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Patient Characteristics Associated with Artifacts in Spectralis Optical Coherence Tomography Imaging of the Retinal Nerve Fiber Layer in Glaucoma

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Abstract

Purpose—To determine patient factors and eye conditions associated with artifacts in Spectralis optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) scans.

Design—Retrospective cross-sectional study.

Methods—The prevalence of twelve artifact types were described in this review of 2313 eye scans from 1188 patients who underwent a complete eye exam with Spectralis OCT scanning during the period of September 2009 to July 2013. Generalized estimating equations model was utilized to analyze associations between increased artifact prevalence and 10 patient characteristics, which included age, sex, race, visual acuity, refractive error, astigmatism, cataract status, glaucoma staging, visual field reliability, and glaucoma diagnosis.

Results—A total of 1070 or 46.3% of the 2313 eye scans had at least one artifact. De-centration error was the most common artifact (27.8%), followed by posterior vitreous detachment artifacts (14.4%). Visual acuity of less than 20/40 ($p<0.0001$), presence of moderate to severe cataracts ($p<0.0001$), advanced stage of glaucoma ($p<0.0001$), and a diagnosis of open angle glaucoma ($p=0.0003$) were associated with increased prevalence of artifacts.

Conclusions—Clinicians should first assess scans for artifacts before making therapeutic decisions based on RNFL thickness measurements.

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Keywords

Spectral domain optical coherence tomography; Spectralis OCT; Artifacts; Glaucoma; Retinal nerve fiber layer (RNFL)

Introduction

Glaucoma is the leading cause of irreversible blindness in the world, affecting more than 2.8 million people in the United States alone.¹ It is an optic neuropathy characterized by the death of retinal ganglion cells, the axons of which converge to form the retinal nerve fiber layer (RNFL).² As a result, glaucoma causes RNFL thinning. Imaging of the RNFL, therefore, has important clinical value for not only diagnosing glaucoma but also for following disease progression.

First developed and described in 1991 by Huang et al.,³ optical coherence tomography (OCT) is a noninvasive imaging technique that uses low-coherence interferometry to generate high-resolution cross-sectional images of any optically accessible tissue. OCT imaging has undergone many significant technological advances, and the current commercially available spectral domain OCT (SD-OCT) machines, such as the Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany), provide ultra-high speed images, with better resolution and sensitivity compared to older time domain OCT (TD-OCT) devices.⁴ Automated SD-OCT measurements allow for quantitative and objective assessments of early RNFL thinning, which can be detected before corresponding visual field loss.^{5–7} However, SD-OCT, or any test, is limited by the quality of the test. Errors either in data acquisition or software analysis may result in erroneous RNFL measurements, which may lead to an inaccurate clinical assessment. Therefore, the goal of this paper is to determine when such imaging artifacts or inaccuracies occur and in which patients these artifacts are most likely to occur.

SD-OCT has been reported to have a decreased incidence of segmentation errors compared to older devices.^{8,9} Han and Jaffe¹⁰ previously performed a study to characterize the types and frequencies of image artifacts with SD-OCT imaging of the macula for the evaluation of retinal diseases. Several types of artifacts were observed, including inner and outer retina misidentification, degraded scan images, cut edge artifacts, incomplete segmentation errors, and retinal image shifts. As many as 90.9% of scans had at least 1 artifact, and clinically significant artifacts were observed in 8.0% of scans.¹⁰ More recently, Asrani et al¹¹ conducted a retrospective cross-sectional study on 277 consecutive patients with a diagnosis of glaucoma and obtained SD-OCT scanning of the RNFL. They found that 19.9% of RNFL scans contained artifacts, and the most common cause of artifacts was related to epiretinal membranes. Our study has a larger study population of 1188 patients. In addition, we evaluated if RNFL artifacts were associated with patient factors or eye conditions. We hypothesize that an increased prevalence of RNFL artifacts in Spectralis OCT imaging is associated with patient factors such as older age, female gender, worse visual acuity, worsen refractive error and astigmatism, and worse glaucoma severity.

Methods

Study population

A retrospective review of patients and their eye scans was conducted with approval from the Massachusetts Eye and Ear Infirmary (MEEI) Institutional Review Board, and the study protocol was in accordance with the Health Insurance Portability and Accountability Act.

Subjects were included in the study if they were seen in the Glaucoma service at MEEI (by TCC) and underwent a complete eye exam with Spectralis OCT scanning during the period of September 2009 to July 2013. A total of 1188 patients met the above criteria and were included in the study. Some patients had multiple scans, but only the most recent SD-OCT scans were used for the study. Both eyes were included in the study if a patient had both eyes scanned. Sixty-three patients only had scans from one eye, so only one scan for these patients was included. As a result, a total of 2313 eye scans were reviewed in this study.

Spectralis optical coherence tomography (OCT) imaging

All patients had peripapillary SD-OCT RNFL thickness measured using a circular scan pattern.^{11,12} The Spectralis OCT is an SD-OCT machine that has a scan speed of 40,000 A-lines per second and an eye tracking system, the TruTrack™ image alignment software, which reduces target motion artifacts and results in more stable captured images. The scan automatically generates a quality score of 0 to 40 decibels (dB). Multiple frames at the same location are obtained and then averaged to reduce speckle noise. The scan circle around the optic nerve is 12 degrees in diameter, and the scan circle diameter in millimeters therefore depends on the axial length. For a typical eye length, the circle would be approximately 3.5 to 3.6 mm in diameter. Scans were acquired in High Speed mode.

The Spectralis OCT software (version 4.0) allows for automatic segmentation of the anterior and posterior borders of the RNFL to calculate the average RNFL thickness for the overall global (360 degrees), for 4 quadrants (superior [S], inferior [I], nasal [N], and temporal [T]), and for four additional sectors (superior-temporal [TS, 45–90 degrees], superior-nasal [NS, 90–135], inferior-nasal [NI, 225–270 degrees], and inferiortemporal [TI, 270–315]).

Evaluation of image artifacts

In this paper, we defined 12 artifact types. A type 1 artifact was defined algorithm failure or incorrect segmentation of the anterior RNFL (Figure 1, top, white arrow), and a type 2 artifact occurred when there was posterior RNFL misidentification (Figure 1, top and middle, yellow arrows). A type 3 artifact occurred when there was incomplete segmentation (Figure 1, bottom), when the algorithm failed to delineate the entire extent of the RNFL, or when the red line on the OCT printout ended before the OCT image ended. Complete absence of segmentation was considered a subtype of artifact type 3.

Spectralis OCT scans were considered de-centered (type 4, Figure 2, top) when the center of the optic nerve head was more than approximately 10% off the center of the peripapillary circular scan. Spectralis SD-OCT automatically generates a quality score from 0 to 40 dB. Type 5 or poor signal artifact (Figure 2, bottom, yellow arrow) was defined as a quality

score of less than 15, as indicated in the Spectralis user's manual.¹³ A type 6 artifact (Figure 3, top, yellow arrow) occurred when part of the scan was missing and when a portion of the RNFL across its entire thickness was completely black or indistinguishable from the background noise. Since glaucoma patients tend to have decreased RNFL thickness, cases where even the slightest signal above background noise was detected were excluded as an artifact. Type 7 cut edge artifacts (Figure 3, middle, yellow arrows) were identified in cases of abrupt lateral edge truncation of the RNFL. Type 8 motion artifacts (Figure 3, bottom) were due to patient movement during scanning. If patient movement caused parts of the OCT scan to be completely out of the rectangular display printout, this was counted as a movement artifact. If the OCT scan was characterized by a wavy or undulating appearance of the entire scan image but if the entire retina was still visible in the displayed scan, this was not considered a motion artifact in this paper.

Patient ocular pathology-associated artifacts types 9 to 12 were identified when the RNFL scan circle involved scanning over areas of clinically documented fundus abnormalities. Type 9 posterior vitreous detachment (PVD) associated artifacts (Figure 4, top, yellow arrow) were identified in scans where a clear PVD was present on the Spectralis OCT printout. Type 10 was a peripapillary atrophy (PPA) associated artifact (Figure 4, upper middle, yellow arrow). Type 11 was a staphyloma-associated artifact (Figure 4, lower middle, yellow arrow). Type 12 was a myelinated nerve fiber layer (MNFL)-associated artifact (Figure 4, bottom, yellow arrow).

Patient factors and eye characteristics

We recorded patient specific factors such as age, sex, race, as well as eye specific factors such as visual acuity (VA), refractive error [with spherical equivalent (SE)], astigmatism (cylindrical refractive errors), cataract status, glaucoma diagnosis, glaucoma staging, and visual field reliability.

Visual acuity was either best corrected visual acuity (cc) or visual acuity without correction (sc) if visual acuity did not improve with correction. Vision was divided into two categories: 1) 20/40 or better, and 2) worse than 20/40.

Refraction, if recorded within 3 months of the OCT scan, was included in this study. If there were multiple refractions, the one closest to the date of the scan was used. Of the 2313 eye scans, 1091 eye scans did not have any documented refraction within the 3 month time period. For the remaining 1222 eye scans, patients were categorized as being either within -6.00 diopters (D) SE to $+5.00$ D SE, inclusive, or worse than -6.00 D SE or worse than $+5.00$ D SE. Astigmatism was evaluated, and patients were categorized as either better than or equal to ± 3.00 D of cylinder, or worse than ± 3.00 D of cylinder.

Cataract status was evaluated on the day of the SD-OCT scan and was classified as being: 1) clear, no cataract, 2) trace to 1+ cataract, 3) 2+ cataract or more, or 4) with a posterior or anterior chamber intraocular lens. If a patient had glaucoma, glaucoma staging was evaluated based on the mean deviation (MD) value from Humphrey visual field testing (SITA-standard 24-2 strategy, model HFAII series 750i, Carl Zeiss Meditec Inc., Jena, Germany), and glaucoma stages were classified using a modified Hodapp-Anderson-Parrish

system which graded fields as 1) normal ($MD \geq 0$), 2) mild ($-6 \leq MD < 0$), 3) moderate ($-12 \leq MD < -6$), or 4) advanced ($MD < -12$). Visual fields were categorized as reliable, if false positives were $\leq 20\%$, false negatives $\leq 20\%$, and fixation losses $\leq 33\%$. Patients were also categorized according to their glaucoma diagnosis. The 4 most common glaucoma diagnoses each were categorized into their own individual groups; pediatric glaucoma was categorized as a separate group, and the rest of the diagnoses were included in the category of “other.”

Statistical analysis

All statistical analysis was performed using SAS version 9.3 (Cary, NC). To quantify the frequency of artifacts among all scans analyzed, the number of scans with at least one artifact was divided by the total number of scans. Scans that had multiple artifacts were only counted once. Analyses were then performed for each artifact type. The frequencies of scans with 1, 2, and 3 or more types of different artifacts were also quantified by dividing the number of corresponding scans by the total number of scans analyzed.

Statistical analyses were performed on a per-eye basis to assess the effects of patient-specific and eye-specific factors on the prevalence and frequency of artifacts in SD-OCT imaging. Generalized estimating equation models were utilized to account for correlations of the paired eyes of the same subjects. Univariable analyses were first conducted to determine the existence of association between each of the patient and eye specific factors (age, sex, race, visual acuity, refractive error, astigmatism, cataract status, glaucoma staging, visual field reliability, glaucoma diagnosis) and the frequency of eye scans with at least one artifact. Variables with a univariable significance of $p < 0.10$ were selected for the model building. Glaucoma diagnosis and glaucoma staging were highly correlated and therefore they were not entered in a model simultaneously.

A manual selection method was utilized, and those maintaining a $p < 0.05$ were kept. The univariable predictors not included in the model were manually re-entered for an assessment of confounding effects. Interaction effects with the significant variables were also assessed. All missing data was excluded from analysis. Of note, 1091 eye scans did not have a recorded refraction, so univariable analyses were carried out with the remaining 1222 eye scans as a separate sub-group analysis.

Results

Patient demographics

There were 1,188 patients in the database with an average age of 61.3 ± 35.3 years, among whom 640 patients (53.9%) were females and 548 (46.1%) were males. In terms of race, a total of 846 patients (71.2%) were white, 143 (12%) were black, 66 (5.6%) were Asian, 37 (3.1%) were Hispanic, and 24 (2.0%) belonged to other racial groups. Seventy-two patients (6.1%) did not disclose their racial information.

Of all 1,188 subjects, 1,125 subjects (94.7%) had two eye scans, one for each eye, and 63 subjects (5.3%) had a scan for one eye. As a result, a total of 2,313 eyes from 1,188 subjects were scanned. There were 1,160 scans from right eyes and 1,153 from left eyes.

Eye characteristics

Eye specific characteristics are shown in Table 1, which showed that most of the scans were associated with better than 20/40 vision (80.9%), mild glaucoma stage (55.5%), reliable visual fields (69.7%), and trace to 1+ cataracts (54.9%). Of the 1222 (52.8% of the total) eye scans from patients who had their refractive errors recorded, 1141 or 93.4% were associated with refractive errors between -6.0 D SE to $+5.0$ D SE while the remaining 81 or 6.6% were associated with refractive error worse than -6.0 D SE or $+5.0$ D SE. Of the 1222 eye scans from patients who had their refraction recorded within 3 months of the OCT scan, 1186 or 97.1% had between -3.0 to $+3.0$ D of cylinder, while the remaining 35 or 2.9% had astigmatism worse than -3.0 or $+3.0$ D of cylinder.

Of the 2313 scans that were obtained from 1188 patients, the most common diagnosis was open angle glaucoma that represented 34.0% of the scans. The second most common condition was glaucoma suspect that included 18.5% of the scans. Following that, in order of descending frequency, the findings included normal (12.6%), ocular hypertension (9.6%), narrow angle glaucoma (8.0%), pediatric glaucoma (0.97%). A total of 16.3% of the scans represented findings in the “other” category including diagnoses of aphakic glaucoma, chronic angle closure glaucoma, physiologic cupping, congenital glaucoma, juvenile open angle glaucoma, mixed mechanism glaucoma, normal tension glaucoma, neovascular glaucoma, pseudoexfoliation glaucoma, pigment dispersion glaucoma, traumatic glaucoma. A small number of patients with other ophthalmic conditions that were seen on the glaucoma service were also included, such as iridocorneal endothelial syndrome, plateau iris configuration, and retinal abnormalities.

Frequency of artifacts

At least one artifact was noted in 1,070 of 2,313 eye scans (46.3%). Amongst them, 820 scans had one artifact, 196 scans had 2 different types of artifact, and 54 scans had 3 or more types of artifact. Of the 12 types of artifacts, de-centration error was the most common artifact (27.8%, Table 2). The next most common artifact was related to the presence of a PVD (14.4%, Table 2).

Univariable analysis of patient demographics and eye characteristics and artifact frequency

Scans with at least one artifact were more likely to occur in patients with vision worse than 20/40 compared to those with vision better than 20/40, with an odds ratio of 1.98 (95% CI [1.59–2.48], $P < 0.0001$, Table 3). The presence of cataracts was also associated with an increased likelihood of artifact. The odds ratios of a scan having at least one artifact in those with trace to 1+ cataract, 2+ cataract, or an intraocular lens compared to no cataract were 1.79 (95% CI [1.32–2.42], $p = 0.0002$), 2.9 (95% CI [1.90–4.44], $p < 0.0001$), and 2.26 (95% CI [1.61–3.16], $p < 0.0001$), respectively (Table 3).

Specifically, univariable analysis was also conducted to determine the effect of cataracts on signal strength (Type 5). There was no statistically significant association between mild (trace to 1+) cataract and increased frequency of poor signal strength, with an odds ratio of 1.26 and 95% confidence interval between 0.50 to 3.17 ($p = 0.6297$). However, having

moderate cataracts (2+ or worse) and having an IOL were both associated with increased frequencies of poor signal compared to not having a cataract. The odds ratio of a scan with poor signal in those with moderate cataract compared to no cataract was 5.33 (95% CI [2.01–14.11], $p = 0.0008$). The odds ratio of poor signal in scans associated an intraocular lens compared to no cataract was 4.15 (95% CI [1.67–10.33], $p=0.022$).

In addition, more advanced glaucoma stage was associated with a greater frequency of artifacts ($p<0.0001$, Table 3). In particular, patients with advanced glaucoma were significantly more likely to have eye scans with at least one artifact compared to patients without glaucoma with an odds ratio of 1.70 (95% CI [1.18–2.43], $p=0.004$, Table 3). Furthermore, normal eyes and diagnoses of glaucoma suspect or ocular hypertension were found to be associated with a decreased likelihood of artifact compared with open angle glaucoma ($p=0.0003$, Table 3). Compared to open angle glaucoma, patients with normal eyes had fewer scans with at least one artifact with an odds ratio of 0.55 (95% CI [0.40–0.75], $p=0.0002$, Table 3). Also, glaucoma suspects tended to have fewer circumpapillary scans with at least one artifact on their eye scans compared to patients with open angle glaucoma with an odds ratio of 0.63 (95% CI [0.48–0.83], $p=0.011$, Table 3). Furthermore, patients with ocular hypertension also had fewer scans with artifacts compared to patients with open angle glaucoma, with an odds ratio of 0.68 (95% CI [0.47–0.97], $p=0.036$, Table 3). Meanwhile, glaucoma suspects and ocular hypertension patients did not have a significant difference in prevalence of their eye scans having at least one artifact, with an odds ratio of 1.08 (95% CI [0.73–1.60], $p=0.704$, Table 3).

The other patient factors, including age, sex, race, refractive error, astigmatism, and visual field reliability were not associated with a significant increase or decrease in the frequency of artifacts (Table 3).

Multivariable analysis of patient demographics and eye characteristics and artifact frequency

The correlation of visual acuity and cataract grading with artifact frequency remained significant in the multivariable model. VA of worse than 20/40 is associated with increased likelihood of artifacts compared with VA better than 20/40 with odds ratio of 1.70 (95% CI [1.34–2.15], $p<0.0001$). Cataract severity is also associated with an increased likelihood of artifacts with $p<0.0001$. Individually, RNFL scans associated with trace to 1+ cataract, 2+ cataract, and intraocular lens have odds ratios of 1.73 (95% CI [1.28–2.34], $p=0.0004$), 2.37 (95% CI [1.53–3.66], $p=0.0001$), and 2.00 (95% CI [1.42–2.81], $p<0.0001$), respectively, of having at least one artifact in SD-OCT scans compared to those with normal slit lamp findings.

Discussion

A total of twelve types of artifacts are described in our study. Five of the artifacts were described previously by Han et al¹⁰ and include misidentification of the anterior RNFL (type 1), incorrect segmentation of the posterior RNFL (type 2), incomplete segmentation (type 3), off-center scans (type 4), and cut edge artifacts (type 7).

A total of 8 artifacts (types 1 to 8) described are independent of patient pathology. Misidentification of the anterior and posterior RNFL and incomplete segmentation were artifacts that are consistently described and observed in multiple prior OCT studies.^{10,14–17} These artifacts represent algorithm failures that directly lead to inaccuracies in RNFL thickness measurements. When peripapillary scans are not properly centered over the optic nerve head (type 4), this can lead to inaccurate interpretations of RNFL thickness measurements, because the RNFL is normally thinner as one moves further away from the optic nerve head. Therefore, for example, if the scanned area is further away from the optic nerve head due to de-centration, the scanned RNFL area may appear artifactually thinner compared to prior centered scans.^{18–20} Improper centration of the peripapillary circle scan is a type of error that can potentially be eliminated by an automated process, which ideally should be integrated into future OCT imaging machines.

Although Han et al did not report any motion artifacts in their Spectralis study, we saw and described motion artifacts caused by patient movement (type 8). Even though a retinal-tracking system is integrated into the commercially available Spectralis SDOCT machine in order to improve scan registration when there is patient movement,²¹ the tracking system does not correct for large degrees of patient movement which can still cause scan artifacts that interfere with accurate RNFL segmentation and thickness measurements. On the other hand, the mirror artifact described by Han et al¹⁰ was not observed in our study. Although mirror artifacts are theoretically possible with RNFL scans, perhaps RNFL scans compared to macular studies are less commonly associated with mirror artifacts.

Two other related artifacts include poor signal (type 5) and missing parts (type 6). Poor signal may lead to missing parts, and missing scan areas may be similar to the concept of “degraded scans” which was described in the study by Han et al.¹⁰ As shown in Figure 3 (top), segmentation in areas of missing scan data resulted in incorrect interpolation of the true RNFL borders.

Poor signal (type 5) was defined by the manufacturer as a quality score of less than 15 dB (range from 0 to 40 dB). It has been shown that both qualitative and quantitative evaluation of OCT images, such as RNFL measurements, are markedly influenced by the signal level.^{22–26} However, signal strength may not always reflect the quality of the image. For example, Figure 2 (bottom) has a poor signal strength of 9 dB, but subjectively there is good visibility of the RNFL against the background. Huang et al proposed a subjective grading scheme for OCT image signal quality composed of 9 questions about the visibility of different retinal layers and the reflectivity between layers generating a total score of 0 to 9 based on the binary answers.²⁷ The grading scheme had good correlation with objective quantitative measurement of signal strength.²⁷ Since subjective assessment of image quality may be clinically relevant and can complement the machine-generated signal strength, the grading scheme by Huang et al may be adapted in the future to Spectralis scanning of the RNFL.

Four artifacts described in this study are related to ocular pathology. Asrani et al recently described 3 artifacts caused by patient ocular pathologies, including epiretinal membranes, posterior vitreous detachments, and high myopia.¹⁴ Epiretinal membranes were not

considered a separate category of artifacts in our study, but were included as artifacts in the category of misidentification of the anterior RNFL layer (type 1). Asrani et al¹⁴ demonstrated that posterior vitreous detachments result in erroneously thickened RNFL measurements by Spectralis. Interestingly, in an earlier study by Aref et al with Cirrus, the presence of PVDs led to falsely thin RNFL thickness values in an area corresponding to the PVD.²⁸ 14.4% of the eye scans in our study contained artifacts caused by the presence of a PVD (type 9). PVDs may interfere with accurate longitudinal assessment of disease progression, because RNFL thickness values may decrease over time from the release of vitreous traction unrelated to glaucoma progression, or because there may be inaccurate RNFL thickness assessments due to PVD-related algorithm failures.

High myopia, or longer axial lengths, can be independently associated with thinner RNFL thickness values.^{29–33} In particular, high myopia, or having longer axial lengths, has been reported to be associated with thinner RNFL values for all 4 quadrants.^{31–33} Therefore, because high myopia and glaucoma can independently cause RNFL thinning, RNFL thickness may be limited as a diagnostic tool for glaucoma in highly myopic patients. Independent of the association between RNFL thinning and high myopia, our paper specifically evaluated whether high myopia is associated with an increased prevalence of RNFL artifacts. Indeed, in a subgroup of 1222 eye scans with documented refraction within a period of 3 months before or after the scan, our evaluation of both spherical equivalent and cylinder failed to establish an association between high myopia and astigmatism with an increased prevalence of artifacts in Spectralis scans. This finding confirms the conclusions of prior studies that RNFL thinning seen in highly myopic patients is due to physiologic changes and not due to artifactual RNFL thinning.”

In addition, we hereby described for the first time three new types of artifacts related to patient ocular pathology, including peripapillary atrophy (type 10), staphyloma (type 11), and myelinated nerve fibers (type 12).

Peripapillary atrophy is thinning of the retina and retinal pigment epithelium in the region immediately surrounding the optic nerve head. The frequency and size of peripapillary atrophy has been shown to be greater in eyes with glaucoma than in normal eyes,^{34,35} and severe peripapillary atrophy has been shown to affect OCT RNFL thickness measurements.^{36,37} In our study, the presence of peripapillary atrophy, in a total of 27 RNFL scans, has been consistently associated with poor RNFL scan quality and inaccuracy of RNFL thickness measurements. Although the current scan circle diameter in OCT machines was selected to be large enough to be outside most areas of peripapillary atrophy but not too large such that the RNFL is too thin to be reliably segmented, OCT RNFL circular scans sometimes still scan over areas of peripapillary atrophy. In our study, most of the 27 scans were associated with artifactually thinner RNFL measurements. Therefore, even though the intent of the peripapillary scan circle was to be large enough to avoid most areas of peripapillary atrophy, artifactually thinner RNFL measurements with peripapillary atrophy is sometimes unavoidable. Clinicians should use caution when interpreting Spectralis RNFL measurements in patients with peripapillary atrophy. Studies should be conducted in the future to better quantitatively assess the full effect of peripapillary atrophy on RNFL thickness measurements.

There have not been any studies done to date to evaluate the effect of staphyloma on OCT RNFL thickness measurements. Staphyloma is an ocular anomaly characterized by deep fundus excavation around the disc or posterior pole. Based on the 1 eye scan with staphyloma in our study, the pathology significantly interfered with accurate signal transmission during scanning, and significantly affected accurate RNFL segmentation. It is therefore a clinically significant artifact that clinicians should keep in mind when interpreting OCT scans.

Similarly, one patient in our study was found to have myelinated nerve fibers, which is a rare finding present in 0.3 to 0.6% of the population and are seen in 1% at postmortem examination.^{38,39} Even though myelinated nerve fibers should theoretically cause an increase in RNFL thickness, we found that myelinated nerve fibers can instead cause artifactually thin RNFL measurements due to incorrect segmentation of the RNFL borders (Figure 4, bottom). Clinicians should be aware that myelinated nerve fibers may cause artifacts in RNFL thickness measurements.

Next, we looked at the correlation of patient factors and eye conditions with frequency of artifact. A total of 10 patient factors and eye conditions were evaluated for correlation with artifact frequency. The patient factors which were not statistically associated with an increase in artifacts were age, sex, race, refractive error, astigmatism, and visual field reliability. On the other hand, factors associated with an increased prevalence of artifacts were worse visual acuity, more severe cataract, having a diagnosis of open angle glaucoma, and having advanced glaucoma.

Although best corrected visual acuity was used for this study, suboptimal patient vision during an eye scan may interfere with patient cooperation during the SD-OCT study and contribute to an increased prevalence of artifacts in eye scans.

Cataract was associated with an increased frequency of artifacts. As cataract severity increased, it was more likely that the corresponding scan would contain at least one artifact. The odds ratio of artifact frequency was 1.79 in eyes with mild cataracts (i.e. trace to 1+ cataracts) compared to normal eyes. This increased to an odds ratio of 2.90 in eyes with moderate to severe cataracts (i.e. 2+ or worse cataract) compared to normal eyes. In an OCT study that compared pre- versus post-operative signal strengths in patients who had undergone cataract surgery, cataracts were found to decrease signal strength.⁴⁰ This finding is consistent with the fact that media opacities of any kind can degrade signal strength. Our data also confirmed this finding by showing that severe cataracts (2+ or worse) are associated with an increased frequency of poor signal strength (type 5). Interestingly, however, our data also showed that patients who have had cataract surgery had an increased frequency of artifacts compared to normal eyes, and this effect was related to its correlation with poor signal strength. There are possible reasons that a PCIOL may be associated with poor signal strength. It is possible that subtle associated posterior capsular opacification that is not visually significant may decrease light source transmission and affect signal strength. Another possibility is that the PCIOL per se may cause light scattering either off the front or back surface of the PCIOL, and this may degrade signal strength.

Our data also showed that patients with severe glaucoma were more likely to have RNFL scans with artifacts, while mild to moderate glaucoma patients were not. This may likely be due to the fact that glaucomatous RNFL thinning is associated with decreased RNFL reflectivity which may lead to more algorithm failures. This finding suggests that when physicians are reviewing Spectralis scans for patients with MD < -12, they should be aware of the increased occurrence of artifacts when interpreting the results.

The diagnosis of open angle glaucoma was associated with a higher prevalence of artifacts compared to normal eyes and other diagnoses such as ocular hypertension and glaucoma suspect. This may also be due to a decrease in RNFL reflectivity, making automated RNFL thickness determinations more difficult. Since patients under 18 years of age were excluded from the study, there were only 22 patients with pediatric glaucoma diagnoses but who were adults at the time their scans were obtained. The smaller number of patients in this diagnostic group probably is the reason that pediatric glaucomas were not significantly associated with artifacts in our study.

Since our study was conducted using Spectralis OCT imaging, our conclusions may not be generalizable to other SD-OCT machines.

In conclusion, 46.3% of eye scans in a total of 2313 had at least one artifact. Of the 12 artifacts described, 4 were related to patient ocular pathology and two of them, staphyloma and myelinated nerve fibers, were described for the first time. Clinicians should look for artifacts and be aware that the two most common types of OCT RNFL artifacts are decentration, with a total frequency of 27.8%, and PVD-associated errors, with a frequency of 14.4%. Also, before making therapeutic decisions based on RNFL thickness measurements, clinicians should note if the patient has any conditions that may be associated with more OCT artifacts or may affect RNFL thickness interpretations, such as the following: 1) de-centered RNFL scan, 2) PVD, 3) visual acuity less than 20/40, 4) moderate to severe cataracts, 5) past cataract surgery, 6) advanced glaucoma stage, 7) open angle glaucoma, and 8) peripapillary atrophy. Ideally, computer algorithms should allow for manual correction of algorithm errors to avoid inaccurate diagnostic information.

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References

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br. J. Ophthalmol.* 2006; 90(3):262–267. [PubMed: 16488940]
2. Friedman, NJ.; Kaiser, PK.; Trattler, B. *Review of Ophthalmology*. Philadelphia: Elsevier Saunders; 2005.

3. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. *Science*. 1991; 254(5035): 1178–1181. [PubMed: 1957169]
4. Chen TC, Cense B, Pierce MC, et al. Spectral domain optical coherence tomography: ultra-high speed, ultra-high resolution ophthalmic imaging. *Arch. Ophthalmol*. 2005; 123(12):1715–1720. [PubMed: 16344444]
5. Quigley HA, Addicks EM, Green WR. Optic nerve damage in human glaucoma. III. Quantitative correlation of nerve fiber loss and visual field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy. *Arch. Ophthalmol*. 1982; 100(1):135–146. [PubMed: 7055464]
6. Quigley HA, Dunkelberger GR, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am. J. Ophthalmol*. 1989; 107(5):453–464. [PubMed: 2712129]
7. Kerrigan-Baumrind LA, Quigley HA, Pease ME, Kerrigan DF, Mitchell RS. Number of ganglion cells in glaucoma eyes compared with threshold visual field tests in the same persons. *Invest. Ophthalmol. Vis. Sci*. 2000; 41(3):741–748. [PubMed: 10711689]
8. Mylonas G, Ahlers C, Malamos P, et al. Comparison of retinal thickness measurements and segmentation performance of four different spectral and time domain OCT devices in neovascular age-related macular degeneration. *Br. J. Ophthalmol*. 2009; 93(11):1453–1460. [PubMed: 19520692]
9. Ho J, Sull AC, Vuong LN, et al. Assessment of artifacts and reproducibility across spectral- and time-domain optical coherence tomography devices. *Ophthalmology*. 2009; 116(10):1960–1970. [PubMed: 19592109]
10. Han IC, Jaffe GJ. Evaluation of artifacts associated with macular spectral-domain optical coherence tomography. *Ophthalmology*. 2010; 117(6):1177–1189. e4. [PubMed: 20171740]
11. Alasil T, Wang K, Keane PA, et al. Analysis of Normal Retinal Nerve Fiber Layer Thickness by Age, Sex, and Race Using Spectral Domain Optical Coherence Tomography. *J. Glaucoma*. 2012
12. Wu H, de Boer JF, Chen TC. Reproducibility of retinal nerve fiber layer thickness measurements using spectral domain optical coherence tomography. *J. Glaucoma*. 2011; 20(8):470–476. [PubMed: 20852437]
13. Heidelberg Engineering. Spectralis HRA + OCT User Guide. Software Version 5.3. Art. No. 19095-001.
14. Asrani S, Essaid L, Alder BD, Santiago-Turla C. Artifacts in Spectral-Domain Optical Coherence Tomography Measurements in Glaucoma. *JAMA Ophthalmol*. 2014; 132(4):396. [PubMed: 24525613]
15. Ghazi NG, Kirk T, Allam S, Yan G. Quantification of error in optical coherence tomography central macular thickness measurement in wet age-related macular degeneration. *Am. J. Ophthalmol*. 2009; 148(1):90–96. e2. [PubMed: 19403111]
16. Keane PA, Mand PS, Liakopoulos S, Walsh AC, Sadda SR. Accuracy of retinal thickness measurements obtained with Cirrus optical coherence tomography. *Br. J. Ophthalmol*. 2009; 93(11):1461–1467. [PubMed: 19574239]
17. Krebs I, Hagen S, Brannath W, et al. Repeatability and reproducibility of retinal thickness measurements by optical coherence tomography in age-related macular degeneration. *Ophthalmology*. 2010; 117(8):1577–1584. [PubMed: 20557937]
18. Vizzeri G, Bowd C, Medeiros FA, Weinreb RN, Zangwill LM. Effect of improper scan alignment on retinal nerve fiber layer thickness measurements using Stratus optical coherence tomograph. *J. Glaucoma*. 2008; 17(5):341–349. [PubMed: 18703942]
19. Yoo C, Suh IH, Kim YY. The influence of eccentric scanning of optical coherence tomography on retinal nerve fiber layer analysis in normal subjects. *Ophthalmol. J. Int. Ophtalmol. Int. J. Ophthalmol. Z. Für Augenheilkd*. 2009; 223(5):326–332.
20. Cheung CYL, Yiu CKF, Weinreb RN, et al. Effects of scan circle displacement in optical coherence tomography retinal nerve fibre layer thickness measurement: a RNFL modelling study. *Eye Lond. Engl*. 2009; 23(6):1436–1441.
21. Hammer DX, Ferguson RD, Magill JC, et al. Active retinal tracker for clinical optical coherence tomography systems. *J. Biomed. Opt*. 2005; 10(2):024038. [PubMed: 15910111]

22. Wu Z, Vazeen M, Varma R, et al. Factors associated with variability in retinal nerve fiber layer thickness measurements obtained by optical coherence tomography. *Ophthalmology*. 2007; 114(8):1505–1512. [PubMed: 17367862]
23. Barkana Y, Burgansky-Eliash Z, Gerber Y, et al. Inter-device variability of the Stratus optical coherence tomography. *Am. J. Ophthalmol*. 2009; 147(2):260–266. [PubMed: 18835473]
24. Sung KR, Wollstein G, Schuman JS, et al. Scan quality effect on glaucoma discrimination by glaucoma imaging devices. *Br. J. Ophthalmol*. 2009; 93(12):1580–1584. [PubMed: 19692363]
25. Huang J, Liu X, Wu Z, Sadda S. Image quality affects macular and retinal nerve fiber layer thickness measurements on fourier-domain optical coherence tomography. *Ophthalmic Surg. Lasers Imaging Off. J. Int. Soc. Imaging Eye*. 2011; 42(3):216–221.
26. Balasubramanian M, Bowd C, Vizzeri G, Weinreb RN, Zangwill LM. Effect of image quality on tissue thickness measurements obtained with spectral domain optical coherence tomography. *Opt. Express*. 2009; 17(5):4019–4036. [PubMed: 19259243]
27. Huang Y, Gangaputra S, Lee KE, et al. Signal quality assessment of retinal optical coherence tomography images. *Invest. Ophthalmol. Vis. Sci*. 2012; 53(4):2133–2141. [PubMed: 22427567]
28. Aref AA, Budenz DL. Spectral domain optical coherence tomography in the diagnosis and management of glaucoma. *Ophthalmic Surg. Lasers Imaging Off. J. Int. Soc. Imaging Eye*. 2010; 41(Suppl):S15–S27.
29. Leung CK-S, Mohamed S, Leung KS, et al. Retinal nerve fiber layer measurements in myopia: An optical coherence tomography study. *Invest. Ophthalmol. Vis. Sci*. 2006; 47(12):5171–5176. [PubMed: 17122099]
30. Rauscher FM, Sekhon N, Feuer WJ, Budenz DL. Myopia affects retinal nerve fiber layer measurements as determined by optical coherence tomography. *J. Glaucoma*. 2009; 18(7):501–505. [PubMed: 19745664]
31. Mohammad Salih PA-K. Evaluation of peripapillary retinal nerve fiber layer thickness in myopic eyes by spectral-domain optical coherence tomography. *J. Glaucoma*. 2012; 21(1):41–44. [PubMed: 21173707]
32. Zhao J-J, Zhuang W-J, Yang X-Q, Li S-S, Xiang W. Peripapillary retinal nerve fiber layer thickness distribution in Chinese with myopia measured by 3D-optical coherence tomography. *Int. J. Ophthalmol*. 2013; 6(5):626–631. [PubMed: 24195037]
33. Savini G, Barboni P, Parisi V, Carbonelli M. The influence of axial length on retinal nerve fibre layer thickness and optic-disc size measurements by spectral domain OCT. *Br. J. Ophthalmol*. 2012; 96(1):57–61. [PubMed: 21349942]
34. Jonas JB, Nguyen XN, Gusek GC, Naumann GO. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. I. Morphometric data. *Invest. Ophthalmol. Vis. Sci*. 1989; 30(5):908–918. [PubMed: 2722447]
35. Jonas JB, Naumann GO. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. II. Correlations. *Invest. Ophthalmol. Vis. Sci*. 1989; 30(5):919–926. [PubMed: 2722448]
36. Lai E, Wollstein G, Price LL, et al. Optical coherence tomography disc assessment in optic nerves with peripapillary atrophy. *Ophthalmic Surg. Lasers Imaging Off. J. Int. Soc. Imaging Eye*. 2003; 34(6):498–504.
37. Doshi A, Kreidl KO, Lombardi L, Sakamoto DK, Singh K. Nonprogressive glaucomatous cupping and visual field abnormalities in young Chinese males. *Ophthalmology*. 2007; 114(3):472–479. [PubMed: 17123617]
38. Kodama T, Hayasaka S, Setogawa T. Myelinated retinal nerve fibers: prevalence, location and effect on visual acuity. *Ophthalmol. J. Int. Ophthalmol. Int. J. Ophthalmol. Z. Für Augenheilkd*. 1990; 200(2):77–83.
39. Straatsma BR, Foos RY, Heckenlively JR, Taylor GN. Myelinated retinal nerve fibers. *Am. J. Ophthalmol*. 1981; 91(1):25–38. [PubMed: 7234927]
40. Mwanza JC, Bhorade AM, Sekhon N, et al. Effect of cataract and its removal on signal strength and peripapillary retinal nerve fiber layer optical coherence tomography measurements. *J. Glaucoma*. 2011; 20(1):37–43. [PubMed: 20179622]

Biographies

Yingna Liu is a third year medical student at Harvard Medical School. She is currently undergoing clinical training in Medicine. She has published several original articles during her undergraduate study and during medical school.

Teresa C. Chen, MD is an Associate Professor of Ophthalmology at the Harvard Medical School. She is on the full-time staff of the Glaucoma Service at the Massachusetts Eye and Ear Infirmary and is the Chief Quality Officer for the Harvard Department of Ophthalmology. Her research expertise is in imaging and the pediatric glaucomas. She edited the book *Glaucoma Surgery* and has published almost 150 original articles, major reviews, and book chapters. She is one of the leaders in spectral domain optical coherence tomography and swept source imaging research.

Figure 1. Examples of 3 types of segmentation artifacts (types 1–3) in Spectralis optical coherence tomography imaging of the retinal nerve fiber layer

A type 1 artifact is an incorrectly segmented anterior retinal nerve fiber layer (top, white arrow). A type 2 artifact is an incorrectly segmented posterior retinal nerve fiber layer (top and middle, yellow arrows). A type 3 artifact is failure to completely segment the borders of the retinal nerve fiber layer (bottom).

Figure 2. Examples of 2 types of scanning artifacts (types 4 and 5) in Spectralis optical coherence tomography imaging of the retinal nerve fiber layer

A type 4 artifact is a de-centered scan with the center of the optic nerve head more than 10% off the center of the peripapillary circular scan (top). A type 5 artifact is a poor signal scan, with Quality value less than 15 (bottom, yellow arrow).

Figure 3. Examples of 3 types of artifacts associated with missing images (types 6, 7, 8) in Spectralis optical coherence tomography imaging of the retinal nerve fiber layer

A type 6 artifact is an image which is missing portions of the retinal nerve fiber layer (top, yellow arrow). A type 7 artifact is an image with abrupt lateral edge truncation of the retinal nerve fiber layer (middle, yellow arrows). A type 8 artifact is when the retinal nerve fiber layer borders are blurred and out of the rectangular display printout due to patient movement (bottom).

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Figure 4. Examples of 4 types of artifacts associated with ocular conditions (types 9, 10, 11, 12) in Spectralis optical coherence tomography imaging of the retinal nerve fiber layer

A type 9 artifact is due to a posterior vitreous detachment (top, yellow arrow). A type 10 artifact is due to peripapillary atrophy (upper middle, yellow arrow). A type 11 artifact is due to a staphyloma (lower middle, yellow arrow). A type 12 artifact is due to myelinated nerve fibers (bottom, yellow arrow).

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Eye characteristics of the study population of 1,188 patients who had a total of 2,313 Spectralis optical coherence tomography scans of the retinal nerve fiber layer.

Table 1

Visual Acuity	Better than 20/40	Worse than 20/40	None recorded
Number of scans	1871	437	5
Percentage (%)	80.9	18.9	0.2
Refractive error	-6.0 SE to +5.0 SE	Worse than -60 SE or +5.0 SE	None recorded
Number of scans	1141	81	1091
Percentage (%)	49.3	3.5	47.2
Astigmatism	-3.0 to +3.0 cylinder	Worse than 3.0 or +3.0 cylinder	None recorded
Number of scans	1186	36	1091
Percentage (%)	51.3	1.56	47.2
Glaucoma stage	Normal	Mild	Moderate
Number of scans	266	1283	341
Percentage (%)	11.5	55.5	14.7
Visual field reliability	Reliable	Unreliable	None recorded
Number of scans	1611	526	176
Percentage (%)	69.7	22.7	7.6
Cataract	No Cataract	Trace or 1+	2+ or worse
Number of scans	324	1271	199
Percentage (%)	14.4	54.9	8.6
			IOL
			487
			21.1
			22
			1.0

SE = spherical equivalent; IOL = intraocular lens

Table 2

Prevalence of the 12 types of artifacts in a total of 2,313 scans from 1,188 patients who underwent Spectralis optical coherence tomography imaging of the retinal nerve fiber layer.

Artifact Number	Artifact	Number of scans	Percentage of scans (%)
1	Anterior RNFL misidentification	73	3.16
2	Posterior RNFL misidentification	177	7.7
3	Incomplete segmentation	14	0.6
4	De-centration	644	27.8
5	Poor signal	118	5.10
6	Missing parts	35	1.51
7	Cut edge	4	0.17
8	Motion artifact	5	0.22
9	PVD-associated error	332	14.4
10	PPA-associated error	27	1.2
11	Staphyloma-associated error	1	0.04
12	MNFL-associated error	1	0.04

RNFL = retinal nerve fiber layer; PVD = posterior vitreous detachment; PPA = peripapillary atrophy; MNFL = myelinated nerve fiber layer; OR = odds ratio

Table 3

Univariable analyses to determine if specific patient factors are associated with an increased frequency of artifacts in 2,313 scans from 1,188 patients who underwent Spectralis optical coherence tomography imaging of the retinal nerve fiber layer.

Factors	OR (95%CI)	P value
Age	1.01 (0.99–1.02)	0.076
Sex (Female vs. Male)	1.12 (0.92–1.35)	0.27
Race		0.65
(Black vs. White)	0.90 (0.66–1.21)	0.47
(Asian vs. White)	1.09 (0.70–1.69)	0.70
(Hispanic vs. White)	0.89 (0.50–1.56)	0.67
(Others vs. White)	0.59 (0.26–1.34)	0.21
VA		
(Worse than 20/40 vs. Better than 20/40)	1.98 (1.59–2.48)	<0.0001
^a Spherical refractive errors (Worse than –6.0 SE or worse than +5.0 SE vs. within –6.0 SE to +5.0 SE)	1.16 (0.69–1.95)	0.5848
^a Cylindrical refractive errors (Worse than –3.0 or worse than +3.0 cylinder vs. within –3.0 to 3.0cylinder)	1.98 (0.93–4.21)	0.0762
Visual field reliability (Reliable vs. Unreliable)	1.05 (0.86–1.30)	0.62
Cataract		<0.0001
(Trace 1+ vs. No cataract)	1.79 (1.32–2.42)	0.0002
(2+ or worse vs. No cataract)	2.90 (1.90–4.44)	<0.0001
(IOL vs. No cataract)	2.26 (1.61–3.16)	<0.0001
Stage of Glaucoma		<0.0001
(Mild vs. Normal)	0.86 (0.65–1.13)	0.2667
(Moderate vs. Normal)	1.10 (0.79–1.54)	0.5678
(Advanced vs. Normal)	1.70 (1.18–2.43)	0.0040
Diagnosis of glaucoma		0.0003
(Narrow angle vs. Open angle)	1.19 (0.81–1.76)	0.38
(OHTN vs. Open angle)	0.68 (0.47–0.97)	0.036
(No glaucoma or normal vs. Open angle)	0.55 (0.40–0.75)	0.0002
(Pediatric childhood vs. Open angle)	0.76 (0.25–2.32)	0.63
(Glaucoma suspect vs. Open angle)	0.63 (0.48–0.83)	0.0011
(Other vs. Open angle)	0.73 (0.54–0.97)	0.030
(OHTN vs. Glaucoma suspect)	1.08 (0.73–1.60)	0.704

VA = visual acuity; SE = spherical equivalent; IOL = intraocular lens; OHTN = ocular hypertension; OR = odds ratio

^a Analyzed using a subgroup of 1,222 eye scans with corresponding refractive errors documented.