Oregon Health & Science University
School of Medicine

Scholarly Projects Final Report

Title *(Must match poster title; include key words in the title to improve electronic search capabilities.)*

A Retrospective Study of Electroretinography (ERG) Utility in Birdshot Chorioretinopathy (BCR)

Student Investigator's Name

Aseel Alsamarraie

Date of Submission *(mm/dd/yyyy)*

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Graduation Year

2022

Project Course *(Indicate whether the project was conducted in the Scholarly Projects Curriculum; Physician Scientist Experience; Combined Degree Program [MD/MPH, MD/PhD]; or other course.)*

Scholarly Project

Co-Investigators *(Names, departments; institution if not OHSU)*

None

Mentor's Name

Dr. Paul Yang

Mentor's Department

Casey Eye Institute

Scholarly Project Final Report

Concentration Lead's Name

Dr. Mark Baskerville

Project/Research Question

What are the sensitivities and specificities of ERG findings in predicting BCR disease worsening requiring treatment escalation?

Type of Project *(Best description of your project; e.g., research study, quality improvement project, engineering project, etc.)*

Research study

Key words *(4-10 words describing key aspects of your project)*

Birdshot chorioretinopathy; retinopathy; electroretinography

Meeting Presentations
If your project was presented at a meeting besides the OHSU Capstone, please provide the meeting(s) name, location, date, and presentation format below (poster vs. podium presentation or other).

None

Publications *(Abstract, article, other)*
If your project was published, please provide reference(s) below in JAMA style.

None

Submission to Archive
Final reports will be archived in a central library to benefit other students and colleagues. Describe any restrictions below (e.g., hold until publication of article on a specific date).

No restrictions

Next Steps
What are possible next steps that would build upon the results of this project? Could any data or tools resulting from the project have the potential to be used to answer new research questions by future medical students?

Statistical analysis

Please follow the link below and complete the archival process for your Project in addition to submitting your final report.

https://ohsu.ca1.qualtrics.com/jfe/form/SV_3ls2z8V0goKiHZP

Scholarly Project Final Report

Student's Signature/Date *(Electronic signatures on this form are acceptable.)*
This report describes work that I conducted in the Scholarly Projects Curriculum or alternative academic program at the OHSU School of Medicine. By typing my signature below, I attest to its authenticity and originality and agree to submit it to the Archive.

X _____

Student's full name

Mentor's Approval *(Signature/date)*

X _____

Mentor Name

Scholarly Project Final Report

Report: *Information in the report should be consistent with the poster, but could include additional material. Insert text in the following sections targeting 1500-3000 words overall; include key figures and tables. Use Calibri 11-point font, single spaced and 1-inch margin; follow JAMA style conventions as detailed in the full instructions.*

Introduction *(≥250 words)*

For a disease that confers relatively high morbidity in the form of irreversible blindness, contrarily little is known about its pathogenesis, treatment, and prognosis: Birdshot chorioretinopathy (BCR) is a progressive binocular disease characterized by round white fundus lesions following a "birdshot" pattern comprising approximately 7% of posterior uveitis cases in America.[1] Beyond a strong association with the HLA-A29 allele (present in over 90% of BCR patients), its etiology is unknown.[1] Symptoms include blurred vision, photopsia, scotomas, nyctalopia, and/or decreased color vision that typically develop(s) years before the fundus findings required for diagnosis.[1] Although BCR can be fully treated with no remission after treatment cessation, visual disturbances and blindness that develop over the disease course are irreversible, leaving 9.8% of patients legally blind at follow-up.[1]

Annual electroretinography (ERG) is a mainstay of BCR monitoring.[1] Research shows that treatment with corticosteroids and/or immunosuppressants can improve BCR ERG findings such as delayed implicit times and decreased signal amplitudes and improve prognosis for central visual acuity and maintenance of visual fields.[1] While ERG findings seemingly correlate with disease status and visual prognosis, research on the relationship is limited with no established standards of what ERG findings indicate disease progression requiring treatment escalation to improve prognosis.

To address this knowledge gap, the research presented aims to determine the sensitivities and specificities of various ERG parameters in predicting BCR disease progression by retrospectively examining the longitudinal relationship between ERG findings and disease status in BCR patients at the authors' institution. If disease progression can be approximated by ERG, then this research may help set standards of ERG findings that guide ophthalmologists to escalate treatment in a timely manner to reduce the incidence of blindness in BCR.

Methods *(≥250 words)*

In 2021, a retrospective analysis of all Casey Eye Institute (CEI) electronic health records (EHR) through 2020 was conducted to identify patients with a diagnosis of BCR and at least one available ERG. Each ERG belonging to these patients was evaluated for 14 total parameters measured in the right eye, measured in the left eye, and averaged between both eyes. Under scotopic and photopic conditions, the b wave amplitude (μV), b wave implicit time (ms), a wave amplitude, a wave implicit time, b:a wave amplitude ratio, and oscillatory potential index (μV) were evaluated. Under photopic conditions, 30-Hz flicker amplitude and implicit time were evaluated.

BCR clinical disease status at the time of each ERG was evaluated using the EHR and categorized using a representative numerical value system: "0" indicates inactive disease naïve to treatment, "1" indicates active disease naïve to treatment, "2" indicates active disease undergoing treatment, "3" indicates remission undergoing treatment, "4" indicates remission off treatment, "5" indicates recurrent/active

disease off treatment.

Statistical analysis of the ERG data in association with disease status was planned to determine the sensitivity and specificity of each parameter in indicating or predicting active disease. The decision of which analytic approach to use was deferred to the statistician – in case it was decided to use a logistic regression or other approach requiring a dichotomous dependent variable, it was planned that disease statuses "1," "2," and "5" would be translated into "active" disease, and "0," "3," and "4" would be translated into "inactive" disease.

Results *(≥500 words)*

In total, 165 ERGs from 32 patients were included in the study: nine individuals contributed one ERG, four contributed two, five contributed three, two contributed four, two contributed five, two contributed seven, two contributed eight, two contributed 11, one contributed 13, one contributed 14, one contributed 16, and one contributed 20. Altogether, the number of ERGs contributed per individual ranges from one to 20 with the mean being five and the mode being nine.

The oldest ERG included dates to 1999. Of the 23 individuals who contributed more than one ERG, two contributed ERGs spanning one year in total, one contributed ERGs spanning two years, three contributed ERGs spanning three years, three contributed ERGs spanning four years, three contributed ERGs spanning five years, one contributed ERGs spanning six years, three contributed ERGs spanning seven years, two contributed ERGs spanning nine years, one contributed ERGs spanning ten years, two contributed ERGs spanning 13 years, one contributed ERGs spanning 15 years, and one contributed ERGs spanning 21 years. Overall, the total number of years spanned by the ERGs contributed by an individual ranges from one to 21 with the mean being approximately seven and the mode including three, four, five, and seven.

Regarding ERG values averaged between both eyes, scotopic b wave amplitude (µV) ranges 38.66-730.75 with a mean of 354.35, scotopic b wave implicit time (ms) ranges 39.00-77.25 with a mean of 55.90, scotopic a wave amplitude ranges 23.10-404.29 with a mean of 208.67, scotopic a wave implicit time ranges 14.75-24.00 with a mean of 17.65, scotopic b:a wave amplitude ratio ranges 0.7-2.7 with a mean of 1.7, scotopic oscillatory protentional index (µV) ranges 3.90-241.80 with a mean of 65.10, light intensity 16 photopic b wave amplitude ranges 7.41-265.96 with a mean of 107.57, light intensity 16 photopic b wave implicit time ranges 29.00-47.20 with a mean of 34.60, light intensity 16 photopic a wave amplitude ranges 5.22-75.37 with a mean of 38.42, photopic a wave implicit time ranges 12.30-19.40 with a mean of 15.37, light intensity 16 photopic b:a wave amplitude ratio ranges 1.1-4.8 with a mean of 2.8, light intensity 16 photopic oscillatory potential index ranges 2.41-126.67 with a mean of 38.82, flicker b wave amplitude ranges 5.08-152.79 with a mean of 60.37, and flicker b wave implicit time ranges 27.04-40.47 with a mean of 32.41.

Regarding disease status, one ERG was associated with status "0," 12 with "1," 30 with "2," 56 with "3," 26 with "4," and 16 with "5," making the most represented status "3." Disease status was unable to be determined due to insufficient records in association with 24 ERGs: the single ERG available from three patients, all three ERGs available from one patient, one of two ERGs available from one patient, two of 11 ERGs from one patient, four of 20 from one patient, five of 13 from one patient, and seven of 16 from one patient.

Statistical analysis was not performed and no data on ERG parameter sensitivity and specificity was produced at the time of this report. It is anticipated that statistical analysis will be performed by a statistician at a later date.

Discussion *(≥500 words)*

Considering the size and complexity of the presented dataset, no significant trends relating ERG findings to disease status can be determined without statistical analysis. Although analysis was planned, the CEI statistician assigned to conduct the analysis left the position abruptly for reasons unrelated to the study. Until another statistician is recruited, the analysis is performed, and the discussion is updated to focus on the subsequent study results, this iteration of the discussion will focus on the study limitations.

To begin, the study methodology itself poses a limitation. In the setting of minimal prior research existing to suggest which ERG parameter(s) may most correlate to disease status, numerous parameters were selected for evaluation. Nonetheless, because not all parameters were evaluated, any conclusions made on the prognostic power of ERG in BCR may only apply to the parameters analyzed.

Despite this limitation in the methodology and the rarity of BCR, significant study results remain possible in the setting of a substantial sample size. Over time, CEI has been able to serve a considerably large portion of BCR patients due to its long-standing status as a) the only academic ophthalmic center serving Oregon and b) a premier national ophthalmic center accepting referrals from Alaska, California, Idaho, Washington, and other states.[2] While other medical centers may not have access to samples of BCR patient data sizable enough or spanning disease courses long enough to produce statistically significant results, CEI may have such access with some exceptions: first, the CEI EHR excludes records prior to 1999 that may include additional BCR data, since paper records prior to CEI HER implementation in 1999 were never digitized; second, any conclusions made based on the data from the BCR patient population of a single institution like CEI may not be generalizable to BCR patients of other institutions.

Further, the sample size must be reduced since it was found that disease status was unable to be determined in association with 24 ERGs. Originally, there were no exclusion criteria applied during data compilation, but moving forward, ERGs unable to be associated with disease status will be excluded, leaving 141 ERGs from 28 patients in the study. It remains to be seen whether this reduction in sample size and data points across time will affect the potential of the study to produce significant results.

A final limitation may be introduced if the compiled ERG data includes artifacts. There is no current indication of artifacts, but the raw dataset is difficult to search efficiently due to its size. Statistical analysis will be used to exclude any artifacts, which may further reduce sample size.

Reflecting on these limitations and devising future research, the next step of this study is statistical analysis. To combat the pending reduction in sample size, another next step entails searching CEI paper charts for additional BCR data meeting inclusion criteria, since including such data in the study will increase its power. Once these steps are taken, determination of ERG sensitivity and specificity in predicting BCR prognosis may be achieved.

Conclusions *(2-3 summary sentences)*

This study aims to correlate ERG findings to BCR disease status. Significance of this correlation is yet to be determined and requires further research.

References *(JAMA style format)*

1. Mirza RG, Jampol LM. White Spot Syndromes and Related Diseases. Retina. December 2012:1337-1380. doi:10.1016/b978-1-4557-0737-9.00076-x.
2. Casey Eye Institute. OHSU.edu. https://www.ohsu.edu/casey-eye-institute/patients-casey-eye-institute. Accessed March 3, 2022.