Evaluating Structural Progression of Retinitis Pigmentosa After Cataract Surgery

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• PURPOSE: To determine whether cataract surgery accelerates disease progression in retinitis pigmentosa (RP).
• DESIGN: Retrospective cohort study.
• METHODS: Seventy eyes of 40 patients with RP were categorized as having had phacoemulsification with intraocular lens implantation vs no cataract surgery at a single tertiary-level institution. Spectral-domain optical coherence tomography (SDOCT) was used to measure the ellipsoid zone (EZ) width, which has been demonstrated to be a reliable marker of RP severity, at baseline and throughout follow-up (median 768 days). RP progression was calculated as the loss of EZ width over time for all patients. Additional postoperative data were collected for the cataract surgery group, including preoperative and postoperative best-corrected visual acuity, incidence of macular edema, posterior capsular opacification, epiretinal membrane, and intraocular lens subluxation.
• RESULTS: Multivariable analysis including age, baseline EZ width, mode of inheritance, and cataract surgery status showed that there was no significant difference in RP progression between the cataract surgery and control groups ($P = .23$). Mode of inheritance was associated with RP progression, with autosomal recessive RP progressing at 148 μm/year and autosomal dominant RP progressing at 91 μm/year ($P = .003$). Visual acuity improved in almost all eyes that underwent surgery (17/19, 89%) and remained stable in remaining eyes (2/19, 11%). There was a high incidence of postsurgical posterior capsular opacification (18/19, 95%). There were no serious complications, such as lens subluxation or endophthalmitis.
• CONCLUSIONS: Our findings suggest that cataract surgery is a safe and effective means of improving visual acuity in RP patients and that it does not seem to be associated with faster disease progression as measured using SDOCT. (Am J Ophthalmol 2017;180:117–123. © 2017 Elsevier Inc. All rights reserved.)

RETINITIS PIGMENTOSA (RP) IS A GENETICALLY HETerogeneous inherited retinal dystrophy characterized by a slow loss of rod followed by cone photoreceptors that leads to a progressive, functional loss of visual acuity and visual field.[1] Common complications in the course of RP are formation of cataracts, cystoid macular edema (CME),[2] and epiretinal membrane (ERM).[3] Cataracts are more commonly seen in patients with RP compared to the general population, occur at an earlier age, are more commonly of the posterior subcapsular cataract (PSC) type, tend to be more visually significant, and often present with significant glare.[4–6]

Cataract surgery is frequently performed in RP patients, but that does not make it benign, as it has been postulated that cataract extraction and intraocular lens placement may increase outer retinal atrophy through light damage[7] and/or anterior chamber inflammation,[8] as well as increase the likelihood or severity of CME formation[6] and posterior capsular opacification (PCO).[9] RP patients may also have a higher prevalence of zonular instability, increasing the risk of intraocular lens dislocation during or after surgery.[10] Despite its potential risks and downfalls in RP patients, cataract surgery has been shown to improve visual acuity in these patients, although to varying degrees.[5,6,9]

In order to measure the structural severity of RP accurately and precisely, special techniques using spectral-domain optical coherence tomography (SDOCT) are being used to measure and monitor ellipsoid zone (EZ) measurements (ie, photoreceptor inner segment/outer segment junction layer measurements). The EZ line, visualized using this technique, is a known correlate of where retinal function is partly or fully intact.[11] The purpose of our study is to determine whether RP progression is altered by cataract surgery by comparing EZ line loss (ie, progression) in RP patients who underwent uncomplicated cataract surgery with RP patients who did not. Our study is the first to quantitatively measure the EZ for this purpose. We will also look at potential complications and other postoperative outcomes to further investigate if cataract surgery is safe and effective in this special population of patients.

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METHODS

• **SUBJECTS:** This retrospective cohort study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Boards of the Harkness Eye Institute and Columbia University. The study protocol adhered to the Health Insurance Portability and Accountability Act.

All study subjects were diagnosed (or confirmed) with RP by the same clinician (S.H.T.), using the same criteria incorporating clinical history, fundus examination, SDOCT, and full-field electroretinogram results. This cohort of typical RP patients was followed in the electrodiagnostics clinic at Columbia University's Harkness Eye Institute for at least 2 visits. Owing to our international referral system for RP, many patients were only seen for 1 visit and care was transferred back to the primary provider. Therefore, these patients did not return for a second visit and were excluded from our study. No cases of unilateral RP, X-linked RP in female patients, or paravenous RP were included in the study. Patients who developed RP before 30 years of age were also excluded, as such cases are often part of a syndrome that does not exemplify typical RP progression. SDOCT was used to evaluate structural disease progression and disease status at every time point. Patients with advanced RP who exhibited no visible EZ line in the 30-degree field were excluded. Exclusionary criteria also included patients with SDOCT scans of poor quality from which the EZ line could not be assessed; however, none of the patients who underwent cataract surgery were excluded for this reason.

The patients were divided into 2 groups: those who had cataract surgery and those who did not. Patients who were included in the cataract surgery group met the following criteria: (1) all cataract surgeries were performed at our institution; (2) all cataracts were removed using similar, typical phacoemulsification technique; and (3) documentation of the preoperative and follow-up visits were available for review. Patients were excluded if they had a second procedure along with cataract surgery, such as glaucoma tube implantation or vitrectomy. All patients undergoing cataract surgery had baseline SDOCTs taken within 3 months before the date of surgery. Sixteen eyes were implanted with SN60WF intraocular lenses (AcrySof IQ Natural SN60WF; Alcon Laboratories, Fort Worth, Texas, USA) and 3 were implanted with SA60AT lenses (Acrysof Natural Single-Piece SA60AT; Alcon Laboratories, Fort Worth, Texas, USA), based on surgeon preference.

• **IMAGE ACQUISITION:** SDOCT and fundus infrared reflectance images were acquired with an 870-nm light source at a resolution of 1536 × 1536 pixels and field of view of 30 degrees, using an automatic real-time registration program from the Spectralis HRA + OCT device (Heidelberg Engineering, Heidelberg, Germany). The horizontal single-line SDOCT (9 mm, ART, average of a minimum of 50 scans) was acquired in high-resolution mode. All images were acquired using a 30-degree lens. The horizontal scan through the fovea was used to evaluate the horizontal width of the residual EZ line using the measuring tool (Heidelberg Eye Explorer, software version 1.9.10.0; Heidelberg Engineering, Heidelberg, Germany). This is further described by Sujirakul and associates.[1] The termination of the EZ was determined using a described protocol.[12] EZ width was measured in the horizontal line SDOCT from the nasal to temporal termination. This is the most sensitive marker of RP progression when the EZ line falls under 3000 μm.[1] The Figure depicts an example of baseline and follow-up SDOCTs in 2 patients, with calculation of EZ lines displayed.

• **STATISTICAL ANALYSES:** The SDOCT scans at baseline and all follow-up visits were independently analyzed by 2 authors (K.S. and T.C.). The authors were masked to the patients' cataract surgery status when interpreting the images. Intraobserver and interobserver reliability was controlled for by measuring the horizontal width of the EZ line (ie, the EZ width) at 2 different times several weeks apart. The average of 4 EZ line measurements at each time point (2 from each author) was used for this analysis. Test-retest reliability using this method has been previously calculated and verified.[1] The baseline time point was deemed "day 0" and corresponded to the first recorded visit in the non–cataract surgery or control group, and it corresponded to the preoperative visit closest to the day of operation in the cataract surgery group. The baseline visits for the latter group all occurred fewer than 90 days prior to the respective surgery date for each patient. All subsequent follow-up visits were recorded in days from baseline examination. Baseline characteristics for the RP patients who underwent cataract surgery vs those who did not were compared with Student t test for continuous variables and χ^2 test for categorical variables. The rate of RP progression was computed by first creating a scatterplot for each eye displaying the change in EZ line width over time. Univariable linear regression analysis was used for each eye to calculate the slope of the best-fit line (unit = micrometers per day). The mean rates of progression in the RP patients undergoing cataract surgery vs those with no surgical intervention were compared using Student t test. The rate of RP progression was also compared with mode of inheritance, sex, and disease severity using Student t test. Shapiro-Wilk test was used to assess normality of data distribution for continuous variables. The association between age or baseline EZ line width and the rate of progression was determined using a univariable linear regression model. Multivariable analyses were used for the covariables found to be significant. All statistical analyses were performed with STATA version 14 (STATA Corp, College Station, Texas, USA).