Peripheral Cryoablation for Treatment of Active Pars Planitis: Long-Term Outcomes of a Retrospective Study

ELLIOTT H. SOHN, BENJAMIN C. CHAON, DOUGLAS A. JABS, AND JAMES C. FOLK

- PURPOSE: To compare the long-term outcomes of peripheral retinal cryoablation to conventional treatment for active pars planitis.
- DESIGN: Retrospective, interventional, comparative case series.
- METHODS: Review at a single institution was conducted to compare the effect of cryotherapy to eyes with pars planitis to those receiving conventional therapy (topical, regionally injected, or oral corticosteroid therapy). Best-corrected visual acuity (VA), complications, resolution of cystoid macular edema (CME), and anterior chamber and vitreous inflammation were assessed.
- RESULTS: One hundred thirty-six eyes were treated conventionally, 50 eyes were treated with cryotherapy. Median follow-up was 60.8 months (range 8.1–223.1 months) in the cryotherapy group and 45.0 months (range 3.1–339.0 months) in the controls. There were no significant differences in baseline VA, anterior chamber and vitreous inflammation, presence of CME, and prior use of regional corticosteroid injections. VA improved over time in the cryotherapy group (slope of \(-0.0018\) logMAR units per month; \(P = .023\)) but declined in the controls (slope of \(+0.0011\) logMAR units per month; \(P = .233\)). Kaplan-Meier survival estimates demonstrated faster times to resolution of anterior chamber cell, vitreous cell, and CME in the cryotherapy-treated eyes. Hazard ratios of remission (adjusted for confounding factors) for vitreous cell and CME for those treated with cryotherapy compared to controls were 4.73 (95% confidence interval 1.63, 13.63; \(P = .004\)) and 6.85 (95% confidence interval 1.06, 44.78; \(P = .044\)), respectively. No ocular complications were identified in the cryotherapy group.
- CONCLUSIONS: These data suggest that peripheral retinal cryoablation therapy is an effective treatment for active pars planitis and may be better than conventional regional corticosteroid injections and oral corticosteroid therapy for induction of remission. (Am J Ophthalmol 2016;162:35–42. © 2016 by Elsevier Inc. All rights reserved.)

PARS PLANITIS IS A SUBSET OF INTERMEDIATE UVEITIS characterized by chronic vitreous inflammation and the accumulation of fibroinflammatory debris over the pars plana, occurring in the absence of any associated infection or systemic disease. Clinically, these collections of inflammatory material resemble yellow-gray or white aggregates visible in the mid- and posterior vitreous and collections of inflammatory debris on the pars plana (particularly inferiorly), known as “snowballs” and “snowbanks,” respectively. The most frequent structural complication of pars planitis is macular edema, and most treatment regimens are directed at controlling macular edema. Other, less common structural complications include traction retinal detachments and vitreous hemorrhage from neovascularization of the snowbank.

Although a subset of patients with pars planitis do not have macular edema or visual impairment and may be observed, the majority of patients need treatment. Conventional treatment regimens typically have used a stepped approach starting with regional corticosteroid injections (either periocular or intravitreal), followed by oral corticosteroids, supplemented with immunosuppression as needed for more difficult or bilateral cases. Regional corticosteroid injections have the potential for elevated intraocular pressure and cataract formation/progression and typically have a duration of effect of 3 months, thereby requiring repetitive injections. Although when used properly, oral corticosteroids and immunosuppression can be administered with minimal to no increase in side effects in adults, in children long-term use of oral corticosteroids is avoided owing to the risk of growth retardation. Furthermore, the chronic nature of the disease often requires long-term therapy; there is a low sustained, drug-free remission rate; and some patients’ uveitis will not be controlled by this approach. Although some clinicians have advocated therapeutic vitrectomy for pars planitis, a review...
concluded that methodological problems and study confounders resulted in insufficient evidence to support or refute its use. In 1973, Aaberg and associates reported in 23 eyes in 14 patients affected by pars planitis that peripheral retinal ablation directed at the inflammatory exudates overlying the pars plana with transconjunctival cryopexy (cryotherapy) was effective at decreasing vitritis and improving visual acuity. These observations subsequently were supported by data from other small case series; however, these studies evaluated the effect of cryotherapy on relatively few eyes and were limited by a relatively short duration of follow-up.

There are limited data on the long-term effectiveness of peripheral retinal cryoablation therapy in controlling intraocular inflammation, improving visual acuity outcomes, and reducing structural complications of pars planitis. Our retrospective study compared the long-term clinical outcomes of eyes receiving cryotherapy to those receiving conventional therapy for active pars planitis. We sought to determine if cryotherapy resulted in better visual outcomes and faster time to resolution of cystoid macular edema, vitreous, and anterior chamber cell compared to conventional therapy.

METHODS

A RETROSPECTIVE, INTERVENTIONAL, COMPARATIVE study of all known patients with active pars planitis treated in the Department of Ophthalmology and Visual Sciences at the University of Iowa from January 1, 1983 (near the time cryotherapy for pars planitis was first used at the University of Iowa) to January 1, 2013 was conducted. The records of patients with ICD-9 diagnosis code 363.21 corresponding to a diagnosis of pars planitis were reviewed for inclusion in this study. Included patients met the following criteria: (1) presence of intraocular inflammation in the vitreous in at least 1 eye; (2) presence of inflammatory vitreous debris with snowbanks on the pars plana of the inflamed eye; and (3) a follow-up ophthalmic evaluation performed at least 3 months after the diagnosis of pars planitis. Exclusion criteria included (1) serologic evidence of an infectious etiology for the ocular inflammation or a known associated systemic disease (eg, sarcoidosis or multiple sclerosis); (2) clinical history or physical examination finding(s) to suggest a diagnosis other than pars planitis (eg, oral lesions in patients with Behc¸et disease); (3) intermediate uveitis without evidence of snowbanks; (4) isolated anterior or posterior uveitis; and (5) significant diabetic retinopathy, macula-off retinal detachment, uncontrolled glaucoma, or a disease other than pars planitis that could account for a loss of visual acuity. Only deidentified data were used in the analyses. Institutional Review Board approval at the University of Iowa was obtained for this project, which adhered to the principles of the Declaration of Helsinki.

Data were extracted from review of patient charts at the time of pars planitis diagnosis (the “baseline” visit) and at consecutive follow-up visits. Follow-up visits were grouped as sequential 3-month “contiguous visit windows” extending until the last follow-up visit (eg, the 3-month follow-up window extended from 1.5 to 4.5 months post-baseline, the 6-month follow-up visit window from 4.5 to 7.5 months post-baseline, etc). Data collected at presentation, baseline, and follow-up visits included (1) best-corrected Snellen visual acuity; (2) presence or absence of cystoid macular edema identified by stereoscopic funduscopic examination and/or fluorescein angiography, which was confirmed by optical coherence tomography imaging when this modality became available (2004); (3) grading of anterior chamber cell; (4) grading of vitreous chamber cell; (5) lenticular status (phakic, aphakic, pseudophakic); (6) use of topical corticosteroid medications; (7) use of oral corticosteroid medications; (8) use of periocular corticosteroid injections within the previous 120 days; (9) treatment of glaucoma with topical medication; (10) interval glaucoma surgery; (11) interval cataract surgery; and (12) presence of retinal detachment. Also noted in treated eyes was the date of the first cryotherapy and the total number of cryotherapy treatments per eye.

Visual acuity data were converted to logMAR (logarithm of the minimal angle of resolution) values (logMAR = log [1/Snellen visual acuity]) to allow for statistical analysis. The following logMAR values were assigned: for hand motion, 3.3 logMAR; light perception, 4.3 logMAR; and no light perception, 5.3 logMAR. Each difference of +0.3 logMAR between the baseline and follow-up visual acuity corresponds to a loss of 3 lines on an Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart and a doubling of the visual angle.

Much of the grading of anterior chamber cell and vitreous chamber cell was performed prior to publication of the Standardization of Uveitis Nomenclature’s (SUN) publication of their standardized grading schema. However, the grading used appears to correspond reasonably well with the SUN schema. The early grading used a 1 × 1 mm beam on the brightest illumination on slit-lamp biomicroscopy and had the following grades: 0 for no cells, 0.5+ for 1–2 cells, 1+ for 5–10 cells, 2+ for 10–20 cells, 3+ for 20–30 cells, and 4+ for over 30 cells. Anterior chamber and vitreous inflammatory activity outcomes were dichotomized based on a threshold of anterior chamber cell or vitreous chamber cell ranking less than or equal to 0.5+, corresponding to “trace” inflammatory activity or less. The proportion of patients with anterior chamber cell or vitreous cell ranking less than or equal to 0.5+ at baseline and the rate at which patients’ anterior chamber and vitreous inflammation fell below this threshold was compared between eyes treated with cryotherapy and eyes treated with conventional therapy alone.
CRYOABLATION PROCEDURE AND CONVENTIONAL THERAPY: With visualization using the indirect ophthalmoscope and condensing lens, single freeze-thaw, confluent, but not overlapping applications of cryotherapy were applied to all areas of snowbanking along involved areas of the pars plana (Figure 1, Left). Procedures were performed by 1 of 2 surgeons (E.H.S. or J.C.F.). A single row of cryotherapy was also applied just posterior to the most posterior aspect of snowbanking (Figure 1, Right). Depending on the amount of snowbanking, the average eye may receive between 10 and 20 spots of cryotherapy. If the snowbanking involved more than 6 clock hours of the periphery, treatment was planned in 2 sessions because of the concern that more extensive cryopexy at a single session could cause exacerbation of the inflammation and/or peripheral retinal traction. A second session of cryotherapy was also performed if the inflammation remained active. All patients received preprocedure topical anesthesia with proparacaine eye drops and, if the cryotherapy was performed in the clinic, subconjunctival 2% lidocaine without epinephrine; those intolerant of this approach were given a peribulbar block with 2% lidocaine without epinephrine. Children under the age of 16 years or those with substantial anxiety or discomfort were brought to the operating room for monitored anesthesia care or laryngeal mask anesthesia for the procedure. No postoperative antibiotic drops were given to patients. To blunt any inflammatory response and the potential for retinal detachment from cryotherapy, some patients not already on oral prednisone received either (1) a posterior superior sub-Tenon injection of 20 mg triamcinolone acetonide or intravitreal 2 mg triamcinolone acetonide injection at the time of cryotherapy (n = 21) or (2) oral prednisone at a dose of 20–60 mg daily for 3 days prior to treatment, then a rapid taper and discontinuation over 9 days after cryotherapy (n = 6).

Patients receiving conventional therapy (ie, controls) received either topical prednisolone acetate 1% eye drops or a posterior superior sub-Tenon or an intravitreal triamcinolone acetonide injection for unilateral active pars planitis. Oral prednisone was used for recalcitrant unilateral cases, eyes with a history of a corticosteroid-related intraocular pressure rise, or bilateral active disease; patients who could not tolerate prednisone or had recalcitrant disease despite prednisone 80 mg daily were started on corticosteroid-sparing immunomodulatory therapy. Relatively few eyes were treated with pars plana vitrectomy with or without adjunctive cryotherapy; any eyes receiving cryotherapy were placed in the cryotherapy group. Some eyes with bilateral active disease received cryotherapy in only 1 eye; in these instances the eye with more severe disease was always selected for cryotherapy.

STATISTICAL ANALYSIS: Kaplan-Meier curves and random-effects Cox proportional hazards models were fit for time-to-event data, such as resolution of macular edema, vitreous cell, and anterior chamber cell. Visual acuity (logMAR after conversion from Snellen) trajectories were obtained using linear model with random effects (ie, mixed model). Resolution was defined as going from a vitreous (or anterior) chamber cell rating greater than 0.5+ at baseline (ie, time of cryotherapy or time or presentation in the control group) to the first occurrence of vitreous (or anterior) cell rating less than 0.5+ at least 3 months after baseline, with additional qualifiers of having no periocular or intravitreal corticosteroid injections within the previous 120 days and no oral corticosteroids or immunosuppressive agents. The 120-day time lag was used to account for the duration of the effect of regional corticosteroid injections in both groups. Baseline for the controls was defined as the time of presentation; for the cryotherapy group it was...
the date the treatment was performed or most recent visit before cryotherapy. Time-varying covariate analysis was performed to account for confounding factors found between the groups at baseline and during follow-up, including bilaterality, vitrectomy, and regional corticosteroid injections given after baseline.

RESULTS

OF THE CHARTS REVIEWED FOR INCLUSION IN THIS STUDY, 58 patients were excluded because they did not meet the diagnostic criteria for pars planitis and 3 patients were excluded owing to follow-up of less than 3 months. The study population consists of 186 eyes (136 control eyes; 50 cryotherapy eyes) from 95 patients (69 control patients, 6 cryotherapy patients with unilateral pars planitis, and 20 patients with bilateral uveitis where 1 eye was treated with cryotherapy and the second eye was in the control group). Characteristics of the study population are shown in the Table. Cryotherapy-treated patients were followed for a median of 60.8 months (range 8.1–223.1 months) and controls were followed for a median of 45.0 months (range 3.1–339.0 months). Ten eyes in the cryotherapy group sustained more than 1 treatment. The 2 groups were relatively well balanced at baseline with no significant differences between the groups in baseline visual acuity, anterior chamber and vitreous inflammation, presence of macular edema, and prior use of regional corticosteroid injections. There were significant differences in the ages of the 2 groups, with the cryotherapy group being somewhat younger (median 17.4 years vs 23.0 years) and in the higher use of oral corticosteroids in the cryotherapy group at baseline (28.2% vs 2.9%, \( P = .001 \)).

Regarding other potential confounders occurring during follow-up, 13 eyes (9.6%) in the control group underwent pars plana vitrectomy, compared to 11 eyes (22%) in the cryotherapy group (\( P = .038 \)). Of the 11 cryotherapy-treated eyes that underwent vitrectomy, 4 underwent it at the time of cryotherapy and 7 underwent it subsequently. The mean number of regional (ie, sub-Tenon or intravitreal) corticosteroid injections after baseline in the cryotherapy-treated group was 2.13/eye and in the control group was 0.85/eye (\( P < .001 \)). Potential confounders at baseline and follow-up between the 2 groups were accounted for using time-varying covariate analyses.

- **VISUAL ACUITY OUTCOMES:** Over time, visual acuity on average improved in the cryotherapy-treated eyes and worsened slightly in the control eyes (Figure 2). Specifically, in the cryotherapy-treated eyes, visual acuity values tended to improve (decreasing logMAR) during follow-up.

![Mean Visual Acuity in Cryo-treated and Control Eyes](image)
by an average of 0.0018 logMAR units per month ($P = .023$). In the control eyes, the visual acuity values tended to worsen (increasing logMAR) during follow-up by 0.0011 logMAR units per month ($P = .023$). A formal test of interaction to see if the slopes were different was significant ($P = .024$). After adjusting for bilateral status, vitrectomy, and regional corticosteroid injections during follow-up, there was still a suggestion that the slopes were different ($P = .069$).

- **VITREOUS CELL:** Resolution of vitreous cell occurred with greater frequency in cryotherapy-treated eyes. At 1 year, 49.8% of eyes in the cryotherapy group had experienced resolution of vitreous cell and were not taking either prednisone or immunosuppressive agents, compared to 22.5% in the control group ($P = .0071$). At 1 year, 43.7% of eyes in the cryotherapy group had resolution of the vitreous cell, were not receiving oral corticosteroids or immunosuppressive agents, and had not received a regional corticosteroid injection within the previous 120 days, compared to 18.5% in the control group ($P = .0115$). Kaplan-Meier survival estimates depicting resolution of vitreous cell are presented in Figure 3. The hazard ratio for “remission” (inactive disease without treatment) for the cryotherapy group compared to the control group was 3.79 (95% confidence interval [CI] 1.47, 9.76; $P = .002$). After adjusting for bilaterality, vitrectomy, and regional corticosteroid use, the hazard ratio for remission with cryoablation vs none was 4.73 (95% CI 1.65, 13.63; $P = .004$).

- **CYSTOID MACULAR EDEMA:** Cryotherapy-treated eyes appeared more likely to obtain resolution of macular edema compared to control eyes. The Kaplan-Meier survival estimates of the resolution of macular edema are shown in Figure 4; differences were significant by 6 months ($P = .007$). At 1 year resolution of macular edema without recurrence and without use of systemic medications or use of regional corticosteroid injections within the previous 120 days occurred in 57.7% of eyes treated with cryotherapy compared to 41.0% of control eyes. At 1 year, resolution of macular edema without systemic medications but allowing regional corticosteroid injections within the previous 120 days occurred in 68.9% of cryotherapy-treated eyes compared to 42.8% of control-treated eyes. These percentages are Kaplan-Meier estimates based on 18 cryotherapy-treated eyes and 58 control eyes. The crude hazard ratio for remission (inactive disease off all therapy) was 4.12 (95% CI 0.87, 19.44; $P = .074$), and after adjustment for bilaterality, vitrectomy, and regional corticosteroid use during follow-up it was 6.85 (95% CI 1.11, 425.68; $P = .043$).

- **ANTERIOR CHAMBER CELL:** Cryotherapy appeared to be associated with resolution of anterior chamber cell when compared to control eyes (Figure 5). Kaplan-Meier survival estimates of resolution of anterior chamber cell were significantly different between the 2 groups by 6 months ($P = .005$). The crude hazard ratio for remission (inactive disease off all therapy) was 12.62 (95% CI 0.96, 165.25; $P = .053$), and after adjustment for bilaterality, vitrectomy, and regional corticosteroid use during follow-up it was 21.74 (95% CI 1.11, 425.68; $P = .043$).

- **COMPLICATIONS AND OTHER TREATMENTS:** Other than transient erythema of the conjunctiva over the treated areas, there were no complications resulting from cryotherapy. No eyes developed retinal detachment as a result of cryotherapy. In fact, 1 eye had an inferior retinal detachment before treatment that resolved 3 months after cryotherapy. Six eyes in the cryotherapy group had posterior subcapsular cataract noted on examination (5 had cataract surgery); 18 of the control eyes had posterior subcapsular cataract (16 had cataract surgery)—the number...
injections. Nevertheless, because of the chronic hypertension/glaucoma from regional corticosteroid disadvantages, including cataracts and ocular Standard approaches to treatment have advantages and ease affecting the pediatric population and has an PARS PLANITIS IS THE THIRD MOST COMMON UVEITIC DIS-

that had cataracts was not significantly different between the 2 groups ($P = .83$).

Four eyes in the control group and 4 eyes in the cryotherapy group needed glaucoma surgery, and all had multiple periocular corticosteroid injections preceding the glaucoma procedure. Five patients started corticosteroid-sparing immunosuppressive agents during follow-up, 2 in the control group and 3 in the cryotherapy group. All 3 of these cryotherapy group patients had bilateral disease with cryotherapy given to only 1 eye.

FIGURE 5. Kaplan-Meier survival estimate showing more rapid resolution of anterior chamber cell in the cryotherapy group compared to control eyes with active pars planitis.

that had cataracts was not significantly different between the 2 groups ($P = .83$).

Four eyes in the control group and 4 eyes in the cryotherapy group needed glaucoma surgery, and all had multiple periocular corticosteroid injections preceding the glaucoma procedure. Five patients started corticosteroid-sparing immunosuppressive agents during follow-up, 2 in the control group and 3 in the cryotherapy group. All 3 of these cryotherapy group patients had bilateral disease with cryotherapy given to only 1 eye.

DISCUSSION

PARS PLANITIS IS THE THIRD MOST COMMON UVEITIC DISEASE affecting the pediatric population and has an overall annual incidence of 2 per 100,000 persons. Standard approaches to treatment have advantages and disadvantages, including cataracts and ocular hypertension/glaucoma from regional corticosteroid injections. Nevertheless, because of the chronic nature of this disease, these treatments often require long-term use. Our data suggest that many eyes treated with peripheral retinal cryoaablation can achieve “inactive” disease without attendant systemic medications and that this rate may be greater than that in eyes treated conventionally. Furthermore, cryotherapy-treated eyes appeared to have faster resolution of macular edema and better visual outcomes. In addition, we did not identify any greater rate of ocular complications in the cryotherapy-treated eyes, suggesting that this treatment can be administered safely.

Some clinicians have employed peripheral laser photoablation instead of cryoaablation for pars planitis, with good results reported in uncontrolled case series. These authors have expressed concern about the complications of cryotherapy, particularly retinal detachment. However, in our series no retinal detachments were identified despite relatively long follow-up. Nevertheless, it is possible, or perhaps even likely, that peripheral retinal ablation by either means (cryotherapy or laser photoablation) may be similarly effective for the treatment of pars planitis, as the key issue is not the mode of ablation but that peripheral retinal ablation was performed.

Histopathologic studies of human eyes with pars planitis have demonstrated fibroglial proliferation and lymphocytic infiltration of the snowbank as well as retinal vasculitis, cyclitis, and choroiditis. Though B cells have been identified posterior to the junction of the iris and ciliary body, there was a predominance of T cells in the pars plana of these donor eyes along with a high ratio of helper T cells to suppressor cells. Elevated levels of specific T cell subtypes in the peripheral blood of patients with pars planitis further implicate the role of T cell activation in this disorder. Thus a mechanism of action for cryotherapy is unknown; hypotheses have included altering the blood-ocular barrier (allowing better ingress of drugs and egress of inflammatory mediators) and destruction or reduction of an antigenic stimulus in the pars plana. The retinal S-antigen that has been used to cause experimental autoimmune uveitis has been suggested as a potential candidate, but antibodies to the S-antigen were not found in a donor eye with pars planitis, suggesting that it may not be important in the pathogenesis. There is no doubt that further research is needed to elucidate the pathogenetic mechanisms involved.

There are several potential limitations to this study, many inherent in its retrospective nature. Although we could not identify any evident selection bias in the eyes chosen for cryotherapy (aside from choosing the “worse” eye for unilateral treatment in a patient with bilateral disease), unidentified selection bias could have influenced the results. Observers were not masked as to treatment, allowing for potential observer bias to influence the results. As this was a retrospective study, it is difficult to know for certain which type of patients would benefit most from cryotherapy. These potential biases can only be addressed through a randomized clinical trial with masked assessment of outcomes. Variable concomitant therapy is a potential confounder. There was a baseline imbalance in oral corticosteroid use, with a higher percentage of patients in the cryotherapy group using oral corticosteroids at baseline. Given our stepwise treatment algorithm, this greater use could reflect more severe disease or the greater frequency of bilateral disease in the cryotherapy group. Given the similarity of vision, macular edema percentage, and inflammation median grades, it is likely that the difference reflects the difference in bilateral disease. As some of these patients were treated before the advent of optical coherence tomography, it is possible that cystoid macular edema could have been present despite not being seen ophthalmoscopically; however, both groups would have been subjected to this.
and thus the effect on the results of this study should be minimal.

Any differential treatment during follow-up also could have influenced the outcomes, including resolution of anterior chamber and vitreous cells, resolution of macular edema, and improvement in vision. For instance, on average there were fewer periocular injections given to the control group during the follow-up period, and pars plana vitrectomy was used in a greater percentage of patients (albeit still a minority) in the cryotherapy group. We sought to mitigate any potential confounding factors in 2 ways. The first was analyzing outcomes that included being off systemic and regional treatments as part of the definition of remission, and the second was adjusting for potential confounders statistically (including postbaseline periocular injections and vitrectomy) using time-varying covariate analysis. In this regard, our data suggest greater rates of resolution of anterior chamber cells, vitreous cells, and macular edema despite discontinuing concomitant oral therapy in the cryotherapy group. Nevertheless, despite the apparent success of cryotherapy and the significant adjusted hazard ratios (favoring cryotherapy), the small sample size led to wide confidence intervals, so that the magnitude of the benefit is less certain. Finally, observers were not masked as to treatment, potentially introducing observer bias. As such, our data should be viewed as highly suggestive rather than conclusive.

There were no standard follow-up protocols, resulting in variable follow-up intervals. We attempted to mitigate this variable follow-up by recording only visits that corresponded to 3-month intervals after baseline and using contiguous visit windows. Heterogeneous follow-up also was addressed by using statistical tools such as Kaplan-Meier product-limit estimation and random-effects modeling. The sample size of eyes treated with cryotherapy was small, so that estimates of side effects also are imprecise. For example, the upper 95% CI on the detachment rate is approximately 6% of eyes treated with peripheral retinal cryoablation.

In conclusion, for eyes with active pars planitis, our data suggest that peripheral retinal cryoablation appears to be an effective treatment that can potentially result in a “remission,” a result that appears to be seen less commonly with conventional corticosteroid treatments. This treatment appears to have a low risk of side effects and to be a reasonable addition to the armamentarium of therapies for pars planitis. Because of the limitations inherent in a retrospective study of this type, its role vis-a`-vis conventional treatment will need to be evaluated in a randomized clinical trial.

**FUNDING/SUPPORT:** NO FUNDING OR GRANT SUPPORT. **FINANCIAL DISCLOSURES:** ELLIOTT H. SOHN: OXFORD BIOMEDICA, Oxford, United Kingdom (research support); GlaxoSmithKline, Middlesex, United Kingdom (research support); Douglas A. Jabs: Applied Genetic Technologies, Inc, Alachua, Florida (Data and Safety Monitoring Committee); James C. Folk: IDx LLC, Iowa City, Iowa (Shareholder, Officer, and Board Member). The following author has no financial disclosures: Benjamin C. Chaon. All authors attest that they meet the current ICMJE criteria for authorship.

The authors thank Jeffrey Dawson, ScD (University of Iowa) for his assistance with statistical analysis and Alton Szeto (altonseto.com) for creation of the eye schematic figure.

**REFERENCES**


Biosketch

Dr Elliott H. Sohn is vitreoretinal surgeon-scientist at the Wynn Institute for Vision Research/University of Iowa with special expertise in inherited retinal degenerations, AMD, and diabetic retinopathy and is surgeon/PI/co-investigator for several gene therapy trials. His laboratory focuses on efficacy and immunologic effects of stem cell and gene therapy and the pathophysiology and novel therapies for AMD. He serves on ARVO, AAO, and ABO committees and is editorial board member for Scientific Reports (Nature Publishing).
Biosketch

Dr James C. Folk is the Judith (Gardner) and Donald Beisner, Professor of Vitreoretinal Disease and Surgery in the Department of Ophthalmology and Visual Sciences and Wynn Institute of Vitreoretinal Research at the University of Iowa. He is an officer of the Macula Society and member of the Retina Society and American Society of Retinal Specialists. Although he treats a wide variety of vitreoretinal disease he has a particular interest in ocular inflammatory diseases. He is active in both clinical and translational research.