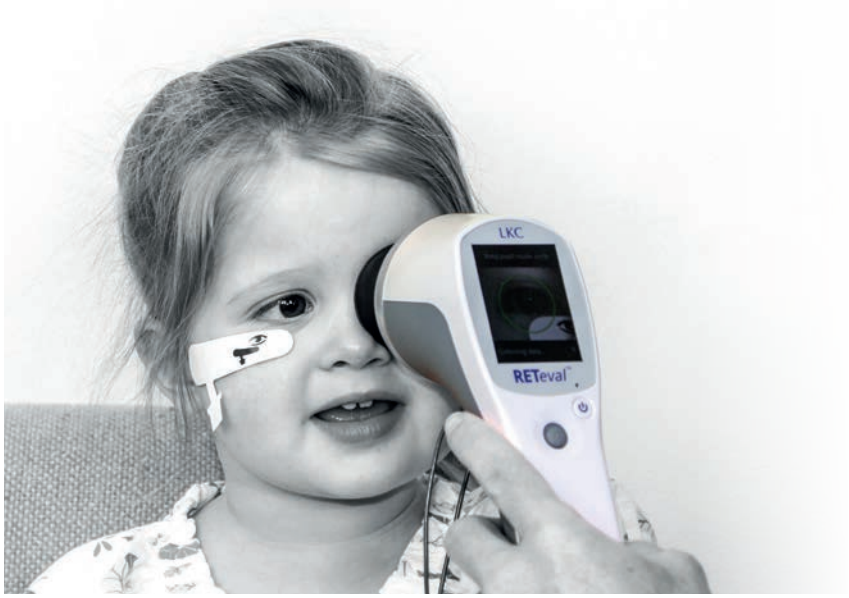
LKC TECHNOLOGIES
VISION DEFINED™

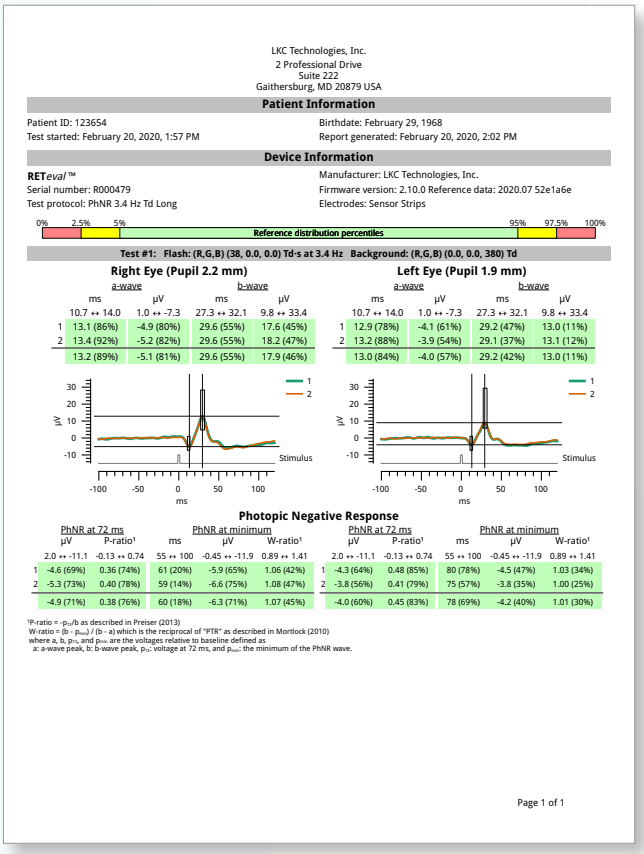
RETeval® Device

CLINICAL INTERPRETATION GUIDE

Disclaimer

The content in this document is based on studies published using the RETeval® device or similar ERG systems. It is provided for informational purposes only. LKC has not been involved in the clinical determination by the authors of these publications and does not assume any liability nor responsibility for completeness or correctness. The RETeval® device is an aid in diagnosis, and not intended to be used as the sole diagnostic for disease. Never draw diagnostic conclusions from a single exam, and heed the subject's medical history. It is the clinician's responsibility to make diagnostic interpretations of RETeval® measurements after they have familiarized themselves with the most recent literature/ guidelines or recommendations, as well as with the RETeval® System according to the most recent product documentation. If you have any questions, please contact your local representative or the LKC Technologies company at info@lkc.com.





LKC Technologies, Inc.
2 Professional Drive
Suite 222
Gaithersburg, MD 20879 USA

Patient Information

Patient ID: 123654
Test started: February 20, 2020, 1:57 PM
Birthdate: February 29, 1968
Report generated: February 20, 2020, 2:02 PM

Device Information

RETeval™
Serial number: R000479
Test protocol: PhNR 3.4 Hz Td Long
Manufacturer: LKC Technologies, Inc.
Firmware version: 2.10.0 Reference data: 2020.07 52e1a6e
Electrodes: Sensor Strips

0% 2.5% 5% 95% 97.5% 100%
Reference distribution percentiles

Test #1: Flash: (R,G,B) (38, 0.0, 0.0) Td·s at 3.4 Hz Background: (R,G,B) (0.0, 0.0, 380) Td

Right Eye (Pupil 2.2 mm)

	a-wave ms	a-wave µV	b-wave ms	b-wave µV
	10.7 ↔ 14.0	1.0 ↔ -7.3	27.3 ↔ 32.1	9.8 ↔ 33.4
1	13.1 (86%)	-4.9 (80%)	29.6 (55%)	17.6 (45%)
2	13.4 (92%)	-5.2 (82%)	29.6 (55%)	18.2 (47%)
	13.2 (89%)	-5.1 (81%)	29.6 (55%)	17.9 (46%)

Left Eye (Pupil 1.9 mm)

	a-wave ms	a-wave µV	b-wave ms	b-wave µV
	10.7 ↔ 14.0	1.0 ↔ -7.3	27.3 ↔ 32.1	9.8 ↔ 33.4
1	12.9 (78%)	-4.1 (61%)	29.2 (47%)	13.0 (11%)
2	13.2 (88%)	-3.9 (54%)	29.1 (37%)	13.1 (12%)
	13.0 (84%)	-4.0 (57%)	29.2 (42%)	13.0 (11%)

Photopic Negative Response

	PhNR at 72 ms µV	PhNR at 72 ms P-ratio¹	PhNR at minimum ms	PhNR at minimum µV	PhNR at minimum W-ratio¹
	2.0 ↔ -11.1	-0.13 ↔ 0.74	55 ↔ 100	-0.45 ↔ -11.9	0.89 ↔ 1.41
1	-4.6 (69%)	0.36 (74%)	61 (20%)	-5.9 (65%)	1.06 (42%)
2	-5.3 (73%)	0.40 (78%)	59 (14%)	-6.6 (75%)	1.08 (47%)
	-4.9 (71%)	0.38 (76%)	60 (18%)	-6.3 (71%)	1.07 (45%)

	PhNR at 72 ms µV	PhNR at 72 ms P-ratio¹	PhNR at minimum ms	PhNR at minimum µV	PhNR at minimum W-ratio¹
	2.0 ↔ -11.1	-0.13 ↔ 0.74	55 ↔ 100	-0.45 ↔ -11.9	0.89 ↔ 1.41
1	-4.3 (64%)	0.48 (85%)	80 (78%)	-4.5 (47%)	1.03 (34%)
2	-3.8 (56%)	0.41 (79%)	75 (57%)	-3.8 (35%)	1.00 (25%)
	-4.0 (60%)	0.45 (83%)	78 (69%)	-4.2 (40%)	1.01 (30%)

¹P-ratio = $-p_{72}/b$ as described in Preiser (2013)
W-ratio = $(b - p_{min}) / (b - a)$ which is the reciprocal of "PTR" as described in Mortlock (2010)
where a, b, p_{72}, and p_{min} are the voltages relative to baseline defined as
a: a-wave peak, b: b-wave peak, p_{72}: voltage at 72 ms, and p_{min}: the minimum of the PhNR wave.

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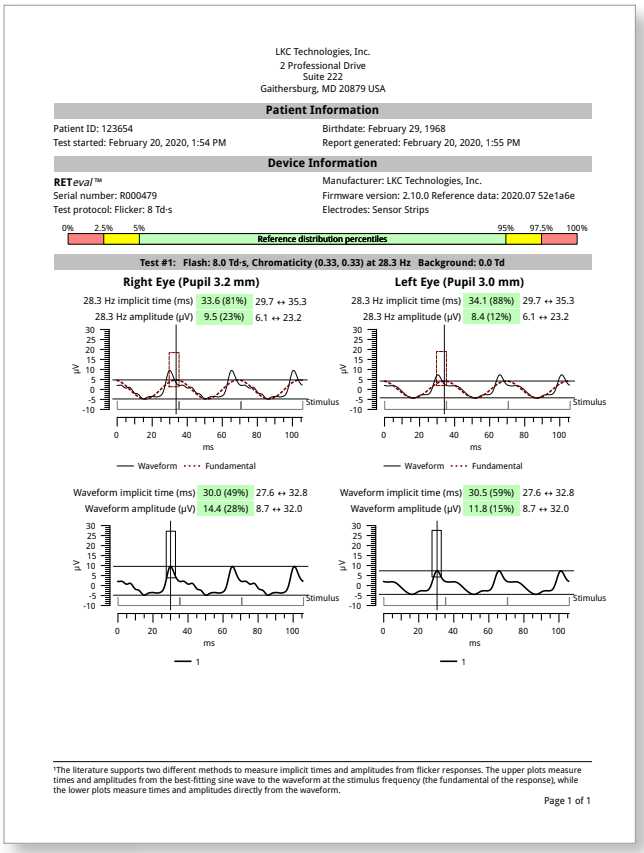

LKC Technologies, Inc.
2 Professional Drive
Suite 222
Gaithersburg, MD 20879 USA

Patient Information

Patient ID: 123654
Test started: February 20, 2020, 1:54 PM
Birthdate: February 29, 1968
Report generated: February 20, 2020, 1:55 PM

Device Information

RETeval™
Serial number: R000479
Test protocol: Flicker: 8 Td·s
Manufacturer: LKC Technologies, Inc.
Firmware version: 2.10.0 Reference data: 2020.07 52e1a6e
Electrodes: Sensor Strips

0% 2.5% 5% 95% 97.5% 100%
Reference distribution percentiles

Test #1: Flash: 8.0 Td·s, Chromaticity (0.33, 0.33) at 28.3 Hz Background: 0.0 Td

Right Eye (Pupil 3.2 mm)

28.3 Hz implicit time (ms) 33.6 (81%) 29.7 ↔ 35.3
28.3 Hz amplitude (µV) 9.5 (23%) 6.1 ↔ 23.2

Waveform implicit time (ms) 30.0 (49%) 27.6 ↔ 32.8
Waveform amplitude (µV) 14.4 (28%) 8.7 ↔ 32.0

Left Eye (Pupil 3.0 mm)

28.3 Hz implicit time (ms) 34.1 (88%) 29.7 ↔ 35.3
28.3 Hz amplitude (µV) 8.4 (12%) 6.1 ↔ 23.2

Waveform implicit time (ms) 30.5 (59%) 27.6 ↔ 32.8
Waveform amplitude (µV) 11.8 (15%) 8.7 ↔ 32.0

¹The literature supports two different methods to measure implicit times and amplitudes from flicker responses. The upper plots measure times and amplitudes from the best-fitting sine wave to the waveform at the stimulus frequency (the fundamental of the response), while the lower plots measure times and amplitudes directly from the waveform.

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> The handheld and portable nature of the device made it easy to bring to multiple office locations. We were able to test many patients at once, and gathering information was seamless for our technicians and patients. We have been able to see more patients and get better information on their retina function since acquiring the RETeval device last year. Our patient profile is improved since we are bridging the gap between structural and functional information, allowing us to see a full picture of eye health."
>
> *Dr. Robert Feig, MD, Brooklyn Eye Center, USA*

> I am using RETeval since about 2 months and in this short time I was able to implement ERG with minimal disruption to clinic. We exams are done by our excellent nurse and she reports that patients are really cooperative."
>
> *Dr. Igor Kozak, Moorfields Eye Hospital, Abu Dhabi, UAE*

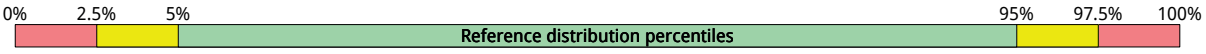
> We were impressed with the ease of acquisition, the quality of the automatic reporting function and the affordability. The ability to download reports into our EMR facilitates timely record keeping and communication with referring doctors. We appreciate the overall quality of the device."
>
> *Dr. Monique Leys, MD EBO, West Virginia University Eye Institute, USA*

General interpretation of results

The reports generated by the RETeval® device include reference range values for a subset of built-in protocols. These reference range values were generated through a clinical trial with over 660 normal subjects. Here is a sample waveform containing reference range values:

RETeval ™
Serial number: R000707
Test protocol: ISCEV Photopic flash/flicker Td

Manufacturer: LKC Technologies, Inc.
Firmware version: 2.8.0rc8 Reference data: 2017.39 89f8cca
Electrodes: Sensor Strips



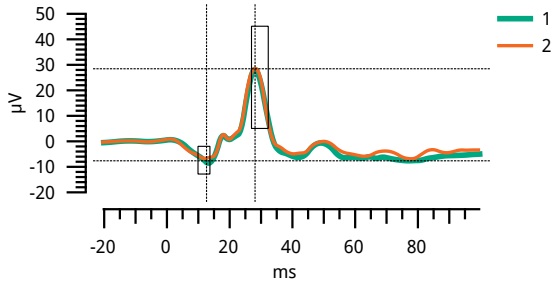
Test #1: Flash: 85 Td·s, Chromaticity (0.33, 0.33) at 2 Hz Background: 850 Td, Chromaticity (0.33, 0.33)

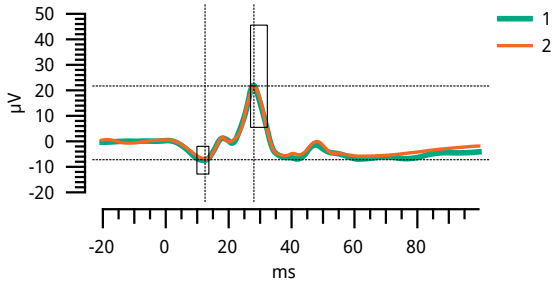
Right Eye

	a-wave		b-wave	
	ms	µV	ms	µV
	9.9 ↔ 13.7	-2.0 ↔ -12.8	27.0 ↔ 32.3	12.7 ↔ 52.8
1	13.2 (92%)	-8.6 (77%)	28.1 (11%)	36.9 (75%)
2	12.0 (62%)	-6.7 (50%)	28.1 (12%)	35.3 (71%)
	12.6 (79%)	-7.6 (66%)	28.1 (12%)	36.1 (72%)

Left Eye

	a-wave		b-wave	
	ms	µV	ms	µV
	9.9 ↔ 13.7	-2.0 ↔ -12.8	27.0 ↔ 32.3	12.7 ↔ 52.8
1	12.2 (66%)	-7.5 (64%)	27.9 (9%)	29.5 (52%)
2	12.8 (86%)	-6.9 (54%)	28.2 (13%)	28.3 (47%)
	12.5 (76%)	-7.2 (59%)	28.0 (10%)	28.9 (49%)





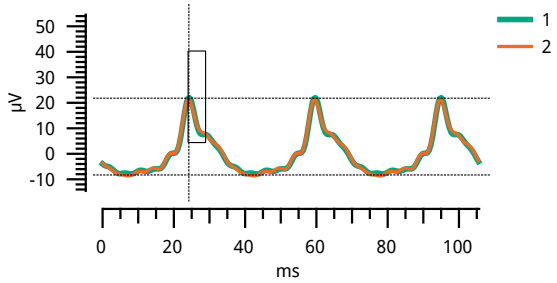
Test #2: Flash: 85 Td·s, Chromaticity (0.33, 0.33) at 28.3 Hz Background: 850 Td, Chromaticity (0.33, 0.33)

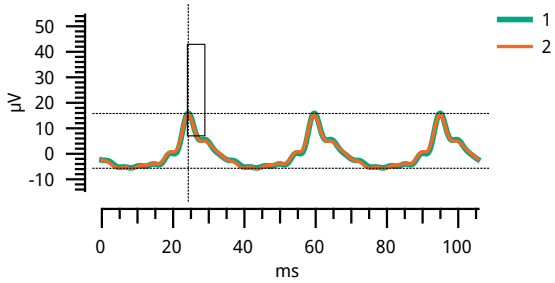
Right Eye

	ms	µV
	24.0 ↔ 28.9	12.7 ↔ 48.6
1	24.3 (5%)	30.2 (65%)
2	24.1 (4%)	30.0 (65%)
	24.2 (4%)	30.1 (65%)

Left Eye

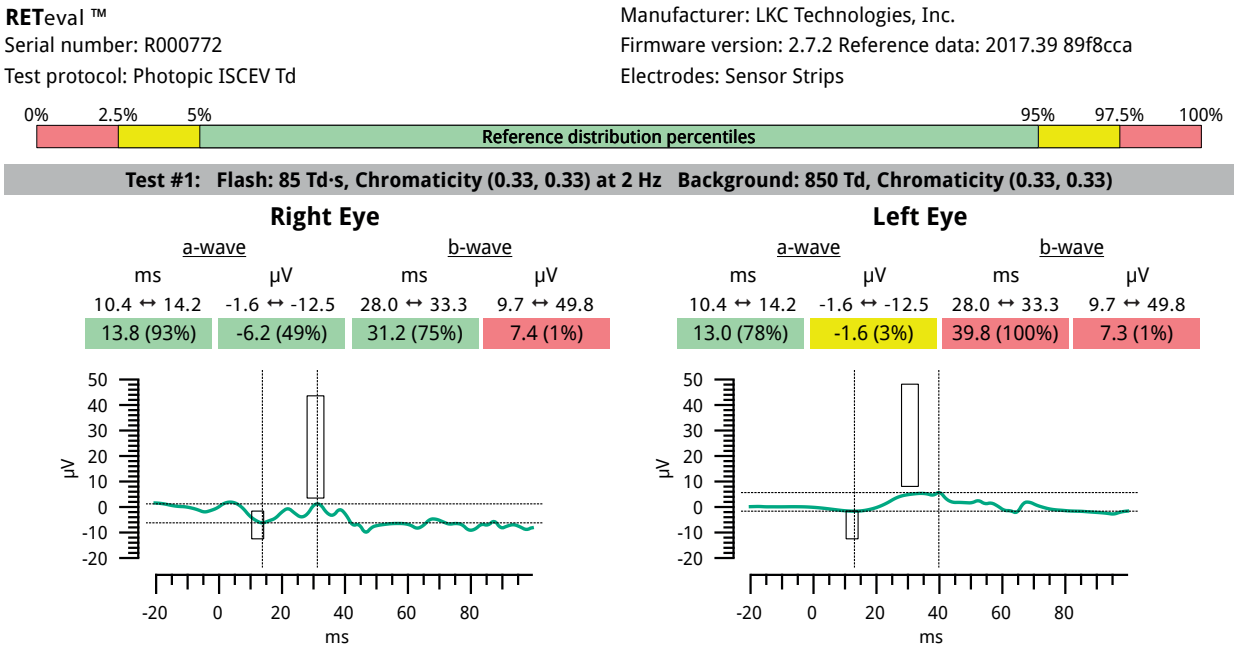
	ms	µV
	24.0 ↔ 28.9	12.7 ↔ 48.6
1	24.3 (5%)	21.6 (26%)
2	24.2 (5%)	21.3 (25%)
	24.2 (5%)	21.5 (25%)





Green – Indicate results fall in the middle 90% of normal subjects.
Yellow – Indicate results fall in the next 5% of normal subjects
Red – Indicate results fall outside of the "normal" 97.5% reference distribution percentile

Example of abnormal patient results indicated with red highlight (Severe non-proliferative diabetic retinopathy):



How do you think about yellow results?

Patient is borderline and may be worthy of a closer diagnostic assessment or more frequent follow-up interval.

How do you think about red results?

Clinically, red results happen 1/20 times for subjects with normal vision, based on how the reference intervals were made (95% specificity). Assuming test was done properly:

Amplitudes

- Too large: Probably ok
- Too small: Indication of cell death

Implicit times

- Too fast: Probably ok
- Too small: Indication of cellular stress

Clinicians must exercise judgement in the interpretation of a patient's result when compared to the reference data. About 1 in 20 visually-normal subjects will be flagged as "red" and another 1 in 20 visually-normal subjects will be flagged as "yellow". Thus, 2 in 20 visually-normal subjects (10%) will not be marked as "green", when they are in fact normal. The RETeval® device is an aid in diagnosis, and not intended to be used as the sole diagnostic for disease. Never draw diagnostic conclusions from a single exam, and heed the subject's medical history. It is the clinician's responsibility to make diagnostic interpretations of RETeval® measurements.

Diabetic Retinopathy

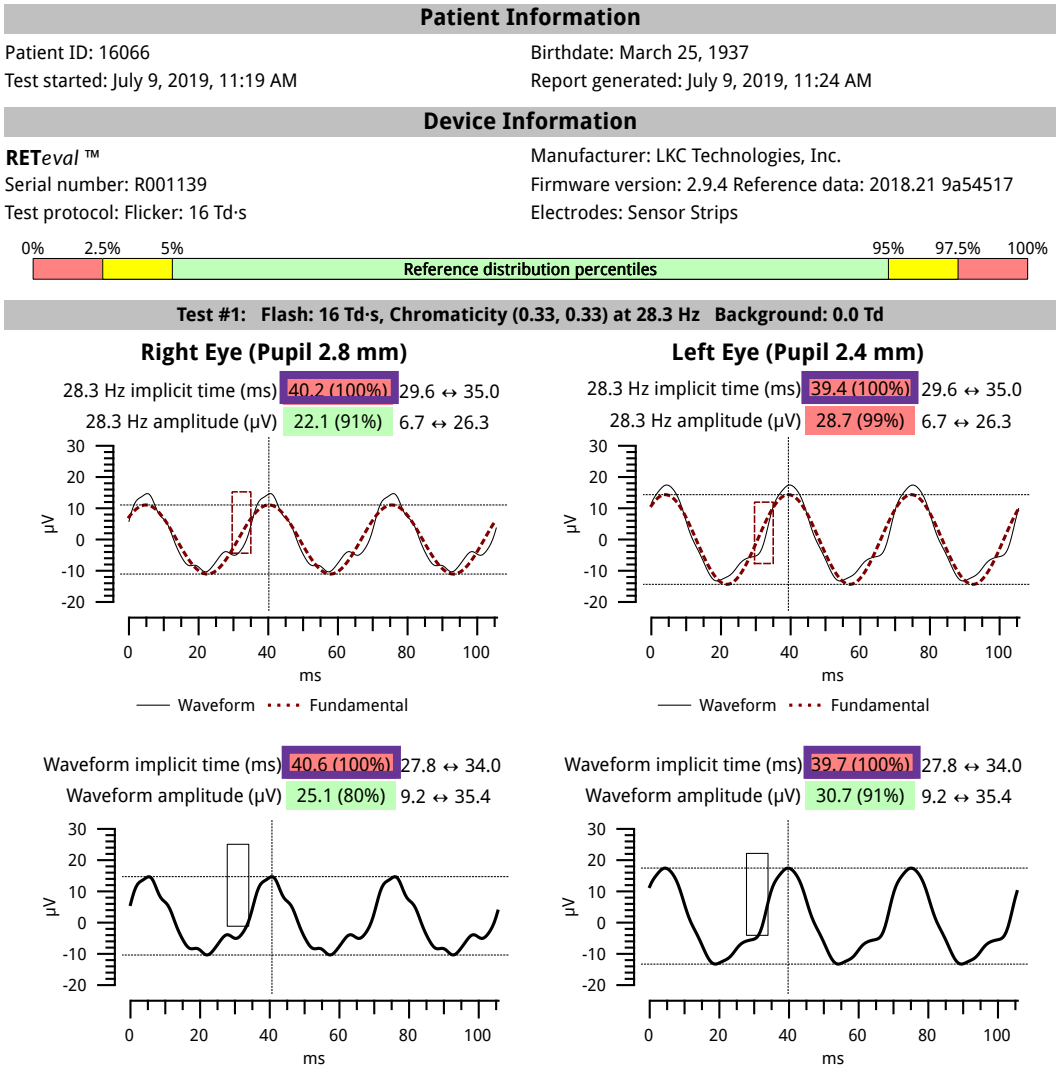
The objective is to predict which patients will develop VT DR and may require intervention. The test result is an age-dependent comparison of Flicker 16 Td•s implicit time.

Source: Zeng et al: Early retinal neurovascular impairment in patients with diabetes without clinically detectable retinopathy. Br J Ophthalmol 2019;0:1-6. doi: 10.1136lbjophthalmol-2018-313582

Patient test conditions: Test is completed un-dilated. Diabetic patient suspected retinopathy.

Protocol: Flicker 16 Td•s (use Flicker 32 Td•s for patients with media opacities)

Results: If the **implicit time** is > 97.5% the patient is at the risk to develop vision threatening DR within the coming 24 months. Results of this type will be highlighted in red.



Glaucoma

The objective of the test is to confirm a glaucoma diagnosis. This can also be used for patients not suitable for perimetry.

Source: Wu et al: Photopic Negative Response Obtained Using a Handheld Electroretinogram Device: Determining the Optimal Measure and Repeatability. TVST, 2016, Vol. 5, No. 4, Article 8

Patient test conditions: Test is done un-dilated. Test performed in combination with tonometry and OCT.

Protocols: PhNR 3.4 Hz Td Long in addition to Flicker16 Td or Flicker 32 Td for eyes with media opacities. If patient is not compliant, choose PhNR 3.4 Hz Td Short.

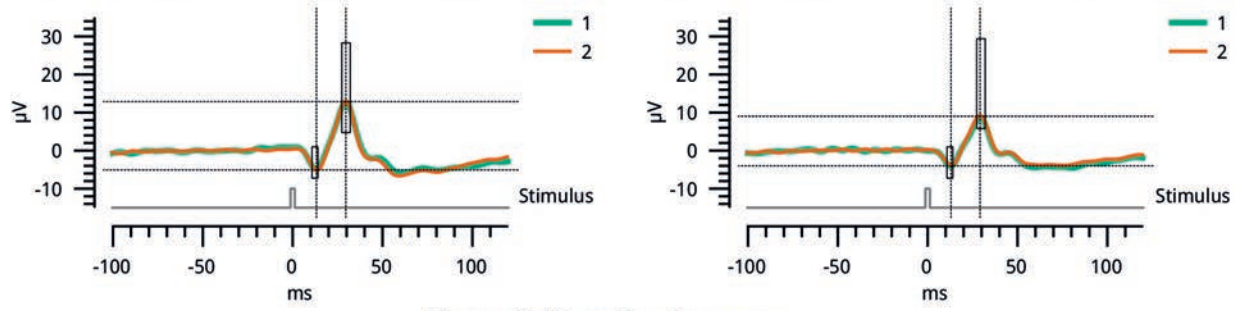
Sample Normal PhNR Waveform:

Right Eye (Pupil 2.2 mm)

	a-wave		b-wave	
	ms	µV	ms	µV
	10.7 ↔ 14.0	1.0 ↔ -7.3	27.3 ↔ 32.1	9.8 ↔ 33.4
1	13.1 (86%)	-4.9 (80%)	29.6 (55%)	17.6 (45%)
2	13.4 (92%)	-5.2 (82%)	29.6 (55%)	18.2 (47%)
	13.2 (89%)	-5.1 (81%)	29.6 (55%)	17.9 (46%)

Left Eye (Pupil 1.9 mm)

	a-wave		b-wave	
	ms	µV	ms	µV
	10.7 ↔ 14.0	1.0 ↔ -7.3	27.3 ↔ 32.1	9.8 ↔ 33.4
1	12.9 (78%)	-4.1 (61%)	29.2 (47%)	13.0 (11%)
2	13.2 (88%)	-3.9 (54%)	29.1 (37%)	13.1 (12%)
	13.0 (84%)	-4.0 (57%)	29.2 (42%)	13.0 (11%)



Photopic Negative Response

	PhNR at 72 ms		PhNR at minimum		
	µV	P-ratio[1]	ms	µV	W-ratio[1]
	2.0 ↔ -11.1	-0.13 ↔ 0.74	55 ↔ 100	-0.45 ↔ -11.9	0.89 ↔ 1.41
1	-4.6 (69%)	0.36 (74%)	61 (20%)	-5.9 (65%)	1.06 (42%)
2	-5.3 (73%)	0.40 (78%)	59 (14%)	-6.6 (75%)	1.08 (47%)
	-4.9 (71%)	0.38 (76%)	60 (18%)	-6.3 (71%)	1.07 (45%)

	PhNR at 72 ms		PhNR at minimum		
	µV	P-ratio[1]	ms	µV	W-ratio[1]
	2.0 ↔ -11.1	-0.13 ↔ 0.74	55 ↔ 100	-0.45 ↔ -11.9	0.89 ↔ 1.41
1	-4.3 (64%)	0.48 (85%)	80 (78%)	-4.5 (47%)	1.03 (34%)
2	-3.8 (56%)	0.41 (79%)	75 (57%)	-3.8 (35%)	1.00 (25%)
	-4.0 (60%)	0.45 (83%)	78 (69%)	-4.2 (40%)	1.01 (30%)

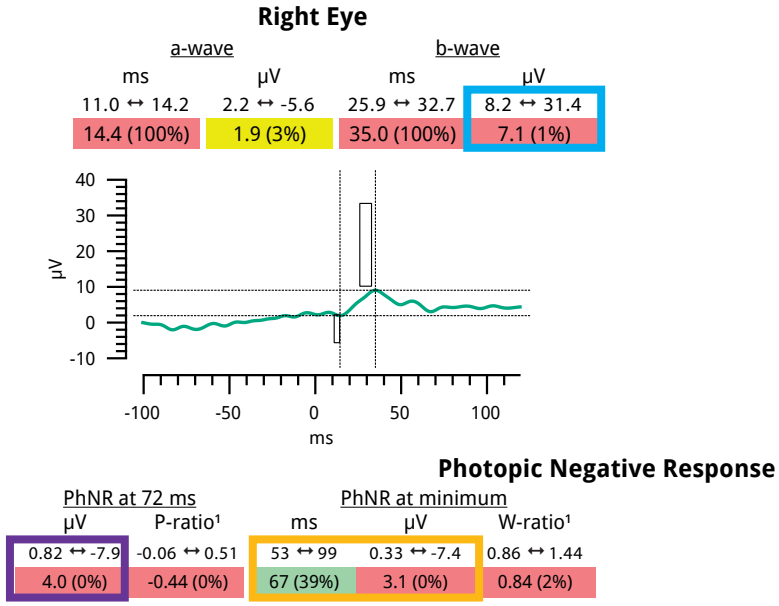
[1]P-ratio = $-p_{72}/b$ as described in Preiser (2013)
W-ratio = $(b - p_{min}) / (b - a)$ which is the reciprocal of "PTR" as described in Mortlock (2010)
where a, b, p_{72}, and p_{min} are the voltages relative to baseline defined as
a: a-wave peak, b: b-wave peak, p_{72}: voltage at 72 ms, and p_{min}: the minimum of the PhNR wave.

PhNR at 72ms: fixed time, only amplitudes to be measured
PhNR at minimum: both implicit time and amplitudes will be measured

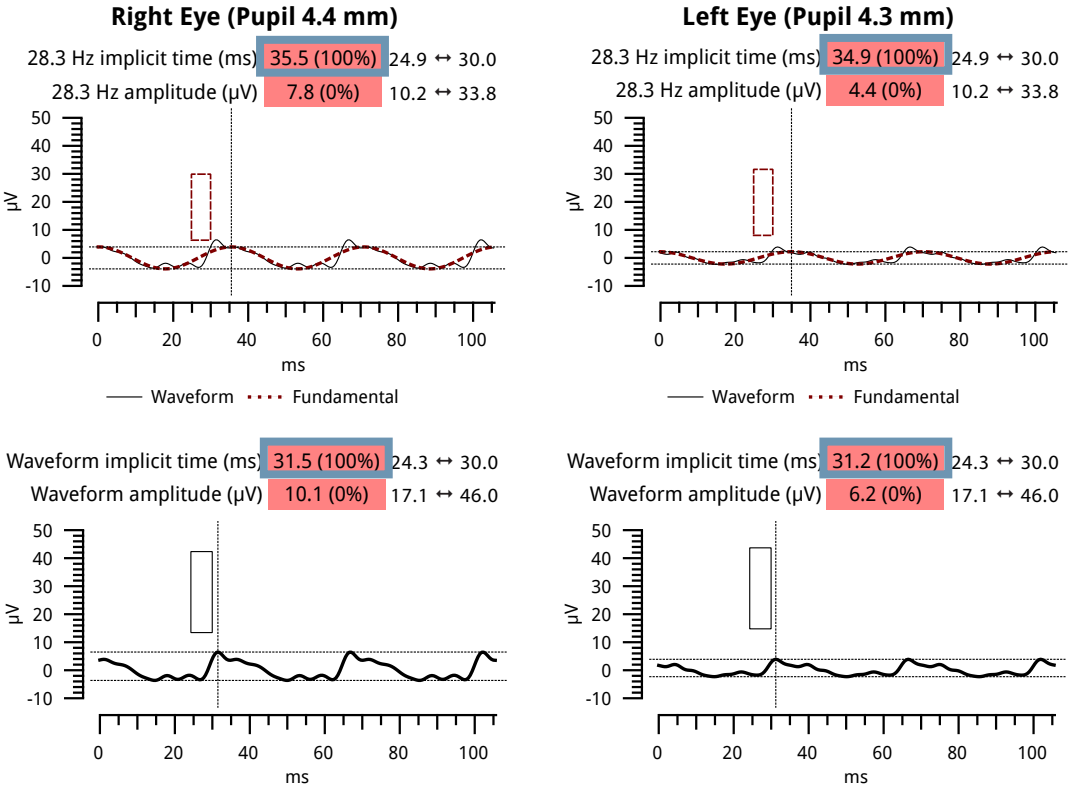
Results: Look at **PhNR at minimum** and suspect glaucoma if ganglion cells responded after 100 ms and amplitude is not within the normative values or amplitude of **PhNR at 72 ms** is not within the normative values

AND

Flash **b-wave** amplitude ≤ 8 %.



This can be confirmed by looking at the Flicker 16/32 Td: the flicker **implicit time** is ≥ 92 % of normative values:



Central Retinal Vein Occlusion (CRVO)

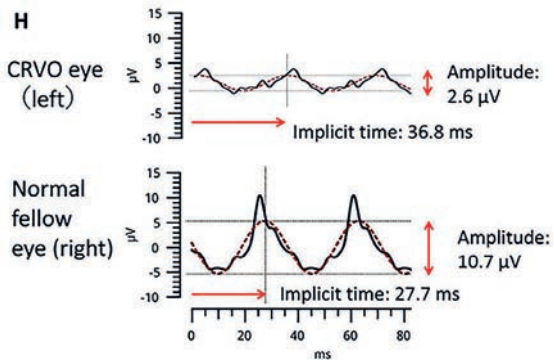
The objective is to differentiate between ischemic and non-ischemic CRVO at the early stage.

Source: Miyata et al: Supernormal Flicker ERGs in Eyes With Central Retinal Vein Occlusion: Clinical Characteristics, Prognosis, and Effects of Anti-VEGF Agent. Investigative ophthalmology & visual science 2018, 59 (15), 5854-5861.

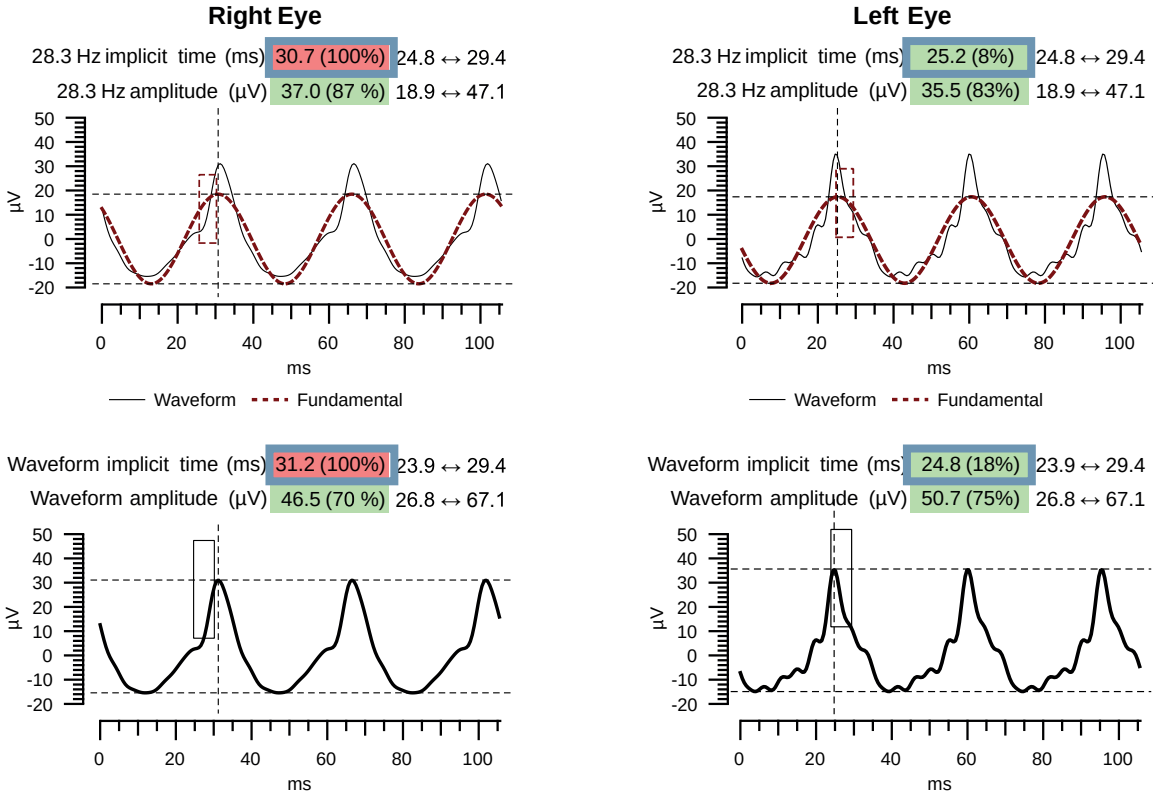
Patient test conditions: Test is done un-dilated. Test is performed longitudinally earliest 3 weeks after detected CRVO.

Protocols: Flicker 16 Td or Flicker 32 Td with cataracts/cornea opacities.

Results: If **implicit time** of affected eye is > 5 ms that of fellow eye, suspect ischemic CRVO



CRVO eye (OD), Normal/Fellow eye (OS)



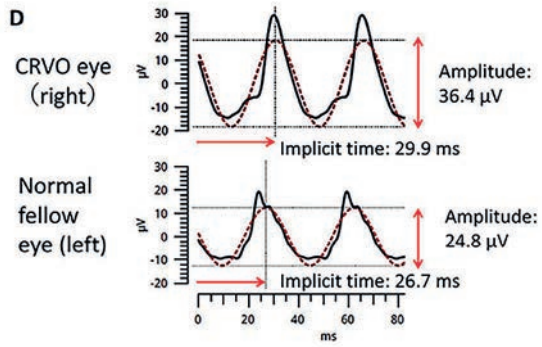
Sample waveform for illustration, not from an actual CRVO patient result

Additional note:

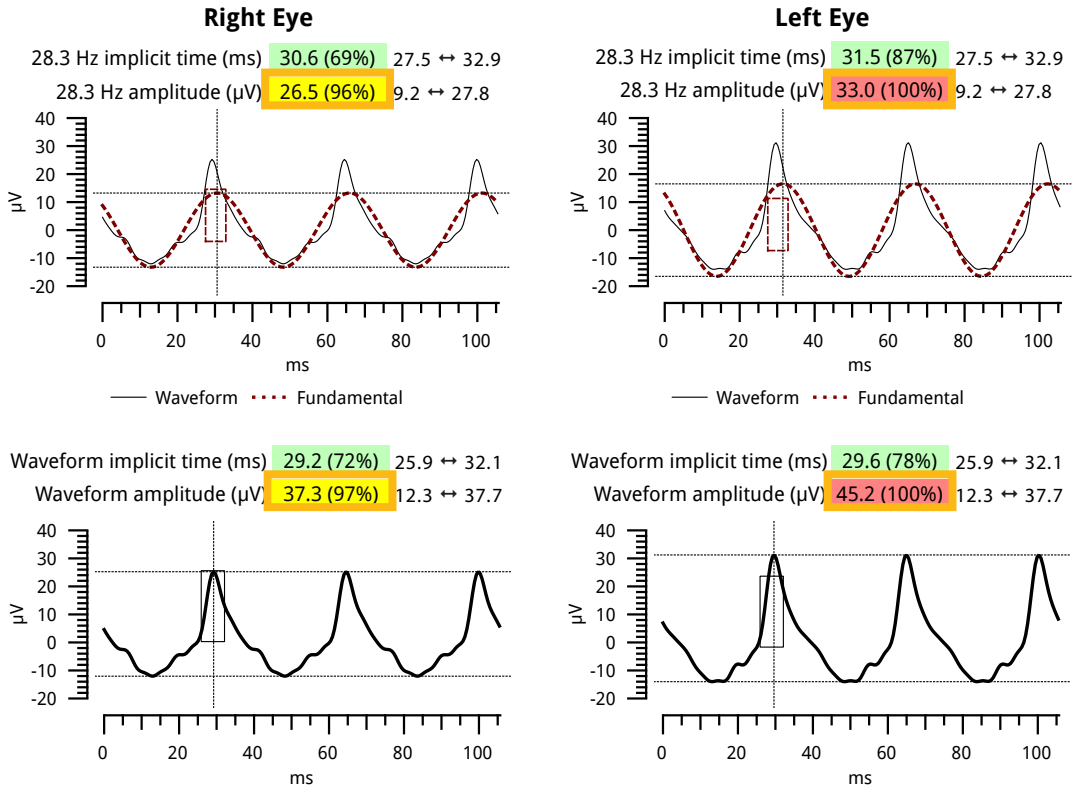
According to the study by Miyata et al., all CRVO eyes with supernormal flicker ERGs had the non-ischemic type of CRVO and tended to have better visual acuities than did the 28 non-ischemic CRVO eyes without supernormal flicker ERGs at 12 months after the treatment.

These results indicated that the supernormal flicker ERGs can be a sign of a mild degree of ischemia, and these eyes have a better prognosis.

If **amplitude** of affected eye is > 117% that of fellow eye ("supernormal" results), subject has better 12-month prognosis in terms of VA.



CRVO eye (OD), Normal/Fellow eye (OS)



Sample waveform for illustration, not from an actual CRVO patient result

Pediatric Nystagmus

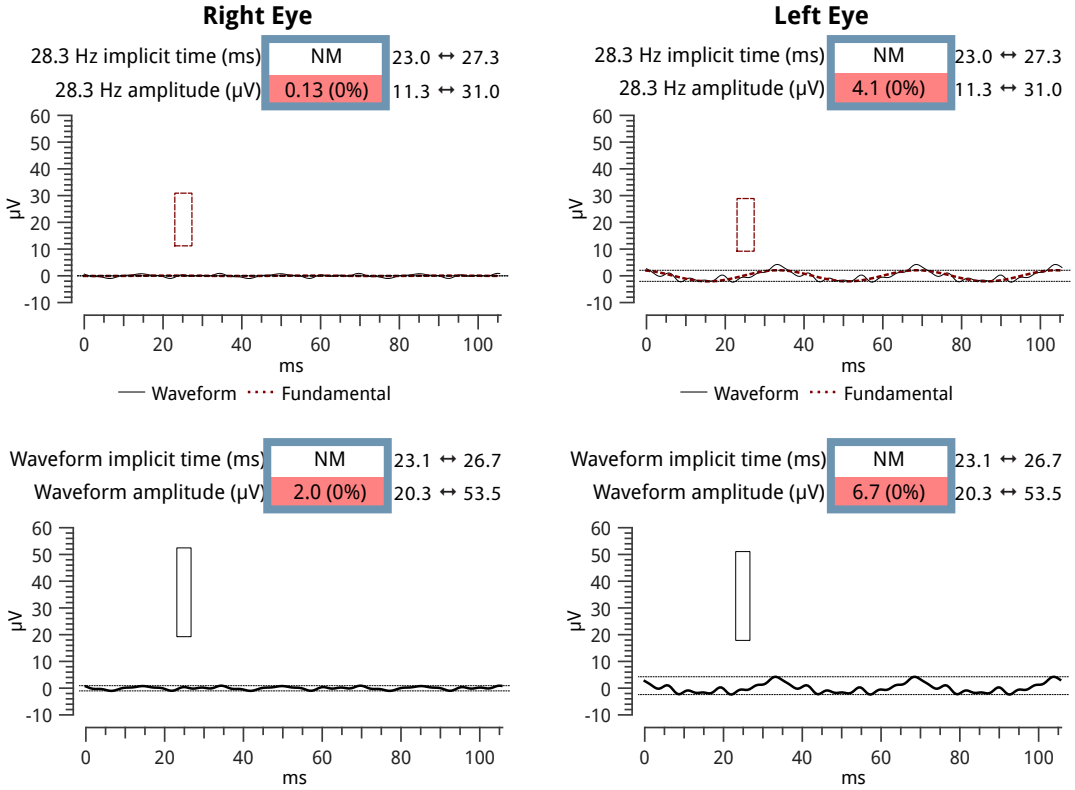
The objective is to differentiate nystagmus related to an ophthalmic disorder (e.g., retinal dystrophy, optic nerve abnormality) versus congenital nystagmus without ophthalmic structural pathology.

Source: Grace, et al: Nonsedated handheld electroretinogram as a screening test of retinal dysfunction in pediatric patients with nystagmus. J AAPOS 2017, 21 (5), 384-388.

Patient test condition: Always dilate, pediatric patient typically unsedated with adequate cooperation.

Protocol: Flicker 3 cd·s/m^2, 30 cd/m^2 background

Results: If **amplitude < 0% or implicit time** (either on Fundamental or on Waveform) **is not measurable or measurable and > 100%,** suspect retinal involvement, assuming patient is reasonably compliant and electrodes are properly placed. Leber's congenitial amaurosis (LCA) is an example retinal degeneration found in pediatric patients with nystagmus and an abnormal ERG.



Generalized assessment of retinal function

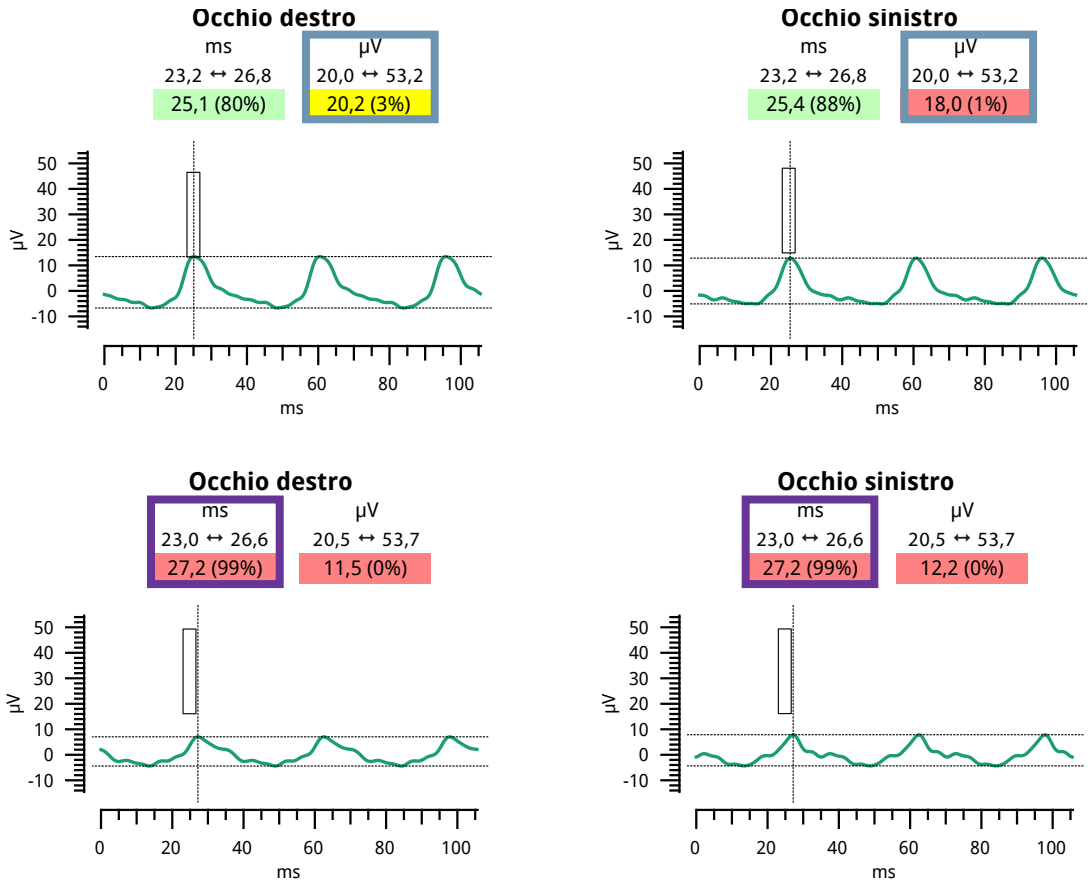
Differential diagnosis of retinal degenerative diseases and dysfunctional pathologies (cone-rod dystrophy, rod-cone dystrophy, Retinitis Pigmentosa, Stargardt disease, Leber's congenital amaurosis, achromatopsia, CSNB)

The objective is to run a fast and effective ERG in order to get a general assessment of overall retinal function and based on its results to decide if further tests (mainly scotopic) are necessary.

Source: Robson et al (2018): ISCEV guide to visual electrodiagnostic procedures. Doc Ophthalmol 136:1–26. doi: 10.1007/s10633-017-9621-y

Protocol: Flicker Protocols
- If dilated, run Flicker 3 cd·s/m², 30 cd/m² background (ISCEV Standard flicker)
- If undilated, run Flicker 16 Td or Flicker 32 Td w / cataract

Results: If **amplitude** < 5 %, suspect retinal involvement
If **timing** is > 95 %, suspect retinal involvement



If retinal involvement is suspected, further testing may be needed:

The RETeval® device contains several built-in protocols in order to provide a full comprehensive retinal examination for differential diagnosis for a number of retinal pathologies.

Protocol	Reference Data available
ISCEV 5 Step Dark First Cd	Yes
ISCEV 5 Step Dark First Td	Yes
ISCEV 5 Step Light First Cd	Yes
ISCEV 5 Step Dark First Td	Yes
ISCEV 6 Step Dark First Cd	Yes
ISCEV 6 Step Dark First Td	Yes
ISCEV 6 Step Light First Cd	Yes
ISCEV 6 Step Dark First Td	Yes

These protocols are compliant with the International Society for Clinical Electrophysiology of Vision clinical standards. For a full complete guide to electrodiagnostic procedures, you may find the resource here: **https://iscev.wildapricot.org/standards**

Scotopic Testing

- Assessment of rod system function
- Requires dark adaptation

Photopic Testing

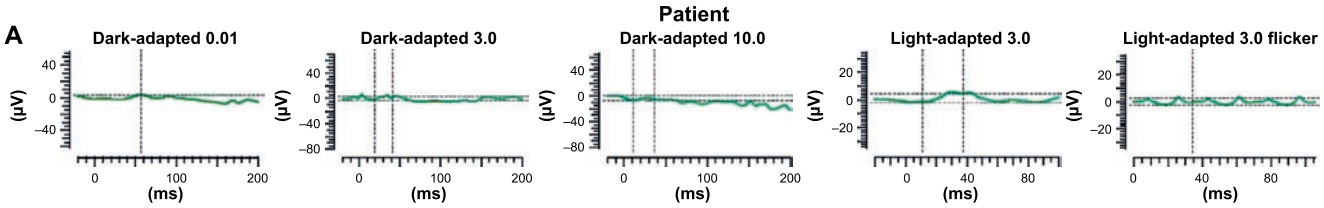
- Assessment of cone system function
- Does not require dark adaptation

ERG results and morphology must be included in the overall clinical context for accurate differential diagnosis.

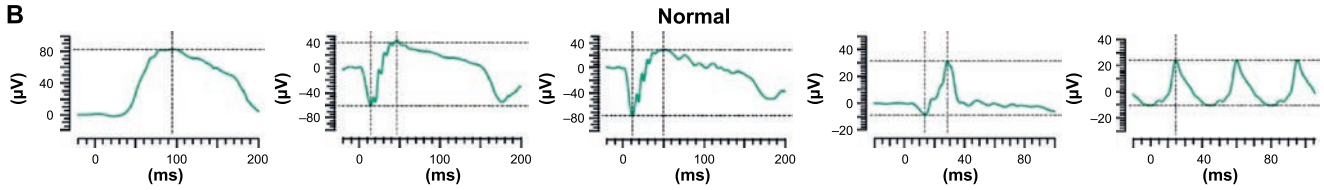
Example Waveforms Scotopic and Photopic tests

Source: Nakamura, et al: Evaluation of cone function by a handheld non-mydriatic flicker electroretinogram device. Clin Ophthalmol 2016, 10, 1175-85.

Retinitis Pigmentosa suspect (A)



And a healthy subject (B)



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