New Handheld, Non-Mydriatic ERG Device to Screen for Diabetic Retinopathy and Other Eye Diseases

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Abstract

Purpose: To evaluate the use of the 30 Hz RET*eval*™ handheld ERG device in diabetic and glaucoma patients in an office setting.

Methods: The RET*eval*™ (LKC Technologies, Inc., Gaithersburg, MD) is a small handheld ERG device using adhesive skin electrodes in lieu of contact lens electrodes to assess cone function in patients without mydriasis. The RET*eval*™ is currently in Phase 2 and 3 clinical trials (US FDA, and EC, respectively). RET*eval*™ (REv) was used in patients with diabetes mellitus and glaucoma in a retina practice in San Jose, CA. Inclusion criteria: Diabetic pts HbA1c > 6.0 mg/dL or FBS > 100 mg/dL; Glaucoma patients were verified by visual field findings. Visual acuity was 20/15-20/40. The Stata statistical software program was used. For each patient, ERG data from only one eye was used based on randomization by coin toss. Informed consent was obtained.

Results: A total of 77 patients and controls were enrolled over 9 months: Control (C): n=36: age range 23-75 yrs, avg=56.1, sd=16.1; Diab (DM): n=20: age range 23-77 yrs, avg=59.8,sd=10.9; Glaucoma (G) n=21: age range=37-76 yrs, avg=61.19, sd=11.82. ERG photopic implicit times were prolonged in both diabetic and glaucoma patients: 2 tailed t-test: Control mean 33.1 msec vs DM mean 34.8 msec, implicit time p=0.043; Control mean 33.1 msec vs G mean 35.4 msec, implicit time p=0.001. No significant differences were noted between implicit times in the diabetic and glaucomatous patients or for difference in response in amplitude: C vs DM: p=0.18.

Conclusions: This small study suggests that prolongation of flicker implicit times in diabetes and glaucoma can be discerned with the RET*eval*™ in a clinical setting. The RET*eval*™ may be of value as a screening tool in nursing homes or facilities where ophthalmic exams are not available.

Figure 1: RET*eval*™ device (LKC Technologies, Inc., Gaithersburg, MD)

Purpose

To evaluate diabetic patients, glaucoma patients and control patients for electrophysiologic changes using a new, handheld ERG device, RET*eval*™, measuring 30 Hz flicker amplitude and implicit times.

Background

Diabetic retinopathy is the leading causes of blindness in Americans aged 20-65 years old. Screening for diabetic retinopathy has involved the use of non-mydriatic cameras and are expensive to purchase, use and maintain. Retinal function testing for diabetic retinopathy with ERG techniques is available in the academic setting. ERG machines are costly and require trained medical technicians thus making electrophysiologic testing a rarely used test in clinical practice.

Tahara et al (1993)[1] and Holopigan et al (1997)[2] has shown that 30 Hz flicker ERG in diabetic patients have longer peak latency than controls. Tahara et al in their work used an LED light to perform the 30 Hz flicker[1].

RET*eval*™ uses LED based 30 Hz flicker test in a handheld device, without corneal contact electrodes, or mydriasis. Glaucoma patients have been studied with multifocal ERG using 30 Hz flicker and the results have shown a difference between glaucoma patients from controls. We postulate that this RET*eval*™ device may be useful in screening for glaucoma from controls (Chu, 2009)[4].

Methods

A small handheld ERG device was used, employing proprietary software and hardware (LKC Technologies, Gaithersburg, MD). It creates a 30 Hz LED-based flicker test. The device, RET*eval*™, is currently in Phase 2 and 3 clinical trials (US FDA, and EC, respectively). The RET*eval*™ uses noncontact skin electrodes.

RET*eval*™ was used in patients with diabetes mellitus and glaucoma in a retina practice in San Jose, CA after informed consent was obtained. Visual acuity was assessed with a Snellen Visual Acuity chart. Non mydriasis was obtained. Non-contact electrodes were placed on the lateral side of the zygoma of the test eye, on the infraorbital rim. One eye was tested at a time. The fellow eye was covered.

Inclusion criteria: Diabetic patients had verification of their diagnosis by FBS or HbA1c within 6 months of evaluation: HbA1c > 6.0 mg/dL or FBS > 100 mg/dL. Glaucoma patients were verified by visual field findings. Visual acuity was 20/15-20/40. Exclusion criteria for patients were optic nerve disease, optic neuritis, and s/p neurosurgical procedures.

Data analysis was performed using the STATA statistical software program. For each patient, ERG data from only one eye was used based on randomization by coin toss.

Controls were normal patient volunteers with no ocular pathology affecting the macula, such as retinal holes or macular laser or macular surgery.

Results

	Males	Females	Age Mean (yrs)	Age SD (yrs)	Age Range (yrs)
Total patients: 77	35	42	55.14	14.55	22-80
Controls: 36	18	18	56.1	16.1	22-75
Diabetics: 20	8	12	59.8	10.9	23-74
Glaucoma: 21	9	12	61.19	11.82	37-80

Figure 2

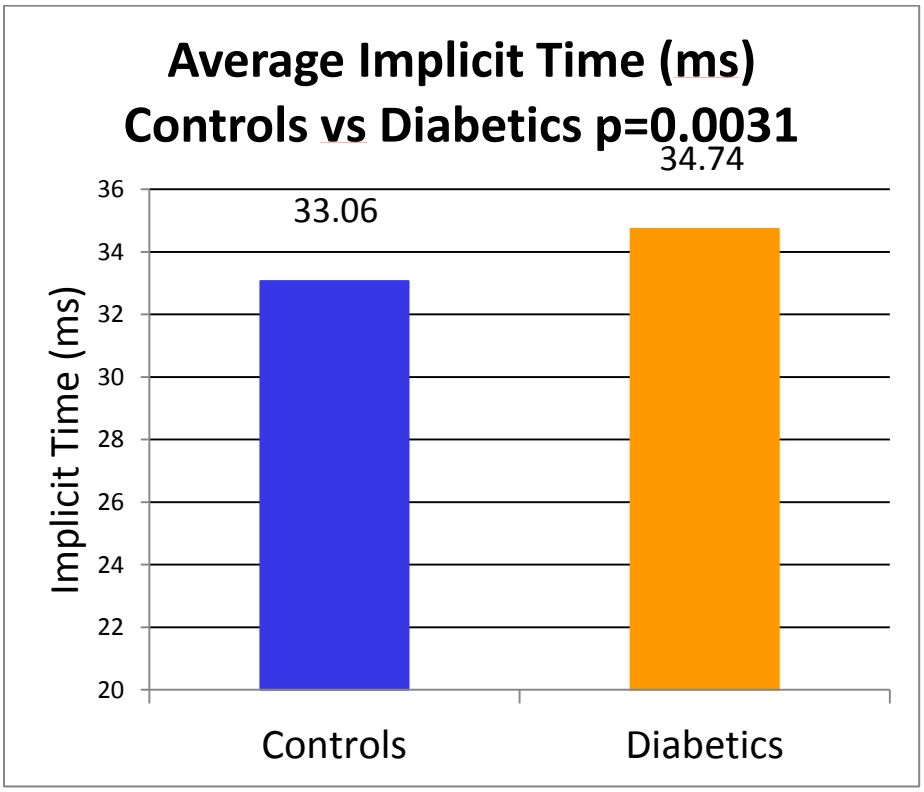


Figure 3: Controls had average of 33.06 ms whereas Glaucoma patients had an average of 34.74 ms.

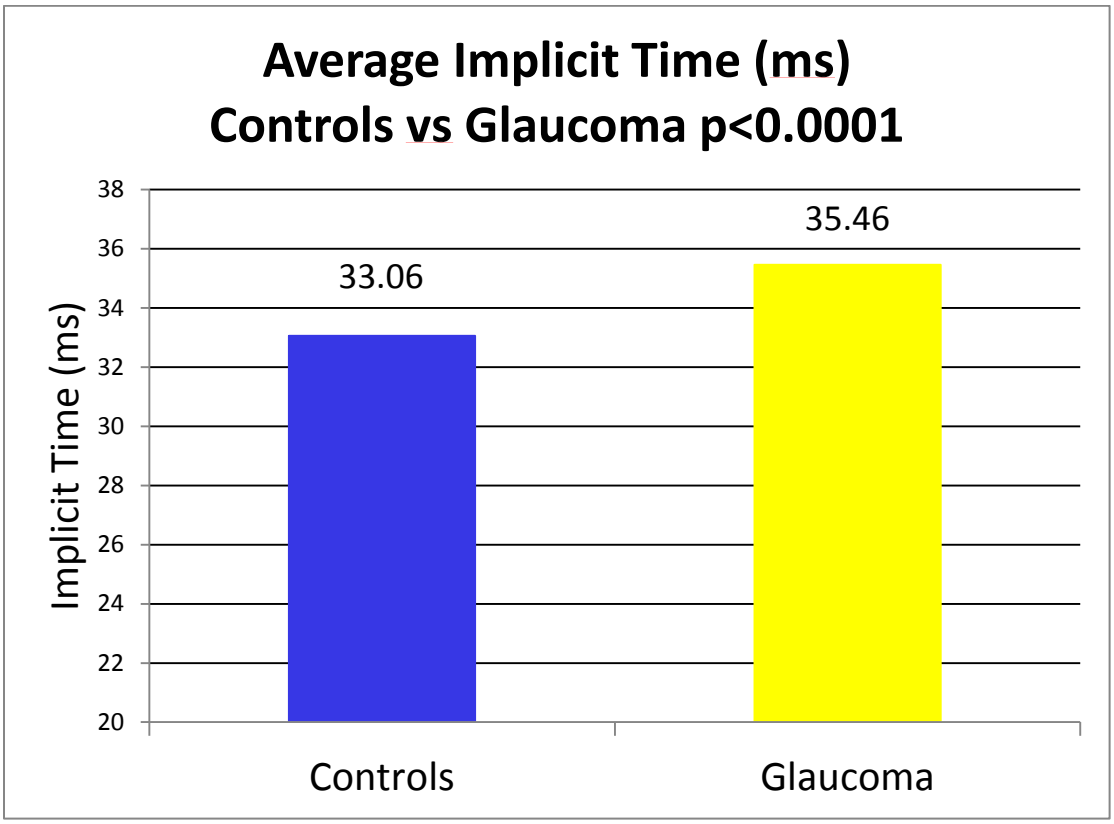


Figure 4: Controls had average of 33.06 ms whereas Glaucoma patients had an average of 35.46 ms.

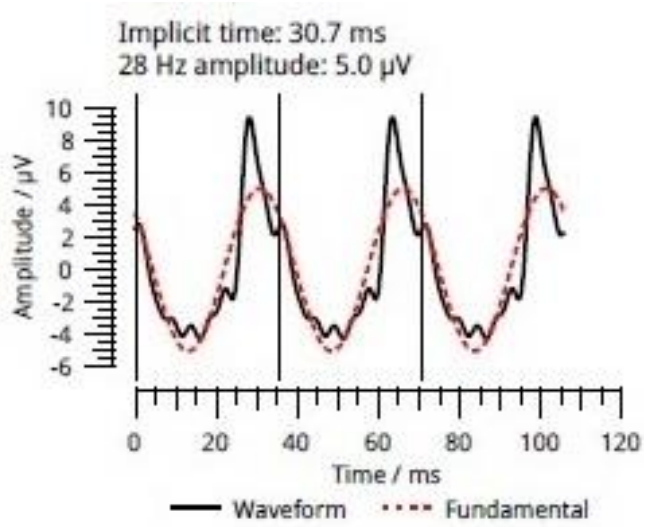


Figure 5: 24 yo WF control OD normal, OS amblyopia. OD was used V_{OD} = 20/20

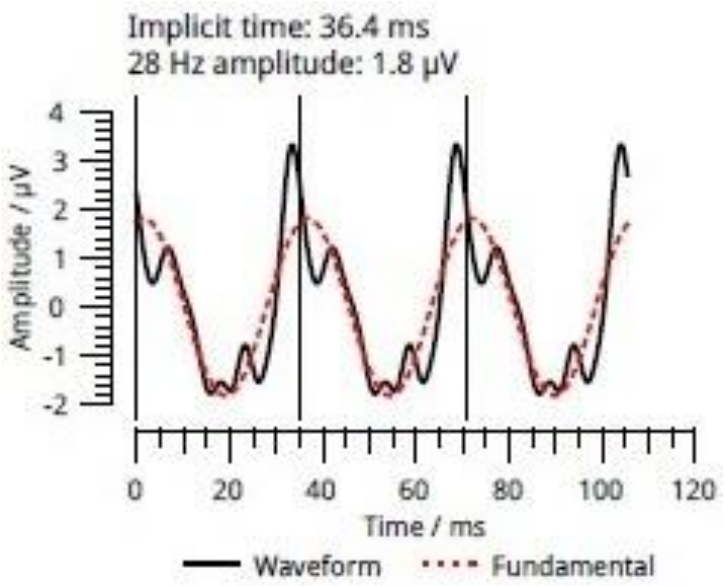


Figure 6: 63 yo diabetic BF OD. V_{OD} = 20/25

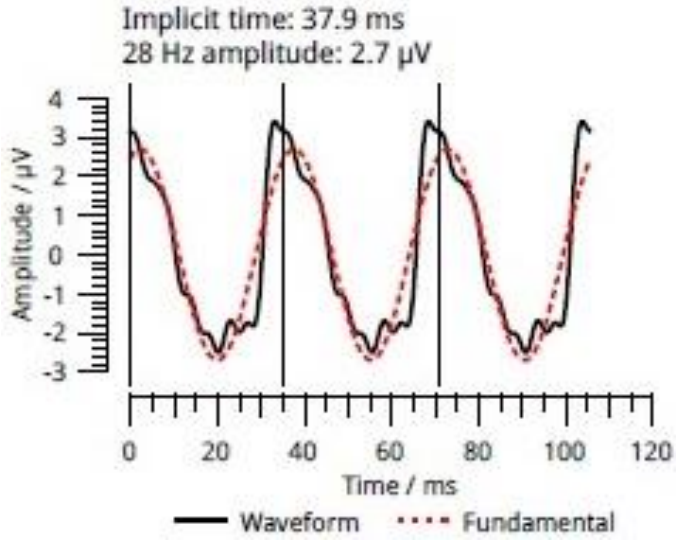


Figure 7: 64 yo AF glaucoma patient OD. V_{OD} = 20/40

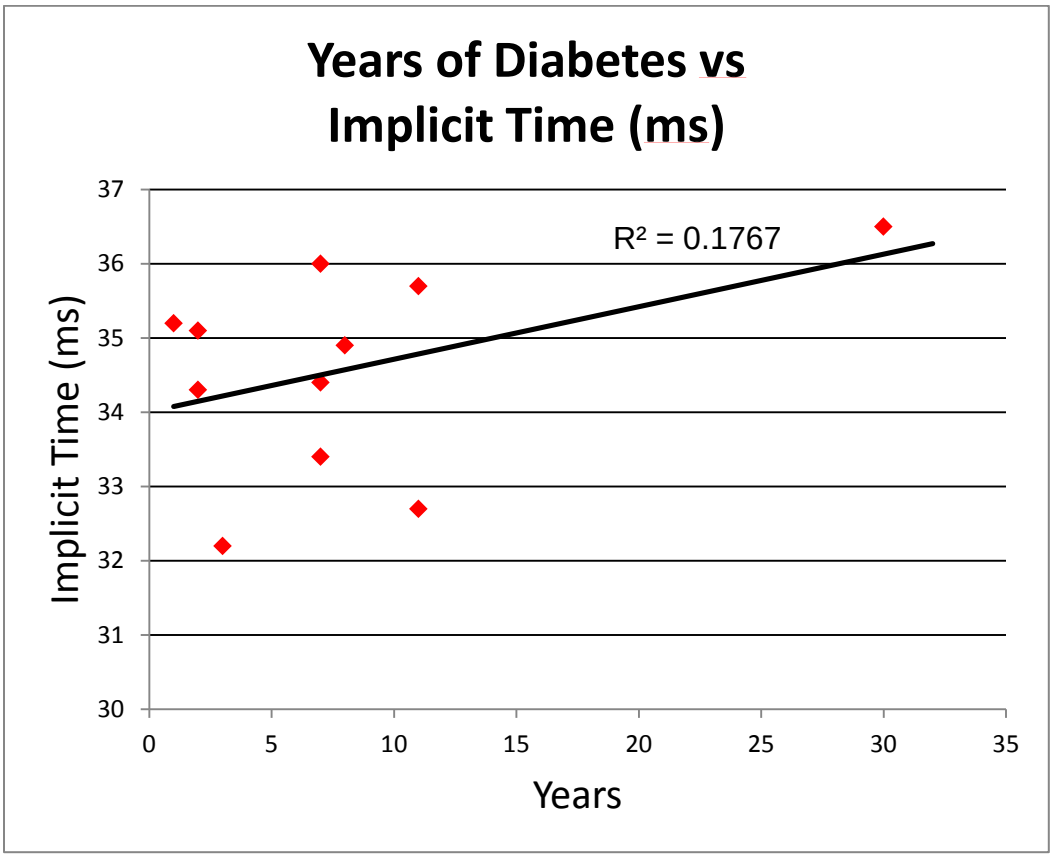


Figure 8: The implicit times are weakly correlated to the duration of diabetes (years)

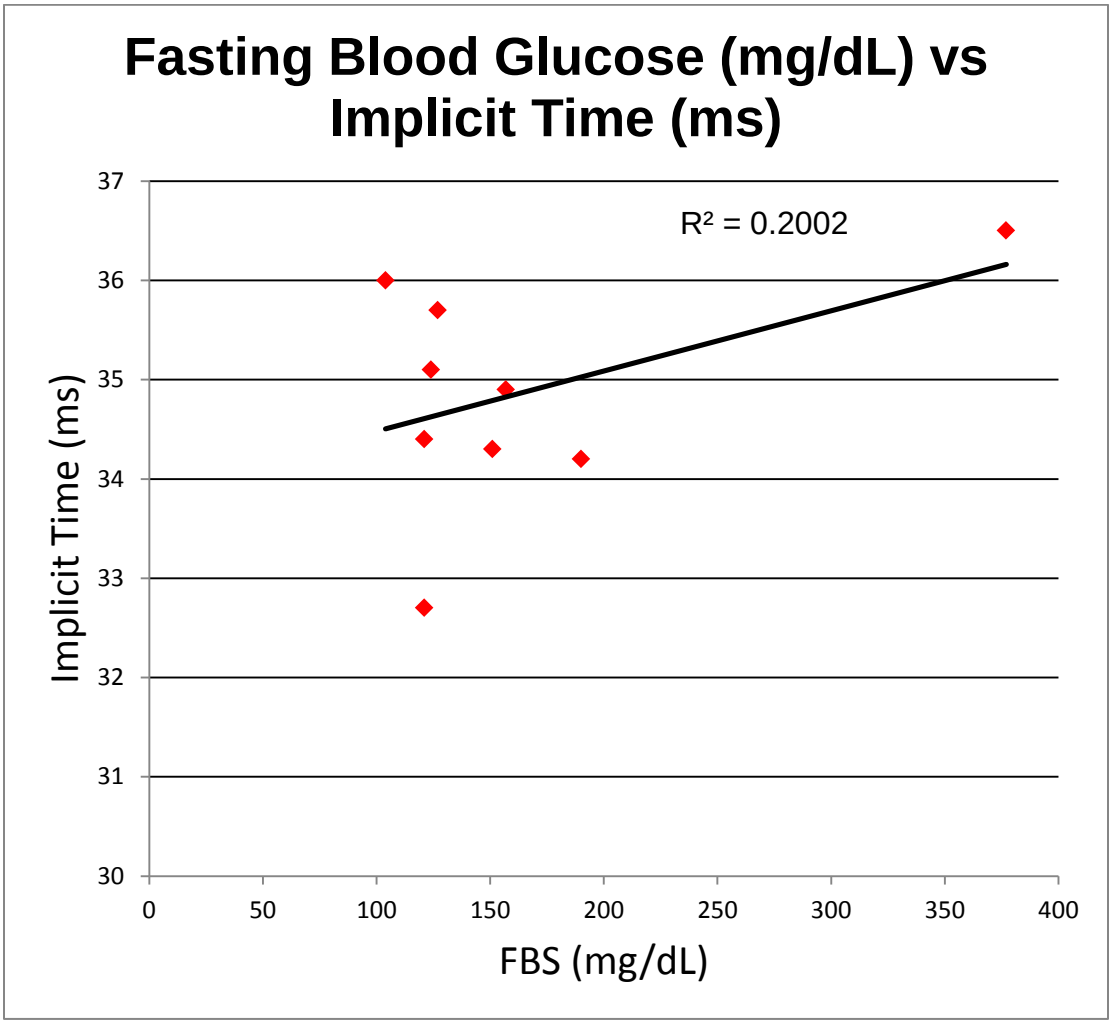


Figure 9: The implicit times are weakly correlated to levels of fasting blood glucose (mg/dL)

Diabetic Patients

	Mean	SD	Range
Hemoglobin A1C (%)	7.3	1.3	6.0 - 11.0
Cholesterol (mg/dL)	167.7	76.5	106 - 377
Triglycerides (mg/dL)	68.1	19.7	62 - 249
Years of Diabetes	8.1	8.1	1 - 30

Figure 10: Diabetic Profile

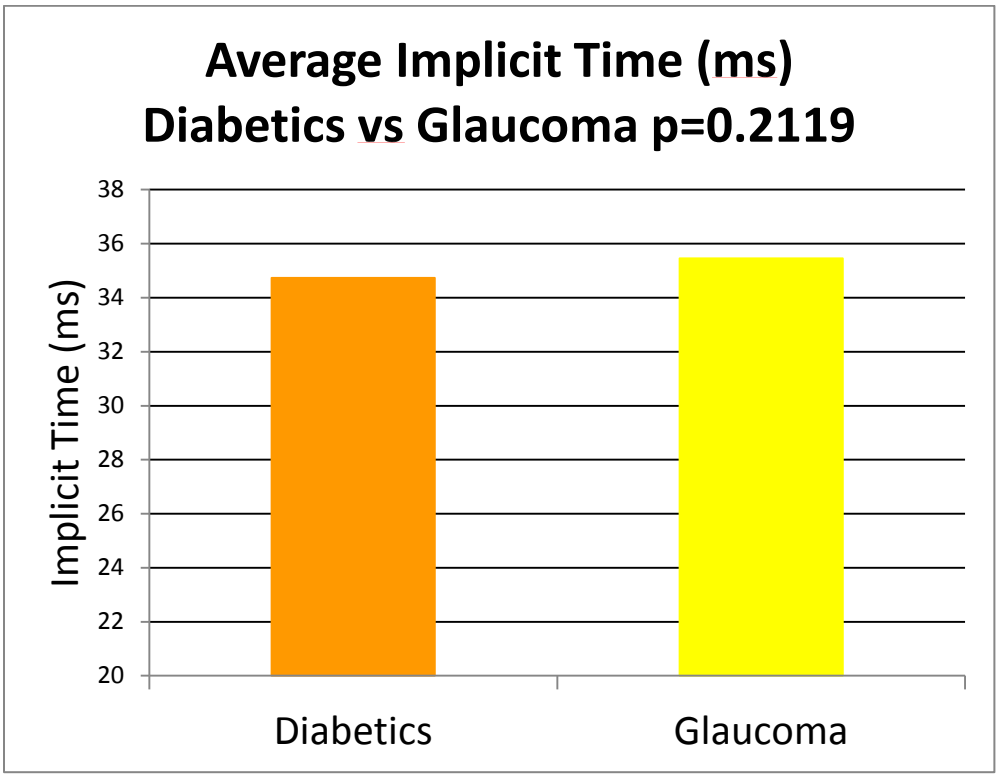


Figure 11: The implicit times for diabetics and glaucoma patients are not significant.

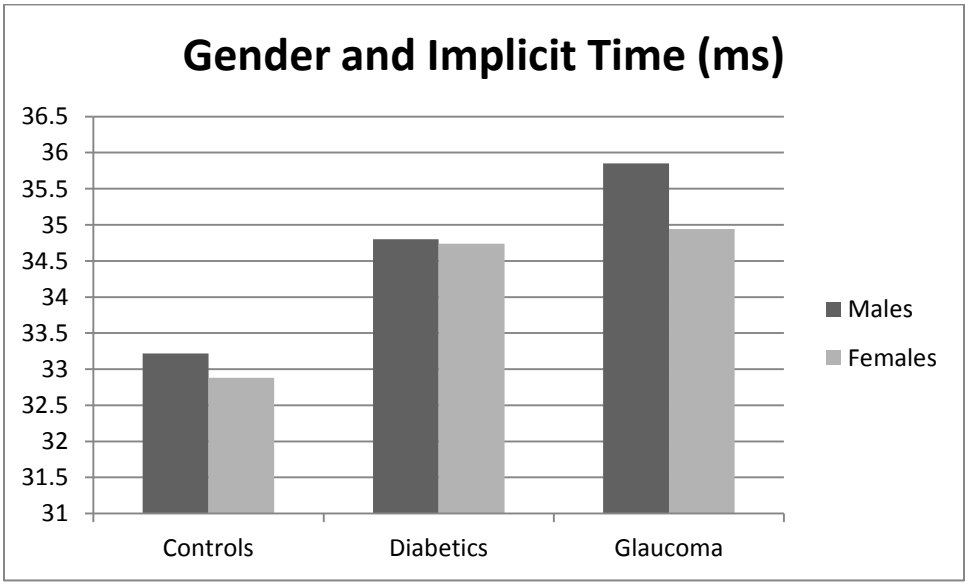


Figure: 12: Gender was not significantly different for diabetics and glaucoma patients because sample size is small. Males n=35 and Females n=42

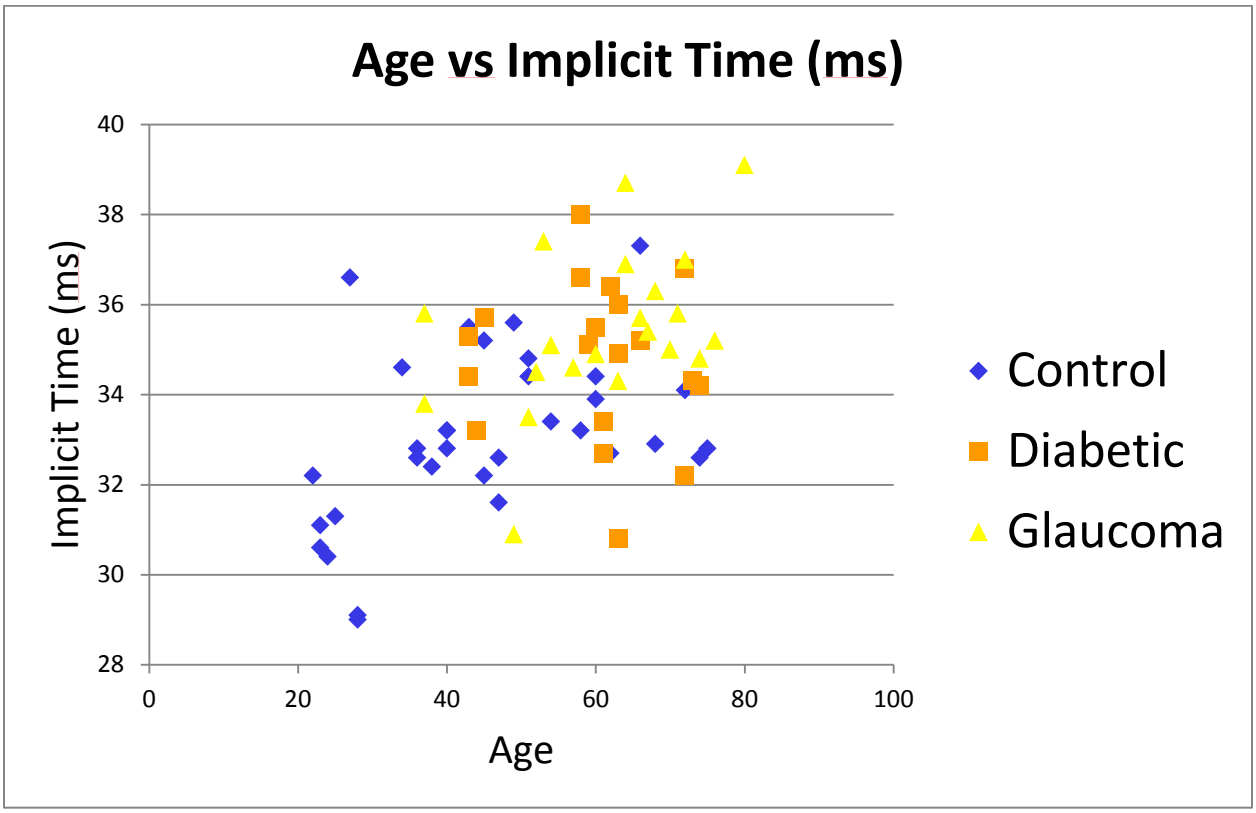
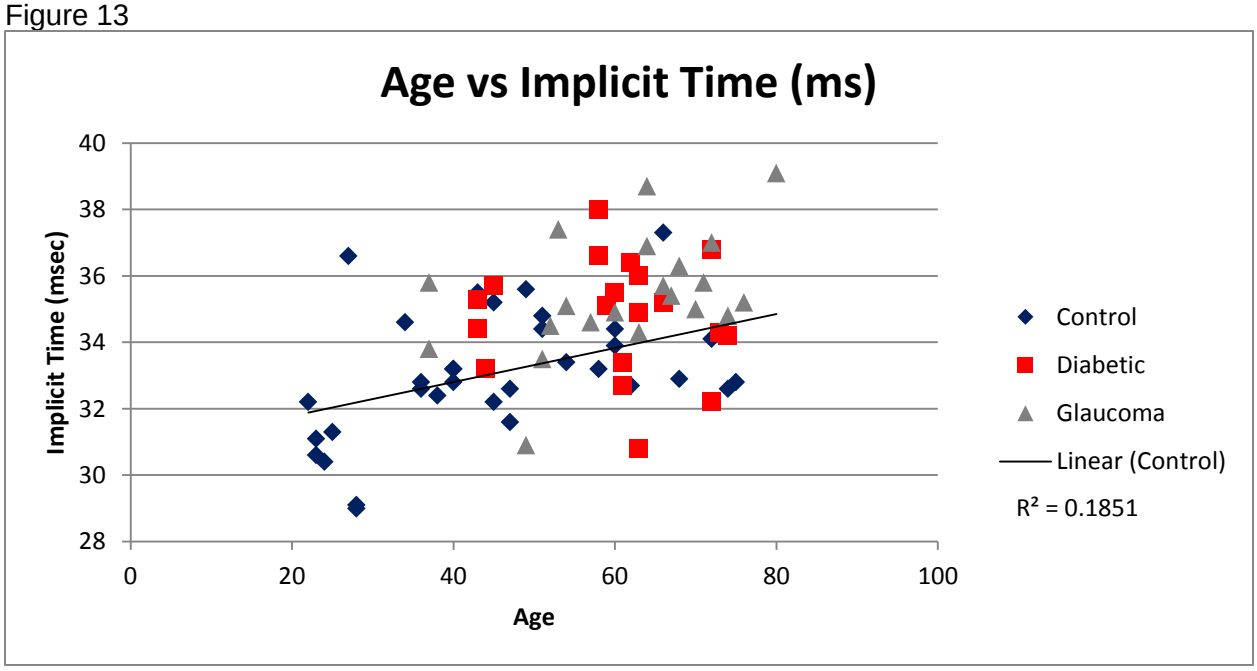

Age vs Implicit Time (ms)
Implicit Time (ms)
40
38
36
34
32
30
28
0
20
40
60
80
100
Age
Control
Diabetic
Glaucoma

Figure 13


Age vs Implicit Time (ms)
Implicit Time (msec)
40
38
36
34
32
30
28
0
20
40
60
80
100
Age
Control
Diabetic
Glaucoma
Linear (Control)
R² = 0.1851

	Diabetes	Control
IT ≥ 33.5 ms	15	11
IT < 33.5 ms	5	25
	Sensitivity = 75%	Specificity = 69.4%

Figure 14: Sensitivity and Specificity of Control vs Diabetes

	Glaucoma	Control
IT ≥ 33.5 ms	19	11
IT < 33.5 ms	2	25
	Sensitivity = 90.4%	Specificity = 69.4%

Figure 15: Sensitivity and Specificity of Control vs Glaucoma

Control vs Diabetics	P values
41~50: C(6) vs D(4)	0.4272
51~60: C(6) vs D(4)	0.0054
61~70: C(3) vs D(7)	0.9483
71~80: C(3) vs D(4)	0.3535
41~80: C(18) vs D(19)	0.0452

Control vs Glaucoma	P values
31~40: C(7) vs G(2)	0.042
41~50: C(6) vs G(1)	N/A
51~60: C(6) vs G(6)	0.126
61~70: C(3) vs G(7)	0.1991
71~80: C(3) vs G(5)	0.0256
31~80: C(25) vs G(21)	0.0003

Figure 16: Age stratification

Discussion

Diabetic retinopathy and glaucoma are leading causes of blindness in America. These patients are first seen in an internal medicine or primary care setting where there may not have been access to optometry or ophthalmology.

Cost effective and efficient screening is needed as our country heads into the Affordable Care Act of 2010. To decrease false positive referrals and to utilize specialty physician's time in the most efficient manner, screening may be necessary in the primary care setting.

The RET*eval*™ is a new device which may screen for diabetic eye disease. Its tracings document implicit time delays in Diabetic and Glaucoma patients. The device in our small study was used in non-mydriatic eyes in patients in general medicine practices or optometry practices where eye disease may be first encountered in a health care setting. The reproducibility is a promising sign that this device may be useful for ophthalmologists, optometrists, general practitioners or screening clinics.

The testing takes 5 to 7 seconds to perform without any eye contact. The ease of use makes this test a possible choice for screening diabetic eye disease. However this is a small study and more diabetic patients need to be tested.

The testing of diabetic patients with the RET*eval*™ device shows delay of implicit time, which is correlated with the literature[1,2]. We are hopeful that this device will be used by primary care physicians and nurses.

While the testing of glaucoma patients showed consistent delay in implicit time, more testing should be done with this group. Theoretically, the glaucoma results suggest that this test evaluates the ganglion cell layer which plays a role in the 30 Hz flicker.

One of the flaws of the study is the small sample size. While the results are interesting we need further studies with a larger study population to verify our pilot study findings. However,

with 77 patients and controls, we are able to identify interesting trends which may suggest that this may be a screening tool for the non-ophthalmic setting.

Conclusions

The RET*eval*™ is a handheld alternative to traditional ERG screening, which only requires 5 to 7 seconds to administer and provides a quick, quantitative screening of diabetic retinopathy and glaucoma. This study shows that implicit times were significantly different in both diabetic and glaucoma patient groups compared with controls. However, further studies with more patients will be needed to further evaluate the capabilities of the RET*eval*™ device.

References

1. Tahara K, Matsuura T, Otori, T. Diagnostic evaluation of diabetic retinopathy by 30-Hz flicker electroretinography. Jpn J Ophthalmol 1993;37:204-10.
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3. Holopigian K, Greestein V, Seiple W, Hood DC, Ritch R. Electrophysiologic assessment of photoreceptor function in patients with primary open-angle glaucoma. J Glaucoma 2000;9:163-8.
4. Chu H, A new approach to early glaucomatous diagnosis by multifocal electroretinogram: luminance-modulation of the global flash stimulation paradigm. Hong Kong Polytechnic University 2009;25:274.