Ophthalmology Times
eBOOK

SHIFTING THE PARADIGM FOR RETINAL DISEASE MANAGEMENT: THE VALUE OF MODERN ELECTRORETINOGRAPHY

by SUBER HUANG, MD, MBA

Dr. Huang is internationally recognized as a retina specialist and is an expert in clinical trials. He founded the Retina Image Bank, now the world's largest and most comprehensive open-access multimedia database of all things retina. Past leadership includes President, American Society of Retina Specialists and Chair, National Eye Health Education Program, NEI, NIH, among many others. Dr. Huang currently practices at the Retina Center of Ohio, Euclid, OH, where is the Founder and CEO.

Dr. Huang is a consultant and researcher for Diopsys.

There has never been a more exciting time in ophthalmology, and especially in the field of retina, because therapeutic advances are enabling our ability to improve outcomes for patients with some of the most serious sight-threatening diseases. These developments intensify the need for a simple non-invasive objective test to measure visual function.

As an objective and reliable test of global retinal function, flicker electroretinography (ERG) may be beneficial in managing patients with pathologies that affect the entire retina, including diabetic retinopathy, central retinal vein occlusion (CRVO), inherited retina dystrophies, and uveitis. Electrophysiology continues to be an invaluable diagnostic test to help evaluate visual function in patients with media opacities, in pre-verbal patients, or those who cannot speak.

In the past, ERG was accessible for patient evaluation mostly through referral to specialized centers and involved a testing protocol that was poorly tolerated by patients. Now with technology available from Diopsys, ERG can be performed as an efficient, painless, patient-friendly, office-based test.

Benefits of ERG

Most of the approaches that are used for assessing patients with retinal disease have stayed largely the same over the past century. Visual acuity remains the gold standard for assessing visual function, but visual acuity is subjective and reflects only central foveal function, which is not a very sensitive measure considering that even when half the fovea is obscured (or non-functional), a patient may still have 20/20 visual acuity.

Standardized automated perimetry, another conventional test for visual function, is also subjective, which can lead to considerable intra-individual variability. In addition, standardized

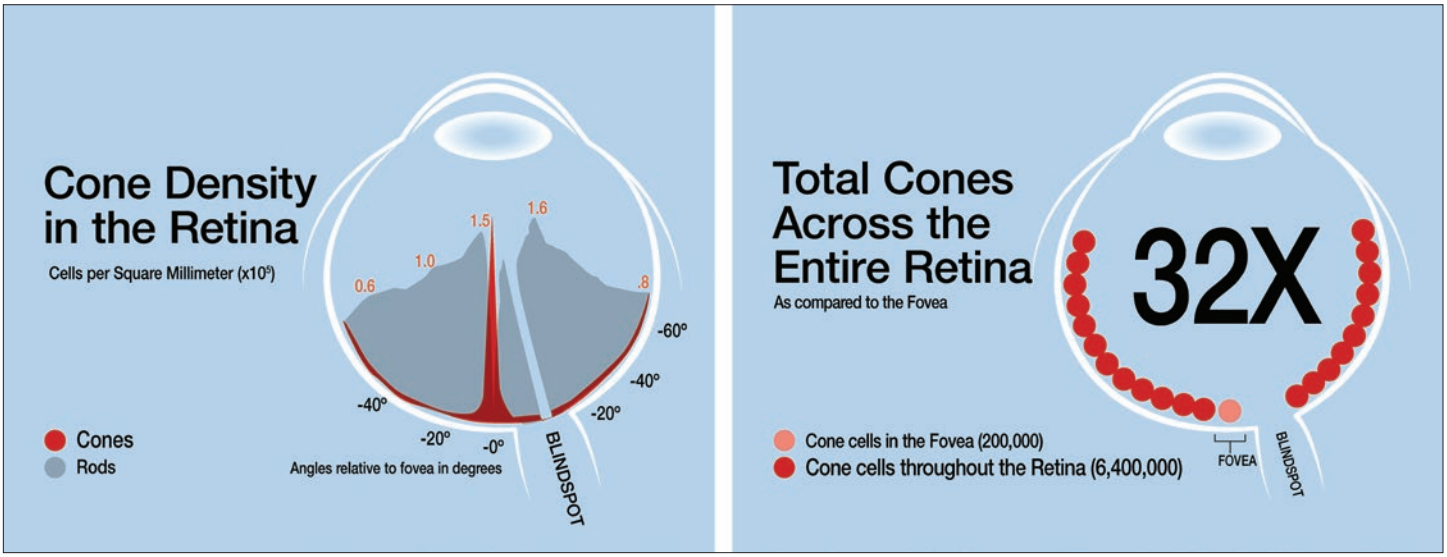
automated perimetry only maps the posterior pole, and so it does not provide a full picture of functional status.

Fundus photography provides a noninvasive method for evaluating retinal anatomy and physiology. Coupled with angiography, it has been a valuable resource to evaluate retinal vascular diseases. Limitations include difficulty evaluating structure through media opacities, retina hemorrhage, and that the findings require (subjective) interpretation. A round retinal hemorrhage may be an isolated fleck of blood, a microaneursym, or the beginning of a vascular anomaly. Similarly, tortuous vessels may constitute early retinal neovascularization, telangiectasia, capillary collateralization, or an intra-retina microvascular abnormality (IRMA).

Optical coherence tomography (OCT) has advanced our ability to evaluate retinal structure in depth. Because it is noninvasive, objective, quick, easy, and reproducible, OCT has become a workhorse in clinical practice for evaluating patients with retinal disease. However, OCT provides information about structure only and only in the posterior pole region, but there may be loss of function before structural changes are detectable with OCT.

None of the previous tests are measures of global retinal function. By measuring a light induced visual-response (LIV), ERG provides information about retinal function. Uniquely, it can be an indicator of the "health" of retinal tissue. It measures the aggregate function of the entire retina and different protocols can identify those conditions that affect rods only, cones only, or both. Moreover, the ability to identify progressive dysfunction (or improvement) related to retinal diseases prior to detectable structural alterations is intriguing, and it may be the key to shifting the treatment paradigm towards effective interventions that occur BEFORE structural pathology becomes manifest.

Flicker ERG (ffERG or full field flicker ERG), uses a flash stimulus of high frequency. Because the frequency of the flash stimulus is higher than the refresh rate of rod photoreceptors, flicker ERG measures cone-driven function. Although cone density is highest in the fovea, cones are distributed throughout the retina (**Figure 1**). Full field flicker ERG measures the stimulation of the entire retina and provides a summated measure of global retinal function. As an objective, reliable,



and quantitative measurement of LIV, flicker ERG can be used in the evaluation and follow-up of patients with conditions that can cause generalized retinal dysfunction.

ERG in the clinic

Integration of ERG testing in our office has been easy with the Diopsys system. The device uses intuitive interfaces and was quickly mastered by the technical staff. Unlike older ERG techniques that use a hard contact lens, the Diopsys system uses disposable sensors that are placed on the lower lid and forehead. The set-up and testing can be completed in less than ten minutes, and the system generates a report in a format that is clear, concise, and intuitive to interpret. Testing is comfortable and well-accepted by patients.

Figure 2 shows sample printouts generated from fixed luminance flicker ERG testing in a healthy eye and one with abnormal retinal function. The report includes an indication of signal quality, which is a measure of proper sensor connection. The results are presented in both graphical and tabular forms. Good function is represented by high and equally spaced peaks on the magnitude graphs and closely packed lines pointing in the vicinity around 5 o'clock in the lower right quadrant of the Mag/Phase plot. The table at the bottom of the report summarizes the raw data, and the values for magnitude and phase are color-coded based on documented reference ranges so that they readily indicate in-range (healthy), borderline, or out of range (abnormal).

With this concise report summary, clinicians can quickly evaluate retinal function and identify changes over time by comparing results from serial tests.

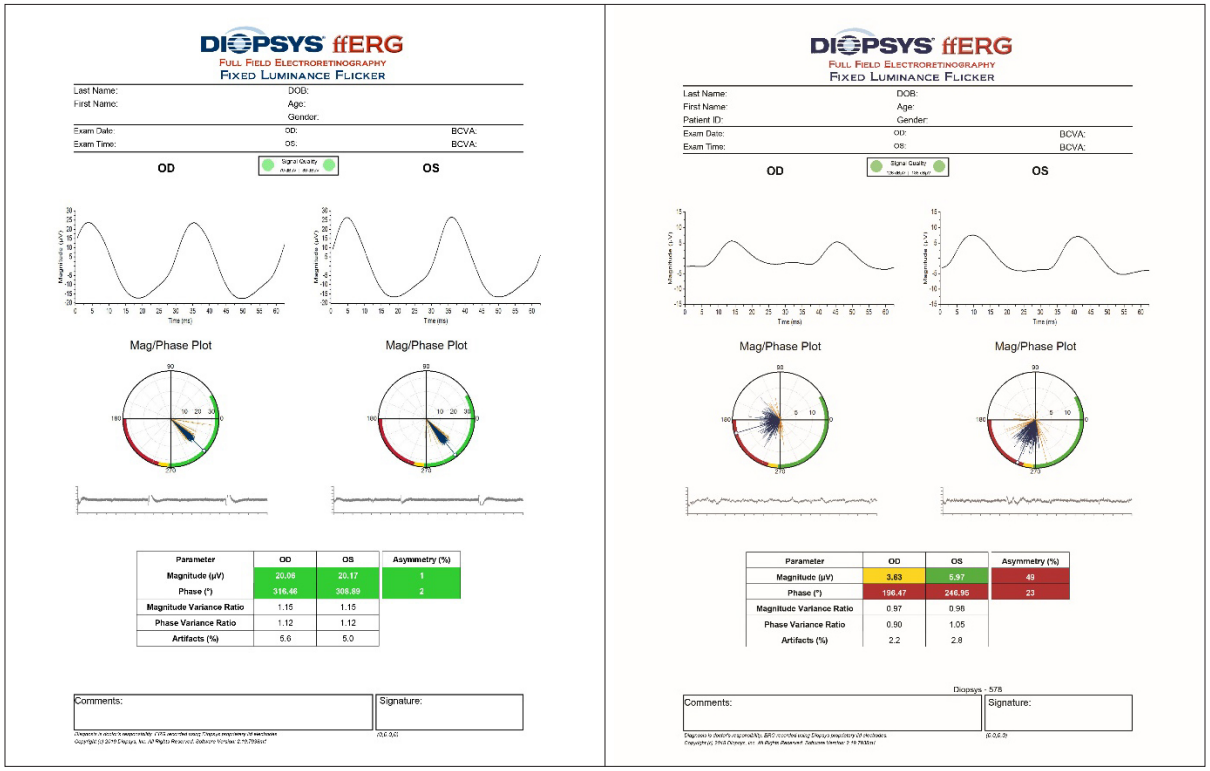


Figure 2. *Sample printouts from fixed luminance flicker ERG testing in a healthy eye (left) and an eye with abnormal retinal function (right).*

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Other indications for performing flicker ERG are to assess visual function in patients in whom visual acuity testing is not possible or unreliable because they are preverbal, unable to speak, malingering, or to evaluate visual potential in patients whose retina cannot be visualized because of media opacity. For example, in a patient with a dense cataract or a history of CRVO, flicker ERG is the only modality that can provide insight as to the patient's visual potential. By performing flicker ERG, the clinician is then able to give the patient a realistic expectation about the possibility of achieving better vision after cataract surgery.

Flicker ERG can also be particularly helpful for understanding poor vision not explained by anatomic findings. In a patient who has established recirculation after a CRVO but continues to have reduced vision, evaluation with flicker ERG to determine retinal function can indicate whether or not the individual has potential for vision improvement. In a patient with nonproliferative DR and 20/20 visual acuity, the finding of reduced retina function using flicker ERG may be a sign of global retinal ischemia associated with capillary dropout in the periphery

The following case involving a patient with CRVO being treated with anti-VEGF therapy shows how the retina specialist used the quantitative measurement of retina function obtained with flicker ERG testing together with other diagnostic findings to guide care decisions.

Case Study

PATIENT PROFILE

An 88-year-old male patient presented with a chief complaint of blurred central vision OD for 1–2 weeks. He had a past medical history of coronary artery disease. Past ocular history consisted of cataract extraction OU, laser posterior capsulotomy OS, chronic open-angle glaucoma OU, dry age-related macular degeneration OU.. The patient was using timolol maleate 0.5% OU qam and latanoprost 0.005% OU qhs.

The table summarizes findings from his ophthalmic examination.

PATIENT FINDINGS ON OPHTHALMIC EXAMINATION

	OD	**OS**
BCVA:	20/40	20/100
Pupils:	No APD	No APD
IOP (mmHg):	14	14
C/D Ratio:	0.4	1.0
Anterior Segment:	PCIOL	PCIOL
OCT:	V.M. adhesion	V.M. adhesion
Fundus Exam:	Hard drusen, disc edema, intraretinal hemorrhages, increased CRVP, dilated venous tree	Hard drusen
Diagnosis:	Central retinal vein occlusion OD	Advanced glaucoma OS

DECISION TO TREAT

The decision was made to initiate intravitreal bevacizumab injection OD to treat the patient's CRVO. The retina specialist was hoping to intervene before substantial structural damage developed that would potentially lead to permanent severe vision loss.

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Case Study

VISIT 1: BASELINE TESTING

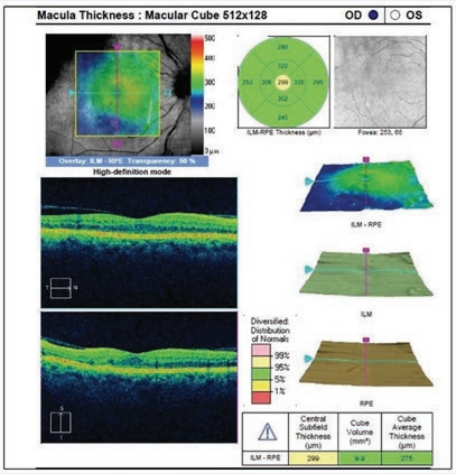
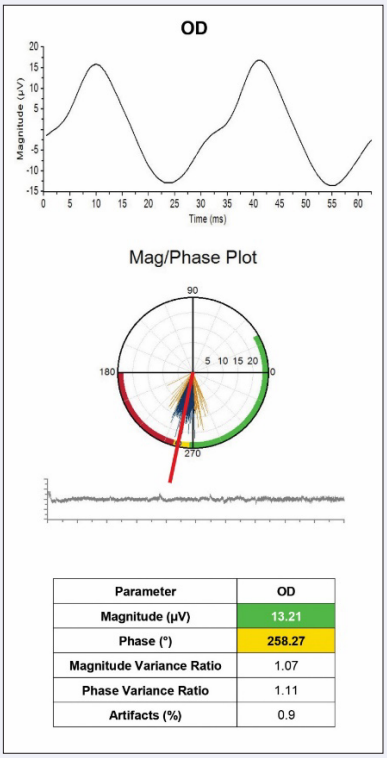


Figure 3. *Baseline OCT*



Parameter	OD
Magnitude (µV)	13.21
Phase (°)	258.27
Magnitude Variance Ratio	1.07
Phase Variance Ratio	1.11
Artifacts (%)	0.9

Figure 4. *Baseline Diopsys® ffERG/Flicker results.*

OCT shows minor macular involvement possibly due to CRVO, but no significant structural abnormalities (**Figure 3**). Diopsys® ffERG/Flicker results show dysfunction with an out of range Phase parameter OD (**Figure 4**). Note the angle of phase responses is 258.27°, with most responses falling in the ***lower, left quadrant*** of the Mag/Phase Plot. In contrast, a healthy eye will typically have similar responses to each flash stimulus so that the responses in the Mag/Phase plot will be tightly packed together close to or within the ***lower, right quadrant***.

VISIT 2: 1-MONTH POST FIRST BEVACIZUMAB INJECTION

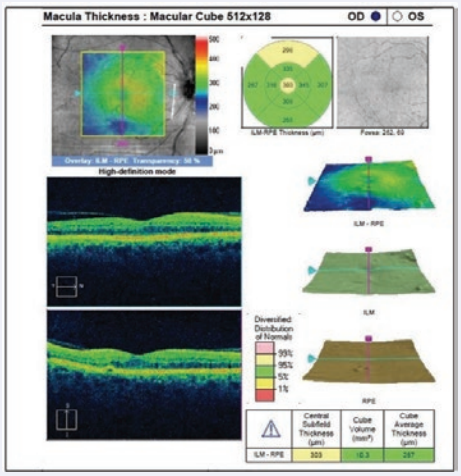
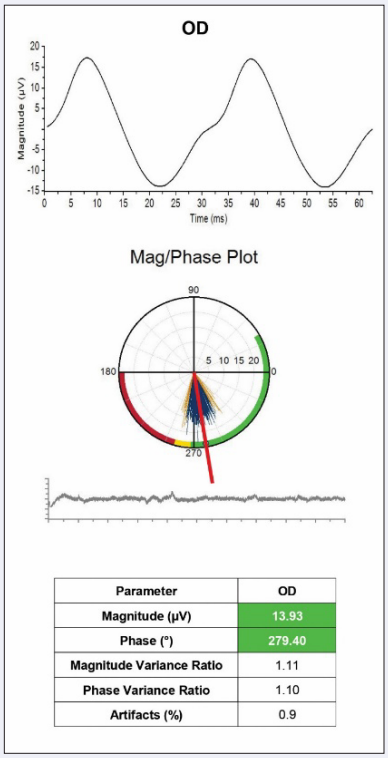


Figure 5. *OCT from 1 month post 1st bevacizumab injection.*



Parameter	OD
Magnitude (µV)	13.93
Phase (°)	279.40
Magnitude Variance Ratio	1.11
Phase Variance Ratio	1.10
Artifacts (%)	0.9

Figure 6. *Diopsys® ffERG/ Flicker results from 1 month post 1st bevacizumab injection.*

OCT shows no significant structural change (**Figure 5**). Diopsys® ffERG results show functional improvement, with an in-range Phase response of 279.40° (now within the lower, right quadrant) (**Figure 6**).

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Case Study

VISIT 3: 1 MONTH POST 2ND MONTHLY BEVACIZUMAB INJECTION (2 MONTHS POST BASELINE)

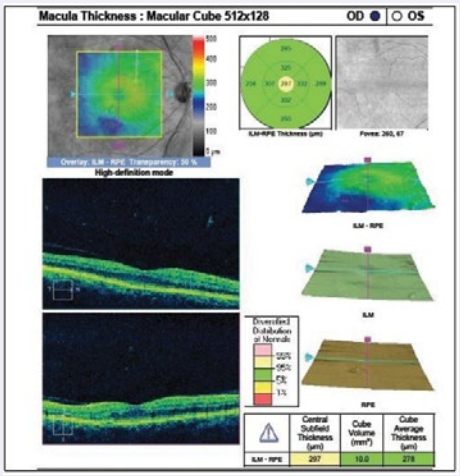
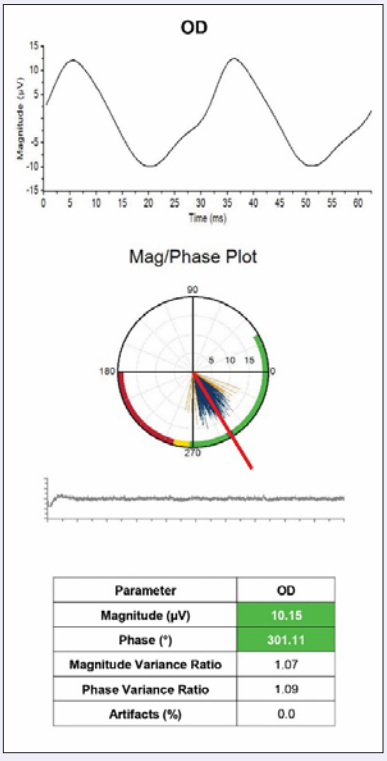


Figure 7. *OCT from 1 month post 2nd monthly bevacizumab injection.*



Parameter	OD
Magnitude (µV)	10.15
Phase (°)	301.11
Magnitude Variance Ratio	1.07
Phase Variance Ratio	1.09
Artifacts (%)	0.0

Figure 8. *Diopsys® ffERG/ Flicker results from 1 month post 2nd monthly bevacizumab injection.*

OCT shows no significant structural change (**Figure 7**). Diopsys® ffERG results show additional functional improvement, with an in-range Phase response of 301.11° (**Figure 8**).

VISIT 4: 1 MONTH POST 3RD MONTHLY BEVACIZUMAB INJECTION (3 MONTHS POST BASELINE)

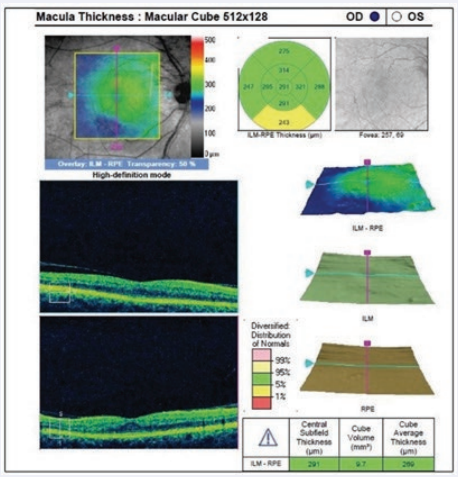
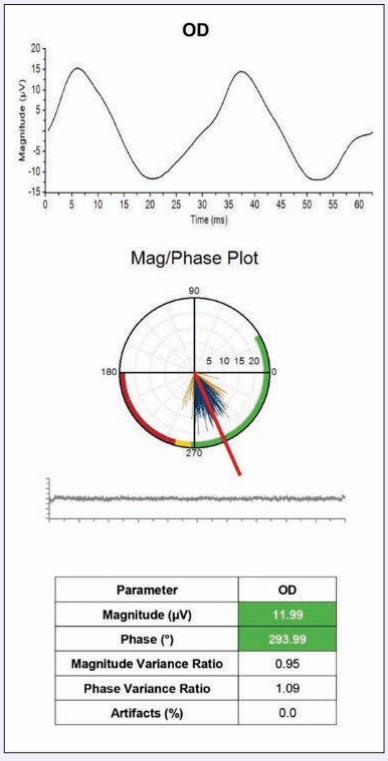


Figure 9. *OCT from 1 month post 3rd monthly bevacizumab injection.*



Parameter	OD
Magnitude (µV)	11.99
Phase (°)	293.99
Magnitude Variance Ratio	0.95
Phase Variance Ratio	1.09
Artifacts (%)	0.0

Figure 10. *Diopsys® ffERG/ Flicker results from 1 month post 2nd monthly bevacizumab injection.*

OCT shows no significant structural change (**Figure 9**). Diopsys® ffERG results show functional stability, with an in-range Phase response of 293.99° (**Figure 10**).

IMPACT ON CARE

On combining information from the OCT and Diopsys® ffERG/Flicker test that showed stability of structure and improvement with stability in function, the retina specialist felt that the patient could stop anti-VEGF treatment and continue care with careful follow-up.

Conclusion

Light induced visual-response is the only readily available modality to objectively measure retinal function. Flicker ERG measures the global function of the retina and is an essential diagnostic test for evaluating visual function. Advances in ERG technology now permit rapid, safe, reproducible, and well-tolerated testing in the office. This capability permits quantitative and longitudinal evaluation of retinal diseases that affect global retinal function. These include many of our most common conditions including diabetic retinopathy, vascular occlusive disease, uveitis, and inherited retinal dystrophies. This capability gives us the power to change how we evaluate disease progression, management, and therapy.

I encourage ophthalmologists to introduce ERG into their practices. The ability to objectively evaluate retinal functional health is important to patients and is a valued test in our diagnostic armamentarium.

LIV: Light Induced Visual-response™

Track progression. Tailor treatment.

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Performing LIV tests allow you to objectively evaluate retinal health now and over time for tailored treatment and more precise disease management.

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