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Effect of Testing Frequency on the Time to Detect Glaucoma Progression with OCT and OCT Angiography

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Abstract

Purpose: To determine how the frequency of testing affects the time required to detect statistically significant glaucoma progression for circumpapillary retinal nerve fiber layer (cpRNFL) with ocular coherence tomography (OCT) and circumpapillary capillary density (cpCD) with OCT angiography (OCTA).

Design: Retrospective, observational cohort study.

Methods: In this longitudinal study, 156 eyes of 98 patients with glaucoma followed up over an average of 3.5 years were enrolled. Participants with 4 or more OCT and OCTA tests were included to measure the longitudinal rates of cpRNFL thickness and cpCD change over time using linear regression. Estimates of variability were then used to recreate real-world cpRNFL and cpCD data by computer simulation to evaluate the time required to detect progression for various loss rates and different testing frequencies.

Results: The time required to detect a statistically significant negative cpRNFL and cpCD slope decreased as the testing frequency increased, albeit not proportionally. cpCD detected progression

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slightly earlier than cpRNFL. 80% of eyes with a cpCD loss of−1%/year were detected after 6.0, 4.2, and 4 years when testing was performed one, two, and three times per year, respectively. Progression in 80% of eyes with a cpRNFL loss of −1 μm /year was detected after 6.3, 5.0., and 4.2 years, respectively.

Conclusions: cpRNFL and cpCD are comparable in detecting progression. As there were only small changes in the time to detect progression when testing increased from two to three times per year, testing twice per year may provide sufficient information for detecting progression with either OCT or OCTA in clinical settings.

Keywords

Optical Coherence Tomography Angiography; optic nerve head vessel density; retinal nerve fiber layer; glaucoma

Introduction

Glaucoma is a slowly progressive optic neuropathy characterized by damage to the retinal ganglion cell (RGC) axons at the level of the optic nerve head (ONH) and subsequent loss of RGCs across the retina.[1, 2] Timely detection of the disease and its progression are essential for effective treatment.[3]

In patients with an established diagnosis of glaucoma, evidence of progression will influence a clinician's decision whether to modify glaucoma therapy.[4] Despite improved testing paradigms for detecting progression, clinicians need practical recommendations for measuring clinically relevant rates of glaucomatous progression.[4–7] In this regard, the maximum number and frequency of testing are limited in real clinical settings because of the burden on the patients, physician, and healthcare system.[8]

Previous studies investigated the time to detect progression according to different test frequencies and follow-up schemes for the visual field (VF). [7, 9–14] Wu et al., suggested that obtaining two reliable tests at baseline followed by semiannual testing and confirmation of progression through repeat testing in the initial years of follow-up may provide a good compromise for detecting progression due to variability of VF.[13]

In clinical practice, testing with OCT and OCTA complements routine VF testing.[15] Optical coherence tomography (OCT), especially optic nerve head OCT is a standard tool for monitoring structural findings in glaucoma.[16, 17] Optical coherence tomography angiography (OCTA), a test that quantifies with good reproducibility vessel density of the optic disc and macula,[18] also can enhance glaucoma diagnosis and monitoring.[19,20] OCTA vessel density measurements has similar performance as cpRNFL to detect glaucoma.[21, 22] Moreover, there can be widely different individual rates of change based on VF and OCT/OCTA in any group of patients.[23] Therefore, timely information about glaucoma progression deriving from both instruments is helpful for management of glaucoma patients.[15]

While some studies investigated how time to detect progression varies according to different test frequencies and follow-up schemes for the VF,[9, 10, 12, 13, 24] ophthalmologists lack guidelines on how frequently patients should undergo OCT and OCTA examinations. The

current study aims to determine the effect of frequency of testing on time required to detect glaucomatous progression for OCT determined circumpapillary retinal nerve fiber layer (cpRNFL) and OCTA determined circumpapillary capillary density (cpCD) by simulating various rates of loss found in clinical settings.

Methods:

Participants

This longitudinal study includes POAG patients enrolled in the Diagnostic Innovations in Glaucoma Study (DIGS)[25, 26] who underwent both OCT and OCTA testing. Institutional review board approval was obtained, and written informed consent was acquired from all participants. This study adhered to the tenets of the Declaration of Helsinki and was conducted in accordance with the Health Insurance Portability and Accountability Act.

Inclusion criteria include 1) diagnosis of open angles on gonioscopy, 2) a best-corrected visual acuity of 20/40 or better, and 3) age more than 18 years old 4) at least 2 years of follow-up a minimum of four follow-up OCTA and OCT scanning sessions. In addition, POAG was defined as the presence of repeatable and reliable (fixation losses and false negatives ≤ 33% and false positives ≤ 15%) abnormal standard automated perimetry tests using the 24–2 Swedish Interactive Thresholding Algorithm with either a PSD outside the 95% normal limits or a GHT result outside the 99% normal limit.[27, 28]

Eyes were excluded that had 1) a history of trauma or intraocular surgery (except for uncomplicated cataract surgery or glaucoma surgery), (2) coexisting retinal disease, (3) uveitis, or (4) non-glaucomatous optic neuropathy. Participants diagnosed with Parkinson's disease, Alzheimer's disease, dementia, or a history of stroke and those with axial length of more than 26 mm or a spherical equivalent of less than −6 diopter were also excluded.

Imaging

Subjects were enrolled who had at least 4 visits with good quality OCT (Optovue Inc, Fremont, California, USA) and OCTA (Optovue Inc, Fremont, California, USA) imaging on the same day. ONH microvasculature was evaluated using the AngioVue OCT system (software version 5.6.3.0). This system previously has been described.[29] The ONH 4.5 × 4.5-mm^2 scans (304 B-scans x 304 A-scans per B-scan) centered on the ONH were obtained. Vessel density was automatically calculated as the proportion of measured area occupied by flowing blood defined as pixels having decorrelation values acquired by the split-spectrum amplitude-decorrelation angiography algorithm above the threshold level. According to the University of California, San Diego, Imaging Data Evaluation and Analysis Reading Center standard protocol, an image quality review was done on all scans. Trained graders reviewed scans and excluded poor-quality images, defined as images with (1) a signal strength index of less than 48, (2) poor clarity, (3) residual motion artifacts visible as irregular vessel pattern or disc boundary on the en face angiogram, (4) local weak signal, or (5) segmentation errors. In addition, the location of the disc margin in the ONH scans was reviewed for accuracy and was adjusted manually if required.

A series of vascular and thickness parameters were measured, including retinal nerve fiber layer (cpRNFL) and circumpapillary capillary density (cpCD).

Computer Simulations

We created a computer simulation to evaluate the time required to detect different cpRNFL and cpCD progression rates. First, the expected variability (noise) of cpRNFL cpCD was derived in the longitudinal clinical data by fitting an ordinary least squares regression to their values over time within-subject. The observed values were subtracted from the fitted value to calculate the residuals, which were then categorized in 5 bins according to the fitted values. The noise component was then sampled randomly from these residuals and added to the simulated values. Then, it was possible to reconstruct how the cpCD and cpRNFL would appear in real-world clinical practice, similarly as previously performed for the VF.[13]

We first evaluated the specificity of clinical protocols using a progression rate of 0 (μm/year or %/year) to simulate glaucoma eyes that were truly stable so that the specificity of the clinical paradigms could be evaluated for different frequencies of testing per year.

For all subsequent simulations, a clinical protocol that met the definition of cpCD and cpRNFL progression (negative slope, and $p<0.05$) was used. This protocol was applied to sequences that assumed progression rates of −0.50, −1.5 −1.00, and −2.00 (%/year or μm/year) for different testing frequencies per year (once, twice, and thrice). A total of 200,000 sequences were generated for each of these conditions, and the time when 80% and 90% of simulated eyes were detected as having progressed was recorded. The percentages of simulated eyes detected as having progressed after 2 and 5 years was also recorded. A similar protocol was performed with normalized data to compare cpCD and cpRNFL change rates, as described previously.[30, 31] In brief, the dynamic range of certain measurement was estimated by calculating the top and bottom 3% of eyes. Percent of dynamic range change= [(visit value − floor value) /dynamic range] × 100/year. The unit of the normalized coefficients is %/year, meaning annual percent change of the dynamic range.

Statistical analysis

Patient and eye characteristics data were presented as mean (95% confidence interval (CI)) for continuous variables and count (%) for categorical variables. Statistical analyses were performed using Stata version 15.1 (StataCorp, College Station, TX), and R version 3.6.3. P values of less than 0.05 were considered statistically significant for all analyses.

Results

This study included 156 eyes of 98 patients with a mean (95% CI) baseline age of 68.6 (66.8, 70.4) years over a mean (95% CI) follow-up time of 3.5 (3.4, 3.6) years. A total of 21 eyes were excluded due to poor image quality. One-hundred twenty-seven eyes (81.4%) had early glaucoma at baseline with MD better than −6.0 dB and 29 (18.6%) eyes had moderate to advanced VF loss (MD worse than −6 dB). The patients were seen over a mean (95% CI) of 5.3 (5.1, 5.5) visits. At the first visit, the mean (95%CI) cpRNFL and cpCD for all the eyes were 78.7 (76.0, 81.3)μm and 43.9 (42.9, 44.8)%, respectively. Demographic and clinical characteristics of the enrolled eyes are displayed in Table 1.

Detection of Progression for Different Rates of Loss with respect to Different Frequency of testing per year

The time required to detect progression of cpCD and cpRNFL change over time in eyes with different rates of loss with respect to various frequencies of testing per year are presented in Tables 2 and 3. Similar results were found with normalized data. Overall, the time required to detect progression was comparable between cpCD and cpRNFL and decreased as the frequency of testing increased for both cpCD and cpRNFL. With similar testing frequency, cpCD detects progression slightly sooner than cpRNFL.

Increasing the testing frequency from two to three times per year showed a smaller gain than an increase from testing once to twice per year. For example, the cpCD showed that 80% of eyes that had a decline of −1%/year progressed over 6, 4.2, and 4.0 years when the testing was performed once, two, and three times per year. In cpRNFL, a total of 6.3, 5.0, and 4.2 years on average were required before significant progression was considered to have occurred in 80% of the eyes that had a decline of −1μm/year when testing was performed one, two, and three times per year, respectively. Figures 1 shows the time required to detect −1%/year of change for cpCD and −1μm/year of change for cpRNFL when the different frequencies of testing are performed. As demonstrated with a similar frequency, cpCD detects progression slightly sooner than cpRNFL.

Table 2 and 3 also shows the proportion of eyes progressing (i.e., power to detect progression) after 2 and 5 years. Similar results were found with normalized data. For example, with the cpCD loss of – 1.5%/year, 11.1% and 34.6% of eyes progressed with one and two tests per year, respectively, at the end of 2 years. Performing 3 tests per year changed the proportion of eyes progressing with −1.5%/year loss to 51.3%. With the cpRNFL thinning of −1.5 μm/year, 10%, and 29.3% of eyes were detected as having progressed when testing was performed one and two times at the end of two years. With a moderate increase in the proportion of eyes progressing, 42.0% of eyes with cpRNFL thinning of −1.5μm/year progressed when the testing frequency was performed three times per year. With a cpCD loss of −1%/year, 7.7%, 21.5%, and 32% of eyes were detected as having progressed at the end of 2 years when testing was performed one and two and three times per year, respectively. Similar results were found with a cpRNFL thinning of −1μm/year, 7.1%, 19.1%, and 27.6% of eyes were detected as having progressed at the end of 2 years when testing was performed one, two, and three times per year, respectively. Figure 2 shows the proportion of eyes progressing (power) based on the time required to detect −1%/year and −1.5%/year of change for cpCD and −1μm/year and −1.5μm/year of change for cpRNFL when 2 testing per year is performed.

Supplementary Table1 and 2 show the results of simulation for early eyes. Similarly, increasing the testing frequency from two to three times per year showed a smaller gain than an increase from testing once to twice per year.

Specificity of the simulation with respect to Different Frequency of Testing Per Year

The specificity of the simulation was evaluated by examining the percentage of stable glaucoma eyes (cpCD or cpRNFL slope of 0 (%/year or μm/year) detected as progressing

with different frequencies of testing per year (Figure 3). The percentage of stable glaucoma eyes that were considered to be progressing increased with an increased frequency of OCT and OCTA testing (Fig 3 A and B). For example, in OCTA, 7.3%, 12.4%, and 15.5% of stable eyes were considered to have progressed after 5 years when testing was performed once, twice, and thrice per year for cpCD, respectively (Fig 3A). Comparable specificities were found for OCT, and 7%, 12.5%, and 16.2 of stable eyes were considered to have progressed after 5 years when testing was performed once, twice, and thrice per year for cpRNFL, respectively (Fig 3B)

Discussion

This study evaluated the time required to detect OCT and OCTA progression in glaucoma eyes using different rates of cpCD and cpRNFL loss with respect to various frequencies of testing per year. We also provided information on how frequently testing should be performed to detect different rates of loss. With a similar frequency of testing, cpCD detected progression slightly sooner than cpRNFL. CpRNFL and CpCD were comparable and complementary in detecting glaucoma progression over time. Two visits per year seemed sufficient for detecting glaucoma using both cpRNFL and cpCD.

Previous studies showed that the average rate of RNFL change in glaucoma patients varies between −0.5 to −1.0μm/year depending on the severity of disease, treatment, and population samples.[32–36] Average rate of cpCD change −0.5 to −1.3 %/year was reported.[37] According to our findings, cpCD OCTA was able to detect progression slightly sooner than OCT cpRNFL, especially with a lower rate of change such as −0.5 or −1, in part, because the rates of change evaluated were relatively faster for cpCD. For example, with the frequency of 2 tests per year, OCTA could detect progression of −1%/year after 4.3 years, while OCT could detect similar rates of change after 5.0 years. As the rates of change increased, OCT and OCTA showed more similar detection of progression. For example, they could detect −1.5 (μm/year or%/year) rate of change after 3.8 and 4.0 years, respectively, when testing was performed twice per year.

Our results also showed that there could be a slight improvement in the detection of progression after 2 years with two and three tests per year with a higher rate of vessel loss as compared to cpRNFL loss (−1.5 and −2 μm/year) and also a subtle improvement in detection of progression with the lower rate of vessel loss (−0.5 and −1 %/year) after 5 years. With the testing frequency of twice per year, OCTA detected half of the eyes as progressed with −2%/year of loss after 2 years and 40% of eyes were detected as progressed by OCT with a similar rate of change. For a −0.5 (μm/year or %/year) loss per year, cpCD in OCTA showed a progression in 60% of eyes after 5 years. However, 49% of eyes were detected as progressed eyes by cpRNFL in OCT at −0.5 μm/year.

Our results only in eyes with early glaucoma showed that two visits per year seemed sufficient for detecting glaucoma using both cpRNFL and cpCD. Reduced peripapillary and macular vessel density were detectable in the perimetrically intact hemiretinae of glaucoma eyes with a single-hemifield defect. [20] Also, it seemed that in the early course of the disease, the dynamic range of RNFL thickness is lower than vessel density.[38] As we included a

population of glaucoma and glaucoma suspects eyes, it is possible that OCTA can detect the changes early in the course of disease progression. Given the possible high intra-session variability in both cpCD and cpRNFL,[39–42] this result should be validated with real data to determine whether cpCD can detect progression sooner than cpRNFL.

Previous studies have shown that glaucoma or glaucoma patients typically are examined at different frequencies according to the severity of their glaucoma. For example, it would be every 6–12 months for stable patients. In contrast, unstable patients (intraocular pressure above goal or disease progression) may have follow-up clinical examinations every 1–2 or 3–6 months.[43] Despite reports of different rates of VF testing per year (typically, once or twice per year),[44–47] there is no report on OCT or OCTA to suggest the time to detect a specific rate of progression according to different testing frequencies per year in clinical settings.[48] A study reported that various glaucoma patients underwent about an average of 1.39 OCTs per year in routine clinical settings.[48] However, the appropriate frequency of testing for OCT and OCTA testing needs to be clarified For example, for a more typical and slower rate of cpCD loss (−1%/year) and cpRNFL (−1μm/year), progression can be detected with 80% power after 6.0 years and 6.3 years vs. 4.3 years and 5.0 years when testing is performed once and twice per year, respectively, and again with a smaller improvement to 4.0 and 4.2 years for cpCD and cpRNFL, respectively when testing is performed 3 times annually. Similar to results by Wu et al. and Gardiner et al. for VF progression, our finding shows that improvements in the time to detection were not proportional to the testing frequency.[13, 49] Proudfoot et al. also showed decreased gains in study efficiency (as measured by total study duration) when increasing observation frequency for fixed effect sizes and samples sizes in the short-term assessment of glaucoma progression model in clinical practice.[50]

Test-retest variability of RNFL has been shown to be around 5 μm.[41, 42] Therefore, a change that exceeds the expected test-retest variability (5 μm) in RNFL is considered a true disease progression by some clinicians.[4] However, this method fails to account for losses in RNFL that may occur because of normal aging.[4] Defining a cut-off for RNFL progression also has been investigated using trend-based analysis.[4, 32–36] Using −1 μm/year as a cut-off takes into account age-related changes over time. Moreover, trend-based analyses used in the current study may be able to adjust for expected age-related losses better than event-based analyses.[4] Also, the trend-based analysis considers the inter-visit variability and provides the possibility to detect progression sooner.[50] Performing OCTA several times in a day may give different, but very close, density values, to each other, but most of the them are within 1–2 % of each other.[39, 40] However, it was recently shown that OCTA has good longitudinal reproducibility in stable glaucoma eyes.[51] Also, we defined −1 %/year as a cut-off for OCTA because it is above the average rate of reported cpCD progression in glaucoma patients.

Some limitations should be considered while interpreting the current study. First, we excluded OCTA scans with poor quality. Consistent, high-quality images are not always available in clinical settings.[52] Therefore, more significant variability in a clinical setting can be expected than in the current study. A previous study showed that around one-third of OCT images had poor quality scans. [52] Second, the frequency of testing can also be influenced by intra-individual test-retest variability. OCT and OCTA measurements

with the instrument used in the current study have acceptable test-retest variability and both differentiate glaucomatous from normal eyes.[15] However, OCTA vessel density is affected by the signal strength index more than OCT cpRNFL measurements.[53] Third, in the current study, we used good quality OCTA scans to reduce the test-retest variability. Inter-session short-term and long-term variability are other crucial factors in the detection of glaucoma progression. Previous studies reported an acceptable short-term and long-term reproducibility for OCTA and OCT, with OCT showing generally better reproducibility than OCTA.[18, 51] Nishida et al., showed that vascular parameters demonstrate good long-term reproducibility, although it was not as high as the reproducibility of OCT parameters. Fourth, imaging devices are not interchangeable in detecting glaucoma progression because of their different analytic algorithms.[5, 17, 51] Therefore, the current results may not be generalizable to other devices and algorithms. Fifth, we used a linear rate of cpRNFL or cpCD loss for simulation to simplify the interpretation of our estimation. In addition, glaucomatous progression is more likely to be nonlinear or bilinear over a long duration of follow-up. Therefore, different simulation methods can also be considered.[54–56] Current simulation can be improved with other models integrating multiple available covariates in clinical practice and even a combination of progression methods such as trend and event-based analysis. Finally, the sample size in our data is limited, and we were not able to compare early vs. advanced stage of glaucoma. So, caution should be exercised when extrapolating this result to the moderate to advanced eyes. In fact, it was recently reported that for detection of progression with 60 % accuracy, 7 measurements are needed to detect both moderate and rapid worsening within a 2-year period if the more efficient “clustered” measurement strategy is used.[57]

Several factors should be considered when defining testing frequency. For example, patients with advanced glaucoma or who have mild damage at a younger age may require more frequent OCT/OCTA testing. Clinicians should consider for decision making other factors such as those for risk of progression including ethnicity, age and life expectancy.[8, 48, 58–60] Although this study presents the time required to detect a statistically significant negative cpRNFL or cpCD slope, the actual time required to detect the progression of glaucomatous damage is likely to be shorter in practice when considering the overall clinical picture. This is because our simulation of cpRNFL and cpCD is one component of known factors in clinical practice that can show the pattern of glaucomatous damage. Previous studies have also shown that combining structure and function can increase the ability to detect and estimate glaucoma progression in clinical practice.[54,55]

These findings provide information on the proportion of progressing eyes and the time required to detect progression in OCT and OCTA for different rates of loss with respect to various frequencies of testing based on trend-based analysis. We found that cpRNFL and cpCD are comparable for the detection of progression. Further, this study showed that increasing the number of tests from two to three does not reduce the time required to detect progression. Two visits per year appear sufficient for detecting glaucoma using both cpRNFL and cpCD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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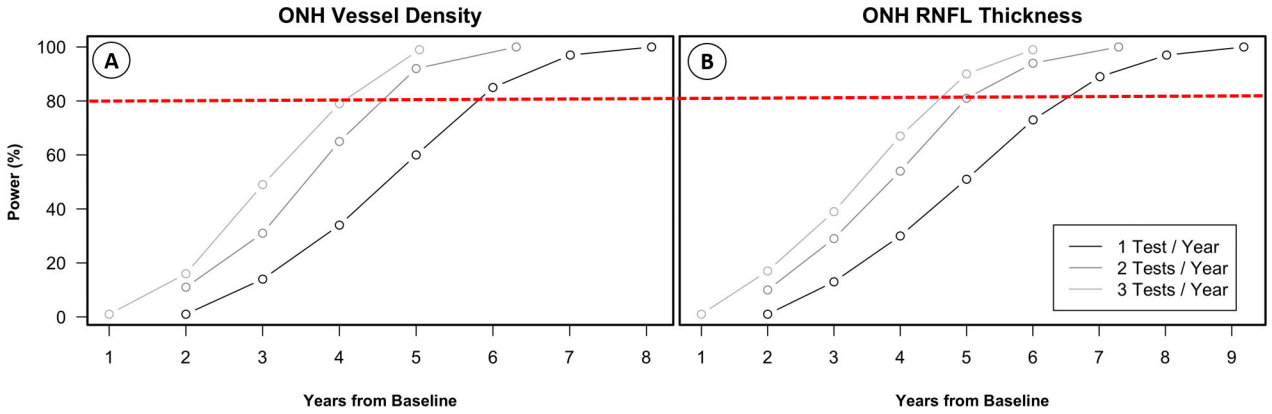

Figure 1.

Power (the proportion of eyes progressing) and required time to detect a significant rate of change (−1%/year for cpCD and −1μm/year for cpRNFL) with respect to different frequencies of testing per year. Red dashed line shows the 80% power to detect −1 (%/year or μm/year) rate of change in (A) circumpapillary capillary density (cpCD) and (B) circumpapillary retinal nerve fiber layer (cpRNFL)

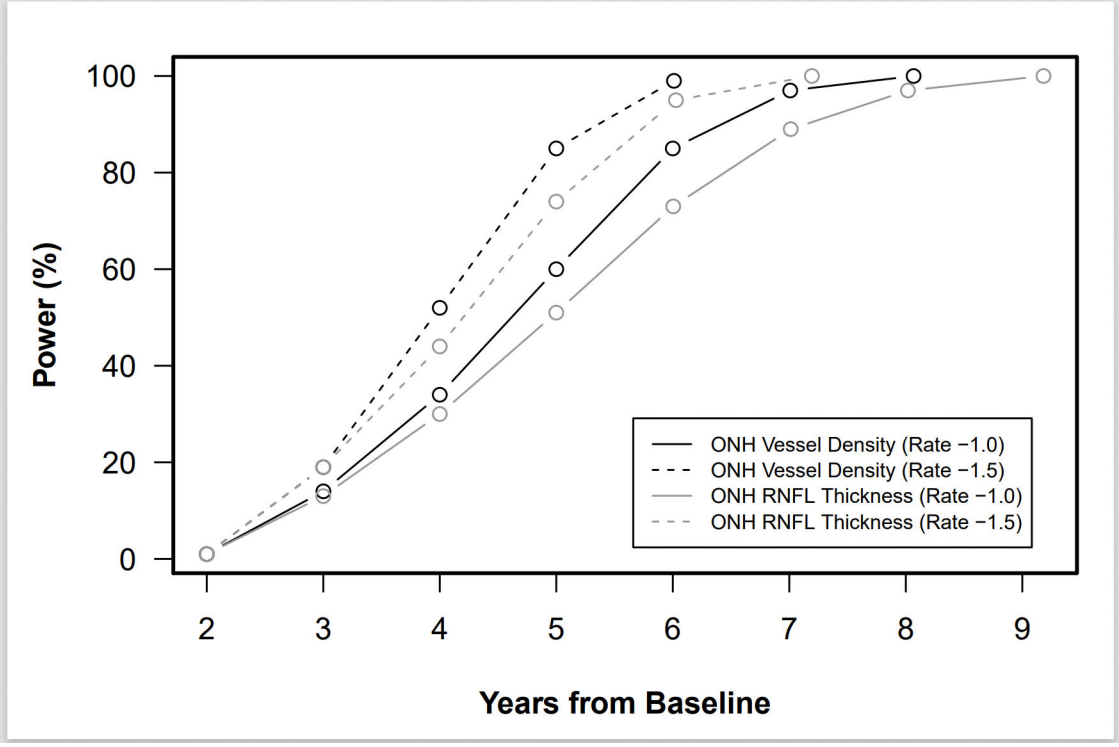

Figure 2.

Power (the proportion of eyes progressing) and required time to detect two significant rates of change (−1 and −1.5 (%/year or μm/year) for circumpapillary capillary density (cpCD) and circumpapillary retinal nerve fiber layer (cpRNFL) when 2 testing per year is performed.

Table 1.

Demographics and Baseline Characteristics of included eyes.

Variables	
Age (years)	69.1 (66.9, 71.2)
Gender (M/F)	51(52.0%)/47(48.0%)
Race	
African Descents (%)	24 (24.5%)
Non-African Descents (%)	74 (75.5%)
Axial Length (mm)	24.3 (24.2, 24.4)
CCT (μm)	534.8 (531.4, 538.2)
Spherical Equivalent (D)	−1 (−1.1, −0.8)
Mean IOP (mmHg)	15.3 (14.6,16.0)
Diagnosis	
Early, n (%)	127 (81.4%)
Moderate to advance, n (%)	29 (18.6%)
Baseline 24–2 VF MD (dB)	−3.3 (−4.1, −2.5)
ONH	
Average cpCD (%)	43.9 (42.9, 44.8)
Average cpRNFL (μm)	78.7 (76.0, 81.3)
Average SSI	62.9 (61.4, 64.3)

CCT = central corneal thickness; CD = capillary density; cp = circumpapillary; D = diopter; F = female; IOP = intraocular pressure; ONH = optic nerve head; RNFL = retinal nerve fiber layer; SSI = signal strength index; VD = vessel density; VF = visual field; M = male; MD = mean deviation. Values are shown in mean (95% confident interval), unless otherwise indicated.

Table 2.

Required time and power (proportion of eyes progressing) to detect different rates of circumpapillary retinal nerve fiber layer (cpRNFL) thickness

	Rate of cpRNFL thinning (μm/year)	Time to Detect progression (Years)				Power to Detect progression (%)	
		Mean	SD	80% power	90% power	2 years	5 years
1 observation/year	−0.5	7.1	2.7	9.6	10.8	4.5	29.8
	−1	4.9	1.6	6.3	7.0	7.1	62.4
	−1.5	4.1	1.2	5.0	5.9	10	85.7
	−2	3.7	1.0	4.5	5.0	13.2	96.5
2 observations /year	−0.5	5.2	2.2	7.6	8.5	11.1	49
	−1	3.5	1.3	5.0	5.8	19.1	87.5
	−1.5	2.8	1.0	4.0	4.5	29.3	99.3
	−2	2.4	0.8	3.3	4.0	40.3	100
3 observations /year	−0.5	4.4	2.0	6.7	7.3	16	61.5
	−1	2.9	1.2	4.2	5.0	27.6	96.3
	−1.5	2.3	0.9	3.6	4.0	42	100
	−2	2.0	0.7	3.0	3.0	56.9	100

Table 3.

Required time and power (proportion of eyes progressing) to detect different rates of circumpapillary capillary density change.

	Rate of vessel density change (%/yr)	Time to Detect progression (Years)				Power to Detect progression (%)	
		Mean	SD	80% power	90% power	2 years	5 years
1 observations/year	−0.5	6.4	2.3	8.2	9.2	4.7	35
	−1	4.5	1.4	6.0	6.1	7.7	75.6
	−1.5	3.8	1.1	5.0	5	11.1	95.1
	−2	3.4	0.9	4	4.5	14.5	99.6
2 observations /year	−0.5	4.7	1.9	6.6	7.2	12	60.5
	−1	3.2	1.1	4.2	5	21.5	96.9
	−1.5	2.6	0.9	3.8	4	34.6	100
	−2	2.3	0.7	3	3.1	49.6	100
3 observations /year	−0.5	3.9	1.7	5.9	6.3	17.3	75.1
	−1	2.7	1.0	4	4.0	32	99.6
	−1.5	2.1	0.8	3	3.2	51.3	100
	−2	1.8	0.6	3	3	69.7	100