ANALYSIS OF RETINAL LAYERS IN FIBROMYALGIA PATIENTS WITH PREMIUM PROTOCOL IN OPTICAL TOMOGRAPHY COHERENCE AND QUALITY OF LIFE.

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RUNNING HEAD: Posterior Pole OCT analysis in fibromyalgia.

KEYWORDS: OCT, optical coherence tomography, retinal nerve fiber layer, ganglion cells, fibromyalgia, retinal layers

All subjects gave detailed consent to participate in this study, which was conducted in accordance with the guidelines determined by the Ethics Committee of the Miguel Servet Hospital and the principles of the Declaration of Helsinki.

ABSTRACT

Purpose: To evaluate the inner retinal layers in fibromyalgia (FM) patients compared to control subjects using posterior pole protocol (PPole) analysis in optical coherence tomography (OCT) and to correlate structural retinal changes with subjective quality of life.

Methods: Seventy-four eyes of healthy subjects and 55 eyes of those with FM were analyzed. All subjects underwent retinal evaluation using the PPole protocol for Spectralis OCT (Heidelberg Engineering) to obtain measurements of the retinal nerve fiber layer (RNFL) and the ganglion cell layer (GCL) in the macular area. The EuroQol (EQ-5D) questionnaire and Fibromyalgia Impact Questionnaire (FIQ) were performed to analyze health-related quality of life. Additionally, the FM group was divided into three groups depending on the disease phenotype (atypical, depressive and biological).

Results: Patients with FM presented with a reduction of the RNFL thickness compared to controls in 17/64 cells of the PPole area, and a reduction of the GCL thickness in 47/64 cells. Depressive FM phenotype showed the greatest number of cells with significant reduction compared with the control group in both RNFL and GCL layers. A correlation between temporal-inferior cells of the GCL and the EuroQol 5D questionnaire results was observed.

Conclusions: Patients with FM present with a reduction of the inner retinal layers in the macular area. This degeneration correlates with disease severity/reduced quality of life in these patients. The PPole protocol for OCT is a non-invasive and fast tool that might help clinicians diagnose and monitor neurodegeneration in FM patients.

INTRODUCTION.

Fibromyalgia (FM) is a disease characterized by chronic muscular pain of unknown origin, accompanied by feelings of fatigue and other symptoms without a well-defined underlying organic disease. Although neither the etiology nor the pathogenesis of fibromyalgia are completely understood, elements such as central and autonomic nervous system dysfunction, alteration in neurotransmitters, hormonal factors, abnormal immune response, external factors and psychiatric disorders, all appear to have influence on the presentation and progression of the disease. [1]

The mainstream opinion holds that women are more prone to fibromyalgia than men. [2] And while there is no cure for fibromyalgia, there are several medications aimed at reducing pain and fatigue, improving sleep and activity levels, promoting adaptation and thus enhancing patient quality of life, as well as maintaining functionality and increasing their ability to cope with the disease and improve psychological well-being. Consequently, FM patients frequently report limitations in activities of daily living, as well as mental impairment.[3,4]

The fact that this disease affects the central nervous system, suggests that the visual system might be involved in these patients. Symptoms like dry eye, double vision, sensitivity to light, eye pain, and blurred vision are commonly reported in fibromyalgia patients.

In recent years, retinal changes in FM patients were observed by optical coherence tomography (OCT). Garcia-Martin et al [5] observed a significant decrease of the retinal nerve fiber layer (RNFL) thickness in patients with FM. Nowadays, the retinal ganglion cell layer (GCL) has become the most sensitive biomarker in other neurodegenerative processes, such as multiple sclerosis, Parkinson's disease and Alzheimer's.[6-9] Due to this, analysis of the outermost layers of the retina could be established as a diagnostic method for FM.

Research on FM and the visual system is very scarce, and there are currently very few studies where neurodegeneration in the retina of these patients was observed. The aim of the present study was to evaluate and obtain objective measurements of the RNFL and the GCL in the macular area of patients with FM using a new protocol for Spectralis OCT, and to analyze the

possible association of structural changes with changes in quality of life caused by FM progression.

METHODS

Patients with FM were recruited from the primary care research group study population of FM patients in Zaragoza, Spain.

All procedures in this study adhered to the tenets of the Declaration of Helsinki; the experimental protocol was approved by the Ethics Committee of Miguel Servet Hospital (CEICA), and all participants provided written informed consent to participate in the study. The protocol designed for this study included a study of the patient's medical history for the years since disease diagnosis, FM phenotype and demographic data, completion of quality of life questionnaires, and a complete neuro-ophthalmologic evaluation including retinal evaluation using optical coherence tomography (OCT).

A total of 55 eyes from 55 FM patients and 74 eyes from 74 healthy individuals were selected for this study. We included patients with FM diagnosis based on the 1990 American College of Rheumatology criteria. [10] Parameters such as type of fibromyalgia and questionnaires dates were recorded. The ophthalmologic evaluation included a best correction visual acuity test (BCVA), intraocular pressure measurement and fundoscopy which was used to detect any ocular alterations such as macular or optic disc damage, and cataract of media opacity which could affect functional vision or captured OCT images. The exclusion criteria were: patients with (BCVA) lower than 0.4 (decimal, measured with Snellen chart), significant refractive errors (>5 diopters of spherical equivalent refraction or 3 diopters of astigmatism), intraocular pressure ≥21 mmHg, media opacifications, concomitant ocular diseases (including history of glaucoma or retinal pathology) and systemic conditions (especially neurodegenerative processes) that could affect the visual system. The healthy controls had no history and no evidence of ocular or neurologic disease of any nature; their best-corrected visual acuity (BCVA) was >0.4. Each eye

was considered independently and only one eye of each subject was randomly included unless only one of the eyes met the exclusion criteria.

Type of FM, disease duration, age at diagnosis and treatment were recorded by a psychiatrist specializing in FM, who evaluated the patients and was blind to the ophthalmology assessment. We classified FM patients into three different subgroups based on the pressure-pain thresholds and psychologic factors described by Giesecke et al.[11] (Group 1, biological; Group 2, depressive; Group 3, atypical).

The subject questionnaire included two validated health-related quality of life questionnaires: EuroQol (EQ-5D) and Fibromyalgia Impact Questionnaire (FIQ) to scale FM's impact of quality in daily life. Five dimensions were evaluated in EQ-5D: mobility, self-care, performance of usual activities, pain or discomfort, and anxiety or depression. The application of the coefficients to each profile allows calculation of the "social rate", which ranges from value 1 (best possible state of health) to value 0 (state of death). [12] The Fibromyalgia Impact Questionnaire (FIQ) measures 10 areas: physical impairment, feel good, work missed, doing work, pain, fatigue/tiredness, rested, stiffness, anxiety, and depression using ranges from 0 to 100. Higher scale scores indicate greater impact of the disease. [13]

The Posterior Pole protocol (PPole) of Spectralis OCT device (Heidelberg Engineering, Germany) was used for all subjects to obtain structural measurements of the retina. Macular thickness is measured using 61 lines (30 ° 25 ° volume OCT scan) in the central area of 20 ° for each eye. Anatomic Positioning System (APS) uses a horizontal line between the axis of fovea to the entrance of Bruch's Membrane ensuring an accurate position of the macula for each individual based on his head tilt and eye cyclotorsion. (Fig 1)

This line marks the reference for 61 parallel explorations that form the area of the retina scan. Analysis shows a color thickness map for an 8x8 grid centered on the foveal depression divided into small squares of 3 ° 3 ° areas, which correspond to a little less than a square millimeter of the retina, showing the average thickness of the retina for each small square. Cells are denominated by row and column starting from left to right and from inferior to top. Cell 1.1 is

located in the inferior left corner, cell 1.8 is in the inferior right corner and so on. Cells on the left are in the temporal area of the retina and cells on the right are in the nasal area of the retina. This protocol is able to detect thickness changes about 1 µm and provides a color map scale in steps of 10 to 15 µm, thus permitting improved detection of small tissue thickness losses to visual inspection of the retinal thickness map. In this study, we evaluated the RNFL and the GCL corresponding to the neuroretina. All measurements were obtained by a single operator blind to the group. Artifacts and quality scores less than 25/40 in the analyses were excluded. [14] The quality of the scans was assessed prior to analysis and poor-quality scans were rejected. Only images scoring higher than 25/40 were analyzed. Descriptive data and 64 cells measurements of both retinal layers, RNFL and GCL, were recorded in a database and analyzed with Statistical Package IBM-SPPS (SPSS Unc, Chicago, IL, USA) software version 20.0. Kolmogorov-Smirnov testing identified that the study variables were not normally distributed. We used a Mann-Whitney U test to compare between patients and the control group. Differences between FM phenotype groups were analyzed with a one-way ANOVA and post hoc test. Due the volume of variables, Bonferroni correction for multiple comparisons was applied and significance was considered with p value < 0.001.

Numerical data obtained from SPSS were analyzed with MATLAB (R2020a, Mathworks, Massachusetts, USA), which allows matrix representation using M language. This program has been previously used in biological tissue research [15] and also in ophthalmic research. [16] Since PPole Protocol analysis is based on an 8*8 grid, which works as a matrix, numerical data can be reassembled and processed in MATLAB.

RESULTS

The study was comprised by 74 eyes of healthy subjects; 10 males (13.5%) and 64 females (86.5%), and 55 eyes of FM patients; 7 males (12.7%) and 48 females (87.3%). The average age of the sample was 53.97 ± 14.16 years, with no age differences existing between groups (p = 0.085). There were no differences in IOP values (p=0.990 and p=0.911). The FM phenotype

distribution was as follows: Group 1 with biological FM, 14 patients (10.90%); Group 2 with depressive FM, 10 patients (7.8%); Group 3 with atypical FM, 18 patients (14%). The FIQ mean score was 61.49±17.96. The EQ-5D mean score was 38.20±13.68 (table 1).

Retinal Nerve Fiber Layer

Patients with FM presented with significant thinning of the RNFL thickness compared to healthy controls in 17/64 cells (p-value <0.05) (table 2) (Fig 2).

The ANOVA test amongst the three subgroups of FM phenotypes and controls also revealed significant differences in 26/64 cells (p-value <0.05) and 8/64 cells (p-value <0.001) (table 3). Post hoc analysis with Bonferroni correction showed significant thinning in subgroup 2 compared to healthy controls in 28 cells. Cells 3.6, 6.5 and 6.6 showed significant thinning in subgroup 2 compared with subgroup 1, Cell 2.8 in subgroup 1 was significantly thinner compared to control group and cells 2.8 and 8.1 were thinner in subgroup 3 but a significant engross was observed in cell 5.2 compared with control. (Table 3) (Fig 3).

Ganglion Cell Layer

Compared with controls, the FM group presented a significant thinning of the GCL in 33/64 cells (p-value <0.05) and 14/64 cells (p-value <0.001) (table 4) (Fig 2).

Several areas of thinning were shown in ANOVA testing amongst the three phenotype subgroups and healthy controls, 27/64 cells with significant differences (p-value <0.05) and 14/64 cells with highly significant differences (p-value <0.001) (table 5) (Fig 2).

Post hoc analysis showed significant thinning (p<0.001) in 27 cells in subgroup 2 and in 14 cells in subgroup 1 compared with control group. Cells 5.6, 6.4 and 6.5 in subgroup 2 showed a significant thinning compared with subgroup 3 and cells 4.3, 5.2 were thinner in subgroup 3 compared with healthy subjects.

Correlation study

Mild significant correlations were observed between GCL and years of evolution of FM disease, in cells 5.8 (0.282), cell 6.8 (0.309), cell 7.8 (0.333) and cell 8.5 (0.327) and only one high positive correlation in RNFL in cell 5.2 (0.389). A significant positive correlation was observed between the RNFL and GCL and the EuroQol-5D questionnaire in inferior and temporal cells and an inverse correlation between the GCL thickness and the FIQ score in nasal, superior and inferior cells. (Table 6) (Fig 3)

DISCUSSION

The aim of this study was to verify that the PPole premium protocol for OCT Spectralis provides objective information about the inner retinal layers in patients with FM and to evaluate possible changes in the neuroretina of these patients caused by the disease. There are other devices that allow wide protocols, such as Triton OCT (Topcon) which also scans big areas but nowadays, this protocol has the most complete analysis. Currently, there is a scarcity of material in the bibliography about this disease and its relationship with the retina, so this could be considered a novel study using a new diagnostic tool that might provide a new scientific contribution to this topic.

Plentiful studies on retinal alterations in FM could not be found. Loss of RNFL thickness in a group of FM patients had previously been observed at this hospital by our own team [5]. In the present study, significant thinning affecting both the RNFL and GCL in FM patients was detected in comparison with control subjects. In RNFL, affected grid cells were observed in the superior and inferior areas along the papillary arch. With regard to the GCL, more affected grid cells in the area of the analysis were detected, especially around the macular area and in the temporal area. In the GCL, a higher level of significance and a larger affected area of thinning were found compared to the RNFL, so it is postulated that, in FM, structural alterations affect the nuclei of the ganglion cells to a greater degree and earlier than the axon of the cell. These findings are important since, up to now, the diagnosis of FM has been made through subjective

tests and there are no quantifiable objective tests. Furthermore, the PPole protocol can determine the exact location of the papillomacular bundle, and therefore supply more accurate results. This area usually shows the first pathological changes established in neurodegenerative diseases, and hence, this new protocol might be a potential tool to provide new biomarkers for early diagnosis. [17]

Neither the etiology nor the pathogenic mechanisms of fibromyalgia are not yet fully determined. It has been reported that in FM the sensitivity of the central and peripheral nervous system is altered in response to tissue stimulation, manifesting as hyperalgesia and allodynia. [18] It has also been mentioned that these disorders of muscular-skeletal pain are not only associated with alteration in functional neural plasticity, but also with changes in brain morphology. [19] Studies such as Mountz et al [20] and Kwiatek et al [21] support the theory that many signs and symptoms of FM originate from central nervous system dysfunction. They found hypoperfusion in the bilateral thalamus and bilateral caudate nucleus, involved in the nociceptive stimulus processing, using single-photon emission computed tomography. Also, Katz et al [22] suggest that FM pain is the product of muscle hypoperfusion secondary to regional vasomotor dysregulation. Prevalence of emotional and affective disorders in FM have presented as depression, anxiety, borderline personality, obsessive-compulsive personality, and post-traumatic stress disorder. It has been suggested that chronic stress may lead to changes in various hormones and neurotransmitters, resulting in various manifestations of FM such as pain and fatigue. [23, 24] We classified our patients into 3 distinct subgroups depending on the Giesecke clasification, and observed no significant difference in RNFL and GCL among subgroups. However, the depressive phenotype presented with the thinnest values in RNFL and GCL measurements compared to healthy subjects. The exact mechanisms underlying the different disease phenotypes is still not well understood, but our results, showing greater neurodegeneration in the depressive subtype, might shed light on current pathophysiological theories on this disease. Two questionnaires about Health-related quality of life were conducted in this study. The EuroQol 5D questionnaire correlated more strongly with the temporal-inferior area of the GCL.

However, the FIQ questionnaire did not correlate with structural data from either retinal layers, despite being more specific on FM than the EuroQol 5D. It is thought that, although the FIQ has the capacity to detect changes in disease progression, the functional elements of the test are oriented towards high levels of disability, which possibly results in false evaluation of mild stages. [25]

Since to this date there is no clear pathophysiological cause, FM has been determined as a state of pain that originates in the central nervous system. This hypothesis was proposed following observations of increased neuronal activity during non-harmful stimulation in brain regions involved in pain processing, and of dysfunctional endogenous pain modulators in FM patients. [26, 27] Following this statement, we believe that the alterations in the central nervous system of FM patients might be reflected in the alterations observed in the neuroretina of these subjects, and thus, might possibly serve as a useful tool to monitor the disease, as neuroretinal changes occur in demyelinating diseases of the central nervous system and in other neurodegenerative diseases.[28-30]

This study also presents some methodological limitations. Firstly, the present study mostly recruited, women, due to incidence; this allowed us to provide greater homogeneity in the sample, but future studies should be replicated including more men with fibromyalgia. Secondly, this is a monocentric study, and has used a single OCT acquisition system. It would be useful to analyze whether the conclusions of this work are generalized to other conditions and other populations and even other OCT devices. Thirdly, it is also important to state that the sample size was limited and so continuing this line of investigation in future studies with a larger sample could support these results. We did not perform comparison of sensitivity in the detection of neurodegenerative changes. More studies using ROC analysis should be performed in the near future comparing the fast protocol, with the RNFL of the peripapillary area. [31,32] And finally, this study did not consider environmental factors, nutritional disorders, and unhealthy sedentary lifestyle habits that may influence axonal loss as described in other studies. [33]

In addition to the present results, an analysis of the superficial plexuses by optical coherence tomography angiography may well be beneficial, to show if vascular flow in the superficial retina is affected by cause or by consequence, as well as providing an analysis of the deeper retinal layers and the choroid, for a much more complete study. Previous research by Ulusoy et al suggested a decrease in the thickness of the choroid in patients suffering from FM. [34] These findings in the vascular retina can be related to other studies that confirm hypoperfusion in the peripheral and central nervous system. [20-22] Today FM diagnosis is only clinical, there are not diagnostic imaging tests or laboratory tests that confirm this syndrome, and so these results might help us to establish quantifiable values to help diagnosis. More studies following this line of research would be useful in advancing understanding and diagnosis of FM.

In conclusion, the PPole in OCT is a useful, safe, easy and quick test for use in FM patients. Given the high sensitivity to measure the loss of nerve fibers and the measurable ganglion cell layer that this protocol has, it may be advantageous to add the PPole test as part of the FM evaluation protocol, to help quantify and monitor this disease in an objective fashion. Further studies with larger sample size to corroborate our findings would be of great benefit.

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DECLARATION OF INTEREST

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

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TABLES LEGENDS

Table 1. Demographic data in fibromyalgia subgroups and control group.

Table 2. Mean and standard deviation thickness in 64 cells of Ppole protocol in retinal nerve fiber layer in control subject and fibromyalgia patients and significative.

Table 3. Mean and standard deviation in RFNL thickness between subgroups of FM and ANOVA test with Post hoc Kruskal-Wallis.

Table 4. Mean and standard deviation thickness in 64 cells of Ppole protocol in Ganglionar cells layer in control subject and fibromyalgia patients and significative.

Table 5. Mean and standard deviation in GCL thickness between subgroups of FM and ANOVA test with Posthoc Kruskal-Wallis.

Table 6. Spearman correlation between cells of grid Ppole and values of Fibromyalgia impact questionnaire and EuroQol 5 dimensions in both, retinal nerve fiber layer and ganglionar cells layer.

FIGURE LEGENDS

Figure 1. Image of Posterior pole protocol. Right image: Color thickness map of the 64 OCT scans measured, and the 8*8 analysis grid positioned in macula for RNFL; Left image: Color thickness map of the 64 OCT scans measured and the 8*8 analysis grid positioned in macula for GCL.

Figure 2. Contour maps of mean thickness represented on the 64-cell grid (8 * 8) and recreated with Mathworks. (A): retinal fiber layer (RNFL) thickness in the control group; (B): RNFL thickness from fibromyalgia (FM) group; (C): differences corresponding to the RNFL between groups along the grid; (D): ganglion cell layer (GCL) thickness in the control group; (e): GCL thickness in the FM group; (F): differences corresponding to GCL comparison between groups. In all maps, color scale represents the thickness of the corresponding retinal layer in μm, the thinner the retinal layer, the warmer the color.

Figure 3. Significance representation of Ppole 64-cells (8 * 8) gird in retinal fiber layer (RNFL) (left) and ganglionar cells layer (GCL) (right) among three different phenotypes of fibromyalgia (FM) an control group. Color scale represents the p value statistical significance between groups using Kurskal-Wallis post hoc test. Asterisk marks represent significance with p value ≤ 0.001 based on Bonferroni correction for multiple comparisons.

Table 1. Demographic data in fibromyalgia subgroups and control group.

	CONTROL	FM		
		1	*2*	*3*
	N = 74	N =14	N =10	N =18
AGE (Years)	55.12 ± 14.25	57.00±8.89	54.60±7.07	56.54±9.82
IOP (mmHg)	15.36 ± 1.95	115.64±2.27	15.50±1.51	15.94±1.51
GENDER	10 (M) / 64 (F)	3 (M) / 11 (F)	2 (M) / 8 (F)	2 (M) / 16 (F)
FIQ	-	69.12±19.53	75.08±9.49	49-88±13.56
EQ-5D	-	36.00±10.22	40.00±13.74	39.33±16.13

Abbreviations: FM. Fibromyalgia; IOP. Intraocular pressure; FIQ. Fibromyalgia Impact Questionnaire ;EQ-5D. EuroQol ;M. Male; F. Female. 1. Subgroup biological; 2. Subgroup depressive; 3. Subgroup atypical.

Table 2. Mean and standard deviation thickness in 64 cells of Ppole protocol in retinal nerve fiber layer in control subject and fibromyalgia patients and significative.

	CONTROL		FM		
	N = 74		N = 57		U Mann-Withnney
	Media(µm)	*Dev. ±*	*Media(µm)*	*Dev. ±*	*P*
Cell 1.1 RNFL	31,08	6,31	30,80	13,50	0,226
Cell 1.2 RNFL	36,7	7,66	35,53	9,74	0,699
Cell 1.3 RNFL	43,58	9,25	40,53	11,89	0,256
Cell 1.4 RNFL	51,14	11,05	47,40	14,08	0,122
Cell 1.5 RNFL	62,97	15,24	58,67	19,49	0,128
Cell 1.6 RNFL	84,58	20,08	76,58	25,05	0,085
Cell 1.7 RNFL	99,58	19,19	87,53	20,45	0,001*
Cell 1.8 RNFL	86,62	16,88	77,95	24,73	0,077
Cell 2.1 RNFL	26,55	5,25	24,78	5,71	0,253
Cell 2.2 RNFL	30,12	5,02	28,25	5,91	0,142
Cell 2.3 RNFL	34,3	5,04	32,75	7,26	0,15
Cell 2.4 RNFL	38,93	5,44	36,87	7,48	0,067
Cell 2.5 RNFL	45,2	6,65	41,82	9,38	0,014
Cell 2.6 RNFL	57,91	11,17	53,85	15,09	0,034
Cell 2.7 RNFL	89,34	19,62	80,93	25,30	0,042
Cell 2.8 RNFL	123,04	20,10	105,02	23,96	<0,001*
Cell 3.1 RNFL	21,39	3,91	21,55	5,69	0,811
Cell 3.2 RNFL	23,95	3,62	23,07	4,78	0,129
Cell 3.3 RNFL	27,32	3,66	26,18	6,14	0,12
Cell 3.4 RNFL	31,39	4,28	29,93	6,69	0,078
Cell 3.5 RNFL	35,69	5,43	33,96	7,26	0,087
Cell 3.6 RNFL	43,65	6,86	41,45	9,44	0,112
Cell 3.7 RNFL	60,47	10,20	56,80	16,05	0,042
Cell 3.8 RNFL	105,62	20,30	97,64	29,72	0,063
Cell 4.1 RNFL	17,7	2,34	18,24	3,04	0,44
Cell 4.2 RNFL	17,92	2,06	18,53	3,28	0,807
Cell 4.3 RNFL	18,97	2,25	19,05	3,34	0,472
Cell 4.4 RNFL	17,15	1,85	16,80	1,98	0,241
Cell 4.5 RNFL	16,84	2,09	16,91	2,99	0,921
Cell 4.6 RNFL	25,14	4,77	24,76	6,60	0,329
Cell 4.7 RNFL	40,41	7,00	39,31	10,29	0,166
Cell 4.8 RNFL	69,22	12,75	67,72	21,48	0,179
Cell 5.1 RNFL	17,7	2,57	19,65	9,93	0,588
Cell 5.2 RNFL	17,12	2,66	20,09	8,76	0,001*
Cell 5.3 RNFL	15,51	1,84	17,24	5,93	0,017
Cell 5.4 RNFL	15,49	1,74	15,62	2,40	0,961
Cell 5.5 RNFL	16,28	1,96	16,38	2,47	0,805
Cell 5.6 RNFL	25,74	4,41	24,91	6,82	0,083
Cell 5.7 RNFL	42,5	6,97	40,04	7,73	0,055
Cell 5.8 RNFL	69,49	11,71	65,59	17,58	0,030
Cell 6.1 RNFL	16,73	1,97	17,13	3,78	0,915
Cell 6.2 RNFL	17,88	2,25	17,95	2,71	0,747
Cell 6.3 RNFL	20,86	2,88	19,87	2,92	0,027
Cell 6.4 RNFL	26,24	3,88	24,44	4,16	0,017
Cell 6.5 RNFL	32,41	5,00	30,64	5,75	0,084
Cell 6.6 RNFL	41,57	6,56	39,51	8,10	0,125
Cell 6.7 RNFL	55,78	8,67	53,07	11,42	0,058
Cell 6.8 RNFL	84,45	15,13	79,98	20,77	0,085
Cell 7.1 RNFL	18,15	3,83	18,02	3,19	0,852
Cell 7.2 RNFL	20,82	4,46	19,96	3,60	0,37
Cell 7.3 RNFL	25,32	5,28	23,82	4,57	0,082
Cell 7.4 RNFL	31,19	5,97	29,29	6,28	0,038
Cell 7.5 RNFL	40,03	7,55	37,09	8,51	0,010
Cell 7.6 RNFL	49,08	8,96	47,11	11,54	0,064
Cell 7.7 RNFL	64,01	13,64	62,67	18,56	0,142
Cell 7.8 RNFL	95,65	19,70	89,78	27,93	0,031
Cell 8.1 RNFL	22,58	1,59	19,61	4,85	<0,001*
Cell 8.2 RNFL	24,93	6,50	23,02	6,05	0,148
Cell 8.3 RNFL	29,86	7,54	27,98	6,88	0,234
Cell 8.4 RNFL	35,78	8,10	34,15	8,43	0,245
Cell 8.5 RNFL	43,93	10,15	41,91	10,86	0,123
Cell 8.6 RNFL	56,24	13,56	53,44	15,61	0,102
Cell 8.7 RNFL	76,68	16,90	69,40	18,45	0,015
Cell 8.8 RNFL	93,32	17,56	83,09	19,29	0,001*

Abbreviations: FM. Fibromyalgia; Dev. Standard Deviation; RNFL. Retinal nerve fiber layer.

Asterisk marks significance based on Bonferroni correction for multiple comparisons

Table 3. Mean and standard deviation in RFNL thickness between subgroups of FM and ANOVA test with Post hoc Kruskal-Wallis.

	CONTROL		1		2		3		*KRUSKAL-WALLIS*
N	74		14		10		18		*P*
	Media(μm)	*Dev. ±*	*Media(μm)*	*Dev. ±*	*Media(μm)*	*Dev. ±*	*Media(μm)*	*Dev. ±*	
Cell 1.1 RNFL	31,08	6,31	27,14	6,09	29,00	8,08	34,18	20,91	0,246
Cell 1.2 RNFL	36,70	7,66	32,14	9,55	35,80	11,80	34,94	7,70	0,436
Cell 1.3 RNFL	43,58	9,25	38,36	13,02	38,80	13,92	39,83	10,63	0,442
Cell 1.4 RNFL	51,14	11,05	45,64	16,29	44,20	11,07	46,33	13,79	0,227
Cell 1.5 RNFL	62,97	15,24	57,29	21,25	51,20	14,27	57,78	19,50	0,136
Cell 1.6 RNFL	84,58	20,08	72,29	27,50	67,80	17,76	77,39	26,35	0,069
Cell 1.7 RNFL	99,58	19,19	86,07	17,34	83,30	20,75	85,83	23,99	0,006
Cell 1.8 RNFL	86,62	16,88	80,79	23,23	81,40	27,93	71,28	23,93	0,075
Cell 2.1 RNFL	26,55	5,25	24,07	6,63	23,40	7,55	24,83	4,37	0,507
Cell 2.2 RNFL	30,12	5,02	27,29	6,20	24,40	7,09	28,39	4,78	0,04
Cell 2.3 RNFL	34,30	5,04	33,14	7,44	27,10	6,98	32,78	6,67	0,017
Cell 2.4 RNFL	38,93	5,44	37,43	7,02	31,00	5,06	36,56	7,38	0,03
Cell 2.5 RNFL	45,20	6,65	42,14	9,65	35,20	5,45	40,78	9,05	0,001*
Cell 2.6 RNFL	57,91	11,17	55,46	16,99	41,80	5,14	52,67	13,63	<0,001*
Cell 2.7 RNFL	89,34	19,62	79,46	29,35	65,30	9,79	81,44	24,58	0,007
Cell 2.8 RNFL	123,04	20,10	101,85	29,79	100,80	10,25	104,50	24,32	<0,001*
Cell 3.1 RNFL	21,39	3,91	23,29	9,60	18,60	3,10	20,67	2,97	0,22
Cell 3.2 RNFL	23,95	3,62	24,07	5,94	19,60	3,60	22,17	3,02	0,007
Cell 3.3 RNFL	27,32	3,66	28,21	8,68	22,90	3,07	25,00	4,78	0,013
Cell 3.4 RNFL	31,39	4,28	32,36	8,38	25,70	3,43	29,06	6,80	0,004
Cell 3.5 RNFL	35,69	5,43	36,21	8,88	29,30	3,53	33,17	7,60	0,007
Cell 3.6 RNFL	43,65	6,86	44,29	11,17	34,70	3,83	39,78	9,27	0,002
Cell 3.7 RNFL	60,47	10,20	57,50	19,29	47,10	5,34	54,67	15,91	0,001*
Cell 3.8 RNFL	105,62	20,30	97,64	32,33	80,20	13,33	96,94	30,50	0,008
Cell 4.1 RNFL	17,70	2,34	18,71	4,78	16,90	1,97	18,28	2,22	0,463
Cell 4.2 RNFL	17,92	2,06	19,36	4,78	16,70	1,77	18,06	2,21	0,141
Cell 4.3 RNFL	18,97	2,25	20,57	4,86	17,00	1,05	18,67	2,85	0,033
Cell 4.4 RNFL	17,15	1,85	17,21	2,39	15,80	1,69	17,22	2,05	0,226
Cell 4.5 RNFL	16,84	2,09	18,14	5,13	15,10	1,60	16,56	1,29	0,066
Cell 4.6 RNFL	25,14	4,77	27,71	10,23	20,50	3,44	23,78	4,40	0,026
Cell 4.7 RNFL	40,41	7,00	42,77	13,59	32,20	5,16	37,17	7,70	0,008
Cell 4.8 RNFL	69,22	12,75	68,00	18,80	54,10	11,91	63,78	19,14	0,015
Cell 5.1 RNFL	17,70	2,57	22,36	15,25	16,70	2,83	18,61	2,57	0,287
Cell 5.2 RNFL	17,12	2,66	23,29	16,19	18,80	3,52	19,67	2,33	0,001*
Cell 5.3 RNFL	15,51	1,84	19,50	10,94	15,80	2,04	16,78	2,58	0,067
Cell 5.4 RNFL	15,49	1,74	16,00	3,94	14,80	1,14	16,06	1,16	0,166
Cell 5.5 RNFL	16,28	1,96	16,86	3,90	15,40	1,17	16,11	1,41	0,561
Cell 5.6 RNFL	25,74	4,41	27,36	11,81	21,10	3,11	24,17	3,62	0,011
Cell 5.7 RNFL	42,50	6,97	39,79	8,54	33,90	4,58	39,56	7,06	0,002
Cell 5.8 RNFL	69,49	11,71	63,77	17,54	54,20	5,43	63,11	14,56	0,001*
Cell 6.1 RNFL	16,73	1,97	18,00	4,13	15,10	1,60	16,83	1,58	0,047
Cell 6.2 RNFL	17,88	2,25	18,43	4,20	17,10	2,03	17,89	1,84	0,72
Cell 6.3 RNFL	20,86	2,88	20,50	3,65	18,80	2,10	19,83	3,37	0,099
Cell 6.4 RNFL	26,24	3,88	25,29	4,73	22,30	2,36	24,72	4,81	0,028
Cell 6.5 RNFL	32,41	5,00	32,64	6,83	26,70	2,75	30,39	5,61	0,007
Cell 6.6 RNFL	41,57	6,56	41,86	9,87	32,90	2,56	39,44	7,87	0,001*
Cell 6.7 RNFL	55,78	8,67	53,64	12,94	45,70	5,38	52,89	10,69	0,005
Cell 6.8 RNFL	84,45	15,13	77,92	21,31	67,60	10,72	80,00	21,15	0,009
Cell 7.1 RNFL	18,15	3,83	18,71	4,16	17,60	2,41	17,72	3,05	0,884

Cell 7.2 RNFL	20,82	4,46	19,86	3,90	19,70	3,20	19,83	4,00	0,775
Cell 7.3 RNFL	25,32	5,28	22,86	4,90	22,90	3,87	24,06	4,63	0,197
Cell 7.4 RNFL	31,19	5,97	28,21	6,33	26,80	3,29	29,78	6,42	0,044
Cell 7.5 RNFL	40,03	7,55	35,86	8,41	33,10	4,25	38,50	8,91	0,008
Cell 7.6 RNFL	49,08	8,96	46,36	11,39	41,00	8,94	48,83	11,84	0,033
Cell 7.7 RNFL	64,01	13,64	66,29	26,39	54,50	11,96	61,50	16,70	0,109
Cell 7.8 RNFL	95,65	19,70	95,00	42,71	83,90	24,24	86,00	20,09	0,1
Cell 8.1 RNFL	22,58	1,59	19,79	7,14	19,40	3,86	20,44	4,15	<0,001*
Cell 8.2 RNFL	24,93	6,50	22,79	8,30	22,30	6,78	24,22	5,12	0,818
Cell 8.3 RNFL	29,86	7,54	27,07	8,50	27,30	8,56	29,61	5,19	0,784
Cell 8.4 RNFL	35,78	8,10	33,64	9,87	32,60	9,51	35,17	6,65	0,795
Cell 8.5 RNFL	43,93	10,15	41,07	14,06	40,40	11,12	42,83	8,62	0,571
Cell 8.6 RNFL	56,24	13,56	53,93	20,62	50,30	16,81	54,50	12,95	0,485
Cell 8.7 RNFL	76,68	16,90	69,50	23,03	66,00	22,84	70,67	13,43	0,118
Cell 8.8 RNFL	93,32	17,56	79,21	26,62	76,70	22,63	89,22	10,13	0,02

RNFL. Retinal nerve fiber layer; Groups of fibromyalgia: Group 1, biological fibromyalgia. Group 2, Depressive fibromyalgia. Group 3, atipic fibromyalgia. Asterisk marks significance based on Bonferroni correction for multiple comparisons

Table 4. Mean and standard deviation thickness in 64 cells of Ppole protocol in Ganglionar cells layer in control subject and fibromyalgia patients and significative.

	CONTROL		FM		
	N = 74		N = 57		U Mann-Withnney
	Media(µm)	*Dev. ±*	*Media(µm)*	*Dev. ±*	*P*
Cell 1.1 GCL	21,34	2,41	20,24	3,62	0,01
Cell 1.2 GCL	22,61	2,26	21,22	3,18	0,019
Cell 1.3 GCL	23,72	2,87	22,07	3,71	0,017
Cell 1.4 GCL	24,50	4,12	22,95	3,41	0,042
Cell 1.5 GCL	24,41	4,09	23,60	3,29	0,452
Cell 1.6 GCL	22,91	3,05	22,58	3,20	0,692
Cell 1.7 GCL	21,26	2,18	22,16	3,60	0,213
Cell 1.8 GCL	21,26	1,81	21,38	3,24	0,707
Cell 2.1 GCL	23,95	2,12	22,13	3,76	0,007
Cell 2.2 GCL	26,66	2,88	24,80	4,00	0,009
Cell 2.3 GCL	30,36	4,04	28,05	4,08	0,008
Cell 2.4 GCL	33,31	5,32	30,44	4,34	0,003
Cell 2.5 GCL	33,80	5,39	30,65	4,63	0,002
Cell 2.6 GCL	30,80	4,77	27,85	4,48	<0,001*
Cell 2.7 GCL	25,66	3,60	24,69	4,70	0,157
Cell 2.8 GCL	21,66	2,79	22,72	4,83	0,218
Cell 3.1 GCL	28,28	3,14	26,47	3,32	0,007
Cell 3.2 GCL	34,99	4,48	32,36	4,81	0,008
Cell 3.3 GCL	43,85	6,01	40,55	5,68	0,009
Cell 3.4 GCL	50,93	5,51	47,09	5,74	<0,001*
Cell 3.5 GCL	50,70	5,37	47,40	6,39	0,002
Cell 3.6 GCL	45,09	5,63	40,89	6,35	<0,001*
Cell 3.7 GCL	34,82	4,24	32,04	5,60	0,003
Cell 3.8 GCL	26,32	3,33	25,60	4,23	0,339
Cell 4.1 GCL	30,54	3,97	27,87	4,59	0,003
Cell 4.2 GCL	41,39	5,78	36,60	7,18	<0,001*
Cell 4.3 GCL	52,73	4,83	48,04	7,27	<0,001*
Cell 4.4 GCL	41,54	7,15	37,64	7,95	0,004
Cell 4.5 GCL	39,99	6,92	37,96	8,13	0,121
Cell 4.6 GCL	55,84	4,58	52,11	5,64	<0,001*
Cell 4.7 GCL	43,88	4,97	40,70	5,33	0,001*
Cell 4.8 GCL	31,58	3,38	30,44	4,17	0,145
Cell 5.1 GCL	25,84	4,83	23,82	4,78	0,012
Cell 5.2 GCL	36,72	6,86	30,96	7,25	<0,001*
Cell 5.3 GCL	49,47	5,48	43,76	7,39	<0,001*
Cell 5.4 GCL	35,09	6,61	31,91	7,57	0,015
Cell 5.5 GCL	37,05	7,57	35,75	6,39	0,183
Cell 5.6 GCL	55,73	5,07	52,31	5,69	0,001*
Cell 5.7 GCL	43,39	4,92	40,35	5,20	0,002
Cell 5.8 GCL	30,07	3,71	30,52	5,23	0,677
Cell 6.1 GCL	26,32	4,13	24,16	3,83	0,003
Cell 6.2 GCL	35,42	5,11	31,51	5,15	<0,001*
Cell 6.3 GCL	46,00	5,08	42,25	6,49	0,001*
Cell 6.4 GCL	53,39	4,87	49,55	6,74	0,001*
Cell 6.5 GCL	53,00	5,37	49,24	5,74	<0,001*
Cell 6.6 GCL	46,00	6,06	42,82	5,46	0,005
Cell 6.7 GCL	35,73	5,47	33,67	4,12	0,059
Cell 6.8 GCL	27,51	4,04	26,94	3,94	0,387
Cell 7.1 GCL	24,12	2,57	22,49	3,38	0,005
Cell 7.2 GCL	28,74	4,35	26,40	4,34	0,006
Cell 7.3 GCL	33,70	5,65	31,31	4,26	0,016
Cell 7.4 GCL	37,95	6,80	34,91	4,42	0,002
Cell 7.5 GCL	37,73	6,57	35,20	4,94	0,034
Cell 7.6 GCL	33,51	6,41	30,84	4,16	0,002
Cell 7.7 GCL	27,88	5,60	26,33	3,43	0,042
Cell 7.8 GCL	23,34	2,92	23,89	4,24	0,510
Cell 8.1 GCL	21,45	2,86	19,70	3,99	0,003
Cell 8.2 GCL	23,69	3,26	22,15	4,35	0,031
Cell 8.3 GCL	26,03	4,58	24,35	4,49	0,053
Cell 8.4 GCL	27,89	5,73	25,87	4,58	0,017
Cell 8.5 GCL	28,53	6,16	26,36	4,38	0,009
Cell 8.6 GCL	25,91	5,52	24,73	3,30	0,089
Cell 8.7 GCL	23,07	3,70	23,33	3,33	0,364
Cell 8.8 GCL	21,27	2,63	22,94	3,18	0,004

Abbreviations: FM. Fibromyalgia; Dev. Standard Deviation; GCL. Ganglionar cell layer. Asterisk marks significance based on U Mann-withnney.

Table 5. Mean and standard deviation in GCL thickness between subgroups of FM and ANOVA test with Posthoc Kruskal-Wallis.

	CONTROL		1		2		3		*KRUSKAL-WALLIS*
N	74		14		10		18		*P*
	Media(μm)	*Dev. ±*	*Media(μm)*	*Dev. ±*	*Media(μm)*	*Dev. ±*	*Media(μm)*	*Dev. ±*	
Cell 1.1 GCL	21,34	2,41	19,57	3,13	19,70	4,52	21,41	4,20	0,137
Cell 1.2 GCL	22,61	2,26	21,36	3,18	20,20	4,78	21,22	2,73	0,129
Cell 1.3 GCL	23,72	2,87	22,50	3,90	20,20	5,12	22,22	3,59	0,090
Cell 1.4 GCL	24,50	4,12	22,64	3,27	22,10	3,35	22,89	4,23	0,073
Cell 1.5 GCL	24,41	4,09	23,21	3,02	23,10	2,42	23,22	4,10	0,509
Cell 1.6 GCL	22,91	3,05	21,93	3,32	22,00	2,63	22,56	3,62	0,699
Cell 1.7 GCL	21,26	2,18	23,21	5,56	21,60	2,27	21,56	3,00	0,857
Cell 1.8 GCL	21,26	1,81	23,07	4,46	20,30	1,89	21,33	3,11	0,377
Cell 2.1 GCL	23,95	2,12	22,14	4,19	20,20	5,59	22,72	2,47	0,041
Cell 2.2 GCL	26,66	2,88	24,64	3,80	21,90	6,17	25,50	3,03	0,017
Cell 2.3 GCL	30,36	4,04	28,07	3,65	25,20	5,87	28,22	3,66	0,010
Cell 2.4 GCL	33,31	5,32	30,00	4,10	28,70	4,99	30,39	4,57	0,007
Cell 2.5 GCL	33,80	5,39	29,50	4,38	28,50	5,46	31,33	4,63	0,003
Cell 2.6 GCL	30,80	4,77	26,07	5,80	27,70	4,72	28,33	3,46	0,002
Cell 2.7 GCL	25,66	3,60	24,64	7,28	24,00	4,35	25,44	3,29	0,601
Cell 2.8 GCL	21,66	2,79	24,08	7,31	21,60	4,01	22,56	4,42	0,639
Cell 3.1 GCL	28,28	3,14	26,50	3,67	24,50	3,69	26,56	2,92	0,008
Cell 3.2 GCL	34,99	4,48	32,07	4,84	29,30	4,81	32,39	4,47	0,003
Cell 3.3 GCL	43,85	6,01	38,93	5,73	37,80	3,29	40,44	6,21	0,001
Cell 3.4 GCL	50,93	5,51	45,57	4,99	44,30	3,13	46,78	6,58	<0,001*
Cell 3.5 GCL	50,70	5,37	45,71	4,87	43,90	2,73	47,33	8,26	<0,001*
Cell 3.6 GCL	45,09	5,63	38,86	5,49	38,10	3,64	41,72	7,66	<0,001*
Cell 3.7 GCL	34,82	4,24	30,71	6,22	30,40	5,32	33,11	5,93	0,015
Cell 3.8 GCL	26,32	3,33	26,14	3,76	23,90	4,04	25,67	5,11	0,473
Cell 4.1 GCL	30,54	3,97	26,79	5,19	25,80	3,23	27,39	3,93	0,001
Cell 4.2 GCL	41,39	5,78	35,79	8,11	33,80	4,52	35,94	7,08	<0,001*
Cell 4.3 GCL	52,73	4,83	47,93	7,51	44,80	4,13	47,83	8,55	<0,001*
Cell 4.4 GCL	41,54	7,15	38,57	7,19	35,00	8,21	38,33	10,00	0,065
Cell 4.5 GCL	39,99	6,92	36,36	6,79	33,10	7,11	39,11	8,60	0,017
Cell 4.6 GCL	55,84	4,58	50,21	6,23	48,20	2,20	52,83	6,23	<0,001*
Cell 4.7 GCL	43,88	4,97	39,69	4,68	37,10	4,86	42,11	5,76	0,001
Cell 4.8 GCL	31,58	3,38	30,85	3,39	28,70	5,08	31,17	4,11	0,416
Cell 5.1 GCL	25,84	4,83	23,36	6,13	21,80	3,29	22,72	3,44	0,002
Cell 5.2 GCL	36,72	6,86	30,21	8,65	28,10	3,76	29,89	6,27	<0,001*
Cell 5.3 GCL	49,47	5,48	43,71	7,43	42,20	4,94	44,78	8,06	<0,001*
Cell 5.4 GCL	35,09	6,61	32,00	5,44	32,60	8,29	33,89	6,56	0,385
Cell 5.5 GCL	37,05	7,57	33,86	3,92	33,20	5,27	37,28	7,00	0,076
Cell 5.6 GCL	55,73	5,07	50,43	5,79	47,60	3,50	53,89	6,37	<0,001*
Cell 5.7 GCL	43,39	4,92	40,29	4,62	36,40	5,52	41,50	5,77	0,002
Cell 5.8 GCL	30,07	3,71	31,54	4,74	28,30	5,62	30,94	6,08	0,669
Cell 6.1 GCL	26,32	4,13	25,21	4,30	23,40	3,20	24,06	3,57	0,044
Cell 6.2 GCL	35,42	5,11	31,71	5,77	29,50	4,70	31,22	4,05	<0,001*
Cell 6.3 GCL	46,00	5,08	42,07	6,81	38,40	4,60	42,33	5,33	<0,001*
Cell 6.4 GCL	53,39	4,87	49,64	5,81	44,40	4,14	50,94	5,53	<0,001*
Cell 6.5 GCL	53,00	5,37	48,50	5,07	44,00	4,35	50,72	5,68	<0,001*
Cell 6.6 GCL	46,00	6,06	41,64	4,31	38,60	5,95	43,94	6,15	0,001*
Cell 6.7 GCL	35,73	5,47	32,93	3,52	31,00	5,14	34,83	4,38	0,029
Cell 6.8 GCL	27,51	4,04	26,92	2,93	25,80	5,03	27,39	5,03	0,784
Cell 7.1 GCL	24,12	2,57	22,64	3,41	21,20	3,82	22,33	2,95	0,008

Cell 7.2 GCL	28,74	4,35	25,86	4,40	24,90	4,61	26,17	3,68	0,006
Cell 7.3 GCL	33,70	5,65	29,79	4,15	29,20	4,59	31,89	3,71	0,004
Cell 7.4 GCL	37,95	6,80	34,14	4,52	32,00	5,77	35,61	3,70	0,002
Cell 7.5 GCL	37,73	6,57	34,43	4,83	32,10	6,37	35,89	4,89	0,014
Cell 7.6 GCL	33,51	6,41	30,57	3,63	28,30	6,09	31,22	3,93	0,005
Cell 7.7 GCL	27,88	5,60	26,50	2,71	25,30	5,14	26,33	3,71	0,208
Cell 7.8 GCL	23,34	2,92	25,79	6,39	22,80	3,46	23,39	3,13	0,593
Cell 8.1 GCL	21,45	2,86	18,71	5,58	19,00	4,40	20,33	2,99	0,034
Cell 8.2 GCL	23,69	3,26	21,00	5,75	20,70	5,29	22,72	2,93	0,091
Cell 8.3 GCL	26,03	4,58	23,36	5,34	22,40	5,84	25,00	3,50	0,117
Cell 8.4 GCL	27,89	5,73	24,36	5,27	23,60	6,19	26,83	3,33	0,007
Cell 8.5 GCL	28,53	6,16	25,43	5,61	23,90	5,67	27,11	3,05	0,009
Cell 8.6 GCL	25,91	5,52	23,79	4,76	24,00	2,49	24,89	2,85	0,099
Cell 8.7 GCL	23,07	3,70	23,21	4,87	23,40	2,76	23,11	3,07	0,938
Cell 8.8 GCL	21,27	2,63	23,21	4,04	23,20	2,53	22,39	2,95	0,075

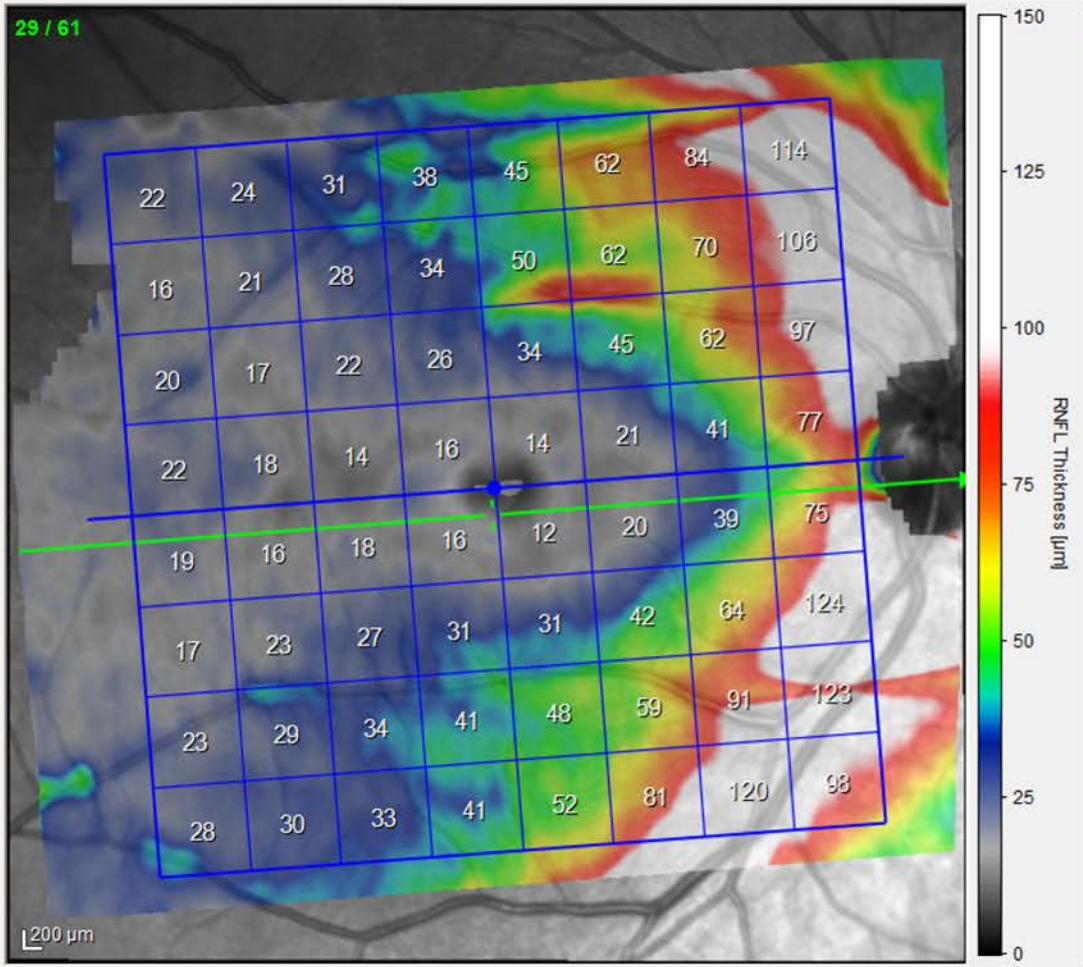
GCL. Ganglionar cell layer; Groups of fibromyalgia:. Group 1, biological fibromyalgia. Group 2, Depressive fibromyalgia. Group 3, atipic fibromyalgia. Asterisk marks significance based on Bonferroni correction for multiple comparisons

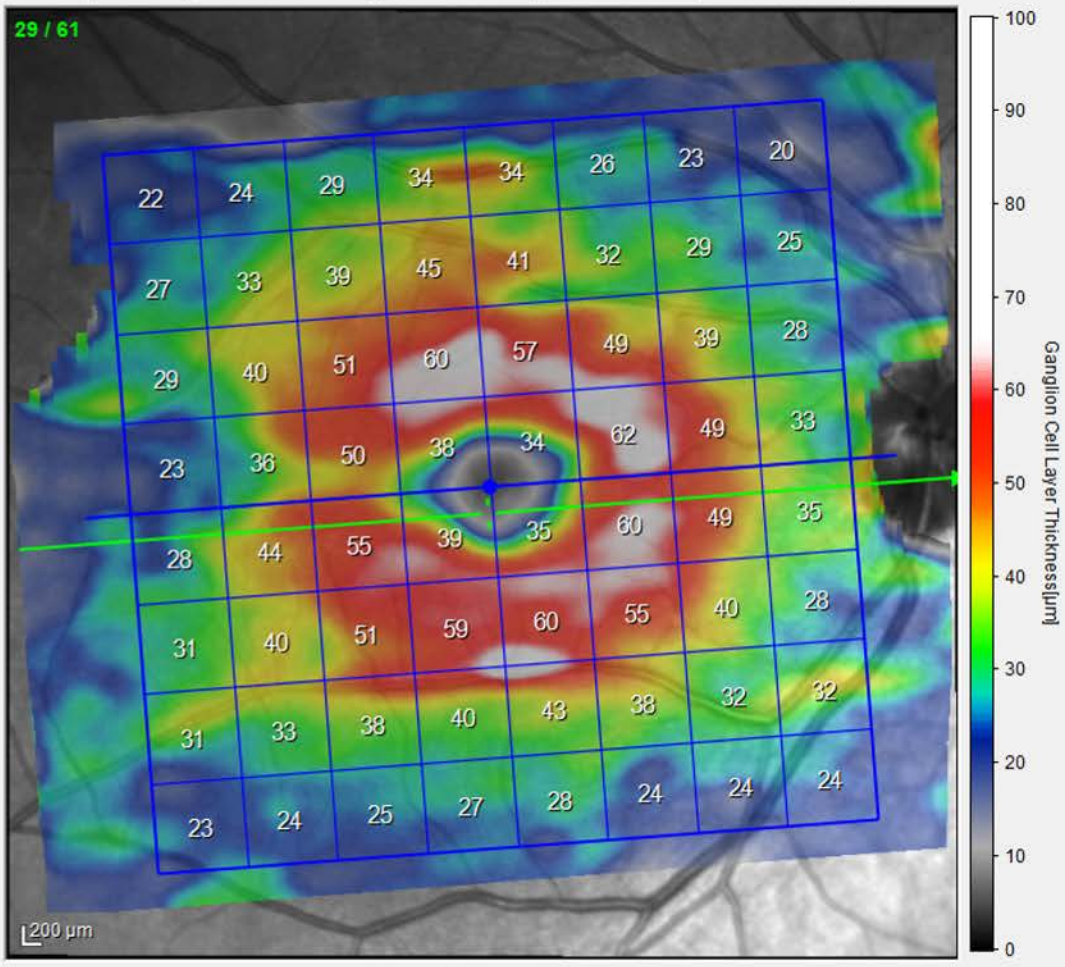
Table 6. Spearman correlation between cells of grid Ppole and values of Fibromyalgia impact questionnaire and EuroQol 5 dimensions in both, retinal nerve fiber layer and ganglionar cells layer.

	RNFL				GCL			
	IMPACTP SFM FIQ		SCALE EQ 5D		IMPACTP FIQ		SCALE EQ 5D	
	Spearman Corrleation	*Sig.*	*Spearman Corrleation*	*Sig.*	*Spearman Corrleation*	*Sig.*	*Spearman Corrleation*	*Sig.*
Cell 1.1	-0,110	0,515	0,293	0,070	0,145	0,384	-0,019	
Cell 1.2	-0,158	0,345	0,298	0,062	-0,173	0,306	,401*	0,011
Cell 1.3	-0,297	0,070	,389*	0,013	-0,122	0,466	,495**	0,001
Cell 1.4	-0,293	0,074	,341*	0,032	-,327*	0,045	,586**	0,000
Cell 1.5	-0,269	0,103	,322*	0,042	-,365*	0,024	,475**	0,002
Cell 1.6	-0,240	0,146	,401*	0,010	-0,152	0,361	,363*	0,021
Cell 1.7	-0,037	0,827	,402*	0,010	-0,191	0,249	0,226	0,161
Cell 1.8	0,224	0,177	,324*	0,041	-0,019	0,909	0,011	0,944
Cell 2.1	-0,126	0,451	0,306	0,055	-0,092	0,582	0,144	0,374
Cell 2.2	-0,291	0,076	0,185	0,253	-0,279	0,089	,426**	0,006
Cell 2.3	-0,196	0,237	0,005	0,976	-0,303	0,065	,342*	0,031
Cell 2.4	-0,139	0,404	0,008	0,962	-0,202	0,225	0,302	0,058
Cell 2.5	-0,174	0,295	0,165	0,310	-0,181	0,276	,314*	0,049
Cell 2.6	-0,164	0,333	0,146	0,376	-0,270	0,102	0,289	0,070
Cell 2.7	-0,227	0,176	0,097	0,556	-0,199	0,230	,493**	0,001
Cell 2.8	-0,116	0,494	0,258	0,113	-0,084	0,616	,388*	0,013
Cell 3.1	-0,083	0,619	-0,067	0,682	-0,084	0,623	0,235	0,149
Cell 3.2	-0,136	0,417	-0,215	0,182	-0,156	0,348	0,301	0,059
Cell 3.3	-0,041	0,807	-0,278	0,083	-0,179	0,283	0,206	0,203
Cell 3.4	0,044	0,795	-0,142	0,383	-0,313	0,056	0,235	0,144
Cell 3.5	-0,069	0,682	-0,087	0,595	-0,296	0,071	0,233	0,148
Cell 3.6	-0,052	0,755	-0,117	0,470	-,388*	0,016	0,212	0,189
Cell 3.7	-0,179	0,283	-0,017	0,919	-,402*	0,012	0,269	0,094
Cell 3.8	-0,161	0,336	0,023	0,888	-0,299	0,068	0,163	0,316
Cell 4.1	-0,009	0,955	-0,058	0,722	-0,099	0,554	0,109	0,502
Cell 4.2	-0,080	0,633	-,341*	0,031	-,398*	0,013	,417**	0,007
Cell 4.3	-0,099	0,554	-0,137	0,401	-0,256	0,121	0,150	0,355
Cell 4.4	-,359*	0,027	0,106	0,515	-0,183	0,272	0,194	0,231
Cell 4.5	-0,212	0,200	0,001	0,996	-0,222	0,179	,392*	0,012
Cell 4.6	-0,105	0,529	-0,124	0,445	-0,305	0,062	0,248	0,123
Cell 4.7	-0,162	0,338	-0,086	0,604	-,417**	0,009	0,248	0,123
Cell 4.8	-0,190	0,267	-0,040	0,810	-,385*	0,019	0,228	0,164
Cell 5.1	0,049	0,770	0,058	0,723	-0,143	0,399	0,275	0,090
Cell 5.2	0,115	0,490	-0,074	0,649	-0,289	0,078	0,176	0,276
Cell 5.3	0,094	0,574	-0,291	0,069	-0,167	0,317	0,076	0,641
Cell 5.4	-0,100	0,549	-,388*	0,013	-0,126	0,449	0,179	0,268
Cell 5.5	0,200	0,228	-0,138	0,395	0,027	0,874	0,199	0,217
Cell 5.6	-0,152	0,361	-0,160	0,323	-0,123	0,462	0,135	0,405
Cell 5.7	-,396*	0,014	-0,035	0,832	-,502**	0,001	0,217	0,178
Cell 5.8	-0,238	0,156	-0,053	0,747	-,321*	0,050	0,175	0,280
Cell 6.1	-0,077	0,647	-0,098	0,548	-0,135	0,427	0,217	0,185
Cell 6.2	0,047	0,779	-0,260	0,106	-0,002	0,989	0,229	0,156
Cell 6.3	0,136	0,416	-,360*	0,022	-0,190	0,253	0,182	0,261
Cell 6.4	-0,021	0,899	-0,304	0,056	-0,288	0,080	0,131	0,419
Cell 6.5	-0,040	0,813	-0,188	0,246	-,332*	0,041	0,066	0,687
Cell 6.6	-0,219	0,188	-0,131	0,421	-,419**	0,009	0,172	0,287
Cell 6.7	-0,277	0,092	0,019	0,906	-,428**	0,007	0,200	0,217
Cell 6.8	-0,287	0,085	0,036	0,829	-,411*	0,010	0,165	0,308

Cell 7.1	-0,093	0,580	0,083	0,612	-0,181	0,285	0,045	0,785
Cell 7.2	-0,067	0,691	0,011	0,947	-0,233	0,158	,430**	0,006
Cell 7.3	0,011	0,946	-0,123	0,449	-0,274	0,096	,358*	0,023
Cell 7.4	-0,004	0,983	-0,136	0,401	-,450**	0,005	0,279	0,081
Cell 7.5	-0,144	0,390	-0,107	0,511	-,443**	0,005	0,188	0,246
Cell 7.6	-0,191	0,250	-0,077	0,638	-,479**	0,002	0,199	0,219
Cell 7.7	-0,091	0,588	-0,006	0,969	-,409*	0,011	0,228	0,158
Cell 7.8	-0,142	0,395	0,075	0,645	-0,266	0,107	0,174	0,283
Cell 8.1	-0,286	0,081	,314*	0,048	-0,072	0,667	0,042	0,797
Cell 8.2	-0,219	0,186	,377*	0,016	-0,195	0,240	0,301	0,059
Cell 3.3	-0,187	0,260	,361*	0,022	-0,294	0,073	,330*	0,038
Cell 8.4	-0,039	0,818	0,215	0,182	-0,260	0,115	0,311	0,051
Cell 8.5	0,028	0,866	0,225	0,163	-,373*	0,021	0,307	0,054
Cell 8.6	-0,034	0,838	0,169	0,298	-0,279	0,090	0,084	0,607
Cell 8.7	-0,224	0,177	0,247	0,124	-0,139	0,406	0,118	0,469
Cell 8.8	-0,256	0,121	0,148	0,363	-0,056	0,739	-0,022	0,892

RNFL. Retinal nerve fiber layer GCL. Ganglionar cell layer; Groups of fibromyalgia:. FIQ. Fibromyalgia Impact Questionnaire EZ-5D. EuroQol 5 dimensions. Asterisk marks significance based on Bonferroni correction for multiple comparisons



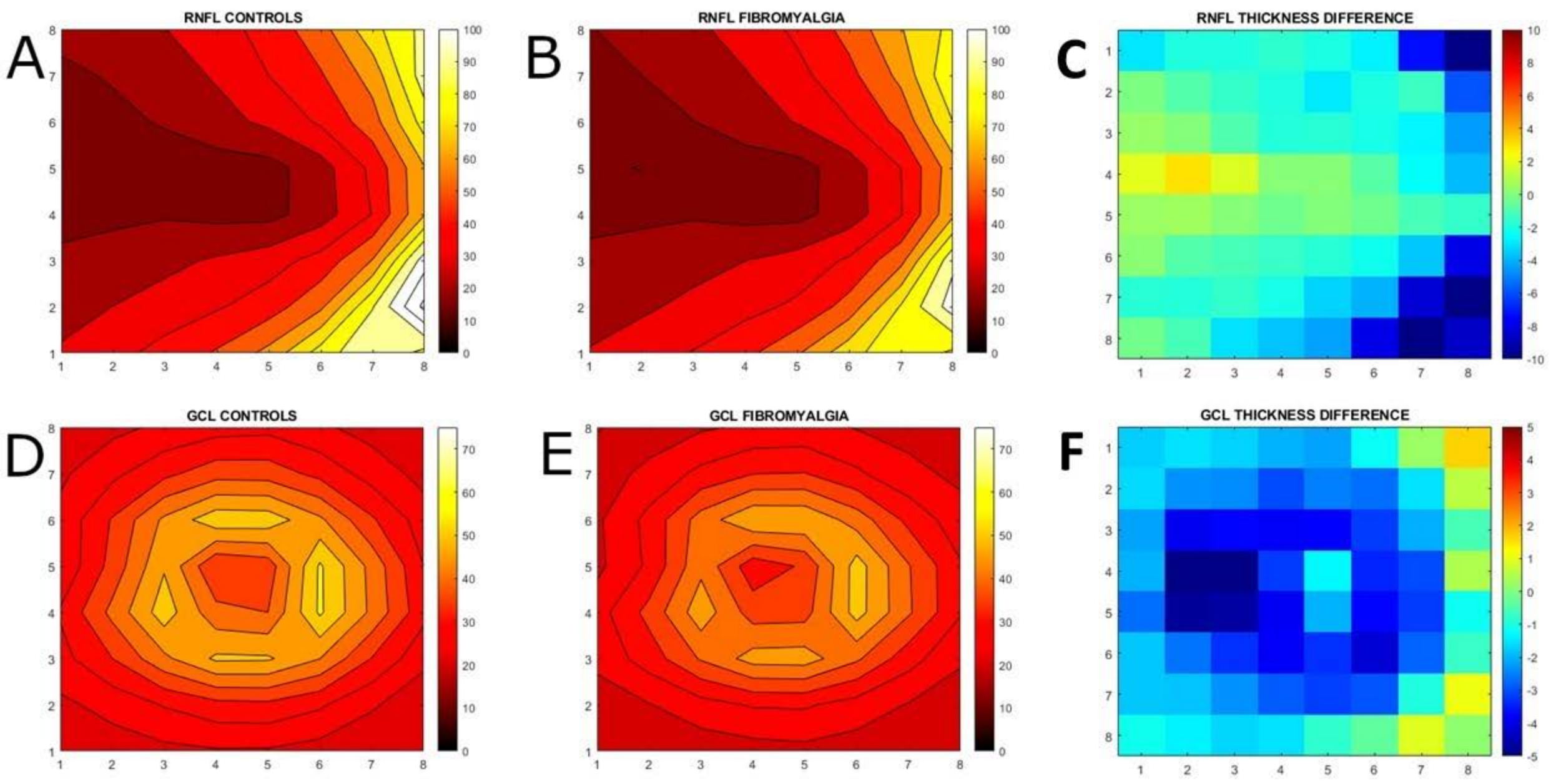


Auto Overlay:

Layer: Nerve Fiber Layer 8x8 Posterior Pole Grid

Auto Overlay:

Layer: Ganglion Cell Layer 8x8 Posterior Pole Grid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B
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C
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D
GCL CONTROLS
E
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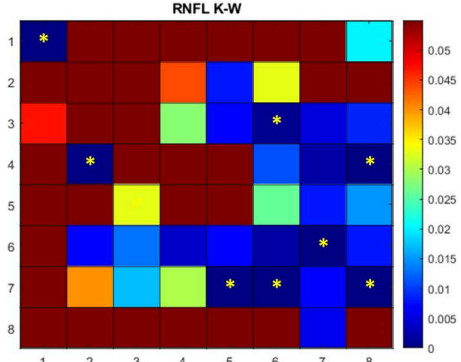
F
GCL THICKNESS DIFFERENCE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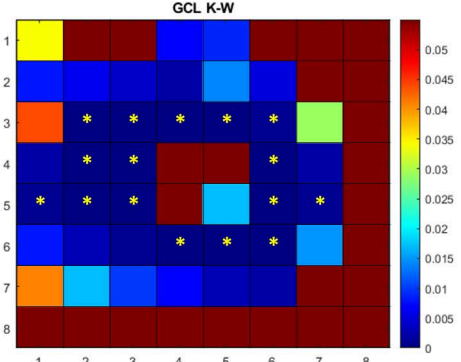
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