Correlation between Metamorphopsia and Epiretinal Membrane Optical Coherence Tomography Findings

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Purpose: To examine the retinal morphologic features of metamorphopsia caused by epiretinal membrane (ERM) and to determine whether spectral-domain optical coherence tomography (SD-OCT) correlated with metamorphopsia.

Design: Retrospective case series.

Participants: This study included 19 eyes of 19 patients with ERM diagnosed by clinical ophthalmic findings and SD-OCT.

Methods: The 19 eyes were classified into 3 groups based on Amsler chart results: no metamorphopsia (n = 4), local metamorphopsia (n = 8), and broad metamorphopsia (n = 7). The thickness of the 3 inner retinal layers: inner nuclear layer (INL), outer plexiform layer (OPL), and outer nuclear layer (ONL), on 5 horizontal SD-OCT cross-sections (1 line through the fovea, 2 regularly spaced lines superior to the fovea, and 2 regularly spaced lines inferior to the fovea) were measured using the electronic calipers of the SD-OCT system.

Main Outcome Measures: Correlation between INL, OPL, and ONL thickness with metamorphopsia and visual acuity.

Results: Metamorphopsia was detected in the same position as edematous areas of the INL with a thickness >50 μm. The maximum INL thickness was relatively significantly different between the subjects with no metamorphopsia and those with local or broad metamorphopsia (vs local, $P = 0.06$; vs broad, $P = 0.04$). Visual acuity significantly correlated with both maximum INL thickness ($A = -0.681$; $P = 0.001$) and maximum ONL thickness ($A = -0.708$; $P<0.001$) in metamorphopsia.

Conclusions: Metamorphopsia induced by ERM may be related to the edematous areas of the INL detected with SD-OCT. The classification of ERM based on INL thickness is a potentially useful indication for surgery.

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Idiopathic epiretinal membrane (ERM) is a disorder in which the vitreomacular interface induces a tangential tractional force on the retina, leading to deformation of the retinal architecture. Generally, ERM is asymptomatic; therefore, most patients with the disease have normal or nearly normal vision with occasional metamorphopsia. The onset of metamorphopsia can be slow and imperceptible, such that an Amsler chart is the only means of detection. Although several possible causes of the metamorphopsia and reduced visual acuity have been considered, including macular distortion, vascular leakage, shallow tractional retinal detachment, opacity owing to ERM itself, and disarray of the photoreceptors in the sensory retina,[1–3] to date there is no direct evidence supporting any of these possibilities.

Metamorphopsia is usually detected as a subjective symptom using an Amsler chart, and there are currently no examinations that provide objective data. Detection of metamorphopsia using an Amsler chart can also be influenced by visual acuity disturbances such as severe cataract or corneal opacity. Metamorphopsia is a symptom associated not only with ERM but with several other diseases as well. For that reason, establishing an objective method for detecting metamorphopsia is clinically important.

In the present study, we evaluated the correlation between the degree of metamorphopsia using an Amsler chart and the thickness of the inner retinal layers based on 3-dimensional (3D) spectral-domain optical coherence tomography (SD-OCT) to determine whether correlates of subjective metamorphopsia in patients with ERM could be objectively detected using SD-OCT. In addition, we attempted to construct an ERM classification scheme based on morphometric and objective OCT findings.

Materials and Methods

Study Participants and Clinical Examination

The study was a nonrandomized, retrospective case series of 19 eyes of 19 patients with idiopathic ERM diagnosed by clinical findings from ophthalmic examination and SD-OCT. Cases with secondary membrane formation owing to diabetic retinopathy and eyes with previous retinal detachment surgery or pars plana vitrectomy were excluded. Eyes with reduced vision owing to other causes, such as severe cataract, glaucoma confirmed by optic nerve head glaucomatous changes, visual field defects, and age-related macular degeneration, were excluded. We also excluded eyes for which accurate OCT images could not be obtained. The mean

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age ± standard deviation (SD) of the 11 women and 8 men diagnosed with ERM was 71.2±6.4 years (range, 55–81). To compare and understand normal retinal morphologic features, healthy patients (5 men, 5 women) were also examined. The mean age ± SD was 69.2±6.2 years (range, 56–75).

All eyes were examined for the presence of metamorphopsia using an Amsler chart. The eyes were classified into 3 groups: no metamorphopsia (defined as not detected by the Amsler chart), local metamorphopsia (defined as metamorphopsia involving less than two thirds of the Amsler chart), or broad metamorphopsia (defined as metamorphopsia involving more than two thirds of the Amsler chart). In addition to comprehensive ophthalmic examination, including best-corrected visual acuity in decimal notation, SD-OCT (3D OCT 1000 Topcon Corp, Tokyo, Japan) was performed to evaluate tomographic features and measure the inner retinal layers.

Optical Coherence Tomography Scanning Procedure

The 3D datasets were obtained using the raster scan protocol of 128 horizontal B-scan images, each composed of 512 axial scans. This raster scan protocol covers an area of 6 mm (horizontal) × 6 mm (vertical) × 1.7 mm (axial) with a horizontal pixel spacing of 11 μm (6 mm/512) and a vertical pixel spacing of 47 μm (6 mm/128). We obtained 3D datasets centered on the fovea for each patient. Volumetric rendering of the dataset was performed using the image processing software provided by the SD-OCT for 3D image reconstruction.

Thickness Measurements of the Inner Retinal Layers

To measure the thickness of the inner retinal layers, 5 horizontal B-scan cross-sections on 3D OCT were examined: 1 horizontal B-scan cross-section through the fovea, 2 regularly spaced horizontal B-scan cross-sections superior to the fovea, and 2 regularly spaced horizontal B-scan cross-sections inferior to the fovea (Fig 1).

The retinal layer borders were determined based on the refractive differences between the inner retinal layers using the macular segmentation algorithm for OCT developed by Ishikawa et al[4] and Tan et al.[5] The thickness of the inner nuclear layer (INL) and outer nuclear layer (ONL), defined as the width of the lowest black-scattering and lowest black-reflection layers, and the thickness of the outer plexiform layer (OPL), defined as the width of the highly reflective line between the INL and ONL, were measured vertically at as many points as possible on each of the 5 horizontal B-scan cross-sections. In particular, the ONL thickness measurement was defined as the vertical length from the highly reflective line corresponding to the junction between the photoreceptor inner and outer segment to the lower edge of the highly reflective line corresponding to the OPL. The INL, OPL, and ONL thickness measurements were carefully obtained at points where there were obvious differences between the black reflective line and the highly reflective line. The thickness measurements of the inner retinal layers were performed manually using the electronic calipers of the 3D-OCT 1000 system.

Statistical Analysis

Statistical analysis was performed using the Pearson correlation factor, Student *t* test, and Welch's *t* test. For all analyses, $P<0.05$ was considered significant. All statistical analyses were performed using Statcel (2nd ed), an add-in module for Microsoft Excel (Statcel 2nd ed, OMS, Tokyo, Japan).

Results

Normal Cases

Mean thickness of the INL, OPL, and ONL, findings of the Amsler chart and SD-OCT through the fovea are presented in Figure 2. The Mean thicknesses of the INL, OPL, and ONL without the central fovea were 31.1±5.1, 18.8±4.1, and 63.0±11.8 μm, respectively. The mean thickness of the ONL at the central fovea was 113.0±10.9 μm. Although the thickness of the ONL was highly variable, the thicknesses of the INL and OPL were almost fixed.

Selected Cases with Epiretinal Membrane

The INL, OPL, and ONL thickness values and findings of the Amsler chart and SD-OCT through the fovea of 3 eyes of the 19 patients included in the study are presented in Figure 2 (case 1 with no metamorphopsia, case 2 with local metamorphopsia, and case 3 with broad metamorphopsia).

In case 1, ERM was observed over a broad retinal region, but no metamorphopsia was detected. The INL, OPL, and ONL thickness ranged from 22 to 39, 11 to 29, and 31 to 116 μm, respectively. The INL and ONL tended to be slightly edematous.

In case 2, local metamorphopsia on the Amsler chart was detected in the same position as edematous areas of the INL that were >50 μm thick. The ONL and OPL in the same position of metamorphopsia tended to be edematous but had varying thicknesses. Edematous areas of the INL that were >50 μm thick were more clearly present in the same position of the metamorphopsia than edematous areas of the ONL and OPL. The position of metamorphopsia on the Amsler chart correlated highly with the edematous areas of the INL.

In case 3, with broad metamorphopsia, the INL, OPL, and ONL had diverse and severe edematous changes. The edematous area of the INL that had a thickness of >50 μm was in almost the same position as the metamorphopsia.

Patient Characteristics

Patient characteristics are summarized in Table 1. The 19 eyes were classified into 3 groups based on Amsler chart results: 4 eyes with no metamorphopsia, 8 eyes with local metamorphopsia, and 7 eyes with broad metamorphopsia.

The maximum thickness of the INL in eyes with no metamorphopsia tended to differ from that in eyes with local metamorphopsia ($P = 0.06$) and significantly differed from that in eyes with broad metamorphopsia ($P = 0.04$). The OPL and ONL tended to be edematous in the area of the metamorphopsia, but there were no significant differences between eyes with no metamorphopsia and those with local or broad metamorphopsia (vs local: OPL, $P = 0.49$; ONL, $P = 0.77$; vs broad: OPL, $P = 0.12$; ONL, $P = 0.10$).

Relationship between Visual Acuity and Inner Nuclear Layer, Outer Plexiform Layer, and Outer Nuclear Layer Thicknesses

There was a significant negative correlation between visual acuity and the maximum thickness of the INL ($A = -0.681$; $P = 0.001$) and ONL ($A = -0.708$; $P<0.001$) in the area of metamorphopsia (Fig 3). There was a slight negative correlation between visual acuity and ONL thickness at the central fovea ($A = -0.527$; $P = 0.043$). Visual acuity and maximum OPL thickness did not correlate in the area of metamorphopsia ($A = -0.179$; $P = 0.463$).

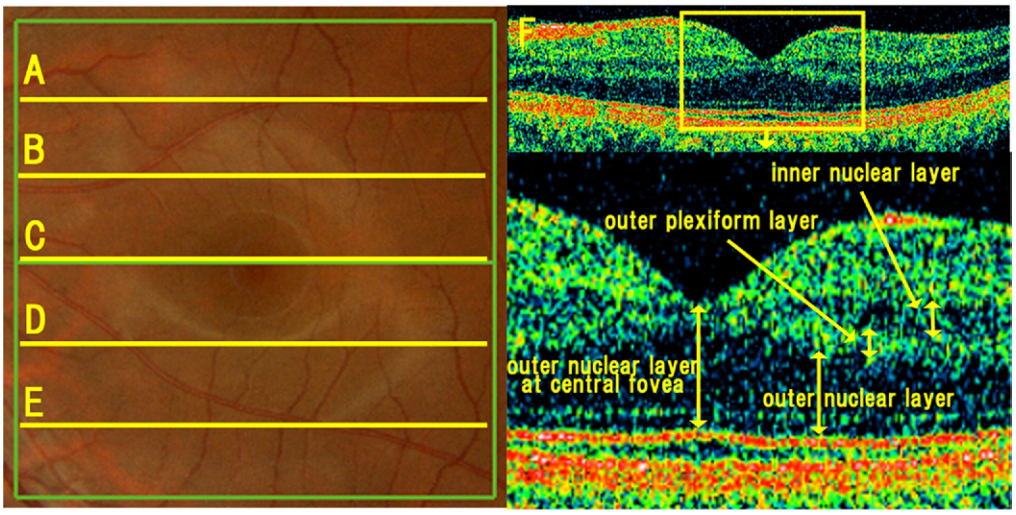

Figure 1. Five horizontal B-scan cross-sections and thickness measurement of the inner retinal layer. Line C is a single horizontal B-scan cross-section through the fovea. Lines A, B and D, E are 4 horizontal B-scan cross-sections, placed at regular intervals superior (**A**, **B**) and inferior (**D**, **E**) to that of the horizontal line through the fovea. **F**, Measurements of the inner retinal layer on line C through the fovea performed using the electronic calipers.

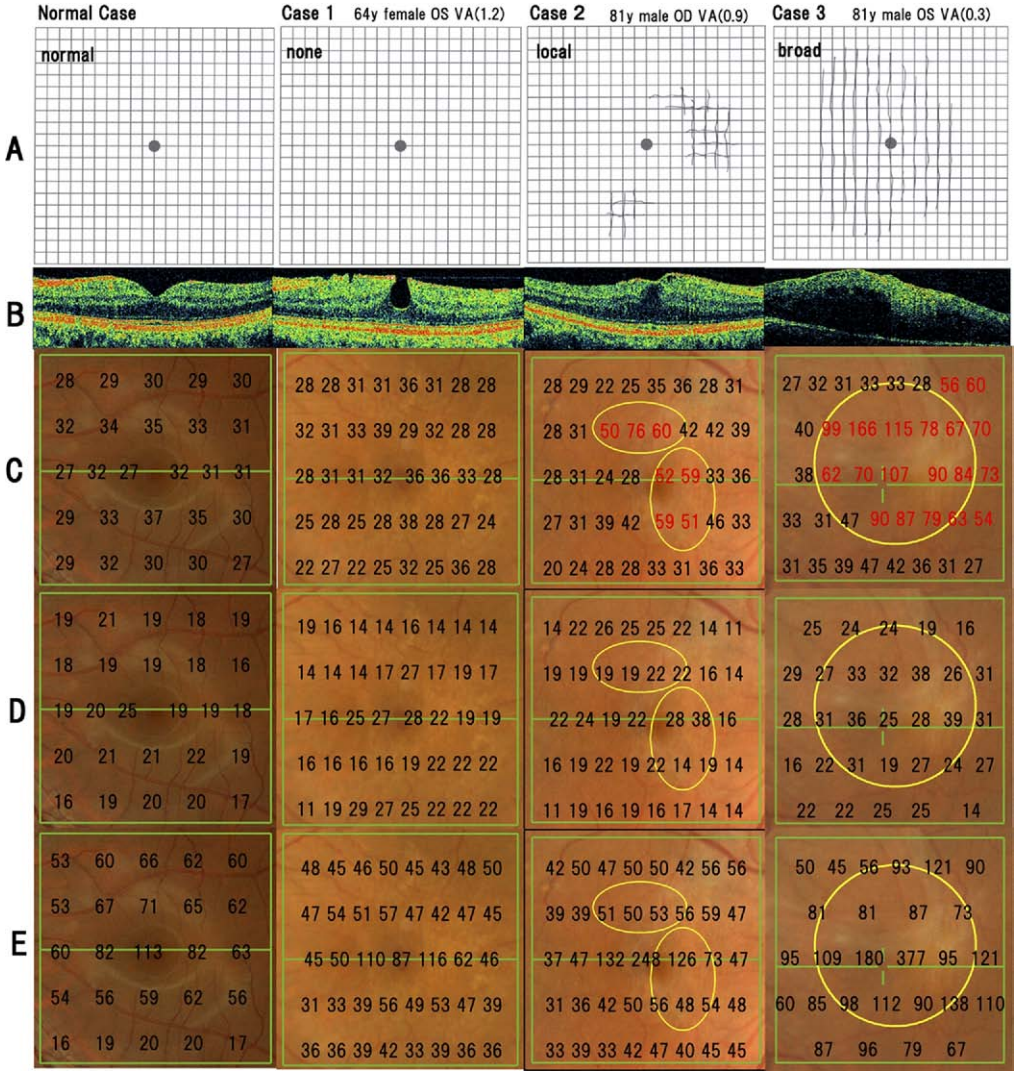

Table 1. Patient Characteristics

Metamorphopsia Findings	None*	Local	Broad
No. of eyes	4	8	7
Mean age, y (range)	69.0 (64–74)	69.8 (55–81)	74.6 (69–81)
Gender			
Male	2	3	3
Female	2	5	4
Mean visual acuity (range)	1.03 (0.9–1.2)	0.83 (0.4–1.0)	0.46 (0.1–1.0)
P vs no metamorphopsia		0.14	0.02
Mean maximum INL thickness ± SD (range) in the area correlating to metamorphopsia	43.8±4.4 (38–48)	68.8±18.8 (50–109)	125.3±81.8 (47–289)
P vs no metamorphopsia		0.06	0.04
Mean maximum OPL thickness ± SD (range) in the area correlating to metamorphopsia	26.0±3.2 (22–29)	30.4±11.7 (14–50)	35.1±13.0 (25–59)
P vs no metamorphopsia		0.49	0.12
Mean maximum ONL thickness ± SD (range) in the area correlating to metamorphopsia	147.8±66.9 (95–245)	134.4±72.8 (52–225)	257.4±108.9 (104–389)
P vs no metamorphopsia		0.77	0.10
Mean maximum ONL thickness ± SD (range) at the central fovea	147.8±66.9 (95–245)	179.6±65.9 (78–248)	258.6±108.4 (87–389)
P vs no metamorphopsia		0.45	0.10

INL = inner nuclear layer; ONL = outer nuclear layer; OPL = outer plexiform layer; SD = standard deviation.
*In the case of metamorphopsia findings "none," the INL, OPL, and ONL thicknesses in the area of metamorphopsia indicate the mean maximum thickness value of INL, OPL, and ONL in the 5 horizontal B-scan cross-sections.

Discussion

In the present study, SD-OCT was useful for detecting objective changes in the inner retinal layers. Metamorphopsia was detected in almost the same position as the edematous areas of the INL, especially areas that were >50-μm thick. Maximum INL thickness differed significantly between eyes with no metamorphopsia and eyes with broad metamorphopsia. The ONL and OPL also tended to be edematous in the area of metamorphopsia, but these changes were not significantly related to the area of metamorphopsia. Therefore, INL thickness mapping based on SD-OCT findings may be a useful and objective method for determining the position of metamorphopsia.

The simplest retinal circuit is a 3-neuron chain: cone to bipolar cell to ganglion cell.[6] This is the so-called vertical pathway, and it is the shortest circuit between the retinal image and one-to-one correspondence with the central nervous system.[6] The INL contains horizontal, bipolar, amacrine, and Müller cell bodies; the OPL is the area in which photoreceptors communicate with the horizontal cells and bipolar cells. The ONL contains the photoreceptor cell bodies, both rods and cones.[6]

Metamorphopsia on the Amsler chart was detected in the same position as the change in INL thickness, which might be due to changes in the bipolar, horizontal, amacrine, and Müller cell bodies. We hypothesize that metamorphopsia begins with changes in INL thickness, which interferes with the one-to-one correspondence between the retinal image and the central nervous system. There were also some edematous changes in the OPL and ONL in the area of metamorphopsia, which may result in insufficient synaptic junctions and low photoreceptor sensitivity, leading to metamorphopsia.

There are some reports about the influence of central retinal thickness on visual acuity in patients with ERM. Suzuki et al[7] reported that foveal thickness and visual acuity in patients with ERM were not related to macular pseudohole. Liu et al[8] reported that central retinal thickness and visual acuity were negatively correlated, and Michalewski et al[9] reported a significant negative correlation between foveal thickness and visual acuity. In the present study, visual acuity and maximum ONL thickness in the area of metamorphopsia or central fovea were significantly negatively correlated. There was also a negative correlation between visual acuity and maximum INL thickness in the area of metamorphopsia. Because the maximum INL thickness position was not at the fovea, however, further study is required to understand this correlation between visual acuity and INL thickness.

In most ophthalmology centers, macular surgery for ERM removal is advocated if the best-corrected visual acuity falls below approximately 20/30 (0.6), but there are no reports of objective indications for surgery, such as OCT findings.[10,11] In this study, eyes with a visual acuity of 20/30 (0.6) showed thickness changes; that is, the INL had a thickness of approximately 100 μm and the ONL had a thickness of approximately 250 μm (Fig 3).

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Figure 2. Normal case and selected cases with epiretinal membrane. The thickness value of the healthy case indicates the mean thickness value of 10 cases. Cases 1 through 3 show selected cases with epiretinal membrane (case 1 with no metamorphopsia; case 2 with local metamorphopsia; case 3 with broad metamorphopsia). **A**, Amsler chart findings. **B**, Spectral domain optical coherence tomography findings through the fovea. **C**, The thickness value of the inner nuclear layer (INL). Red number indicates a greater than 50-μm thickness. **D**, The outer plexiform layer (OPL) thickness value. **E**, The outer nuclear layer (ONL) thickness value. Area enclosed by yellow line indicates the area correlating to metamorphopsia. OD, right eye; OS, left eye; VA = visual acuity.

According to these results, we classified ERM into 1 of 4 stages based on the INL thickness. Stage 0 represents ERM without metamorphopsia and INL thickness ≤50 μm. In stage 1, there is ERM with local metamorphopsia, a maximum INL thickness between 50 μm and 100 μm, and visual acuity >0.6. In stage 2, there is ERM with broad metamorphopsia, an INL thickness >100 μm, and visual acuity between 0.6 and 0.4. In stage 3, there is ERM with severe and broad metamorphopsia, varying INL thickness, and visual acuity <0.4 (Table 2).

In previous studies, ERM was classified based on a clinical scale or on OCT findings.[12,13] Gass proposed classifying ERM severity on a clinical scale with grades 0 through 2.[12] Wilkins et al[13] and Mori et al[12] classified ERM into 2 groups based on OCT findings. With regard to the classification of metamorphopsia on vertical and horizontal center lines, Matsumoto et al[14] divided ERM into 3 groups based on scanning laser ophthalmoscope images, fundus photographs, and the metamorphopsia chart (M-chart). Our classification based on the degree of metamorphopsia, visual acuity, and OCT findings is a new classification that may be useful in determining ERM cases with indistinct metamorphopsia due to cataracts or corneal opacity. Once the maximum INL thickness is >50 μm, patients may become aware of metamorphopsia.

Table 2. Epiretinal Membrane Classification

Stage	Degree of Metamorphopsia	Maximum Thickness of Inner Nuclear Layer (μm)	Visual Acuity
0	None	<50	Without vision loss
1	Local	50–100	>0.6
2	Broad	>100	0.4–0.6
3	Broad and severe	Varied	<0.4

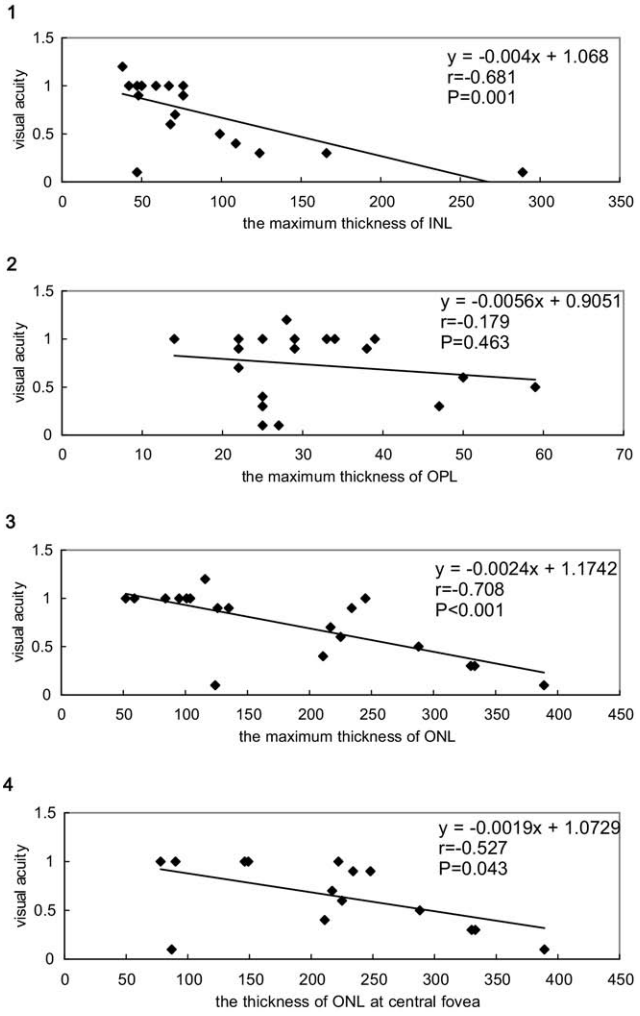

Figure 3. Relationship between visual acuity and thickness of inner nuclear layer (INL), outer plexiform layer (OPL), and outer nuclear layer (ONL). In the area correlating with metamorphopsia, 1, 2, and 3 show the relationship between visual acuity and maximum thickness of the INL, OPL, and ONL, respectively; 4 shows the relationship between visual acuity and thickness of the ONL at the central fovea.

In our preliminary data, postoperative metamorphopsia was detected in 10%, 33%, and 100% of eyes with a preoperative ERM classification of stages 1, 2, and 3, respectively. The applicability of this new classification system for determining the indications for surgery and predicting postoperative visual function must be further investigated.

To apply this ERM classification clinically, the position of the maximum thickness of the INL must be determined from B-scan cross-sections by dragging the mouse across a 3D data map, then measuring the INL thickness using the electronic calipers of the 3D OCT 1000, and finally classifying the ERM stage according to INL thickness, visual acuity, and degree of metamorphopsia.

The limitations of the present study include a relatively small sample size, measurements based on only 5 horizontal B-scan cross sections, inclusion of erroneous values based on measurements of layers with indistinct signals, and manual measurement using electronic calipers. Future studies with a large sample size and improved OCT are needed.

In conclusion, metamorphopsia induced by ERM may be caused by edematous changes of the INL, especially INL with a >50-μm thickness. Our new ERM classification scheme may help clinicians to better understand the retinal changes that underlie the subjective symptoms.

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