Standardization of the Electroretinogram in the Michigan College of Optometry Electrodiagnostics Clinic

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Outline

The purpose of this project was to obtain electroretinographic data using the standard set of clinical protocol developed by the International Standard for Clinical Electroretinography. Using this accepted protocol, a range of "normal" values were obtained for each of the components of the electroretinogram tests so that the Michigan College of Optometry (MCO) will conform with these published standards and will be able to more accurately compare its results with that of other institutions.

To collect the data, 12 fourth year optometry students between the ages of 23 and 32 were used as patients. Each patient had their pupils maximally dilated and underwent 20 minutes of dark adaptation in accordance with the standards for recording scotopic ERG waveforms. Next, mesopic recordings were measured, as well as oscillatory potential waveforms, and finally, following a 10 minute period of light adaptation per eye, photopic recordings were obtained. In following these steps, as well as the numerous other requirements outlined in the published standards, a complete, accurate set of normal values were developed that may be used in the Optometry Clinic on real patients in the future.

The procedures and protocol used in the MCO Electrodiagnostics Clinic in the past, although acceptable because they provided consistent results based upon its own established normal values, did not meet the requirements outlined in the published Standard in many areas. Each of these areas was addressed in this report, the most significant of which include the following:

- In the past, patients were not dilated prior to being tested. For this study, each of the test subjects were maximally dilated with 1% Tropicamide and 2.5% Phenylephrine.
- Patients used to be dark adapted only 10 minutes before recording scotopic ERG's; the Standard calls for a 20 minute dark adaptation period to ensure maximum rod response.
- The Standard also calls for a 10 minute light adaptation period (per eye) before measuring photopic ERG's. This was never done at MCO in the past.
- Separate cone responses to both a single flash stimulus and to a flickering light stimulus were measured for this study in accordance with the Standard. Previously, only a flickering stimulus was used to assess cone function.
- Oscillatory potentials were never recorded in the past. Although their clinical significance is still not completely understood, it is thought that they can play a role in predicting the liklihood of a patient with nonproliferative diabetic retinopathy progressing to the proliferative stage. This, along with other aspects of oscillatory potentials, is currently being researched, but since they were included in the published Standard, they were also included in this study.

In addition to these changes, calibration of the light sources using a digital photometer and an oscilloscope was also performed to ensure compliance with the Standard. These calibrations involved measurements of flash intensity, bowl illumination, duration between flashes, and flicker frequencies. Of these, only the flicker frequency had to be modified to meet

the Standard, which calls for a frequency of 30 flashes per second (30 Hz). In the past, the computer that is used to produce the flickering stimuli was programmed incorrectly and it was determined that the rate of flickering was actually in the range of 15-16 Hz. This error was corrected by creating a new test stimulus program on the computer which actually is 30 Hz, and therefore is capable of more accurately measuring the cone responses. Aside from this modification, the current test setup already met the necessary requirements, which called for a standard test flash of 1.5 to 3.0 $cd \cdot m^{-1} \cdot sec$ for measuring the maximum ERG, the cone ERG, and the oscillatory potentials. The rod ERG should be a 2.5 log unit decrease in intensity from the standard flash. The duration between flashes varies from test to test, but each were determined to meet the Standard, as was the background/bowl illumination, which had to be in the range of 17 - 34 $cd \cdot m^{-1}$ to meet the Standard.

In order for ERG recordings to be consistently and reliably measured from clinician to clinician, the same step by step procedures should be followed from start to finish. The following is a complete listing of the procedures that should be used in the MCO Electrodiagnostics Clinic to comply with the official Standard for Clinical Electroretinography:

1. Initial Preparation

   - The patient enters and has the procedure explained to them so that they will know what to expect. This greatly reduces patient apprehension while they are waiting in the dark room.
   - The patient removes contact lenses if they are wearing them.
   - The patient sits on the stool facing the Ganzfeld bowl and the proper height adjustment is made.
   - A drop of 0.5% Proparacaine is instilled in each eye, followed by a drop of 1% Tropicamide and 2.5% Phenylephrine (this assumes there are no contraindications to dilating the patient and that pupils, angles, and IOP's have already been assessed).
   - The patient enters the dark room and remains there for 20 minutes.

2. Equipment Preparation (while the patient is dark adapting)

   - The contact lens electrode, the ground electrode, and the chin rest are all sterilized with an alcohol swab.
   - The computer, if not already running, should be turned on and prepared to run an ERG. This includes entering the patient data information (name, age, reason for test, and type of test [OD1, OD2, etc.]) on the introductory screen. It is also important to sure that the correct experiment is displayed on the right hand side of this screen. It should include the 5 different stimulus components from Rod.ERG to Cone.FLK. If it is not correct, this experiment first needs to be retrieved by using the "Get" and "Experiment" commands. The correct experiment that should be selected is "JAG".
   - The lower Grass Preamplifier, the Grass Photostimulator and the red lamp should all be turned on.

- The room lights should be turned off and the door closed to allow the clinician to dark adapt. The computer screen should also be dimmed as much as possible.

3. Patient Preparation

- When the 20 minutes of dark adaptation is complete, the patient is brought out of the dark room and instructed to sit down on the stool.
- 2 drops of 0.5% Proparacaine are instilled in each eye.
- The ground electrode with conductive paste applied to it is taped to the patient's forehead and the wire lead is taped to the patient's shoulder to keep it out of the way.
- 1 drop of 0.5% Cellufresh is placed on the contact lens electrode.
- The contact lens electrode is placed into the patient's right eye. To do this, have the patient tip their head back and look down. With your thumb, retract the patient's upper lid and insert the upper edge of the electrode under the lid and pin the lid as far up as possible. Next, instruct the patient to look up. With your thumb again, pull down the lower lid and insert the lower edge of the electrode. Release the lid and have the patient look straight ahead. The electrode wire should be taped to the patient's cheek to remove the tension (leave a little slack in the wire).
- The patient's left eye is patched with care taken not to dislodge the ground electrode on the forehead.
- The patient is helped into the chin rest and instructed to look straight ahead.

4. Measuring the Rod ERG

Recording a rod only response is accomplished by using a dim light flashed at a low frequency. The standard calls for a 2.5 log unit decrease in intensity from the standard flash with a minimum interval between flashes of 2 seconds. To do this, the Grass Photostimulator intensity should be turned to 1. The computer will create 5 flashes, 2 seconds apart, each of which will generate a waveform. The 5 waveforms get averaged together.

5. Measuring the Maximum ERG (rods and cones)

Obtaining the maximum ERG is done using a bright flash (the standard flash) at a low frequency. The Grass Photostimulator intensity should be turned to 16. The computer will create 5 flashes, 5 seconds apart. These will also generate an average waveform.

6. Measuring the Oscillatory Potentials

The oscillatory potentials (OP's) are small wavelets that ride on the B-wave of the scotopic, mesopic and photopic ERG's. They are still not clearly understood, but are thought to come from depolarizing amacrine cells and depolarizing interplexiform cells. The trick to the measurement of the OP's is thru the use of selective filters. This will be discussed later under Analyzing the Data. To record the OP's, the computer will create 3 standard flashes (Grass

Photostimulator intensity set at 16) with an interval of 15 seconds between flashes. Only the last 2 of the 3 flashes will be used to generate the average waveform. The first is simply a conditioning test flash. This is done to comply with the Standard.

7. Light Adaptation

Next, a 10 minute period of light adaptation is necessary before proceeding to test the cone ERG's. To do this, turn the Grass Photostimulator intensity back to 1, the frequency to its maximum value (300 Hz) and the test flash switch to "Repeat".

8. Measuring the Cone-Single Flash ERG

After the 10 minutes of light adaptation, shut off the test flash switch and return the intensity to 16. The computer will create 5 standard flashes with a 5 second interval in between. These responses will be averaged.

9. Measuring the Cone-Flickering ERG

This test also uses the standard flash (intensity at 16) but with a flickering stimulus. In accordance with the Standard, the flickering is at a rate of 30 flashes per second. The response to the first 5 flashes are not recorded to allow for more stable conditions.

10. Testing the Other Eye

- First remove the patch from the left eye.
- The electrode should then be removed from the right eye. Have the patient look up. With your thumb, pull down on the patient's lower lid and then pull out the lower edge of the electrode. Next, instruct the patient to look down. The electrode will come away easily.
- Instill 2 drops of 0.5% Proparacaine in each eye again.
- A drop of 0.5% Cellufresh is placed in the electrode lens.
- The electrode is inserted into the left eye and the wire lead is taped to the cheek.
- The patch is placed over the right eye and the patient is once again put into the chin rest.
- Repeat the testing as above starting with the Rod ERG. Be sure to switch the Photostimulator intensity back to 1.

11. Analyzing the Data

Correctly analyzing the data is a critical step in the testing process. In most cases, it is just a matter of positioning the cursors in the correct locations to match the waveforms' peaks and troughs. Some cases, however, require a little more clinical judgement and experience.

Filtering procedures may even have to be used to remove bad data or uncorrelating records. Explaining this more advanced analysis using filters is beyond the scope of this report, however, and therefore the focus will remain on summarizing the basic ways in which to analyze the data from the 5 different ERG waveforms.
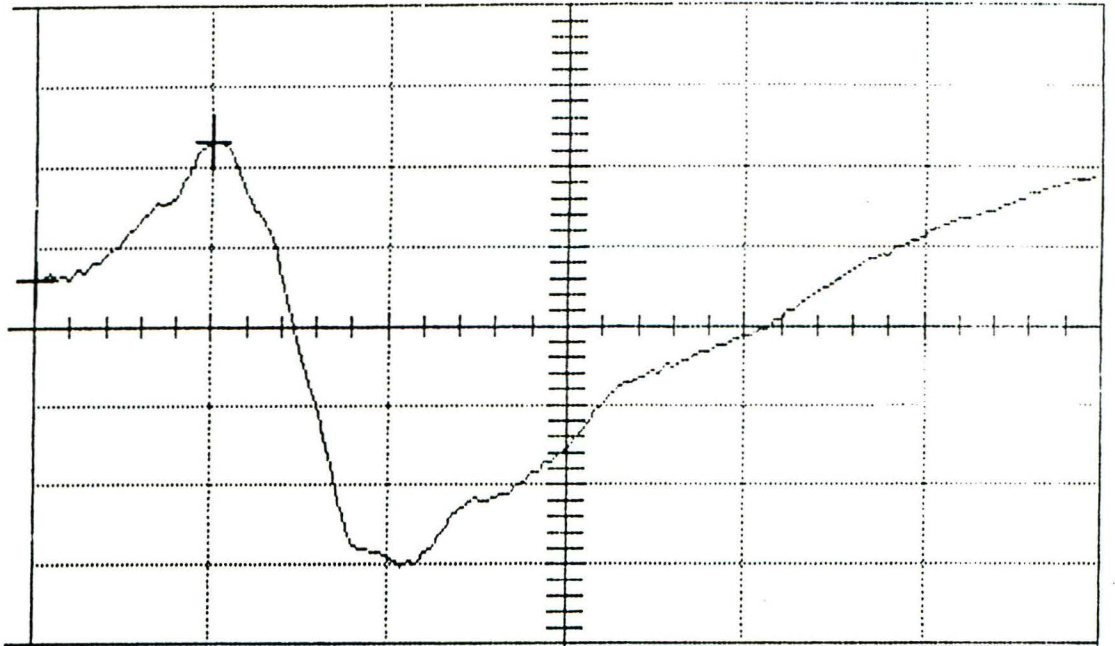
For the Rod ERG, the Maximum ERG, and the Cone-Single Flash ERG, the analysis is virtually the same. Once you have reached the main analysis screen on the computer where you can move the cursors, place the left cursor at the trough of the beginning wave. This point will usually be the farthest left point on the graph. The other cursor is placed at the peak of the B-wave. From here, the amplitude (in red) and implicit time (in purple) can be read from the data box.

For the Cone-Flicker ERG, the principal is the same, however, the shape of the waveform is slightly different. This ERG is a more rounded, sloping waveform with either a plateau or a small dip (trough) in the wave before the rising B-wave. The left cursor is placed at the lowest point of this dip, or in the middle of the plateau, if that is the case. The right cursor, as would be expected, is positioned at the peak of the B-wave. At this point, the amplitude and implicit time are read from the data box.
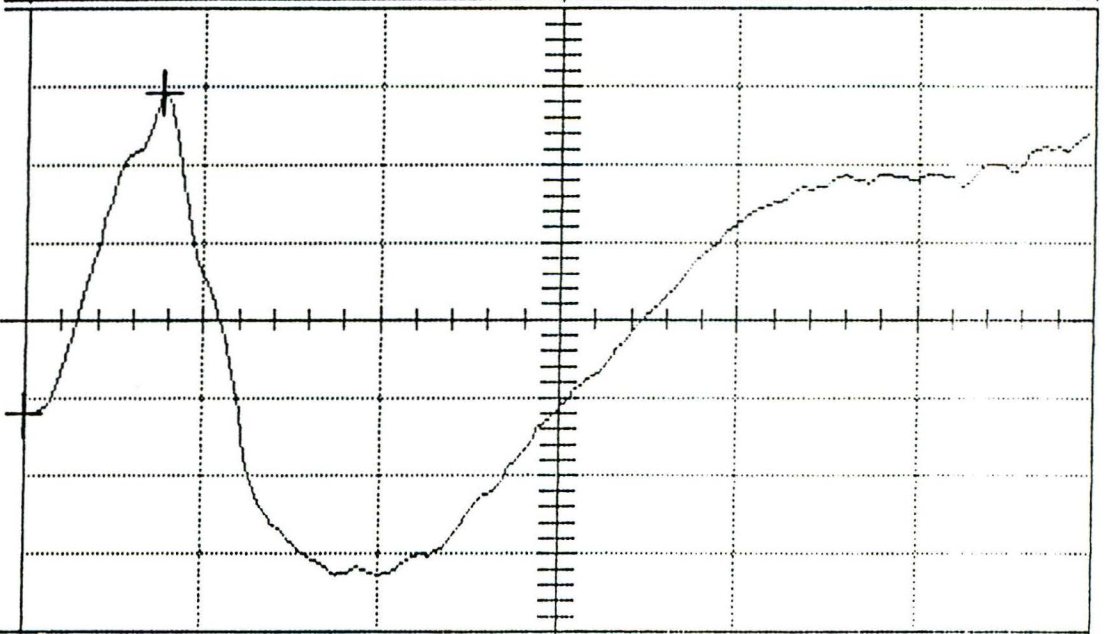
The oscillatory potentials are relatively unique to analyze, because before they can be assessed, bandpass filters must be used to narrow down the frequencies that are displayed in the waveform. In doing this, it eliminates the large B-wave characteristics of the wave and draws out and magnifies the small wavelets (OP's) that ride on the B-wave. In order to do this, the "View" function should be highlighted from the main analysis screen. This will bring you to the filter selection screen. From here a lowpass frequency filter should be run that is set at 300 Hz (or as close to this as possible). This cuts off any frequencies above 300 Hz. Then, a highpass frequency filter should be used that is set at 70 Hz (or as close as possible). This cuts off any frequencies below 70 Hz. The combination of these two filters allows a specific range of selected frequencies (70-300 Hz). It is by using this specific range that the oscillatory potentials are brought into view. So once this is done, hit "escape" to return back to the main analysis screen. There should now be a much different looking waveform present. To measure the amplitude, again place the right cursor at the top of the tallest peak. The left cursor is put at the trough just to the left of the peak. Again, the amplitude and implicit time are read from the data box.

The following are example printouts of each of the components of the electroretinogram. They were each obtained on subjects in this study and can be used to not only see the appearance of the typical waveforms, but also to indicate the proper placement of the cursors in each of the situations. After the printouts, the actual data from this study of each of the 12 tested subjects is presented, including the normal range values for the 5 different ERG tests.
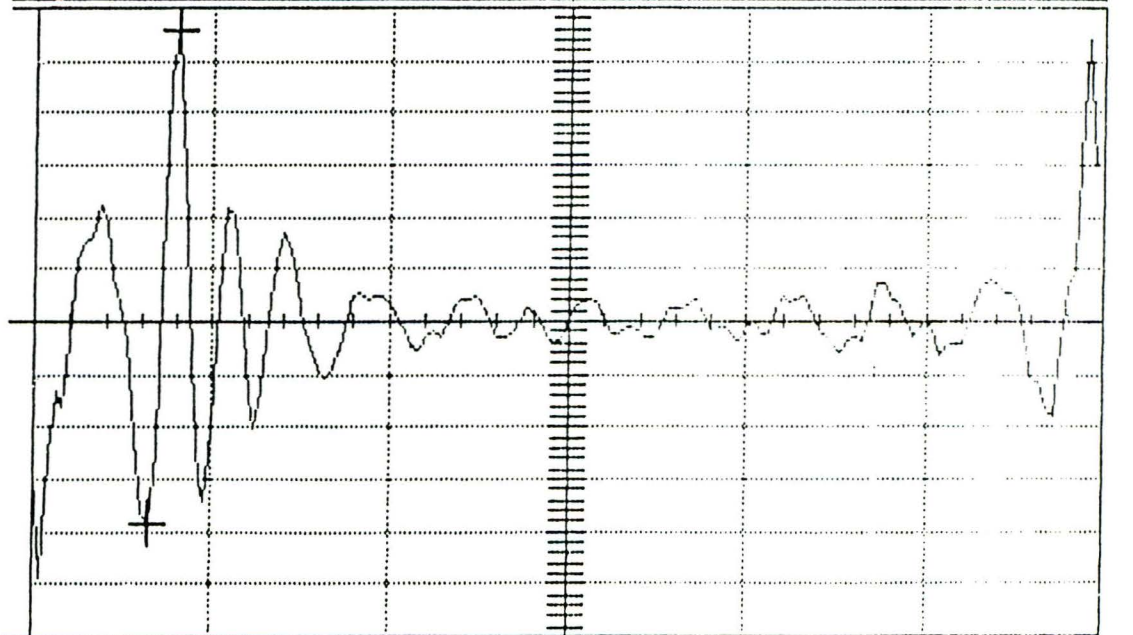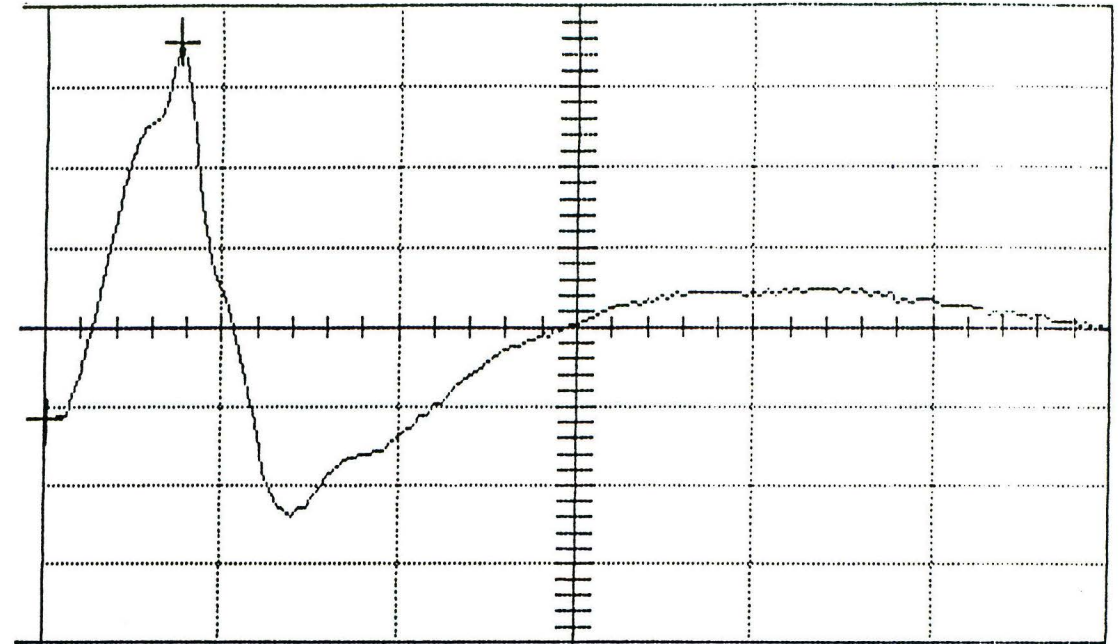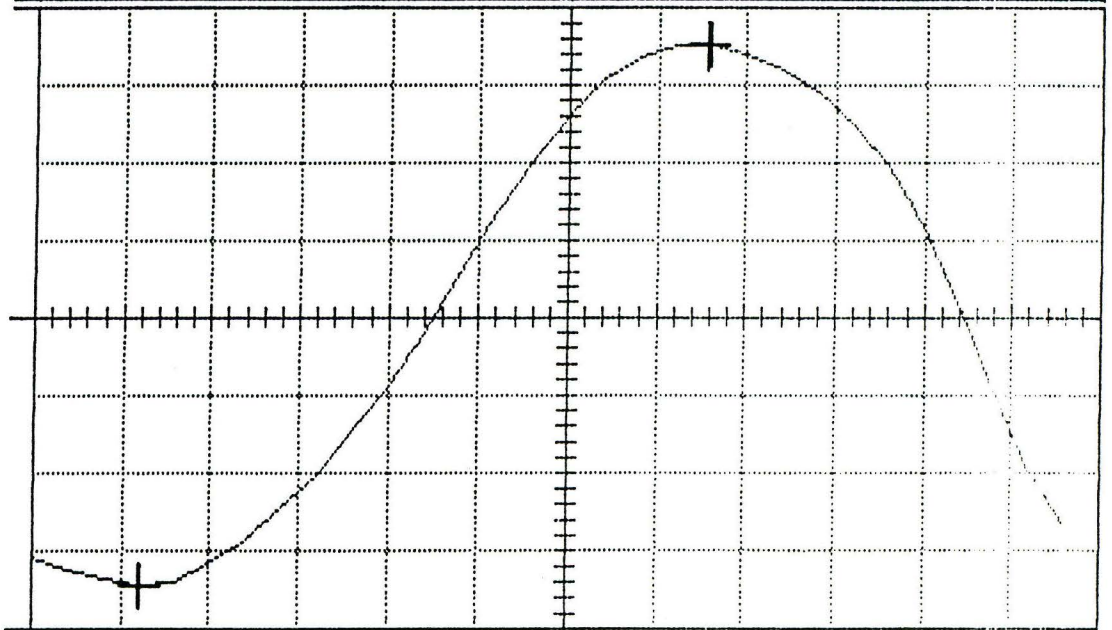
ROD.ERG

MAX.ERG

OSC.POT

6.

CONE.SFL

CONE.FLK

	A	B	C	D	E	F	G
1		Rod ERG		Max ERG		Osc Pot	
2	Subject	Amplitude	Implicit Time	Amplitude	Implicit Time	Amplitude	Implicit Time
3	1--OD	41.976	25	132.882	19	19.279	20
4	OS	36.098	26	125.977	20	20.636	20
5	2--OD	20.508	24	148.926	20	39.334	20
6	OS	xxxxxx	xxx	xxxxxx	xxx	23.601	20
7	3--OD	42.481	24	155.204	20	44.759	20
8	OS	63.965	23	177.017	20	55.026	20
9	4--OD	63.651	25	161.675	19	42.589	20
10	OS	47.701	24	145.954	19	36.369	19
11	5--OD	59.814	24	174.696	19	21.459	20
12	OS	xxxxxx	xxx	xxxxxx	xxx	xxxxxx	xxx
13	6--OD	74.192	24	206.543	19	58.899	20
14	OS	77.237	24	210.961	19	55.135	20
15	7--OD	65.918	25	130.005	19	39.063	26
16	OS	79.753	23	143.155	19	24.127	19
17	8--OD	75.684	22	100.403	18	29.419	25
18	OS	55.106	23	134.82	18	24.858	19
19	9--OD	55.339	24	148.315	19	58.594	19
20	OS	71.777	24	125.488	19	53.711	20
21	10--OD	87.402	25	247.007	19	48.191	20
22	OS	93.217	24	248.068	19	47.485	19
23	11--OD	66.223	23	212.891	19	41.504	19
24	OS	66.528	23	205.078	19	31.836	20
25	12--OD	58.105	23	154.351	18	33.081	19
26	OS	48.828	24	155.317	19	37.435	19
27							
28							
29							
30							
31							
32							
33	Mean	61.432	23.909	165.129	19.042	38.539	20.13
34	Std Dev	16.944	0.8998	39.146	0.562	12.506	1.607
35							
36	Norm Range						
37	Low	27.544	22.109	86.837	17.917	13.527	16.915
38	High	95.32	25.709	243.421	20.167	63.551	23.345
39							
40							
41	Amplitudes measured in microvolts; Implicit Times measured in milliseconds.						
42	X's indicate poor recordings or improperly saved data that could not be used in the study.						
43							

	H	I	J	K	L	M	N
1		Cone-Single Flash ERG		Cone-Flicker ERG			
2	Subject	Amplitude	Implicit Time	Amplitude	Implicit Time		
3	1--OD	129.395	19	34.587	17		
4	OS	117.187	19	36.236	17		
5	2--OD	159.912	20	31.738	16		
6	OS	150.391	19	31.738	19		
7	3--OD	158.128	19	48.828	19		
8	OS	151.367	19	48.828	16		
9	4--OD	151.978	18	48.828	16		
10	OS	168.457	18	54.525	16		
11	5--OD	176.086	18	xxxxxx	xxx		
12	OS	xxxxxxx	xxx	xxxxxx	xxx		
13	6--OD	168.457	19	69.716	18		
14	OS	181.641	19	86.67	19		
15	7--OD	118.164	18	37.842	17		
16	OS	106.201	18	48.421	19		
17	8--OD	131.836	18	68.766	18		
18	OS	127.441	18	67.817	18		
19	9--OD	163.574	19	79.346	19		
20	OS	142.648	20	81.264	20		
21	10--OD	223.123	19	72.168	16		
22	OS	235.374	19	75.412	16		
23	11--OD	194.336	18	76.294	16		
24	OS	198.975	18	70.452	16		
25	12--OD	141.113	18	51.27	14		
26	OS	140.612	19	58.507	14		
27							
28							
29							
30							
31							
32							
33	Mean	158.104	18.652	58.148	17.091		
34	Std Dev	32.101	0.633	17.017	1.621		
35							
36	Norm Range						
37	Low	93.903	17.386	24.114	13.849		
38	High	222.305	19.918	92.182	20.333		
39							
40							
41	Amplitudes measured in microvolts; Implicit Times measured in milliseconds.						
42	X's indicate poor recordings or improperly saved data that could not be used in the study.						
43							

In conclusion, this study was done to provide the MCO Electrodiagnostics Clinic with a step by step approach to obtaining accurate electroretinographic data in a manner that complies with the International Standard of Clinical Electroretinography. Although the normative values determined in this study can be used to reliably compare with real patients test data results, it should be suggested that another study be done with a larger sample population and wider age range of subjects to possibly narrow the normal ranges down even further. In addition, with more and more research being done into the sources and clinical implications of the different waveforms of the electroretinogram, new and improved standard protocols will no doubt be on the way. The MCO Electrodiagnostics Clinic should change along with these new standards and continue to provide their patients with the best possible eyecare today and on into the future.

Acknowledgement

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Disease Entity	ERG	EOG	VER
Stargardt's macular degeneration	normal	variable	abnormal
Leber's Congenital Amaurosis	abnormal	abnormal	abnormal
Albinism	normal	normal	abnormal
Foveal hypoplasia	normal	normal	abnormal
Rod monochromatism	normal rod abnormal cone	normal	abnormal
Retinitis Pigmentosa	abnormal	abnormal	normal
Retrobulbar Neuritis	normal	normal	abnormal
Amblyopia	normal	normal	abnormal
Psychogenic Problems	normal	normal	normal