussion

This study demonstrated that significant loss of the RNFL was detected by OCT several years before the development of visual field loss. By following up a cohort of glaucoma suspects over time, we were able to quantify neural losses at different times before development of the earliest signs of visual field damage. Our approach allowed us to evaluate the lead time that could be gained by applying OCT in diagnosing glaucoma before a visual field defect is detectable by SAP. These results may be important in the assessment of OCT as an ancillary diagnostic tool in glaucoma.

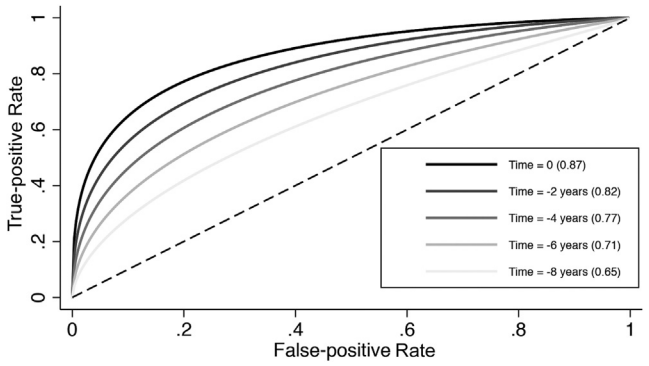

Figure 1. Receiver operating characteristic curves for discriminating glaucomatous from control eyes. Time 0 corresponds to the date of conversion to the earliest detectable visual field defect in glaucoma cases and last follow-up date for controls. Negative time values correspond to years before time 0.

To be able to estimate RNFL thickness abnormalities associated with the earliest detectable visual field losses on SAP, we followed up a cohort of glaucoma suspects longitudinally over time until they showed evidence of repeatable visual field defects. The criteria used to define visual field losses were those applied by the Ocular Hypertension Treatment Study[30,31] and are widely used in clinical practice, requiring confirmation of abnormalities in 3 consecutive visual fields. This greatly decreases the chance that the abnormalities seen on perimetry may represent just variability rather than true defects. At the time of development of the earliest visual field defect, mean average RNFL thickness was 75 μm in glaucomatous eyes, compared with 90 μm from the age-matched healthy group ($P < 0.001$). Interestingly, this value is almost identical to the threshold for RNFL thickness loss (75.3 μm) where visual field defects become detectable as estimated in a previous cross-sectional study.[32] Importantly, OCT showed good ability to discriminate glaucomatous from healthy eyes at this point, with a ROC curve area of 0.87. At specificities of 80% and 95%, the sensitivities were 77% and 53%. A sensitivity of 53% for specificity at 95% implies a positive likelihood ratio of $0.53 / (1 - 0.95) = 10.6$, which is considered quite large and able to change the probability of disease substantially.[12,33]

When used as an ancillary tool to diagnose disease, it is important to evaluate the benefit that OCT assessment can provide in addition to standard diagnostic tools, such as funduscopy and visual field testing. By including only cases with confirmed visual field defects, most previous studies on diagnostic accuracy of OCT failed to evaluate this issue. For example, in the study of diagnostic accuracy published by Leung et al,[6] the average MD of the visual field of glaucoma cases was −8.66 dB, indicating that most glaucoma patients had at least moderate visual field damage. For comparison, the average MD of our patients at the time of the earliest field defect was −1.97 dB. It should be obvious that if a

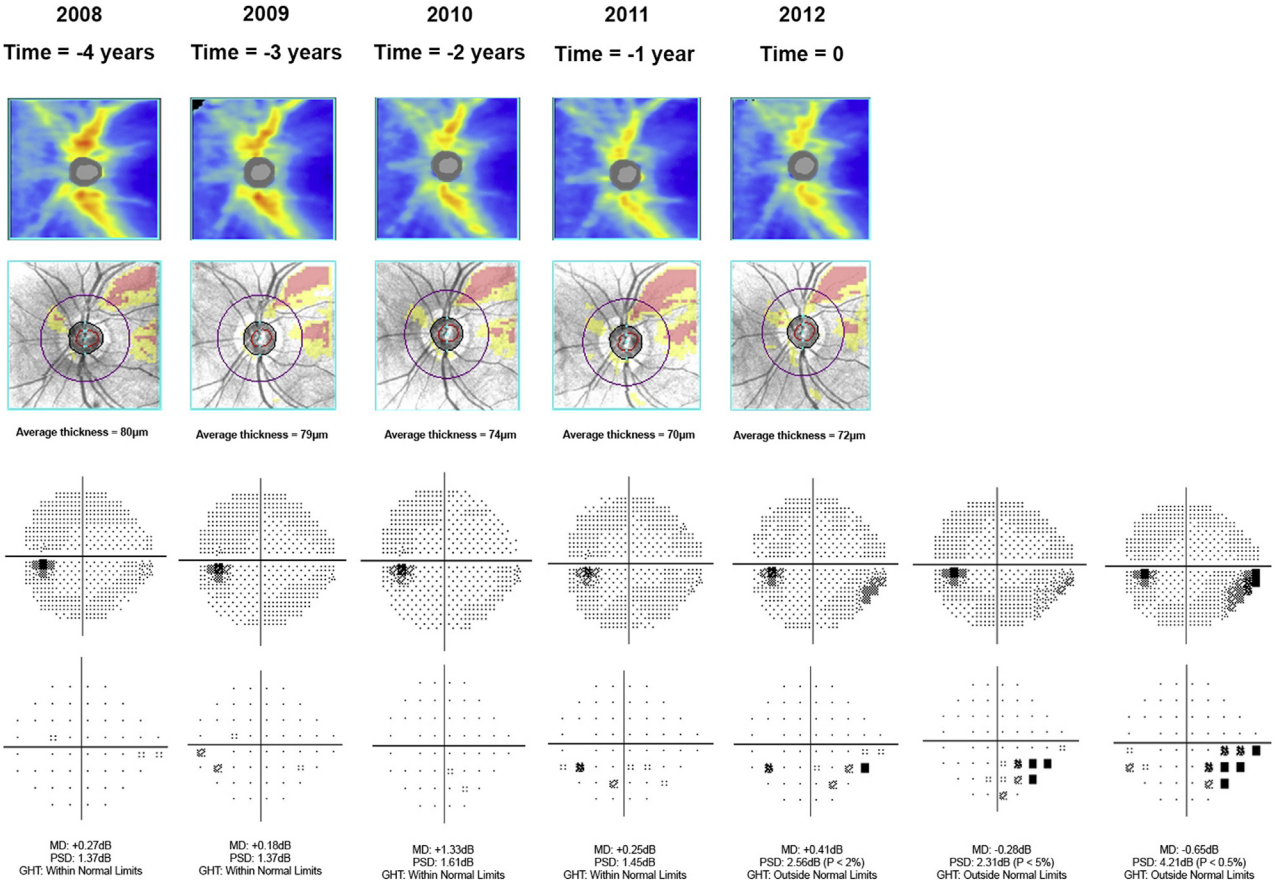

Figure 2. Example of a glaucomatous eye included in the study. The figure shows the color-coded retinal nerve fiber layer thickness map and mean deviation (MD) map from spectral-domain optical coherence tomography, as well as grayscale and pattern standard deviation (PSD) plots from standard automated perimetry. Time 0 corresponds to the date of conversion to the earliest detectable visual field defect, which occurred in 2012 for this eye. The subsequent visual fields confirmed the defect. Spectral-domain optical coherence tomography results for this eye were available up to time −4 years, that is, 4 years before development of visual field defect. GHT = glaucoma hemifield test.

repeatable glaucomatous visual field defect is present, the defect itself is already diagnostic, so there is no need to apply another potentially costly tool for this purpose in clinical practice. Therefore, the design of our study attempted to evaluate the ability of OCT in detecting neural loss before repeatable visual field defects would become clearly apparent. We demonstrated that significant differences between glaucomatous eyes and controls were seen for several years preceding the earliest field defect. However, as expected, the diagnostic ability decreased with increase in the time before field losses.

Our results may have important implications in considering whether the use of OCT as an ancillary test for diagnosis is justifiable. If the lead time that could be gained by applying OCT is too short, its use in this circumstance may not be justifiable, because one could as easily monitor subjects until repeatable visual field defects would become recognizable, without being penalized by late detection of damage. In our study, we demonstrated that a lead time of up to 8 years could be obtained in some patients by using OCT. However, it is important to note that the proportion of patients showing abnormal results with OCT before development of field loss decreased progressively with increase in the time before the appearance of a field defect. For example, at 95% specificity cutoff, up to 44% of subjects had abnormal average RNFL thickness at 2 years before development of a field defect (Table 3). This number reduced to 35% at 4 years and to 19% at 8 years. Although 19% may be seen as an apparently small proportion, it is important to consider that 8 years is a relatively large amount of time and such lead time could have significant management implications to a significant group of patients. In fact, our results suggest that OCT could detect damage in approximately one-third of glaucoma patients up to 5 years before the appearance of the earliest visual field defects. However, it is important to emphasize that the benefit of treatment at this stage in preventing future functional disability from glaucoma has not yet been demonstrated. Regardless, detection of early damage may still have important implications in management decisions, such as establishing frequency of follow-up and patient counseling.

Only 53% of glaucoma patients could be declared to have abnormal OCT results at the time of earliest development of

field defects using a 95% specificity cutoff. It is likely that this number could be higher if multiple OCT parameters investigating damage by hemifields or by localized regions had been used. However, use of multiple parameters may also increase false-positive results. Subjects in our study were followed up carefully over time until development of field defects. It is possible that in clinical practice, the frequency of visual field testing would be lower, resulting in longer delays in detecting a confirmed visual field defect. Therefore, the benefit provided by OCT on the percentage of subjects detected before field damage and on lead times could be higher in clinical practice. Despite this, our results should not be seen as indicating that OCT should replace visual field as a diagnostic tool for glaucoma, but rather that it can provide useful information as an ancillary diagnostic tool. It is likely that many patients who still have OCT results within normal limits at the time of development of earliest field losses may have had progressive RNFL thickness change over time. This highlights the importance of longitudinal monitoring of glaucoma suspects over time. A recent study by Miki et al[34] showed that eyes of suspects who converted to glaucoma had a rate of RNFL thickness change of −2.02 μm/year compared with −0.82 μm/year ($P < 0.001$) for eyes that did not convert to glaucoma. Detection of longitudinal change may improve the ability of OCT in both diagnosing the disease and detecting progression. However, the purpose of our study was not to investigate longitudinal changes over time, but rather to assess the validity of OCT as an ancillary diagnostic tool when used in a cross-sectional assessment, as commonly performed in clinical practice. Approaches that combine structure and function also have been shown to improve diagnosis both in cross-sectional,[35,36] as well as longitudinal[37–40] investigations, and it would be interesting to assess whether they can increase the lead time for diagnosis before a field defect is apparent.

It is important to emphasize that the analysis of diagnostic accuracy provided in our study should be evaluated in the appropriate context of use of OCT. Our study targeted subjects who would be considered glaucoma suspects and referred for further evaluation at a tertiary center. Our purpose was not to evaluate the accuracy or benefit that could be provided by using OCT as a diagnostic tool in population-based screening. The concept of lead time also would be different in a screening situation. From a public health perspective, early diagnosis actually would mean diagnosis at a stage earlier than would have presented symptomatically. Given that symptomatic presentation of glaucoma is likely to occur only very late in the course of the disease, detecting cases with even moderate damage could still increase the lead time until appearance of symptoms substantially, facilitating appropriate treatment to prevent functional impairment.

Our study had limitations. To maximize the amount of OCT data available, we included scans obtained with the older version of the technology, time-domain OCT, and a conversion factor to SD OCT was applied. This was necessary because of the relatively recent introduction of SD OCT. Although it could be argued that this approach may introduce bias, the cross-sectional diagnostic accuracy of time-domain OCT was reported to be comparable with SD OCT in previous studies.[4,6,19,41] In addition, cases and controls were matched by number of OCT tests during follow-up, and we did not attempt to estimate longitudinal changes over time, which could be more problematic when mixing tests from different versions of OCT. It also should be noted that our ability to estimate the lead time was limited by the duration of follow-up of the study. It is possible that longer lead times could have been obtained for some subjects with longer follow-up times. Another limitation of our study is that some of the suspects had different treatments, which were introduced at different periods during follow-up at the discretion of the attending ophthalmologist. The treatments may have lengthened the lead time until development of visual field loss. However, our estimates of diagnostic accuracy would still be valid and the lead times would still represent those expected for patients following standard clinical care.

In conclusion, assessment of RNFL thickness with OCT was able to detect glaucomatous damage before the appearance of visual field defects on SAP. In many subjects, significantly long lead times would be gained when applying OCT as an ancillary diagnostic tool. Future research should evaluate the implications of OCT-assisted decision making in preventing functional impairment and disability in glaucoma.

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Abbreviations and Acronyms:
MD = mean deviation; **OCT** = optical coherence tomography; **RNFL** = retinal nerve fiber layer; **ROC** = receiver operating characteristic; **SAP** = standard automated perimetry; **SD** = spectral-domain.

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