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Abstract

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OF CORNEAL THICKNESS

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A STUDY ON DIURNAL VARIATION

OF CORNEAL THICKNESS

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ABSTRACT

Central corneal thickness measurements were taken on both eyes of seven subjects, every four consecutive hours, for as long as the subjects were available. The corneal thickness data were analyzed for influences of sex and age, ocular dominance in thickness, and periodicity of the corneal thickness fluctuations.

Age and sex were two factors which did not affect the corneal thickness of the seven subjects. In five of the seven subjects neither eye seemed to dominate in corneal thickness, one subject consistently had the left eye thicker, and one subject consistently had the right eye thicker. No repetitive pattern or periodicity was discovered on any corneal thickness fluctuation of any subject. The fluctuations were on the order of ten percent of the mean corneal thickness in almost all subjects. A significantly high co-variation of the corneal thickness fluctuations between the left eye and right eye was found on five of the seven subjects.

INTRODUCTION

In the past, many authors have considered corneal thickness a constant value and have failed to record baseline data on any of their corneal thickness research. (Mishima and Maurice, 1961), (Ytteborg and Dohlman, 1969), (Maurice, 1969) (Mandell, 1965), (Carney, 1974), (Marlota and Baum, 1968).

> "The normal cornea does not undergo significant changes in curvature or hydration throughout the day except for a slight thinning upon awakening."
> (Polse, 1972)

Yet, there is a tremendous variability in the average central corneal thickness that has been reported in the literature. Table I shows the average corneal thicknesses reported by the named investigators.

What could explain these wide variations? Each investigator used one specific instrument to measure the thickness and not all of the above investigators used the same instrument. Each instrument has its own inherent error of measurement and inaccuracies of repeatability, and each investigator has his own inherent errors of measurement. But, it does not appear that the combination of even the extreme cases of inherent errors accounts for such wide variations on corneal thickness reported.

Some investigators have reported the presence of a diurnal variation in corneal thickness. (Hara, 1970), (Peterson, 1968), (Kikkawa, 1973, 1974, 1975,), (Stone, 1974),

Table I

Investigator	Date	Corneal thickness(mm)	No.of eyes
Blix	1880	.482-.576	10
Gullstrand	1909	.460-.510	2
Koby	1928	.466-.733	20
Fincham	1930	.480-.590	12
Lobranski	1934	.400-.570	20
Von Bohr	1948	.565±.035	224
Maurice & Giardini	1951	.507±.028	44
Cook & Langham	1953	.536±.040	10
Lanergen & Kelecom	1962	.510±.040	198
Donaldson	1966	.522±.041	268
Martola & Baum	1968	.523±.039	209
Mishima & Hedbys	1968	.518±.020	40
Lowe	1968	.517±.034	157
Giglio	1968	.522±.033	?
Peterson	1968	.566±.029	53
Baum & Levene	1968	.568±.048	103
Harris	1970	.520±.008	4
Alsbirk	1974	.512±.032	839

(Gerstman, 1972). Is it possible that diurnal variation of corneal thickness could contribute to the wide variability in reported average corneal thickness?

The purpose of this research project is to study diurnal variations in corneal thickness; to try to determine if there is cyclic rhythm, and if there is, to quantify it.

BACKGROUND

There is much controversy in the literature about the presence or absence of a diurnally varying corneal thickness. There is also controversy regarding the relationships between corneal thickness and; age, sex , differences between the two eyes of one individual, refractive errors, time of day, and the mechanism for regulation of corneal thickness.

Corneal thickness is controlled by the balance between passive movement of water into the stroma under its swelling force and the active movement of fluid out of the cornea by metabolic action. (Maurice, 1969). Two other factors which also contribute to corneal thickness have been shown to be tear tonicity and oxygen tension. (Mandell and Harris, 1968), (Hill and Fatt, 1964)

A small number of researchers have reported the presence of a diurnal variation in corneal thickness. In man, Gerstmann (1972) found it to vary about seven percent, Mandell and Fatt (1965) found a four percent variation, Peterson (1968) found an eight to fourteen percent variation, and Hara (1970) found a diurnal corneal variation but had failed to quantify it. Kikkawa (1973.1974, 1975) found a definite pattern, or cycle, in the diurnal variation of rabbit corneas, but reported the magnitude of the variation to be inconsistent.

Hara (1970) reported no regular pattern in the diurnal variation. Mandell and Fatt (1965) found the cornea to thicken overnight and subsequently thin during the day, with the most rapid thinning occurring in the early morning. Peterson (1968) reported a thickening of the cornea early in the morning, a thinning in the early afternoon, and a thickening in the late afternoon. Kikkawa (1973) discovered the rabbit corneas to be thickest in the forenoon and thinnest in afternoon, followed by an increase in thickness throughout the night. One can see from these findings that while the times of thickening or thinning appear to vary, the occurance of a corneal thickness diurnal change is evident in each study.

Right and left eye corneal thickness in the same individual are not statistically different. Nor are corneal thicknesses between male and female and different age groups statistically different (Martola and Baum,1968), (Maurice and Giardini,1951). Von Bohr(1948) found myopes greater than four diopters to have thinner central corneas than all other subjects of less refractive error, but Martola and Baum (1968) found myopes of the same magnitude to have thicker corneas than all others.

As to the controversy regarding the control of diurnal variation, there appears two schools of thought. One opinion is that the daily variations in corneal thickness is controlled mainly by tear tonicity and oxygen tension. The reason given for the finding of thicker corneal measurements in the morning is that at night, with the eye lids closed, the tears become hypotonic and there is a reduced oxygen supply to the cornea, which causes absorption of water by osmotic pressure of the hypertonic cornea, producing an increased thickness. The thinning that occurs during the daytime is proposed to be due to an increase in hypertonicity and oxygen supply of the tears and an extraction of water from the cornea by the osmotic pressure of the hypertonic tears. (Mandell and Fatt, 1965)

Kikkawa (1973, 1974, 1975) believes that he has shown corneal diurnal thickness variation to be independent of oxygen supply or tear tonicity. He has shown definite diurnal corneal thickness variations in controlled environments of 93% humidity, rabbits whose lids have been sutured shut for many days; rabbits whose lids have been sutured open for many consecutive days; rabbits living in an environment of constant light; and rabbits living in an environment with a normal dark-light cycle. He also believes that he has found that the cornea appears to have a twenty-four hour rhythm regardless of whether the eye lids blink normally. Changing the normal dark-light daily cycle can have profound effects upon the magnitude of corneal thickness and the normal twenty-four hour periodicity. Corneal dehydration occurred in rabbits that were active while corneal hydration occurred during periods of relaxation or drowsiness, independent of lid closure.

INSTRUMENTATION

The instrument used to measure corneal thickness is the pachometer. History about the development of the pachometer can be found in Donaldson's "A New Instrument for the Measurement of Corneal Thickness", and the doctoral thesis of Blomquist, Keene, Zook, "Diurnal Variation in Corneal Thickness." Since the history has been covered so extensively in the above mentioned sources it will not be described in this paper.

The instrument used in this study is the Haag-streit pachometer. This pachometer does not measure absolute corneal thickness, but instead measures the relative corneal thickness. To determine the true value, a correction must be made for corneal refractive index, front surface power, and obliquity of angle at which the corneal section is viewed. Front surface power has a negligible effect (Arner and Rengstorff, 1972), (Fatt and Harris, 1973), and correcting according to conversion charts for index of refraction and obliquity of angle rarely produces any statistically significant difference.(Alsbirk, 1974) This paper reports <u>relative</u> corneal thickness changes, rather than changes in <u>absolute</u> corneal thickness, so the conversion charts were not used.

The pachometer was mounted on a Mentor slit lamp. The narrowest possible slit beam was used and, to facilitate observation, the illumination system was set at maximum intensity. The slit beam to ocular angle was set at forty degrees. The pachometer had incorporated into it a doubling device which was controlled by a rotational scale on its upper surface facing the experimentor. When the scale was adjusted the image of the slit beam was seen to double. A replacement eye-piece which obscures the upper half of one section and the lower half of the other, thus making vernier alignment of the corneal sections possible, was inserted into the right ocular of the biomicroscope.

The patient placed his head onto the chin-rest and was asked to remain still for the thirty seconds to one minute required to take the three measurements. He was directed to fixate directly into the slit beam. The first Purkinje image of the slit beam was seen approximately at the front surface of the crystalline lens and the height of the instrument was adjusted till the upper and lower halves of the field were seen to bisect the Purkinje image. The purkinje image was centered laterally in the middle of the pupil, and the slit beam of the corneal section was brought into clear focus. The scale was rotated till two images of the corneal section were seen and a vernier-type setting was made aligning the back surface of one corneal section with the front surface of the other corneal section. (Stone, 1974)

Maurice and Giardini (1951) have stated that the central area of the cornea ± 1.5 mms has the same thickness, so small fixation tremors of the patient should not affect measurement results. However, Alsbirk (1374) states that small significant differences between the neasurements of two eyes do occur due to the fact that for the readings the patient must fixate both eyes to the right. This difference between the two eyes is on the order of 0.019mm, and is directly correlated to angle kappa.

Three consecutive measurements were made on each eye of the subjects in this research project. Alsbirk(1974) found a standard deviation between three consecutive readings of .007, and Stone(1974) determined accuaracy to be ± 0.01 in any set of three readings.

INVESTIGATOR RELIABILITY

Ten consecutive measurements on each eye were made on one subject prior to the beginning of the research to test the reliability of the findings made by the investigator. The results are listed on Table II.

Table II

Reading	RE(mm)	LE(mm)
1	.585	.590
2	.600	.590
3	.600	.590
4	.600	.590
5	.590	.595
6	.600	.590
7	.585	.600
8	.590	.600
9	.590	.590
10	.590	.600
Mean	.593	.593
Standard deviation	.006	.004
Variance	.000036	.000002

EXPERIMENTAL PROCEDURE

To accomplish the stated purpose of this study it was necassary to obtain thickness measurements for as many consecutive four hour intervals as possible 'around the clock'. A 'pilot study' was done to confirm the value and practicality of further investigation. The results of the pilot study are not included in this paper.

The methodological format included obtaining contributory histories on each subject and measurements every four hours for as many hours as they were able to participate. Three measurements were obtained on each eye, each time, with the right eye measured first. The data were recorded and a resulting average figure was computed from each set of three readings.

The subjects were asked not to change their daily routines - the only inconveniences being that they were asked to report every four hours for measurements to be taken. All subjects agreed to be awakened at four AM and reported having slept well prior to awakening. Subjects returned to sleep following the 4am readings.

All measurements were obtained prior to major daily meals. This was a stipulation because it has not been shown what the resulting effect of eating a major meal may have on corneal fluctuation, if any.

Some of the participants in this study were successful habitual hydrophilic contact lens wearers as a part of their life routine. It was determined that this factor not be altered for this study based on findings of Kikkawa (1975), wherein a normal diurnal corneal variation was obtained on rabbits which daily wore hydrophilic contact lenses. The normal variation was seen superimposed on an increased level of corneal thickness due to hydrophilic lens use.

RESULTS

Table III contains information about each subject's sex, age, correction, medication, general health, total time of participation, total number of thickness measurements, right and left eye mean and ranges of thickness, and the extent of covariation between the thickness measurements of the right and left eyes, represented by the correlation coefficient.

TABLE III

SUBJECT	A	B	C	D	E	F	G
SEX	M	F	M	F	F	M	F
AGE	59	60	25	20	48	24	23
CORRECTION	Hyperope Spects.	Emmetrope	Myope Soft CL's	Myope Soft CL's	Myope Spects.	Myope Spects.	Myope Soft CL's
MEDICATION	Buff. ASA Inderol Hydrodiuril Zyloprim	None	None	Lo/Ovral	Premarin Phenergin Indocin	None	Norinyl
GENERAL HEALTH	Essential Hypertension	Good	Good	Good	Good	Good	Good
TOTAL TIME	84 hrs	84 hrs	40 hrs	60 hrs	60 hrs	64 hrs	148 hrs
# OF READINGS	22	22	11	16	16	17	38
MEAN R.E. THICKNESS	.571±.015	.576±.015	.533±.013	.565±.017	.543±.023	.595±.008	.571±.018
MEAN L.E. THICKNESS	.568±.015	.580±.012	.541±.015	.574±.019	.567±.021	.595±.016	.572±.018
TOTAL RANGE OF R.E. THICKNESS	.550-.600	.550-.600	.500-.553	.540-.600	.512-.610	.576-.606	.517-.610
TOTAL RANGE OF L.E. THICKNESS	.530-.596	.563-.630	.513-.560	.540-.603	.526-.610	.557-.636	.540-.610
CORRELATION COEFFECIENT RE vs. LE	.401	.448	.337	.502	.387	.461	.606

DISCUSSION

The results of this research have been organized into five major areas for discussion;

1) A total of 284 corneal measurements were made. The mean corneal thickness of the subjects of this research project was .570 ± .038mm. This central thickness was in close agreement with those measurements made by Von Bohr, Peterson , Baum and Levene, and within the tolerances of those measurements made by Donaldson, Martola and Baum, Giglio, Annergen and Kelecom, and Alsbirk. (see Table I) The corneal thickness measurements over all the subjects ranged from .512 mm as the thinnest to .636mm as the thickest.

Mandell has hypothesized that contact lenses which produced between four and nine percent swelling of the cornea represents an inadequate contact lens fit. The data in this research project strongly contradicts Mandell's supposition. The corneal thickness fluctuations in these subjects usually ranged on the order of ten percent of the mean corneal thickness.

2) There was no definate pattern as to one eye's cornea being predominately thicker than the other when all the subjects' eyes were collectively compared. In two individual cases, subjects A and E, one eye's cornea had the tendency to be thicker than the other, but in subject A the right eye was predominantly thicker and in subject E the left eye was predominantly thicker. The absence of a predominantly thicker eye

Figure 1a

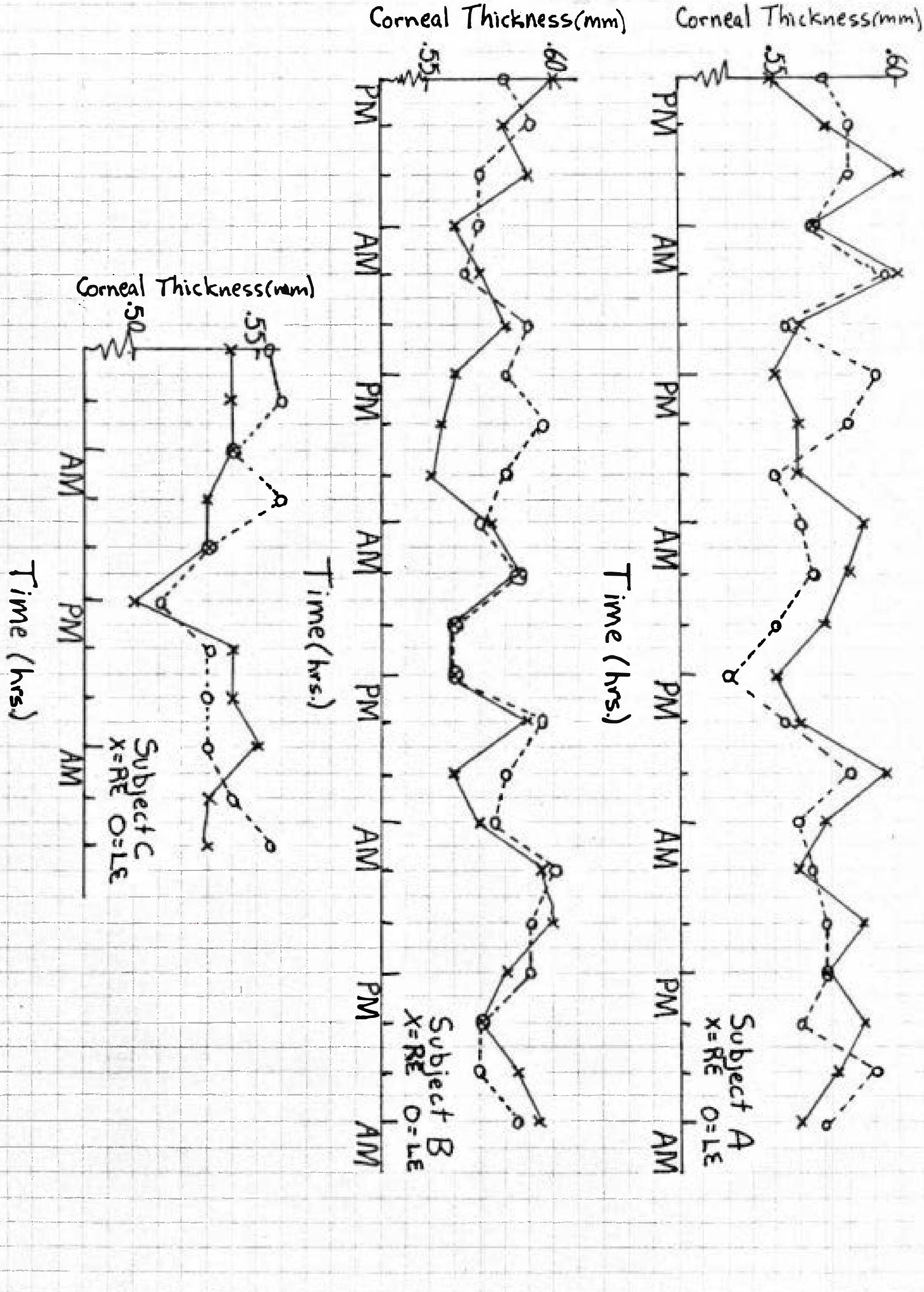
Corneal Thickness(mm)
.55
.60
PM
AM
Time (hrs.)
Subject A
x=RE O=LE
Corneal Thickness(mm)
.55
.60
Time(hrs.)
Subject B
x=RE O=LE
Corneal Thickness(mm)
.50
.55
Time (hrs.)
Subject C
x=RE O=LE

Figure 1b

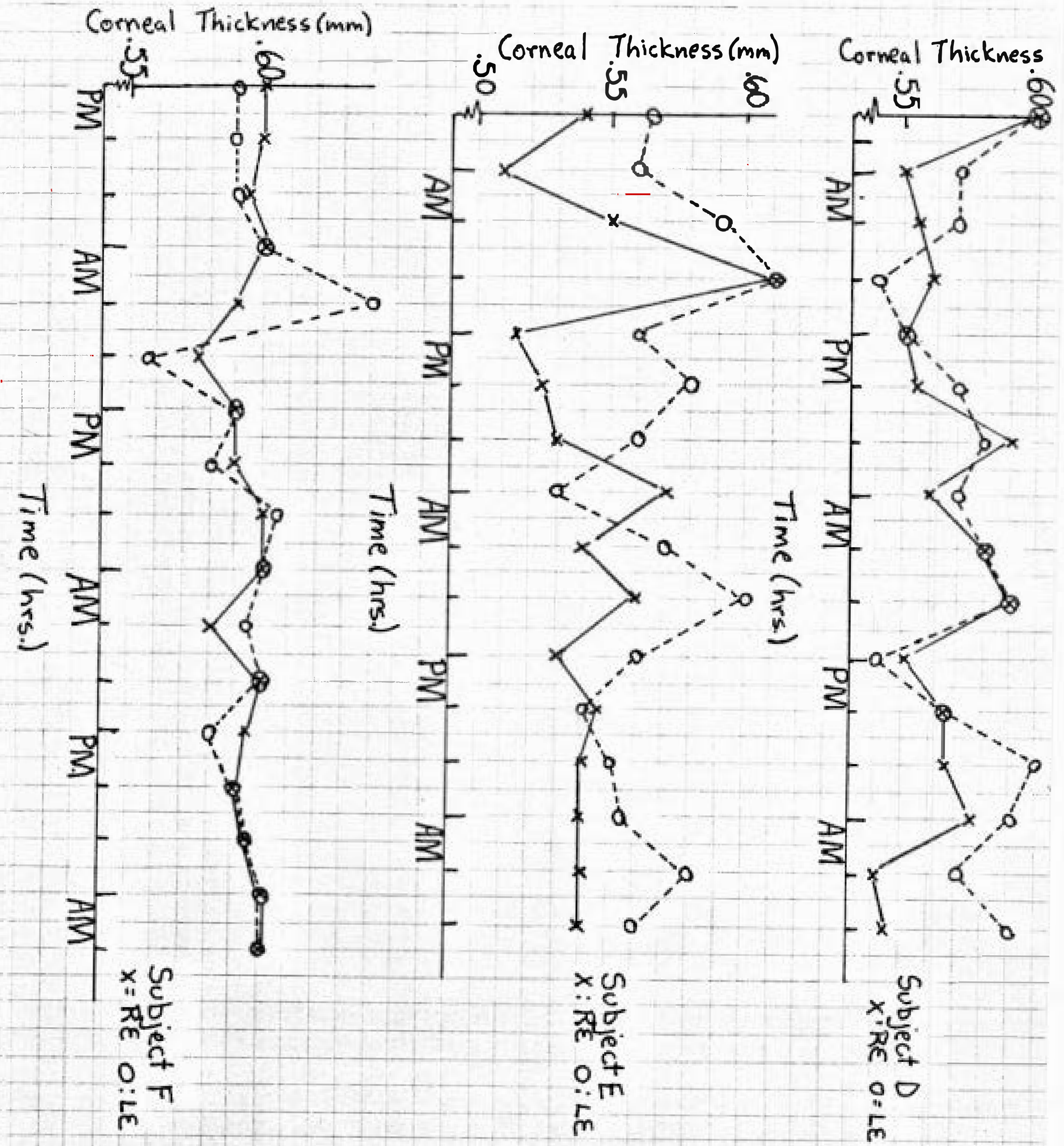
Corneal Thickness (mm)
.55
.60
PM
AM
PM
AM
PM
AM
Time (hrs.)
Subject F
x: RE o: LE
Corneal Thickness (mm)
.50
.55
.60
AM
PM
AM
PM
AM
Time (hrs.)
Subject E
x: RE o: LE
Corneal Thickness
.55
.60
AM
PM
AM
PM
AM
Time (hrs.)
Subject D
x: RE o: LE

Figure 1c

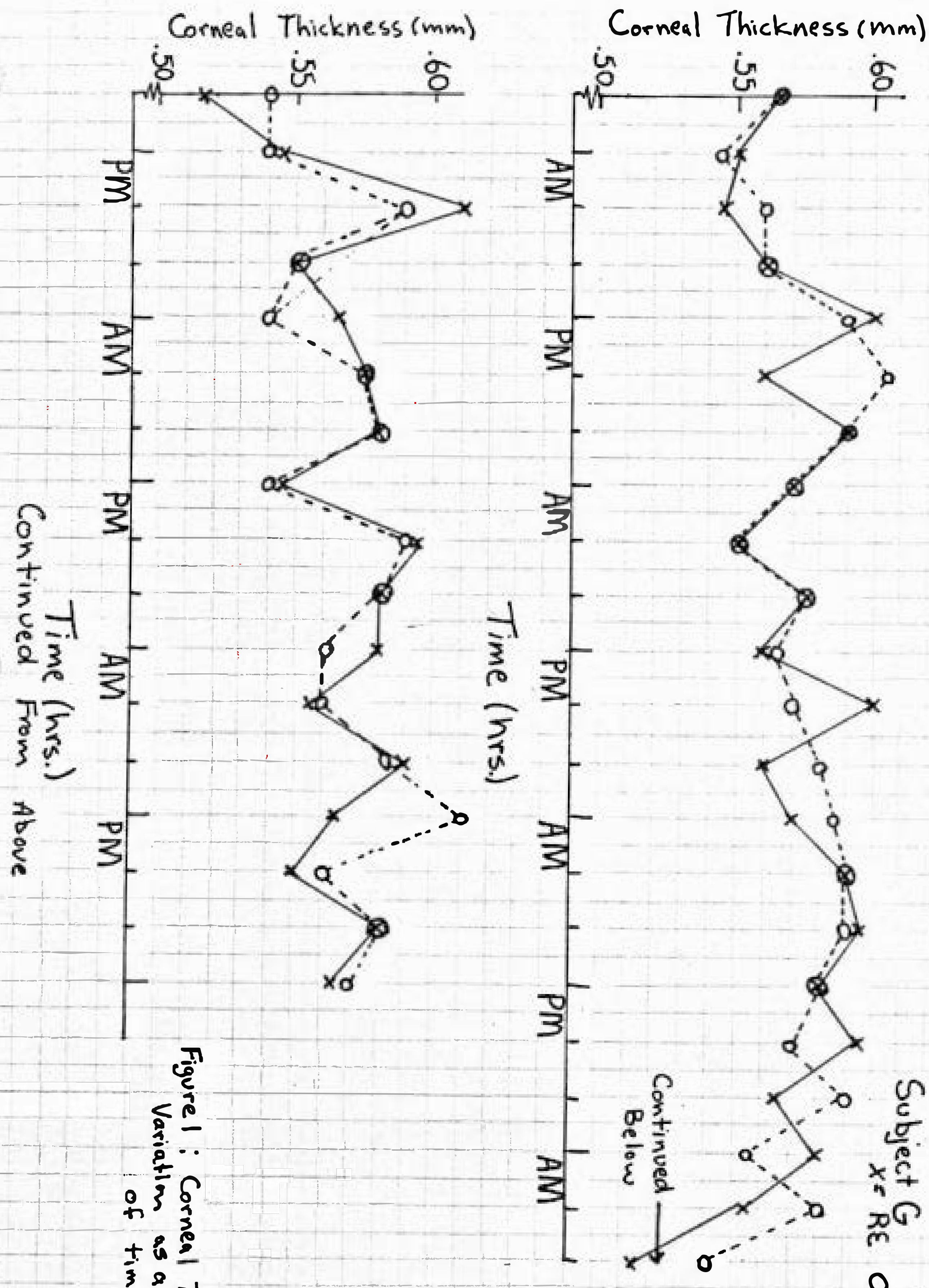

Figure 1: Corneal Thickness Variation as a function of time.

Figure 2

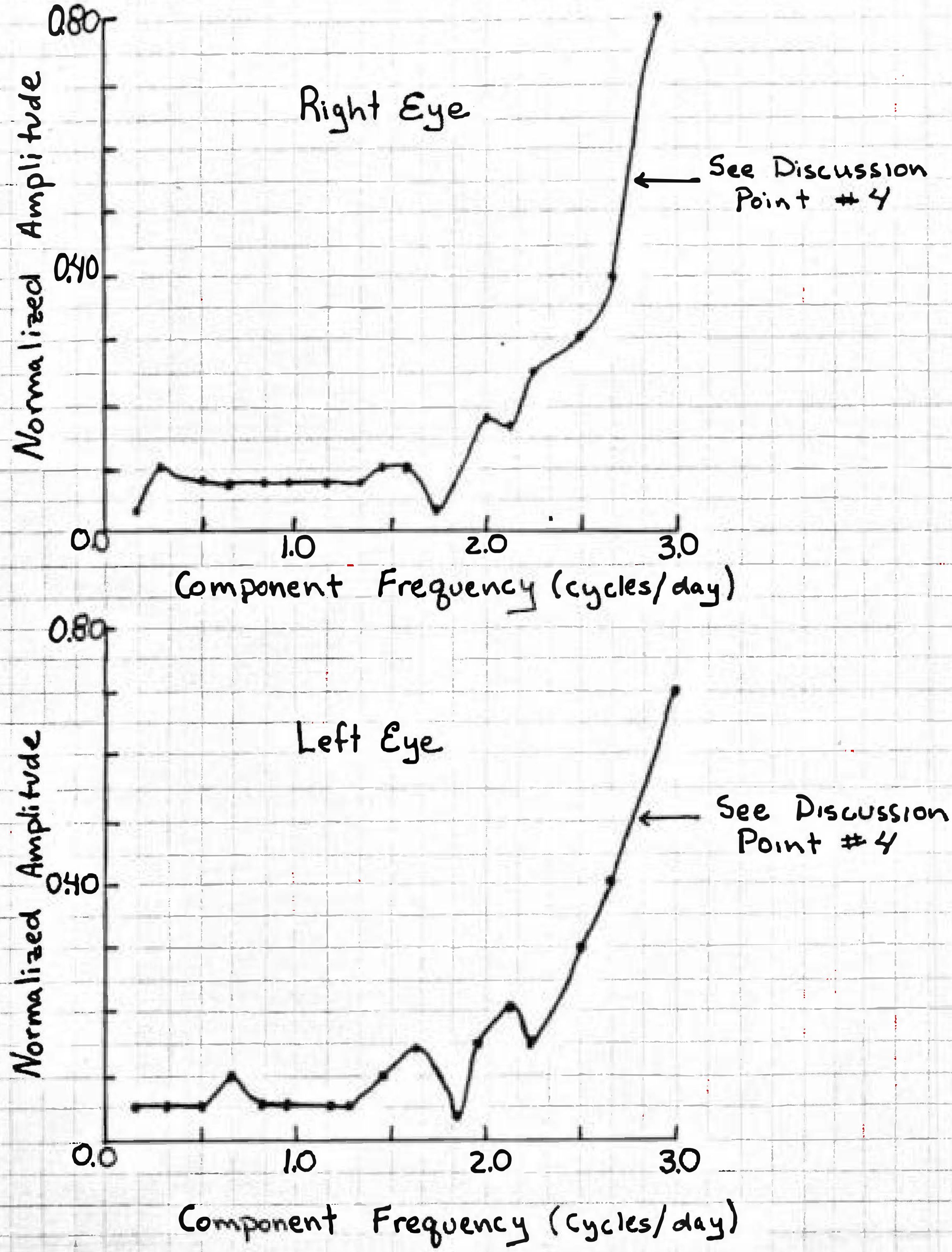

Figure 2: Fourier Analysis of Subject G's thickness vs. time data.

corneal thickness. Since subject G had the highest left eye vs right eye correlation coefficient (as seen on Table III), the greatest number of thickness measurements, and the longest time course of the study, subjects G's data would best indicate any periodic oscillations in corneal thickness, if present. Results of the fourier analysis are suggestive rather than conclusive. The functions in Figure 2 show no rise at 1 cycle/day, indicating the absence of a twenty-four hour oscillation, however, there is a slight rise at 1.5 cycles/day suggesting a possible thirty-six hour thickness oscillation. The fact that both the left eye and the right eye had a rise in the function at 1.5 cycles/day and no rise at 1 cycle/day adds reliability to the suggestion of a thirty-six hour repetitive pattern instead of a twenty-four hour repetitive pattern. The large rise on figure 2 at 3 cycles/day is an artifact of the limited sample size and not statistically significant. In order to determine and study the time course of corneal thickness oscillations in man, it would be necessary to take thickness measurements over more than a 148 hour period, especially if one wished to study the possibility of a thirty-six hour corneal oscillation.

The findings in this study have definite clinical implications. These are illustrated using a hypothetical researcher in the following example. Suppose a researcher wished to study the affect of corneal contact lenses on corneal thickness. He takes corneal thickness measurements at the same time each day in an attempt to avoid or control diurnal variation as a factor compounding or complicating the experimental procedure.

This researcher then draws conclusions about the contact lenses affect on corneal thickness while assuming that diurnal variation does not contaminate the experiment. The findings in this study conclusively show that measuring corneal thickness at the same time each day on the days measured does not eliminate or control the normal random variation in corneal thickness. The researcher might draw false conclusions concerning the affects of contact lenses on corneal thickness.

5) The most significant results of this research is shown in the scattergrams and the left eye vs. right eye correlation coefficients in Figures 3a, 3b and 3c. In almost all of the subjects' data, and especially those subjects with the most measurements, the correlation coefficient indicates a covariation of the subjects' two eyes' corneal thicknesses. When one cornea changes thickness, either thicker or thinner, the other cornea usually changes thickness in the same direction.

That the covariation is not an artifact or experimental error, but does occur, is supported by Kikkawa's rabbit studies where covariation was so predictable that he could use one eye of the rabbit as a control for the various experimental situations presented to the other eye of the same rabbit. Further evidence comes by inspecting Table III and noting that the more measurements taken, the higher the resultant correlation coefficient becomes; observe the scattergrams in Figures 3a, 3b, and 3c and notice the more linear tendency of the points on the graphs with the most measurements.

Figure 5a

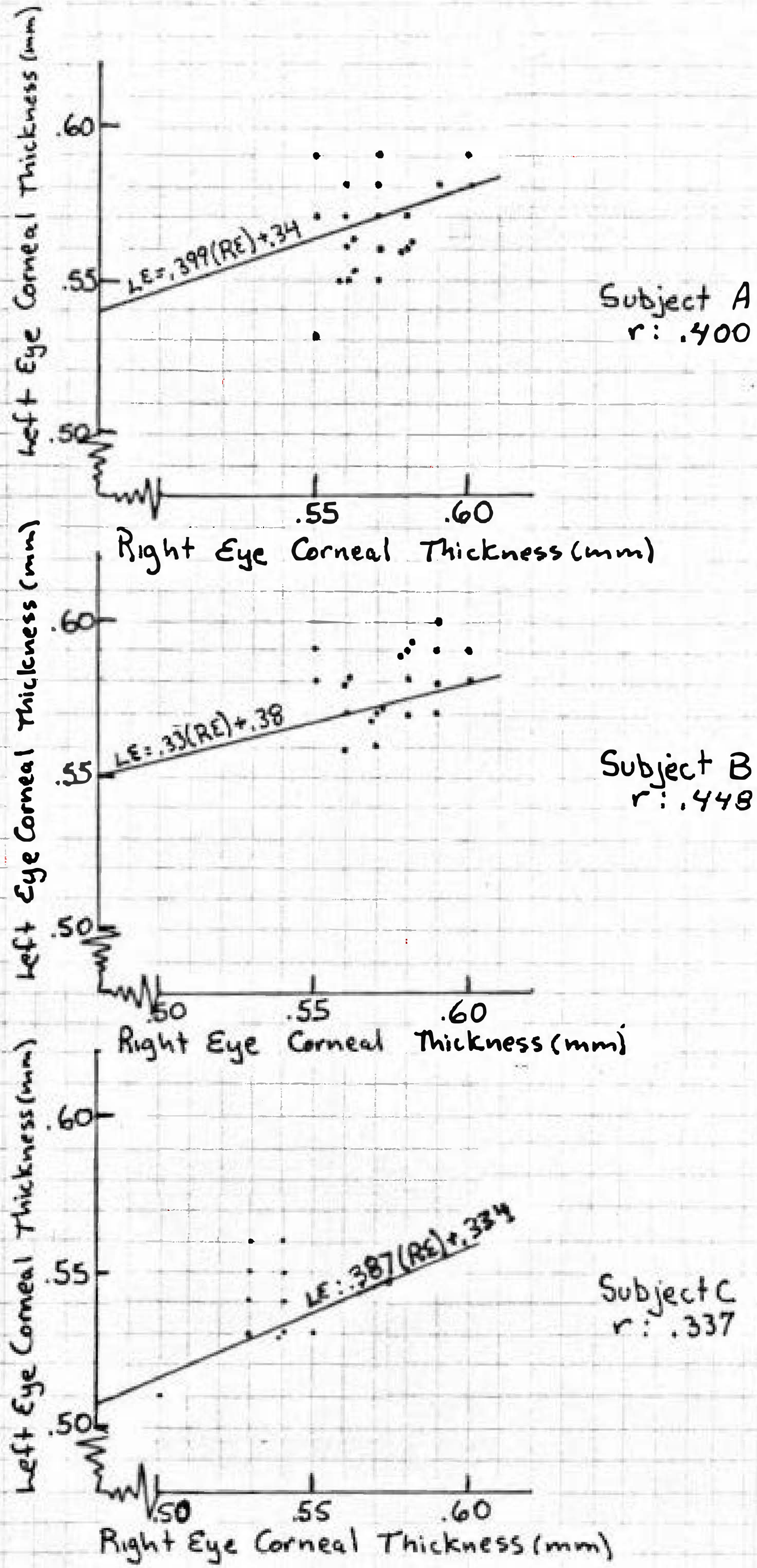
Left Eye Corneal Thickness (mm)
.60
.55
.50
LE=.399(RE)+.34
.55
.60
Right Eye Corneal Thickness (mm)
Subject A
r: .400
Left Eye Corneal Thickness (mm)
.60
.55
.50
LE=.33(RE)+.38
.50
.55
.60
Right Eye Corneal Thickness (mm)
Subject B
r: .448
Left Eye Corneal Thickness (mm)
.60
.55
.50
LE=.387(RE)+.334
.50
.55
.60
Right Eye Corneal Thickness (mm)
Subject C
r: .337

Figure 3b

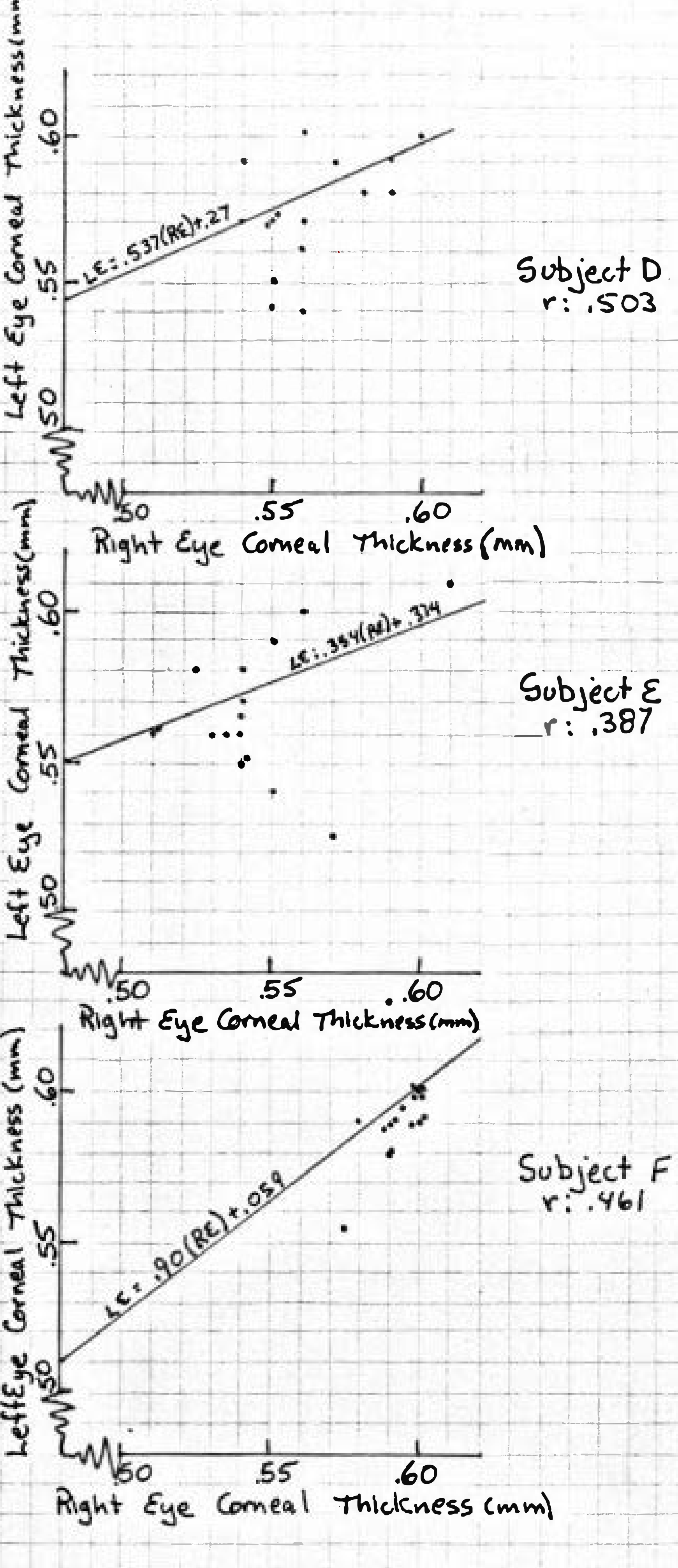
Left Eye Corneal Thickness (mm)
.50
.55
.60
LE: .537(RE)+.27
.50
.55
.60
Right Eye Corneal Thickness (mm)
Subject D
r: .503
Left Eye Corneal Thickness (mm)
.50
.55
.60
LE: .354(RE)+.374
.50
.55
.60
Right Eye Corneal Thickness (mm)
Subject E
r: .387
Left Eye Corneal Thickness (mm)
.50
.55
.60
LE: .90(RE)+.059
.50
.55
.60
Right Eye Corneal Thickness (mm)
Subject F
r: .461

Figure 3c

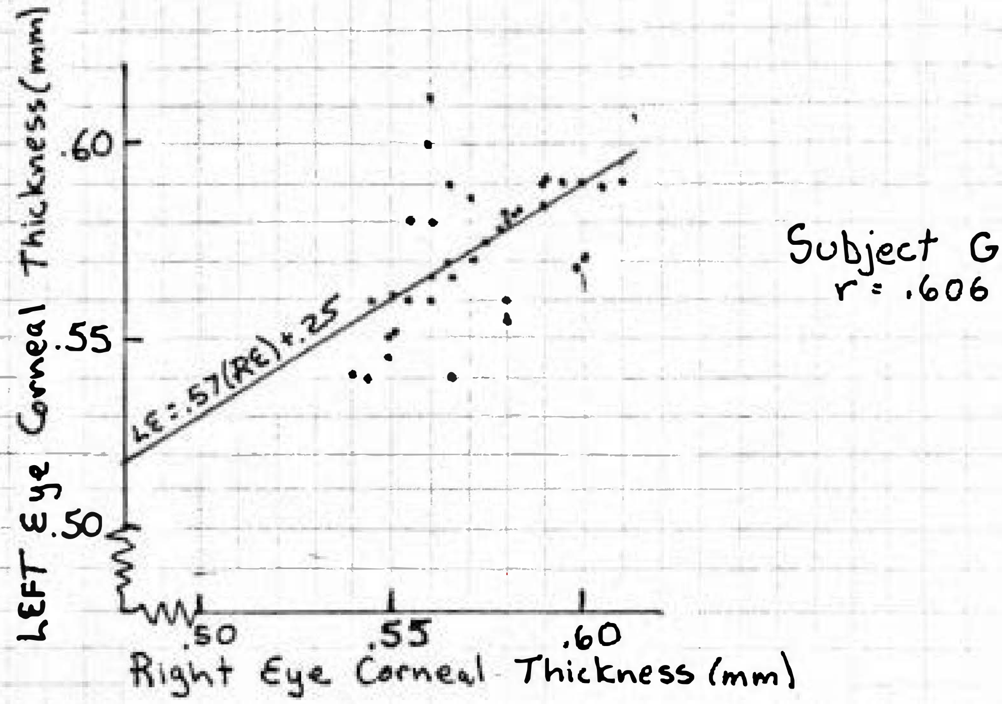

Figure 3: Scattergrams and least squares line (best fit) of left eye corneal thickness vs. right eye corneal thickness.

(To be more correct two linear regression lines should be plotted. However, only the line representing the LE thickness as a function of the RE thickness is plotted here.)

CONCLUSION

It has been shown in this research that daily corneal thickness oscillations are unpredictable. No cyclic corneal thickness diurnal variations were found on any subject measured. This knowledge, coupled with the knowledge of a tendency toward corneal thickness covariation, leads to suggest that the best predictor of what one eye's corneal thickness does may come from observing what the other eye's corneal thickness does and not based on the time of the day. Further study should be done to determine the extent of covariation between the two eyes and to determine whether covariation can be a useful tool in studying the effects of various factors upon corneal thickness.

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