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Diurnal variation in corneal thickness

Robert Blomquist
Pacific University

Jeff Keene
Pacific University

Thomas Zook
Pacific University

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DIURNAL VARIATION IN CORNEAL THICKNESS

by
Robert Blomquist
Jeff Keene
Thomas Zook

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Introductory Statement.

In the past most authors have assumed that corneal thickness is a constant value. (Polse, 1972) (Mishima and Maurice, 1961) (Ytteborg and Dohlman, 1965) (Maurice, 1969)

More recently researchers have been studying diurnal variation of corneal thickness in rabbits. They contend that there is a definate diurnal cycle. (Kikkawa, 1973)

In reviewing the literature nothing has been found concerning studies of diurnal variation of corneal thickness in humans. Our research project is primarily directed at this topic.

Kikkawa (1973) also noted that there are other functions which have diurnal cycles. He mentioned aqueous production, and intraocular pressure. A study by Kruse (1971) found that the relationship between an increase in corneal thickness and an increase in intraocular pressure is statistically significant. Therefore, a second consideration of our research project was to determine if there is a correlation between the diurnal corneal thickness values and the diurnal intraocular pressure values.

Introduction of Background Material.

1. Instruments used to measure corneal thickness.

The earliest measurements of corneal thickness were made during post mortem examinations. According to ancient literature the thickness of the central cornea is about one millimeter. This corresponds fairly well to the thickness of the maximally swollen human cornea. (Ehlers, 1966)

The first person to measure corneal thickness by optical means was Blix in 1880. (Ehlers and Hansen, 1971) The method used by Blix involved the observation of the specular reflection from the epithelial and endothelial surfaces of the cornea. The difference in instrument adjustment gave the apparent distance between the two surfaces. The real distance was then calculated knowing the radius of corneal curvature and the index of refraction of the cornea. (Donaldson, 1966) The biggest disadvantage of this method is that any movement of the cornea during the successive focusing invalidated the results. (Ehlers and Hansen, 1971)

Gullstrand in 1909 was the next to measure corneal thickness by a new method. His method involved simultaneous observation of the specular reflexes. (Ehlers and Hansen, 1971) Although his method was accurate, it involved the use of complicated equipment and was quite time consuming. (Donalson, 1966)

In 1916 Lindstedt developed a method of measuring anterior chamber depth. He used an astigmatic light bundle with one focal line on the cornea and the other on the lens. The principle, although apparently accurate, has not been used to study corneal thickness. (Ehlers and Hansen, 1971)

During the 1920's Hartinger was the first person to use the slit lamp beam to measure corneal thickness. The apparent thickness of the optical section can be used to calculate the actual thickness. (Ehlers and Hansen, 1971)

A similar method was used by Juillerat and Koby. They made use of an eyepiece micrometer to measure the apparent thickness. (Donaldson, 1966)

In the early 1930's Goldman developed a split ocular to measure the optical section of the slit lamp beam as it passed through the cornea. (Donaldson, 1966)

In 1948, von Bahr published the results of his extensive study of corneal thickness. His apparatus optically was similar to that of Blix. However, instead of making successive adjustments to obtain a reading, his instrument had a simultaneous adjustment of both the illumination and observation systems. This eliminated the movement problem that affected Blix's instrument. (Donaldson, 1966)

Maurice and Giardini, in 1951, used the same principles as von Bahr in the design of their pachometer, but their modifications eliminated many of the poorer features of von Bahr's instrument. Maurice and Giardini's pachometer was designed to be attached to the Haag-Streit Model 360 slit lamp. (Ehlers and Hansen, 1971)

In 1962 Hedbys and Mishima designed an instrument similar to Maurice and Giardini's. It was used for experimental purposes only. (Ehlers and Hansen, 1971)

Donaldson (1966) designed a special ocular which contained a split field lens. The ocular had a micrometer incorporated in its structure. The main advantage of his invention is that the ocular can be exchanged with any regular ocular of any slit lamp.

According to Ehlers and Hansen (1971) there are three instruments available commercially which measure corneal thickness by optical means. These are the Maurice-Giardini pachometer mentioned previously; an attachment to the Zeiss slit lamp; and a pachometer which attaches to the Haag-Streit Model 900 slit lamp. The latter shows the smallest measuring error, and appears to be the easiest to use.

The investigators using optical techniques have made several simplifying assumptions. First, they assume that the anterior and posterior corneal surfaces are parallel. They are not. However, Arner and Rengsdorff (1972) believe this factor produces only negligible changes in the apparent corneal thickness. They feel that variations in the index of refraction of various areas of the cornea are of more importance. They found that the cornea may change in thickness by about 3% based upon the limits of corneal indices of refraction of 1.333 and 1.419.

The above evidence of corneal thickness determination concerned the use of so called optical techniques. High freque ncy sound waves producing a graphic representation have been used to determine intraocular distances, namely, anterior chamber length, lens thickness, posterior segment length, and most important to this study, corneal thickness. The determination of these intraocular distances, excepting corneal thickness, utilizing echo feedback techniques have been made as long ago as the mid 1950's,(Mundt and Hughes, 1956) however, it wasn't until 1967 that corneal thickness measurement was made with the ultrasound device. (Giglio and Ludlam, 1967) Because of greater magnification (without the introduction of time errors) and greater resolution it was possible to achieve accurate and repeatable corneal thickness measurements. (Giglio and Ludlam) It is on this latter development that this present study is possible.

Repeatability and validity are certainly characteristics that need to be considered when accessing methods of corneal thickness measurements. In 1969 Giglio and Ludlam repeated at least seven measurements at one sitting on intraocular component dimensions using an ultrasonic devise on various subjects. The standard deviation of these measurements showed at the most

.0086mm and the least .0033mm, thereby, indicating a high degree of repeatability. At the same time a measurement on a ping pong ball was made with the ultrasound and this was copared with caliper determinations. There was a difference of less then 0.10% when comparing overall length thus indicating a high degree of validity.[7]

Sound is the mechanical vibration of particles of a medium around a position of equilibrium. The highest frequency of vibration audible to the human ear is 20 Kilo Hertz(Kc) - vibrations of higher frequency are called ultrasound. Although basic principles of piezoelectric phenomena date from the work of the Curie brothers and Galton in the 1880's, the first practical applications were put to use by a French scietist, Paul Langevin, during World War I when he used ultrasonics for the detection of submarines. Later this same device was applied for depth derminations and iceburg detection. A revolutionary discovery was made in 1929 when Sokolov found that ultrasonics reflections from the boundries in metal media of various densities could be the means of detecting flaws. From this work and other engineering principles developed by Sokolov in the late 1930's SONAR was utilized in World War II. Since 1945, manifold use has been made of ultrasound in cleaning devices, for drilling, welding, and in chemical and biological processes. The principles of echo ranging have been applied to flaw detection in metals, for

for thickness gauging, liquid level switches, and flow meters.

From the early 1940's to the mid 1950's, medical explorations with ultrasound were largely directed toward tumar and foreign body detection. Attention to the eye began slowly with notation of the damaging effects in the late 1930's to diagnostic considerations of retinal detachment, foreign body, neoplasm and cyst detection, and intraocular component and axial length measurements in the 1950's and 1960's.

Certain natural and synthetically manufactrued substances change dimensions when an electrical charge is placed across its surface. These materials are called piezoelectric elements and include quartz, lithium sulfate, and Rochelle salt in the natural state and barium titanate and lead zirconate in manufactured ceramic crystals. Since piezoelectric materials convert electrical energy to mechanical energy and reciprocally convert mechanical energy to electrical energy, they are well suited for both transmission and reception of ultrasound signals. The response of the crystal to the changing pressure of the returning echo is not necessaraly equal to its efficiency in converting electrical to mechanical energy. Quartz is not nearly as sensitive as barium titanate to a change in voltage, however, quartz is more sensitive to the returning echoes. Since applications of ultrasonics usually employ the same crystal for transmission and reception, the concept of "loop gain" is used in the selection of a transducer material.

When an electrical signal is placed across the transducer, the piezoelectric element expands and contracts in response to the excitation waves. This motion generates mechanical compression and rarefaction waves, the direction of which depends on the number of wavelengths across the diameter of the driving element. When energy is initiated from a single source, it is as though a stone were thrown into the water. Ringlets or waves propagate awy from the source. As the energy source is increased, the sound beam becomes directive. Variables influencing propagation of the sound beam through examined structures include transducer diameter and frequency, sonic velocity in the medium, impedance of penetrated materials, contour of the speciman, attenuation and beam properties.

The oscilloscope is usually the instrument for the display of the returning acoustic reflections. There are two modes of display. One is the B-scope, B-scan or intensity modulated ultrasonagraphy(IMU). It gives an entire cross section of the eye as a configuration of dots on the scope face. The other, which we will be concerned with in this study, is the A-scope, A-scan or time amplitude ultrasonagraphy(TAU). The returning signal is amplified and fed into the oscilloscope and becomes a voltage increase on the vertical plates. This deviates the electron beam from its normal horizontal sweep to form a signal trace. Since the sweep time of the electron beam is very regular, the measurement of the distance signal trace can be utilized as a measure of the time elapsed between signals. Knowing the velocity of ultrasound in various intraocular media enables one to convert the time between the echo signals on the scope to distances between the interfaces within the eye.

2. Comparison of the results obtained by the various investigators.

Table A

This table gives a comparison of the corneal thickness values obtained by some of the investigators. (Donaldson, 1966) (Kruse, 1971)

Author	Date	Corneal Thickness	No. of Eyes
Blix	1880	0.482-0.576	10
Gullstrand	1909	0.46-0.51	2
Koby	1928	0.466-0.733	20
Fincham	1930	0.48-0.59	12
Solanski	1934	0.40-0.57	20
von Bahr	1948	0.565±0.035	224
Maurice & Giardini	1951	0.507±0.028	44
Cook & Langham	1953	0.536±0.04	10
Lanergen & Kelecom	1962	0.51±0.04	198
Donaldson	1966	0.522±0.041	268
Martola & Baum	1968	0.523±0.039	209
Mishima & Hedbys	1968	0.518±0.02	40
Lowe	1968	0.517±0.034	157

3. Primary clinical uses of corneal thickness measurements.

One clinical use of corneal thickness measurements is in the detection and periodic evaluation of corneal thickness of keratoconus patients. (Cardona and DeVoe, 1971)

Another use is in the determination of the thickness of the cornea in patients having bullous keratopathy. If the thickness exceeds 1.2 mm, the prognosis is favorable for either a keratoplasty or a prosthokeratoplasty. (Cardona and DeVoe, 1971)

For optometrists fitting contact lenses it has been shown that the area of corneal thickening corresponds to the observed area of central circular clouding after two hours of wearing steep fitting contact lenses. Therefore there is justification for using corneal thickness measurements as an index of corneal edema if edema formation is considered essentially a hydration process. (Mandell and Polse, 1971)

Further clinical use for corneal thickness measurements in contact lens therapy would involve orthokeratology. The use of corneal thickness measurements could be used as an added criteria for evaluating the change in refractive power and as a key to help guide the change in the contact lens-cornea fitting relationship.

Methods and Materials

1. Ultrasonography equipment and procedures

The instrument used in determining the corneal thickness consists of two main parts which is shown in figure I. The topmost unit is called an Ocular Reflectoscope consisting of a Hewlett-Pachard model 175A oscilloscope with a 1754A four channel amplifier. A camera is attached to the oscilloscope utilizing Polaroid Black and White Type 107 film with one sixtieth/second shutter speed setting. In the lower portion of the picture are located a pulser/reciever unit, calibrated delay lines, and finally the display gate generator.

The probe consists of an open ended, flexible, cone shaped device made of clear transparent silicone rubber which fits snugly on a lithium sulfate 20 Kc transducer.

Maximum amplitude reflections are obtained when the probe has as angulation of less then $\pm$ 2 degrees in both the horizontal and vertical meridians and a horizontal/vertical translation of less then $\pm$ ½mm. The axis of maximum amplitude approximates the region of the optic axis of the eye therefore an unacceptable is easily recognized as illustrated in figure II. Figure III shows an acceptable pattern.

The subject is seated next to the instrument. After anesthesia has been applied to both corneas the patient is directed to fixate a target fourteen feet away and at eye level. The probe is brought up to one eye and a water bridge between the probe and the cornea is formed. Asecond investigator views the oscilloscope and when an acceptable picture appears the is operated. A picture is likewise taken on the other eye.

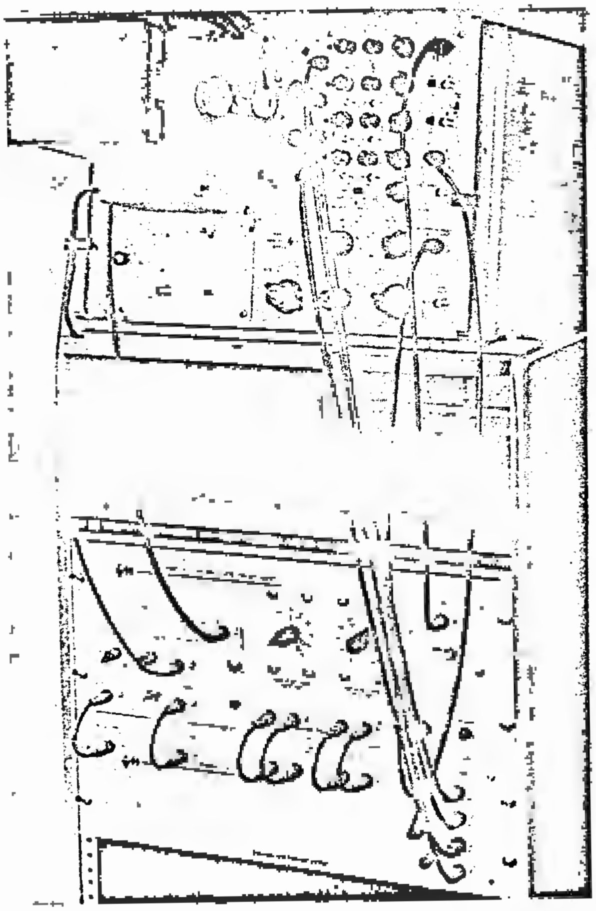


FIGURE I - The Ultrasonic Unit

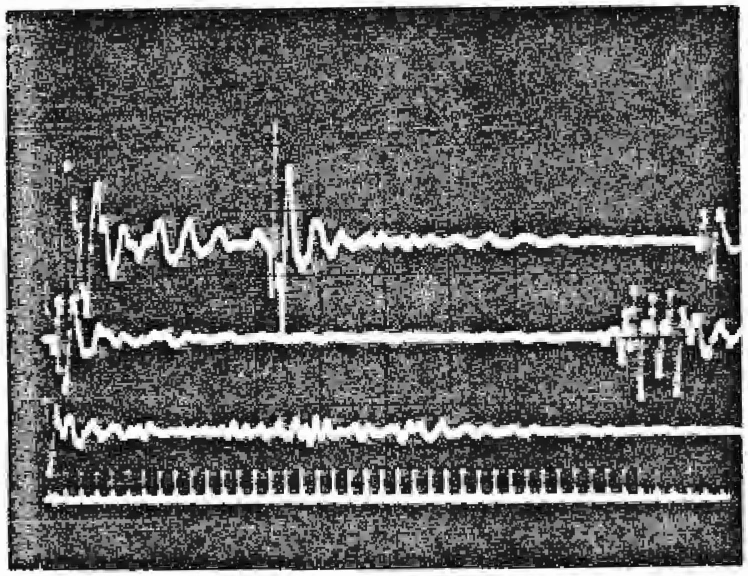


FIGURE II - An unacceptable ultrasonograph

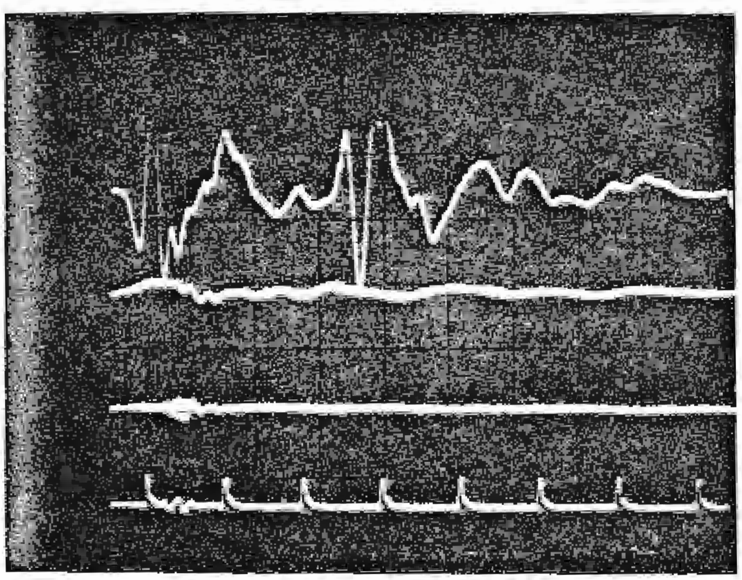


FIGURE III - An acceptable ultrasonograph

2. Anaesthetic used and procedures.

The anaesthetic used was Ophthaine Solution (Proparacaine Hydrochloride Ophthalmic Solution 0.5%). It is a rapid acting local anaesthetic. With a single drop, the onset of anaesthesia occurs in approximately 13 seconds and persists for 15 minutes or longer. (PDR, 1971)

One drop was placed in each eye about one minute before ultrasonography measurements were taken.

3. Procedures and Equipment Used to Measure the Photographs

The corneal thickness display on the cathode-ray tube was photographed using Polaroid film. The measurement of the corneal thickness dimension can be made directly from the photograph by being compared with a time reference included on the photograph. To measure the corneal thickness and the time reference directly from the photograph, a traveling microscope was used (microscope from Scientific Instruments; catalog number 6147; serial number 93709; W. G. Pye and Co., Ltd.; Granta Works; Cambridge, England).

To obtain the most accurate photographic measurements, an expanded trace of the oscilloscope pattern must be used. With the display being expanded on the photograph, direct measurement is more easily made. In reference to this study, two points should be mentioned if the research is done again. First, as mentioned, the most expandable trace will be the more accurate, and second, centering on the photograph of the first channel involving the corneal thickness will help do away with any distortions present from the cathode-ray tube.

In making the measurements from the photographs, the first measurements that were taken involved the time reference marks. The distance between five time marks were measured on the photograph to give distance in centimeters per micron. For each subject, a minimum of six photographs was measured using the mean of the six values to determine the time reference scale. The corneal measurements were then made in centimeters using the first negative wave of the front surface of the cornea and the first positive wave of the back surface of the cornea. The negative and positive waves were both measured an equal distance on each wave; for example if the negative wave was measured ten per cent down from the baseline then the positive wave was measured ten per cent up from the baseline. The measurements were taken twice on each wave allowing three different corneal thickness values to be calculated.

4. Instruments used to measure IOP and procedures.

The instrument used to measure intraocular pressure was the American Optical Non-Contact Tonometer. It was used because it probably causes less corneal trauma then any other type of tonometer.

Tonometry measurements were made before the ultrasonography measurements.

The instrument was allowed to warm for several minutes. Then with the setting on demonstration a reading of 57±1 was obtained. Next, three measurements were taken of the IOP of each of the subjects eyes.

RESULTS:

To help show the results obtained, Table B for subjects 1, 2, and 3 are provided. Two pictures were taken at each time period, one picture for the right eye and one picture for the left eye. The picture was numbered on the back of the photograph; for example picture number 1A with the number (1) standing for the subject and the letter (A) indicating which eye was measured.

From the use of the traveling microscope, the time reference scale and the corneal measurements were taken in centimeters. The first negative wave was measured of the front surface of the cornea and the first positive wave of the back surface of the cornea was measured. Two measurements of each wave were taken allowing the calculation of three different corneal thickness values. To complete the corneal thickness values, the time reference scale was measured and found to be 4.112 cm./micron for each subject. The time reference scale must be used for the corneal thickness measurements are calibrated against the time reference to provide the appropriate time distance. This fact means that the distances between the echoes on the oscilloscope refer only to the differences in time that the echoes must take to return to the transducer after being reflected from the corneal surfaces. The time intervals are multiplied by the velocity of sound in the cornea (1.6 usec/mm.) to provide the corneal dimensions. The dimensions are divided in half because of the return trip of the echoes from the corneal surfaces. Hence, the complete formula used to calculate corneal thickness was:

$$\frac{\left(\frac{\text{Corneal Measurements in cm.}}{\text{Time Reference in cm./micron}}\right)(1.6\ \text{usec./mm.})}{2} = \text{Corneal Thickness in mm.}$$

The arithmetic mean of the three corneal thickness values was then taken to give the corneal thickness for that picture.

Table C of intraocular pressure shows the time the pressures were taken, the three pressure readings from each eye, and the arithmetic mean for the three pressure readings for all three subjects.

The changes in corneal thickness involving the maximum and minimum corneal thickness values are found in Table D. The minimum value was subtracted from the maximum value giving the change in millimeters. The average corneal thickness change was figured from the six corneal values listed in the table and found to be 0.0386 mm.

Table E shows the average corneal thickness values for each subject calculated from all the thickness values taken. From these averages, the overall average for the three subjects combined was 0.4864 mm. The midrange value was 0.4759 ± 0.0538 mm.

The graphs in the report show corneal thickness vs. time and intraocular pressure vs. time. The slope values are also shown and were obtained by the graphical three - point mean method of curve smoothing adapted to drawing a best-fit straight line.

The average slope values from the graphs for corneal thickness and pressure are found in Table F. If 0.01 mm. of thickness equals one unit value and if 1.0 mm. of mercury equals one unit value, then the average negative slope value for corneal thickness is -0.18075 units/hour and the average negative slope value for intraocular pressure is -0.22845 units/hour. Also shown in Table F are the changes of the right and left eyes of all three subjects of millimeters of corneal thickness per change of one millimeter of intraocular pressure. These values were calculated from the slope values obtained from the graphs of corneal thickness and intraocular pressure.

Discussion.

The normal cornea has been considered to maintain a constant thickness (Mishima and Maurice, 1961a) (Ytteborg and Dohlman, 1965) (Maurice, 1969) On the other hand, Hara (1970) reported that the corneal thickness changed both within a period of hours and from day to day. However, he failed to find any regular pattern of diurnal variation, although a pattern of daylight thinning appeared in his results. Hara's long-term experiments were exclusively concerned with the measurements of thickness before noon. The number of experiments done on the measurement of diurnal variation was small, therefore it might be difficult to draw adequate conclusions from the literature.

During daytime some thinning of the cornea on keeping the eyes open can be explained on the basis of the effect of evaporation on corneal thickness (Mishima and Maurice, 1961b). In accordance with this Kikkawa's (1973) experiments with rabbit eyes sutured closed showed that the level of corneal thickness depends largely on evaporation. However, Friedman (1972) challenged the concept of constant corneal thickness from the theoretical viewpoint. He considered that the cornea is never in a steady-state condition, because there are variations in tear tonicity as a result of the sleep-awake cycle, and he expected the daytime thinning from this cause alone.

However, the effects of tear tonicity or evaporation do not seem to explain the daytime process of progressive corneal dehydration found in Kikkawa's closed lid experiments, nor does it explain the process of corneal hydration found in rabbits during the night, with their eyes open wide. (Kikkawa, 1973)

It is known that biological clocks within cells are geared to the rhythmic changes of nature, and are found in all life (Luce and Segal, 1966). It is well known that the human intraocular pressure shows a slight diurnal variation. Diurnal variations are also found in the rate of aqueous secretion and in protein concentration in the aqueous humor (Davson, 1969).

In Kikkawa's (1973) experiments, the corneal swelling during the night was found to be closely related to the resting of bodily activities. It is reasonable to consider that the diurnal variations in corneal thickness are in part related to biological rhythms that revolve around an interval of about 24 hours.

Kikkawa (1973) measured corneal thickness at three different times of day in rabbits. The rabbit cornea showed a significant diurnal variation regarding thickness. In most cases, the cornea was thickest in the forenoon, and then thinning followed. It usually became thinnest in the afternoon, but sometimes at about noon. The decrease in thickness was reversed during the night. The amount of the diurnal change was inconsistent. The average value in rabbits was 0.014 mm.

As stated before the primary purpose of this research paper was to investigate the "natural" diurnal changes of corneal thickness in man using ultrasonography, a more accurate instrument then the Maurice-Giardini pachometer used by the previously mentioned investigators. Secondly we measured intraocular pressure to see if there was any evidence of a similar diurnal cycle.

The results of our study show inconsistencies between the three subjects and between the two eyes of each subject. This is partially due to some inadequate ultrasonographs. We feel that if several ultrasonographs could have been taken at each reading many of the inconsistencies would have been eliminated.

Our findings do suggest that corneal thickness does have a diurnal cyclic nature. The corneal thickness is higher in the morning, but not necessarily highest. The corneal thickness is thinnest in the afternoon, then increases in the evening. Maximal thickness is either at midnight or in the early morning hours. The amount of diurnal change is quite inconsistent between the three subjects. The average change is 0.0386 mm which is considerably more than found in the rabbit. Our average corneal thickness for the three subjects is 0.4864 mm. The midrange value is 0.4759 ± 0.0538 mm. These values are lower than the values found by other investigators. (See Table A) One subject has thin corneal readings which lowered the average considerably.

Tonometry was done immediately prior to ultrasonography. As can be seen on the graphs, the tonometry findings do correlate with the corneal thickness findings. There is a tendency for the IOP to be reduced in the afternoon and to increase toward midnight. Pressures in the morning generally are higher, but not necessarily the highest. Corneal thickness is also the lowest in the afternoons with the higher readings near midnight and early in the morning. A further comparison between the two can be made using the average of the negative slope values from the graphs. The slope value for thickness equals 0.18075 units per hour, while the slope value for intraocular pressure equals 0.22845 units per hour indicating a reasonable correlation between the two.

To improve this research project the following should be done. First, as mentioned before, two or three ultrasonographs should be taken at each testing period.

Second, more subjects should be used. Fifty subjects would seem to be an adequate number. Third, testing should be done on more than two twenty four hour periods. Kikkawa tested one group of rabbits for over a month and another group for ten days, however he did not test as frequently in a twenty four hour period. To improve the project in the ways I have indicated would cost several hundred dollars for the Polaroid film alone.

Other areas to be studied are: (1) change in corneal thickness during orthokeratology; (2) changes in corneal thickness in relationship to menstrual cycles; (3) changes in corneal thickness in relationship to increased intra-ocular pressure induced by provocative tests; and (4) readings to be taken at three o'clock in the morning because this is where the upward trend seems to occur for an increase in corneal thickness. The readings should be taken in two different instances, with the person sleeping from midnight until three a.m. and with the person being awake from midnight until three a.m. to check upon any change that may occur as a result of sleep time.

Summary.

Three male optometry students, age 26, 26, and 31, were used in this study of diurnal corneal thickness changes in man. Six ultrasonography measurements and non-contact tonometry measurements were made in one twenty four hour period. Four measurements were made in a second twenty four hour period. The early morning readings were taken after the subjects had at least six hours of sleep with a half hour minimum time allowed between sleeping and the taking of the first readings. Because of this, a three a.m. reading of corneal thickness was not made. The results of the study indicated that there is a diurnal cyclic nature to both corneal thickness changes and IOP. The maximum thickness is usually from midnight to the morning hours. The minimum thickness was in the afternoon. There were inconsistencies between subjects and between the two eyes of any one subject. The average corneal thickness was 0.4864 mm. The average diurnal change in corneal thickness was 0.0386 mm. Intraocular pressure also showed inconsistency between subjects and between the two eyes of any one subject. It also was cyclic in nature, with the lowest readings in the after noon and the highest readings in the morning or night hours. The negative slope values of 0.18075 units/hour for corneal thickness and 0.22845 units/hour for

pressure is a reasonable indication of the correlation between both thickness and pressure.

LIST OF TABLES

TABLE B: Results of ultrasound procedure; Subject # 1.; Time reference= 4.112cm/micron; R=right; L=left

PICTURE NUMBER	EYE	TIME	CORNEAL MEASUREMENTS(cm)	CORNEAL THICKNESS(mm)	MEAN(X̄) OF CORNEAL THICKNESS
1A	R	10:30AM	8.8532 - 13.6752 8.8680 - 13.6757 8.8680 - 13.6869	0.40268 0.40350 0.40260	0.40260
1B	L	10:30AM	8.8255 - 11.0913 8.8062 - 11.0913 8.8062 - 11.0636	0.42470 0.42579 0.42601	0.42550
1C	R	1:20PM	8.8142 - 11.2040 8.8211 - 11.2040 8.8211 - 11.2044	0.42315 0.42315 0.42135	0.42315
1D	L	1:20PM	8.7830 - 11.0408 8.7885 - 11.0408 8.7885 - 11.0365	0.41909 0.41825 0.41860	0.41864
1E	R	4:25PM	9.0085 - 10.9717 9.0062 - 10.9717 9.0062 - 10.9735	0.40835 0.40820 0.40717	0.40791
1F	L	4:25PM	9.0466 - 11.1033 9.0479 - 11.1033 9.0479 - 11.1041	0.42015 0.41976 0.41964	0.41985
1G	R	7:35PM	8.9674 - 11.1935 8.9748 - 11.1935 8.9748 - 11.1945	0.40155 0.40105 0.40097	0.400119
1H	L	7:35PM	9.0331 - 11.0712 9.0432 - 11.0712	0.41305 0.41352	0.41337
1I	R	11:50PM	9.0296 - 11.0003 9.0339 - 11.0003 9.0359 - 11.0005	0.40330 0.42136 0.40107	0,40191
1J	L	11:50PM	9.0273 - 11.0971 9.0282 - 11.0971 9.0282 - 11.0976	0.45060 0.44951 0.44916	0.44976
1K	R	7:15AM	9.0408 - 11.2238 9.0352 - 11.2238	0.43027 0.42951 0.43311	0.42957
1L	L	7:15AM	9.0375 - 11.2124 9.0375 - 11.2125 9.0375 - 11.2135	0.43179 0.43279	0.43256
1M	R	12:25PM	8.3662 - 105274 8.3815 - 10.5274 8.3815 - 10.5292	0.44023 0.44419 0.43886	0.44109
1N	L	12:25PM	8.1670 - 10.2675 8.1678 - 10.2675	0.46539 0.46368 0.46404	0.46443
1O	R	7:30PM	8.2210 - 10.3806 8.2230 - 10.3806 8.8830 - 10.3800	0.43950 0.43843	0.43851
1P	L	7:30PM	8.1872 - 10.2512 8.1898 - 10.2512 8.8198 - 10.2508	0.38194 0.38239 0.38274	0.38236
1Q	R	10:45PM	8.1717 - 10.2947 8.1693 - 10.2947 8.1969 - 10.2950	0.40013 0.39988 0.40003	0.40001
1R	L	10:45PM	8.1725 - 10.2455 8.1825 - 10.2455 8.1825 - 10.2440	0.43309 0.43165 0.43126	0.43200
1S	R	6:25AM	8.2047 - 10.5280 8.2107 - 10.5208	0.39561 0.39455 0.39339	0.39482
1T	L	6:25AM	8.1449 - 10.3565 8.1488 - 10.3565 8.1488 - 10.3565	0.38340 0.38217 0.38217	0.38258

TABLE B: Results of ultrasound procedures; Subject Number two
Time reference = 4.112cm/micron; Right=R; Left=L

Picture Number	Eye	Time	Corneal Measurements(cm)	Corneal Thickness(mm)	Mean($\bar{X}$) of Corneal Thickness
3A	R	10:45AM	8.7541 - 11 3582 8.7761 - 11.3582 8.7761 - 11.3815	0.50663 0.50235 0.50688	0.50529
3B	L	10:45AM	8.7430 - 11.3815 8.7305 - 11.3815 8.7305 - 11.3810	0.51332 0.51576 0.51566	0.51491
3C	R	1:35PM	8.7955 - 11.4877 8.8042 - 11.4877 8.8042 - 1148921	o.52398 0.52208 0.52237	0.52281
3D	L	1:35PM	8.7804 - 11.3222 8.7921 - 11 3222 8.7391 - 11.4310	0.49381 0.49219 0.48589	0.49396
3E	R	4:30PM	8.8022 - 11.3215 8.8240 - 11.3215 8.8300 - 11.4460	0.49013 0.48589 0.50894	0.48727
3F	L	4:30PM	8.8300 - 11.4460 8.8476 - 11.4460 8.8469 - 11.4467	0.50894 0.50566 0.50579	0.50677
3G	R	7:40PM	8.7910 - 11.3700 8.7850 - 11.3700 8.7850 - 11.3738	0.50175 0.50291 0.50365	0.50277
3H	L	7:40PM	8.7795 - 11.5260 8.7981 - 11.5260 8.791 - 11.5308	0.53433 0.53071 0.53165	0.5323
3I	R	12:10AM	8.7930 - 11.4700 8.8121 - 11.4700	0.52081 0.51710	0.5184
3J	L	12:10AM	8.7540 - 11.3158 8.7790 - 11.3158 8.8500 - 11.3210	0.49840 0.49354 0.49455	0.4955
3K	R	7:25AM	8.8509 - 11.5266 8.8590 - 11.5260 8.8590 - 11.5260	0.52044 0.51887 0.51887	0.5194
3L	L	7:25AM	8.1300 - 10.8555 8.1377 - 10.8355 8.1377 - 10.8380	0.52508 0.52369 0.52407	0.5243
3M	R	12:40PM	8.1280 - 10.8149 8.1300 -,10.8149 8.1200 - 10.8190	0.52274 0.52236 0.53316	0.5228
3N	L	12:40PM	7.9740 - 10.5972 7.9820 - 10.5872 7.9820 - 10.6020	0.51035 0.58091 0.50972	0.5096
3O	R	7:36PM	79745 - 10.6326 7.9810 - 10.6326 7.9810- 10.6325	0.51714 0.51587 0.51587	0.5163
3P	L	8:36PM	8.0215 - 10.6970 8.0105 - 10.6970 8.0105 - 10.7010	0.52247 0.52266 0.52344	0.5228
3Q	R	10:55PM	8.0182 - 10.6660 8.0220 - 10.6660 8.0220 - 10.6879	0.51388 0.51314 0.51662	0.5145
3R	L	10:55PM	7.9610 - 10.5899 7.9665 - 10.5899 7.9665 - 10.5920	0.51145 0.51607 0.51679	0.5109
3S	R	6:40AM	7.9572 - 10.6460 7.9630 - 10.6480 7.9630 - 10.6480	0.53331 0.52237 0.52237	0.5224
3T	L	6:40AM	8.1280 - 10.8149 8.1377- 10.8355 8.1300 - 10.8149	0.52274 0.52369 0.53336	0.51998

TBBLE B: Results of ultrasound procedure; Subject Number Three;
Time reference = 4.114cm/micron; R = right; L = Left

Picture Number	Eye	Time	Corneal Measurements(cm)	Corneal Thickness(mm)	Mean(X) of Corneal Thickness
2A	R	10:50AM	8.7730 - 11.5125 8.7791 - 11.5125 8.7791 - 11.5100	0.53319 0.53200 0.53152	0.5322
2B	L	10:50AM	8.7452 - 11.4660 8.7348 - 11.4660 8.7348 - 11.4670	0.53011 0.53155 0.53175	0.53116
2C	R	1:40PM	8.8171 - 11.4605 8.8320 - 11.4605 8.8320 - 11.4767	0.51428 0.51138 0.51543	0.5134
2D	L	1:40PM	8.7888 - 11.5060 8.7930 - 11.5060 8.7930 - 11.5140	0.52836 0.52783 0.52937	0.5286
2E	R	4:35PM	8.8220 - 11.4958 8.8265 - 11.4958 8.8265- -11.4940	0.52019 0.51931 0.51896	0.5195
2F	L	4:35PM	8.7629 - 11.5101 8.7760 - 11.5105 8.7760 - 11.5143	0.53447 0.53183 0.53274	0.5330
2G	R	7:50PM	8.7600 - 11.4799 8.7683 - 11.4979 8.7698 - 11.5038	0.53266 0.53947 0.53061	0.5309
2H	L	7:50PM	8.7960 - 11.4925 8.8021 - 11.9011	0.52333 0.52215	0.5225
2I	R	12:20AM	8.7870 - 11.5470 8.7872 - 11.5470 8.7852 - 11.5521	0.53566 0.53566 0.53661	0.5359
2J	L	12:20AM	8.7600 - 11.4845 8.7628 - 11.4845	0.52877 0.52833	0.5288
2K	R	7:30AM	8.7767 - 11.5100 8.2850 - 11.5100 8.6998 - 11.5190	0.53048 0.52886 0.53061	0.52996
2L	L	7:30AM	8.8128 - 11.5010 8.8060 - 11.5010 8.8060 - 11.5135	0.51722 0.53420 0.52547	0.5234
2M	R	12:50PM	8.1340 - 10.8258 8.1233 - 10.8250 8.1323 - 10.8292	0.523333 0.52366 0.52444	0.5328
2N	L	1250PM	8.0840 - 10.8220 8.1098 - 10.8220	0.53268 0.53245	0.5327
2O	R	7:40PM	8.0071 - 10.7190 8.0110 - 1071903	0.52760 0.52357	0.5269
2P	L	7:40PM	7.9942 - 10.7522 7.9970 - 10.7522 7.9960 - 10.7595	0.53527 0.53473 0.53614	0.5353
2Q	R	11:00PM	7.9948 - 10. 7300 8.0025- 107300	0.53084 0.52935	0.5290
2R	L	11:00PM	7.9986 - 10.7035 7.9987 - 10.7035 7.9986- 10.7035	0.52623 0.52623 0.52663	0.52623
2S	R	6:55AM	8.0011 - 10.7290 8.0051 - 107290 8.0051 - 107268	0.52543 0.52822 0.52822	0.5288
2T	L	6:55AM	7.9541 - 10.7130 7.9546 - 10.7130 7.9547 - 10.7172	0.53544 0.53533 0.5361[illegible]	0.5356

TABLE C: INTRAOCULAR PRESSURE IN MILLIMETERS OF MERCURY

R = Right Eye; L = Left Eye; A = Average

3 Hour Interval	SUBJECT #1				SUBJECT #2				SUBJECT #3			
TIME	R	A	L	A	R	A	L	A	R	A	L	A
10:30 AM	11	9.6	12	11	16	17	16	17	14	13	11	11.6
	9		8		19		19		12		12	
	9		13		16		16		13		12	
1:20 PM	9	8.3	9	9.6	17	16.3	16	15.6	12	12.6	12	12.6
	8		11		17		15		13		12	
	8		9		15		16		13		14	
4:25 PM	8	8	9	9.3	14	14.3	15	16.3	11	10.6	10	11
	7		10		16		16		11		11	
	9		9		13		18		10		12	
7:35 PM	10	9.3	10	8.6	12	12.3	13	12.6	10	10.3	11	11.3
	10		8		13		13		10		12	
	8		8		12		12		11		11	
11:50 PM	7	7.3	9	8.3	12	12	13	12.3	9	8.6	10	10.6
	8		6		12		12		8		11	
	7		10		12		12		9		11	
7:15 AM	8	8	10	10	14	14	14	13.6	12	12	12	12.6
	8		10		14		14		12		12	
	8		10		14		13		12		14	
6 Hour Interval												
12:25 PM	8	8.6	8	9.6	16	16.6	17	17.6	13	14	12	13
	9		9		15		17		15		13	
	9		12		19		19		14		14	
7:30 PM	9	7.6	8	8.3	14	15	15	15	11	12	11	11.6
	7		9		15		16		12		12	
	7		8		16		14		13		12	
10:45 PM	10	8.3	6	6.6	15	13.6	16	15.6	10	10.6	17	14
	7		7		13		15		11		13	
	8		7		13		16		11		12	
6:25 AM	9	8.6	7	6.3	15	15.6	18	17.6	11	13	12	12
	9		6		16		18		15		10	
	8		6		16		17		13		14	

TABLE D: CHANGES IN CORNEAL THICKNESS

		RIGHT EYE	LEFT EYE
PATIENT #1	MAXIMUM	0.4644	0.4411
	MINIMUM	0.3824	0.3948
	CHANGE	0.0820	0.0463
PATIENT #2	MAXIMUM	0.5323	0.5228
	MINIMUM	0.4939	0.4873
	CHANGE	0.0384	0.0321
PATIENT #3	MAXIMUM	0.5359	0.5356
	MINIMUM	0.5134	0.5226
	CHANGE	0.0225	0.0131

AVERAGE CHANGE IS 0.0386 mm.

TABLE E: AVERAGE CORNEAL THICKNESS

	RIGHT EYE	LEFT EYE
PATIENT #1	0.4221	0.4141
PATIENT #2	0.5125	0.5131
PATIENT #3	0.5271	0.5297

AVERAGE CORNEAL THICKNESS FOR THE THREE SUBJECTS IS 0.4864 mm.

THE MIDRANGE VALUE IS 0.4759 ± 0.0538 mm.

TABLE F: AVERAGE SLOPE VALUES COMPUTED FROM GRAPHS

AVERAGE SLOPE VALUE OF CORNEAL THICKNESS IS -0.0018075 mm./hour or -0.18075 units/hour.

AVERAGE SLOPE VALUE OF INTRAOCULAR PRESSURE IS -0.22845 mm of Hg/hour or -0.22845 units/hour.

CHANGE IN MILLIMETERS OF CORNEAL THICKNESS PER CHANGE OF ONE MILLIMETER OF MERCURY OF INTRAOCULAR PRESSURE.

	RIGHT EYE	LEFT EYE
SUBJECT #1	0.03328	0.0152
SUBJECT #2	0.00354	0.0104
SUBJECT #3	0.00283	0.0024

AVERAGE CHANGE IS 0.01128 mm./mm. of Hg.

LIST OF FIGURES

FIGURE IV: A GRAPH OF CORNEAL THICKNESS IN MILLIMETERS VS. TIME IN HOURS. SUBJECT #1.

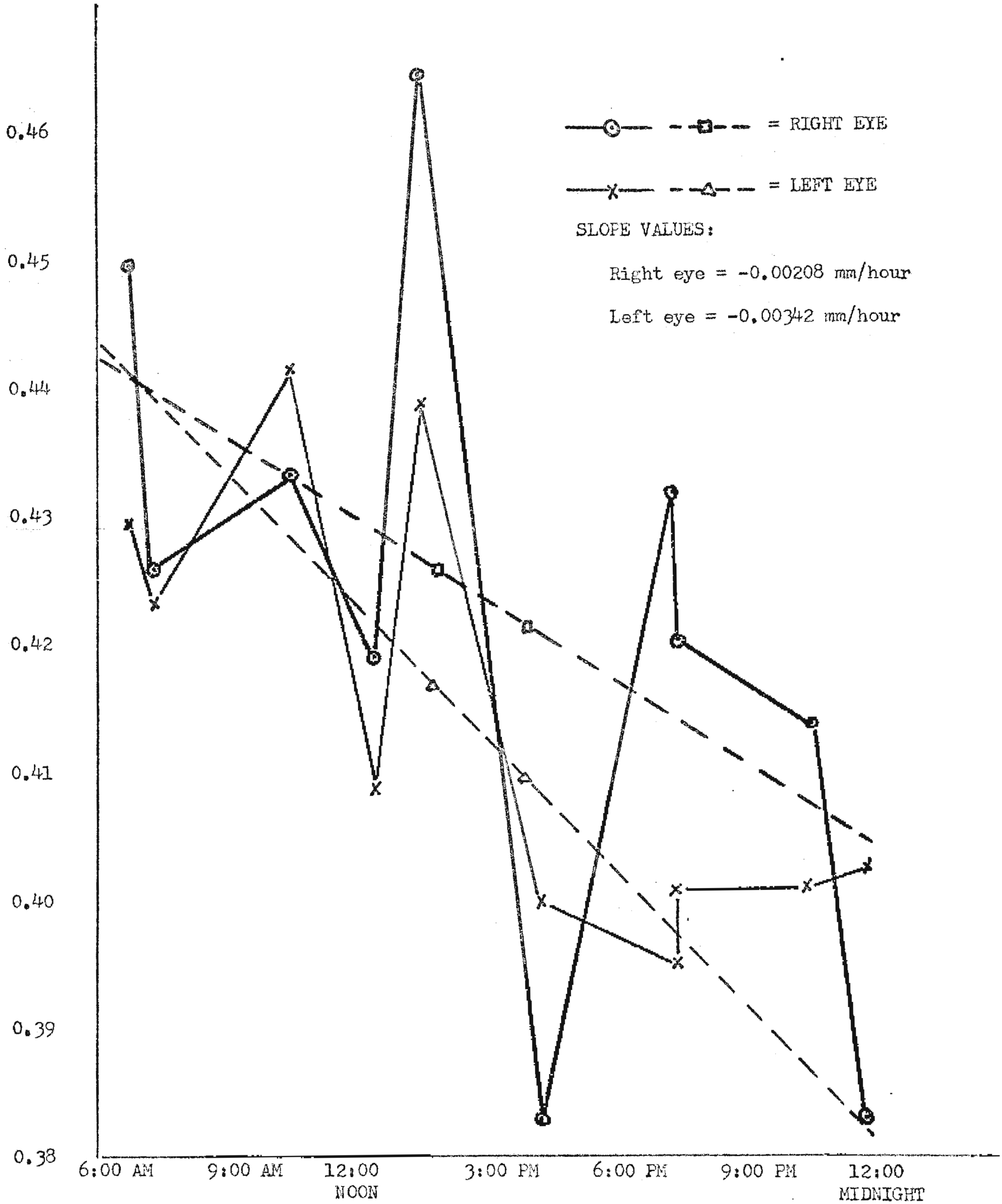


FIGURE V: A GRAPH OF INTRAOCULAR PRESSURE IN MILLIMETERS OF MERCURY VS. TIME IN HOURS. SUBJECT #1.

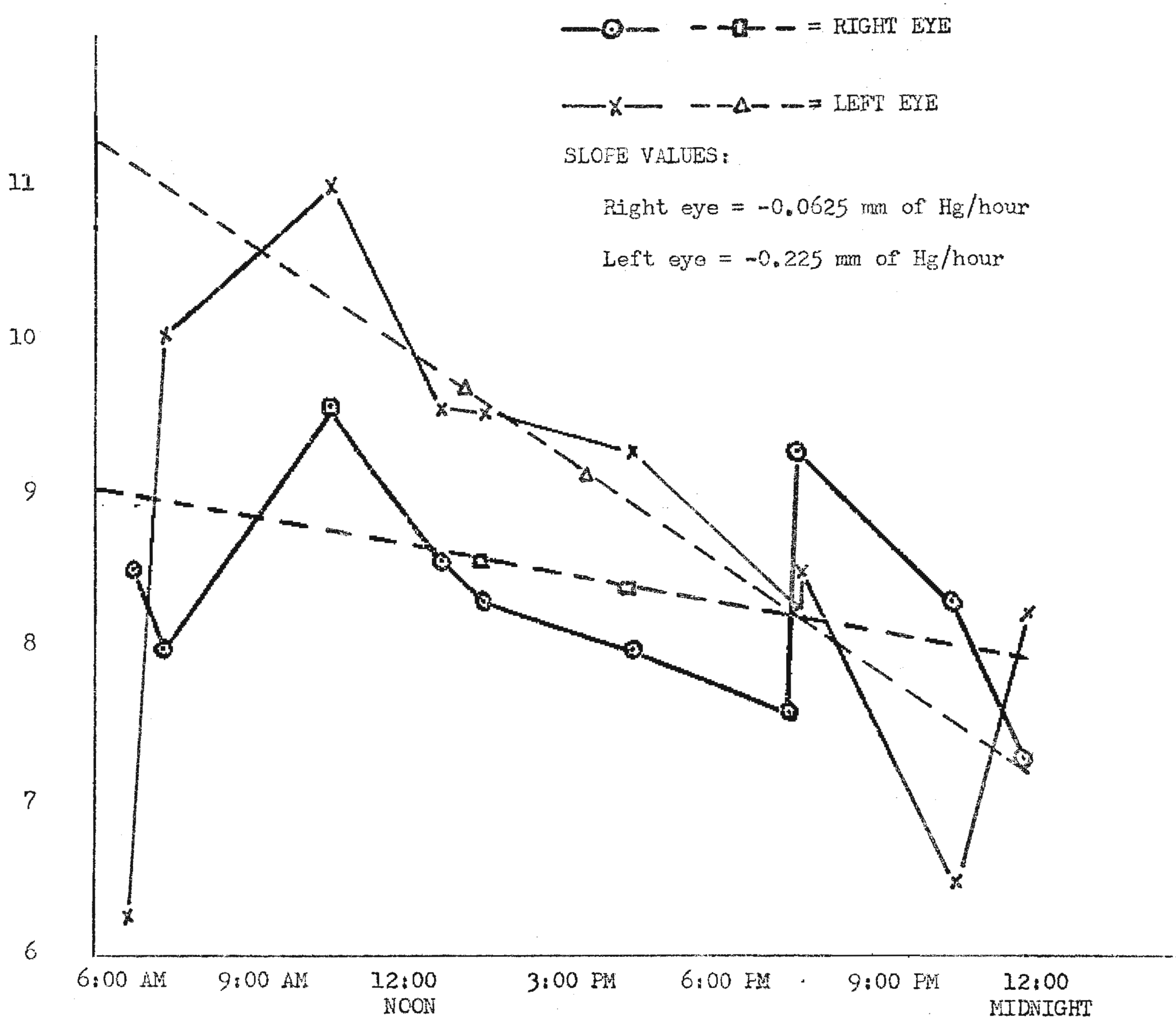


FIGURE VI: A GRAPH OF CORNEAL THICKNESS IN MILLIMETERS VS. TIME IN HOURS. SUBJECT #2.

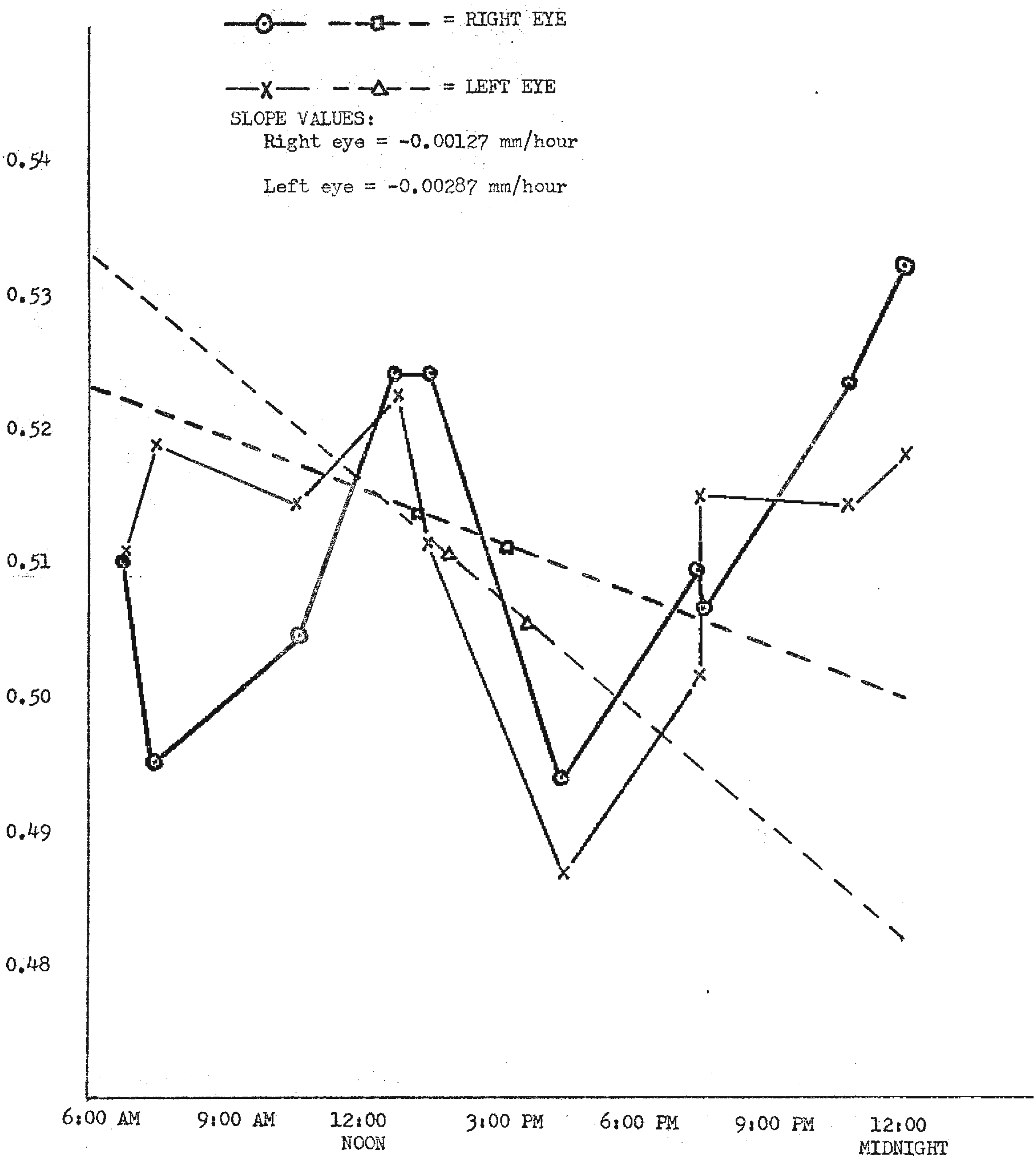


FIGURE VII: A GRAPH OF INTRAOCULAR PRESSURE IN MILLIMETERS OF MERCURY VS. TIME IN HOURS. SUBJECT #2.

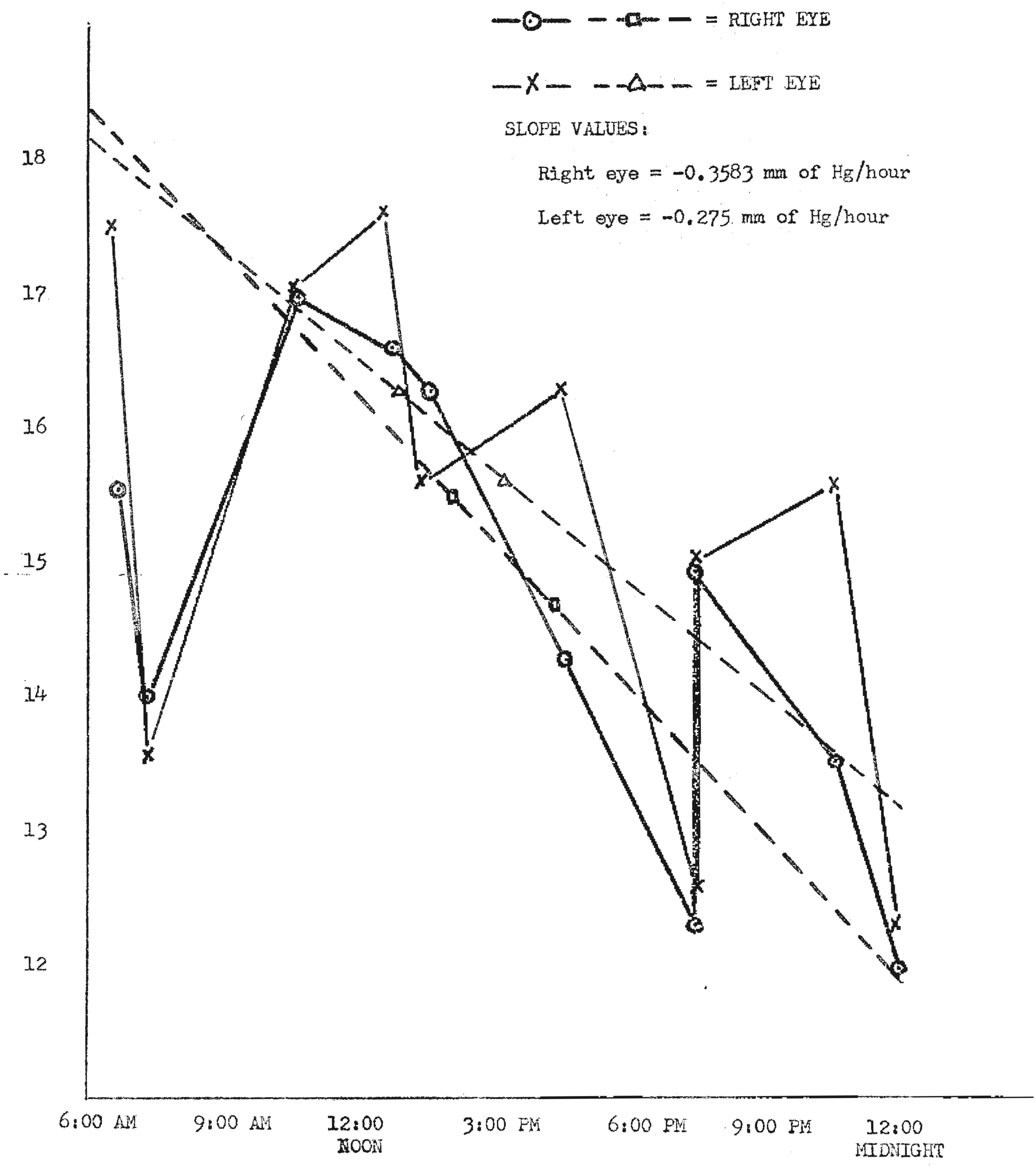


FIGURE VIII: A GRAPH OF CORNEAL THICKNESS IN MILLIMETERS VS. TIME IN HOURS. SUBJECT #3.

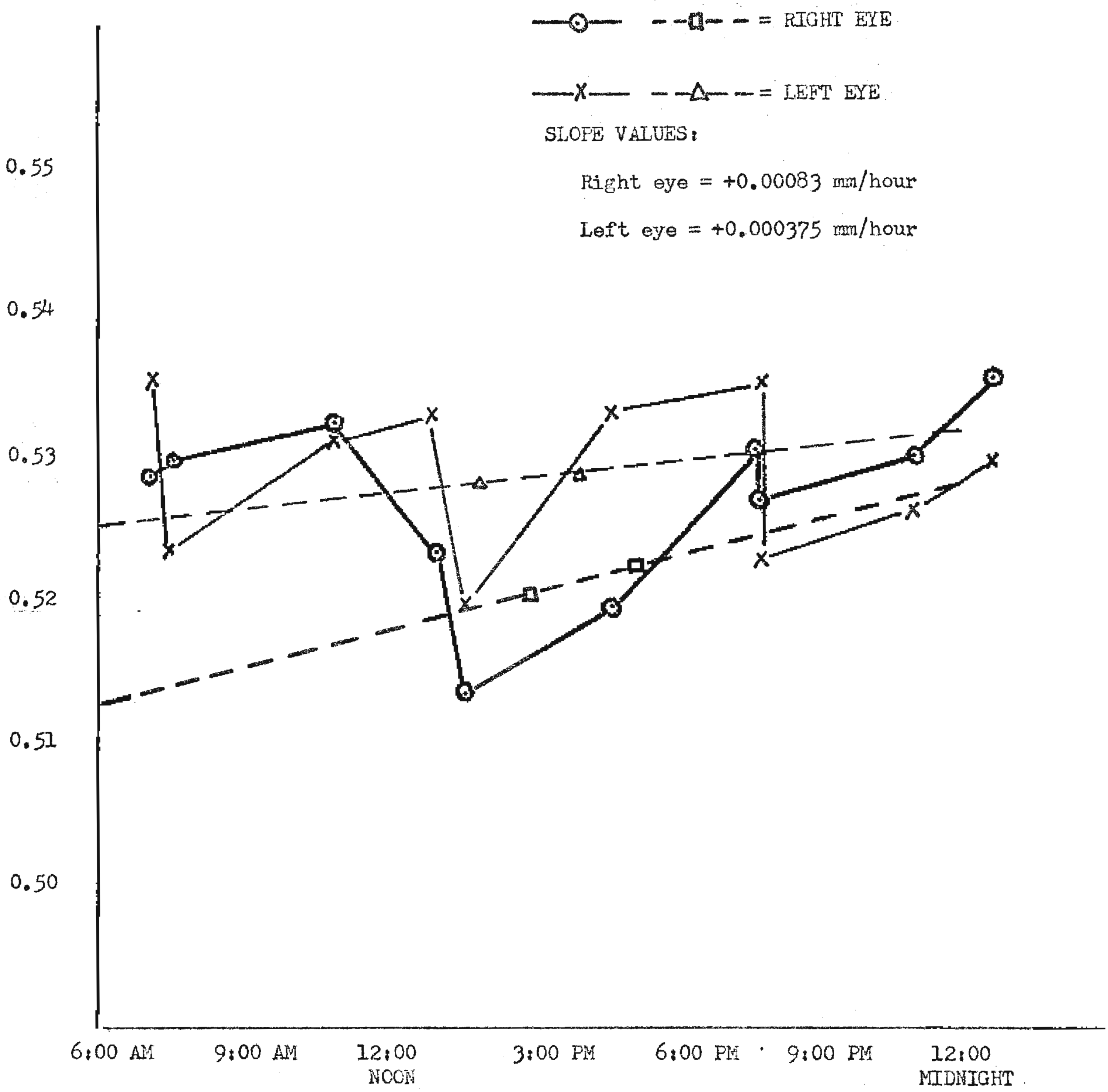
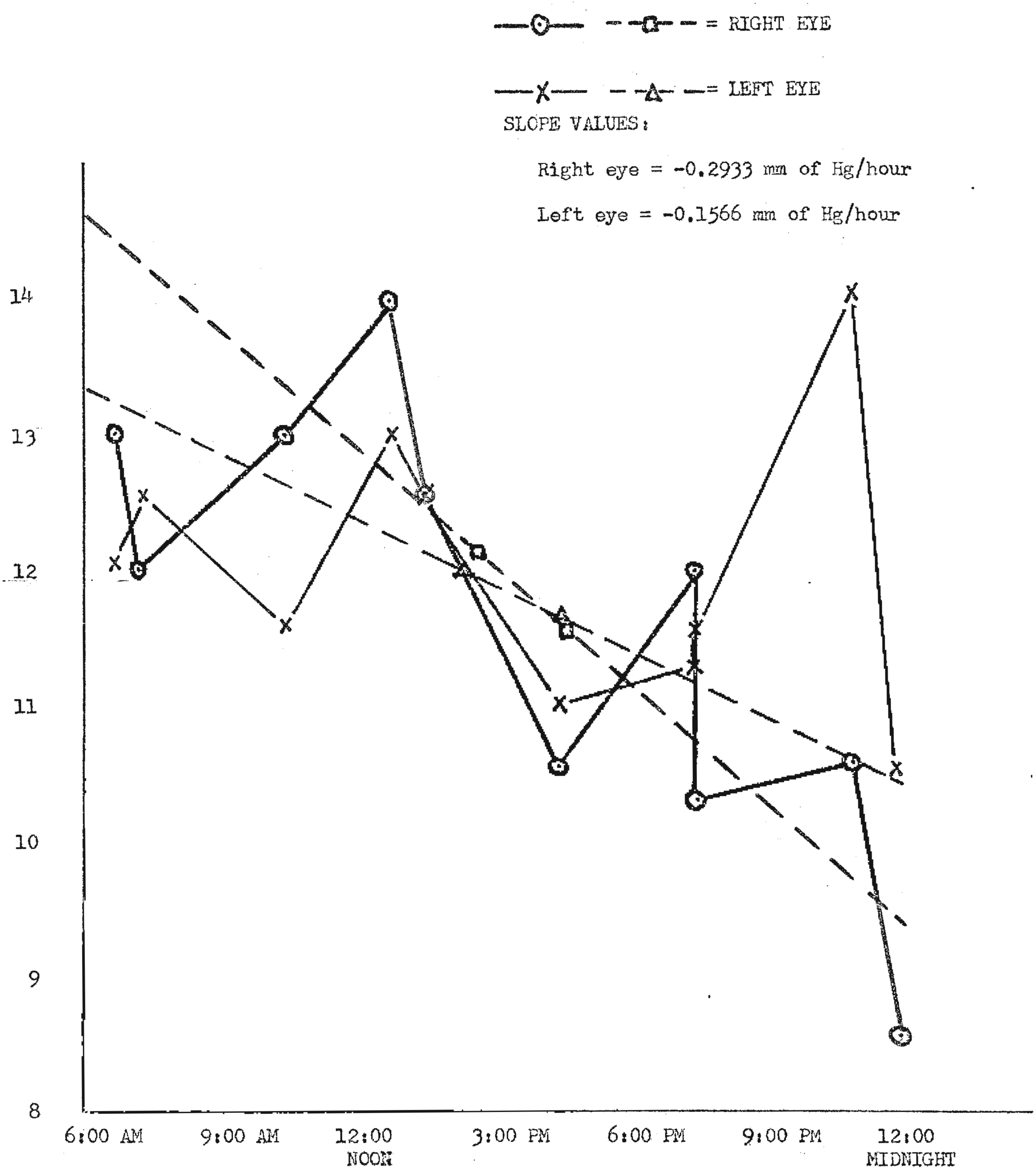


FIGURE IX: A GRAPH OF INTRAOCULAR PRESSURE IN MILLIMETERS OF MERCURY VS. TIME IN HOURS. SUBJECT #3.



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