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Lacrimal equilibration time (LET): Clinical application in the assessment of dry eye

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Abstract

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Lacrimal Equilibration Time (LET):

Clinical Application in the Assessment of Dry Eye

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ABSTRACT:

This study investigates the Lacrimal Equilibration Time (LET) test, a procedure proposed in 1994 by Lavaux and Keller to aid in the diagnosis of dry eye. The test evaluates the time required for a patient to regain his or her habitual monocular distance visual acuity after the instillation of a Celluvisc lubricating drop. In this study, the LET test is compared to rose bengal staining and to a dry eye patient questionnaire. No statistically significant relationship was found between any of these variables for the 58 subjects. In addition, the LET test was found to be highly variable within subjects.

KEY WORDS: dry eye, lacrimal equilibration time (LET), rose bengal, dry eye questionnaire, Celluvisc

INTRODUCTION

In today's arena of managed care, where cost effectiveness and productivity are key, inexpensive clinical tests that are both easily administered and interpreted have become very important. While many clinical tests provide evidence about the presence of dry eye, none definitively diagnose the condition.[1-3] Keratoconjunctivitis sicca is one of the most frequently encountered problems by eye care practitioners,[4-5] with one 1997 survey reporting that approximately 25% of the population could be symptomatic to some degree.[6] In addition, keratoconjunctivitis sicca is the most commonly encountered tear film abnormality.[1] Despite these facts, the condition is underdiagnosed[7] and often misinterpreted.[8] The ideal dry eye test would quickly, easily, and inexpensively diagnose keratoconjunctivitis sicca with a high degree of sensitivity and specificity.

This study investigates a simple and inexpensive procedure presented in 1993 by Levaux and Keller called the Lacrimal Equilibration Time (LET) test. The LET test was designed to measure lacrimal system function by evaluating the amount of time required for a patient to regain his or her baseline visual acuity after the instillation of a Celluvisc lubricating drop. Using twenty subjects, Lavaux and Keller discovered that symptomatic dry eye patients required statistically significant ($p=0.0002$) longer time intervals to regain their baseline acuities than did asymptomatic patients, and that the LET test showed "a very predictable identification of dry eye symptomatic patients when LET's exceeded five minutes." They concluded that "the LET test may prove to be the easiest, least invasive, quickest, most reliable, and most cost effective dry eye test currently available to the eye care practitioner."[9] Lavaux and Keller recommended that their study be repeated, to include more subjects, to include comparisons with other dry eye tests, to

precisely measure the Celluvisc drop volume, and to include intrapatient and interpatient variations, in order to validate the LET test's reliability. The current study has been modified to include these recommendations.

Lavaux's and Keller's study also assessed the clinical usefulness of the Schirmer test in diagnosing keratoconjunctivitis sicca; they found that the test did not clearly identify their symptomatic dry eye patients (p=0.019). Numerous investigators have found large variations in Schirmer values between subjects[1,10-14] and even within subjects.[1,10,12,15-16] Several researchers have also found the test to have a low reliability, low specificity, and/or low sensitivity for diagnosing dry eye.[11,13, 17-21] In addition, the discomfort and invasiveness of the Schirmer test have been well documented.[9,15, 22] The test has a poor correlation with both patient symptoms[2,11, 23] and with the severity of corneal damage.[24] Additionally, the Schirmer's test, even when performed with anesthesia, is not truly independent of reflex tearing components due to stimulation of the cilia and the lid margin.[11] For all of these reasons, this study does not include an assessment of the Schirmer test.

Rose bengal staining is one of the most frequently used dry eye tests in routine clinical practice.[23,25] The dye has long been known to stain dead, devitalized or degenerating cells, in addition to mucus.[9,26-34] More recently it has been demonstrated to stain living cells devoid of mucus-coating,[27, 35] and its staining can be blocked by albumin or tear substitutes such as carboxymethylcellulose. [35] In patients with dry eye, rose bengal gives a characteristic interpalpebral staining of the cornea and conjunctiva. The staining often appears as two triangles lying on either side of the cornea, with their bases toward the limbus.[1,24,28] When the cornea stains, it occurs primarily in its lower two-thirds.[24,28]

One investigator has proposed that staining should be considered positive only if both the cornea and conjunctiva stain.[24] Using his own method for scoring staining, van Bijsterveld estimated a false positive diagnostic error in the range of 4-5% for rose bengal, as compared to a false positive result of 16.67% with the Schirmer test.[20] Goren et al found rose bengal staining to have a specificity of 87.9% in diagnosing dry eye, when used as an individual test. In addition, rose bengal stain has been observed to correlate with decreased corneal sensitivity, reflecting corneal disease severity.[36] Unfortunately the dye has been demonstrated to have intrinsic cytotoxicity that is directly proportional to the concentration of and length of exposure to the dye.[27, 30-31, 35] However, this toxicity has been reported to occur to a minimal degree.[30] Because rose bengal stain has been considered by various investigators to be one of the most important diagnostic aids in the diagnosis of dry eye,[20, 32, 35, 37-40] and has also been recognized by some as the most reliable clinical method for its diagnosis,[41] rose bengal staining has been chosen as the objective measure of dry eye for this study.

Dry eye patients often have a wide range of characteristic symptoms.[42] These can include, but are not limited to, irritation, burning, soreness, itching, redness, pain, dryness, foreign body sensation, mild discomfort, vision disturbances,[5, 43-44] and most commonly ocular fatigue.[44] Because symptomology is well accepted as an indicator for dry eye disease,[6, 42, 45-48] a patient questionnaire developed by McMonnies has also been included in this study. This questionnaire, reported to have a sensitivity of 98% and a specificity of 97%, attempts to identify dry eye and the risk for dry eye. It assesses age, sex, contact lens wear, previous dry eye treatment, symptoms, symptoms brought on by provocative situations, systemic or ocular conditions associated with dry eye, and

medications which have been proven to provoke dry eye.[49] The results of this questionnaire will be compared to both the LET test results and to the rose bengal staining results. The latter two of these tests will also be compared to each other. It is our hypothesis that the LET test will accurately diagnose symptomatic dry eye patients at a statistically significant level, and that it will be more effective than the Rose Bengal test in making this diagnosis.

MATERIALS AND METHODS

Fifty-eight subjects were recruited from the student and staff population at Pacific University. Their ages ranged from 21 to 45 years of age, with a mean age of 27.3 years. Thirty of the subjects were male, and 28 were female. Candidates with ocular surface disease (other than keratoconjunctivitis sicca), such as blepharitis, infectious keratoconjunctivitis, and acne rosacea, were excluded from the study. Those with punctal occlusion were also excluded. Four different testing appointments were required for each subject, all on different days. Only two examiners administered testing in order to decrease variability within the study. The rose bengal test was administered on the first day of testing, and the LET test was administered one time on each of the three following visits. Contact lens wearers were asked to discontinue lens wear five days prior to the first day of testing, in order to ensure that any rose bengal staining was due to dry eye and not to contact lens related conditions. Lens wearers were permitted to resume lens wear after rose bengal testing, but could not wear their lenses at any time during a day when the LET test was to be administered.

To administer the rose bengal test, a single strip of "Rosets" Rose Bengal Dye was wetted with Allergan Preservative Free Saline Solution. A small amount of dye was instilled into the lower conjunctival sac of each of the subject's eyes, with care taken to minimally touch the strip to the conjunctiva. After approximately thirty seconds, staining of the ocular surface was assessed using a biomicroscope and the Van Bijsterveld scoring method. With this method, the ocular surface is divided into three vertical sections. The cornea is included in the middle section, while the nasal and temporal conjunctiva comprise the other two sections. Each of these sections is then divided horizontally into three sections. The result resembles a tic-tac-toe grid, with the cornea filling the middle square. The number of quadrants containing staining are counted, and a maximum score of 9 is possible per eye. A score greater than 3.5 is considered positive for keratoconjunctivitis sicca.[20] Because some research indicates that the test should be positive only when the cornea and conjunctiva both have staining,[24] the presence or absence of corneal staining was also recorded.

At each of the three administrations of the LET test, the subject's best habitual monocular distance acuities were measured with distance spectacles. Next, the following standardized set of instructions was read to each subject in order to attempt to decrease the variability inherent in the test's highly subjective endpoint: "For the LET test, we are going to test each eye separately. First I am going to put a drop of Celluvisc into your eye. I am going to immediately start the timer. After I put in the drop, I want you to put your glasses back on (if the subject has any), and to cover your other eye. Please tell me when you can first see all of the letters on that line again. You may notice that after you blink, the letters are clear for just a second and then become blurry again. I want you to

tell me when the letters are *constantly* clear, not just after you blink. While we do this, please blink as you normally would, and do not wipe your eyes."

A maximum of 30 microliters of fluid can be held in the average adult eye without drainage of excess fluid.[26] Eyes of smaller sizes, including those of children, can hold less than this amount. In addition, excess tearing can be stimulated by a drop larger than 20 microliters.[50] Therefore, twenty microliters was chosen as the volume of each Celluvisc drop used in this study. After reading the instruction set, 20 microliters of Celluvisc Lubricating Drops were instilled into the lower conjunctival sac of the subject's right eye using a micropipette. The subject then immediately put on his or her distance correction, if the subject wore any glasses, the stopwatch was started, and the subject covered his or her left eye with an opaque occluder. The time was recorded when the subject regained the baseline habitual monocular acuity for the right eye. This was the lacrimal equilibration time (LET) for the right eye. The process was then repeated for the left eye and the entire test was repeated for each subject on two more days. Neither the results of the testing nor the theory behind the LET test was revealed to subjects until all testing was completed in order to prevent subjects from unknowingly altering their results. In addition, examiners did not have access to previous LET or rose bengal results. This measure was taken to prevent examiner bias during the study.

A copy of the McMonnies questionnaire (Appendix A) was given to each subject during the first visit and was collected during one of the following visits.[46] The questionnaires were not evaluated, other than to assess completeness, until all testing was completed in order to maintain the objectiveness of the examiners. The questionnaires were later scored using the arbitrary point system developed for the questionnaire by

McMonnies, as shown in Appendix A, and the total score for each questionnaire was recorded. Scores of greater than 20 were classified as dry eye and those less than 10 were non-dry eye. Scores between 10 and 20 fell into the marginal dry eye group.[46] Based on his or her score, each subject was placed into the dry eye, marginal dry eye, or non-dry eye group.

RESULTS

The subjects' data, including ages, gender, rose bengal staining, LET times, overall LET averages per eye, LET standard deviations, and questionnaire scores are displayed in Table 1. The overall mean LET for a given trial does not differ significantly from day to day. It differs by a maximum of 10.8 seconds for the right eye and 11.3 seconds for the left eye. The overall mean LET of the subjects' left eyes is 29 seconds longer than the mean of their right eyes. The data for subject #37 includes only one LET measurement for the right eye because this subject had punctal plugs inserted in her right eye during the course of this study. The subject was kept in the study since data had already been gathered for rose bengal staining and since the left eye had not received any treatment. In addition, left eye data for subject #55 was omitted because the subject had a history of marked amblyopia in that eye, therefore making the endpoint of the LET tests difficult to measure for that eye.

As a measure of LET variability within each subject, the percentage of subjects that had a standard deviation greater than 10%, 25%, 50% and 100% of their mean LET was calculated. These results, for subjects' right and left eyes, are displayed in Table 2. LET scores for the subjects' right eyes show that 4% of subjects had standard deviations

greater than 100% of a single LET measurement. Right eye data also shows that 93% of subjects tested had standard deviations greater than 10% of a single LET measurement. LET results for subjects' left eyes show similar patterns in that, although no patients had a standard deviation greater than 100% of their mean LET, 95% of subjects had standard deviations greater than 10% of a single LET measurement. This indicates the variability inherent within a single subject for the LET test. A one factor ANOVA for repeated measures was performed using right and left eye LET's from trial 1, 2, and 3, as well as mean LET data from each eye. A within-subjects level of significance of $p = 0.8725$ for right eye LET's and 0.8143 for left eye LET's was calculated. When analyzed as a group, this indicates a statistically significant similarity within subjects.

An ANOVA for repeated measures performed on the mean group data from right eye and left eye shows a between-subjects level of significance of $p = 0.0001$. This indicates that the mean LET between each patient in the group is significantly different. After determining that the data, when analyzed as a group, was not statistically different within subjects, and that there is a significant statistical difference between subjects, a correlation analysis was performed, and a correlation matrix was formulated to determine if the LET's obtained on different trials were similar. A strong correlation exists between the LET's for trials 1, 2, and 3 for each eye, and among the mean LET's between right and left eye, as shown in Table 3. This indicates that the LET's obtained on different days of testing are similar and that the LET's are similar between eyes.

Figure 1 represents a histogram of scored questionnaire values for the 58 subjects. Scores ranged from a minimum of 0 to a maximum of 19, with a modal value of 8 and a median value of 8. The mean value of scoring was 7.9 with a standard deviation of 4.76

displayed in Figures 6 and 7, of questionnaire scores versus rose bengal staining demonstrates this finding.

In addition to correlating rose bengal staining with questionnaire results, staining results were correlated with LET findings (Table 3). Again, no significant correlation was demonstrated. A scatter plot was generated using the results of staining of each eye and the mean LET for right and left eyes (Figures 8 and 9). As illustrated, no relationship exists between the results.

No statistically significant correlation exists between age and rose bengal staining of either eye. Additionally, as can be seen in Table 3, no relationship was found among age and LET for either right or left eye.

DISCUSSION

Statistical analysis of the variability of the LET test within subjects shows paradoxical results. When analyzed as a group via ANOVA testing, results indicate that the LET test is very repeatable within subjects, with right eye LET yielding a level of significance of $p=0.8725$, and left eye data yielding a similar level of $p=0.8143$. The ANOVA test assesses the similarity of the LET test results for each individual by calculating the difference between the LET's from day-to-day for the entire group. Hence, it is possible for the mean to remain stable even if a number of patients had increased LET's, as long other patients had decreased LET's by approximately the same average amount of time. Upon closer evaluation of the subjects' individual results, via percentage standard deviations, the marked variability between LET measurements within subjects is apparent. The number of patients who had standard deviations greater

than 10%, 50%, and 100% of single LET trials is illustrated in Table 2. The variability inherent in the test necessitates repeated testing of patients, in order to use average LET's as a diagnostic tool. This variability may be the result of the high degree of subjectivity in the endpoint of the LET test.

The results of this study also indicate that a patient's lacrimal equilibration time does not accurately predict the occurrence of dry eye symptoms, and dry eye symptoms do not allow a predictable estimate of equilibration time. Our study found no statistically significant relationship between LET's and the presence of marginal dry eye, or between LET's and the absence of dry eye (as classified by the McMonnies questionnaire). This lack of correlation between times and questionnaire scores can be explained by the variability inherent in the LET test, as previously described. Since the LET test in not repeatable and is highly variable, no correlation can be expected between any variables tested. The measures taken to ensure the examiners' objectivity prevented detection of the fact that no definitive dry eye subjects were included in this study. Specifically, subjects were not screened for dry eye at the start of the study, and questionnaires were not scored until all testing was completed. Due to the high variability of the LET test, in conjunction with the fact that no correlation was found between LET's and marginal or non-dry eye patients, it is predicted that no correlation exists between LET's and subjects classified as dry eye by the McMonnies questionnaire. Further testing is indicated to prove or disprove this conclusion.

ANOVA testing also indicates that a statistically significant difference exists between subjects, indicating that the lacrimal equilibration time is not identical from person to person. Statistical analysis also reveals that the mean group LET of each trial is

repeatable. This indicates that little external variability was introduced into the study via materials, methods, examiners, or environment conditions such as humidity and temperature.

The mean overall LET's between right and left eyes differs by 29 seconds and, although slightly less, corresponds to the difference of 43.8 seconds found by Lavaux and Keller.[9] In both cases, the mean LET's for the left eyes was longer than for the right eyes. The cause of this difference, other than a greater incidence of dry eye in patients' left eyes, is not clearly evident. One possible cause is that the blur is induced when pressure is placed on the eye during occlusion. In both studies, the LET for subjects' right eyes was measured first, with concurrent occlusion of their left eyes. If a patient exerted pressure on his or her left eye with the occluder, time would be needed to overcome this induced blur, in addition to the time needed to clear the Celluvisc drop. The overall result would be an increased LET for the left eye. Instructing patients not to place pressure on the occluded eye would eliminate this variable from the test, if that truly were the cause.

Rose bengal staining, as assessed by the van Bijsterveld method, did not correlate significantly with LET's or with questionnaire scores. Again, the variability inherent in the LET test, as previously described, may contribute considerably to this lack of correlation. Another contributing factor may be the use of rose bengal-impregnated strips instead of rose bengal solution. While research indicates that rose bengal-impregnated ophthalmic paper strips do minimize patient discomfort,[40] some researchers suggest that 1% rose bengal solution should be used in the assessment of dry eye in order to attain a high enough concentration of solution to provide adequate staining.[25,30] Another possible

cause of the poor correlation between rose bengal staining and the LET test is the possibility that two tests assess different tear deficiencies. Rose bengal staining strongly indicates a loss of preocular mucin protection,[27,35] while it is our opinion that the LET test most likely assesses aqueous layer deficiencies, reduced tear production abilities, or lacrimal system outflow capabilities. Another cause of the poor correlation between rose bengal staining and LET's or questionnaire scores may be the use of the stain to diagnose basic dry eye cases. Some investigators believe that rose bengal staining may be useful in diagnosing Sjogren's syndrome specifically and not in other tear film instability problems.[25] If this is the case, since none of the patients assessed in this study had Sjogren's syndrome, less of a correlation would be expected between rose bengal staining and LET scores.

Statistical analysis also shows that a marked asymmetry exists between right and left eye group rose bengal staining. Fifteen subjects were classified as dry eye via van Bijsterveld's method based on their right eyes' staining, while only 3 subjects were given the same classification based on their left eyes' staining. This was most likely caused by using only one rose bengal strip per patient, with right eye instillation always occurring first. Therefore, the amount and concentration of rose bengal that was instilled into subjects' left eyes was probably much less than that instilled into their right eyes, correlating to less staining in their left eyes.

Only eight patients had any degree of rose bengal corneal staining, illustrated as (+) or (-) in Table 1, under the heading of COD and COS, for right and left eye data respectively. No correlation exists between this staining and the questionnaire scores or the LET's (Table 3). Therefore, the inclusion of corneal involvement in the assessment

of rose bengal staining may not provide any useful information as to the presence of dry eye. Williamson also found that in the majority of patients suffering from keratoconjunctivitis sicca, there is no clinical evidence of corneal epithelial involvement.[51] However, the presence or absence of corneal staining would undoubtedly be affected by the amount of rose bengal stain instilled, so the data obtained in this study regarding corneal staining must be considered with caution.

Lavaux and Keller state that the LET test stresses the lacrimal system because the instillation of Celluvisc increases tear volume and viscosity. This stress may induce reflex tearing that aids in the removal of the lubricating drop. If true, those patients with the greatest induced reflex tearing would be expected to have shorter lacrimal equilibration times. If this test truly measures tear outflow, variables such as punctal size, punctal stenosis, and blink rate would also influence equilibration time. The size of the eye may also affect the LET time. Spreading a constant volume over a larger area will result in a thinner layer of Celluvisc and an expected lower LET, as compared to a thicker layer over a smaller area.

Further testing, specifically more trials on a similar or larger number of subjects, is indicated to more thoroughly assess the repeatability and variability of the LET test. The ideal study would include numerous pre-diagnosed dry eye subjects, as well as marginal and non-dry eye subjects, with their identities unknown to a single examiner. Rose bengal testing should also be repeating using precisely measured amounts of 1% rose bengal solution.

CONCLUSIONS

The LET test was initially conceived of as a cost effective, quick, easy, and accurate test to aid practitioners in the diagnosis of dry eye. This study shows that the LET test is a highly variable test, and therefore would need to be repeated several times on a single patient in order to obtain an average score for diagnostic use. The increased chair time required for repeated testing ultimately defeats the LET test's usefulness as a quick test, even though the test would still be cost effective and easy to administer. The results of this study also indicate that the LET test does not adequately correlate with patient's dry eye symptoms, when these symptoms are mild to moderate in nature. Because no dry eye patients were included in this study, no definite statement can be made about the relationship of the LET test with highly symptomatic patients. Despite this, a clinically useful test should accurately identify those patients who are even mildly symptomatic and asymptomatic; a result not conferred by the LET test. The LET test also has no correlation with rose bengal staining. Overall, the LET test was found to be highly variable with a highly subjective endpoint, and correlates poorly with patient symptoms and rose bengal staining, limiting the clinical usefulness of the test.

Table 1: Right Eye Data

Subject	M/F	Age	RB OD	C OD	LET OD 1	LETOD 2	LET OD 3	Mean LET OD	STDDEV Let OD	STDEV/MeanLET%	q-sc
1	f	22	3	-	85.48	127.78	129	114.09	24.78	21.72	0
2	f	29	1	-	77.00	74.34	116.6	89.31	23.67	26.50	12
3	m	28	6	+	14.78	51.29	35.81	33.96	18.33	53.96	8
4	m	31	7	+	358.28	518.39	285.69	387.45	119.06	30.73	4
5	f	26	0	-	137.69	120.62	101.22	119.84	18.25	15.23	18
6	m	45	5	-	61.60	201.38	156.41	139.80	71.36	51.04	6
7	f	26	4	+	156.53	94	214.53	155.02	60.28	38.88	11
8	m	27	0	-	380.46	292.66	405.38	359.50	59.21	16.47	2
9	f	27	1	-	76.19	116.19	99.22	97.20	20.08	20.65	12
10	f	24	1	-	84.57	109.37	135.49	109.81	25.46	23.19	9
11	m	27	4	+	377.06	217.51	399.57	331.38	99.25	29.95	8
12	f	27	3	-	30.02	13.19	52.54	31.92	19.74	61.86	4
13	f	37	3	-	131.96	183.19	125.25	146.80	31.69	21.59	7
14	m	27	0	-	90.85	189.96	267.28	182.70	88.44	48.41	3
15	m	25	1	-	103.47	167.44	211.31	160.74	54.23	33.74	1
16	m	25	2	-	137.75	44.85	74.07	85.56	47.50	55.52	1
17	m	26	0	-	76.00	62.40	105.72	81.37	22.15	27.23	10
18	f	33	4	-	434.78	245.37	173.75	284.63	134.87	47.38	16
19	f	26	1	-	179.00	337.37	160.19	225.52	97.32	43.15	4
20	f	23	3	+	84.60	132.03	99.81	105.48	24.22	22.96	3
21	m	24	4	-	55.28	22.69	37.69	38.55	16.31	42.31	5
22	m	24	2	-	87.98	97.04	17.37	67.46	43.62	64.65	7
23	m	25	2	-	391.19	204.84	287.55	294.53	93.37	31.70	2
24	f	42	3	-	512.47	584.53	1017.41	704.80	273.11	38.75	11
25	f	28	1	-	477.32	345.19	331.42	384.64	80.56	20.94	14
26	m	27	2	-	70.08	46.54	20.75	45.79	24.67	53.88	1
27	m	24	0	-	56.03	91.03	42.97	63.34	24.85	39.23	3
28	f	24	0	-	19.56	26.53	39.53	28.54	10.14	35.51	4
29	f	25	0	-	494.59	121.60	69.69	228.63	231.79	101.38	13
30	m	29	0	-	78.75	95.12	156.06	109.98	40.74	37.04	14
31	m	25	0	-	544.60	171.31	77.06	264.32	247.26	93.54	12
32	f	25	1	-	27.90	104.21	74.01	68.71	38.43	55.93	5
33	m	22	4	+	426.07	864.22	506.25	598.85	233.29	38.96	9
34	m	25	4	-	36.25	47.72	45.47	43.15	6.08	14.09	8
35	f	21	3	-	72.44	34.97	48.34	51.92	18.99	36.58	8
36	m	25	1	-	53.69	50.41	34.97	46.36	10.00	21.56	5
37	f	27	0	-	98.25			98.25		0.00	13
38	f	24	0	-	692.34	766.69	757.97	739.00	40.64	5.50	10
39	m	28	3	-	430.18	110.12	493.62	344.64	205.56	59.65	2
40	m	29	5	-	119.34	612.78	291.6	341.24	250.44	73.39	10
41	f	26	5	+	542.47	413.41	372.13	442.67	88.86	20.07	17
42	m	29	4	-	146.06	688.40	102.75	312.40	326.34	104.46	7
43	f	24	3	-	120.44	153.31	164.31	146.02	22.83	15.63	13
44	m	27	0	-	20.91	50.75	62.34	44.67	21.37	47.85	9
45	m	45	6	+	147.47	135.53	138.03	140.34	6.30	4.49	2
46	m	27	2	-	108.07	65.50	155.41	109.66	44.98	41.01	9
47	f	36	1	-	556.59	485.16	345.22	462.32	107.52	23.26	9
48	f	27	8	-	79.46	80.51	80.09	80.02	0.53	0.66	5
49	f	24	2	-	63.78	118.68	84.43	88.96	27.73	31.17	14
50	m	25	0	-	97.00	279.97	315.63	230.87	117.30	50.81	8
51	f	24	0	-	28.57	66.25	127.16	73.99	49.75	67.23	8
52	f	26	0	-	114.81	133.25	99.62	115.89	16.84	14.53	11
53	m	23	5	-	637.72	987.87	914.72	846.77	184.70	21.81	19
54	m	28	0	-	56.85	33.1	58.15	49.37	14.10	28.57	3
55	m	23	3	-	26.90	38.59	40.68	35.39	7.43	20.98	13
56	m	36	1	-	13.40	12.97	14	13.46	0.52	3.84	0
57	f	23	3	-	548.18	308.19	322.85	393.07	134.53	34.22	7
58	f	32	2	-	601.75	245.34	280.5	375.86	196.41	52.26	9

Table 1: Left Eye Data

Subject	M/F	Age	RB OS	C OS	LET OS 1	LET OS 2	LET OS 3	Mean LET OS	STDDEV LET OS	STDEV/MeanLET%	q-sc
1	f	22	2	-	47.53	69.88	99	72.14	25.81	35.78	0
2	f	29	0	-	286.28	49.16	171.19	168.88	118.58	70.22	12
3	m	28	5	+	15.19	107.47	90.54	71.07	49.13	69.13	8
4	m	31	4	-	550.32	540.28	235.82	442.14	178.75	40.43	4
5	f	26	0	-	288.06	133.19	114.84	178.70	95.15	53.25	18
6	m	45	2	-	118.75	206.92	233.25	186.31	59.97	32.19	6
7	f	26	0	-	290.5	195.02	204.97	230.16	52.49	22.81	11
8	m	27	0	-	673.09	360.22	431.96	488.42	163.90	33.56	2
9	f	27	1	-	189.25	85.19	108.17	127.54	54.67	42.86	12
10	f	24	1	-	98.03	159.37	178.87	145.42	42.19	29.01	9
11	m	27	2	-	360.75	382.06	550.28	431.03	103.82	24.09	8
12	f	27	1	-	31.44	11.03	28.06	23.51	10.94	46.53	4
13	f	37	2	-	137.25	149.19	275.25	187.23	76.46	40.84	7
14	m	27	0	-	169.5	275.00	382.32	275.61	106.41	38.61	3
15	m	25	0	-	117.65	205.50	271.25	198.13	77.06	38.90	1
16	m	25	2	-	98.28	38.50	110.75	82.51	38.62	46.81	1
17	m	26	2	-	81.79	83.47	81.50	82.25	1.06	1.29	10
18	f	33	3	-	343.84	182.69	244.48	257.00	81.30	31.63	16
19	f	26	1	-	197.41	351.53	246.07	265.00	78.79	29.73	4
20	f	23	3	+	59.75	200.41	297.47	185.88	119.52	64.30	3
21	m	24	2	-	49.33	39.16	33.71	40.73	7.93	19.46	5
22	m	24	3	-	152.43	144.60	27.06	108.03	70.23	65.01	7
23	m	25	0	-	277.63	252.6	310.71	280.31	29.15	10.40	2
24	f	42	3	-	718.01	670.56	750.75	713.11	40.32	5.65	11
25	f	28	3	-	238.54	441.56	363.22	347.77	102.39	29.44	14
26	m	27	1	-	114.56	32.38	77.56	74.83	41.16	55.00	1
27	m	24	0	-	64.36	57.28	72.65	64.76	7.69	11.88	3
28	f	24	0	-	54.07	25.56	20.03	33.22	18.27	54.99	4
29	f	25	3	-	420.34	235.32	312.41	322.69	92.94	28.80	13
30	m	29	0	-	31.62	127.93	124.03	94.53	54.51	57.67	14
31	m	25	0	-	393.90	209.01	116.28	239.73	141.34	58.96	12
32	f	25	1	-	114.31	51.81	89.78	85.30	31.49	36.92	5
33	m	22	3	-	567.25	499.28	394.69	487.07	86.93	17.85	9
34	m	25	3	-	56.49	81.04	179.78	105.77	65.26	61.70	8
35	f	21	2	-	66.63	43.82	51.41	53.95	11.62	21.53	8
36	m	25	0	-	26.13	59.5	49.62	45.08	17.14	38.02	5
37	f	27	1	-	81.53	89.95	108.56	93.35	13.83	14.82	13
38	f	24	0	-	960.63	671.38	863.87	831.96	147.24	17.70	10
39	m	28	1	-	302.34	320.03	562.56	394.98	145.40	36.81	2
40	m	29	3	-	640.81	612.87	417.59	557.09	121.62	21.83	10
41	f	26	3	+	288.61	494.44	317.13	366.73	111.52	30.41	17
42	m	29	3	-	130.56	704.31	438.91	424.59	287.14	67.63	7
43	f	24	1	-	103.88	88.56	50.21	80.88	27.65	34.18	13
44	m	27	0	-	38.62	63.18	77.91	59.90	19.85	33.13	9
45	m	45	2	-	184.59	170.47	138.81	164.62	23.44	14.24	2
46	m	27	2	-	90.03	127.71	164.41	127.38	37.19	29.20	9
47	f	36	2	+	530.06	503.91	589.88	541.28	44.07	8.14	9
48	f	27	6	-	64.62	49.47	67.68	60.59	9.75	16.09	5
49	f	24	1	-	81.19	109.25	148.78	113.07	33.96	30.03	14
50	m	25	0	-	151.97	529.02	305.97	328.99	189.58	57.62	8
51	f	24	0	-	35.03	52.03	78.87	55.31	22.10	39.96	8
52	f	26	0	-	242.32	194.62	140.72	192.55	50.83	26.40	11
53	m	23	3	-	575.28	926.78	1347.84	949.97	386.80	40.72	19
54	m	28	1	-	35.72	80.51	93.31	69.85	30.24	43.29	3
55	m	23	1	-							13
56	m	36	1	-	10.65	12.94	17.75	13.78	3.62	26.30	0
57	f	23	1	-	696.00	328.62	423.28	482.63	190.75	39.52	7
58	f	32	1	-	440.78	265.63	115.41	273.94	162.84	59.45	9

Table 2: LET Standard Deviation Percentages

	OD #	OD %	OS #	OS %
SD > 100% LET Mean	2/57	4%	0/57	0%
SD > 50% LET Mean	15/57	26%	13/57	23%
SD > 25% LET Mean	37/57	65%	42/57	74%
SD > 10% LET Mean	53/57	93%	54/57	95%

Table 3: Correlation Matrix

Correlation Matrix for all Variables

	Age	RB OD	RB OS	LET OD.1	LET OD.2	LET OD.3	MeanLETOD	LET OS.1	LET OS.2	LET OS.3	MeanLETOS	Q.Score
Age	1											
RB OD	0.268	1										
RB OS	0.175	0.76	1									
LET OD 1	0.078	0.086	0.133	1								
LET OD 2	0.076	0.264	0.273	0.657	1							
LET OD 3	0.15	0.148	0.099	0.729	0.779	1						
MeanLETOD	0.112	0.187	0.189	0.875	0.906	0.926	1					
LET OS 1	0.112	0.088	0.062	0.826	0.745	0.77	0.863	1				
LET OS 2	0.123	0.229	0.244	0.693	0.931	0.818	0.906	0.741	1			
LET OS 3	0.087	0.153	0.153	0.7	0.811	0.889	0.888	0.717	0.868	1		
MeanLETOS	0.116	0.168	0.164	0.802	0.897	0.897	0.96	0.887	0.941	0.938	1	
Q.Score	-0.065	-0.011	0.102	0.362	0.322	0.28	0.355	0.292	0.314	0.287	0.322	1

Figure 1: Histogram of Questionnaire Scores

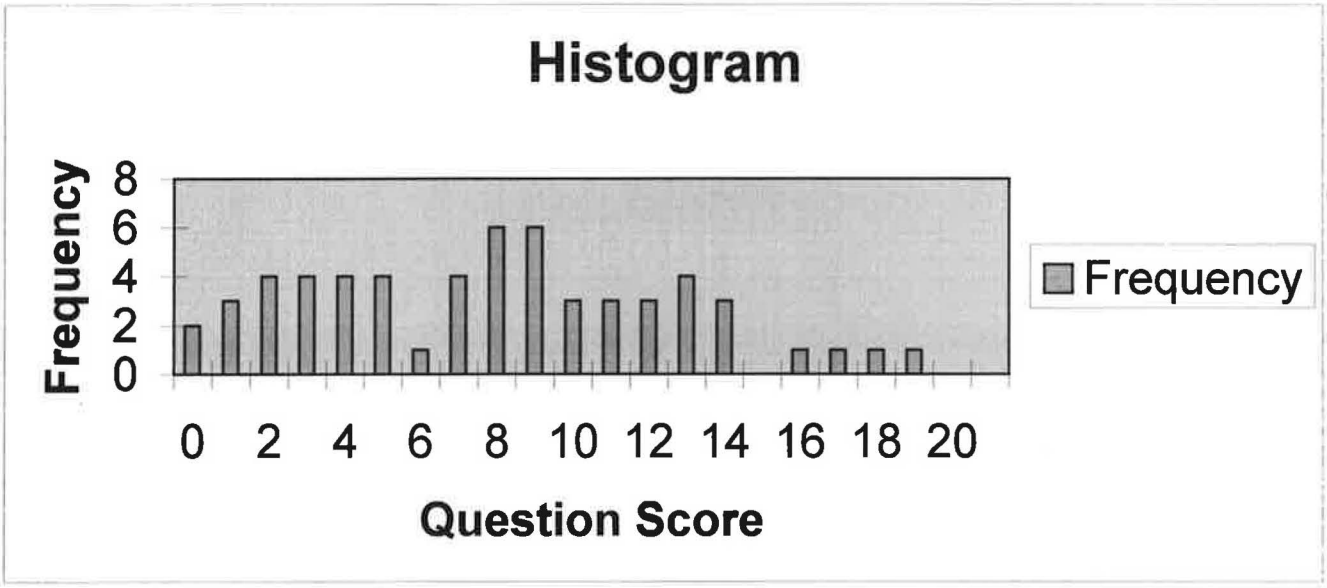


Figure 2: Scatter Plot of Questionnaire vs LET OD

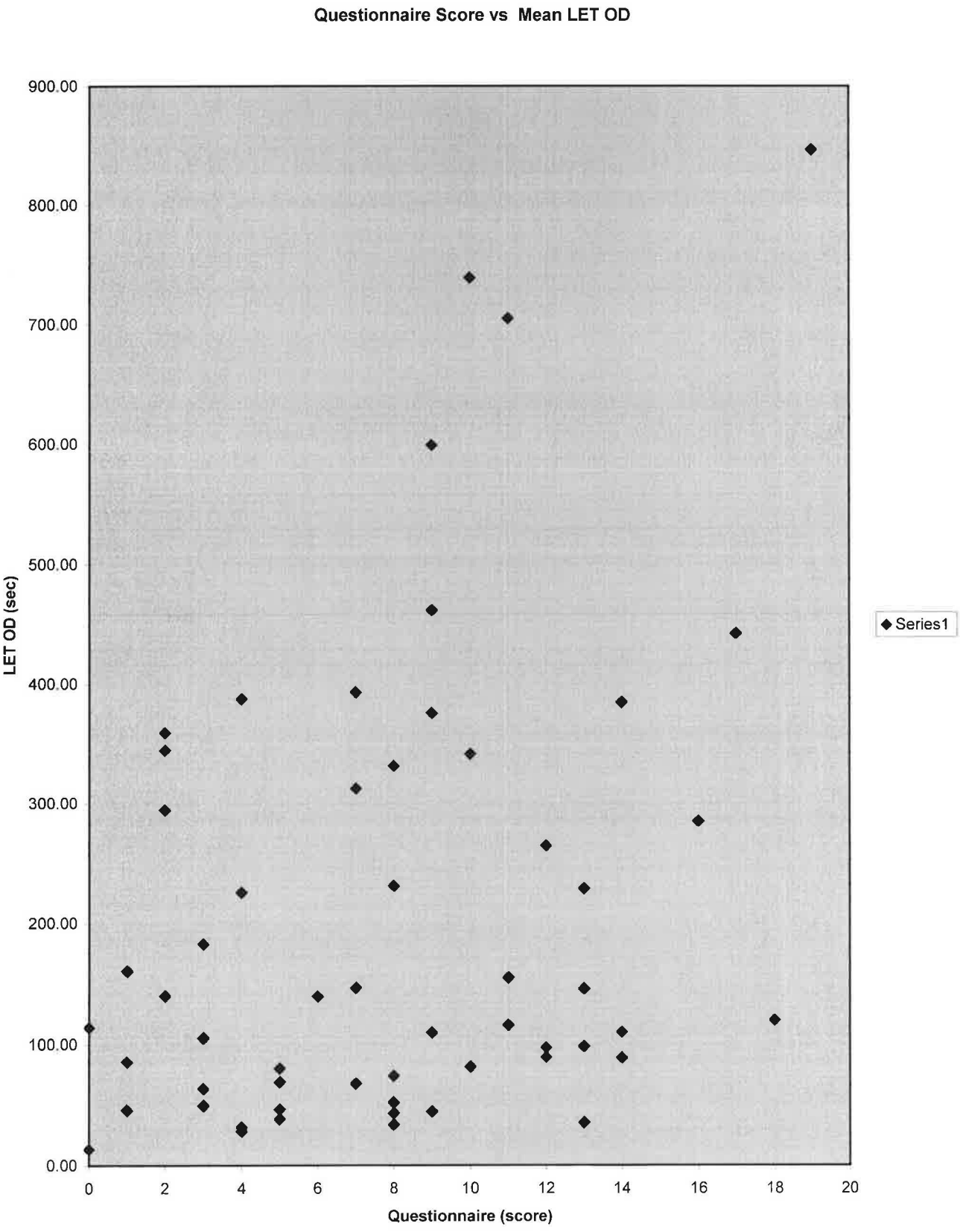


Figure 3: Scatter Plot of Questionnaire vs LET OS

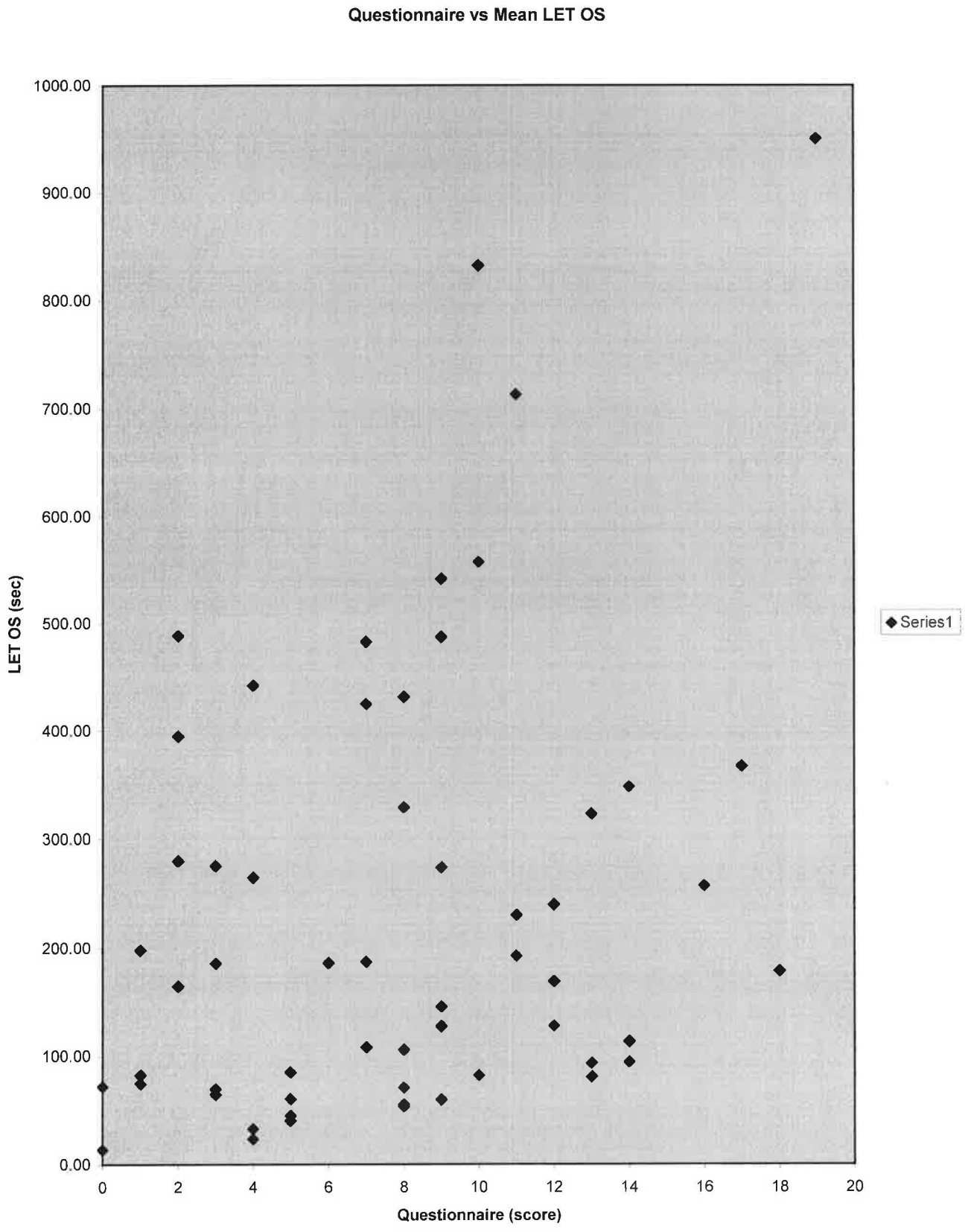


Figure 4: Histogram of OD Rose Bengal Staining

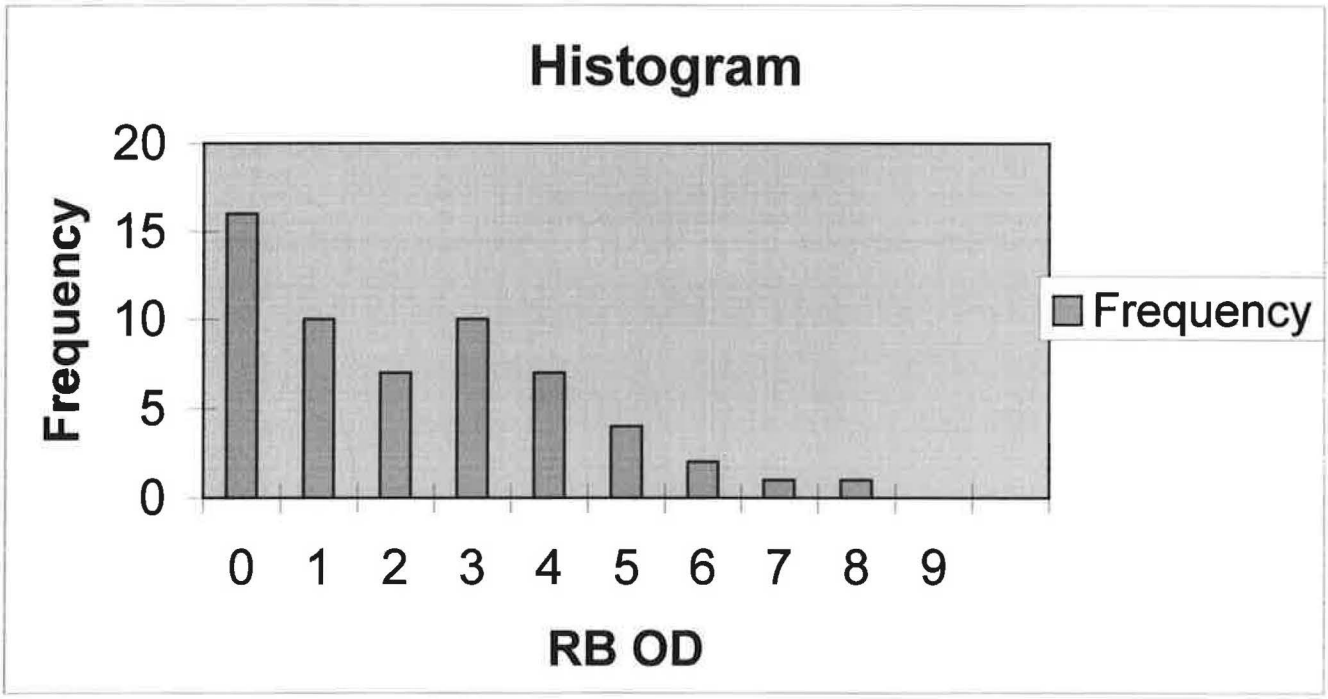


Figure 5: Histogram of OS Rose Bengal Staining

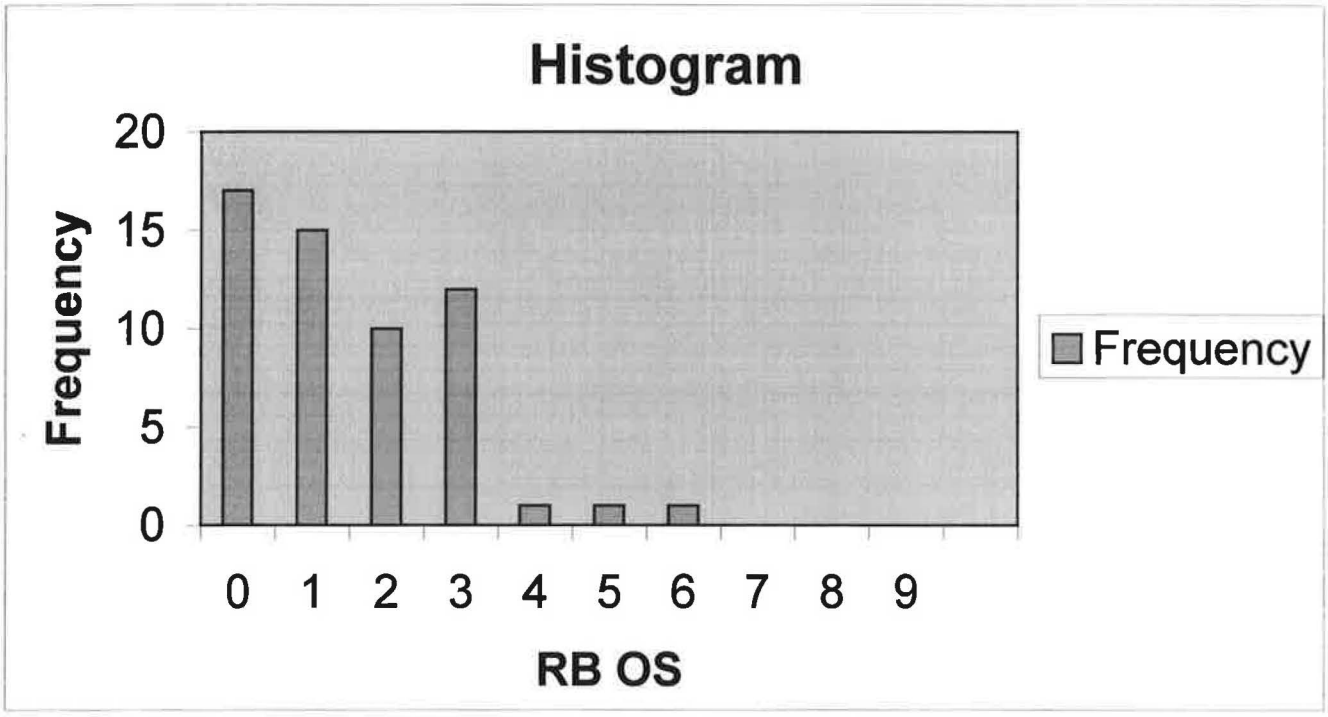


Figure 6: Scatter plot of Question Score vs RB OD

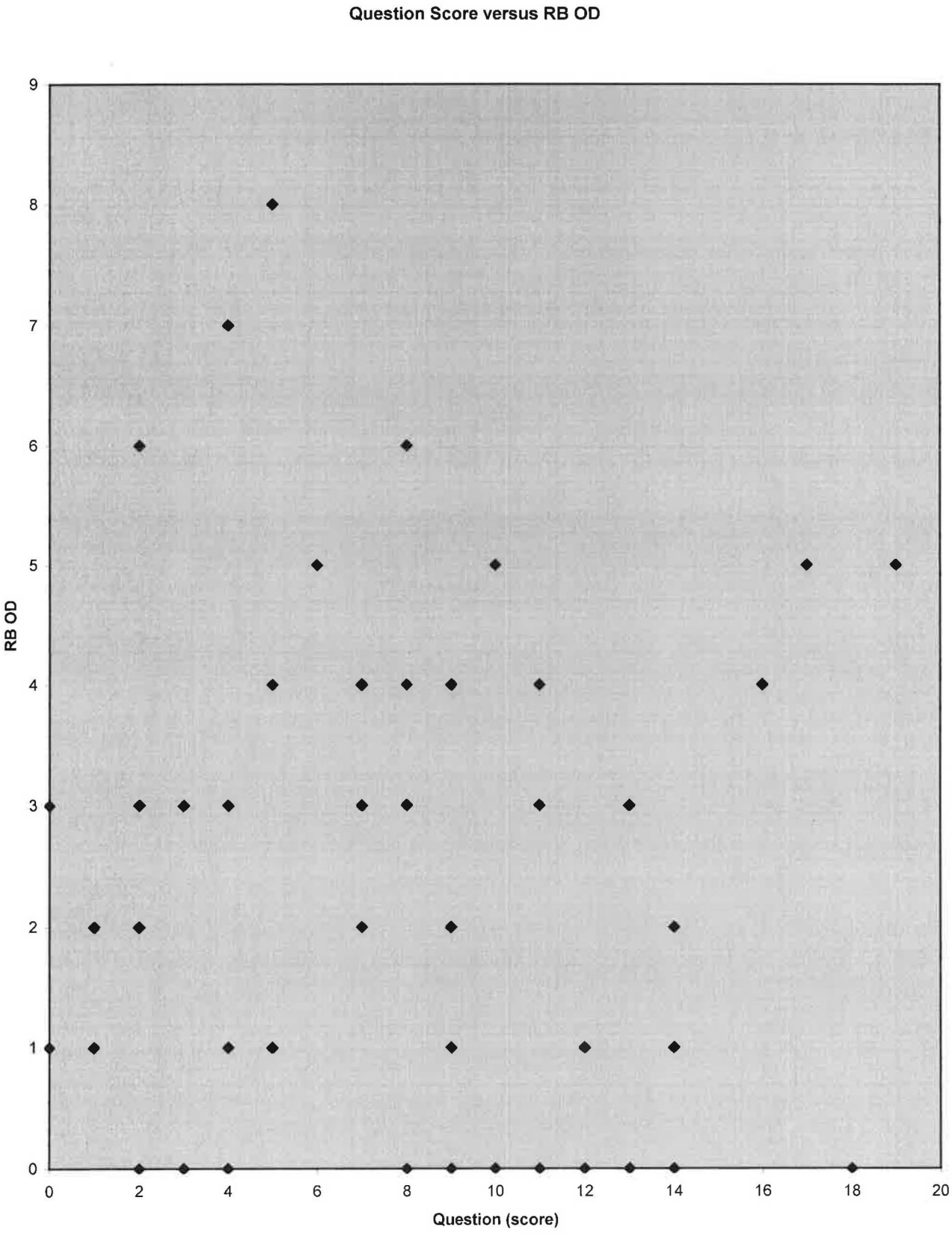


Figure 7: Scatter plot of Question Score vs RB OS

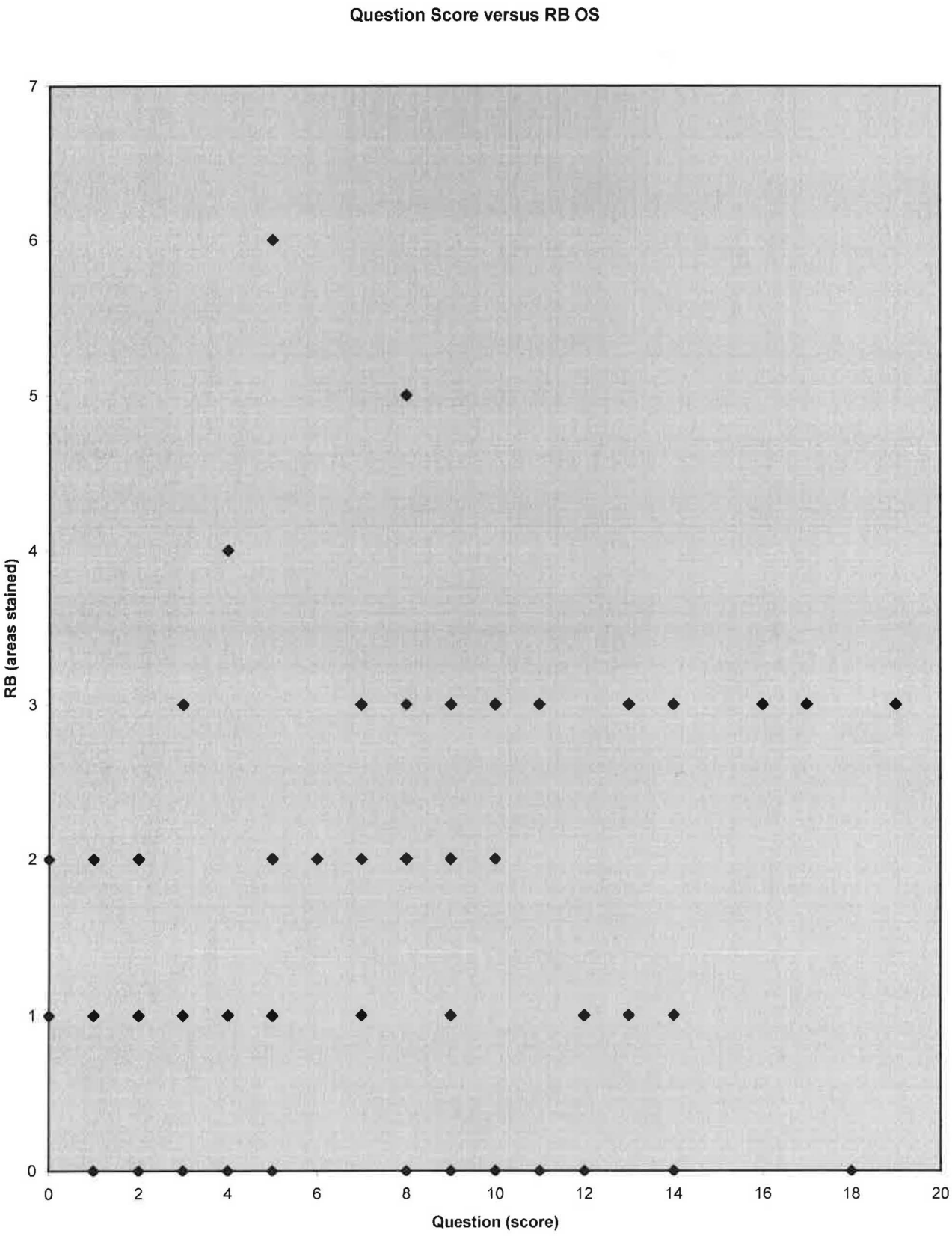


Figure 8: Scatter Plot of OD Rose bengal staining vs Mean LET OD

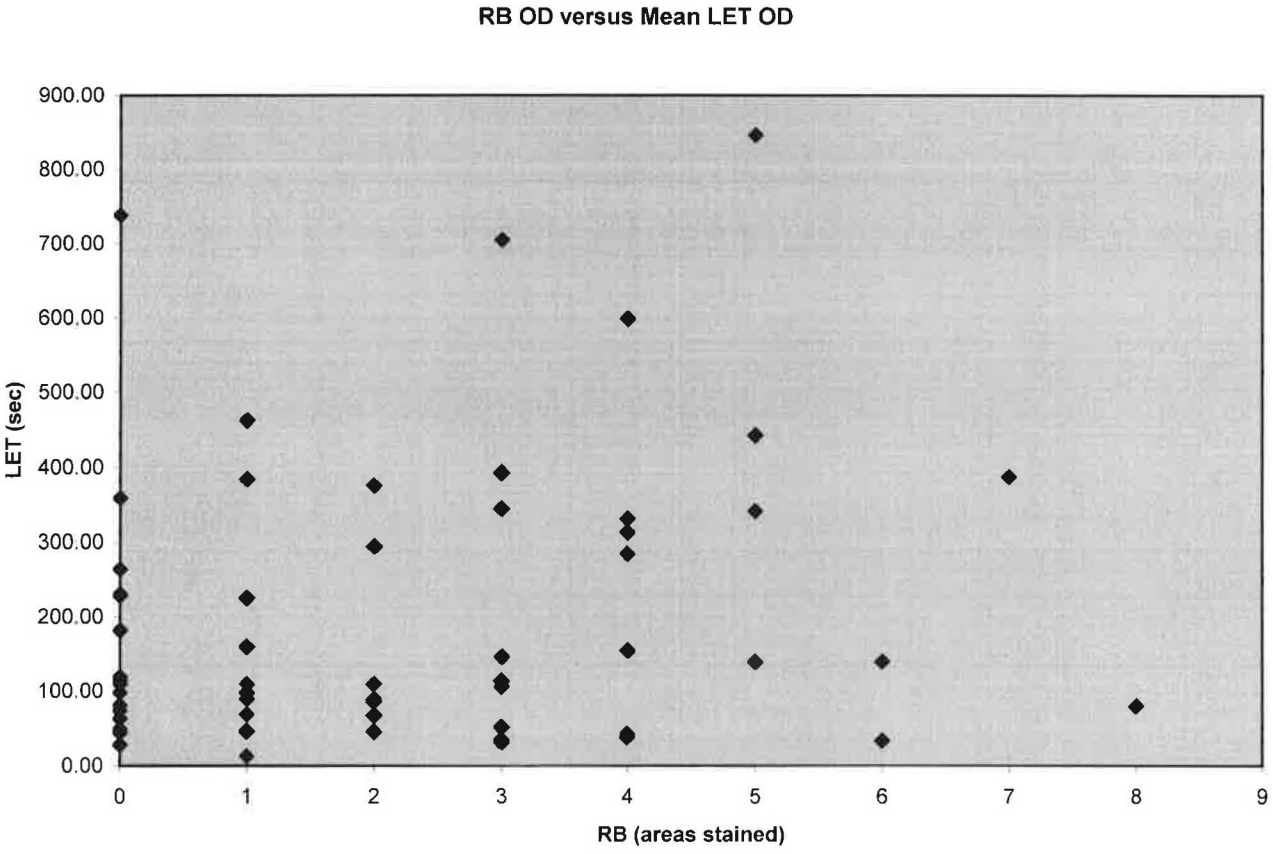
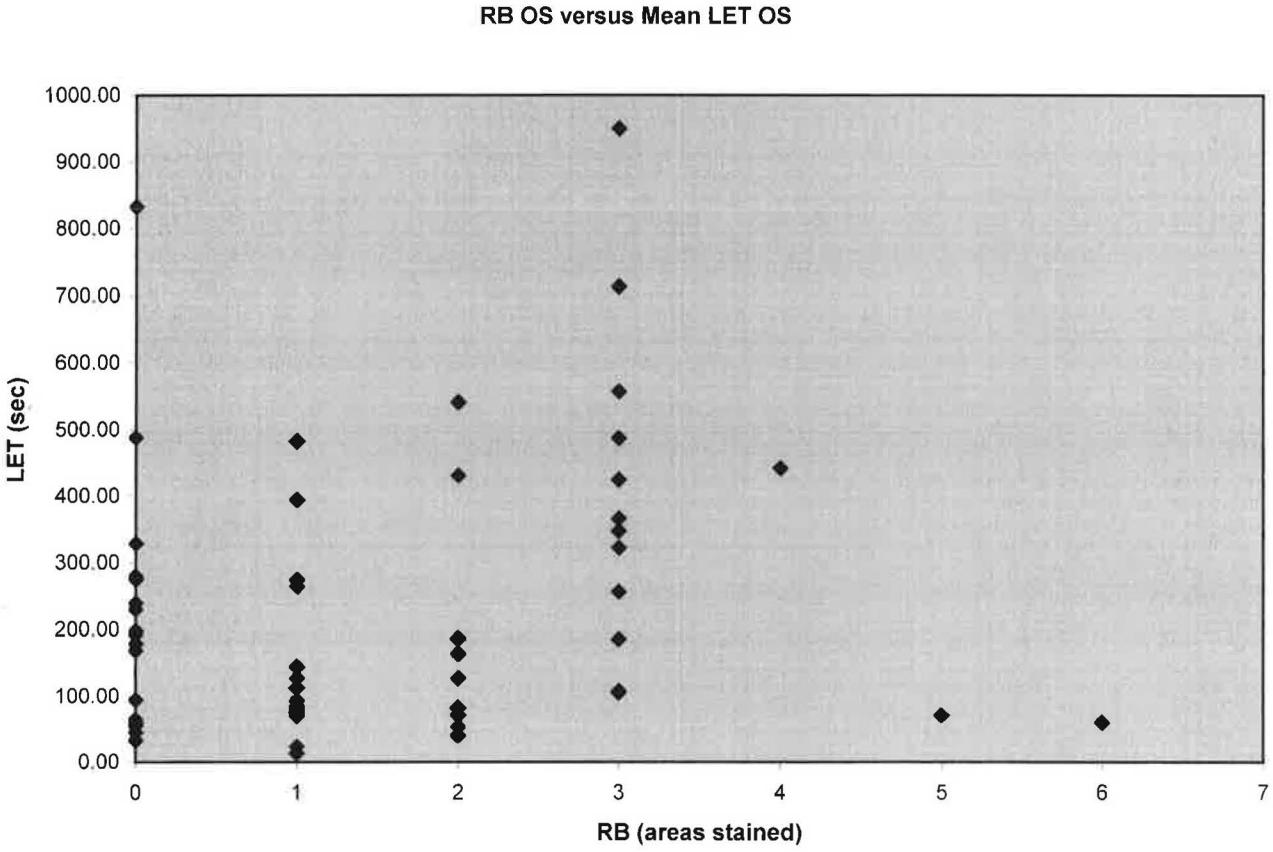


Figure 9: Scatter Plot of OS Rose Bengal Staining vs Mean LET OS



APPENDIX A: Dry Eye Questionnaire[42]

Please circle your responses to the following questions:

Currently wearing contact lenses? Hard Soft None

1. Have you ever had drops prescribed or other treatment for dry eyes?
   Yes(2), No(0), Uncertain(1)

2. Do you ever experience any of the following eye symptoms? (circle)
   Soreness(1), Scratchiness(1), Dryness(1), Grittiness(1), Burning(1)

2. How often do your eyes have these symptoms?
   Never(0), Sometimes(1), Often(2), Constantly(3)

4. Are your eyes *unusually* sensitive to cigarette smoke, smog, air conditioning, or central heating?
   Yes(2), No(0), Sometimes(1)

5. Do your eyes easily become very red and irritated when swimming in chlorinated fresh water?
   Yes(2), No(0), Sometimes(1), Not Applicable

6. Are your eyes dry and irritated the day after drinking alcohol?
   Yes(2), No(0), Sometimes(1), Not Applicable

7. Do you currently take or use any of the following medications? (please circle)
   Antihistamine tablets(1), Antihistamine eyedrops(1), Diuretics(fluid tablets)(1),Sleeping tablets(1), Tranquilizers(1), Oral Contraceptives(1), Medication for duodenal ulcer(1), Medication for digestive problems(1), Medication for high bloodpressure(1), Other_____

8. Do you suffer from arthritis? Yes(2), No(0), Uncertain(1)

9. Do you experience dryness of the nose, mouth, throat, chest, or vagina?
   Never(0), Sometimes(1), Often(2), Constantly(3)

10. Do you suffer from thyroid abnormality? Yes(2), No(0), Uncertain(1)

11. Are you known to sleep with your eyes partly open? Yes(2), No(0), Uncertain(1)

12. Do you have eye irritation as you wake from sleep? Yes(2), No(0),Uncertain(1)

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