

# Visual Performance and Predictive OCT Biomarkers in Epiretinal Membrane Assessment: Beyond Distance Visual Acuity

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**PURPOSE.** This study aimed to comprehensively assess visual performance in eyes with idiopathic epiretinal membrane (iERM). Additionally, it sought to explore the associations between optical coherence tomography (OCT) imaging biomarkers and visual performance in patients with iERM.

**METHODS.** In this prospective, non-interventional study, 57 participants with treatment-naïve iERM from the University of Turin, between September 2023 and March 2024 were enrolled. Visual performance was measured using distance best-corrected visual acuity (BCVA), near BCVA, and maximum reading speed (MaxRS). Structural retinal imaging biomarkers were obtained from OCT, focusing on retinal layer thicknesses and epiretinal membrane characteristics. Statistical analyses, including linear regression and multivariate analysis, were used to determine relationships between visual function and imaging metrics.

**RESULTS.** Monocular distance BCVA ( $0.37 \pm 0.23$  LogMAR), near BCVA ( $0.59 \pm 0.18$  LogMAR), and MaxRS (108.88 [68.38] words per minute [wpm]) in patients with iERM were significantly reduced compared with reference values. Both near BCVA and reading speed exhibited a greater percentage reduction than distance visual acuity. Patients with phakic showed worse visual acuity than patients with pseudophakia, although their reading performance was similar. Higher outer plexiform layers thickness and inner retinal thickness were associated with decreased distance and near visual acuity and reduced reading speed (beta, *P* value).

**CONCLUSIONS.** The iERM predominantly impacts near visual performance, with near visual acuity and reading speed being more affected than distance visual acuity. Structural OCT biomarkers, particularly retinal thickness in specific regions, correlate with worse functional impairments. This highlights the importance of near vision assessments and imaging biomarkers for a comprehensive evaluation of visual impairment in iERM.

**Keywords:** idiopathic epiretinal membrane (iERM), reading performance, reading speed, retinal biomarkers, structural optical coherence tomography (OCT)

Idiopathic epiretinal membrane (iERM), commonly known as macular pucker, is a retinal disorder characterized by the growth of a thin layer of fibrous tissue over the macula. This fibrocellular proliferation often results from pathological vitreoretinal separation, leading to retinal distortion and visual impairment.<sup>1</sup> The iERM is a frequent condition, with a prevalence estimated between 2% and 34% among individuals aged 50 years and older.<sup>2–5</sup> Structural optical coherence tomography (OCT) has advanced the characterization of iERM, enabling its classification into four stages according to the Govetto classification. This classification helped identify inner and outer imaging biomarkers associated with

a poorer prognosis.<sup>1,6–12</sup> The primary symptoms of iERM included decreased distance visual acuity<sup>10</sup> and the development of metamorphopsia,<sup>13</sup> which is characterized by distorted perception of lines. These symptoms have traditionally been used to indicate retinal alterations and determine the timing of surgical intervention.<sup>1</sup> However, it is important to note that anatomic changes may not always correlate with symptoms, and relying solely on distance visual acuity may not fully capture a patient's visual impairments.<sup>1,14</sup> Recent studies highlighted the importance of additional functional assessments, such as near visual acuity and reading speed, to quantify near visual performance

impairment in macular disorders, including central serous chorioretinopathy<sup>15</sup> and age-related macular degeneration (AMD).<sup>16–22</sup> Indeed, near visual performance significantly impacts the quality of life, affecting daily activities, such as reading and writing.<sup>15</sup> The aim of this prospective, non-interventional study was to provide a comprehensive assessment of visual performance, including distance visual acuity, near visual acuity, and reading speed, in eyes with iERM. More importantly, this study sought to investigate the associations between OCT imaging biomarkers and visual performance in patients with iERM.

## METHODS

In this prospective non-interventional non-randomized study (protocol number 0042010), the authors enrolled consecutive patients with treatment-naïve iERM at the “Città della Salute e della Scienza” hospital, University of Turin, Turin, Italy, between September 2023 and March 2024. The diagnosis of iERM was based on clinical examination, including the use of structural OCT. In the presence of bilateral iERM, one eye was randomly included in the study in order to minimize inter-eye confounding factors. All patients gave their consent to be included in this study. Finally, the research adhered to the 1964 Helsinki Declaration and its later amendments.

Exclusion criteria included: (i) history or evidence of any concurrent retinal or optic nerve disorders, including diabetic retinopathy and high myopia (greater than  $-6.00$  diopters [D]); (ii) clinical evidence of a macular pseudohole, lamellar macular hole, full-thickness macular holes, or foveoschisis; and (iii) any evidence of ocular pathologies causing secondary ERM.

## Tests of Visual Performance

Distance best-corrected visual acuity (BCVA) was assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) acuity charts. Patients received either retinoscopy or autorefractometer measurements to determine the best refractive correction. Subsequently, conventional subjective refraction was performed to achieve the optimal correction. During the testing process, background illumination and room setting were standardized for each evaluation. The BCVA measurements were directly recorded in the logarithm of the minimal angle of resolution (LogMAR) for statistical analysis.

Near BCVA was measured using a Jaeger near-point test card at a distance of 35 centimeters (approximately 14 inches) from the patient's face. This test followed the addition of a positive lens, ranging from  $+2.00$  D to  $+2.75$  D, to the lens used in the distance BCVA test, based on the patient's age. Subsequently, conventional subjective refraction was performed to achieve the optimal correction. The Jaeger units were then converted to Snellen equivalents using the equivalencies reported on the Rosenbaum near-vision screening card,<sup>23</sup> and subsequently converted to LogMAR units for statistical analysis. Throughout the testing process, background illumination, room setting, and reading position were standardized for each evaluation.

Monocular reading performance was tested using the Italian version of the Radner reading charts. The Radner charts consist of 41 sentences with uniform grammatical structure

and a consistent level of lexical and syntactical complexity. The print sizes increase geometrically from 0.25 M to 6.3 M (equivalent to 20/320 to 20/12.5 Snellen at 35 cm). Each sentence comprises 3 lines and 14 words, aligned in blocks. The line structure follows these guidelines: (i) each line includes 27 to 29 characters, spaces included; (ii) the first and second lines each contain exactly 5 words, whereas the third line has 4 words; (iii) the initial word of the first line is a 2-letter, 1-syllable word, followed by a medium-length word of 6 to 8 letters and 3 syllables; (iv) the third and fourth words must also have 3 syllables; (v) the first word of the second line is a 2 or 3-letter, 1-syllable word, different from the first word of the first line; (vi) the second word in the second line is a long 4-syllable word, followed by a comma; (vii) after the comma, there should be 2 one-syllable words of 2 or 3 letters each, plus a 3-syllable word; and (viii) the third line begins with a 6 to 8 letter word with 3 syllables.

During this test, the patients utilized the same best refractive correction used for near BCVA. The background illumination, room setting, and reading position were also standardized. Additionally, the chart luminance was maintained at  $120 \text{ cd/m}^2$ , and the reading distance was set at 35 cm, corresponding to 14 inches used in the near BCVA examination.

During the evaluation, the patients were instructed to read the sentences on the Radner reading charts as quickly as possible. They were asked to continue reading until they could no longer proceed, even if they made errors (such as mispronunciations or unread syllables), which were recorded by the examiner. The examiner also noted the time taken to read each sentence. After completing the examination, the maximum reading speed (MaxRS) was obtained, which is defined as the fastest speed achieved across the various print sizes and is measured in words per minute (wpm). This metric was demonstrated to be characterized by high inter-session repeatability in patients with neovascular AMD.<sup>20</sup>

Each participant also underwent individual Amsler grid testing, conducted at a distance of 35 cm under consistent lighting conditions and using the same best refractive correction used for near BCVA assessment. A positive Amsler grid test result was defined by the patient reporting interrupted or curved lines on the grid, or squares appearing distorted in shape or size.

## Structural OCT Assessment

All patients underwent structural OCT scans using the spectral domain (SD) Heidelberg Spectralis HRA + OCT (Heidelberg Engineering, Heidelberg, Germany). The scanning protocol included the following 3 scans: (i) 73 horizontal B-scans spaced 60 microns apart, spanning an area of 20 degrees  $\times$  15 degrees centered on the fovea; (ii) 49 horizontal B-scans spaced 120 microns apart, spanning an area of 20 degrees  $\times$  20 degrees centered on the fovea; (iii) and 2 high-definition vertical and horizontal B-scans centered on the fovea. Only images with a signal strength of at least 25, as per the manufacturer's recommendation, were considered.

Two experienced and unbiased graders (authors F.G. and E.R.) independently evaluated the OCT images for qualitative and quantitative features without knowledge of the visual outcomes. In cases of disagreement, an experienced clinician (author M.R.) made the final decision. In details,

graders assessed the central subfield and the four para-central subfields of the ETDRS grid centered on the fovea for the presence of: (i) central foveal bouquet abnormalities; (ii) disruption of the external limiting membrane (ELM) and the ellipsoid zone (EZ), defined as any interruption in their hyper-reflective bands, regardless of the size; and (iii) the presence of degenerative intra retinal cysts. Additionally, using structural OCT images, the two graders classified each case of iERM into one of the four stages according to the Govetto classification.<sup>24</sup>

Quantitative retinal metrics were obtained using the 20 degrees  $\times$  20 degrees OCT scan. Individual retinal layer thicknesses were obtained within five sectors of the ETDRS grid (i.e. inner-superior, inner-right, inner-inferior, inner-left, and central) using the Heidelberg Spectralis built-in software. Segmentation of each layer was adjusted manually in all cases. The retinal layers measured included the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), and outer nuclear layer (ONL).

Additionally, each study eye underwent en face structural OCT examination using the Cirrus 6000 (Carl Zeiss Meditec, Dublin, CA, USA) device, which performed  $6 \times 6$  mm scans centered on the foveal region. This scan provided an en face structural image of the vitreoretinal interface, allowing visualization of the epiretinal membrane's adhesion to the inner retina, referred to as the "A-zone."<sup>25</sup> If necessary, segmentation of vitreoretinal interface slab was adjusted manually. These en face OCT images were imported in ImageJ and the area of the A-zone was calculated in mm<sup>2</sup>, as previously described.<sup>25</sup>

### Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 28.0.1.0, developed by IBM SPSS Statistics Inc. in Chicago, IL, USA. Normal data distribution was assessed using the Shapiro-Wilk test. All quantitative and qualitative variables are reported in the "Results" section as mean (M) and standard deviation ( $\pm$ SD) for variables with a normal distribution, and as median (Mdn) and interquartile range (IQR), for those with a non-normal distribution. The level of statistical significance was set at  $P < 0.05$ .

A linear regression was conducted among the three functional reading performance variables: (i) distance BCVA (logMAR) versus near BCVA (logMAR), (ii) MaxRS (wpm) versus distance BCVA (logMAR), and (iii) MaxRS (wpm) versus near BCVA (logMAR). Comparative analysis between patients who were phakic and those who were pseudophakic was conducted using the independent samples *t*-test for distance BCVA (LogMAR) and near BCVA (LogMAR), and the Mann-Whitney *U* test for MaxRS (wpm). The percentage of reduction in visual performance was calculated using the formula: Percentage (%) Reduction = ((Reference Value (RV)–Disease Group Value)/RV)  $\times$  100. For distance and near visual acuity, an RV of 0.01 LogMAR was used instead of 0 LogMAR to avoid division by zero. A univariate analysis was performed to investigate the independent factors influencing MaxRS (wpm), distance BCVA (LogMAR), and near BCVA (LogMAR). Distance BCVA and near BCVA, as well as MaxRS, were each considered as dependent variables. Independent variables (Table 1) that were statistically significant in the univariate analysis ( $P < 0.05$ ) were included, for each dependent variable, in a backward multiple regression.

**TABLE 1.** Independent Variables Analyzed in Univariate Analyses

AGT
A-zone, mm <sup>2</sup>
Central foveal bouquet abnormalities:
Cotton ball sign
Subfoveal hyporeflective detachment
Acquired vitelliform lesion
ELM/EZ integrity in central ETDRS subfield
ERM staging
ETDRS subfield thickness of:
RNFL
GCL
IPL
INL
OPL
ONL

AGT, Amsler grid testing; ELM, external limiting membrane; ERM, epiretinal membrane; ETDRS, Early Treatment of Diabetic Retinopathy Study; EZ, ellipsoid zone; GCL, ganglion cell layer; INL, inner nuclear layer; IPL, inner plexiform layer; LogMAR, logarithm of the minimum angle of resolution; ONL, outer nuclear layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

### RESULTS

Fifty-seven patients (57 eyes) were enrolled in this study. Demographic and clinical characteristics are summarized in Table 2.

### Functional Metrics

The mean ( $\pm$ SD) BCVA was 0.37 LogMAR ( $\pm$ 0.23) for distance and 0.59 LogMAR ( $\pm$ 0.18) for near, whereas the median (IQR) for MaxRS was 108.88 wpm (68.38). Table 2 summarizes the mean and median values of these three functional variables the whole cohort of patients, as well as separately for the phakic and pseudophakic subgroups. Statistically significant differences were found between the phakic and pseudophakic groups for both distance (independent samples *t*-test,  $P = 0.003$ ) and near visual acuity (independent samples *t*-test,  $P = 0.029$ ), whereas no significant differ-

**TABLE 2.** Demographic and Clinical Characteristics of Enrolled Patients

No. of patients	57
No. of eyes	57
Age, y, mean ( $\pm$ SD)	73.18 ( $\pm$ 5.69)
Gender, <i>n</i>	
Male	35
Female	22
Eye laterality, <i>n</i>	
Right	35
Left	22
Lens status, <i>n</i>	
Phakic	32
Pseudophakic	25
Distance best-corrected visual acuity, LogMAR, mean (SD)	0.3 ( $\pm$ 0.23)
Near best-corrected visual acuity, LogMAR, mean (SD)	0.59 ( $\pm$ 0.18)
Maximum reading speed, wpm, median (IQR)	108.88 (68.38)

*n*, number; SD, standard deviation; wpm, words per minute.

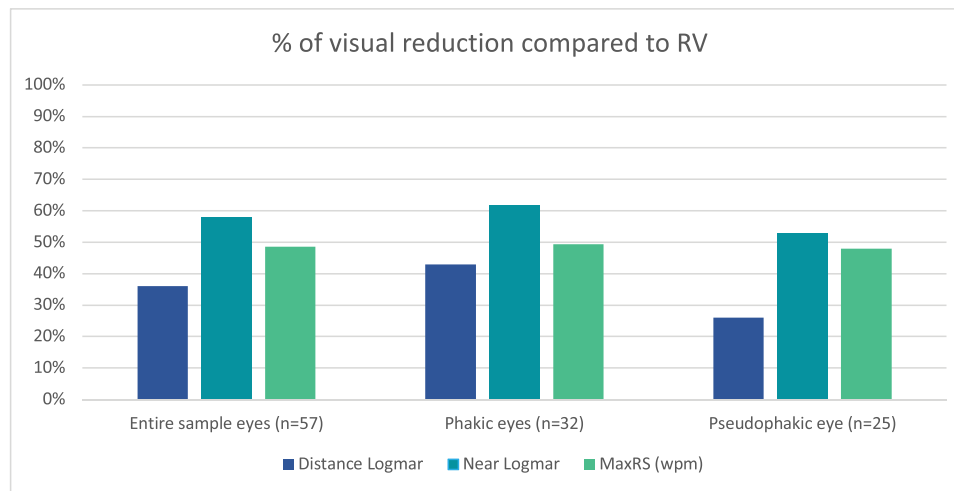
**TABLE 3.** Visual Performance in Patients With iERM and Percentage of Reduction of Each Functional Variable From the Reference Value

		Distance Visual Acuity, LogMAR	Near Visual Acuity, LogMAR	MAX Reading Speed, WPM
Entire sample ( <i>n</i> = 57)	Mean ( $\pm$ SD) or median (IQR)	0.37 $\pm$ 0.23	0.59 $\pm$ 0.18	108.88 (68.38)
Phakic eyes ( <i>n</i> = 32)		0.44 $\pm$ 0.22*	0.63 $\pm$ 0.16*	107.28 (49.80)*
Pseudophakic eyes ( <i>n</i> = 25)		0.27 $\pm$ 0.22*	0.54 $\pm$ 0.20*	110.14 (84.61)*
Difference between groups		<b><i>P</i> = 0.003*</b>	<b><i>P</i> = 0.029*</b>	<i>P</i> = 0.766*
	RV	0.01	0.01	211.8 $\pm$ 34.1
Entire sample ( <i>n</i> = 57)	% of reduction compared to the RV	36%	58%	48.59%
Phakic eyes ( <i>n</i> = 32)		43%	62%	49.35%
Pseudophakic eyes ( <i>n</i> = 25)		26%	53%	47.99%

%, percentage; IQR, interquartile range; RV, reference value.

\* Independent samples *t*-test.

# Mann-Whitney *U* test.

**FIGURE 1.** Histogram showing percentage (%) of reduction of each functional variable from the reference value (RV).

ences were observed between these two groups in terms of MaxRS (Mann-Whitney *U* test, *P* = 0.766). Greater percentage reductions from the RV were observed in near visual performance compared to distance visual acuity, as summarized in Table 3 and Figure 1.

Linear regression analysis tests were conducted among the three functional metrics in order to investigate the following associations: (i) distance BCVA (logMAR) with near BCVA (logMAR), (ii) MaxRS (wpm) with distance BCVA (logMAR), and (iii) MaxRS (wpm) with near BCVA logMAR. The results yielded linear correlation models with Pearson's values (*r*) of 0.794 ( $r^2 = 0.631$ , *P* < 0.001), 0.477 ( $r^2 = 0.228$ , *P* < 0.001), and 0.629 ( $r^2 = 0.395$ , *P* < 0.001), for the three above-mentioned associations, respectively (Fig. 2).

Finally, in our cohort, 43 patients (75%) presented with a positive Amsler test, whereas 14 patients (25%) had a negative Amsler grid testing (AGT). The mean area of the A-zone was 13.29 mm<sup>2</sup> ( $\pm 7.49$ ).

### Imaging Metrics

Twenty-one patients (21 eyes, 36.8%) had a stage II iERM, whereas 32 patients (32 eyes, 52.1%) had a stage III iERM, and 4 patients (4 eyes, 7%) had a stage IV iERM. As for the central foveal bouquet abnormalities, 22 patients (22 eyes,

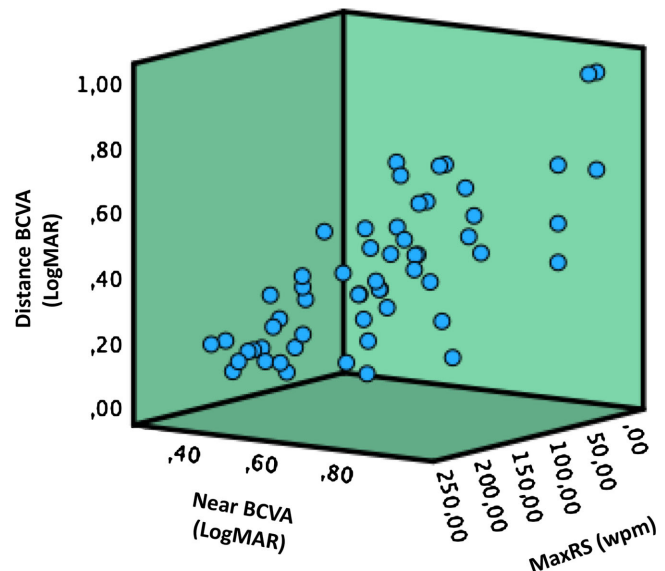
**FIGURE 2.** Three-dimensional scatter plot illustrating the linear regression among three functional reading performance variables. BCVA, best correct visual acuity; MaxRS, maximum reading speed; LogMAR, logarithm of the minimum angle of resolution.



TABLE 4. Retinal Layers Thickness of 57 Eyes Using the ETDRS SD-OCT Grid Centered on Fovea

Retinal Layer Thickness, $\mu\text{m}$	ETDRS Subfield				
	I-S	I-R	I-I	I-L	C
RNFL mean ( $\pm$ SD)	59.54 ( $\pm$ 28.71)	49.70 ( $\pm$ 38.80)	55.21 ( $\pm$ 31.32)	43.70 ( $\pm$ 29.92)	34.47 ( $\pm$ 29.91)
GCL mean ( $\pm$ SD)	59.02 ( $\pm$ 16.13)	62.96 ( $\pm$ 21.57)	57.81 ( $\pm$ 16.77)	61.77 ( $\pm$ 24.69)	46.77 ( $\pm$ 21.25)
IPL mean ( $\pm$ SD)	47.14 ( $\pm$ 10.82)	49.09 ( $\pm$ 13.34)	46.04 ( $\pm$ 10.98)	51.00 ( $\pm$ 14.75)	44.44 ( $\pm$ 19.10)
INL mean ( $\pm$ SD)	55.60 ( $\pm$ 10.69)	57.16 ( $\pm$ 11.76)	58.63 ( $\pm$ 17.85)	59.58 ( $\pm$ 23.20)	66.32 ( $\pm$ 25.76)
OPL mean ( $\pm$ SD)	39.16 ( $\pm$ 9.09)	39.89 ( $\pm$ 9.53)	42.05 ( $\pm$ 12.46)	41.82 ( $\pm$ 11.57)	43.91 ( $\pm$ 16.66)
ONL mean ( $\pm$ SD)	79.77 ( $\pm$ 13.99)	86.53 ( $\pm$ 25.11)	76.95 ( $\pm$ 22.64)	81.67 ( $\pm$ 15.70)	127.98 ( $\pm$ 26.33)

$\mu\text{m}$ , micron; C, central; I-I, inner-inferior; I-L, inner-left; I-R, inner-right; I-S, inner-superior; SD-OCT, structural spectral domain optical coherence tomography.

TABLE 5. Factors Contributing to Reading Performance by Multivariable Analyses

	Multivariable								
	Distance Visual Acuity			Near Visual Acuity			Reading Speed		
	B	SE	P Value	B	SE	P Value	Coefficient	SE	P Value
OPL thickness in central ETDRS subfield	0.004	0.002	<b>0.019</b>	–	–	–	–	–	–
ERM stage III/IV	0.143	0.050	<b>0.006</b>	0.075	0.040	<b>0.002</b>	0.093	0.044	<b>0.039</b>
RNFL thickness in inner right ETDRS subfield	–	–	–	0.002	0.001	<b>0.007</b>	0.005	0.002	<b>0.011</b>
INL thickness in inner superior ETDRS subfield	–	–	–	–	–	–	0.005	0.002	<b>0.039</b>

B, coefficient beta; SE, standard error B; B, SE and *P* values of excluded cases in the backward multivariable analysis were not reported. Statistically significant *P* values are highlighted in bold.

38.6%) were graded to exhibit the cotton ball sign on structural OCT, whereas 6 patients (6 eyes, 10.5%) had a subfoveal hyporeflective serous detachment. Moreover, 48 patients (48 eyes, 84.2%) had evidence of ELM or EZ interruption in the central ETDRS grid subfield and 17 patients (17 eyes, 29.8%) presented with degenerative intraretinal cysts.

The segmentation of the retinal layers' thickness ( $\mu\text{m}$ ), expressed as mean ( $\pm$ SD), within the ETDRS SD-OCT grid subfields, is detailed in Table 4.

### Linear Regression Analyses Between Visual Performance and Other Factors

Table 5 reports the results of multivariate regression analyses. Distance BCVA (dependent variable) was significantly associated with the OPL thickness within the central ETDRS grid subfield ( $P = 0.019$ ) and with evidence of iERM stage III/IV ( $P = 0.006$ ). Near BCVA (dependent variable) was significantly associated with the RNFL thickness in the inner right sector of the ETDRS grid ( $P = 0.007$ ) and with evidence of iERM stage III/IV ( $P = 0.002$ ). Finally, MaxRS (dependent variable) was significantly associated with the RNFL thickness in the inner right sector ( $P = 0.011$ ) and INL thickness in the inner superior sector ( $P = 0.039$ ), and with evidence of iERM stage III/IV ( $P = 0.039$ ; Fig. 3).

### DISCUSSION

In the present study, we provided a comprehensive assessment of the visual performance in patients with treatment-naïve iERM, observing a greater decline in near visual performance compared to distance visual acuity and identifying specific OCT biomarkers associated with functional performance.

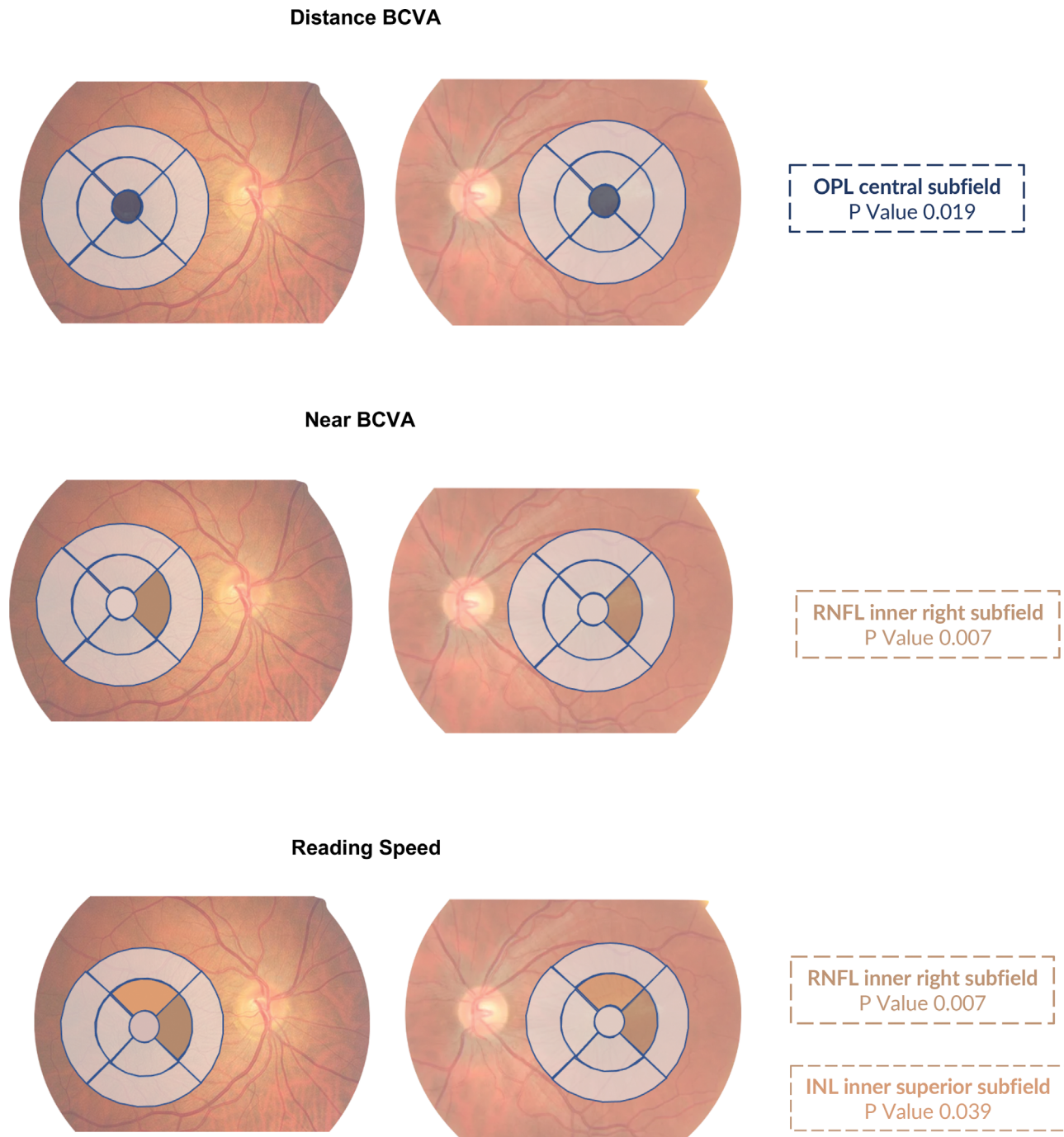
The decision to recommend surgery in patients with iERM is primarily based on distance visual acuity (ranging from

20/40 to 20/60) and the presence of debilitating metamorphopsia.<sup>26</sup> Additionally, contrast sensitivity and binocular function have been proposed as relevant factors to consider in determining the most appropriate timing for surgery.<sup>13</sup> However, it is crucial to note that the main clinical criterion for determining the timing of surgery, distance visual acuity, showed no correlation with the preoperative presence of metamorphopsia, contrast sensitivity, or binocular function.<sup>26</sup> In fact, when assessing a patient with iERM, a decline in one of these functional parameters does not necessarily correlate with deterioration in the others.<sup>13</sup> This variability has led to a lack of standardized functional criteria for timing surgery, often relying on the surgeon's personal experience.

In our study, we initially found a linear relationship among distance visual acuity, near visual acuity, and reading speed in patients with iERM. Specifically, a decrease in distance visual acuity was associated with a corresponding decrease in near visual acuity and in reading speed. However, the observed linear correlations among these functional variables were not perfect, indicating differences among these measures. This discrepancy in reading performance might be due to the activation of different macular areas for each test, individual variability, impact of age, and other cognitive factors.

Therefore, we did calculate the percentage reduction in each functional variable compared to the reference values of healthy eyes, analyzing both the entire cohort and subgroups stratified into patients who were phakic and patients who were pseudophakic (see Table 3; Fig. 1). Interestingly, a more pronounced and comparable percentage decline in near visual performance, including near visual acuity and reading speed, was observed compared to distance visual acuity across all groups.

These findings suggest that iERM may have a greater impact on near visual performance compared to distance performance. Consequently, near visual performance may be



**FIGURE 3.** Significance of retinal layers thickness and their topographic relationship on the ETDRS structural OCT grid correlated with visual performance. BCVA, best corrected visual acuity; ETDRS, Early Treatment of Diabetic Retinopathy Study; INL, inner nuclear layer; OCT, optical coherence tomography; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

a more sensitive measure in these patients, with significant clinical implications, as its impairments may critically affect daily activities requiring good near vision, such as writing, reading, and using computers or smartphones. Further, near visual performance may be a reproducible preoperative indicator as, differently from distance BCVA, it was less influenced by the patient's lens status. Indeed, one of the most significant findings from our study was that patients with iEMR who were phakic had worse distance and near visual acuity compared to patients who were pseudophakic.

However, when examining reading speed, despite patients who were phakic reading fewer words per minute than patients who were pseudophakic, this difference was not statistically significant, eliminating the potential confounding influence of nuclear cataracts.

Moreover, we add to the literature by identifying potential structural retinal OCT biomarkers of visual function in patients with iEMR. In detail, for distance visual acuity, we observed a significant association with increased OPL thickness in the central ETDRS subfield. Previous studies have

established that alterations in the OPL are linked to diminished distance visual acuity in various retinal pathologies, including macular holes,<sup>27</sup> diabetic retinopathy,<sup>28</sup> and retinal vein occlusion.<sup>29</sup> Additionally, as iERM progresses from stage 1 to stage 4, the increase in central foveal thickness (CFT), the presence of ectopic inner foveal layer (EIFL) in the central foveal region, and the thickening of the outer fovea were associated with reduced distance visual acuity.<sup>24,30,31</sup> These observations align with our findings, suggesting a direct correlation between outer retinal thickness and distance visual acuity.<sup>32</sup>

Additionally, our study identified a statistically significant association between near visual acuity and MaxRS with an increase in RNFL thickness in the inner right ETDRS subfield. Moreover, an increase in INL thickness in the inner superior ETDRS subfield was specifically associated with MaxRS. It is well established that iERM may lead to increased parafoveal<sup>33</sup> and perifoveal<sup>34</sup> inner retinal thickness, which may alter retinal sensitivity.<sup>7</sup> However, findings regarding the impact of these changes in retinal thickness on distance visual acuity have been inconsistent.<sup>33,34</sup> To date, no studies have examined the parafoveal and perifoveal retinal thickness effect on near visual performance in patients with iERM. Notably, Mieno et al. is the only study that assessed reading performance using MNREAD-J charts in patients with iERM undergoing surgery, reporting improvements at 3, 6, and 12 months postoperatively.<sup>35</sup>

During the reading process, the number of letters that can be sharply recognized without moving the eyes is referred to as the reading span. Meanwhile, the letters to the right of fixation that remain identifiable fall within the perceptual span.<sup>36,37</sup> Anatomically, the visual span is located within the central two degrees of the fovea in both eyes, whereas the perceptual span extends up to five degrees into the temporal parafovea in the left eye and the nasal parafovea in the right eye.<sup>36,37</sup> These regions correspond to the inner right subfield of the ETDRS grid in structural OCT. Furthermore it has been demonstrated that reading speed is closely correlated with the size of the perceptual span and retinal eccentricity.<sup>38,39</sup> This observation may explain how traction of the RNFL layer in the inner right ETDRS subfield could lead to alterations in near visual acuity and reading speed, reducing the reading perceptual span and consequently increasing the recognition and reading time of these words.

Furthermore, during rapid reading of the Radner chart, the eyes move both horizontally and vertically, transitioning quickly from the main sentence to the smaller sentence below. This movement may shift the perceptual span from the foveal region to the upper parafoveal region in both eyes. This phenomenon could explain how alteration of the INL in the inner superior ETDRS subfield may lead to a reduction in reading speed in the presence of iERM. Alterations in the parafoveal and perifoveal INL have been reported in the literature to affect both BCVA<sup>40</sup> and the M-Chart test,<sup>33</sup> a near functional test. Our findings could thus suggest that modifications in the INL thickness may be also associated with the reading speed.

It is important to recognize the limitations of our study when interpreting the results. First, our assessments were conducted monocularly, which may not accurately reflect binocular reading performance in real-world settings. Additionally, the small sample size and the qualitative assessment of metamorphopsia using the Amsler grid, rather than quantitative tools like M-charts, may have influenced our findings. The lack of microperimetry to assess fixation patterns

is another limitation, although we utilized a validated OCT-based method to evaluate central fixation stability. A further limitation lies in the conversion method for visual acuity measurements to LogMAR units. Whereas distance visual acuity was directly measured using ETDRS charts, near visual acuity was converted from Jaeger units to Snellen equivalents and then to LogMAR. Despite using standardized conversion charts, variability could arise when comparing visual acuity data obtained through different sources and multi-step conversions. Future studies could benefit from the development of direct conversion methods from Jaeger to LogMAR for improved consistency and accuracy in visual acuity assessments. Another limitation is the use of 0.01 LogMAR as a reference value to avoid division by zero when calculating percentage reductions in visual acuity. Although this approach prevents computational issues, it may slightly underestimate the results by not fully capturing ideal visual acuity. Last, the reference value for MaxRS was derived from a young, healthy population (aged  $21 \pm 3.8$  years), which may not be fully representative of other age groups.<sup>41</sup> This could introduce bias when applied to our study sample, which consists of older adults, as age-related changes in visual processing and reading speed may not be fully accounted for, potentially leading to an overestimation of the reading performance deficit. Future studies are necessary to identify the reference value in an elderly population, providing a more accurate comparison.

In summary, our study showed reduced visual performance in patients with iERM, with a particular impact on near visual performance, as reflected by near BCVA and MaxRS. Additionally, the three functional tests could reveal changes in specific retinal layers across different subfields of the ETDRS grid, indicating distinct anatomic and topographic cellular responses in patients with iERM. These findings suggest that near visual performance may represent a valuable functional end point for future interventional clinical trials and the surgical management of iERM.

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