

Supplementary Online Content

Radwan SH, Soliman AZ, Tokarev J, Zhang L, van Kuijk FJ, Koozekanani DD. Association of disorganization of retinal inner layers with vision after resolution of center-involved diabetic macular edema. *JAMA Ophthalmol*. Published online May 7, 2015. doi:10.1001/jamaophthalmol.2015.0972.

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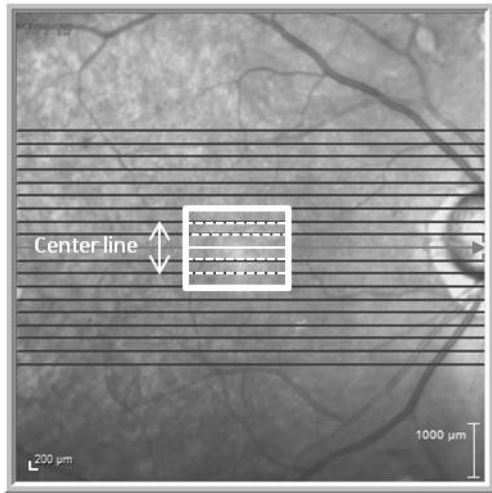
eTable 1. Study Eye Characteristics

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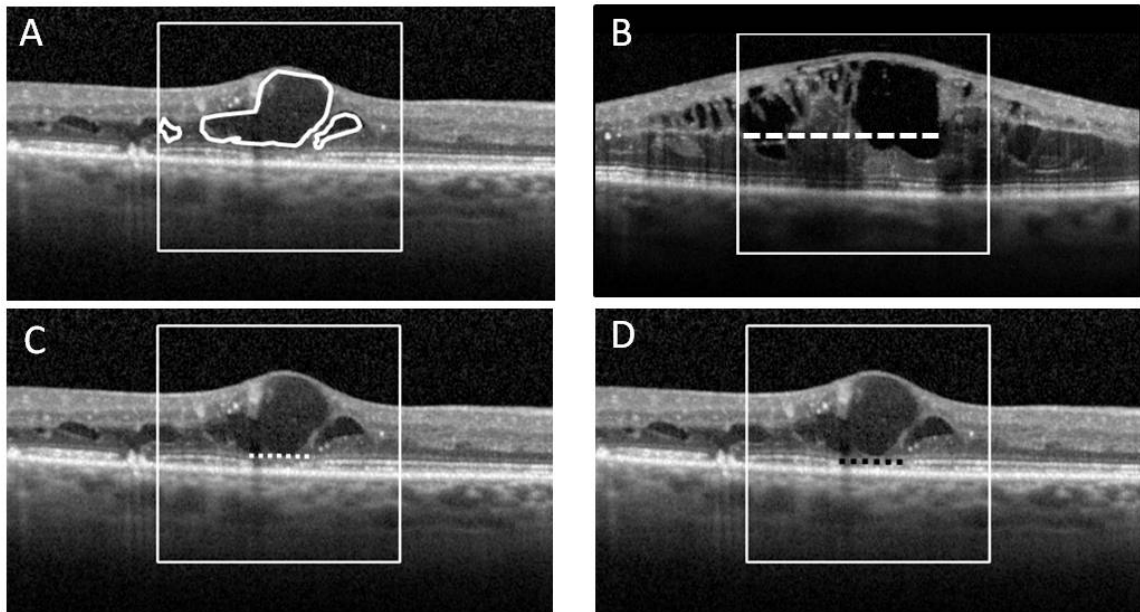
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. An infrared image demonstrating the 1500 μm analysis region bounded by the white box:



The analysis included the central line (marked solid white) and extended to include 2 scans immediately above and below (marked dashed line)

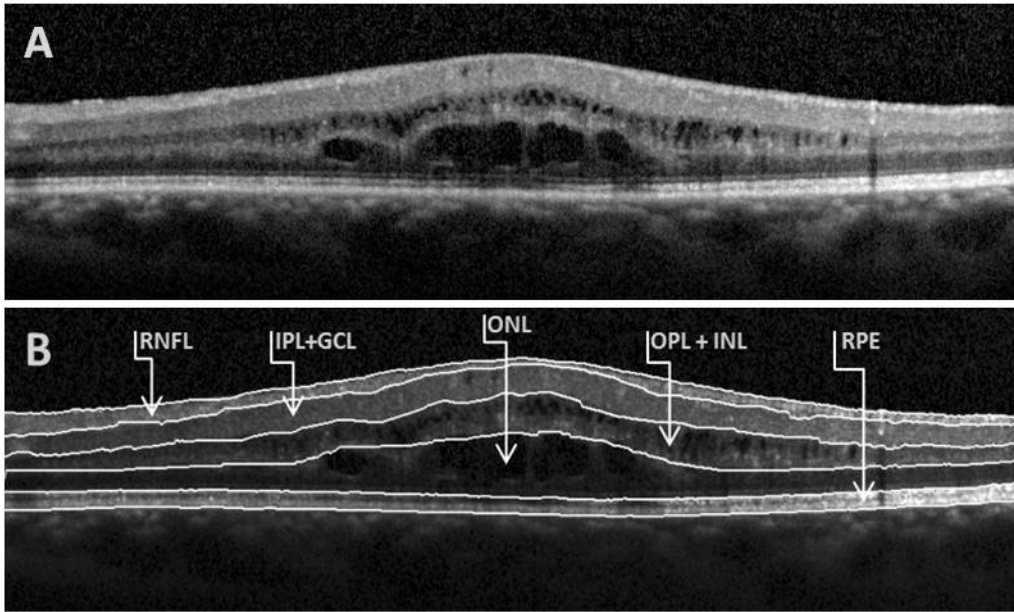
eFigure 2. Representative spectral domain optical coherence tomography (SDOCT) images for the variables measured in this study.



Measurement of:

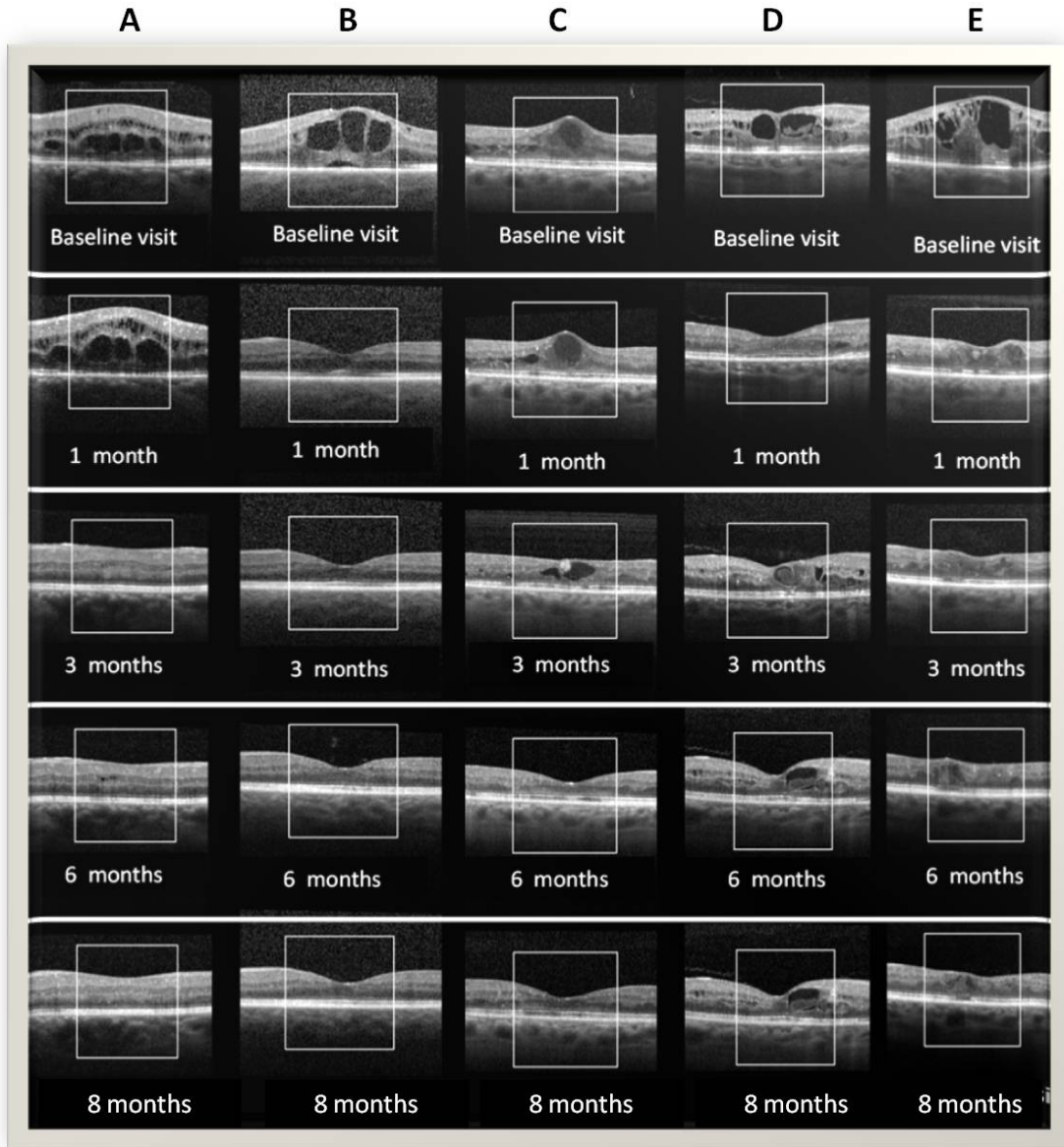
- a) The size and reflectance of intraretinal cysts
- b) The horizontal length of Disorganization of retinal inner layers (DRIL)
- c) The horizontal length of External limiting membrane (ELM) disruptions.
- d) The horizontal length of ellipsoid zone (EZ) disruption.

eFigure 3. Segmentation analysis performed in eyes with no or minimal Disorganization of retinal inner layers (DRIL)



- a) Retinal layers before segmentation.
- b) Retinal layers annotated after segmentation (RNFL=retinal nerve fiber layer, IPL+GCL=inner plexiform ganglion cell layer complex, ONL=outer nuclear layer, OPL+INL=outer plexiform inner nuclear layer complex, RPE=retinal pigment epithelium layer).

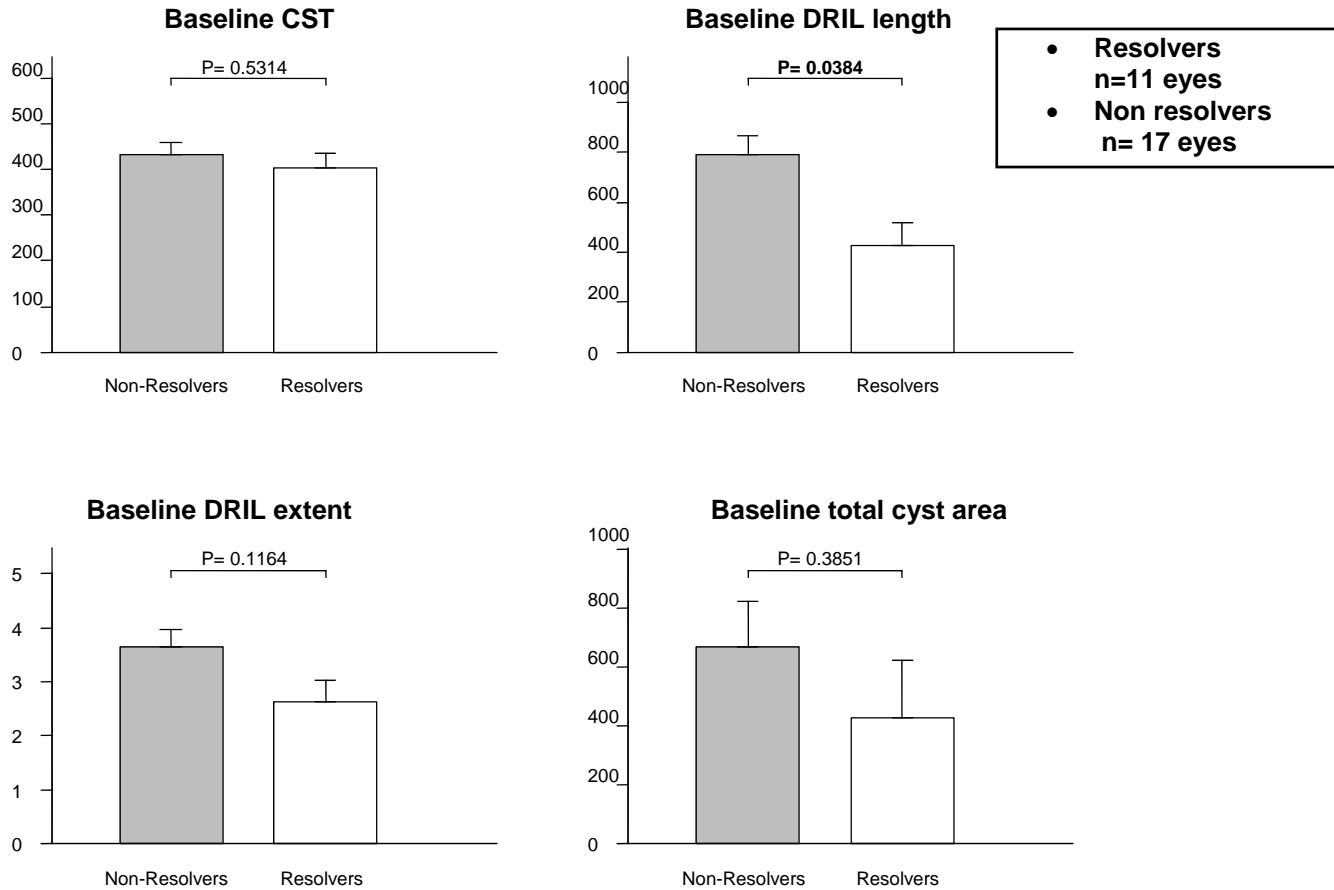
eFigure 4. Representative spectral domain optical coherence tomography (SDOCT) images for Disorganization of retinal inner layers (DRIL) resolution patterns



A= no baseline disorganization group, B= early resolvers, C= late resolvers, D= inconsistent, E= persistent. Note that in group A, inner retinal layers are distinguishable in baseline scans. Unlike columns B,C,D,E where images belong to the baseline DRIL group.

eFigure 5. Baseline variables measured on spectral domain optical coherence tomography (SDOCT) among resolvers and nonresolvers

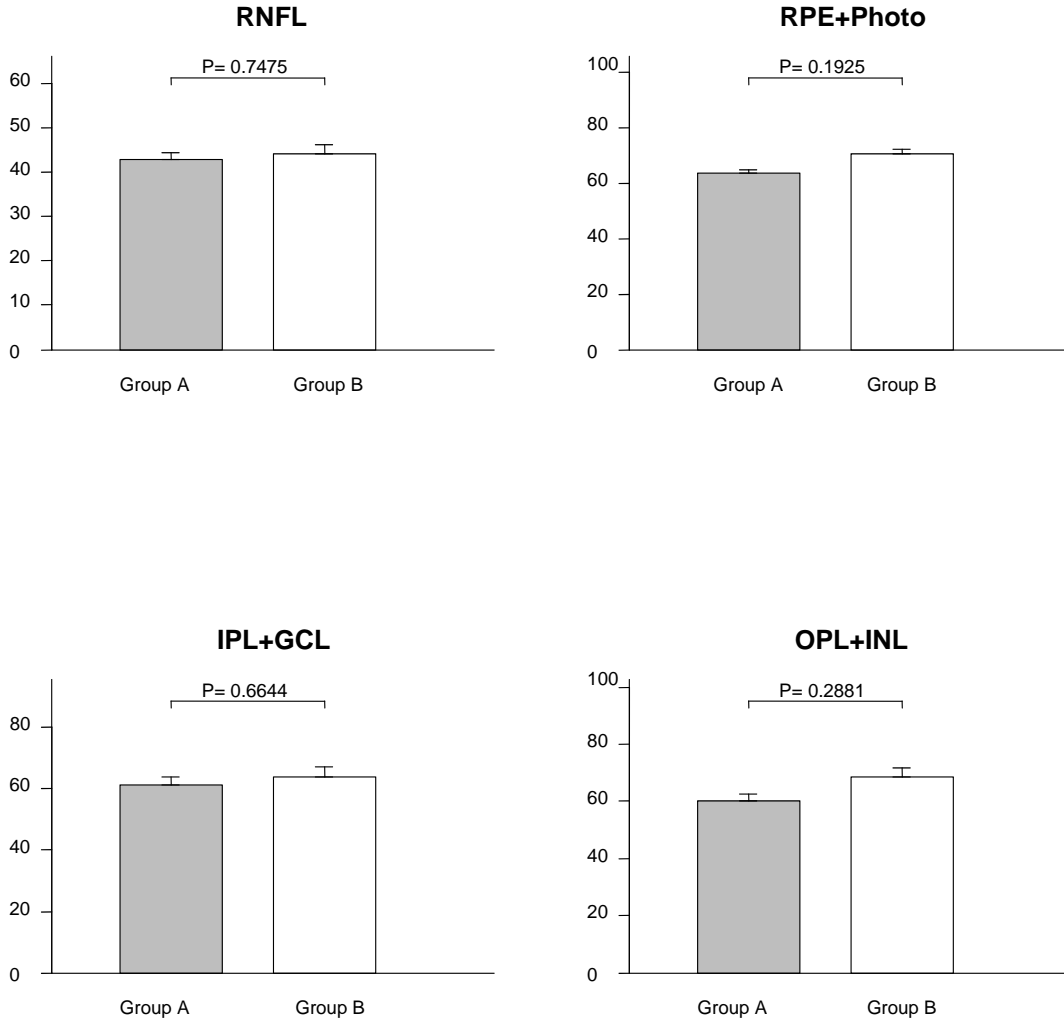
Group A eyes with baseline DRIL (n= 28)



Bar charts showing the difference between the mean baseline total Disorganization of retinal inner layers (DRIL) length, Center subfield thickness (CST), total cyst area, and DRIL extent when comparing the non resolvers versus the resolvers.

eFigure 6. Retinal layer thicknesses in both groups A and B.

Group A and B eyes without baseline Disorganization of retinal inner layers (DRIL)



(RNFL=retinal nerve fiber layer, IPL+GCL=inner plexiform ganglion cell layer complex, ONL=outer nuclear layer, OPL+INL=outer plexiform inner nuclear layer complex, RPE=retinal pigment epithelium layer),

eTable 1. Study Eye characteristics

CST = central subfield thickness. N=number of non-missing observations. Log MAR = Logarithm of the Minimum Angle of

e-table 1 : Study Eye characteristics				
Mean ± SD (N) or N (%)				
Diabetic center involved macular edema (Group A)	N		43 (62%)	
	Etiology of edema	DM	43 (100%)	
	logMAR VA at baseline visit		0.38±0.2	
	CST at baseline visit		407±100	
	Treatment received	No treatment		17 (40%)
		IV antivegef Injection		24 (56%)
		Laser		1 (2%)
		IV antivegef +Laser		1 (2%)
Non Diabetic center involved macular edema (Group B)	N		27 (39%)	
	logMAR VA at baseline visit		0.53±0.3	
	CST at baseline visit		517±150	
	Etiology of edema	BRVO		9 (33%)
		CRVO		4 (15%)
		ERM		1 (4%)
		Idiopathic		1 (4%)
		Post surgery CME		5 (19%)
	Uveitis		7 (26%)	

Resolution. IV anti-VEGF Injection=intravitreal injection of anti-VEGF (bevacizumab, Ranibizumab or aflibercept). VEGF = vascular endothelial growth factor. SD = standard deviation. Percentages may not add to 100 % due to approximation.

eTable 2. Bivariate regression analysis of the correlation of logMAR VA after resolution of edema and baseline variables in all group A eyes

Predictor (n=44 eyes)	Parameter estimate	SE	Lower 95% CI	Upper 95% CI	P-value
AGE	-7.20E-03	6.60E-03	-2.17E-	7.30E-03	0.30
Gender: F vs. M	4.36E-02	1.67E-01	-3.24E-	4.11E-01	0.80
Baseline Log Mar VA	9.45E-01	1.35E-01	6.44E-01	1.25E+00	<0.001
CST (μm)	7.00E-04	5.00E-04	-6.00E-	1.90E-03	0.25
Total DRIL length (μm)	5.00E-04	1.00E-04	3.00E-04	8.00E-04	<0.001
Total DRIL extent (# of B-scans out of 5)	6.52E-02	2.85E-02	1.60E-03	1.29E-01	0.05
Total cyst areas (μm ²)	0.00E+00	1.00E-04	-2.00E-	2.00E-04	0.94
Total of cyst areas reflectivity	-1.48E+01	1.88E+01	-	2.70E+01	0.45
Total ELM disruption length (μm)	4.00E-04	1.00E-04	2.00E-04	6.00E-04	0.003
Total EZ disruption length(μm)	4.00E-04	1.00E-04	2.00E-04	6.00E-04	0.003
Presence of SRF(# of B-scans out of 5)	2.98E-02	3.50E-02	-4.82E-	1.08E-01	0.42
Presence of COST (# of B-scans out of 5)	-2.92E-02	5.17E-02	-1.44E-	8.59E-02	0.58
Presence of Hard Exudates (# of B-scans)	5.24E-02	2.44E-02	-1.90E-	1.07E-01	0.06
Presence of ERM (# of B-scans out of 5)	-6.03E-02	7.31E-02	-2.23E-	1.03E-01	0.43
Inner Superior quadrant thickness (μm)	1.40E-03	9.00E-04	-6.00E-	3.50E-03	0.15
Inner Nasal quadrant thickness (μm)	9.00E-04	9.00E-04	-1.00E-	2.90E-03	0.32
Inner Inferior quadrant thickness (μm)	-4.00E-04	9.00E-04	-2.50E-	1.60E-03	0.67
Inner temporal quadrant thickness (μm)	2.00E-04	7.00E-04	-1.50E-	1.90E-03	0.80
Outer Superior quadrant thickness (μm)	5.00E-04	7.00E-04	-1.20E-	2.20E-03	0.55
Outer Nasal quadrant thickness (μm)	1.00E-03	1.10E-03	-1.40E-	3.50E-03	0.37
Outer Inferior quadrant thickness (μm)	-2.00E-04	1.40E-03	-3.30E-	2.80E-03	0.87
Outer temporal quadrant thickness	-5.00E-04	9.00E-04	-2.50E-	1.50E-03	0.60

F= female . M=Male. SE=Standard error. CST = central subfield thickness. ELM = external limiting membrane. EZ =ellipsoid zone . DRIL= Disorganization of Retinal Inner Layers. ERM = epiretinal membrane .SRF=sub retinal fluid. COST=cone outer segment tips. Log MAR = Logarithm of the Minimum Angle of Resolution. N=number of non-missing observations.

eTable 3. Bivariate regression analysis of the correlation of logMAR visual acuity after resolution of edema and baseline variables in all group B eyes.

Predictor (n=27 eyes)	Parameter estimate	SE	Lower 95% CI	Upper 95% CI	P-value
AGE	9.13E-03	4.85E-	-	2.46E-	0.16
Gender: F vs. M	2.20E-02	1.38E-	-	4.04E-	0.88
CST (µm)	-3.30E-05	3.20E-	-	1.00E-	0.92
Baseline Log Mar VA	5.81E-01	1.31E-	1.63E-	9.99E-	0.02
Total DRIL length (µm)	-7.20E-05	1.40E-	-	4.00E-	0.65
Total DRIL extent (# of B scans out of 5)	-4.67E-04	3.37E-	-	1.07E-	0.99
Total ELM disruption length (µm)	-5.30E-05	1.66E-	-	5.00E-	0.77
Total ellipsoids layer disruption	1.00E-05	1.66E-	-	5.00E-	0.96
Presence of SRF (# of B scans out of 5)	5.13E-02	3.45E-	-	1.61E-	0.23
Presence of COST (# of B scans out of 5)	-6.94E-02	3.31E-	-	3.60E-	0.13
Presence of Hard Exudates (# of B scans out of 5)	-4.04E-02	4.40E-	-	9.97E-	0.43
Presence of ERM (# of B scans out of 5)	1.82E-02	3.30E-	-	1.23E-	0.62
Inner Superior quadrant thickness	-4.77E-04	4.56E-	-	1.00E-	0.37
Inner Nasal quadrant thickness (µm)	-1.89E-04	5.60E-	-	1.60E-	0.76
Inner Inferior quadrant thickness (µm)	2.09E-04	5.65E-	-	2.00E-	0.74
Inner temporal quadrant thickness	7.90E-05	4.72E-	-	1.60E-	0.88
Outer Superior quadrant thickness	-2.64E-04	4.39E-	-	1.10E-	0.59
Outer Nasal quadrant thickness (µm)	1.76E-04	6.65E-	-	3.00E-	0.82
Outer Inferior quadrant thickness (µm)	3.68E-04	6.92E-	-	2.60E-	0.63
Outer temporal quadrant thickness	4.51E-04	6.20E-	-	2.40E-	0.52

F= female . M=Male. SE=Standard error. CST = central subfield thickness. ELM = external limiting membrane. EZ =ellipsoid zone. DRIL = Disorganization of Retinal Inner Layers. ERM = epiretinal membrane .SRF=sub retinal fluid. COST=cone outer segment tips. Log MAR = Logarithm of the Minimum Angle of Resolution. N=number of non-missing observations.