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Agreement in Quantitative Anterior Chamber Angle Metrics between RTVue and Cirrus Spectral Domain Optical Coherence Tomography

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Abstract

Purpose: To investigate the agreement between two spectral domain optical coherence tomography (SD-OCT) instruments in Schwalbe's line (SL) based anterior chamber angle parameters and to evaluate their repeatability and reproducibility.

Methods: The inferior irido-corneal angle of 114 eyes from 59 participants (29 glaucoma and 30 normal) were scanned twice with the Optovue SD-OCT and Cirrus SD-OCT under controlled low luminance conditions. SL angle opening distance (SL-AOD) and SL trabecular-iris-space area (SL-TISA) were graded by masked certified graders at the Doheny Image Reading Center.

Results: The mean SL-AOD/SL-TISA was 623±271µm/ 0.221 ± 0.106 mm^2 for the Cirrus and 611 ± 267 µm/ 0.215 ± 0.112 mm^2 for the RTVue. Excellent repeatability (intraclass correlation coefficient ICC>0.934), excellent intragrader reproducibility (ICC>0.957) and very good intergrader reproducibility (ICC>0.877) were observed with both instruments in SL-AOD and SL-TISA. The agreement between Cirrus and RTVue was excellent (ICC 0.943 for SL-AOD and 0.900 for SL-TISA).

Conclusion: Both instruments provide consistent and reproducible measurement of SL-AOD and SL-TISA. The excellent agreement between them allows for direct comparisons of angle measurements acquired with different SD-OCTs and can lead in the introduction of criteria that could be valid across different platforms.

Keywords: Anterior chamber angle; Glaucoma; Schwalbe's line; Angle opening; Optical coherence tomography; Anterior-segment OCT; Reproducibility; Agreement

Introduction

Assessment of the configuration of the anterior chamber angle (ACA) structures is important in glaucoma. Gonioscopy remains the gold standard for the evaluation of the ACA, allowing the observer to directly visualize the anatomic relationships of the aqueous outflow structures, the cornea and the iris. However it requires a skilled clinician and is considered a highly subjective test with variable agreement reported between examiners [1,2]. Additionally, it provides quantitative assessment of the angle subtended by the inner angle recess and the iris, however it cannot provide measures of the distance between them. The development of ultrasound biomicroscopy allows for an objective and quantitative assessment of the angle and eventually optical coherence tomography (OCT) with its application in anterior segment imaging can provide real-time, non-contact, cross-sectional high resolution scans of the cornea, iris, lens, and angle [3]. It enables qualitative and quantitative analysis of anatomical relationships in the anterior segment, with various clinical applications, including imaging of narrow angles and angle abnormalities, assessment of tube positioning, quantification of peripheral anterior synechiae, but lacking the ability to image the ciliary processes or structures behind the pigmented epithelium of the iris [4-6].

Over the past years, the technology of OCT has evolved rapidly from time-domain to spectral domain (SD) OCT. Commercially available SD-OCT device use a shorter wavelength and allows higher scanning speed and increased axial and transverse resolution. Despite the fact that shadowing artifacts over the angle structures and decreased ability to image the scleral spur (SS) can still occur with SD-OCT, the improved image resolution has facilitated a more detailed and comprehensive analysis of ACA structures, with visualization of the termination of the endothelium at Schwalbe's Line (SL) and the trabecular meshwork. This improvement has led to the introduction of new quantitative parameters that describe anterior segment structures based on SL; the SL-angle opening distance (SL-AOD) and the SL-trabeculum iris space area (SL-TISA) [7].

Since angle imaging with SD-OCT devices is increasingly used both in research and in clinical practice, it is important to characterize the performance of quantitative measures of the angle with this technology. Therefore, this study was undertaken to examine the repeatability, intra- and inter- grader reproducibility in quantitative measurements of the ACA between two widely-available SD-OCT instruments, the Cirrus HD-OCT (Carl Zeiss Meditec, Inc. Dublin, CA) and the RTVue (Optovue Inc. Fremont, CA) and to evaluate the agreement between them.

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Methods

Participants were recruited from the Comprehensive Ophthalmology and the Outpatient Glaucoma clinics in the Doheny Eye Institute in a consecutive if eligible fashion. The study was approved by the Institutional Review Board and was conducted in accordance with the tenets of the Declaration of Helsinki. A written informed consent was obtained from all subjects before entering the study. Patient anonymity was preserved.

All participants underwent a complete ophthalmic examination, including slit lamp biomicroscopy, gonioscopy and dilated funduscopy. Exclusion criteria were the presence of ocular pathology other that senile cataract or glaucoma, previous ocular surgery, laser procedures, trauma, narrow angles or presence of peripheral anterior synechiae on gonioscopy.

Imaging of the angle

All subjects underwent non-mydriatic anterior segment OCT imaging of both eyes using the Cirrus High Definition OCT (Carl Zeiss Meditec, Inc. Dublin, CA) and the RTVue Spectral Domain OCT (Optovue Inc. Fremont, CA) in a randomized order, with two consecutive acquisitions with each instrument (Figures 1A and B). Scans were obtained in a darkened room, with lighting standardized to 1 cd/m^2 at the imaging plane, and confirmed with a light meter with a reading of ≤ 0.2 foot candles at the eye (Light Meter FC-840021, Sper Scientific, Scottsdale, AZ).

For the Cirrus SD-OCT, 3 mm scan length, 5-line anterior segment raster scans were captured, with a 0.25 mm distance between lines (or 1mm between the 1st and 5th scan line). Scans of the inferior angle were performed in a perpendicular fashion by choosing the scan line at the 6 o'clock position of the corneal limbus (270°). For the RTVue SD-OCT, a single line IC 270° angle-scan, with a length of 3 mm, was obtained. The instrument automatically records 16 line scans and after image processing and averaging, the internal software provides the final image. The OCT B-scan images were then exported for subsequent masked grading.

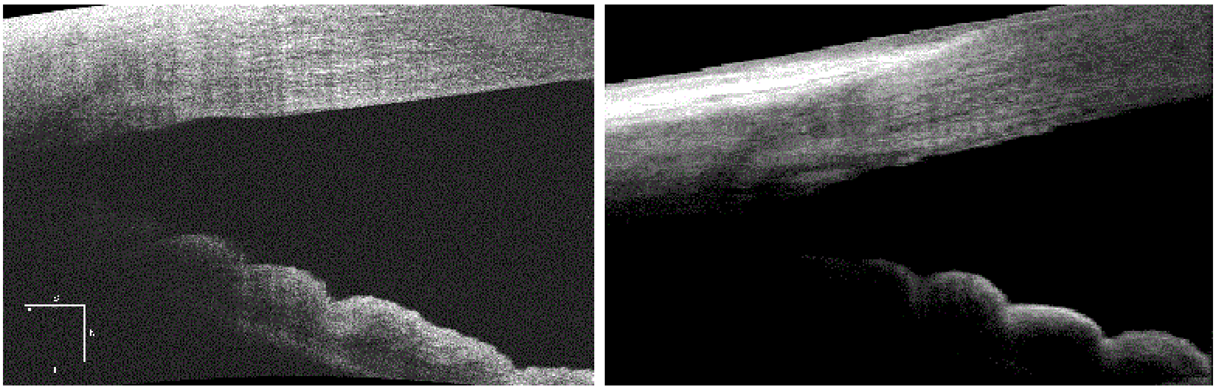


Figure 1: OCT image of the inferior angle of the same eye with the Cirrus (1A) and RTVue (1B) SD-OCT.

OCT grading procedures

Images from the Cirrus and RTVue SD-OCT instruments were graded independently in a masked fashion by certified anterior segment OCT graders using validated grading software (Image J-1.44p; developed by Wayne Rasbands, National Institutes of Health, USA) at the Doheny Image Reading Center. SL-AOD and SL-TISA of the inferior angle were measured for each selected image. For the Cirrus SD-OCT the grader chose the 6 o'clock line scan of the 5-raster set (the other four line scans were used as needed to refine the position of SL on the chosen scan, in case of uncertainty on the exact location) and single line scan in the RTVue SD-OCT. SL-AOD was calculated as the distance between the trabecular meshwork and the iris at SL, perpendicular to the inner corneal/trabecular meshwork interface. SL-TISA was measured as the area circumscribed by SL-AOD, a second line parallel to SL-AOD 500 microns posteriorly from SL, the inner trabeculum surface and the anterior surface of the iris space, and defined the filtration area.

Statistical analysis

The mean ± standard deviation was computed for all continuous variables. Instrument repeatability, intra- and inter-grader reproducibility for SL-AOD and SL-TISA were evaluated, by mean differences with 95% limits of agreement (LoA), intraclass correlation coefficients (ICC) testing for absolute agreement and Bland-Altman plots. ICC values and 95% confidence intervals are presented. All parameters were analysed both for the entire cohort, as well as separately for the glaucoma and non-glaucoma group. All statistical analyses was performed using commercial software (Statistical Package for Social Science, version 18.0; SPSS Inc., Armonk, NY).

Results

Patients characteristics

Fifty-nine participants, 24 men and 35 women (totaling 114 eyes) with a mean age of 50 ± 10 years were enrolled. The study cohort included both glaucoma patients (30 patients, 56 eyes), and non-glaucoma patients (29 patients, 58 eyes). In 4 participants (2 non glaucoma and 2 glaucoma patients), only 1 eye was included in the study, because the fellow eye had undergone previous surgery.

Repeatability

In the images with Cirrus, the mean SL-AOD in the first acquisition was 623 ± 271 µm and 617 ± 259 µm in the second acquisition, with a mean difference of 6 (LoA-154/165) µm (Table 1). The mean SL-AOD for the first acquisition on the RTVue was 611 ± 253 µm and 609 ± 261 µm for the second acquisition, with a mean difference of 2 (LoA -160/164) µm. Both the Cirrus and RTVue showed an excellent repeatability in SL-AOD, with ICC values of 0.955 and 0.953 respectively.

	1st acquisition	2nd acquisition	Mean Difference (LoA)	ICC (95% CI)
Cirrus SL-AOD (µm)	623 ± 271	617 ± 259	6 (-154/165)	0.955 (0.935-0.969)
RTVue SL-AOD (µm)	611 ± 253	609 ± 261	2 (-160−164)	0.953 (0.933-0.968)
Cirrus SL-TISA (mm^2)	0.221 ± 0.106	0.215 ± 0.103	0.006 (-0.069−0.081)	0.934 (0.906-0.954)
RTVue SL-TISA (mm^2)	0.215 ± 0.104	0.216 ± 0.108	-0.001 (-0.069/0.068)	0.951 (0.930-0.966)

Table 1: Intra-instrument reproducibility with the Cirrus SD-OCT and the RTVue SD-OCT. Data are presented as mean ± standard deviation. (SL: Schwalbe's Line, AOD: Angle Opening Distance, TISA: Trabecular-Iris-Space Area, ICC: Intraclass Correlation Coefficient, LoA: Limits of Agreement, CI: Confidence Interval).

The mean SL-TISA on Cirrus on the first acquisition was 0.221 ± 0.106 mm^2 and 0.215 ± 0.103 mm^2 for the second acquisition (Table 1). For RTVue, the mean SL-TISA on the first acquisition was 0.215 ± 0.104 mm^2 and 0.216 ± 0.108 mm^2 on the second acquisition. The ICC was excellent (higher than 0.934) for both instruments.

Considering each group separately, all ICC values were >0.934 in the glaucoma group and >0.913 in the non-glaucoma group.

Intra-Grader and Inter-Grader reproducibility

For SL-AOD, the mean difference between the first and second grading was -4 (-122/115) µm with Cirrus and -5 (-123/133) µm with RTVue. For SL-TISA, the mean difference was -0.002 (-0.060/0.056) mm^2 for Cirrus and 0.001 (-0.062/0.064) mm^2 for RTVue. The intragrader reproducibility was excellent for both devices when examining SL-AOD and SL-TISA, with ICC values greater than 0.957 (Table 2). All these values were calculated based on data from grader 1. Similar values were found when analyzing data from grader 2 (data not shown).

	1st grading	2nd grading	Mean Difference (LoA)	ICC (95% CI)
Cirrus SL-AOD (µm)	623 ± 271	626 ± 277	-4 (-122/115)	0.977 (0.966-0.984)
RTVue SL-AOD (µm)	611 ± 267	606 ± 253	5 (-123/133)	0.970 (0.957-0.979)
Cirrus SL-TISA (mm^2)	0.221 ± 0.106	0.223 ± 0.109	-0.002 (-0.060/0.056)	0.964 (0.948-0.975)
RTVue SL-TISA (mm^2)	0.215 ± 0.112	0.214 ± 0.104	0.001 (-0.062/0.064)	0.957 (0.938-0.970)

Table 2: Intra-observer reproducibility with the Cirrus SD-OCT and the RTVue SD-OCT. Data are presented as mean ± standard deviation. (SL: Schwalbe's Line, AOD: Angle Opening Distance, TISA: Trabecular-Iris-Space Area, ICC: Intraclass Correlation Coefficient, LoA: Limits of Agreement, CI: Confidence Interval).

In addition, considering each group separately, all ICC values for intraobserver reproducibility were excellent. ICC values were >0.970 for the glaucoma group and >0.926 for the non-glaucoma group.

High values for ICC were also observed in the inter-observer comparisons, based on analysis of data from the first grading from each grader. The mean difference for SL-AOD was 10 (-202/223) µm and 17 (-169/203) µm for Cirrus and RTVue respectively. For SL-TISA, the mean difference was 0.002 (-0.092/0.097) mm^2 and 5079 (-0.102/0.112) mm^2 for Cirrus and RTVue respectively. The ICC values were over 0.877 for all between-graders comparisons (Table 3).

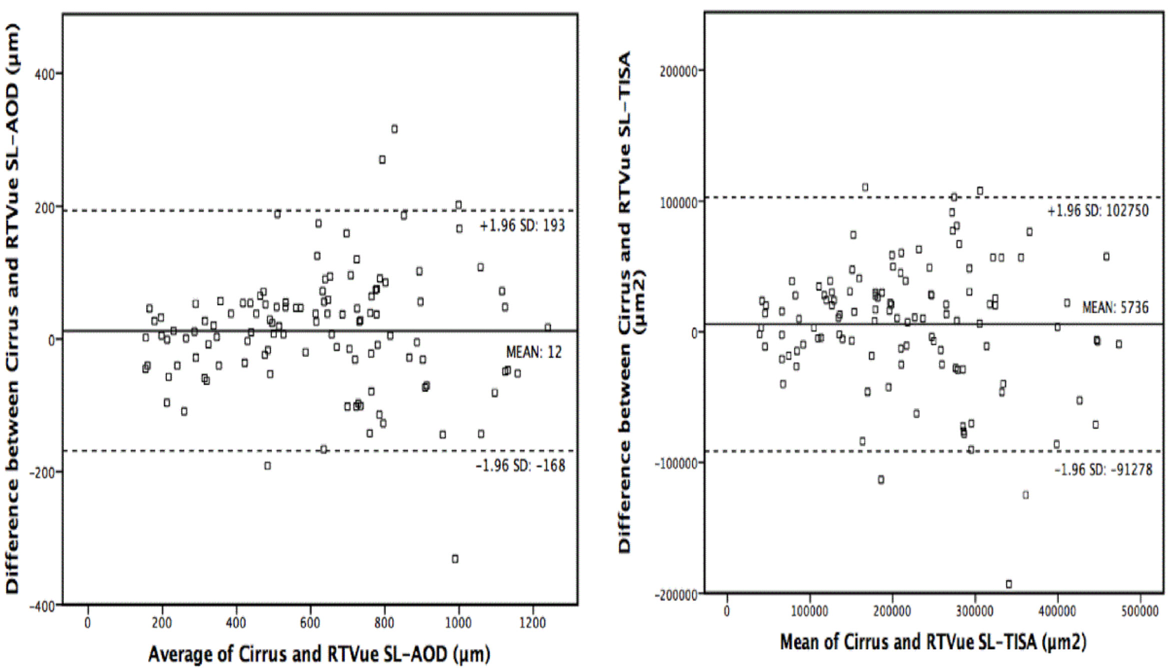
	1st grader	2nd grader	Mean Difference (LoA)	ICC (95% CI)
Cirrus SL-AOD (µm)	623 ± 271	613 ± 285	10 (-202/223)	0.927 (0.896-0.949)
RTVue SL-AOD (µm)	611 ± 267	593 ± 260	17 (-169/203)	0.936 (0.909-0.956)
Cirrus SL-TISA (mm2)	0.221 ± 0.106	0.219 ± 0.111	0.002 (-0.0092/0.097)	0.905 (0.865-0.933)
RTVue SL-TISA (mm2)	0.215 ± 0.112	0.210 ± 0.105	0.005 (-0.102/0.112)	0.877 (0.826-0.913)

Table 3: Inter-observer reproducibility with the Cirrus SD-OCT and the RTVue SD-OCT. Data are presented as mean ± standard deviation. (SL: Schwalbe's Line, AOD: Angle Opening Distance, TISA: Trabecular-Iris-Space Area, ICC: Intraclass Correlation Coefficient, LoA: Limits of Agreement, CI: Confidence Interval).

Considering each group separately, all ICC values for interobserver reproducibility were >0.864 for the glaucoma group and >0.848 for the non-glaucoma group.

Agreement between the two instruments

The mean SL-AOD measurements were 611 ± 267 µm for RTVue and 623 ± 271 µm for Cirrus, based on data from the 1st grading of images by the first grader. This was translated to a mean difference of 12 (LoA -168-13) µm (Figure 2A). SL-TISA was 0.221 ± 0.106 mm^2 for the Cirrus and 0.215 ± 0.111 mm^2 for the RTVue, with a mean difference of 0.006 (LoA-0.091–0.103) mm^2 (Figure 2B). The ICCs for comparisons between the two instruments were 0.943 (0.919-0.960) for SL-AOD and 0.900 (0.859-0.930) for SL-TISA. Similarly, for grader 2, the ICC for comparisons between the two instruments were 0.895 (0.851-0.926) and 0.935 (0.907-0.955) respectively.



Figures 2A and 2B: Bland-Altman plots demonstrate agreement in SL-AOD and SL-TISA measures between Cirrus and RTVue. The horizontal lines indicate the mean difference (solid line) and the limits of agreement (dotted lines) (SL: Schwalbe's Line; AOD: Angle Opening Distance; TISA: Trabecular-Iris-Space Area).

Considering each group separately, ICC values for intrer-instrument agreement were similar. In the glaucoma group, ICC was 0.958 (0.930-0.975) for SL-AOD and 0.931 (0.885-0.959) for SL-TISA and in the non-glaucoma group ICC was 0.912 (0.856-0.947) for SL-AOD and 0.843 (0.749-0.904) for SL-TISA.

Discussion

The present study presents data to support excellent consistency and reproducibility of both Cirrus and RTVue OCT devices in the quantitative assessment of the angle, suggesting that the influence of variability between consecutive acquisitions, between different graders or within the same grader is small. All imaging was performed under tightly controlled dark conditions to minimize the effect of illumination and grading was performed by masked graders in the Doheny Image Reading Center [8]. Consistency in measurements is essential in order to assess the instrument's ability to provide reliable measurements for use in clinical practice, both for diagnosis and for patients' follow up. Furthermore, an excellent agreement between the two devices was demonstrated, suggesting that they can be used interchangeably to quantify the angle opening. Our results provide data on the magnitude of variability between them and suggest that it is possible to directly compare measurements from these different SD-OCTs, which could also help to introduce uniform criteria for angle classification based on OCT.

The assessment of short-term variability between consecutive acquisitions was performed mainly to assess the influence of factors, such as head tilting or small differences in gaze direction that might occur and could play an important role in clinical practice. Also, the excellent between and within graders reproducibility is important since the SL-AOD and SL-TISA seem to be robust and reliable new parameters to quantify in SD-OCT angle images. Reproducibility indices have been assessed before for SD-OCT instruments.9-10 In a previous study, Qin et al showed a high inter- and intra-grader reproducibility of SL-AOD and SL-TISA for images acquired with the RTVue OCT in agreement to the present study [9]. Our group has also reported excellent reproducibility values for SD-OCT SL-based quantitative angle metrics [10]. All these studies justify the adoption of SL-based metrics in SD-OCT instruments operating at wavelengths around 850 nm [7]. In addition, Liu et al reported a high intra- and inter-observer reproducibility of the swept-source OCT, that operates at 1310 nm [11]. This is particularly important since the quantitative assessment of the images with all these instruments is semiautomatic and relies on the subjective recognition of anatomic landmarks, either the SS or SL.

It is also important that the reliability indices achieved with both SD-OCT devices are superior to the ones reported in previous studies for time domain OCT instruments, like Visante and slit-lamp OCT [12-17]. Based on the ability to visualize the SS, the metrics used to characterize an angle were SS angle, AOD500, AOD750, TISA500 and TISA750. Lower speed and image resolution, as well as differences in visibility of different anatomical landmarks due to the longer wavelength in time domain OCT may account for some of the discrepancies between the two modalities. This is especially important, taking into consideration the greatly improved resolution on SD-OCT that enables us to detect even small changes in the configuration of the angle, in the magnitude of 10 μm.

In a previous study, Wylegala et al compared AOD and TISA measured from the SS between the RTVue SD-OCT and Visante time domain OCT, reporting good agreement between them using correlation analysis [18]. However, limited data are available regarding the agreement between different SD-OCT instruments in the quantitative assessment of the angle.

Previous studies have also reported moderate agreement between different OCTs in the qualitative assessment of angle closure. Looking at the agreement between RTVue, Visante and gonioscopy, the authors concluded that there was moderate agreement among them in the assessment of angle closure [19]. Images were acquired with the high-resolution corneal scan mode in that study and the visibility of SL was superior in the former compared to the latter. The authors do not specify if SL visibility was different in narrow compared to open angles. It is also interesting that an overall decreased visibility of SS and SL was observed in that study compared to other studies [9,20]. In another study assessing the agreement between iVue (Optovue, Inc.) and Cirrus for the qualitative assessment of the angle, an increased visibility of SS and SL was found compared to the previous study and the agreement between the OCT devices moderate, while the agreement with gonioscopy was fair [20]. Hu et al. investigated the performance of Cirrus and Visante OCT in angle closure assessment and reported moderate agreement between them with fair agreement with gonioscopy [21]. However, the surprising result of this study was the really low percentage of angle landmarks' identification, both for SS and SL with both modalities. Overall, the SS is the main anatomic landmark used to identify angle closure in all these studies and it is clear that the SS visibility is poor in a percentage of images. In addition, the criteria to identify angle closure are not consistent in OCT and gonioscopy. Furthermore, OCT imaging of a narrow area and sampling of only one or a few areas of the angle circumference might be a reason for the discrepancies found between different modalities in some patients. The better visibility of SL in SD-OCT images may provide a rationale for using the SL as a landmark. Interestingly, Qin et al found a high correlation between the quantitative SL-based AOD and gonioscopic angle grading [9].

In the present study, all measurements were performed on images of the inferior angle, suggesting that reliable and reproducible measurements can be obtained from the inferior angle with both instruments. Usually the temporal and nasal angles are easier to image, mainly because they do not require lid manipulation. In a previous study with Visante, the reproducibility was tested for the nasal, inferior and temporal angle scans, and it was superior in the horizontal scans compared to the inferior angle, largely due to the decreased visibility of the SS in the latter [14]. In another study, the SL was visible in only 26% of the inferior angle scans, which is different from our study where SL was identified in all images [19]. However, the present study shows that SL visibility was excellent and placement of measurement tools was reproducible in this location. This might also result from the fact that images were acquired by an ophthalmologist who checked image quality after the acquisition. It is also important that the variability in measurement was independent from the actual angle opening, since the Bland Altman plots showed no bias relative to the degree of angle opening.

Another important issue is that the SD-OCT instruments used in the study provide high resolution line scans but they do not yet provide tracking or image registration which would also improve the reproducibility, by helping capture the exact same location. However, in a previous study, we reported no measurement differences between OCT scans with local variability. Specifically, we found no significant differences in measurements between individual OCT scans that were placed up to 1 mm apart with the Cirrus SD-OCT or up to 10 degrees apart with the Visante, but it remains unknown whether this is true in eyes with irregular anatomy, iris atrophy, or narrow angles [22].

Finally, the present study provides evidence for excellent repeatability, intra- and inter- observer reproducibility, as well as agreement in SL-based measures between the Cirrus and RTVue SD-

OCT. This is especially important with increasing adoption of OCT imaging in clinical practice since it offers the great advantage of noncontact angle imaging under strictly controlled light conditions.

Declaration of Interest

S. R. Sadda reports consulting agreements unrelated to the submitted work with Carl Zeiss Meditec; grants/grants pending with Carl Zeiss Meditec and Optovue. No other author has a financial or proprietary interest in any material or method mentioned.

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