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Progressive Constriction of the Hyperautofluorescent Ring in Retinitis Pigmentosa

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Abstract

Purpose—To evaluate the constriction of the hyperautofluorescent ring over time in patients with retinitis pigmentosa (RP).

Design—Prospective study.

Methods—Fourteen eyes of 14 RP patients with a hyperautofluorescent ring were studied. Ring constriction was evaluated by measurements of its external and internal boundaries along the vertical and horizontal axes at baseline, 12, 24, 36, and 48 month follow-ups. Repeat fundus autofluorescence was obtained at 12, 24, 36 and 48 months in 13, 7, 5 and 1 eyes respectively. Spectral domain optical coherence tomography (SD-OCT) images were obtained on 8 eyes and the horizontal extent of the inner segment/outer segment (IS/OS) junction was measured. SD-OCT was repeated at 12 and 24 months in 6 and 4 eyes respectively.

Results—The external boundaries of the ring were identified along the horizontal axis in 12 eyes and along the vertical axis in 13. Internal boundaries were identified in 7 eyes. Constriction was demonstrated in all patients except one who demonstrated minimal expansion of the internal boundary along the horizontal axis. SD-OCT measurements showed a decrease in the IS/OS junction length.

Conclusion—Progressive constriction of the hyperautofluorescent ring and a concordant decrease in IS/OS junction length were observed over time.

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Retinitis pigmentosa (RP) is a group of retinal degenerative diseases that are genetically heterogeneous and characterized by an association of progressive visual acuity and photoreceptor loss.^{1,2} The presence of hyperautofluorescent rings in patients with RP has been reported to vary between 59% and 94% of patients³⁻⁵ and probably represent an abnormal perifoveal accumulation of lipofuscin in the retinal pigment epithelium (RPE) due to an increased outer segment dysgenesis as a precursor of apoptosis in RP.^{6,7} The structural assessment of the retina outside the hyperautofluorescent ring reveals absence of the inner segment/outer segment junction (IS/OS), external limiting membrane (ELM) and outer nuclear layer (ONL).⁶ At the edge of the hyperautofluorescent ring, breakdown or disorganization of the IS/OS junction, decreased thickness of ONL, and decreased detection of ELM are seen. In the retinal region within the hyperautofluorescent ring, intact IS/OS junction and ELM are detected.⁶

It has been suggested that the hyperautofluorescent ring may be an indicator of prognosis.^{4,8-10} Retinal degeneration in RP begins in the periphery and it has been shown that the preserved visual fields of eyes with larger rings are greater than those for eyes with smaller rings.⁷ Therefore, the size of the hyperautofluorescent ring seems to have prognostic value for the rate of visual field loss in RP, and the absence of hyperautofluorescent ring constriction in RP patients may reflect milder or less progressive macular involvement.⁶ Determining the rate of ring constriction may form the basis for defining parameters to measure outcomes in an interventional trial.

A decrease in the hyperautofluorescent ring diameter was first reported in 3 cases of RP at follow-up examinations.⁷ Although other studies of the quantification of constriction and change in IS/OS structure observed with spectral domain-optical coherence tomography (SD-OCT) have been reported, they are limited.^{5,11,12} The purpose of this study is to demonstrate progressive constriction of the hyperautofluorescent ring and changes in retinal structure in patients with RP, using fundus autofluorescence (FAF) and spectral domain optical coherence tomography (SD-OCT).

Methods

Subjects

This prospective cross-sectional study included 14 eyes of 14 patients with a clinical diagnosis of RP and hyperautofluorescent rings of different diameters on FAF where expansion, constriction or no change of the ring diameter was documented at follow-up. The patients (6 females, 8 males) ranged in age from 10 to 68 years. The clinical findings of the study patients were evaluated by one retina specialist and the full-field scotopic and photopic electroretinograms (ERGs) were performed according to the International Society for Clinical Electrophysiology of Vision standards.¹³ Both clinical features and ERGs tracings were consistent with the diagnosis of RP in all patients. All eyes in the study had clear media facilitating FAF and SD-OCT imaging. Eyes were excluded if there was a refractive error greater than +/- 6.0 diopters spherical or +/-2.0 diopters cylindrical, evidence of cystoid macular edema, an epiretinal membrane, and evidence or a history of other ocular diseases (e.g. glaucoma, diabetes).

All patients were screened for genetic mutations. RPar genotyping microarray (Asper Ophthalmics, Tartu, Estonia) were used to screen for 585 mutations in *CERKL*, *CNGA1*, *CNGB1*, *MERTK*, *PDE6A*, *PDE6B*, *PNR*, *RDH12*, *RGR*, *RLBP1*, *SAG*, *TULP1*, *CRB*, *RPE65*, *USH2A*, *USH3A*, *LRAT*, *PROM1* genes; RPad genotyping microarray (Asper Ophthalmics, Tartu, Estonia) were used to screen 370 mutations in the following genes, *CA4*, *FSCN2*, *IMPDH1*, *NRL*, *PRPF3*, *PRPF31*, *PRPF8*, *RDS*, *RHO*, *ROM1*, *RP1*, *RP9*, *CRX*, *TOPORS*, *PNR*; early onset retinal dystrophy array was used to screen for 495

mutations in *AIPL1*, *CRB1*, *CRX*, *GUCY2D*, *LRAT*, *TULP1*, *MERTK*, *CEP290*, *RDH12*, *RPGRIPI*, *LCA5* and *RPE65* genes. Usher array and Bardet Biedl array (Asper Ophthalmics, Tartu, Estonia) were applied to selected cases.

Fundus autofluorescence

FAF imaging was performed using a confocal scanning laser ophthalmoscope Heidelberg Retina Angiograph (HRA) 2 or Spectralis HRA+OCT (Heidelberg Engineering, Dossenheim, Germany) after pupil dilation with topical 0.5% tropicamide and 2.5% phenylephrine eye drops. FAF imaging was performed using a 30° field of view at a resolution of 1536 × 1536 pixels. An optically pumped solid-state laser (488 nm) was used for excitation and a 495 nm barrier filter was used to modulate the blue argon excitation light. A standard procedure was followed for the acquisition of FAF images, including focus of the retinal image in the infrared reflection mode at 820 nm, sensitivity adjustment at 488 nm, and acquisition of 9 single 30° × 30° FAF images encompassing the entire macular area with at least a portion of the optic disc. The 9 single images were computationally averaged to produce a single frame with improved signal-to-noise ratio.

The external and internal boundaries of the hyperautofluorescent ring in both horizontal and vertical axes were defined as the visible limits seen on FAF. The external and internal diameters of the hyperautofluorescent ring were measured along the horizontal and vertical axes that passed through the fovea. The baseline and follow-up FAF images were registered using commercial software (MatLab R2006; The MathWorks, Inc., Natick, MA). We tested the accuracy of each registration by superimposing the baseline and follow-up image as a layered image in Photoshop CS2 (Adobe Systems Inc., San Jose, CA) and flickering the superficial layer on and off.¹⁴ The requirements for accuracy were that constant features i.e. the retinal vasculature, and corresponding vessels should remain stationary. If registration was inaccurate, a new registration was performed until the result was satisfactory. Because they were precisely superimposed, both image scales were identical and exact spatial relations between FAF abnormalities in the initial and follow-up images could be determined. The external and internal boundaries for each hyperautofluorescent ring along both the horizontal and vertical axes were measured at baseline and at 12, 24, 36 and 48-month follow-up examinations. Distances were measured using the measuring tool contained in Photoshop. A fovea to optic disc margin distance of 3000 microns was used as a reference. Of the 14 eyes studied, 12 eyes were examined at 12 months, 7 eyes at 24 months, 5 eyes at 36 months and 1 eye at 48 months follow-up. The percentage change in diameter of the ring on FAF at each follow-up examination was compared to the baseline measurement in all subjects and calculated.

The decrease in the diameter of the hyperautofluorescent ring was defined as the value at the baseline subtracted from the value obtained at 12, 24 and 36-month follow-up visits. The 95% confidence interval was calculated as the mean of the differences ± 1.96 multiplied by the standard deviation of the difference. The general linear model (GLM) with t-tests was used to determine the significance of the changes in the hyperautofluorescent ring diameter in both horizontal and vertical axes at follow-up examinations. The Bonferroni test was also applied since there was difference in follow-up examination time among the study patients.

Spectral-domain optical coherence tomography

SD-OCT was obtained at baseline examination in 8 eyes. Of these, 6 had follow-up examinations at 12 months and 4 at 24 months. SD-OCT was performed with the Cirrus SD-OCT (Carl Zeiss Meditec Inc., Dublin, CA, USA). The acquisition protocol consisted of a five-line raster scan and a macular cube 512 × 128 scan pattern in which a 6 × 6 mm region of the retina was scanned (a total of 65,536 sampled points) within a scan time of 2.4

seconds. After image acquisition, those with a signal strength ≤ 8 were excluded. Horizontal line scans through the center of the foveal region were repeated three times.

The measurements obtained using the Cirrus were confirmed with the Spectralis HRA+OCT in 3 eyes. The simultaneous acquisition of OCT and FAF images facilitates point to point correlation between the en-face and cross-sectional images. Spectralis SD-OCT imaging was acquired by a broadband 870 nm superluminescent diode that scanned the retina at 40,000 A-scans per second with an optical depth resolution of 7 μm . The standard protocol included 25 OCT scans averaged to improve the signal-to-noise ratio.

The length of the intact IS/OS junction was measured at baseline and follow-up examinations using the horizontal foveal scan at the same precise landmark. The length of the IS/OS junction was defined as the distance between the nasal and temporal limits of the hyperreflective band that represents the IS/OS junction layer on SD-OCT. The horizontal length of the intact IS/OS junction lamina was measured using the caliper available on the SD-OCT software. The horizontal length of the IS/OS junction at each follow-up examination was compared to that at baseline, and the percentage change in measurement was calculated.

The diameter of the hyperautofluorescent ring and the length of the IS/OS junction lamina were measured independently by two of the authors (LL and TB) who were masked to the other findings and data of the patients. In the event of disagreement, a third investigator (ST) was consulted for the final determination. The FAF and OCT data were analyzed at the baseline and follow-up visits.

Pearson's correlation was performed to correlate the length of the intact IS/OS junction on SD-OCT with both external and internal boundaries of the hyperautofluorescent ring along the horizontal axis at baseline. A p value < 0.05 was considered statistically significant. All analyses were performed using SPSS software version 3.1 (SPSS Inc., Chicago, IL).

Results

Eight patients had autosomal dominant RP, 5 patients had autosomal recessive RP, and 1 patient had Bardet Biedl syndrome. All patients were screened for genetic mutations with the RPar or RPad arrays. Patient 9 carried compound heterozygosity with R102C and S303C mutations in *PDE6A*; patient 1 had the D190N mutation in *RHO*. Snellen best-corrected visual acuity for all tested eyes was 20/20 (see Table 1 for details).

External and internal boundaries of the hyperautofluorescent parafoveal ring were identified in the eyes. External boundaries of the hyperautofluorescent parafoveal ring were identified in the horizontal axis in 12 eyes and in the vertical axis in 13 eyes, and the internal boundaries were identified in 7 eyes.

A decrease in the diameter of the external boundaries of the hyperautofluorescent ring was observed in both horizontal and vertical axes during the follow-up examinations in all patients with a visible external boundary. At baseline, the external boundary of the ring on its horizontal axis had a diameter that ranged from 2280 μm to 6930 μm . At the 12-month follow-up the diameter of the external boundary of the ring had decreased compared to the baseline measurement. The change ranged from 20 μm to 230 μm . At the 24-month follow-up the decrease ranged from 110 μm to 210 μm compared to baseline, and at 36-months from 190 μm to 1040 μm . Patient #2 continued to demonstrate constriction at 48-months with a reduction of 590 μm from baseline. The external boundary of the ring on its vertical axis had a diameter that ranged from 1640 μm to 6030 μm . At the 12-month follow-up the diameter had decreased compared to baseline. The change ranged from 20 μm to 190 μm . At

the 24-month follow-up, the change ranged from 80 μm to 270 μm , and at 36-months from 140 μm to 440 μm (see Table 2 for details). A constriction of 240 μm was noted in the vertical axis at 48-months in patient # 2. Examples of hyperautofluorescent ring constriction are shown in both horizontal and vertical axes at follow-up examinations in Patients #2, 4, 7 and 10 (see Figures 1, 2 and 3).

The mean % decrease in diameter of the external boundary for the horizontal and vertical axes was compared to baseline. The mean % decrease in the horizontal axis compared to baseline was 2.47% (95% CI: 1.40;3.16), 4.10% (95% CI: 1.40;5.48) and 7.85% (95% CI: 3.28;12.42) at the 12, 24, and 36-month follow-up examinations. The mean % decrease in the vertical axis was 2.12% (95% CI: 1.47;2.65), 6.05% (95% CI: 3.08;8.46) and 6.97% (95% CI: 4.05;9.89) at 12, 24 and 36-month follow-up examinations, respectively. Box plot graphs showing the % change in diameter for individual eyes along the horizontal and vertical axes with time are shown in Figures 4 and 5, respectively. Results demonstrated a significant decrease in the horizontal diameter of the external edge when comparisons such as 12-month $\times$ 36-month follow-up ($p=0.005$) and 24-month $\times$ 36-month ($p=0.039$) follow-up were performed. The vertical diameter of the external edge of the hyperautofluorescent ring also decreased significantly when 12-month was compared to 24-month follow-up ($p=0.049$) and to 36-month follow-up ($p=0.020$). Due to the availability of follow-up scans for a single patient at 48-months, mean values could not be calculated for this follow-up period. Determination of the inner boundary of the hyperautofluorescent ring proved more difficult than determination of the outer boundary due to the gradual rather than sharp transition from hyper to hypo-fluorescence seen at the inner compared to the outer boundary respectively. The inner limits of the ring could be determined in 5 of the 14 patients in the horizontal axis and 7 in the vertical axis. Patient #4 showed a minor increase along the horizontal axis (126 μm) compared to baseline. The results for the internal boundary of the ring on its horizontal and vertical axes are shown in Table 3.

The measurements of the IS/OS junction length were determined in 7 eyes with SD-OCT follow-up examinations. At baseline, the IS/OS junction length ranged from 1533 μm to 5725 μm . At the 12-month follow-up the minimal decrease in the IS/OS junction length in comparison to the baseline was 73 μm and the maximum decrease was 390 μm . At the 24-month follow-up, the minimum decrease in comparison with baseline was 204 μm and the maximum was 397 μm (see Table 4). The mean % decrease in the length of the IS/OS junction from baseline was 10.92% (range: 4.73% - 19.83%) at 12-month and 13.03% (range: 5.68% - 20.18%) at 24-month follow-up. Figure 6 shows an example of the progressive decrease in the length of IS/OS junction band over a two-year and one-year follow-up examinations for Patient #6 and #7, respectively.

Correlation of IS/OS junction length with the internal and external diameters of the hyperautofluorescent ring along the horizontal axis, at baseline, was performed. Of the 7 patients with data available for this analysis, correlation with the internal diameter was possible in only 3 of the 7 patients given the difficulty in accurately determining the internal boundary of the ring in 4 of the 7 patients. Although an $r=-0.614$ was calculated, this was not significant ($p=0.579$) due to the small numbers available for correlation. In contrast, correlating the IS/OS junction length with the external boundary diameter for all 7 patients was possible and $r=0.956$ ($p=0.001$) was calculated.

Discussion

The hyperautofluorescent ring found in RP patients is reported to represent a transition between abnormal paracentral and normal central cone function and it delineates a retinal region with visual field preservation.^{9,15,16} The abnormal autofluorescence represented by

the hyperautofluorescent ring observed in RP patients may suggest an anomalous high rate of photoreceptors phagocytosis^{3,17} and the changes in the RPE function may be a secondary phenomena from increased metabolic load on the RPE due to photoreceptor apoptosis.^{4,6,18} The high load of lipofuscin that causes a maximum intensity of hyperautofluorescence would lead to the RPE atrophy with a subsequent loss of lipofuscin granules. Photoreceptor loss along with RPE atrophy is seen outside the ring and is represented by hypoautofluorescence on FAF.³ This photoreceptor death followed by RPE degeneration was previously suggested³ although clinicopathologic analysis is essential to determine an association between the hyperautofluorescent ring and the photoreceptor status in RP patients.

Our study demonstrated that the dimensions of the hyperautofluorescent ring on FAF and the IS/OS junction lamina length on SD-OCT constrict in RP patients at yearly intervals. The results indicate that the constriction of the ring may reflect progression of RP. In a single patient, #4, the diameter of the internal boundary along the horizontal meridian demonstrated a slight increase over a 12-month period. There was a concurrent reduction in the IS/OS junction length and a decrease in the diameter of the external boundary of the ring in the horizontal meridian during this time. In this exceptional case, the increase in diameter of the internal boundary may have reflected an early metabolic overload of the RPE which occurred focally inside the ring, at a stage when lipofuscin levels were reaching those critical levels usually detectable in the hyperautofluorescent ring itself, and thus caused an increase in the area of relative hypofluorescence within the ring with an increase in the diameter of the internal boundary in this case. Alternatively, as the outer segment disc membranes of abnormal photoreceptors are known to contribute to FAF,¹⁹ perhaps a focal accelerated outer segment shedding from these pathological photoreceptors within the ring was responsible for the increase in the diameter of its internal boundary.

Although three recent publications have studied progressive ring constriction in RP patients, measurements of such constriction were not performed. Aizawa et al showed progressive hyperautofluorescent ring constriction in 26 patients and correlated the internal edge of the ring constriction with IS/OS junction lamina length assessed with time-domain OCT.¹¹ Wakabayashi et al has recently correlated progressive constriction of the hyperautofluorescent ring with IS/OS junction length in 5 patients, but without quantification of the rate of constriction.⁵ In addition, Robson et al demonstrated hyperautofluorescent ring constriction over time and hypothesized that the ring surrounded an area of preserved outer retinal structure and photopic function.¹² As in this study, those authors found that the decrease in the diameter of the hyperautofluorescent ring was accompanied by a concurrent decrease in the length of the IS/OS junction lamina. While these three reports correlated internal ring diameter along the horizontal meridian with IS/OS junction length, due to insufficiency of data points, this correlation was not possible in our patient cohort. However, a clear correlation between the external ring diameter and IS/OS junction length was demonstrated. This data supports the hypothesis that progressive constriction of the hyperautofluorescent ring reflects the structural disorganization of photoreceptors during the progression of RP.

The rate of constriction of the AF ring may prove to be a useful surrogate measure of progression for clinical trials. However, it should be kept in mind that the presence of the ring/arc and rate of constriction is likely to be genotype dependent. It is possible that the relationship between FAF, retinal structure and functional measurements will vary in different genetic types; function may deteriorate before structure (*GUCY2D*)²⁰ or structure may deteriorate before function (*CRUMBS1*).²¹ Our study does have some limitations; one of them was the lack of follow-up examination in some of the study patients. A second limitation was that we did not compare our data with changes in visual function changes in

the study patients. A third limitation of this study was that we studied the FAF and IS/OS junction lamina only in eyes with a hyperautofluorescent ring. FAF and SD-OCT changes were not examined in RP eyes with other patterns of abnormal FAF.

In summary, there was evidence of ring constriction in all RP patients along most meridians. This was associated with a shortening of the length of the IS/OS junction lamina. Therefore, FAF and SD-OCT may be important non-invasive imaging techniques to monitor RP patients. Also, the constriction of the hyperautofluorescent ring in RP may differentiate “rapid progressors” from “slow progressors” and provide better counseling regarding prognosis for patients with RP disease.

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Figure 1.

Progressive constriction of the hyperautofluorescent rings in retinitis pigmentosa. Fundus autofluorescence images showing progressive constriction of perifoveal hyperautofluorescent rings at the external boundaries in the horizontal axis. **Top Left and Bottom Left.** Hyperautofluorescent ring in the left eye of Patient #2 measured 3270 μm at baseline (**Top Left**) and 2890 μm at 36-month follow-up in the horizontal axis (**Bottom Left**). Note the constriction of the external boundaries nasally and temporally in the horizontal axis three years later (arrows). **Top Middle and Bottom Middle.** Hyperautofluorescent ring in the right eye of Patient #7 measured 2330 μm at baseline (**Top Middle**) and 2260 μm at 24-month follow-up in the horizontal axis (**Bottom Middle**). Note the constriction of the external boundary temporally in the horizontal axis two years later (arrow). **Top Right and Bottom Right.** Hyperautofluorescent ring in the left eye of Patient #4 measured 2460 μm at baseline (**Top Right**) and 2400 μm at 12-month follow-up in the horizontal axis (**Bottom Right**). Note the constriction of the external boundaries nasally and temporally in the horizontal axis one year later (arrows).

Figure 2.

Progressive constriction of the hyperautofluorescent rings in retinitis pigmentosa. Fundus autofluorescence images showing progressive constriction of perifoveal hyperautofluorescent rings at the external boundaries in the vertical axis. **Top Left and Top Right.** Hyperautofluorescent ring in the right eye of Patient #2 measured 2400 μm at baseline (**Top Left**) and 2320 μm at 24-month follow-up (**Top Right**). Note the constriction of the external boundary inferiorly in the vertical axis two years later (**arrow**). **Bottom Left and Bottom Right.** Hyperautofluorescent ring in the right eye of Patient #10 measured 5360 μm at baseline (**Bottom Left**) and 4920 μm at 36-month follow-up (**Bottom Right**). Note the constriction of the external boundary inferiorly in the vertical axis three years later (**arrow**).

Figure 3.

Different genetic background can affect the rate of constriction of hyperautofluorescent rings in retinitis pigmentosa. A slower progressive constriction of the hyperautofluorescent ring in patient #4. Fundus autofluorescence images of Patient #4 demonstrated minimal constriction of the hyperautofluorescent ring at follow-up. White arrows point to regions of hypoautofluorescence which developed after ring constriction. Images **Top Left, Top Middle, and Top Right** demonstrate the hyperautofluorescent ring at baseline, 12 and 24-month follow-ups respectively. The other images (**Bottom Left, Bottom Middle, and Bottom Right**) give magnified views of the temporal edges of the ring at baseline, 12 and 24-month follow-ups respectively. Note in the magnified images (**Bottom Left, Bottom Middle, and Bottom Right**) an increase in the hypoautofluorescence immediately external to the ring (**white arrows**).

Figure 4. Constriction of external boundaries of the hyperautofluorescent ring along the horizontal axis in retinitis pigmentosa. Box plot graph showing the % change in the external diameter of hyperautofluorescent rings for the 12 eyes along the horizontal axis at baseline, 12, 24 and 36-month follow-up examinations.

Figure 5.

Constriction of external boundaries of the hyperautofluorescent ring along the vertical axis in retinitis pigmentosa. Box plot graph showing the % change in external diameter of the hyperautofluorescent rings for the 13 eyes along the vertical axis at baseline, 12, 24, and 36-month follow-up examinations.

Figure 6.

Progressive constriction of the hyperautofluorescent rings and concurrent photoreceptor inner segment/outer segment junction lamina shortening in retinitis pigmentosa. Spectral domain optical coherence tomography and corresponding fundus autofluorescence images showing progressive shortening of the photoreceptor inner segment/outer segment junction lamina length on Patients #6 and #7. **First and Second Rows.** Spectral domain optical coherence tomography and corresponding fundus autofluorescence imaging of Patient #6 at baseline (**First Row**) and at 24-month follow-up (**Second Row**). The photoreceptor inner segment/outer segment junction lamina length in the right eye of Patient #6 measured 1543 μm at baseline and 1339 μm at 24-month follow-up. Note the disorganization of the outer limit of the photoreceptor inner segment/outer segment junction lamina nasal to the fovea two years later in a magnified view of spectral domain optical coherence tomography (**arrow** indicates the same retinal location at baseline and follow-up). **Third and Fourth Rows.** Spectral domain optical coherence tomography and corresponding fundus autofluorescence images of Patient #7 at baseline (**Third Row**) and at 12-month follow-up (**Fourth Row**). The photoreceptor inner segment/outer segment junction lamina length in the right eye of Patient #7 measured 1533 μm at baseline and 1405 μm at 12-month follow-up. Note the disorganization of the outer limit of photoreceptor inner segment/outer segment junction lamina temporal to the fovea one year later in a magnified view of spectral domain optical coherence tomography (**arrow** indicates the same retinal location at baseline and follow-up).

Table 1

Clinical characteristics of 14 patients with retinitis pigmentosa and hyperautofluorescent ring

Patient (#)	Diagnosis	Age (yrs)	BCVA (study eye)
1	Autosomal Dominant RP	50	20/20
2	Autosomal Dominant RP	47	20/20
3	Autosomal Recessive RP	60	20/20
4	Bardt-Biedel syndrome	17	20/20
5	Autosomal Dominant RP	29	20/20
6	Autosomal Dominant RP	22	20/20
7	Autosomal Recessive RP	68	20/20
8	Autosomal Dominant RP	45	20/20
9	Autosomal Dominant RP	31	20/20
10	Autosomal Recessive RP	13	20/20
11	Autosomal Dominant RP	47	20/20
12	Autosomal Recessive RP	53	20/20
13	Autosomal Recessive RP	10	20/20
14	Autosomal Dominant RP	50	20/20

Abbreviations: #, number; yrs, years; BCVA, best-corrected visual acuity; RP, retinitis pigmentosa

Table 2

Diameter of the external boundaries of the hyperautofluorescent ring in both horizontal and vertical axes in retinitis pigmentosa patients. External boundaries of the hyperautofluorescent parafoveal ring were identified in the horizontal axis in 12 eyes and in the vertical axis in 13 eyes using fundus autofluorescence. The percent change in diameter of the ring on fundus autofluorescence at each follow-up examination were compared to the baseline measurement and calculated.

Patient	Horizontal axis (μm)				Vertical axis (μm)				
	Baseline	12-month follow-up	24-month follow-up	36-month follow-up	Patient	Baseline	12-month follow-up	24-month follow-up	36-month follow-up
# 1	6020	5970 (0.83%)	5910 (1.83%)	5830 (3.16%)	# 1	6030	5930 (1.66%)	5870 (2.65%)	5820 (3.48%)
# 2	3270	3130 (4.28%)	3060 (6.42%)	2890 (11.62%)	# 2	2400	2360 (1.67%)	2320 (3.33%)	2260 (5.83%)
# 3	4990	4760 (4.61%)		4710 (5.61%)	# 3	3580	3510 (1.96%)		
# 4	6110	6090 (0.33%)	6060 (0.82%)		# 4	6110	6030 (1.31%)	5860 (4.09%)	
# 5	2460	2400 (2.44%)			# 5	1910	1870 (2.09%)		
# 6					# 6	5220	5030 (3.64%)	4970 (4.79%)	
# 7	2330	2300 (1.29%)	2260 (3.0%)	2240 (3.86%)	# 7	1930	1880 (2.59%)	1800 (6.74%)	1730 (10.36%)
# 8	2330	2270 (2.58%)	2210 (5.15%)		# 8	1640	1620 (1.22%)	1420 (13.41%)	
# 9	3180	3090 (2.83%)			# 9	2930	2800 (4.44%)		
# 10	6120	6050 (1.14%)			# 10	3930	3900 (0.76%)		
# 11	6930			5890 (15.01%)	# 11	5360			4920 (8.21%)
# 12					# 12	5030	4960 (1.39%)	4760 (5.37%)	
# 13	2280	2260 (0.88%)			# 13	2060	2020 (1.94%)		
# 14	4440	4270 (3.83%)			# 14				

Abbreviations: #, number; μm , microns

Table 3

Diameter of the internal boundaries of the hyperautofluorescent ring in both horizontal and vertical axes in retinitis pigmentosa patients. Constriction of internal boundaries of the hyperautofluorescent parafoveal ring in 7 study patients in both horizontal and vertical axes. The absolute value and percent change in diameter of the ring on fundus autofluorescence at each follow-up examination (12, 24 and 36-month) were compared to the baseline measurement.

Patient	Horizontal axis (μm)				Patient	Vertical axis (μm)			
	Baseline	12-month follow-up	24-month follow-up	36-month follow-up		Baseline	12-month follow-up	24-month follow-up	36-month follow-up
# 2	2295	2182 (4.92%)	1918 (16.43%)	1913 (16.64%)	# 2	1611	1480 (8.13%)	1187 (26.32%)	1214 (24.64%)
# 3	3750	3704 (1.23%)			# 3	2898	2676 (7.66%)		
# 5	1917	2043 (-6.57%)			# 5	1433	1384 (3.42%)		
# 7	1385		1274 (8.01%)	1287 (7.08%)	# 7	983		852 (13.33%)	815 (17.09%)
# 9	2382	2222 (6.72%)			# 9	2418	2151 (11.04%)		
# 11					# 11	4162			3517 (15.50%)
# 12					# 12	4145	3757 (9.36%)		

Abbreviations: #, number; μm , microns

Table 4

The measurements of the inner segment/outer segment junction length in microns in 8 eyes with retinitis pigmentosa and hyperautofluorescent ring using spectral-domain optical coherence tomography. The absolute value and percent change in the inner segment/outer junction length at each follow-up examination (12 and 24-month) were compared to the baseline measurement

Patient	Baseline (μm)	12-month follow-up (μm)	24-month follow-up (μm)
#1	5725		5400 (5.68%)
#2	1967	1577 (19.83%)	1570 (20.18%)
#3	4736	4432 (6.42%)	
#4	5103		5035 (1.33%)
#5	2267	2092 (7.72%)	
#6	4957	4200 (15.27%)	
#7	1543	1470 (4.73%)	1339 (13.22%)
#8	1533	1405 (8.35%)	

Abbreviations: μm , microns