

# Relationship Between Optical Coherence Tomography Parameter and Visual Function in Eyes With Epiretinal Membrane

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**PURPOSE.** To investigate the associations between visual function and the optical coherence tomography (OCT) parameters in eyes with idiopathic epiretinal membrane (ERM).

**METHODS.** Thirty-nine consecutive eyes with ERM were enrolled. In addition to OCT parameters, such as central retinal thickness (CRT), the area of gap between the ERM and the retinal surface (SUKIMA) was newly defined and calculated from the vertical and horizontal OCT images (SUKIMAv and SUKIMAh). The average of SUKIMAv and SUKIMAh (SUKIMAave) was used for the statistical analysis. The vertical and horizontal metamorphopsia scores (MV, MH) and the average of MV and MH (Mave) were also used for the analysis.

**RESULTS.** The Mave was not significantly associated with logMAR visual acuity (VA) ( $P = 0.57$ , linear regression analysis). Analysis using second-order bias-corrected Akaike information criterion model selection identified the age, CRT, and SUKIMAave as being associated with logMAR VA. On the other hand, among the OCT parameters, SUKIMAave and CRT were associated with the Mave. In addition, there was a significant relationship between SUKIMAh and MV ( $P = 0.011$ ) and between SUKIMAv and MH ( $P = 0.0014$ ).

**CONCLUSIONS.** We identified SUKIMA as a novel OCT parameter that is useful to predict both VA and metamorphopsia in patients with ERM.

Keywords: OCT parameter, metamorphopsia, visual function, epiretinal membrane

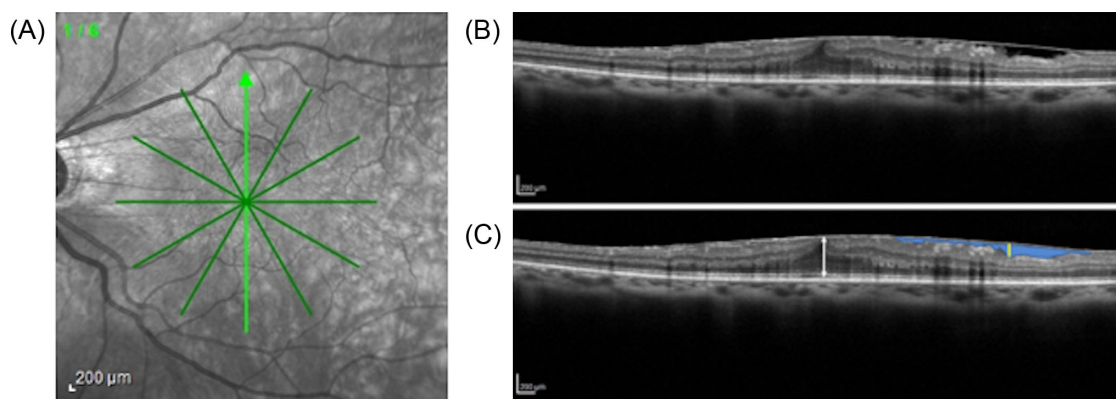
Metamorphopsia is one of the common symptoms associated with epiretinal membranes (ERMs) and other macular disorders, such as age-related macular degeneration. ERMs are among the most common of macular disorders encountered in the elderly population around the world, occurring at a reported prevalence rate of 2% to 12%.<sup>1-6</sup> Patients with ERMs usually manifest no symptoms in the early stages; however, as the condition advances, the patients often develop visual disturbances, including reduced visual acuity and metamorphopsia.

With the development of optical coherence tomography (OCT), researchers have investigated the relationships between several OCT parameters in the affected eyes and the degree of metamorphopsia in patients with ERMs. Watanabe et al.<sup>7</sup> reported that the inner nuclear layer was thicker in patients with ERMs who complained of metamorphopsia than in those without metamorphopsia. One study reported the existence of correlations between the metamorphopsia score and the central retinal thickness (CRT), inner nuclear layer thickness, and thickness of the outer nuclear layer plus outer plexiform layer in patients with ERMs.<sup>8</sup> A more recent study suggested a close association between the metamorphopsia score and the maximum depth of the retinal fold in eyes with ERMs, measured in en face images obtained by swept-source OCT.<sup>9</sup>

M-CHARTS (Inami Co., Tokyo, Japan) have been applied in several previous research studies to quantify the degree of metamorphopsia.<sup>10-13</sup> M-CHARTS enable measurement of the horizontal (MH) and vertical (MV) metamorphopsia scores. Arimura et al.<sup>11</sup> reported that, based on measurements using M-CHARTS, the degree of horizontal retinal contraction was related to the MV score, but the degree of vertical retinal contraction was associated with the MH score in patients with ERMs. Considering that metamorphopsia is one of the major complaints in patients with ERMs, it would be useful if the severity of metamorphopsia could be predicted using OCT images. However, the precise correlations between the OCT parameters and severity of metamorphopsia still remain unclear.

The aim of the current study was to investigate the OCT parameters that were associated with visual function (visual acuity and metamorphopsia) in patients with ERMs. In addition to the CRT and maximum depth of the retinal fold, the area of the gap between the ERM and the retinal surface

metamorphopsia score and the maximum depth of the retinal fold in eyes with ERMs, measured in en face images obtained by swept-source OCT.<sup>9</sup>



**FIGURE 1.** Measurement of OCT parameters in eyes with ERMs. (A) Vertical and horizontal scans 5.8 mm in length (scan angle 20°) were used for the analysis. (B) Each OCT image through the fovea (1024 × 496 pixel) was obtained in eyes with idiopathic ERMs. (C) The following OCT parameters were calculated using ImageJ software: CRT (*white arrow*), maximum retinal fold depth (*yellow bar*), and SUKIMA (*blue area*).

(SUKIMA; “gap” in Japanese) was newly defined and calculated from the vertical and horizontal OCT images. Then, we attempted to identify the parameters in the affected eyes that were closely associated with visual functions in patients with ERMs.

## METHODS

This retrospective observational study was conducted in consecutive patients with idiopathic ERMs seen at our institution. The exclusion criteria were patients with other retinal diseases, such as diabetic retinopathy or retinal vein occlusion, and patients who had undergone vitreoretinal surgery. All of the procedures adhered to the tenets of the Declaration of Helsinki. The study was conducted with the approval of the Ethics Committee of Yokohama City University, Kanagawa, Japan. Written informed consent was obtained from each of the participating patients.

In addition to comprehensive ophthalmologic examinations, including visual acuity measurements, indirect and contact lens slit-lamp biomicroscopy, and spectral domain OCT (Heidelberg Engineering, Heidelberg, Germany), M-CHARTS were used to measure the degree of metamorphopsia. The M-CHART examination was performed for both vertical and horizontal lines at a distance of 30 cm with refractive correction. From the vertical and horizontal metamorphopsia scores (MV and MH, respectively), the mean of MV and MH (Mave) was calculated and used for the statistical analysis. CRT was measured as the distance between the internal limiting membrane and the surface of the retinal pigment epithelium at the fovea. The measurement of maximum retinal fold depth described by Hirano et al.<sup>9</sup> was modified in the current study. Using radial scans with 5.8-mm length centered at the fovea, the deepest retinal surface from the surrounding retina was measured as maximum retinal fold depth for each eye (Fig. 1, yellow bar). The average value of those measured by two independent investigators (AM and KN) was used for the analysis. In addition to the CRT and maximum retinal fold depth, we calculated SUKIMA using Fiji software (ImageJ, National Institutes of Health, Bethesda, MD, USA) (Fig. 1).<sup>14</sup> SUKIMA was manually measured in both the vertical and horizontal OCT scan images through the fovea (SUKIMAv and SUKIMAh, respectively). The scan length was 5.8 mm (scan angle 20°), and

the number of averaging was 30. To investigate the inter-rater agreement, two independent investigators (RA and TI) measured SUKIMA for each eye, and the intraclass correlation coefficient was calculated.

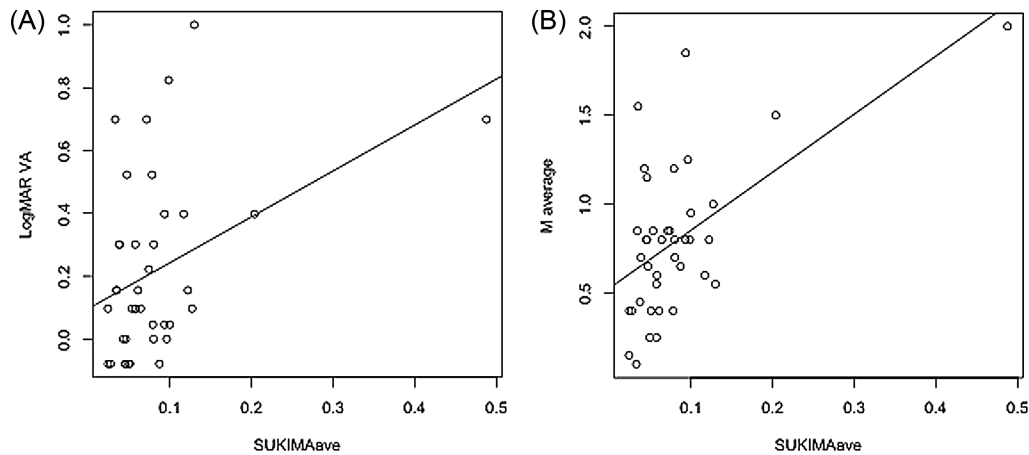
Statistical analyses were conducted to investigate the correlations between the OCT parameters (CRT, maximum retinal fold depth, and SUKIMA) and the visual functions (logMAR visual acuity [VA], metamorphopsia). Multivariate analysis was followed by model selection using the second-order bias-corrected Akaike information criterion (AICc) index. In multivariate regression models, the degrees of freedom decrease as the number of variables increases; hence, the model selection method is recommended to improve the model fit by removing redundant variables, particularly when the number of explanatory variables is large, compared with simple multivariate regression analysis.<sup>15</sup> The AIC is an established statistical measure used to evaluate the relationships among variables, and the AICc represents a corrected AIC, which provides an accurate estimate even when the sample size is small.<sup>16,17</sup> All statistical analyses were performed using R 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

The present study was conducted in 39 eyes of 39 patients (18 females and 21 males) with idiopathic ERMs. Table 1 shows the demographic data for the patients. The mean age

**TABLE 1.** Subject Demographics (N = 39 Eyes; 24 Right, 15 Left)

Variable	Mean ± SD (Range)
Age (y)	69.6 ± 8.9 (52–88)
Refractive error (diopter)	−1.12 ± 3.14 (−9.875 to 3.00)
logMAR visual acuity	0.21 ± 0.28 (−0.079 to 1.0)
Mave score	0.79 ± 0.43 (0.1–2.0)
MH score	0.78 ± 0.50 (0–2.0)
MV score	0.80 ± 0.44 (0.2–2.0)
Maximum retinal fold depth (μm)	89.5 ± 37.5 (25–193)
Central retinal thickness (μm)	400.1 ± 98.1 (154–585)
SUKIMAh (mm <sup>2</sup> )	0.060 ± 0.044 (0.0068–0.22)
SUKIMAv (mm <sup>2</sup> )	0.10 ± 0.12 (0.026–0.76)
SUKIMAAve (mm <sup>2</sup> )	0.081 ± 0.076 (0.024–0.49)



**FIGURE 2.** Correlation between SUKIMAAve and visual functions. There were significant correlations between (A) SUKIMAAve and logMAR VA ( $r = 0.397$ ; 95% CI, 0.0936–0.633;  $P = 0.012$ ) and (B) SUKIMAAve and degree of metamorphopsia (Mave) ( $r = 0.578$ ; 95% CI, 0.322–0.756;  $P = 0.00012$ , linear regression analysis).

**TABLE 2.** Relationship Between the OCT Parameters and logMAR Visual Acuity

Variable	Univariate Analysis			Optimal Model		
	Coefficient	SE	<i>P</i>	Coefficient	SE	<i>P</i>
Age	0.0089	0.0050	0.080	0.012	0.0042	0.0074
Refractive error	0.020	0.014	0.18	N.S.	N.S.	N.S.
Central retinal thickness	0.0012	0.00043	0.007	0.0011	0.00041	0.015
Maximum retinal fold depth	0.0030	0.0011	0.0099	NS	NS	NS
SUKIMAAve	1.46	0.56	0.012	1.12	0.53	0.041

of the participants was  $69.6 \pm 8.9$  years. The logMAR VA was  $0.21 \pm 0.28$ . The spherical equivalent of refractive error was  $-1.12 \pm 3.14$  diopter. The Mave was not significantly correlated with logMAR VA ( $P = 0.57$ , linear regression analysis), and there was no significant correlation between either the MV and logMAR VA ( $P = 0.87$ ) or the MH and logMAR VA ( $P = 0.40$ , linear regression analysis).

The intraclass correlation coefficient value of SUKIMAAve was 0.797 (95% confidence interval [CI], 0.477–0.953), suggesting relatively high reproducibility of our current method. Univariate analysis suggested that CRT ( $P = 0.0070$ ), maximum retinal fold depth ( $P = 0.0099$ ), and SUKIMAAve ( $P = 0.012$ , linear regression analysis) were significantly associated with logMAR VA (Fig. 2A). Multivariate analysis using AICc model selection identified age, CRT, and SUKIMAAve as being significantly correlated with logMAR VA (Table 2). The optimal model for logMAR VA was as follows.

$$\begin{aligned} \text{logMAR VA} = & -1.14 + 0.012 (\pm 0.0042) \times \text{age} \\ & + 0.0011 (\pm 0.00041) \times \text{CRT} + 1.12 (\pm 0.53) \\ & \times \text{SUKIMAAve (AICc} = 3.2) \end{aligned}$$

On the other hand, univariate analysis identified SUKIMAAve as being significantly associated with Mave ( $r = 0.578$ ;  $P = 0.00012$ , linear regression analysis) (Fig. 2B). Multivariate analysis identified CRT and SUKIMAAve among the OCT parameters as being significantly associated with Mave (AICc = 33.0) (Table 3). The optimal model for the

Mave was as follows:

$$\begin{aligned} \text{Mave} = & 0.96 - 0.012 (\pm 0.00061) \times \text{CRT} \\ & + 3.87 (\pm 0.79) \times \text{SUKIMAAve} \end{aligned}$$

Furthermore, although there were significant correlations between SUKIMAAve and MH score ( $r = 0.494$ ;  $P = 0.0014$ ) and between SUKIMAAve and MV score ( $r = 0.405$ ;  $P = 0.011$ ), significant relationships were also observed between SUKIMAAve and MH ( $r = 0.599$ ;  $P < 0.0001$ ) and between SUKIMAAve and MV ( $r = 0.486$ ;  $P = 0.0017$ , linear regression analysis) (Fig. 3). There was a significant association between the maximum retinal fold depth and SUKIMAAve ( $r = 0.600$ ;  $P < 0.0001$ , linear regression analysis) (Fig. 4A). Moreover, SUKIMAAve was significantly related to CRT ( $r = 0.385$ ;  $P = 0.016$ , linear regression analysis) (Fig. 4B).

## DISCUSSION

In the present study, we identified a novel OCT parameter, SUKIMAAve, which means “gap” in Japanese, as a clinically significant parameter in eyes with idiopathic ERMs. The gap area between the ERM and the retinal surface was measured for both the vertical and horizontal lines in each patient (SUKIMAAve and SUKIMAAh, respectively), and the average of SUKIMAAve and SUKIMAAh (SUKIMAAve) was calculated for each eye. Our analysis revealed that the SUKIMAAve was closely associated with logMAR VA and metamorphopsia score.

TABLE 3. Relationship Between OCT Parameters and Mave

Variable	Univariate Analysis			Optimal Model		
	Coefficient	SE	P	Coefficient	SE	P
Age	0.0032	0.0079	0.69	N.S.	N.S.	N.S.
Refractive error	0.0086	0.022	0.70	N.S.	N.S.	N.S.
Central retinal thickness	-0.000059	0.00072	0.94	-0.0012	0.00061	0.055
Maximum retinal fold depth	0.0038	0.0018	0.038	NS	NS	NS
SUKIMAave	3.27	0.76	0.00012	3.87	0.79	<0.0001

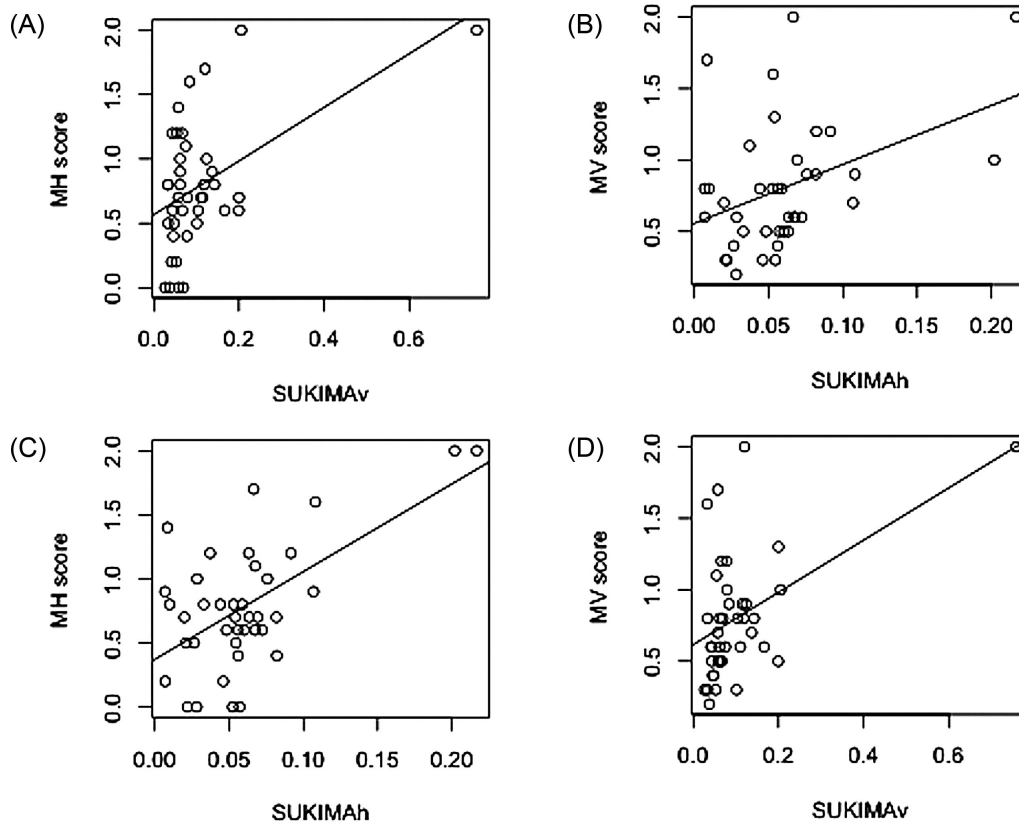


FIGURE 3. Relationships between SUKIMA and metamorphopsia score. There were significant correlations between (A) SUKIMAv and MH score ( $r = 0.494$ ; 95% CI, 0.211–0.700;  $P = 0.0014$ ), (B) SUKIMAh and MV score ( $r = 0.405$ ; 95% CI, 0.103–0.639;  $P = 0.011$ ), (C) SUKIMAh and MH score ( $r = 0.599$ ; 95% CI, 0.349–0.769;  $P < 0.0001$ ), and (D) SUKIMAv and MV score ( $r = 0.486$ ; 95% CI, 0.202–0.695;  $P = 0.0017$ , linear regression analysis).

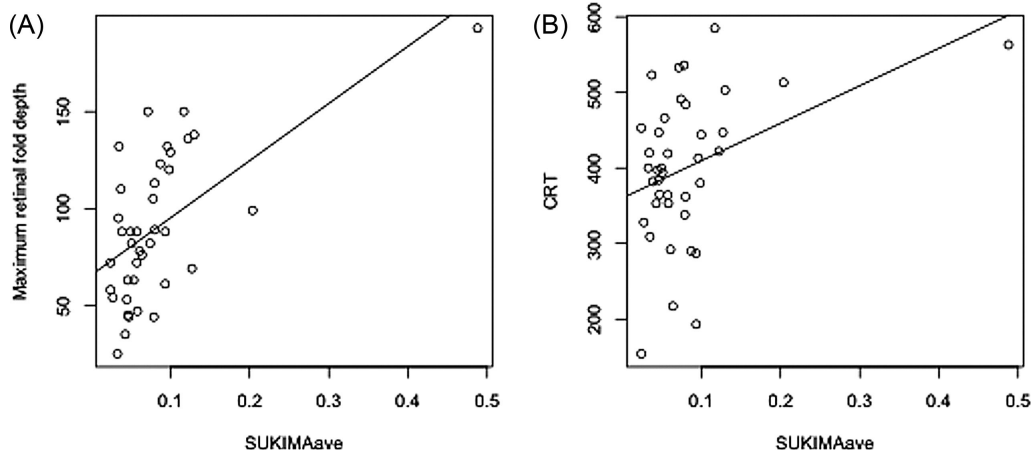
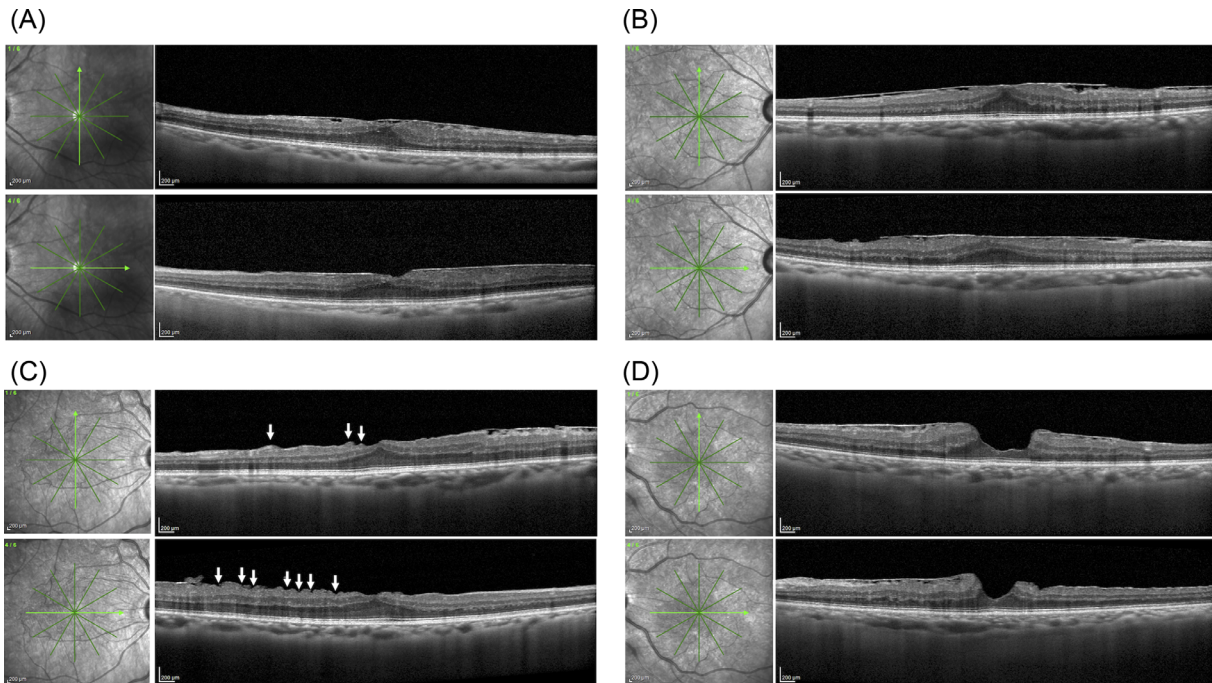


FIGURE 4. Relationships between SUKIMA and OCT parameters. (A) There was a significant relationship between SUKIMAave and the maximum retinal fold depth ( $r = 0.600$ ; 95% CI, 0.350–0.769;  $P < 0.0001$ ). (B) A significant correlation was also observed between SUKIMAave and CRT ( $r = 0.385$ ; 95% CI, 0.0792–0.625;  $P = 0.016$ , linear regression analysis).



**FIGURE 5.** Representative cases with good and poor correlation between SUKIMA and metamorphopsia score. **(A)** Vertical and horizontal scans of 85-year-old female with a good correlation between SUKIMA and metamorphopsia score. SUKIMAv, SUKIMAh, and SUKIMAave were 0.062, 0.033, and 0.047 mm<sup>2</sup>, respectively. MH, MV, Mave score, and logMAR VA were 0.8, 0.5, 0.65, and 0.523, respectively. **(B)** This 71-year-old female showed a good correlation between SUKIMA and metamorphopsia score. SUKIMAv, SUKIMAh, and SUKIMAave were 0.137, 0.107, and 0.122 mm<sup>2</sup>, and MH, MV, Mave score, and logMAR VA were 0.9, 0.7, 0.8, and 0.155, respectively. **(C)** This 72-year-old female showed a poor correlation between SUKIMA and metamorphopsia score. SUKIMAv, SUKIMAh, and SUKIMAave were 0.061, 0.0083, and 0.035 mm<sup>2</sup>, and MH, MV, Mave score, and logMAR VA were 1.4, 1.7, 1.55, and 0.155, respectively. Of note, ERM was not fully identified in both vertical and horizontal scans, whereas retinal folds were observed (*white arrows*). **(D)** This 84-year-old male showed a poor correlation between SUKIMA and metamorphopsia score. SUKIMAv, SUKIMAh, and SUKIMAave were 0.120, 0.067, and 0.093 mm<sup>2</sup>, and MH, MV, Mave score, and logMAR VA were 1.7, 2.0, 1.85, and 0.398, respectively. ERM at the temporal region was not identified, and it is possible that the SUKIMA score might have been underestimated in this case.

SUKIMA is an easy-to-measure parameter from the horizontal and vertical OCT images of eyes with ERMs. Previous studies have suggested that the CRT and maximum retinal fold depth are related to the degree of metamorphopsia in eyes with ERMs.<sup>8,9</sup> Our results with AICc model selection indicated significant correlations between the CRT and the degree of metamorphopsia but not between the maximum retinal fold depth and the degree of metamorphopsia. This discrepancy might be due to the relatively small sample size in our study. However, SUKIMA was significantly related to both CRT and maximum retinal fold depth (Fig. 4). As compared with these metamorphopsia-related OCT parameters, SUKIMA was found to be the parameter closely associated with the degree of metamorphopsia in patients with ERMs. The entire reason why SUKIMA was a better parameter compared to the maximum retinal fold depth and/or CRT still remains elusive; however, it is possible that SUKIMA is simply a two-dimensional parameter and its measurement is highly reproducible. In any case, it appears that SUKIMA is a useful parameter to predict the degree of metamorphopsia in eyes with ERMs. Compared with typical cases that have demonstrated a good correlation between SUKIMA value and metamorphopsia (Figs. 5A, 5B), some ERM patients have demonstrated a poor correlation, because the ERMs were not partially identified in OCT images (Figs. 5C, 5D). In such cases, SUKIMA might be underestimated; therefore, it is important that other metamorphopsia-related parameters, such as CRT and maximum retinal fold depth, be taken into consideration.

Arimura et al.<sup>11</sup> suggested the existence of a significant association between the degree of retinal contraction and the metamorphopsia scores in patients with idiopathic ERMs. In their report, 29 eyes with ERM were carefully observed for at least 3 years, and the degrees of horizontal and vertical retinal contractions were calculated by measuring the changes in the retinal vessel location on images of the fundus. The results revealed that the degree of vertical retinal contraction was correlated with the MH score and the degree of the horizontal retinal contraction was correlated with the MV score. However, it takes much time to measure the degree of retinal contraction. On the other hand, it is simpler to measure SUKIMA from the vertical and horizontal OCT images, and it has the potential to predict the degree of retinal contraction and degree of metamorphopsia in ERM eyes. We initially hypothesized that the SUKIMAh measured in horizontal OCT images might reflect horizontal retinal contraction and the SUKIMAv might reflect vertical retinal contraction. Our results demonstrated significant correlations between the SUKIMAh and MV score, and between the SUKIMAv and MH score (Fig. 3). On the other hand, we also found significant associations between SUKIMAh and MH score and between SUKIMAv and MV score. It would be of interest to clarify the relationship between SUKIMA and the direction of retinal contraction in eyes with ERM. Further investigation with a larger sample size is needed in the future.

Our current results indicate that SUKIMA was significantly correlated with logMAR VA, whereas SUKIMA was

not always found in the fovea. The reason why SUKIMA was associated with VA still remains unclear; however, one possibility is that SUKIMA was associated with VA by influencing CRT. Another possibility is that parafoveal SUKIMA might affect the foveal microstructure to some extent in eyes with ERMs. Further studies are needed to clarify the effect of SUKIMA on the foveal structure in ERMs.

There were some limitations of the current study. First, the study was retrospective in nature, and the number of eyes enrolled was relatively small. Second, the study was a cross-sectional study, and we did not evaluate the ERM patients postoperatively. Several reports have suggested that the degree of metamorphopsia improved significantly after surgical treatment of the ERMs.<sup>18–21</sup> Fukuyama et al.<sup>21</sup> reported significant improvement of the metamorphopsia by 1 month after vitrectomy. It would be of interest to evaluate the relationship between SUKIMA at baseline and the degree of improvement of the metamorphopsia postoperatively and also to investigate the usefulness of measuring SUKIMA to predict the visual outcomes. Finally, the axial length was not measured in the current study. The variability of axial length causes differences in the magnification of OCT or OCT angiography images<sup>22</sup>; therefore, more accurate measurements of SUKIMA are possible when the axial length is taken into account.

In conclusion, we identified a novel OCT parameter, SUKIMA, as a useful parameter in patients with idiopathic ERMs. SUKIMA is easy to measure from vertical and horizontal OCT images and was found to be more closely associated with metamorphopsia as compared with other metamorphopsia-related OCT parameters. SUKIMA is a useful parameter for predicting the degree of metamorphopsia in patients with ERMs.

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