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Repeatability of On- and Off-Axis Eye Length Measurements using the Lenstar

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Abstract

Purpose—To determine the repeatability of eye length measurements made centrally and off-axis using a low-coherence interferometer.

Methods—Eye length was measured (left eye) in twenty-nine adults with a Haag-Streit Lenstar LS 900. Five measurements were made centrally, 10° temporally, and 10° nasally on the retina by the same examiner at two separate visits. Inter-visit repeatability was assessed by plotting the difference versus the mean of each pair of measurements (bias) and calculating the 95% limits of agreement (LoA). Within-session repeatability was determined by calculating the within-subject standard deviation (Sw) of five consecutive measurements at a visit. Due to variability noted 10° nasally, the Sw was also determined on a subset of 10 subjects using five measurements at one visit 30° nasally and 30° temporally.

Results—The mean $\pm$ SD age, spherical equivalent refractive error, and central axial length (at visit 1) were 24.0 ± 1.4 years, -3.46 ± 2.69 D, and 24.91 ± 1.10 mm, respectively. There was no significant bias for central, 10° nasal, or 10° temporal measurements between visits (all $p > 0.09$). The 95% LoA were: ± 0.05 mm central, ± 0.12 mm 10° nasal, and ± 0.05 mm 10° temporal. The Sw (visit 1) were: 0.025 mm central, 0.045 mm 10° nasal, and 0.028 mm 10° temporal. The Sw in the subset of subjects with 30° measurements were 0.023 mm (30° nasal) and 0.030 mm (30° temporal).

Conclusions—Lenstar central and off-axis eye length measurements are very repeatable, though repeatability was not as good 10° nasally on the retina as indicated by the larger 95% LoA between visits and larger Sw. The Sw for measurements centrally and 30° off-axis were similar, suggesting the reduced repeatability 10° nasally is anatomical in nature. Despite greater variability 10° nasally, Lenstar off-axis repeatability is still superior to the repeatability of on-axis ultrasonography.

Keywords

axial length; repeatability; eye shape; off-axis eye length; low-coherence interferometry; Lenstar

Accurate measurements of ocular axial length are important in studies of the development of refractive error, studies of myopia progression, and in cataract surgery. Recent work in animal models and humans has also demonstrated that measurements of peripheral eye length are of interest in studies of human refractive error development. There is convincing

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evidence in animal models that the visual experience in the peripheral retina plays an important role in emmetropization.^{1, 2} Work in rhesus monkeys has shown that relative peripheral hyperopic defocus is capable of altering central refractive error development³ and that retinal regions are capable of responding to local defocus signals.⁴ Based on previous work in children measuring eye length 15° off axis, it has also been suggested that relative peripheral eye length may be associated with central changes in myopia.⁵ Both on-axis (central) and off-axis eye length measurements can be used to determine relative peripheral eye length (retinal shape) and whether changes in relative peripheral eye length occur due to optical treatments that manipulate peripheral defocus.⁶ Although many studies have examined central (on-axis) eye length, very limited information is available on the repeatability of off-axis peripheral eye length measurements.

Since the introduction of a low coherence (also partial coherence) interferometry-based method of measuring axial length, non-contact interferometry has replaced ultrasonography as the gold standard for measuring axial length due to its superior repeatability.⁷ The IOLMaster (Carl Zeiss Meditec, Dublin CA) was the only commercially available interferometer for measuring eye length in the United States until the recent introduction of the Lenstar LS900 (Haag-Streit USA, Mason OH). In addition to measuring axial length using low coherence interferometry, the Lenstar also simultaneously measures corneal thickness, anterior chamber depth, and lens thickness using the same interferometry-based method. Studies evaluating the Lenstar have found it to be a repeatable instrument when measuring on-axis eye length;^{8, 9} however, these studies did not evaluate the repeatability of off-axis eye length measurements.

This study assessed the within-session and between-visit repeatability of the Lenstar for both on-axis and off-axis eye length measurements.

METHODS

Subjects

Twenty-nine adults (age range: 22 to 28 years) participated in this study. The study protocol was approved by the University of Houston Committee for the Protection of Human Subjects and was conducted in accordance with the tenets of the Declaration of Helsinki. Subjects provided written informed consent before being enrolled in the study. Subjects were required to be free of ocular disease, have no history of ocular surgery, and be correctable to at least 20/25. None of the subjects wore rigid gas permeable contact lenses. Subjects who wore soft contact lenses were instructed to wear glasses the day of each visit.

Lenstar Eye Length Measurement

Data for this study were obtained on two separate visits. A standardized subjective refraction was used to determine the most plus (least minus) spectacle prescription that provided the subject with best visual acuity. Eye length was measured on all subjects using a Lenstar LS 900. Five consecutive, non-cycloplegic measurements were made on the left eye centrally, 10° temporally, and 10° nasally on the retina by the same examiner at two separate visits scheduled at the same time of day. Return visits occurred between 1 and 20 days later. For on-axis measurements, subjects viewed the Lenstar's internal fixation target. For off-axis measurements, subjects turned their eye to fixate the center of circular fluorescent-colored targets affixed to the instrument 10° nasally and temporally to the line of sight. Subjects were instructed that they should not try to focus or clear the target, should allow it to remain blurry, and should look at the center of the target. The Lenstar uses a green circle of variable diameter and directional arrows to aid in achieving optimal focus. Directional arrows instruct the operator to move the instrument toward or away from the eye when necessary to

achieve optimal focus, which is indicated by obtaining the smallest circle possible. For each measurement, the instrument was focused until the smallest circle was achieved with no directional arrows present, which is important to ensure that the external targets are at the appropriate angle from the line of sight. By ensuring that the Lenstar was focused within the range where no directional arrows were present before making measurements, possible errors in the location of the off-axis targets were minimized to no more than $\pm 0.2^\circ$ from the desired angle from the line of sight.

Toward the end of data collection, it was noted that the within-session variability was greater when measuring 10° nasally on the retina. To evaluate whether the greater within-session variability at the 10° nasal retinal location was anatomical in nature (e.g., due to the proximity of the optic nerve), five measurements were made 30° nasally and 30° temporally on the retina at one visit on a subset of 10 subjects. The 30° nasal and temporal targets used the same setup as described for the 10° targets.

Statistical Analyses

Statistical analyses were performed using STATA 12.0 (Stata Corp, College Station TX). To assess within-session repeatability, the within-subject standard deviation (S_w) at each visit was calculated using the five sequential measurements made at each location.¹⁰ The coefficient of variation (the ratio of the standard deviation of the five measurements to the mean of the five measurements) was also calculated to allow for comparison to previously published papers of on-axis within-session repeatability using the Lenstar.

The between-visit repeatability was assessed by comparing the mean of the five measurements at each retinal location at the first visit to the mean of the five measurements at each retinal location at the second visit. The difference versus the mean of each pair of measurements was plotted to determine the bias (mean of the differences relative to zero) centrally, 10° nasally, and 10° temporally on the retina. A t-test was used to compare each mean difference to zero. The 95% limits of agreement (LoA) were calculated for each location as mean difference $\pm 1.96 \times$ standard deviation of the differences.¹¹

RESULTS

The mean ($\pm$ SD) age of the 29 subjects was 24.0 ± 1.4 years. The mean ($\pm$ SD) spherical equivalent refractive error and axial length of the left eye were -3.46 ± 2.69 D (range: $+2.63$ D to -8.50 D) and 24.91 ± 1.10 mm (range: 22.93 mm to 27.66 mm), respectively. Of the 29 subjects, 23 were myopes and 6 were non-myopes with myopia defined as greater than -0.75 D of myopia in both meridians of the eye. The mean $\pm$ SD eye length by retinal location for each measurement session is shown in Table 1.

Repeatability of Lenstar Axial Eye Length Measurements

Table 2 shows the within-subject standard deviation and coefficient of variation (CV) for each measured direction at visit one and visit two as well as the S_w and CV for the 30° temporal and 30° nasal measurements in the subset of 10 subjects. The S_w for both 30° temporal and nasal measurements was similar to the S_w for central and 10° temporal measurements. The S_w for the 10° nasal measurement was larger than for the other locations.

Figure 1 shows difference versus mean plots for eye length measurements made centrally (along the line of sight), 10° temporally, and 10° nasally on the retina. There was no significant bias for central, 10° temporal, or 10° nasal measurements made by one examiner on two separate occasions using the same instrument (all $p > 0.09$). Table 3 shows the mean $\pm$ SD difference between visits and the 95% LoA (repeatability) for the three eye length

measurements derived from the plots. The central and 10° temporal retinal eye length measurements were more repeatable than the 10° nasal retinal eye length measurements, as indicated by the larger 95% LoA between visits for the nasal location.

DISCUSSION

Accurate axial length measurements are important for studies of myopia progression, refractive error development, and cataract surgeries. The repeatability of non-contact, interferometry-based measurements of axial length has been shown to be superior to A-scan ultrasonography;^{7, 12, 13} however, the majority of studies have only examined central (primary gaze) axial measurements of eye length and have not evaluated the repeatability of off-axis eye length measurements. Evidence from animal studies has shown that local retinal defocus is capable of altering peripheral eye shape,⁴ and there have been suggestions that peripheral eye shape may be associated with axial elongation in children.⁵ Non-contact, interferometry-based biometers have been suggested as a method of measuring retinal shape.¹⁴ As expected, the mean eye length in this study was longer centrally than at the off-axis locations, which corresponds to the mean refractive error being myopic. In this study, we found excellent repeatability for both on-axis (central) and off-axis eye length measurements using the Lenstar LS900, though measurements made 10° nasally on the retina were not as repeatable as at other locations.

Many studies have utilized A-scan ultrasonography with great success to measure axial eye length in children.^{15–17} That being said, with growing interest in the shape of the eye, A-scan ultrasonography has several disadvantages compared to low coherence interferometry biometers. A-scan ultrasonography requires the use of a local anesthetic and direct contact with the cornea. If used to make both central and peripheral measurements to evaluate retinal shape, the A-scan probe would need to contact the cornea multiple times for each point being measured, increasing the potential for disruption of the corneal epithelium or abrasions. Each applanation of the cornea using the A-scan probe also has the potential to cause corneal indentation, which can alter measurements of eye length.¹⁸ When making off-axis measurements, it would also be difficult to ensure that the A-scan probe was applanating the cornea at the appropriate field angle. The non-contact nature of the Lenstar and IOLMaster alleviates these issues.

Within-session Repeatability of Lenstar Measurements

The central within-session repeatability as assessed by the S_w in this study for visit one and visit two (0.025 mm and 0.026 mm, respectively) is between those reported in recent studies (0.010 mm to 0.017 mm) and the S_w reported in the manufacturer's user manual (0.035 mm).^{8, 9, 19–21} The S_w for measurements made centrally, 10° temporally, 30° temporally, and 30° nasally (range: 0.023 mm to 0.030 mm) are smaller than the S_w found when making measurements 10° nasally (0.045 mm visit 1 and 0.058 mm visit 2), which suggests that the reduced within-session repeatability 10° nasally on the retina is anatomical in nature and associated with proximity to the optic nerve.

Between-Visit Repeatability of Lenstar Measurements

Based on the Gullstrand #1 model eye, a change in axial length of approximately ± 0.10 mm in an emmetropic eye is equivalent to a roughly 0.25-D change in refractive error. Assuming a longitudinal study design, to be able to state that a change of 0.10 mm in axial length between visits only has a 5% probability of being due to measurement error alone, it is necessary for the between-visit repeatability (95% LoA) to be less than ± 0.10 mm. Between-visit repeatability for the ocular component measurements used to determine axial length with A-scan ultrasonography (i.e., anterior chamber depth, crystalline lens thickness, and

vitreous chamber depth) has been reported to range from ± 0.20 and ± 0.37 mm.²² Another study found the axial length between-visit repeatability for A-scan ultrasonography to be between ± 0.30 mm and ± 0.41 mm, depending on the experience level of the examiner, while the between-visit repeatability for the IOLMaster in the same study was between ± 0.06 mm and ± 0.09 mm.¹²

Although several studies have reported the within-session repeatability of the Lenstar, few have examined between-visit repeatability. Between-visit repeatability using the Lenstar was the same for central and 10° temporal eye length measurements (± 0.05 mm), but was greater (± 0.12 mm) for measurements made 10° nasally on the retina (near the optic nerve). The between-visit repeatability of ± 0.05 mm for central measurements in this study was the same as the repeatability reported for central Lenstar measurements by another study that made biometry measurements on two separate days (95% LoA = ± 0.05 mm).⁹ The between-visit repeatability was also similar to previously reported between-examiner repeatability for central measurements made at the same visit (± 0.02 mm).⁸ Despite greater variability 10° nasally, the off-axis repeatability of the Lenstar is still superior to the between-visit repeatability of central A-scan ultrasonography.¹²

Increased between-visit repeatability when making peripheral measurements nasally on the retina was also noted in a previous study utilizing the IOLMaster to make measurements 20° from the line of sight superiorly, inferiorly, nasally, and temporally on the retina.²³ Noble and Walline²³ reported that between-visit repeatability for central measurements made using the IOLMaster was between ± 0.06 mm (cycloplegic) and ± 0.07 mm (non-cycloplegic) while between-visit measurements at the nasal retinal location were less repeatable (± 0.17 mm cycloplegic and ± 0.24 mm non-cycloplegic). They also reported no systematic differences in repeatability across locations between cycloplegic and non-cycloplegic measurements. Between-visit repeatability at peripheral locations other than nasally in their study was between ± 0.10 mm and ± 0.14 mm regardless of cycloplegia, with the exception of poorer repeatability noted for superior measurements made with cycloplegia.²³

Variability of 10° Nasal Lenstar Measurements

The greater variability seen when measurements were made 10° nasally on the retina may be due to a combination of anatomical factors. Small anatomical variations in the size and location of the optic nerve and blind spot have been noted^{24, 25} and may have partially contributed to the increased variability seen at this location. Small errors in fixation combined with the location of the subject's optic nerve could have yielded some of the variability.

The Lenstar measures axial length to the retinal pigment epithelium (RPE),²¹ and another source of variability involves the method by which the RPE is identified from the retinal waveform. Lenstar A-scans generally show 2 to 3 peaks in the retinal region presumed to correspond to (from anterior to posterior) the internal limiting membrane (ILM), RPE, and the boundary between the choroid and sclera,²⁶ though the third peak was not always visible in our study. The Lenstar software appears to select the highest retinal peak as the location of the RPE (Figure 2A). When measurements were made close to the optic nerve, it was noted that the first retinal peak (the ILM peak) was higher in some scans than the second retinal peak (the RPE peak), leading the software to incorrectly select the ILM peak as the location of the RPE when in reality the first peak represents the ILM (Figure 2B). The increase in nerve fiber layer thickness when approaching the optic nerve may be responsible for the amplitude of the ILM peak being greater than that of the RPE in this retinal location. Figure 3 displays an OCT scan in the plane of the fovea and optic nerve showing the anatomical increase in nerve fiber layer thickness when approaching the optic nerve. Although incorrect identification of the RPE peak did not occur in all subjects with

increased within-session variability at the 10° nasal location, it does appear to contribute to the overall increased variability at this location.

While within-session repeatability was assessed at both 10° and 30° from the line of sight, a limitation of this study is that we did not assess the between-visit repeatability of peripheral measurements past 10°. That being said, the only difference between the setup and measurement protocol for the 30° and 10° locations was the location of the target. Given that the within-session repeatability for the measurements that were made 30° nasally and temporally on the retina were very similar to those for the central and 10° temporal measurements, it is reasonable to expect that the between-visit repeatability at the 30° locations is similar to the between-visit repeatability of the central and 10° temporal locations. Future studies could confirm this by evaluating between-visit repeatability at additional peripheral points.

One of the potential sources of reduced repeatability between central and peripheral measurements is the fixation target (internal point of light for central measurements versus fluorescent dots on the instrument for peripheral locations). The within-session repeatability at all locations other than the 10° nasal location (Table 2) were similar, and the between-visit repeatability at the central and 10° temporal locations were both ± 0.05 mm (Table 3). The within-session results show that there is no reason to believe that a subject's ability to consistently fixate the same location during a series of measurements differed between the internal versus external target or was a clinically significant source of variability during a measurement session in this study. The between-visit repeatability data collected in this study do not suggest that subjects were any less accurate at fixating the center of the circular external targets at each visit as they were at fixating the instrument's internal point source. Not finding a difference in either within-session or between-visit repeatability between the two targets (internal versus external) is consistent with previous work finding that subjects can fixate a medium size disc target as accurately as they can fixate a small point.²⁷

Another study limitation is that we did not use a cycloplegic agent. Despite being instructed not to focus on the off-axis targets affixed to the instrument, it is important to consider any effect that residual accommodation or variability in the accommodative response could have had on both the repeatability and accuracy of off-axis measurements. If fluctuations in accommodation had influenced the within-session repeatability of eye length measurements at off-axis points, a meaningful increase in the within-subject SD (S_w) at off-axis locations would have been observed compared to the central location for which the subject viewed the Lenstar's internal, non-accommodative target. In this study (Table 2), the S_w for all off-axis points are the same as for the central measurements (0.03 mm), with the exception of the 10° nasal location where proximity to the optic nerve increased variability. The between-visit repeatability for the central and 10° temporal measurements was also the same (both ± 0.05 mm) despite the central target being internal (no accommodative stimulus) and the off-axis targets being affixed to the instrument head. These data demonstrate that the target used (internal Lenstar target versus off-axis fluorescent target) did not result in a difference in either within-session or between-visit repeatability.

Because a cycloplegic agent was not used, it is possible that the off-axis targets resulted in an accommodative response even though subjects were instructed not to attempt to focus or clear the target and to allow it to remain blurry. Differences in anterior chamber depth and crystalline lens thickness due to accommodation may lead to errors when determining eye length using interferometry-based ocular biometers.²⁸ A recent study investigating the effect of accommodation on axial length measurements with the Lenstar found that a 3.0-D accommodative stimulus resulted in a 0.01 mm change in measured axial length, while a 6.0-D accommodative stimulus resulted in a 0.02 mm change in axial length.²⁹ Both of these

reported changes in measured eye length are clinically small and below the ± 0.05 mm between-visit limits of agreement (repeatability) of the Lenstar found in this study and another by Shammas and Hoffer (2012)⁹; however, utilizing a cycloplegic agent would ensure that the most accurate eye length measurements possible are obtained by eliminating any potential accommodative response. In addition, cycloplegia would also allow for easier off-axis measurements in subjects with smaller pupil sizes.

Since this study was conducted, the instrument manufacturer has upgraded the Lenstar software such that consecutive measurements can be made without the operator having to complete the gross focusing and alignment step before each measurement. The operation is now similar to the operation of the IOLMaster in that the gross focusing is completed before the first measurement of each eye, and subsequent measurements can be made after adjusting the fine focus without requiring complete realignment. This has greatly increased the speed of acquiring measurements with the Lenstar, which could potentially further improve repeatability.

CONCLUSIONS

Central and off-axis eye length measurements made with the Lenstar are feasible and very repeatable. Although repeatability was not as good when measurements were made 10° nasally in the vicinity of the optic nerve, the repeatability at this location was still superior to the repeatability of central A-scan ultrasound measurements. The reduced repeatability 10° nasally on the retina near the optic nerve is partially due to the Lenstar incorrectly selecting the ILM peak on the A-scan as the location of the RPE due to increased nerve fiber layer thickness at this location. The increased variability of eye length measurements near the optic nerve should be taken into account when interpreting changes found in longitudinal studies seeking to measure changes in off-axis eye length.

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Figure 1.

Difference vs mean plots for repeated measures of eye length measured (A) centrally, (B) 10° temporally, and (C) 10° nasally on the retina on two separate visits. The solid horizontal line represents the mean difference (bias) between one examiner on two separate visits. The mean difference was not significantly different than zero for the central, temporal, or nasal location ($p = 0.09$, $p = 0.58$, and $p = 0.33$, respectively). The dashed lines represent the 95% limits of agreement for repeatability.

Figure 2.

Two separate retinal waveforms taken on the same subject consecutively on the same day at the 10° nasal location. (A) shows the Lenstar correctly choosing the second and highest peak as the RPE. (B) shows the Lenstar choosing the first peak as the RPE because it is higher than the second peak.

Figure 3.
An OCT B-scan at the level of the optic nerve (left) and fovea showing the increase in nerve fiber layer (NFL) thickness when approaching the optic nerve (arrow).

Table 1

Mean $\pm$ SD eye length (mm) by retinal location obtained at each measurement visit. Measurements made 30° temporally and 30° nasally on the retina at one visit on a subset of 10 subjects are included under Visit 2.

	30° Nasal (n = 10)	10° Nasal (n = 29)	Central (n = 29)	10° Temporal (n = 29)	30° Temporal (n = 10)
Visit 1	-	24.87 $\pm$ 1.17	24.91 $\pm$ 1.10	24.77 $\pm$ 1.07	-
Visit 2	24.41 $\pm$ 1.51	24.89 $\pm$ 1.16	24.90 $\pm$ 1.10	24.77 $\pm$ 1.07	24.02 $\pm$ 1.08

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Table 2

Within-subject SD (S_w) and coefficient of variation (CV) in mm at visit one and visit two for eye length measurements made centrally, 10° temporally, and 10° nasally on the retina on all 29 subjects. S_w for measurements made 30° temporally and 30° nasally on the retina at one visit on a subset of 10 subjects are included under Visit 2.

	30° Nasal (n= 10)	10° Nasal (n = 29)	Central (n = 29)	10° Temporal (n = 29)	30° Temporal (n = 10)
S_w Visit 1	-	0.045	0.025	0.028	-
S_w Visit 2	0.023	0.058	0.026	0.028	0.030
CV Visit 1	-	0.002	0.001	0.001	-
CV Visit 2	0.001	0.002	0.001	0.001	0.001

Table 3

Mean $\pm$ SD difference between visits (bias) and repeatability for on- and off-axis eye length measurements. None of the mean differences were statistically different than zero.

	Difference (Visit 1 – Visit 2)	Repeatability*
10° Nasal Retina	-0.01 ± 0.06 mm	± 0.12 mm
Central (Line of sight)	0.01 ± 0.02 mm	± 0.05 mm
10° Temporal Retina	0.00 ± 0.03 mm	± 0.05 mm

* $1.96 \times$ standard deviation of mean difference between visits