Retinal Sensitivity and Structural Changes after Focal Photocoagulation for Diabetic Macular Edema: A Multisectorial Comparison

João Marques^a Ana Marta^a Pedro Manuel Baptista^a Diana José^a
Daniel Almeida^a António Ribeiro^{a, b} Irene Barbosa^{a, b}

^aOphthalmology Department, Centro Hospitalar Universitário do Porto, Porto, Portugal; ^bInstituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal

Keywords

Microperimetry · Retinal layers · Focal photocoagulation · Diabetic retinopathy · Retinal sensitivity

Abstract

Introduction: The hindrance of a macular laser treatment for diabetic macular edema (DME) remains unclear. Our purpose was to evaluate macular functional and structural changes after focal macular photocoagulation for DME.

Methods: This is a prospective cohort study that included patients with mild diabetic retinopathy, submitted to focal macular laser treatment as monotherapy for DME. Patients underwent optical coherence tomography and microperimetry after the necessary number of treatment sessions for complete resolution of DME. Eyes were compared in each macular sector (superior, temporal, and inferior 1- to 3-mm parafoveal ring) according to the presence of laser spots. Relative sensitivity was calculated as sectorial sensitivity divided by general sensitivity. **Results:** Sixty-four eyes were included. In sectors submitted to focal photocoagulation, we observed a significant reduction in absolute sensitivity (–1.0 to –0.4 dB, depending on the sector analyzed) and relative sensitivity (–2.1 to –0.6%) together with a reduction in the outer nuclear layer (ONL) thickness (–8 to –3 μm). The number of laser spots correlated with both functional and structural changes. **Conclusion:** In macular sectors that

underwent photocoagulation, we found a small reduction in retinal sensitivity together with a reduction in the corresponding ONL thickness.

© 2021 The Author(s).
Published by S. Karger AG, Basel

Introduction

Diabetic retinopathy affects about one-third of diabetes mellitus patients [1], which makes it the leading cause of visual loss in the working-age population [2]. Vision loss occurs most frequently due to diabetic macular edema (DME).

The ETDRS study showed that focal photocoagulation was beneficent in mild to moderate nonproliferative retinopathy with clinically significant macular edema, with small nonsignificant adverse effects on central visual fields [3]. The laser light is mainly absorbed by the retinal pigment epithelium, but energy may also dissipate to the adjacent neuroretina. Therefore, concern remains about the functional impact on the macula, even after successful resolution of the edema. Using standard automated perimetry to study retinal sensitivity after focal or grid photocoagulation, conflicting results have been reported: in a 2-year follow-up period, Tababat-Khani et al. [4] found no increase in the number of depressed points, as opposed

Fig. 1. Radial grid showing the evaluated macular sectors (superior, temporal, and inferior) and matching tested locations in microperimetry with sensitivity threshold values (white numbers). **a** A case with superior laser spots. **b** A case with temporal and inferior laser spots.

to Hudson et al. [5] and Striph et al. [6] who, in shorter follow-up periods, found a generalized loss of sensitivity across the central 10°. A randomized clinical trial using microperimetry showed reduced retinal sensitivity in the perifoveal 4° and 12° tested points, 12 months after laser focal/grid photocoagulation [7]. On the other hand, Greenstein et al. [8] detected changes in retinal function using multifocal electroretinogram, despite no repercussion in the perimetric tests. Given unclear consequences of an effective focal laser treatment for DME, our purpose is to evaluate macular function and structure in different sectors after focal photocoagulation treatment, using microperimetry and optical coherence tomography, respectively.

Methods

Study Design and Population

This is a cross-sectional cohort study in Centro Hospitalar Universitário do Porto. Patients with mild nonproliferative diabetic retinopathy, according to fundus and fluorescein angiography findings, submitted to focal macular laser treatment as the first and only treatment for DME, were consecutively included from our ocular diabetes practice, from January 2019 to July 2020. Patients were included after the necessary number of treatment sessions for complete resolution of DME. No control group of patients was included.

Exclusion Criteria

Eyes were excluded if additional treatment modalities were required such as intravitreal injections or photocoagulation out of the macula. Further exclusion criteria were best-corrected visual acuity (BCVA) under logMAR 0.5, active DME, visible macular cotton-wool spots or exudates, ischemia and neovascularization in previous fluorescein angiography, disorganization of retinal layers in optical coherence tomography or concomitant ocular hypertension, glaucoma, age-related macular degeneration, or other retinal vascular diseases. Perimetric tests with any false positives or false

negatives, as well as, unstable fixation (defined as fixation within 2° of the central fovea inferior to 75%) were considered unreliable and were excluded. OCT macular scans included in this study had an automatic real time (ART) of 16 and signal strength ≥ 20 dB and were devoid of gross artifacts.

Photocoagulation Treatment

All eyes had been treated with focal macular photocoagulation located at least 500 μm from the center of the fovea. A unique Zeiss Visulas 532 nm laser system was used by a single, experienced clinician. The spot size was set to 50 or 100 μm . Timing and power were set individually to allow visualization of whitish retinal marks after the impact (full threshold). A Mainster focal lens (Ocular®) was used for the procedure. The number and location of impacts were decided by the clinician, with the support of previous fluorescein angiography and optical coherence tomography findings.

Study Protocol

Patients underwent all examinations in the same visit.

1. Laser spots: Infrared (830 nm) confocal scanning laser fundus imaging (Heidelberg Spectralis, Germany) was captured, and visible laser spots were enumerated by a single investigator inside a radial grid with the following sectors: nasal (N), superior (S), temporal (T), and inferior (I) sectors of a 1- to 3-mm parafoveal ring.
2. Retinal light sensitivity: Microperimetric light sensitivity (MP-3; Nidek, Japan) was tested with a red circle of 1° as fixation target, a background luminance of 31.4 apostilbs, a stimulus size equivalent to Goldmann III, a stimulus time of 200 ms, and a 4–2 double staircase strategy. The threshold was converted to the decibel scale. The position of the retina was automatically tracked, and the target was aligned accordingly. We tested 45 locations in the central 12°, but each grid sector was attributed only the corresponding 4 tested locations (Fig. 1). All perimetric tests were performed between 2 p.m. and 4 p.m.
3. Retinal layer thickness: A high-resolution spectral-domain optical coherence tomography scan (Heidelberg Spectralis, Germany) was performed. Individual retinal layers were automatically segmented and measured in each sector of the grid, with proprietary Heidelberg Eye Explorer® software. Each scan was checked for erroneous segmentation.

Statistical Analysis

A multisectorial comparison was performed: light sensitivity and retinal layer thickness were compared in each sector, according to the presence of laser spots. This means that one eye was the control group in one sector but was the test group in another.

Deviation of sectorial sensitivity from general macular sensitivity was also calculated to control diffuse sensitivity loss and is further designated as relative sensitivity (sectorial sensitivity divided by general macular sensitivity). Mann-Whitney U tests were used to compare groups (with vs. without laser in each sector). Pearson's coefficient (r) or linear regression unstandardized coefficient (β) was calculated to access correlations. A p value (p) under 0.050 was considered significant. Values are shown as mean $\pm$ standard deviation (minimum–maximum).

Results

Seventy-six eyes were initially included. Twelve eyes were then excluded due to unreliable perimetric testing (8 eyes) or presence of recurrent macular edema at the study visit (4 eyes). Therefore, 64 eyes from 32 patients were analyzed. The time between the last treatment session and the study visit was 24 ± 21 (2–40) months.

Characteristics of the study subjects are summarized in Table 1. No patients had visual complains suggestive of scotomata after the treatment.

Peripapillary retinal nerve fiber layer thickness was 94.7 ± 8.3 (76–113) μm , and no eye presented thickness values under the normal age-adjusted values (under percentile 5 in the proprietary OCT device database).

BCVA was logMAR 0.06 ± 0.11 (–0.08; 0.52). Mean retinal sensitivity in the central 12° was 24.8 ± 2.6 (12.9; 29.9) dB and was associated with both logMAR BCVA and age (multivariate linear regression: $\beta = -0.06$ dB/year of age, $p = 0.005$, and $\beta = -8.57$ dB/logMAR unit, $p = 0.035$).

Differences in light sensitivity and retinal structure according to the presence of laser spots are shown in Table 2. Correlations with the number of laser spots are shown in Table 3.

In sectors with laser spots, the outer nuclear layer (ONL) thickness correlated with sensitivity ($\beta = 160$ $\mu\text{m}/\%$, $r = 0.544$, $p = 0.006$ for relative sensitivity and $\beta = 2.2$ $\mu\text{m}/\text{dB}$, $r = 0.412$, $p = 0.045$ for absolute sensitivity for the superior sector). We found no other significant correlations, and we found no significant differences between the sensitivity of each sector regarding the presence of laser spots in every other sector.

The time since the last treatment session and the study visit did not correlate with relative or absolute sensitivity ($p > 0.287$). Comparing groups with different time since the last treatment session, we found no differences in sen-

Table 1. Demographic and clinical characterization of the sample

Eyes, n	64
Age, years	63.1 ± 11.5 (35–88)
Type of DM 1/2, n	14/50
Time with DM, years	22.3 ± 11.4 (6–50)
HbA1c, %	7.5 ± 1.2 (5.1–10.5)
Time with DR, years	4.9 ± 4.1 (1.0–15.0)
BCVA, logMAR	0.06 ± 0.11 (–0.08; 0.52)
Spherical equivalent, D	-0.67 ± 2.3 (–9.5; 2.5)

BCVA, best-corrected visual acuity; HbA1c, glycated hemoglobin; DM, diabetes mellitus; DR, diabetic retinopathy; D, diopters.

sitivity ($p > 0.590$ for 1-year cutoff point, $p > 0.104$ for 2 years cutoff point).

Discussion

To our knowledge, this is the first study to evaluate retinal function and corresponding layer's thickness in a controlled sample of eyes treated exclusively with focal macular photocoagulation for DME. We found a significant but small reduction in absolute (–1.0 to –0.4 dB) and relative (–2.1 to –0.6%) sensitivity in sectors submitted to focal photocoagulation. These changes seem to be accompanied by a reduction in the retinal ONL thickness (–8 to –3 μm), perceptible in Figure 2. The number of laser spots seems to correlate with both functional and structural changes. These changes are independent of visual acuity and imperceptible by the patients.

Comparing the overall sensitivity results with to another report that used the same microperimetry device in healthy and younger subjects [9], we found reduced central sensitivity in our sample but similar values in the 6-degree ring (age 33.4 ± 5.9 vs. 63.1 ± 11.5 dB, $p < 0.001$; sensitivity in the fovea 28.0 ± 2.2 vs. 24.3 ± 3.0 dB, $p < 0.001$; sensitivity in the 2-degree ring 25.9 ± 1.5 vs. 24.6 ± 2.5 dB, $p < 0.001$; sensitivity in the 6-degree ring 25.3 ± 0.8 vs. 25.1 ± 2.6 dB, $p = 0.961$ for Wilcoxon one sample tests).

To our best knowledge, it is the first time that microperimetry is used to evaluate sensitivity after focal photocoagulation in macular sectors (superior, temporal, and inferior). The use of different macular sectors increases the power of the study (avoiding a type II error), without the need to increase the number of eyes. The significant differences we found were not observed in all sectors, which may be explained by the asymmetrical sample size and variance among sectors. We used the present grid

Table 2. Comparison of eyes with and without laser spots in each region

	Superior 1–3 mm parafoveal ring		Temporal 1–3 mm parafoveal ring		Inferior 1–3 mm parafoveal ring	
Laser spots	Yes	No	Yes	No	Yes	No
Eyes, <i>n</i>	24	42	29	35	14	50
Laser spots, <i>n</i>	4.5±3.7	0	3.9±3.1	0	3.6±2.9	0
Age, years	63.6±11.3 <i>p</i> = 0.950	62.8±11.8	63.7±10.8 <i>p</i> = 0.556	62.5±12.5	66.6±9.7 <i>p</i> = 0.308	62.1±11.9
BCVA, logMAR	0.045±0.072 <i>p</i> = 0.615	0.066±0.122	0.037±0.086 <i>p</i> = 0.058	0.084±0.122	0.042±0.086 <i>p</i> = 0.768	0.063±0.112
Absolute sensitivity, dB	24.7±2.5 –0.4 <i>p</i> = 0.169	25.1±3.2	24.7±3.4 –0.9 <i>p</i> = 0.125	25.8±2.8	24.7±2.5 –1.0 <i>p</i> = 0.049	25.7±2.2
Relative sensitivity, %	99.2±4.4 <i>p</i> = 0.024	101.3±5.5	100.4±8.6 <i>p</i> = 0.069	103.1±6.2	102.6±5.5 <i>p</i> = 0.454	103.2±6.7
Retinal thickness, µm	331±20 <i>p</i> = 0.142	340±26	328±24 <i>p</i> = 0.492	328±22	328±32 <i>p</i> = 0.086	336±18
ORL thickness, µm	81±4 <i>p</i> = 0.416	81±4	79±3 <i>p</i> = 0.071	80±4	80±4 <i>p</i> = 0.260	79±4
ONL thickness, µm	61±14 <i>p</i> = 0.076	66±14	68±14 <i>p</i> = 0.084	71±13	55±12 <i>p</i> = 0.015	63±10
OPL thickness, µm	32±5 <i>p</i> = 0.394	32±5	32±6 <i>p</i> = 0.218	30±4	36±7 <i>p</i> = 0.129	34±7
INL thickness, µm	41±4 <i>p</i> = 0.445	41±5	41±4 <i>p</i> = 0.671	40±4	42±4 <i>p</i> = 0.062	40±4
IPL thickness, µm	40±5 <i>p</i> = 0.306	40±4	42±5 <i>p</i> = 0.087	40±5	40±7 <i>p</i> = 0.487	40±5
GCL thickness, µm	51±7 <i>p</i> = 0.342	52±6	48±7 <i>p</i> = 0.093	47±6	50±9 <i>p</i> = 0.426	51±6
NFL thickness, µm	27±6 <i>p</i> = 0.465	27±5	18±3 <i>p</i> = 0.420	19±3	30±7 <i>p</i> = 0.263	30±6

Relative sensitivity was calculated as sensitivity in each sector divided by general macular sensitivity. Significant values are highlighted as bold. BCVA, best-corrected visual acuity; ORL, outer retinal layer, from the external limiting membrane to the Bruch membrane; ONL, outer nuclear layer; OPL, outer plexiform layer; INL, inner nuclear layer; IPL, inner plexiform layer; GCL, ganglion cell layer; NFL, nerve fiber layer.

system to be able to gather corresponding thickness information from the OCT scans.

Other studies using microperimetry that applied a similar design compared healthy macular sectors with other abnormal sectors [10, 11]. However, comparing different sectors is subject to inter-sector variability. This variability has been shown to occur in both light sensitivities due to different photoreceptor densities [12], as well as in retinal layer thickness [13]. We compared thickness and sensitivity always in the same sector (intra-sector), according to the presence of laser spots.

The presence of visible macular cotton-wool spots or exudates may decrease focal sensitivity [10] and was part of our exclusion criteria. Previous prospective studies that compared retinal sensitivity before and after laser treatment in DME were biased by the presence of macular

edema in the pretreatment evaluation, which influences sensitivity per se [14–16]. Conversely, the use of healthy eyes as controls is not the best strategy because macular dysfunction may exist in diabetic patients, despite the presence of edema or laser treatments [17]. Therefore, we believe that the best design to uncover the effects of photocoagulation is to compare eyes in the same stage that underwent treatment in different sectors. Moreover, we only included eyes with good vision, highly reliable tests, and inactive macular edema. This way, secondary factors that might influence the results were minimized.

The reduction found in the ONL thickness may be due to its thermal destruction by the laser impact or due to the loss of subjacent pigmented epithelium. Either way, ONL thickness may be a biomarker for retinal function after photocoagulation. Interestingly, another study that used

Table 3. Correlations between the number of laser spots and light sensitivity and retinal structure

	Superior 1–3 mm parafoveal ring	Temporal 1–3 mm parafoveal ring	Inferior 1–3 mm parafoveal ring
Eyes, <i>n</i>	24	29	14
Laser spots, <i>n</i>	4.5±3.7	3.9±3.1	3.6±2.9
Absolute sensitivity, dB	<i>r</i> = −0.139 <i>p</i> = 0.276	<i>r</i> = −0.336 <i>p</i> = 0.007	<i>r</i> = −0.182 <i>p</i> = 0.153
Relative sensitivity, %	<i>r</i> = −0.253 <i>p</i> = 0.046	<i>r</i> = −0.404 <i>p</i> = 0.001	<i>r</i> = −0.070 <i>p</i> = 0.585
Retinal thickness, μm	<i>r</i> = −0.239 <i>p</i> = 0.062	<i>r</i> = 0.037 <i>p</i> = 0.777	<i>r</i> = −0.148 <i>p</i> = 0.252
ORL thickness, μm	<i>r</i> = −0.024 <i>p</i> = 0.855	<i>r</i> = 0.015 <i>p</i> = 0.908	<i>r</i> = 0.071 <i>p</i> = 0.582
ONL thickness, μm	<i>r</i> = −0.319 <i>p</i> = 0.012	<i>r</i> = −0.068 <i>p</i> = 0.598	<i>r</i> = −0.266 <i>p</i> = 0.037
OPL thickness, μm	<i>r</i> = 0.003 <i>p</i> = 0.982	<i>r</i> = 0.049 <i>p</i> = 0.704	<i>r</i> = 0.162 <i>p</i> = 0.209
INL thickness, μm	<i>r</i> = −0.015 <i>p</i> = 0.908	<i>r</i> = 0.077 <i>p</i> = 0.552	<i>r</i> = 0.123 <i>p</i> = 0.341
IPL thickness, μm	<i>r</i> = −0.010 <i>p</i> = 0.940	<i>r</i> = 0.168 <i>p</i> = 0.193	<i>r</i> = −0.076 <i>p</i> = 0.559
GCL thickness, μm	<i>r</i> = −0.035 <i>p</i> = 0.786	<i>r</i> = 0.047 <i>p</i> = 0.717	<i>r</i> = −0.090 <i>p</i> = 0.486
NFL thickness, μm	<i>r</i> = −0.155 <i>p</i> = 0.228	<i>r</i> = 0.163 <i>p</i> = 0.206	<i>r</i> = −0.042 <i>p</i> = 0.744

Relative sensitivity was calculated as sensitivity in each sector divided by general macular sensitivity. Significant values are highlighted as bold. BCVA, best-corrected visual acuity; ORL, outer retinal layer, from the external limiting membrane to the Bruch membrane; ONL, outer nuclear layer; OPL, outer plexiform layer; INL, inner nuclear layer; IPL, inner plexiform layer; GCL, ganglion cell layer; NFL, nerve fiber layer.

Fig. 2. Infrared (830 nm) confocal scanning laser fundus image showing mainly superior laser spots (left side) and corresponding optic coherence tomography horizontal B-scan showing loss of the ONL and of subjacent photoreceptors and pigmented epithelium (right side), without segmentation (top) and with automatic segmentation (bottom). ONL, outer nuclear layer.

microperimetry in epiretinal membrane eyes found an inverse correlation between the mean retinal sensitivity in the central 4° and ONL thickness [18]. The ONL seems to be the best structural predictor for retinal sensitivity.

Considering the distribution of the retinal nerve fibers (aimed at the optic disk), a laser impact might disturb the neuronal transmission upstream. However, we found no significant differences, when we compared the sensitivity of each sector regarding the presence of laser in every other sector. We hypothesize that since 532 µm light is transmitted through the internal retinal layers and mainly absorbed by the pigmented epithelium, its disturbance in the nerve fiber layer is minimal.

The time interval since the last treatment session was not associated with the outcomes, which might suggest that the effects of photocoagulation in retinal structure and function are everlasting. Our results are valid for full-threshold 532 µm laser treatments but may not be reproducible after subthreshold treatments or treatments using a different wavelength. Vujosevic et al. [7] showed different autofluorescence patterns after subthreshold micropulsed versus conventional photocoagulation which suggest a different mechanism and site of action. Future studies comparing different types of laser should access both functional (with microperimetry) and structural (with OCT) results.

Visual acuity is commonly the main outcome in investigational ophthalmology. However, it does not provide a complete assessment of the visual function. We believe that microperimetry may be a useful additional tool to evaluate and monitor eye conditions and their treatment.

Conclusion

Multisectorial evaluation is a suitable and powerful tool in cases where the study factor spreads in different macular regions, asymmetrically in the sample. We found a small reduction in retinal sensitivity in macular sectors that underwent photocoagulation for DME. These changes are followed by a reduction in the ONL thickness.

References

- 1 Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35(3):556–64.
- 2 Antonetti DA, Klein R, Gardner TW. Diabetic retinopathy. *N Engl J Med*. 2012;366(13):1227–39.
- 3 Early Treatment Diabetic Retinopathy Study Research Group. Early photocoagulation for diabetic retinopathy. ETDRS report number 9. Early Treatment Diabetic Retinopathy Study Research Group. *Ophthalmology*. 1991 May;98(5 Suppl):766–85.
- 4 Tababat-Khani P, Bengtsson B, Agardh E. Effects of focal/grid laser treatment on the central visual field in diabetic macular oedema: a 2-year follow-up study. *Acta Ophthalmol*. 2016;94(3):240–5.
- 5 Hudson C, Flanagan JG, Turner GS, Chen HC, Young LB, McLeod D. Influence of laser photocoagulation for clinically significant diabetic macular oedema (DMO) on short-wavelength and conventional automated perimetry. *Diabetologia*. 1998;41(11):1283–92.

Acknowledgements

The authors would like to thank the Head of the Ophthalmology Department of Centro Hospitalar Universitário do Porto, Prof. Dr. Pedro Menéres, for the support granted for this study.

Statement of Ethics

The study adhered to the tenets of the Declaration of Helsinki and it was approved by our Institutional Review Board and Ethics Committee – *Departamento de Ensino, Formação e Investigação do Centro Hospitalar Universitário do Porto* ID 144-20 (114-DEFI/116-CE). The need for written informed consent was waived due to total anonymization and confidentiality of the data and the absence of detailed individual clinical information. All examinations performed were considered noninvasive and performed in the routine clinical setting.

Conflict of Interest Statement

The authors declare that they have no conflict of interests.

Funding Sources

No funding was obtained for this study.

Author Contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. All authors contributed to the draft of the manuscript, critically reviewed for intellectual content, and approved the final version submitted for publication.

Data Availability Statement

The data that support the findings of this study are available anonymously from the corresponding author, J.M., upon request.

- 6 Strioph GG, Hart WM, Olk RJ. Modified grid laser photocoagulation for diabetic macular edema: the effect on the central visual field. *Ophthalmology*. 1988;95(12):1673–9.
- 7 Vujosevic S, Bottega E, Casciano M, Pilotto E, Convento E, Midena E. Microperimetry and fundus autofluorescence in diabetic macular edema: subthreshold micropulse diode laser versus modified early treatment diabetic retinopathy study laser photocoagulation. *Retina*. 2010;30(6):908–16.
- 8 Greenstein VC, Chen H, Hood DC, Holopigian K, Seiple W, Carr RE. Retinal function in diabetic macular edema after focal laser photocoagulation. *Invest Ophthalmol Vis Sci*. 2000 Oct;41(11):3655–64.
- 9 Balasubramanian S, Uji A, Lei J, Velaga S, Nittala M, Sadda S. Interdevice comparison of retinal sensitivity assessments in a healthy population: the CenterVue MAIA and the Nidek MP-3 microperimeters. *Br J Ophthalmol*. 2018;102(1):109–13.
- 10 Kim JS, Maheshwary AS, Bartsch DU, Cheng L, Gomez ML, Hartmann K, et al. The microperimetry of resolved cotton-wool spots in eyes of patients with hypertension and diabetes mellitus. *Arch Ophthalmol*. 2011; 129(7):879–84.
- 11 Sachdev A, Edington M, Morjaria R, Chong V. Comparing microperimetric and structural findings in patients with branch retinal vein occlusion and diabetic macular edema. *Retina*. 2019;39(3):446–51.
- 12 Supriya D, Shwetha M, Kiran Anupama K, Kummelil Mathew K, Berendschot TT, Schouten JS, et al. Structural and function correlation of cone packing utilizing adaptive optics and microperimetry. *Biomed Res Int*. 2015;2015:968672.
- 13 Invernizzi A, Pellegrini M, Acquistapace A, Benatti E, Erba S, Cozzi M, et al. Normative data for retinal-layer thickness maps generated by spectral-domain OCT in a white population. *Ophthalmol Retina*. 2018;2(8):808–15.e1.
- 14 Vujosevic S, Midena E, Pilotto E, Radin PP, Chiesa L, Cavarzeran F. Diabetic macular edema: correlation between microperimetry and optical coherence tomography findings. *Invest Ophthalmol Vis Sci*. 2006;47(7):3044–51.
- 15 Okada K, Yamamoto S, Mizunoya S, Hoshino A, Arai M, Takatsuna Y. Correlation of retinal sensitivity measured with fundus-related microperimetry to visual acuity and retinal thickness in eyes with diabetic macular edema. *Eye*. 2006;20(7):805–9.
- 16 Hatef E, Colantuoni E, Wang J, Ibrahim M, Shulman M, Adhi F, et al. The relationship between macular sensitivity and retinal thickness in eyes with diabetic macular edema. *Am J Ophthalmol*. 2011;152(3):400–5.e2.
- 17 De Benedetto U, Querques G, Lattanzio R, Borrelli E, Triolo G, Maestranzi G, et al. Macular dysfunction is common in both type 1 and type 2 diabetic patients without macular edema. *Retina*. 2014;34(11):2171–7.
- 18 Cacciamani A, Cosimi P, Di Nicola M, Di Martino G, Ripandelli G, Scarinci F. Correlation between outer retinal thickening and retinal function impairment in patients with idiopathic epiretinal membranes. *Retina*. 2019; 39(2):331–8.