The Relation of Axial Length and Intraocular Pressure Fluctuations in Human Eyes

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Purpose. To determine in human eyes whether diurnal fluctuations in axial length are related to fluctuations in intraocular pressure (IOP) by studying these fluctuations in both eyes of individual subjects and by assessing the regularity of both rhythms on two separate study days.

Methods. Ten subjects, ages 18 to 24 years, underwent serial axial length and IOP measurements using highly precise, noncontact partial coherence interferometry and Goldmann applanation tonometry, respectively. Both eyes were measured at six 3-hour intervals during each of two study days, and significant fluctuations were modeled by sine curves.

Results. Of the 40 data sets, 29 had significant axial length high–low differences and 32 had significant IOP high–low differences (ANOVA, $P < 0.05$ for each). The magnitude of the significant high–low differences were 38 ± 22 μm for axial length and 6.0 ± 1.9 mm Hg for IOP (mean ± SD). Neither axial length nor IOP fluctuations necessarily occurred bilaterally on the same day, and neither rhythm was regularly observed on two separate days in individual eyes. In eyes in which both parameters fluctuated on the same day, there were no correlations in the amplitude, period or phase of the two rhythms.

Conclusions. Both axial length and IOP fluctuate during the day much of the time in most subjects. However, diurnal IOP fluctuations do not appear to cause diurnal axial length fluctuations. (*Invest Ophthalmol Vis Sci.* 2006;47:1778–1784) DOI:10.1167/iovs.05-0869

Diurnal fluctuations in axial length occur in many species, including chicks,[1–5] rabbits,[6] marmosets,[2] and humans.[7] In human eyes in particular, the axial length undergoes daily fluctuations of some 15 to 40 μm, with a mean period of approximately 21 hours.[7]

Although diurnal fluctuations in axial length have been observed in many species, the underlying physiologic control mechanisms are unknown. One possibility is that the ocular coats could expand and contract passively in response to diurnal oscillations in IOP. In chicks, the compliance of the ocular coats in response to IOP variations is consistent with this type of mechanism, and averaged peak times suggest that these two rhythms may occur synchronously. However, phase differences in the two rhythms occur in individual eyes, and autonomic denervations effectively dissociate the two rhythms.[1,3,8] Together, these observations suggest that diurnal axial length fluctuations do not arise from a simple IOP-mediated expansion and contraction of the eye, at least in chicks.

In the present study, we sought to learn whether the diurnal fluctuations in axial length of human eyes are related to fluctuations in IOP by studying the temporal relation of the two rhythms. We also evaluated whether axial length and IOP fluctuations occur bilaterally in individual subjects on single days and assessed the regularity of the two rhythms on two separate study days.

Methods

Subjects

Subjects were 10 University of Pennsylvania undergraduate student volunteers, aged between 18 and 24 years, with no history of glaucoma or other eye disease. All had best corrected visual acuity of 20/20 or better in each eye. Refractions were obtained by neutralizing the subjects' glasses or, if no spectacles were worn, from autorefraction without cycloplegia. The spherical equivalent refractions of the subjects on the first measurement day ranged from −2.75 to +1.00 D with a mean of −0.68 D. Inclusion criteria were astigmatism less than 1 D, astigmatism that was bilaterally symmetric (<0.5 D and 15° axis difference), and spherical equivalent refractions within 1.0 D between eyes. The protocol was reviewed and approved by the Institutional Review Board at the Children's Hospital of Philadelphia and was in accord with the Declaration of Helsinki.

Measurement Procedures

Axial length and IOP measurements were obtained during each study day on both eyes of each subject at six 3-hour intervals, starting at 7 AM and ending at 10 PM. (i.e., 7 and 10 AM and 1, 4, 7, and 10 PM). The right eye was always measured first. The axial length measurements were obtained using partial coherence interferometry (PCI) without cycloplegia, using our previously described instrument and protocol, with a precision of approximately 8 μm.[9] Each subject fixated on the alignment beam of the PCI, and five series of 16 individual PCI tracings were obtained from the right and left eyes of each subject at each time point.[9] After obtaining the PCI readings for both eyes at each time point, 1 drop of 0.5% proparacaine was instilled in each eye for topical anesthesia, fluorescein dye was instilled into the cul de sac, and an experienced clinician (GEQ, ELF) measured IOP three times with a slit lamp–mounted Goldmann applanation tonometer.

Subjects returned for a second day of measurements, with identical procedures used for axial length and IOP measurements. The second visit occurred 2 weeks later in seven subjects and 5 months later in the other three subjects. The differing time intervals were the result of conflicts with our subjects' school and vacation schedules.

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Supported in part by EY00402 (GEQ), EY01583 (GSY), EY07354 (RAS); grants from Pennsylvania Lions Club (GEQ); Ethel B. Foerderer Fund for Excellence (GEQ); Research to Prevent Blindness (RAS); the Paul and Evanina Bell Mackall Foundation Trust (RAS); and the Doris Duke Charitable Foundation (LBW).

Submitted for publication July 7, 2005; revised August 26 and September 22, 2005; accepted March 17, 2006.

Disclosure: **L.B. Wilson**, None; **G.E. Quinn**, None; **G.-s. Ying**, None; **E.L. Francis**, None; **G. Schmid**, None; **A. Lam**, None; **J. Orlow**, None; **R.A. Stone**, None

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TABLE 1. Axial Length and Intraocular Pressure Fluctuations in All Subjects

			Significant Sine Curve Modeling ($P < 0.05$)					
			Axial Length			Intraocular Pressure		
Subject-Eye-Day	Axial Length High–Low Difference	IOP High–Low Difference (mm Hg)	Amplitude (μm)	Peak Time (h:mins)	Period (h)	Amplitude (mm Hg)	Peak Time (h:mins)	Period (h)
A-OD-1	24.2*	3.0‡	—	—	—	—	—	—
A-OS-1	27.0*	3.7‡	22.9	11:45	13.5	—	—	—
A-OD-2	18.0*	3.7‡	9.7	5:42	25.5	—	—	—
A-OS-2	26.2*	7.7*	18.1	5:45	24.9	6.19	17:49	13.1
B-OD-1	81.8†	5.3†	59.5	9:55	12.0‖	4.81	15:25	12.3
B-OS-1	96.2†	5.7†	78.8	15:35	16.4	—	—	—
B-OD-2	30.5†	4.0†	28.9	16:37	20.3	4.19	21:19	17.7
B-OS-2	26.0‡	4.7§	—	—	—	—	—	—
C-OD-1	21.8‡	8.3†	—	—	—	5.67	9:07	16.1
C-OS-1	22.8*	5.0‡	21.5	14:04	17.6	—	—	—
C-OD-2	9.8‡	6.7§	—	—	—	6.29	18:53	17.6
C-OS-2	6.0‡	2.3‡	—	—	—	—	—	—
D-OD-1	31.4‡	3.3§	—	—	—	—	—	—
D-OS-1	47.8*	3.7*	40.4	18:20	20.1	—	—	—
D-OD-2	45.7*	5.3*	40.2	18:24	22.4	5.91	18:00	20.2
D-OS-2	47.3*	4.7*	39.8	18:32	24.4	4.75	18:04	21.8
E-OD-1	43.9†	7.0§	—	—	—	—	—	—
E-OS-1	79.9*	4.0†	56.6	6:19	36.0‖	—	—	—
E-OD-2	63.3*	3.3†	—	—	—	—	—	—
E-OS-2	56.3*	4.7†	42.0	4:10	19.3	3.76	10:36	12.9
F-OD-1	27.0†	4.7*	26.3	17:47	17.9	—	—	—
F-OS-1	36.0*	6.7*	33.4	19:47	26.0	—	—	—
F-OD-2	25.3†	0.7‡	18.3	15:46	19.5	—	—	—
F-OS-2	25.4*	4.0‡	24.5	18:12	22.0	—	—	—
G-OD-1	28.0‡	9.3*	—	—	—	—	—	—
G-OS-1	39.5‡	8.0*	—	—	—	—	—	—
G-OD-2	58.8‡	2.3‡	48.3	16:29	23.6	—	—	—
G-OS-2	18.3‡	5.0*	—	—	—	4.46	18:22	16.3
H-OD-1	14.2†	3.7§	—	—	—	—	—	—
H-OS-1	7.4‡	6.3*	—	—	—	4.76	5:37	36.0‖
H-OD-2	42.2†	9.3*	—	—	—	9.61	18:39	17.1
H-OS-2	19.8†	10.0*	20.2	16:36	17.8	8.82	5:16	13.9
I-OD-1	44.5*	6.7*	38.8	17:17	22.2	5.79	10:24	25.5
I-OS-1	33.6*	7.7*	33.1	16:27	22.1	5.53	11:04	17.4
I-OD-2	22.8†	8.0*	22.7	14:46	19.9	—	—	—
I-OS-2	29.4*	7.3*	31.8	2:19	14.0	4.89	5:07	36.0‖
J-OD-1	9.0‡	4.0*	—	—	—	3.67	9:04	20.4
J-OS-1	11.6§	6.0*	—	—	—	5.54	11:40	14.9
J-OD-2	14.6†	7.0*	—	—	—	6.64	17:04	12.8
J-OS-2	6.4‡	5.7*	—	—	—	4.84	17:04	12.8‖
Mean ± SD	38 ± 22	6.0 ± 1.9						

* One-way ANOVA; $P \leq 0.001$.
† One-way ANOVA; $P \leq 0.01$.
‡ Not significant by ANOVA; ($P \geq 0.05$).
§One-way ANOVA; $P < 0.05$.
‖ Period reached 12- or 36-hour modeling restraint.
—Model not provided, either high-low difference by ANOVA or sine curve modeling is not significant.

Data Analysis

As described previously,[9] the PCI tracings were processed by a semiautomated algorithm to calculate axial length, corresponding to the distance from the corneal surface to a reflective surface located at the region of the interface of Bruch's membrane and the retinal pigment epithelium interface.[9–11] This protocol provides an axial length that differs from that of ultrasonography, because ultrasound measures to the retinal surface.[12]

Average daily axial length and IOP were calculated for each data set by using the mean of all measurement series taken on each day for each eye. High–low differences during the day for each data set for both axial length and IOP were calculated as the difference between the mean value at the time of largest parameter value and that of the smallest. A one-way analysis of variance (ANOVA) with replicate measures using a generalized linear model (SAS 8.2; SAS Institute, Inc., Cary, NC) was fit to each data set to determine whether the axial length measured at any of the time points differed significantly from the others. We used a criterion of $P < 0.05$ from the ANOVA to identify data sets that showed significant daily high–low differences in either parameter. Unless otherwise noted, all mean data are presented as the mean ± SD.

To obtain estimates of the period and phase of the daily fluctuations, the data sets with a statistically significant high–low difference in axial length and/or IOP were modeled with a sine curve (Table 1). Sine and cosine curves are traditionally used to model diurnal rhythms.[6,13,14] To achieve this modeling, an adjusted value was calculated by subtracting the mean daily axial length or IOP from the measured value at each time point, and sine curve functions were fit to

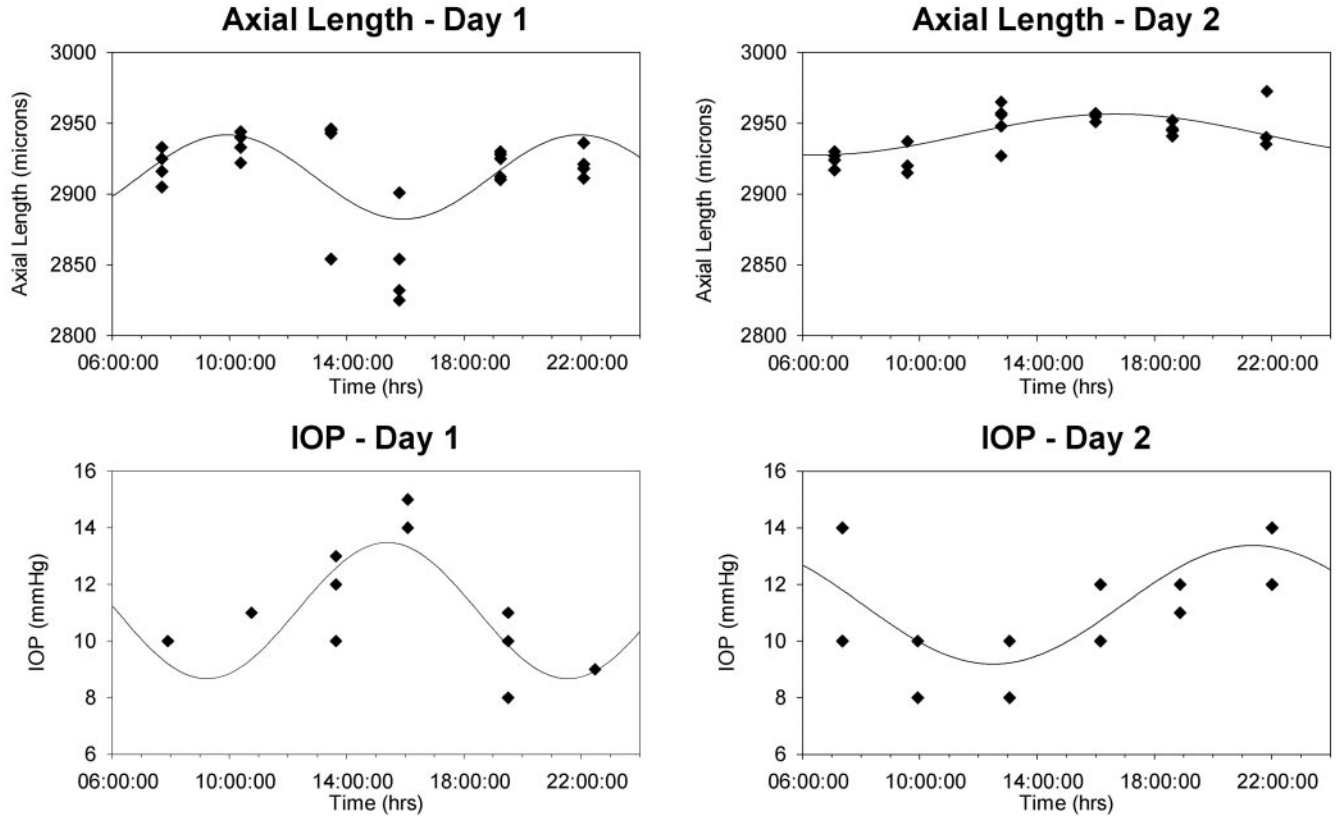

Figure 1. Representative tracings of axial length and intraocular pressure (IOP) fluctuations in a single eye. The data points indicate the measured axial length or IOP values at each time point on the two measurement days for the right eye of subject 2. The line on each graph represents the modeled sine curve.

the adjusted value versus time of day by a nonlinear model (PROC NLIN; SAS 8.2; SAS Institute, Inc.). The following equation was used to curve-fit the data for both axial length and IOP:

$$y = (a/2) \cdot \sin(2\pi \cdot \text{time}/b + c),$$

where y represents the adjusted parameter (either axial length or IOP), a represents the peak-to-trough difference, b represents the period, and c represents the phase of the sine curve. The period was constrained in the model to be 24 ± 12 hours. The model yielded estimates with 95% confidence intervals for the amplitude of the peak-to-trough difference, the period and phase for each individual and, as indicators of goodness-of-fit of the model, the correlation coefficient (R^2) and the probability of the model fit. In addition, the time of maximum axial length or IOP was estimated by solving the equation $\sin(2\pi \cdot \text{time}/\hat{b} + \hat{c}) = 1$ for time, with the constraint of time between 0 and 24 hours and where $\hat{b}$ and $\hat{c}$ were the period and phase estimated from the sin-curve fitting, respectively.

Results

Axial Length Measurements

As 20 eyes were each measured twice, 40 data sets of axial length measurements were collected overall (Table 1). The mean axial length of all eyes was 23.9 ± 0.5 mm (range, 23.1–24.9). From the 40 data sets, 29 eyes had significant axial length high–low differences (Table 1, second column; ANOVA, $P < 0.05$). Of these eyes with a statistically significant fluctuation, the mean magnitude of the axial length high–low differences was 38 ± 22 μm.

Daily axial length fluctuations of 22 of the 29 eyes with significant diurnal measured high–low axial length differences could be successfully modeled by sine curves (Table 1, columns 4 to 6 for amplitudes, peak times, and periods). These sine curve models had a mean amplitude of 34 ± 16 μm, a mean period of 20.8 ± 5.1 hours, and a mean peak time of 14 hours 12 minutes ± 5 hours 6 minutes. Figure 1 shows examples of axial length fluctuations on two examination days in a single subject.

Intraocular Pressure

Forty data sets of diurnal IOP measurements also were collected overall (Table 1). The mean IOP was 13.9 ± 1.3 mm Hg (range, 9.7–17.7). From the 40 data sets, 32 eyes had significant IOP high–low differences (Table 1, third column, ANOVA, $P < 0.05$). The mean magnitude of the significant measured IOP high–low differences was 6.0 ± 1.9 mm Hg.

Daily IOP fluctuations of 19 of the 32 eyes with significant measured high–low differences in diurnal IOP readings could be successfully modeled by sine curves (Table 1, columns 7 to 9 for amplitudes, peak times, and periods). These sine curve models had a mean amplitude of 5.6 ± 1.5 mm Hg, a mean period of 18.6 ± 7.1 hours, and a mean peak time of 14 hours 24 minutes ± 4 hours 54 minutes. Figure 1 shows examples of IOP fluctuations on two examination days in a single subject.

Axial Length versus IOP Fluctuations

As shown in Table 1 and Figure 2, axial length and IOP did not always fluctuate in the same eye on the same day. Whereas the mean peak times of both axial length and IOP fluctuations in these subjects were similar (slightly after 1400 hours), there

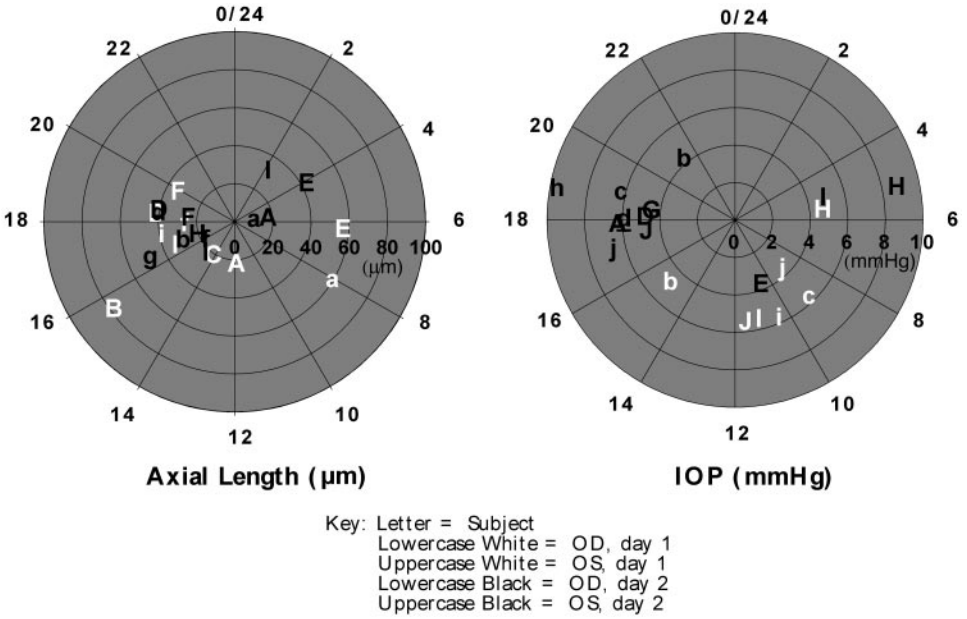

FIGURE 2. Polar plots of axial length and IOP peak time versus amplitude. Both peak time and amplitude are calculated from sine curve modeling of the data of the patients in Table 1. The angular position of each point represents the time of maximum axial length or IOP for each data set. The distance from the origin of each graph represents the amplitude of the axial length or IOP fluctuation for each data set.

was considerable variability between subjects. Examination of the time interval of 1000 to 1800 hours, which brackets the mean peak time for both axial length and IOP, provided evidence of the variability in both axial length and IOP patterns. For axial length, only 11 of the 22 fluctuating data sets successfully fit by a sine curve had a peak length between 1000 and 1800 hours (Fig. 2); and for IOP, only 9 of the 19 fluctuating data sets successfully fit by a sine curve had a peak IOP in this time interval (Fig. 2). As further evidence of the variability, the peak times for both axial length and IOP in a single daily recording session for an individual eye occurred in this rather broad time interval on only two occasions (subject 1, right and left eyes on study day 1; see Table 1).

In the 10 eyes that had both significant axial length and IOP sine curve fittings on the same day, no correlations were found between their peak times, amplitudes or periods. Figure 3 illustrates the lack of correlation for peak times. Similarly, eyes with higher axial length fluctuation amplitudes did not tend to have higher IOP fluctuation amplitudes, and the periods of the axial length and IOP correlations did not correlate.

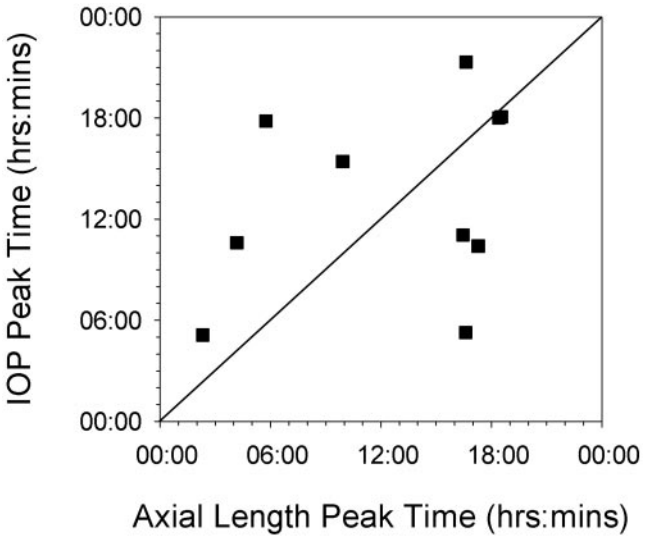

FIGURE 3. Axial length peak time versus IOP peak time. Axial length and IOP peak times are from the 10 data sets that were successfully modeled by sine curves for both axial length and IOP rhythms. The unity line emphasizes the lack of correlation of the axial length and IOP peak times.

Bilaterality of Axial Length and IOP Fluctuation

Table 2 shows the number of times, of 20 possible measurement instances (10 subjects × 2 measurement days/subject), that axial length or IOP fluctuations occurred in both eyes on a single examination day. For axial length, significant diurnal fluctuations occurred in both eyes on the same day 11 times for the actual measurements and 7 times for the sine curve fits. For IOP, significant diurnal fluctuations occurred in both eyes on the same day 14 times by the actual measurements and 5 times by the sine curve modeling.

Regularity of the Rhythms

Table 2 shows the number of times, of 20 possible instances (10 subjects × 2 eyes/subject), that axial length and IOP fluctuated for each individual eye on both days. For axial length, there was a significant fluctuation on both days in 11 eyes by the actual measurements and in 7 eyes by the sine curve modeling. For IOP, there was a significant fluctuation on both days in 14 eyes by the actual measurements and in 5 eyes by the sine curve modeling.

Analytical Efforts to Simplify Data Collection

To learn whether diurnal axial length fluctuations could be identified and modeled using fewer than the six time points measured on each study day, we resampled the existing data sets in various patterns. However, the use of either two (7 AM and 1 PM) or three (7 AM, 10 AM, and 1 PM) time points revealed significant high–low differences in axial length in only approximately 75% of the data sets that had significant fluctuations based on all six readings. To model the axial length data with only three time points, one sine curve parameter (i.e., amplitude, period, or phase) had to be set. Because the period was relatively consistent, it was set to the mean period from the initial analysis, 21 hours. When this setting was used, only 68% of the 22 data sets originally fit successfully by a sine curve could still be modeled.

TABLE 2. Bilaterality and Regularity of Diurnal Axial Length and IOP Fluctuations

	Bilaterality* *n* (%)			Regularity† *n* (%)		
	Axial Length	IOP	Axial Length and IOP	Axial Length	IOP	Axial Length and IOP
Data sets with significant high–low difference	11 (55)	14 (70)	8 (40)	11 (55)	14 (70)	7 (35)
Data sets with significant sine curve modeling	7 (35)	5 (25)	2 (10)	7 (35)	5 (25)	2 (10)

* The number of times, of 20 possible measurement instances (10 subjects × 2 measurement days/subject), that axial length or IOP fluctuations occurred in both eyes on a single examination day.

† The number of times, out of 20 possible measurement instances (10 subjects × 2 eyes/subject), that axial length and IOP fluctuations occurred on both days for each individual eye.

n = number of eyes.

To determine measurement variability in axial length, the absolute axial lengths were compared between the two study days in 14 eyes. Only eyes from those seven subjects with 2 weeks between study days were included in this analysis, to eliminate confounding from possible eye growth. The difference between mean axial lengths for individual eyes on the two measurement days was similar at all time points, ranging from 23 to 30 μm with standard deviations of 29 to 42 μm.

DISCUSSION

Axial length and IOP both fluctuate in a diurnal pattern, occurring much of the time in most subjects. Approximately three fourths of the axial length and IOP datasets showed evidence of fluctuations during the day, as manifested by significant high–low differences in the actual measurements. Although the majority of data sets without identifiable fluctuations in axial length came from only two subjects, these subjects do not appear to have characteristics that distinguish them from the other subjects.

Almost two thirds of these fluctuations in each parameter could be modeled by a sine curve, permitting estimates of period and peak times. It is not clear why some of the eyes exhibiting significant high–low differences in either parameter could not be fit with sine curve models, but we identified no clear differences between those that could be modeled and those that could not. It is possible that the patterns of specific intraday fluctuations were affected by some of the physiologic phenomena, including fluid intake and the sleep cycle.

Diurnal Variation in Axial Length and IOP

Supporting the utility of sine curve fitting for axial length data, the significant measured high–low differences of the axial length fluctuations and the amplitudes from the sine curve modeling were similar: 38 ± 22 μm vs. 34 ±16 μm, respectively. Based on the sine curve modeling, the mean time of the maximum diurnal axial length occurred in the early afternoon, although there was a wide range in the peak times for individual diurnal data sets (Table 1). Axial length variations of similar magnitude and peak time were also seen in a previous study using the same sampling strategy, instrument, and measurement protocol, though a less restricted age range.[7]

Likewise, the significant measured high–low differences of the IOP fluctuations and the amplitudes from the sine curve modeling were similar: 6.0 ± 1.9 mm Hg vs. 5.6 ±1.5 mm Hg, respectively. From the sine curve modeling, the mean time of the diurnal IOP peak occurred in the afternoon in this study. Diurnal IOP oscillations of similar amplitude have been reported in normal human eyes. [13–18]

In our particular sample, the time of peak IOP varied considerably (Fig. l), with a mean peak time between noon and 1 PM. Much data on diurnal IOP rhythms has addressed suspected or known glaucoma, and variability between diurnal curves in the time of maximum IOP has been noted.[19] Fewer studies are available for normal eyes, but these also have commented on the variability in diurnal IOP rhythm, especially the time of maximum IOP.[15,16,18] Two separate diurnal IOP studies using Schiotz tonometry[15,16] found almost 30% of the normal eyes examined (161/536 normal eyes in these two studies) peaked between 12 and 6 PM, a time that includes almost half of the IOP peaks in our study. Given the small sample size, our study results thus are consistent with the available reports of the temporal patterns of diurnal IOP fluctuations in normal, nonglaucomatous human eyes.

Regularity of Rhythms

Only approximately half of the eyes demonstrated a measured diurnal axial length fluctuation on both study days. Subjects with a 2-week interval between the first and second study days exhibited regularity similar to those with a 5-month interval. In the only previous study of diurnal axial length oscillations in human eyes, 9 of the 10 eyes with a second day of measurements showed fluctuations on both study days.[7] Although the two studies used the same instrument and measurement protocol, the age range of subjects from the previous study was less restricted and included subjects aged from 7 to 53 years. It is unclear whether differing age ranges, statistical sampling, or some other factor accounts for the differences in the consistency of the rhythm between these two studies. Determining whether diet, fluid intake, sleep pattern, menstrual cycle, or some other physiologic parameter influences this rhythm requires further study.

As indicated in the Methods section, the present PCI axial length measurements corresponded to the distance from the anterior corneal surface to the RPE/Bruch's membrane junction, the most reliably present and robust peak in the PCI retinal signal. It is currently unknown whether the axial length rhythms described herein are a result of variations in the overall length of the eye from anterior cornea to posterior sclera, variations in choroidal thickness, or both, as separate or combined changes in either parameter could influence the cornea-to-RPE distance and would be indistinguishable by the present PCI protocol.[7]

In addition, we found that diurnal axial length fluctuations could not be identified and modeled by using only two or three

time points per study day. Possible explanations for the inability to detect and model these fluctuations with fewer time points include the diminished power to detect the fluctuation because of a reduced number of data points and the obscuring of fluctuations because of the exclusion of certain data points.

In our study, the IOP rhythm was also not necessarily observed on the two study days. Although IOP variations have been measured on consecutive days in other studies, the regularity of the IOP diurnal rhythm over more than 1 day has only been reported for aggregate data[15,20,21] and not for the regularity of diurnal IOP fluctuations in individual normal subjects, to our knowledge.

We also found that neither axial length nor IOP fluctuations necessarily occurred in both eyes on the same day in our study population. In our prior study of diurnal axial length variation,[7] only one eye was measured, so this issue was not previously addressed for axial length fluctuations.

The issue of the bilaterality of IOP fluctuations in normal eyes also has not been adequately addressed, and only a few studies are pertinent. In Wilensky et al.,[21] the IOP fluctuations of normal eyes were classified into one of three patterns, based on the time of peak IOP: morning (peaking 4–10 AM), day (10 AM–4 PM), and biphasic. Ninety-four percent of their normal subjects exhibited a time of maximum IOP within the broad 6-hour range between 10 AM and 4 PM in both eyes. Another study[18] found maximum IOP measurements in both eyes that fell within 1 hour of each other in less than half of their data sets. In other studies,[6,13,14] in which IOP was measured over the day in both eyes, the right and left measurements were averaged to examine diurnal patterns, thus obscuring potential differences between the two eyes. Our results suggest that diurnal IOP fluctuations may not be as symmetrical as commonly supposed, at least in nonglaucomatous subjects, and indicate a need for direct study of the issue.

Relation of Axial Length and IOP Rhythms

Although axial length and IOP mean peak times were similar, neither the axial length nor the IOP rhythm necessarily occurred on both study days in any individual eye, and neither rhythm necessarily occurred in both eyes of a subject on the same day. The presence or absence of a rhythm in one parameter did not seem to depend on the presence or absence of a rhythm in the other. On the occasions when both parameters fluctuated in the same eye on the same day based on sine curve modeling, there was no correlation between the axial length and IOP amplitudes, periods, or peak times of the two rhythms. Based on these findings, the diurnal oscillations in the axial length of human eyes do not seem to reflect passive expansion and contraction of the ocular coats in response to changing IOP. Diurnal IOP variations thus do not appear to cause diurnal axial length fluctuations. Based on these observations, the diurnal oscillations in the axial length of human eyes do not seem to reflect passive expansion and contraction of the ocular coats in response to changing IOP.

Implications for Future Studies of Refractive Development

High-resolution measurement methods have now identified diurnal fluctuations in the dimensions of the eyes of laboratory animals[1–6] and fluctuations of comparable amplitude in the eyes of humans.[7] In experimental animals, the oscillation patterns of eye dimensions may be pertinent to patterns of refractive development.[1–6]

To adapt high-resolution measurement methods like PCI as novel techniques to study refractive development in children requires improved understanding of the nature and mechanisms of the diurnal oscillations in human eye size. The irregular presence and absence of axial length fluctuations, as well as the variability in peak times, limits the precision with which axial growth can be measured. The 20- to 30-μm variability in axial lengths of individual eyes between two measurement days, even when measured at the same time, reflects the irregularities in the axial length rhythm, masks the higher precision of our PCI protocol and seemingly prevents a strategy for improving measurement precision by controlling measurement time.

Despite these technical considerations in the utility of high-precision axial length measurements, we emphasize that the diurnal axial length rhythms we measured seem as robust as the diurnal IOP rhythm in the normal subjects in our study. For both rhythms, we applied quite strict statistical criteria for both defining the presence/absence of a rhythm and for establishing its characteristics, stricter criteria than often applied in the literature on IOP.[6,13–18,20–22] Further research will be needed to define how highly precise axial length measurements may be used optimally in clinical research and whether the diurnal oscillations in eye size can provide a useful novel parameter for studying refractive development in children.

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E R R A T U M

Erratum in: "Downregulation of IRS-1 Expression Causes Inhibition of Corneal Angiogenesis" by Andrieu-Soler et al. (*Invest Ophthalmol Vis Sci.* 2005;46:4072–4078).

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