



Photoreceptor Damage and Reduction of Retinal Sensitivity Surrounding Geographic Atrophy in Age-Related Macular Degeneration

AYAKO TAKAHASHI, SOTARO OOTO, KENJI YAMASHIRO, AKIO OISHI, HIROSHI TAMURA, HIDEO NAKANISHI, NAOKO UEDA-ARAKAWA, AKITAKA TSUJIKAWA, AND NAGAHISA YOSHIMURA

- **PURPOSE:** To quantify the area of photoreceptor damage surrounding geographic atrophy (GA) and evaluate the relationship between structural abnormalities and retinal function in eyes with GA.
- **DESIGN:** Prospective cross-sectional study.
- **METHODS:** Twenty-five eyes of 25 patients with GA associated with age-related macular degeneration underwent a full ophthalmologic examination, including spectral-domain optical coherence tomography (SDOCT), fundus autofluorescence (FAF), and microperimetry. ImageJ software was used to quantify the disruption of the ellipsoid zone on SDOCT images. Hypofluorescent areas of the FAF images indicated areas of retinal pigment epithelium (RPE) loss. Areas of interest graded by SDOCT (photoreceptor damage) and FAF (RPE loss) were registered with microperimetry within a 6-mm circle centered on the fovea.
- **RESULTS:** The mean area of photoreceptor damage was $7.69 \pm 5.36 \text{ mm}^2$, which was significantly greater than the mean area of RPE loss ($4.57 \pm 4.07 \text{ mm}^2$, $P < .001$). The average retinal sensitivity of the area with photoreceptor damage outside the area of RPE loss was lower than that of the area without photoreceptor damage ($6.57 \pm 4.13 \text{ dB}$ vs $11.27 \pm 3.78 \text{ dB}$, $P < .001$). The area of photoreceptor damage surrounding the area of RPE loss was larger in eyes with pseudodrusen than in eyes without pseudodrusen (4.96 mm^2 vs 1.91 mm^2 , $P = .008$). The only significant predictor of decreased retinal sensitivity was the area of the photoreceptor damage ($P < .001$).
- **CONCLUSIONS:** Widespread photoreceptor damage surrounding sites of RPE loss occurred in eyes with GA, and it correlated with visual function. Evaluation of photoreceptor damage surrounding sites of RPE loss using OCT

is important in patients with GA associated with AMD. (Am J Ophthalmol 2016;168:260–268. © 2016 Elsevier Inc. All rights reserved.)

AGE-RELATED MACULAR DEGENERATION (AMD) IS A major cause of blindness in developed countries, particularly in people older than 60 years.^{1,2} AMD manifests in 2 forms, neovascular AMD and nonneovascular or dry AMD. Geographic atrophy (GA) represents the end stage of dry AMD, and is characterized by the loss of retinal photoreceptors, retinal pigment epithelium (RPE), and choriocapillaris. GA pathophysiology remains unclear, partly because of its multifactorial etiology. Biochemical, histologic, and genetic studies have implicated several mechanisms, such as oxidative damage, chronic inflammation, excessive lipofuscin accumulation, and complement system malfunction.²

Fundus photographs and fundus autofluorescence (FAF) are standard approaches for diagnosing and monitoring GA. On fundus photographs, GA is detected as a sharply delineated area of hypopigmentation, depigmentation, or apparent absence of the RPE, resulting in clearly visible choroidal vessels. On FAF, GA exhibits sharply demarcated hypofluorescent areas, owing to the atrophy of the RPE and thus the loss of fluorophores. These 2 modalities are useful for evaluating RPE loss, and historically GA has been attributed to RPE loss. However, using spectral-domain optical coherence tomography (SDOCT), Fleckenstein and associates noted an ellipsoid zone (EZ) that terminated distal to the RPE beyond the edge of the GA in some patients with dry AMD, indicating that photoreceptor cell death may occur earlier than the loss of RPE cells.³ In 2014, Bird and associates described the novel observation of a marked loss of photoreceptor cells at variable distances distal from the edge of the GA.⁴ This observation indicates that photoreceptor loss may occur in areas with an RPE monolayer. In addition, it is known that retinal sensitivity is reduced beyond the borders of GA.^{5–7} Thus, the relationship between photoreceptors and RPE in eyes with GA has not been well understood, and warrants further investigation.

The purpose of this study was to quantify the areas of photoreceptor and RPE loss, and evaluate the relationship

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From the Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan (A.Takahashi, S.O., K.Y., A.O., H.T., H.N., N.U.-A., A.Tsujikawa, N.Y.); and Department of Ophthalmology, Kagawa University Faculty of Medicine, Kagawa, Japan (A.Tsujikawa).

Inquiries to Sotaro Ooto, Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, 54 Kawahara-cho Syogoin Sakyo-ku, Kyoto 606-8507, Japan; e-mail: ohoto@kuhp.kyoto-u.ac.jp

between structural abnormalities and retinal function in eyes with GA associated with dry AMD. To understand the manifestation of GA, we investigated GA using a combination of 3 imaging modalities: FAF, SDOCT, and microperimetry (MP). These 3 modalities allowed us to quantitatively evaluate the status of RPE and photoreceptor cells in vivo and assess their relationship with visual function.

METHODS

THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH THE tenets of the Declaration of Helsinki. This study was approved prospectively by the Institutional Review Board and the Ethics Committee of Kyoto University Graduate School of Medicine. Written informed consent was obtained from all patients. They are registered under the Cohort Study of the Clinical Course of Macular Diseases in Japanese Patients ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02081339) identifier: NCT02081339).

- **PARTICIPANTS:** For this prospective cross-sectional study, we recruited consecutive patients with GA associated with dry AMD who visited the Kyoto University Hospital between March 6, 2014 and February 5, 2015. All patients had been previously diagnosed with GA associated with dry AMD by experienced retinal specialists. We excluded eyes with RPE atrophy secondary to neovascular AMD, idiopathic choroidal neovascularization, angioid streaks, high myopia (axial length ≥ 26.5 mm), other types of secondary choroidal neovascularization (CNV), central serous chorioretinopathy, hereditary macular dystrophy, uveitis, trauma, and any history or sign of retinal surgery, including laser treatment. We also excluded eyes with coexistent ocular abnormality that would cause decreased visual function, such as significant cataracts greater than NO2, NC2, C2, or P2 in the Lens Opacities Classification System III; epiretinal membrane; diabetic retinopathy; and glaucoma. If both eyes were eligible for the study, 1 eye with better best-corrected visual acuity (BCVA) was selected. Pseudodrusen were diagnosed using multimodal imaging modalities including color fundus photography, FAF, infrared reflectance (IR), and SDOCT.

- **MULTIMODAL IMAGING METHODS:** All patients underwent a comprehensive ophthalmologic examination, including BCVA measurement, intraocular pressure determination, indirect ophthalmoscopy, slit-lamp biomicroscopy with a noncontact lens, axial length measurement (IOLMaster 500; Carl Zeiss Meditec, Dublin, California, USA), color fundus photography, FAF, IR, SDOCT, and MP during the same visit.

Color fundus photographs (field, 40 degrees) were obtained digitally using a Topcon TRC NW6S

nonmydriatic retinal camera (Topcon, Tokyo, Japan) after medical dilation of the pupil (phenylephrine, 0.5% and tropicamide, 0.5%). The FAF images were acquired using a confocal scanning laser ophthalmoscope (SLO) (HRA2; Heidelberg Engineering, Heidelberg, Germany), with an excitation wavelength of 488 nm and with a barrier filter beginning at 500 nm. The field of view was set to 30×30 degrees, centered on the fovea. IR and SDOCT imaging were conducted simultaneously using a Spectralis HRA + OCT (Heidelberg Engineering). The IR images were obtained at a wavelength of 820 nm, and the field of view was set to 30×30 degrees, centered on the fovea. The SDOCT images were acquired with 49 horizontal raster scans covering a 20×30 -degree oblong rectangle, averaging 24 scans for each image to reduce speckle noise.

ImageJ software (National Institutes of Health, Bethesda, Maryland, USA) was used to objectively quantify the extent of the disruptions of the EZ band on an SDOCT image.⁸ The signal intensity of the EZ band was measured, and the EZ band was quantified using the plot profile function of the ImageJ software. The border of the EZ disruption was defined as the line on the grayscale image along which the EZ reflectivity diminished by 2 standard deviations from the reflectivity of the EZ band in the unaffected retina (Figure 1). A sequence of OCT scans in each data set was examined, and the areas with a disrupted EZ band were identified. As Spectralis HRA + OCT combines the confocal SLO and SDOCT, it allows the integration of information obtained from a SLO fundus image and SDOCT in a pixel-by-pixel manner,⁹ thus enabling the determination of the exact sites of the disrupted EZ band regions. An area of interest (ie, the area exhibiting EZ disruption) was defined by manually drawing a line in each B-scan image and projecting it onto the IR image (Figure 1). Each projected image was merged into 1 en face image, and then the area of photoreceptor damage was measured. The hypofluorescent areas on the FAF image were defined as the areas of RPE loss. For images with multiple areas of hypofluorescence, all areas of more than 0.5 mm in the greatest linear diameter were outlined and the measurements were summed and recorded. Areas of interest graded by SDOCT (photoreceptor damage) and FAF (RPE loss) were registered with MP findings within the 6-mm Early Treatment Diabetic Retinopathy Study (ETDRS) sector (Figures 1–3) where major vessels were completely matched.

- **MICROPERIMETRY:** Fundus-monitoring MP was used to measure retinal sensitivity. The MP-1 software (NIDEK, Padova, Italy) was set to automatically track eye movements and to evaluate each frame for shifts in the directions of the x and y axes of the fundus, with a reference image obtained by an infrared camera at the beginning of the examination. The 4-2-staircase strategy with Goldmann size III stimuli against a white background

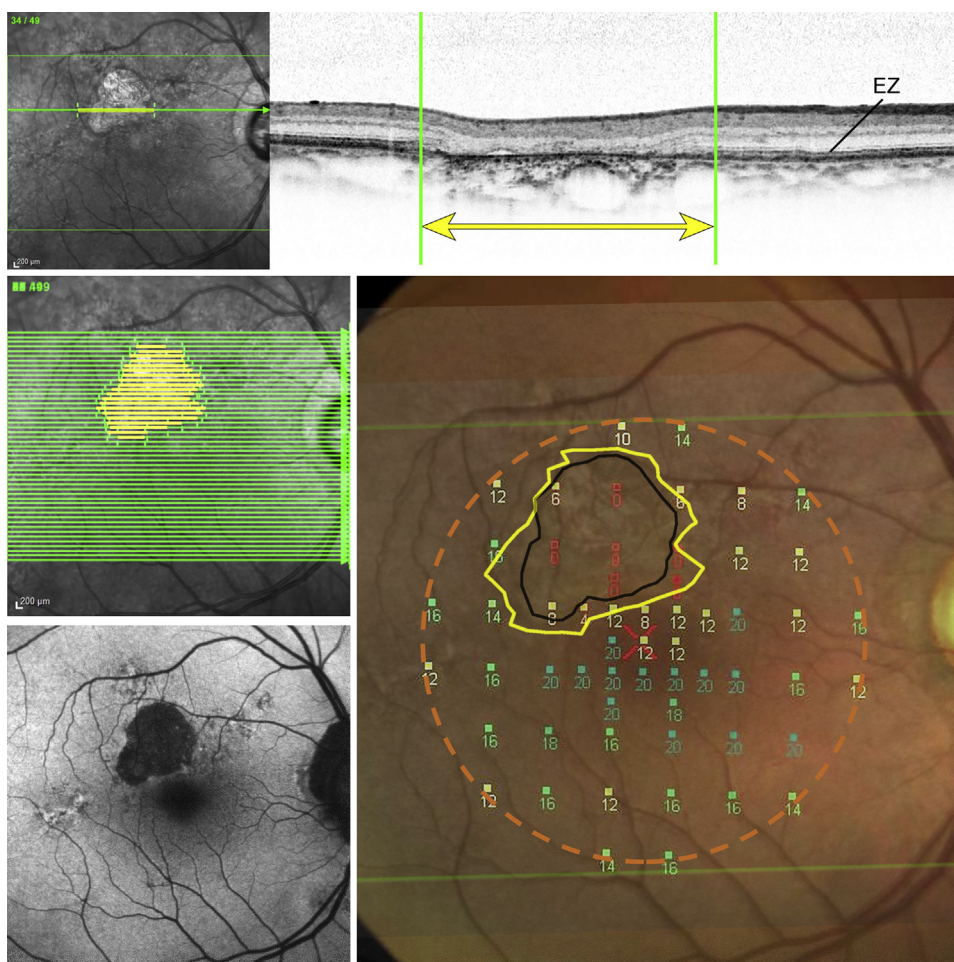


FIGURE 1. Multimodal imaging methods. (Top) The ellipsoid zone (EZ) band on spectral-domain optical coherence tomography (OCT) was objectively evaluated using ImageJ software. The reflectivity of the EZ band was measured, and the EZ band was quantified using the plot profile function of the ImageJ software. The border of the EZ disruption was defined as the line on the grayscale image along which the EZ reflectivity diminished by 2 standard deviations from the reflectivity of the EZ band in the unaffected retina. Areas with a disrupted EZ band were determined and projected onto the infrared (IR) image. (Middle, left) Each projected IR image was merged into 1 en face image and measured as the area of photoreceptor damage. (Bottom, left) The hypofluorescent areas of the fundus autofluorescence images were measured as the area of retinal pigment epithelium (RPE) damage. (Bottom, right) Photoreceptor damage (Middle left, yellow line) and RPE loss (Bottom left, black line) were registered as the retinal sensitivity determined using microperimetry. The image was analyzed within the 6-mm Early Treatment Diabetic Retinopathy Study sector (orange broken line).

with 1.27 cd/m² illumination was used to examine 57 stimulus locations covering the central 20 degrees. The differential luminance, defined as the difference between the stimulus luminance and the background luminance, was 127 cd/m² at 0 dB stimulation, and the maximum stimulus attenuation was 20 dB. The stimulus duration was 200 ms. If the results of the MP examination were not reliable owing to poor fixation, the eye was excluded from this study.

• **STATISTICAL ANALYSES:** All statistical evaluations were carried out using SPSS v. 17 (SPSS, Chicago, Illinois, USA). Significance was defined as $P < .05$. BCVA measured using the Landolt chart was expressed as the

logarithm of the minimal angle of resolution (logMAR). The Wilcoxon signed-rank test was used to compare areas of photoreceptor and RPE loss, and average retinal sensitivity with or without photoreceptor or RPE loss. We calculated the Spearman rank correlation coefficient to determine the associations between the mean retinal sensitivity and the area of photoreceptor and RPE loss, and between the distance from the fovea to the nearest area of photoreceptor damage and BCVA. For comparison of GA with and without pseudodrusen, the Mann-Whitney test was used. Multiple regression analysis was performed with age, sex, lens status, axial length, and areas of the regions of photoreceptor and RPE loss as independent factors and average retinal sensitivity as a dependent factor.

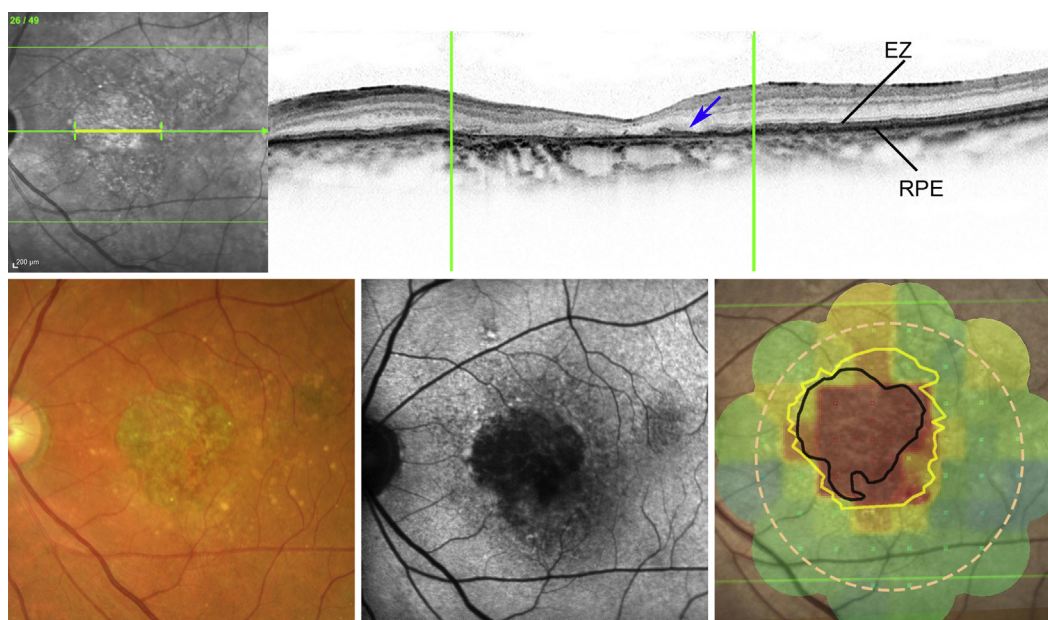


FIGURE 2. Photoreceptor damage detected surrounding the retinal pigment epithelium (RPE) damage in an eye with geographic atrophy without pseudodrusen. Images of the left eye of an 84-year-old man with geographic atrophy without pseudodrusen. (Top) Spectral-domain optical coherence tomography. The ellipsoid zone is disrupted even in the area where the RPE is present (blue arrow). (Bottom, left) Color fundus photography. (Bottom, middle) Fundus autofluorescence. (Bottom, right) Photoreceptor damage (yellow line) and RPE loss (black line) were registered as the retinal sensitivity measured by microperimetry. Photoreceptor damage is widely seen in the area surrounding sites of RPE loss. Note that retinal sensitivity is decreased in the area with photoreceptor damage outside the area with RPE loss.

RESULTS

TWENTY-FIVE EYES OF 25 PATIENTS (19 MEN AND 6 WOMEN) with GA were included in this study. Patient characteristics are shown in Table 1. The mean age was 80.3 ± 6.7 years (range: 62–89 years). All patients were Japanese. Fourteen eyes were phakic and 11 eyes were pseudophakic. The mean best-corrected visual acuity (logMAR) was 0.48 ± 0.41 (range: -0.18 to 1.22), which is equivalent to 20/50 (range: 20/12 to 20/320) in Snellen visual acuity. The mean axial length was 23.48 ± 1.01 (range: 21.58–24.78 mm).

The mean area with photoreceptor damage was $7.69 \pm 5.36 \text{ mm}^2$, which was significantly greater than the mean area with RPE loss ($4.57 \pm 4.07 \text{ mm}^2$, $P < .001$). The mean area with photoreceptor damage outside the area of RPE loss was $3.13 \pm 3.05 \text{ mm}^2$, which had no correlation with the area of RPE loss ($P = .148$). The distance between the fovea and the nearest area of photoreceptor damage negatively correlated with BCVA ($P = .032$, $r = -0.45$).

The areas of RPE loss and photoreceptor damage were negatively correlated with the mean retinal sensitivity of all stimulus points ($R = 0.772$, $P < .001$, and $R = 0.831$, $P < .001$, respectively). The mean retinal sensitivity of the area with RPE loss was lower than that of the area

without RPE loss ($1.84 \pm 2.68 \text{ dB}$ vs $11.27 \pm 3.78 \text{ dB}$, $P < .001$). The mean retinal sensitivity of the area with photoreceptor damage was $3.28 \pm 2.70 \text{ dB}$, which was also lower than that of the area without photoreceptor damage, $10.52 \pm 4.12 \text{ dB}$ ($P < .001$). The average retinal sensitivity with hyperautofluorescence surrounding RPE loss was $7.16 \pm 3.77 \text{ dB}$, which was lower than that of the area without hyperautofluorescence, $11.03 \pm 3.86 \text{ dB}$ ($P < .001$). Furthermore, the average retinal sensitivity of the area with photoreceptor damage outside the area with RPE loss was worse than that of the area without photoreceptor damage ($6.57 \pm 4.13 \text{ dB}$ vs $11.27 \pm 3.78 \text{ dB}$, $P < .001$) (Figures 2 and 3).

The number of stimulus points with hyperautofluorescence surrounding RPE loss was 116 points out of all 1425 stimulus points in 25 patients. Eighty-one points with hyperautofluorescence out of 116 (69.8%) accompanied photoreceptor damage. On the other hand, the number of stimulus points with photoreceptor damage was 198 points in all patients. Out of 198 points, 81 points (40.9%) accompanied hyperautofluorescence.

Multiple regression analysis revealed that among the possible predictors (age, sex, lens status, axial length, area of photoreceptor damage, and area of RPE loss), the only significant predictor of decreased retinal sensitivity was the area of photoreceptor damage ($P < .001$).

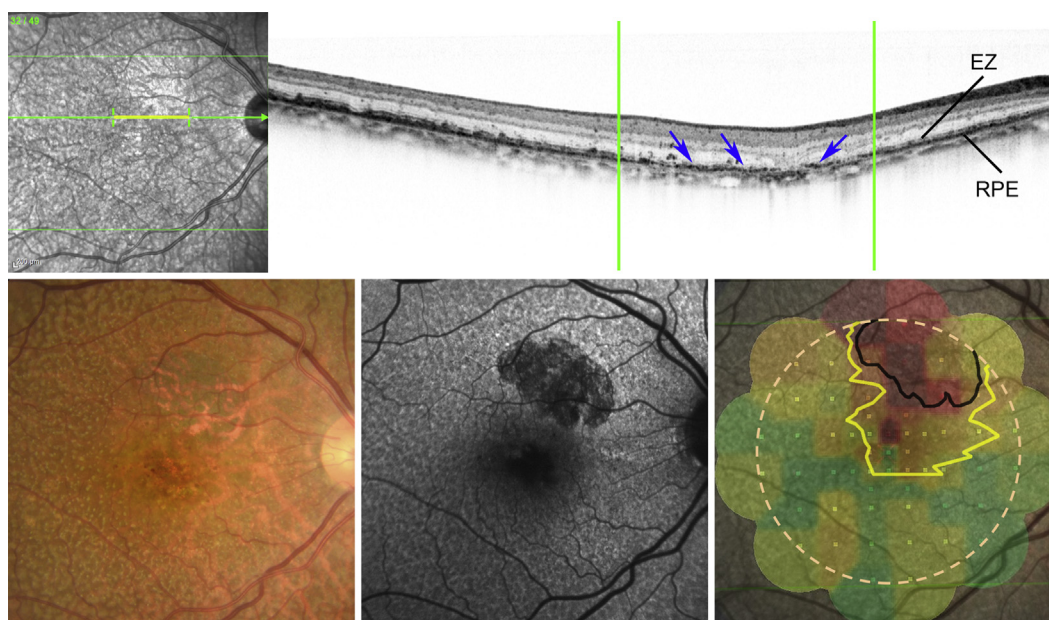


FIGURE 3. Photoreceptor damage surrounding retinal pigment epithelium (RPE) loss in an eye with geographic atrophy accompanied by pseudodrusen. Images of the right eye of an 82-year-old man with geographic atrophy accompanied by pseudodrusen. The images shown are similar to those in [Figure 2](#). (Top) Spectral-domain optical coherence tomography. The ellipsoid zone is disrupted even in the area where the retinal pigment epithelium (RPE) is present (blue arrow). (Bottom, left) Color fundus photography. (Bottom, middle) Fundus autofluorescence. (Bottom, right) The area with photoreceptor damage (yellow line) outside the area of RPE loss (black line) is larger in the eye with pseudodrusen, as illustrated in this figure, than in the eye without pseudodrusen ([Figure 2](#)). Retinal sensitivity is decreased in the area with photoreceptor damage outside the area with RPE loss, and in the area with pseudodrusen.

([Table 2](#)). The area of photoreceptor damage inversely correlated with retinal sensitivity.

We compared the GA patient characteristics between those with and without pseudodrusen ([Table 3](#)). Ten eyes with GA had pseudodrusen and 15 eyes did not. The mean area of photoreceptor damage was greater in eyes with pseudodrusen, compared with eyes without pseudodrusen ($10.82 \pm 6.69 \text{ mm}^2$ vs $5.61 \pm 2.99 \text{ mm}^2$, $P = .031$), though the mean area of RPE loss did not differ significantly ($P = .539$). The mean area of photoreceptor damage outside the region with RPE loss was greater in eyes with pseudodrusen than in eyes without pseudodrusen ($4.96 \pm 4.18 \text{ mm}^2$ vs $1.91 \pm 0.86 \text{ mm}^2$, $P = .008$) ([Figures 2](#) and [3](#)). The mean retinal sensitivity of the area without RPE loss was lower in eyes with pseudodrusen than in eyes without pseudodrusen ($9.29 \pm 2.84 \text{ dB}$ vs $12.41 \pm 3.97 \text{ dB}$, $P = .027$). The mean retinal sensitivity of the area without photoreceptor damage and RPE loss was lower in eyes with pseudodrusen than in eyes without pseudodrusen ($8.10 \pm 3.30 \text{ dB}$ vs $11.82 \pm 4.06 \text{ dB}$, $P = .013$).

DISCUSSION

CLINICALLY, HYPOFLUORESCENCE ON FAF IS ASSUMED TO be an indicator of GA in eyes with dry AMD, with an

established view that GA results from damage to the RPE. FAF has been used for monitoring the progression of GA in many clinical trials. However, several OCT studies showed that the EZ terminates beyond the GA margin.^{3,10} In the current study, photoreceptor damage was observed in widespread areas surrounding sites of RPE loss, and was correlated with visual function. Also, the area of photoreceptor damage outside the region with RPE loss was greater in eyes with pseudodrusen.

In 1988, Sarks and associates reported histologic findings of 5 donor eyes with GA¹¹ that the reduction in photoreceptor nuclei paralleled RPE loss beside and inside the region of GA. However, there were insufficient descriptions of the photoreceptor status outside the GA region. In 2014, Bird and associates histopathologically demonstrated that photoreceptor damage extended beyond the margin of the area of RPE loss, though there was no quantitative assessment of photoreceptor loss.⁴ In the current study, using SDOCT and ImageJ software, we objectively measured the disrupted EZ area as the photoreceptor damage area because the EZ, which contains the mitochondria,¹² reflects photoreceptor physiology and health. In all eyes with GA, photoreceptor damage extended beyond the area of RPE loss to varying degrees. The mean area of photoreceptor damage was significantly greater than the mean area of RPE loss;

TABLE 1. Characteristics of Patients With Geographic Atrophy in This Study

Number of eyes	25
Age (y)	80.3 ± 6.7 (62–89)
Sex (male/female)	19/6
Race (Japanese/other)	25/0
Lens status (phakia/IOL)	14/11
Axial length (mm)	23.48 ± 1.01 (21.58–24.78)
Best-corrected visual acuity (logMAR)	0.48 ± 0.41 (–0.18 to 1.22)
Best-corrected visual acuity (Snellen equivalent)	20/50 (20/12 to 20/320)
Area with photoreceptor damage (mm ²)	7.69 ± 5.36 (0.83–22.32)
Area with RPE loss (mm ²)	4.57 ± 4.07 (0.35–14.08)
Area with photoreceptor damage outside RPE loss (mm ²)	3.13 ± 3.05 (0.52–15.99)
Mean retinal sensitivity of:	
Area of all stimulus points (dB)	8.42 ± 4.24 (0.67–18.98)
Area with photoreceptor damage (dB)	3.28 ± 2.70 (0.00–13.00)
Area without photoreceptor damage (dB)	10.52 ± 4.12 (2.06–19.30)
Area with RPE loss (dB)	1.84 ± 2.68 (0.00–10.00)
Area without RPE loss (dB)	11.27 ± 3.78 (3.54–19.20)
Area with hyperautofluorescence surrounding RPE loss (dB)	7.16 ± 3.77 (0.00–16.00)
Area without hyperautofluorescence surrounding RPE loss (dB)	11.03 ± 3.86 (2.97–19.20)
Area with photoreceptor damage outside RPE loss (dB)	6.57 ± 4.13 (0.00–16.00)

Data are presented as n or mean ± standard deviation (range).
GA = geographic atrophy; IOL = intraocular lens; RPE = retinal pigment epithelium.

thus these in vivo results support the histopathologic findings of Bird and associates.⁴

In eyes with GA, loss of visual acuity has been explained by foveal involvement of RPE loss.^{13,14} This study showed that the linear distance from the fovea to the area of photoreceptor damage correlated with BCVA. The mean retinal sensitivity of the area with photoreceptor damage was significantly lower than that of the area without photoreceptor damage. The average retinal sensitivity with hyperautofluorescence surrounding RPE loss was lower than that of the area without hyperautofluorescence. These results are consistent with previous reports describing the point-to-point correlation of SDOCT/FAF findings and retinal sensitivity on MP.^{5–7,15–20} Landa and associates showed a high inverse correlation between retinal sensitivity

and disruption of the EZ on OCT.¹⁵ Querques and associates showed reduced retinal sensitivity on the points graded as decreased or increased FAF and near-infrared autofluorescence.⁶ In the current study, in assessing the stimulus points in MP, 69.8% of points with hyperautofluorescence corresponded to points with photoreceptor damage. Thus, most areas with hyperautofluorescence mainly reflect photoreceptor damage, but some do not. Hyperautofluorescence in some such lesions may be explained by bilaminar RPE cells.^{10,21} Furthermore, the current study revealed that the mean retinal sensitivity of the area with photoreceptor damage outside the area with RPE loss was lower than that of the area without photoreceptor damage. Multiple regression analysis showed that the area of photoreceptor damage was the only predictor of decreased retinal sensitivity. These findings suggest that photoreceptor damage is more important than RPE loss when evaluating visual function in eyes with GA.

Several studies reported a high prevalence of pseudodrusen among eyes with GA.^{22–24} Finger and associates assessed the impact of pseudodrusen on late AMD in the fellow eyes of patients with CNV, and showed that the presence of pseudodrusen was an independent risk factor for GA development.²⁵ Pseudodrusen are closely associated with GA, though the ratio of coincidence of pseudodrusen in patients with GA may be lower in Asian populations.²⁴ In the current study, 10 of 25 eyes (40%) presented with pseudodrusen. The area with photoreceptor damage outside the site of RPE loss was larger in eyes with pseudodrusen compared with eyes without pseudodrusen, though the area of RPE loss did not differ. These results suggest that pseudodrusen are associated with photoreceptor damage, rather than RPE loss, in GA. This hypothesis is supported by results of previous histologic and imaging studies.^{26–30} Curcio and associates reported on photoreceptor abnormalities in specimens with subretinal drusenoid deposits, a candidate histologic correlate of pseudodrusen. In some eyes, photoreceptor morphology is disturbed over subretinal drusenoid deposits, which manifests as shortening of the outer segment and outer segment loss with inner segment deflection and absence.²⁶ Spaide investigated the long-term clinical course of pseudodrusen and reported that eyes with regression of subretinal drusenoid deposits had decreased photoreceptor length, EZ band loss, and reduction of the underlying choroidal thickness.²⁸ Adaptive optics imaging also revealed that photoreceptors were disturbed in eyes with subretinal drusenoid deposits.^{29,30} Several reports have shown that retinal sensitivity is reduced in eyes with pseudodrusen.^{31–34} Consistent with these reports, the mean retinal sensitivity of the area without photoreceptor damage and RPE loss was lower in eyes with pseudodrusen compared with eyes without them. All these results indicate that pseudodrusen themselves may cause retinal sensitivity reduction.

TABLE 2. Retinal Sensitivity Prediction Model After Stepwise Selection in Eyes With Geographic Atrophy

Variable	Unstandardized Coefficient Beta	Standardized Coefficient Beta	95% CI	P Value
Constant	13.13		11.13–15.14	1.89×10^{-12}
Age	Not selected			
Sex	Not selected			
Lens status (phakia/IOL)	Not selected			
Axial length	Not selected			
Area with photoreceptor damage	–0.61	–0.78	–0.83 to –0.40	5.18×10^{-6}
Area with RPE loss	Not selected			

GA = geographic atrophy; IOL = intraocular lens; RPE = retinal pigment epithelium.

TABLE 3. Comparison Between Patients With Geographic Atrophy With and Without Pseudodrusen

	GA With Pseudodrusen	GA Without Pseudodrusen	P Value
Number of eyes	10	15	
Age (y)	83.3 ± 4.9	78.3 ± 7.2	.079
Sex (male/female)	7/3	12/3	.574
Lens status (phakia/IOL)	4/6	10/5	.197
Axial length (mm)	23.14 ± 0.89	23.71 ± 1.05	.445
Best-corrected visual acuity (logMAR)	0.44 ± 0.40	0.52 ± 0.43	.636
Best-corrected visual acuity (Snellen equivalent)	20/50	20/63	
Area with photoreceptor damage (mm ²)	10.82 ± 6.69	5.61 ± 2.99	.031*
Area with RPE loss (mm ²)	5.86 ± 5.57	3.70 ± 2.56	.579
Area with photoreceptor damage outside RPE loss (mm ²)	4.96 ± 4.18	1.91 ± 0.86	.008*
Mean retinal sensitivity of:			
Area of all stimulus points (dB)	6.85 ± 3.59	9.47 ± 4.42	.174
Area with photoreceptor damage (dB)	3.64 ± 2.15	3.35 ± 3.08	.437
Area without photoreceptor damage (dB)	8.10 ± 3.30	11.82 ± 4.06	.013*
Area with RPE loss (dB)	0.98 ± 1.29	2.11 ± 3.10	.539
Area without RPE loss (dB)	9.29 ± 2.84	12.41 ± 3.97	.027*
Area with photoreceptor damage outside RPE loss (dB)	6.24 ± 2.42	6.72 ± 5.03	.824

Data are presented as n or mean $\pm$ standard deviation (range).

GA = geographic atrophy; IOL = intraocular lens; RPE = retinal pigment epithelium.

*Statistically significant.

Our study has several limitations. First, this study included a relatively small sample size because patients with GA are relatively rare in Asian populations compared to white populations.¹ Therefore, the GA findings in Asian populations may or may not correlate with findings in white populations or those of different ethnicities. Second, we analyzed the area of the macula covering the central 20 degrees. In some eyes, photoreceptor damage outside the area of RPE loss extended beyond the central 20 degrees. In such cases, the area of photoreceptor damage was underestimated. Despite these limitations, we were able to show that photoreceptor damage extended to widespread areas surrounding RPE loss and correlated with retinal function in eyes with GA. In eyes with pseudodrusen, the area of

photoreceptor damage was larger, and the retinal sensitivity was decreased, compared with eyes without pseudodrusen. As Bird and associates mentioned, these observations are important to assess the benefits in therapeutic trials for GA eyes; photoreceptor damage may occur in the absence of changes in the RPE and may be due to disease processes intrinsic to the neuroretina.⁴ A therapeutic strategy to prevent RPE loss only may not be effective for patients in whom photoreceptor damage extends outward beyond the RPE loss. FAF is useful to detect RPE abnormalities, but it is not a reliable indicator of the extent of photoreceptor damage. The evaluation of photoreceptor damage surrounding sites of RPE loss using SDOCT is important in patients with GA associated with AMD.

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