
Medical Policy



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***Current Policy Effective Date: 5/1/25**
(See policy history boxes for previous effective dates)

Title: Electrophysiology (ERG), Multifocal Electrophysiology (mfERG) and Pattern Electrophysiology (pERG)

Description/Background

The electroretinogram (ERG) introduces a brief flash of light to the retina in order to elicit a mass electrical response. Electrophysiology testing assesses the function of the visual pathway from the photoreceptors of the retina to the visual cortex of the brain. The information obtained is for use in diagnosing or ruling out a variety of inherited retinal and ophthalmic diseases, toxic drug exposure, inflammatory conditions, intraocular foreign bodies and retinal vascular occlusions.

Visual Images

Light rays are transferred through the lens of the eye to the retina. The retina is made up of rods and cones (photoreceptors) that are sensitive to light. The retina converts the light (images) to electrical impulses. These electrical impulses then travel along the optic nerve to the brain and form a visual image.

Electrophysiology provides overall performance information about the retina (the light detecting portion of the eye) by measuring the electrical response of the photoreceptors (eye's light-sensitive cells). The obtained information helps to identify retinal degeneration and dystrophies.

Different Types of Testing

There are 3 types of electroretinogram: the full-field ffERG, the multifocal electroretinography (mfERG) and the pattern electroretinography (pERG).

The full-field ERG (ERG) uniformly scatters light over the entire retina and the response is recorded. ERG testing is proposed for use in diseases that have widespread retinal dysfunction (e.g., rod/cone dystrophies, cancer associated retinopathy, toxic retinopathies). It is used to detect loss of retinal function or distinguish between retinal and optic nerve lesions.

Multifocal electroretinography (mfERG) is an advanced form of electroretinography which produces a higher resolution and measures the photoreceptors activity. The mfERG provides a measure of cone system function over 61 or 103 discrete hexagonal retinal areas within the central 40–50° of the posterior pole centered on the macula. It enables the stimulation of multiple retinal areas simultaneously and recording of each response independently, providing a topographic measure of retinal electrophysiological activity.

Multifocal electroretinography (mfERG) helps to distinguish between diseases of the retina and diseases of the optic nerve when the retina appears normal. Due to the difficulties encountered in recording and analyzing mfERG it is recommended that they are performed by centers with an electrophysiologist familiar with mfERG testing.

Pattern ERG (pERG) is derived largely from the macular retinal ganglion cells and was designed to complement the full-field ERG in differentiating between maculopathy and generalized retinopathy. pERG uses an alternating pattern-reversal stimuli (i.e., checkerboard pattern) to assess the central retina region. It has been used as a sensitive indicator of dysfunction to detect subtle optic neuropathies. It has been proposed that pERG can be useful for assessing retinal ganglion cell function in conditions (i.e., glaucoma, ischemic optic neuropathy) and may be abnormal in diabetic retinopathy and idiopathic intracranial hypertension.

Regulatory Status

The following class II devices have received Federal Drug Administration (FDA) 510(k) approval. This may not be an all-inclusive list.

- Electroretinograph (Mchenry, IL) - 1976.
- GLAID Ocular Electrophysiology Device (Clearwater, FL) (2005) for use in the measurement of visual electrophysiologic potentials, including electroretinogram (ERG), pattern electroretinogram (pERG), visual evoked potential (VEP) and electrooculogram (EOG), as an aid in the diagnosis and management of Glaucoma when used in conjunction with other established methods of diagnosis and disease management.
- EDI VERIS System (Los Altos, CA.) (1999 - K983983) and modified in 2001 (K003442).
- RETeval Visual Electrodiagnostic Device (2015). The RETeval-DR™ is not currently marketed in the U.S.

Medical Policy Statement

The safety and effectiveness of full-field electroretinography (ffERG) and multifocal electroretinography (mfERG) has been established. They may be considered a useful diagnostic option for selected indications.

Pattern electroretinography (pERG) is considered experimental/investigational for all indications. There is insufficient scientific evidence in the current medical literature to indicate that this technology is as beneficial as the established alternatives.

Inclusionary and Exclusionary Guidelines

Inclusions:

Full-field electroretinography may be considered medically necessary when used to:

- Detect loss of retina function
- Distinguish between retinal and optic nerve lesions

Multifocal electroretinography may be considered medically necessary when used to detect chloroquine (Aralen®) and/or hydroxychloroquine (Plaquenil®) toxicity.

Note: See policy guidelines for more information regarding diagnosis of loss of retinal function or distinguishing between retinal lesions and optic nerve lesions.

Exclusions:

- Any indications not listed above
- Full-field electroretinography (ERG), multifocal ERG and pattern ERG used to evaluate, monitor or screen suspected or confirmed glaucoma
- Pattern electroretinography for any indication

Policy Guidelines

Full-Field Electroretinography (ffERG)

To diagnose loss of retinal function or distinguish between retinal lesions and optic nerve lesions:

- Toxic retinopathies, including those caused by intraocular metallic foreign bodies and Vigabatrin
- Achromatopsia
- Assessment of retinal function after trauma, especially in vitreous hemorrhage, dense cataracts, and other conditions where the fundus cannot be visualized photoreceptors; absent b-wave indicates abnormality in the bipolar cell region.
- Autoimmune retinopathies such as Cancer Associated Retinopathy (CAR), Melanoma Associated Retinopathy (MAR), and Acute Zonal Occult Outer Retinopathy (AZOOR)
- Choroideremia
- Cone dystrophy
- Congenital stationary night blindness
- Diabetic retinopathy
- Disorders mimicking retinitis pigmentosa
- Goldmann-Favre syndrome
- Gyrate atrophy of the retina and choroid
- Ischemic retinopathies including central retinal vein occlusion (CRVO), branch vein occlusion (BVO), and sickle cell retinopathy
- Leber's congenital amaurosis
- Retinal detachment
- Retinitis pigmentosa and related hereditary degenerations
- Retinitis punctata albescens
- Usher Syndrome

- X-linked juvenile retinoschisis

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

92273 92274

Other codes (investigational, not medically necessary, etc.):

0509T

Note: Code(s) may not be covered by all contracts or certificates. Please consult customer or provider inquiry resources at BCBSM or BCN to verify coverage.

Rationale

Clinical electrophysiological testing of the visual system are noninvasive tests and provide an objective indication of function relating to different locations and cell types within the visual system.

ERG measures the electrical activity generated by neural and non-neuronal cells in the retina in response to a light stimulus. ERGs are usually obtained using electrodes embedded in a corneal contact lens, or a thin wire inside the lower eyelid, which measure a summation of retinal electrical activity at the corneal surface.

The full field electroretinogram (ffERG) detects loss of retinal function or distinguishes between retinal and optic nerve lesions. The global response of the retina to brief flashes of light provide an assessment of generalized retinal function under light- and dark- adapted conditions. ffERG's have input from both rod and cone systems, but the dark-adapted rod system contribution dominates in a normal retina. The ffERG helps to distinguish retinal degeneration and dystrophies. Multi-focal electroretinography (mfERG) is a higher resolution form of the ffERG, enabling assessment of ERG activity in small areas of the retina. Pattern ERG (pERG) uses pattern-reversal stimuli (i.e., checkerboard) and is used to detect subtle optic neuropathies.

During the ERG test, the photoreceptors produce tiny amounts of electricity in response to brief flashes of light. The amount of light that enters the eye measured against the electrical response that is generated indicates how well the rods and cones are working. Differences in responses are analyzed to differentiate diseases which affect the rods from those which affect the cones or other cells in the retina.

ERG

The full-field ERG enables the distinction between generalized outer and inner retinal dysfunction and predominate rod or cone system dysfunction. ERGs can help differentiate between a wide range of disorders when symptoms and/or clinical signs suggest a retinopathy.

Garcia et al (2018) summarized the characteristics of the pathologies in which a negative response of a full field electroretinogram can be useful. The definition of the negative response of the full field electroretinogram is the presence of a b-wave with less amplitude than the a-wave (b/a ratio <1) in the combined response of cones and rods. The presence of this pattern reflects an alteration in the bipolar cells, the Müller cells, or in the transmission of the stimulus from the photoreceptors to the bipolar cells, with preserved photoreceptor function. Alterations in the different ERG waves help to indicate which layer of the retina is producing the alteration. Hereditary disease (i.e., different types of congenital stationary night blindness (CSNB), X-linked juvenile retinoschisis and Duchenne and Becker muscular dystrophies (DMD/BMD) are typical of the negative bilateral and symmetric ERG. Acquired diseases (i.e., some types of immunomediated retinitis such as Birdshot retinochoroidopathy, autoimmune retinopathy or retinal toxicity induced by different drugs or siderosis can be found in negative unilateral ERGs.

Robson et al (2018) provided an introduction to standard visual electrodiagnostic procedures in widespread use and describes the common clinical indications for which these tests are applicable. Full-field ERGs are global responses of the retina to brief flashes of light and provide an assessment of generalized retinal function under light- and dark-adapted conditions. A Ganzfeld (German for “whole field”) stimulator, provides a uniformly illuminated field by delivering a range of flash stimuli that evenly illuminates the maximal area of retina. ERG arises in the inner retinal rod bipolar cells and is the only standard test that selectively monitors rod system function. Abnormality of the dark-adapted ffERG can be caused by either rod photoreceptor dysfunction or selective dysfunction occurring post-phototransduction or at the level of the inner retinal rod bipolar cells. ffERGs have input from both rod and cone systems, but the dark-adapted rod system contribution dominates in a normal retina. The cone system contribution to both dark-adapted ffERG a- and b- waves is minor in a normal retina but can be of greater significance in patients with disease primarily or exclusively affecting the rod system. The full-field ERG enables the distinction between generalized outer and inner retinal dysfunction and predominant rod or cone system dysfunction. It is stressed that the full-field ERG is largely generated by the retinal periphery and there is minimal contribution from the macula. Electrophysiological assessment of the macular function requires the use of different techniques such as the pattern ERG or multifocal ERG. pERG is derived largely from the macular retinal ganglion cells and complements the full-field ERG, in differentiating between maculopathy and generalized retinopathy. The pERG is recorded to an alternating high-contrast checkerboard using a corneal electrode. The transient pERG has 2 major components of diagnostic value. Both components reflect macular retinal ganglion cell function. Furthermore, comparison of responses to standard and additional large-field stimulus may help characterize the area of macular dysfunction, although spatial resolution is lower than for the mfERG. The multifocal ERG provides a measure of cone system function, within the central 40°–50° of the posterior pole centered on the macula. The spatial resolution of the mfERG is better than for the pERG and full-field ERGs, and thus enables improved characterization of focal central, annular, hemifield or discrete paracentral areas of posterior pole dysfunction. In conclusion, the published studies do not support pERG nor ffERG as diagnostic for glaucoma.

The American Academy of Ophthalmology (2022) recommendations utilizing full field ERG to evaluate and/or monitor inherited retinal degenerative diseases including rod-cone degenerations/dysfunctions (e.g., retinitis pigmentosa, congenital stationary night blindness), cone-rod degenerations (e.g., achromatopsia), chorioretinal degenerations (e.g., CHM-associated retinal degeneration - choroideremia) and gyrate atrophy, inherited dystrophies that involve the macula (e.g., cone degeneration, X-linked retinoschisis, ABCA4-associated

macular degeneration [Stargardt disease], and PRPH2-associated macular degeneration [pattern dystrophy]). Full-field ERG is not necessary in Best disease, North Carolina macular dystrophy or in cases of pattern dystrophy limited to the macula. However, if electro-oculogram testing is not available, full-field ERG should be normal in Best disease. A full-field ERG is appropriate for a patient with macular changes for whom 1 is considering cone or cone-rod dystrophy in the differential diagnosis. Also, a non-detectable ERG is not recommended to be repeated.

mfERG

Retinal toxicity is unpredictable and can occur even at relatively low doses of medications known to be retinal toxic (i.e., hydroxychloroquine, chloroquine). If early recognition is detected, most ocular side effects are reversible after cessation of the medication in drug-induced ocular toxicity. Failure to detect toxic effects in the early stages, may cause potentially irreversible ocular dysfunction with associated visual loss.

mfERG is a useful tool in detecting early abnormalities in the macular, perimacular and mid-peripheral retina which may not be obvious on fundus examination, such as those caused by chloroquine (CQ) or hydroxychloroquine (HCQ) toxicity. CQ and HCQ are antimalarial drugs with a well-established beneficial role in the treatment of rheumatoid arthritis, systemic lupus erythematosus and other connective tissue and skin disorders. CQ and HCQ are melanotropic drugs that become concentrated in melanin containing structures of the eye, such as the iris, ciliary body, retinal pigment epithelium and choroid. The ocular side effects range from keratopathy to potentially blinding retinopathy.

Wallace (2024; UpToDate) indicated the earliest retinal abnormalities are asymptomatic and can only be detected by ophthalmologic examination. “Premaculopathy” changes consist of macular edema, increased pigmentation, increased granularity, and loss of the foveal reflex. Subtle functional loss in the paracentral retina can occur before biomicroscopic changes in the RPE. Detection of changes at this stage, using techniques such as...multifocal electroretinography, is desirable since such changes are likely to stabilize without loss of visual acuity and, in some cases, retinopathy may be completely reversible upon discontinuation of the medication. With the advanced electrophysiological screening methods, up to 7 percent of individuals taking HCQ have retinal changes after 5 years of use. These are rarely symptomatic but may require alterations in the dosing regimen and drug discontinuation.

The American Academy of Ophthalmology (2016) recommendations utilizing mfERG for monitoring of CQ and HCQ retinopathy. The goal of screening is to recognize toxicity at an earlier stage. Chloroquine, and less frequently HCQ, can cause whorl like intraepithelial deposits (verticillata) in the cornea. These corneal changes are not a direct marker for retinal damage, are not associated with visual loss, and in contrast to retinopathy are usually reversible. If drug exposure continues, the area of functional disturbance expands, retinal pigment epithelium loss occurs with eventual loss of visual acuity. Retinopathy (retinal pigment epithelium loss) is not reversible, and there is no present therapy. Recognition at an early stage (before any retinal pigment epithelium loss) is important to prevent central visual loss.

pERG

Bowd et al (2009) assessed the ability of the new pERG optimized for glaucoma detection (PERGLA) paradigm to discriminate between healthy individuals and individuals with glaucomatous optic neuropathy (GON) in a cross-sectional study. One hundred forty-two eyes

of 71 participants (42 healthy and 29 with GON in at least 1 eye) enrolled in the University of California, San Diego. Healthy individuals were identified as those with healthy-appearing optic disc by examination and masked stereoscopic optic disc photograph evaluation.

Glaucomatous optic neuropathy was defined based on stereophotograph evaluation. The PERGLA recordings were obtained within 6 months of standard automated perimetry (SAP) testing. Dependent variables were PERGLA amplitude, phase, amplitude asymmetry, phase asymmetry, and SAP pattern standard deviation (PSD) and mean deviation (MD). Diagnostic accuracy (sensitivity and specificity) of the PERGLA normative database for classifying healthy and glaucomatous individuals was determined. In addition, performance (areas under receiver operating characteristic curves [AUCs]) of PERGLA amplitude and phase for classifying healthy (n=84) and GON (n=50) eyes was determined. Results from both analyses were compared with those from SAP. Sensitivity and specificity of the PERGLA normative database were 0.76 and 0.59, respectively, compared with 0.83 and 0.77 for SAP. The AUCs for PERGLA amplitude and phase were 0.75 and 0.50 (chance performance). The AUCs for SAP PSD and MD were 0.83 and 0.78. Authors concluded that pERG recorded using the PERGLA paradigm can discriminate between healthy and glaucoma eyes, although this technique performed no better than SAP at this task. Low specificity of the PERGLA normative database suggests that the distribution of recordings included in the database is not ideal.

Sehi et al (2009) examined the relationship between retinal ganglion cell (RCG) function measured using PERGLA, retinal nerve fiber layer thickness and optic nerve head topography. Twenty-nine individuals with healthy eyes, 28 patients with glaucoma, and 37 people who were suspected of having glaucoma were enrolled. All subjects underwent optical coherence tomography, scanning laser polarimetry with enhanced corneal compensation, confocal scanning laser ophthalmoscopy using the Heidelberg retina tomograph, and pattern electroretinogram examination optimized for glaucoma screening. Only 1 eye per subject was enrolled. If both eyes met eligibility criteria, 1 eye was randomly selected. RCG function measured using PERGLA was reduced in glaucoma but only demonstrated modest correlations with central SAP sensitivity values and structural measures of optic nerve topography and retinal nerve fiber layer thickness. Authors concluded that, longitudinal studies are warranted in order to better understand the role of pERG as a surrogate measure of RGC dysfunction in glaucoma suspects and patients with glaucomatous optic neuropathy.

Tafreshi et al (2010) compared the diagnostic accuracy of the PERG to that of SAP, short-wavelength automated perimetry (SWAP), and frequency-doubling technology (FDT) perimetry for discriminating between healthy and glaucomatous eyes in 83 eyes of 42 healthy individuals and 92 eyes of 54 glaucoma patients. Subjects were tested with pattern ERG for glaucoma detection, SAP, SWAP, and FDT within 9 months. Receiver operating characteristic (ROC) curves were generated and compared for pattern ERG amplitude and SAP, SWAP and FDT mean deviation and pattern standard deviation (PSD). The area under the ROC curve for pattern ERG amplitude was 0.744 (95% Confidence Interval = 0.670, 0.818). The ROC curve area was 0.786 (0.720, 0.853) for SAP PSD, 0.732 (0.659, 0.806) for SWAP PSD and 0.818 (0.758, 0.879) for FDT PSD. At 95% specificity, sensitivities of SAP and FDT PSD were significantly higher than that of pattern ERG amplitude; at 80% specificity, similar sensitivities were observed among tests. Agreement among tests was slight to moderate. Authors concluded that pattern ERG amplitude using the pattern ERG for glaucoma detection paradigm is significantly different between healthy eyes and early glaucoma eyes, and the diagnostic accuracy of pattern ERG amplitude likely is similar to that of SAP and SWAP and somewhat worse than FDT. Pattern ERG (and other electrophysiological

techniques) has the advantage of being a mainly objective visual function test and may be useful for patients who are unable to perform reliably on psychophysical tests. Further high quality studies with larger populations are needed to assess the comparative efficacy and acceptability of pERG in individuals with glaucoma.

Banitt et al (2013) conducted a longitudinal cohort study that included 107 adults (201 eyes) at risk of glaucoma. pERG amplitudes, optical coherence tomography (OCT) imaging of retinal nerve fiber layer (RNFL) and standard automated perimetry testing were compared at 6-month intervals. Over a 4-year period, determinations were made regarding the time lag between loss of RGC function and loss of RNFL thickness. The RNFL thickness did not decrease until the pERG amplitude had lost at least 50% of its normal value for age, indicated by post hoc comparisons showing highly significant differences between RNFL thicknesses of eyes in the stratum with the most severely affected pERG amplitude ($\leq 50\%$ of normal) and the two strata with the least affected pERG amplitudes ($> 70\%$). The authors concluded from the results of the study that there was an approximate time lag of 8 years between a 10% loss in pERG amplitude and a 10% loss in RNFL thickness. In patients who are glaucoma suspects, pERG signal anticipates an equivalent loss of OCT signal by several years although this study did not confirm the utility of such findings in improving care and outcome of patients.

Jafarzadehpour et al (2013) explored RGC dysfunction in glaucoma suspects and patients with early primary open angle glaucoma (POAG) using pERG. Twenty glaucoma suspects (glaucomatous optic disc appearance), 15 early POAG (based on abnormal discs and abnormal visual fields) and 16 normal controls were enrolled. Transient pERG was recorded in response to 0.8° and 16° black and white checkerboard stimuli. Amplitude and peak time (latency) of the P50 and N95 components of the PERG response, and the ratio of N95 amplitude in response to 0.8° and 16° checks were measured. N95 peak time (latency) was significantly increased in both early manifest POAG and glaucoma suspects as compared to normal controls ($p < 0.001$). In early POAG, N95 amplitude in response to small (0.8°) checks and the small/large check ratio were reduced in comparison to normal eyes ($p < 0.05$). However, in glaucoma suspects no significant N95 amplitude reduction was observed. No significant difference was observed among the study groups in terms of P50 amplitude or peak time. The N95 PERG response demonstrated uncoupled peak time and amplitude alterations in glaucoma. N95 peak time was significantly increased both in glaucoma suspects and early POAG; N95 amplitude reduction was present only in early POAG. PERG may detect RGC dysfunction (increased latency) before cell death (decreased amplitude) occurs. The sample size in this study is too small to prove efficacy of pERG as a diagnostic tool.

Preiser et al (2013) compared photopic negative response (PhNR) and pERG in different stages of the glaucoma. Eleven eyes with preperimetric glaucoma (glaucomatous optic disc with normal field); 18 eyes with glaucoma; and 26 normal eyes were included in the study. PhNR (flash strength from 0.1-4 $\text{cd} \cdot \text{s}/\text{m}^2$) and steady-state pERG and analyzed PhNR amplitude (baseline to 72 ms trough); PhNR/b-wave ratio; pERG amplitude; and pERG ratio ($0.8^\circ/16^\circ$) were obtained. Identification of PhNR structure was only reliable $\geq 1 \text{ cd} \cdot \text{s}/\text{m}^2$ flash strength; amplitude and receiver operating characteristics (ROC) area under curve (AUC) changed little from 1 to 4 $\text{cd} \cdot \text{s}/\text{m}^2$. Both PhNR and pERG (amplitude and ratio) were reduced in preperimetric and more so in manifest glaucoma. AUCs based on PhNR/pERG amplitudes were not significantly different from chance in preperimetric glaucoma (AUCs 0.61/0.59) but were significant in manifest glaucoma (0.78/0.76); ratios were significant in both glaucoma groups (0.80/0.73 and 0.80/0.79). In spite of that, PhNR ratio and pERG ratio were not

significantly correlated ($r = 0.22$ across all groups); an ROC based on a combination of both reached AUCs of 0.85/0.90 for preperimetric/manifest glaucoma. Authors concluded that both PhNR and pERG performed similarly to detect glaucoma; for both, ratios performed better than amplitudes. PhNR had the advantage of not requiring clear optics and refractive correction. pERG had the advantage of being recorded with natural pupils. Evidence is limited by a small study population.

Glaucoma

Glaucoma is a progressive optic neuropathy associated with injury to retinal ganglion cell axons, frequently due to elevated intraocular pressure.

Jacobs (2022) published guidance on the epidemiology, clinical presentation, and diagnosis of open-angle glaucoma. The guidance indicates there is not a "gold standard" test for identifying glaucoma. There is controversy regarding which (if any) populations should be screened, what screening tests should be performed, and with what frequency. The guidance adopted the American Academy of Ophthalmology (AAO) recommendations that individuals over age 40 undergo periodic comprehensive eye evaluations by an ophthalmologist to screen for glaucoma. To date, automated perimetry has become the standard of care for optometric and ophthalmic practice in the detection and monitoring of glaucoma.

Jampel et al (2011) reviewed the published literature to summarize and evaluate the effectiveness of visual function tests in diagnosing and monitoring the progression of glaucoma. The authors concluded that advances in technology and analytic tools over the past decade had provided them with more rapid and varied ways of assessing visual function in glaucoma, but they have yet to produce definitive guidance on the diagnosis of glaucoma or its progression over time. The authors determined that further research on an objective measure of visual function is needed.

Bach et al (2013) reported on non-invasive monitoring of the function of most processing stages along the visual pathway. The multifocal electroretinogram (mfERG), although often employed, is less affected in glaucoma than the 2 direct measurements of retinal ganglion cell function, namely the pattern ERG (pERG) and the photopic negative response (PhNR) of the ERG. For the PhNR, no longitudinal study is available as yet. The multifocal pERG can spatially resolve ganglion cell function but its glaucomatous reduction is typically pan retinal, even with only local field changes therefore, its topographic resolution is of no advantage in glaucoma. The multifocal visual evoked potential promises objective perimetry and shows sensitivity and specificity comparable with standard automated perimetry but has not been established as a routine tool to date.

Nouri-Mahdavi (2014) stated that testing the peripheral field of vision is the mainstay for detection of glaucoma deterioration. Various methods and algorithms are currently available for detection of early glaucoma or establishing disease progression. ERG/mfERG was not mentioned as a management tool.

Wilsey et al (2016) reviewed the different types of electroretinography (Full-field ERG, multifocal ERG and pattern ERG) and their role in glaucoma screening and monitoring. Historically, the full-field flash ERG has not been useful for glaucoma diagnosis since it is dominated by the responses of neurons of the distal retina, namely photoreceptors and bipolar cells. Generally the full-field ERG does not reflect the responses of retinal ganglion cells

(RGCs), which are the primary neuron affected by glaucoma. Though it remains a matter of some mild controversy, the evidence that outer retinal (e.g., photoreceptor) damage occurs in glaucoma is limited, at least until later-stages of disease with long-standing vision loss secondary to RGC death and axon degeneration. In this regard, the mfERG can be a useful adjunct for glaucoma management in so far as it can help to determine if a patient is also suffering from additional disease processes affecting the outer retina. The multifocal technique enables assessment of multiple independent stimulus locations (up to hundreds) simultaneously, thereby vastly decreasing the time required to accomplish a topographic representation of ERG and visual evoked cortical responses. One might predict that a combination of a patterned stimulus with the multifocal technique would prove to be highly effective for glaucoma diagnosis. Though abnormalities can be readily detected in mfERG recordings from glaucomatous eyes, the advantage of topographic analysis offered by the technique has not proven important for glaucoma diagnosis. Results to date reveal only a general amplitude reduction centrally with little or no topographic relationship to even advanced visual field loss. pERG like any test of RGC function depends on a cascade of intact outer retinal signals, so without a multifocal ERG to evaluate specifically the macular cone and cone bipolar responses, the pERG alone is not a specific assay of RGC function. The pERG will yield abnormal findings in patients with middle and outer retinal damage. This is important since most glaucoma patients are older and may suffer concomitant age-related decline of outer retinal function too. pERG was mentioned as potentially the most beneficial adjunct in the diagnosis and management of glaucoma suspects (with normal or near normal visual fields and/or RNFL thickness) by helping to stratify risk: for those suspect eyes with a severely reduced pERG (and no other evidence of outer retinal dysfunction), it may be prudent to increase frequency of follow-up and/or initiate therapy.

Salgarello et al (2018) evaluated the clinical ability of pERG to detect functional losses in the affected hemifield of open-angle glaucoma patients with localized perimetric defects. Thirty-two eyes of 29 glaucomatous patients with a perimetric, focal 1-hemifield defect, 10 eyes of 10 glaucomatous patients with a diffuse perimetric defect, and 18 eyes of 18 age-matched normal subjects were selected. Hemifield pERG (h-pERG) amplitudes, perimetric deviations, and retinal nerve fiber layer thicknesses showed losses ($p < 0.001$) when comparing affected with unaffected hemifields of localized glaucomatous eyes. No differences were found in h-pERG amplitudes between hemifields of normal or diffuse glaucomatous eyes. h-pERG amplitude ratios (affected/unaffected hemifield) in localized glaucoma were lower ($p < 0.001$) than the ratios from normal or diffuse glaucomatous eyes. The areas under the receiver operating characteristic curves for h-pERG amplitude ratios, comparing localized-defect glaucomatous eyes with normal or diffuse glaucomatous eyes, were 0.93 and 0.91, respectively. Authors acknowledged being the first study to evaluate the clinical use of steady-state h-pERG in a cohort of glaucomatous patients with well-defined hemifield losses. Limitations were also discussed and it was concluded that these issues should be further addressed in future studies.

Amarasekera et al (2018) reported on a cross sectional study of 41 healthy volunteers with 41 glaucoma patients. Steady-state pERG parameters compared were MagnitudeD, MagnitudeD/Magnitude ratio, and the signal-to-noise ratio. Short-duration transient visual evoked potential parameters compared were amplitude and latency. MagnitudeD was the most accurate steady state-pERG parameter for discerning glaucomatous dysfunction across all stimuli. Authors concluded that steady-state pattern electroretinogram was effectively able to discern between glaucomatous and healthy eyes.

Senger et al (2020) conducted a systemic review searching for articles published from January 1, 2014 to July 1, 2019. A total of 38 studies were selected and the data of 30 of them were tabulated. Among the 30 studies selected, the photopic negative response and the reversal pattern electroretinogram were found to be the major methods used to record the electroretinographic responses generated by the retinal ganglion cell. Their multifocal versions and the multifocal visual evoked potential were also proposed during this period. In general, the results underscored a consistent but general correlation between the amplitude and latency measures and routine tests for glaucoma, such as perimetry and optical coherence tomography. In agreement with previous reviews, clinical electrophysiological testing of the visual system reasonably matched with both the structural and functional analyses for glaucoma. Authors concluded that no definitive indications of these tests have been established either at early detection or during follow-up of the disease, and easier protocols and better topographical correspondence with current glaucoma tests are warranted.

Summary

The full-field ERG enables the distinction between generalized outer and inner retinal dysfunction and predominate rod or cone system dysfunction. ERGs can help differentiate between a wide range of disorders when symptoms and/or clinical signs suggest a retinopathy.

For those individuals utilizing hydroxychloroquine and chloroquine, mfERG is widely used for the evaluation of drug-induced retinopathy. It is particularly useful for the diagnosis of retinal toxicity limited to the central retina. mfERG findings have demonstrated that early retinal toxicity is reversible. The prognosis of those with early retinopathy was better: the changes stabilized and the risk of progression to visual loss was minimal. Guidelines for screening, (e.g., AAO) are increasingly emphasizing the use of newer objective tests annually to supplement clinical examination and perimetry.

For individuals with glaucoma, the 3 different types of electroretinography were evaluated. Very limited roles for specific types of ERG emerged from the recently published literature which aid clinicians in caring for glaucoma individuals. Multiple, recent, small, single-center studies, short in duration indicated positive results for the identification of early stages of glaucoma using pERG. Larger, longer duration, multi-center studies are needed to confirm these findings. There is insufficient evidence in the peer-reviewed medical literature to establish the role of ERG, mfERG or pERG in glaucoma screening or monitoring.

Supplemental Information

American Academy of Ophthalmology

The AAO (2011) concluded that ERG has yet to produce definitive guidance on the diagnosis of glaucoma or its progression over time and that further research specific to objective measures of visual function is needed.

The 2015 AAO Preferred Practice Guidelines, “Primary Open-Angle Glaucoma Suspect” and the “Primary Open-Angle Glaucoma,” recommend comprehensive eye examinations for individuals that have risk factors for glaucoma, but neither mention ERG as a diagnostic tool.

AAO (2016) Comprehensive Adult Medical Eye Evaluation Guideline states “electrophysiologic testing” is not part of a routine comprehensive medical eye evaluation but does acknowledge it as an “additional option for diagnostic testing”. Furthermore, the guideline does not specifically address ERG or offer any grade of evidence specific to electrophysiologic testing.

AAO (2020) Summary Benchmarks for Preferred Practice Pattern Guidelines do not mention electroretinopathy in their initial physical examination or diagnostic testing recommendations.

AAO (2022) guidelines recommend the following:

- Full-field electroretinogram (ERG) is important for diagnosis and staging of diffuse photoreceptor disease, evaluating the retina-wide function of rods and cones.
 - Delays in cone b-wave implicit times are an early sign of disease and reflect retina-wide involvement.
 - Young patients with disease that appears to be limited to the macula benefit from full-field ERGs to rule out retina-wide disease.
 - Multifocal or pattern ERG testing can be useful for detection and monitoring disease progression for diseases that primarily affect the macula. However, its accuracy can be limited in those patients with notable loss of central vision who are unable to maintain steady fixation.
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Government Regulations

National:

No National Determination available.

Local:

Local Coverage Determination: Visual Electrophysiology Testing (L37015) Effective date: 7/17/17; Revision effective date: 10/1/23

Coverage Indications, Limitations, and/or Medical Necessity:

ELECTRORETINOGRAPHY (ERG)

1. To diagnose loss of retinal function or distinguish between retinal lesions and optic nerve lesions:
 - a. Toxic retinopathies, including those caused by intraocular metallic foreign bodies and Vigabatrin
 - b. Diabetic retinopathy
 - c. Ischemic retinopathies including central retinal vein occlusion (CRVO), branch vein occlusion (BVO), and sickle cell retinopathy
 - d. Autoimmune retinopathies such as Cancer Associated Retinopathy (CAR), Melanoma Associated Retinopathy (MAR), and Acute Zonal Occult Outer Retinopathy (AZOOR)
 - e. Retinal detachment
 - f. Assessment of retinal function after trauma, especially in vitreous hemorrhage, dense cataracts, and other conditions where the fundus cannot be visualized photoreceptors; absent b-wave indicates abnormality in the bipolar cell region.
 - g. Retinitis pigmentosa and related hereditary degenerations
 - h. Retinitis punctata albescens

- i. Leber's congenital amaurosis
- j. Choroideremia
- k. Gyrate atrophy of the retina and choroid
- l. Goldmann-Favre syndrome
- m. Congenital stationary night blindness
- n. X-linked juvenile retinoschisis
- o. Achromatopsia
- p. Cone dystrophy
- q. Disorders mimicking retinitis pigmentosa
- r. Usher Syndrome

2. To detect chloroquine (Aralen) and hydroxychloroquine (Plaquenil) toxicity (mfERG) per the American Academy of Ophthalmology (AAO) guidelines

ERG in Glaucoma (non-covered)

Limitations:

Testing shall be performed by physicians who have evidence of knowledge, training, and expertise to perform and interpret these tests. This training and expertise must have been acquired within the framework of an accredited school, residency or fellowship program.

Local Coverage Article: Billing and Coding: Visual Electrophysiology Testing (A57599)

Original effective date: 11/1/19; Revision effective date: 11/30/23

The billing and coding information in this article is dependent on the coverage indications, limitations and/or medical necessity described in the related LCD.

Code	Description
92273	Electroretinography (erg), with interpretation and report; full field (i.e., ffERG, flash erg, ganzfeld erg)
92274	Electroretinography (erg), with interpretation and report; multifocal (mfERG)
0509T	Electroretinography (ERG) with interpretation and report, pattern (PERG)

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

Corneal Hysteresis Measurement for Glaucoma
 Ophthalmologic Techniques that Evaluate the Posterior Segment Glaucoma
 Optical Coherence Tomography Imaging, Anterior Eye
 Retinal Care for Diabetic Retinopathy

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 12/26/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/1/21	2/16/21		Joint policy established
5/1/22	2/15/22		Routine maintenance
5/1/23	2/21/23		Routine maintenance (slp) Vendor Managed: N/A
5/1/24	2/20/24		Routine maintenance (slp) Vendor managed: N/A
5/1/25	2/18/25		Routine maintenance (slp) Vendor managed: N/A

Next Review Date: 1st Qtr, 2026

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: ELECTRORETINOGRAPHY (ERG), MULTIFOCAL ELECTRORETINOGRAPHY (MFERG) AND PATTERN ELECTRORETINOGRAPHY (PERG)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	Refer to the Medicare information under the Government Regulations section of this policy.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.
- *Duplicate (back-up) equipment is not a covered benefit.*