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Optical Coherence Tomography Angiography to Evaluate Anti–Vascular Endothelial Growth Factor Therapy In Myopic Choroidal Neovascularization

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ABSTRACT:
Background*: Myopia is a common disorder estimated to affect approximately 1.6 billion people worldwide. It is defined as a refractive condition in which the image of a distant object is formed anterior to the retina of the unaccommodated (relaxed) eye.*
Objective:*Evaluation of anti–vascular endothelial growth factor therapy in myopic choroidal neovascularization using optical coherence tomography angiography by detecting the changes of shape, size, and flow area.*
Patients and methods:*The study was conducted on 20 myopic eyes (11 left, 9 right) at 20 patients who were referred to the ophthalmologic clinic, faculty of medicine, Menoufia University during the period from February 2021 till April 2022.*
Results:*Central macular thickness was significantly decreased after treatment with intravitreal ranibizumab than before treatment, with mean difference 45.55±71.27 (9.62%), (P=0.010). Intraretinal fluid, subretinal fluid were significantly decreased after treatment with intravitreal ranibizumab than before treatment with changes 22.11% and 16.21%, respectively (P<0.05).*
Conclusion:*It was approached to obtain binarized and skeletonized OCTA images of mCNV lesion for fully quantitative analysis to elucidate the morphological changes of mCNV after anti-VEGF therapy.*
Keywords:*Optical coherence tomography angiography, Anti–vascular endothelial-GF, Myopic choroidal neovascularization*

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I. Introduction

Myopia is a common disorder estimated to affect approximately 1.6 billion people worldwide. This disorder is becoming by time prevalent and it is estimated that up to 2.5 billion people will be affected **(Ruiz-Medrano et al., 2019).** It is defined as a refractive condition in which the image of a distant object is formed anterior to the retina of the unaccommodated (relaxed) eye. Hine classified myopia by degree (low, medium, or high) **(Grzybowski et al., 2020)**. Others classified it according to its clinical entity into (simple myopia, nocturnal myopia, pseudomyopia, degenerative myopia, and induced myopia) **(De Jong, 2018).** Or by age of onset (congenital, youth-onset, early adult-onset, and late adult-onset) **(Ruan et al., 2019)**.

Pathologic myopia (PM) is defined as eyes having atrophic changes equal to or more severe than diffuse atrophy.PM is different from other types of myopia in the sense that PM causes the loss of best-corrected visual acuity, not only the loss of uncorrected visual acuity **(Ohno-Matsui, 2016**). Pathologic myopia is an important cause of visual impairment. Development of myopic choroidal neovascularization (CNV) is one of the most common complications that lead to central vision loss in patients with pathologic myopia. If left untreated, it can cause scarring with expanding macular atrophy leading to irreversible visual loss in a period as short as 5 years (**Ohno-Matsui, Ikuno, Lai, & Cheung, 2018)**.

Vascular endothelial growth factor (VEGF) has an important role appeared in mobilization of endothelial progenitor cells from the bone marrow to distant sites of neovascularization **(Asahara & Masuda, 2017).**The targeting of VEGFA as an essential regulator of both normal and pathological angiogenesis has revealed advanced therapeutic approaches in oncology and ophthalmology. The first VEGFA inhibitors in ophthalmology, pegaptanib and ranibizumab, were approved in 2004 and 2006, respectively**(Ferrara & Adamis, 2016).**

Optical coherence tomography (OCT) angiography is one of the first non-invasive imaging techniques capable of detecting changes in thefoveal avascular zone **(Freiberg et al., 2016).**Use of OCT angiography in

everyday clinical practice allows for the accurate analysis of the chorioretinal vascular situation, with the identification of new vessels that could remain misdiagnosed(**Savastano, Rispoli, & Lumbroso, 2021)**.
OCT angiography is a simple, noninvasive, and practical technique for the informative evaluation and understanding of the underlying mechanisms of various pathologic changes related to myopia, such as lacquer cracks, atrophy and myopic CNV **(Al-Sheikh et al., 2017).**So, the aim of the study is to evaluate anti–vascular endothelial growth factor therapy in myopic choroidal neovascularization using optical coherence tomography angiography by detecting the changes of shape, size, and flow area.

II. Patients And Methods

The study was conducted on 20 myopic eyes (11 left, 9 right) at 20 patients who were referred to the ophthalmologic clinic, faculty of medicine, Menoufia University during the period from February 2021 till April 2022.
Ethical consideration: Written informed consent from patients and care givers after explaining the aim of study. Approval of the study protocol obtained by Ethical Scientific Committee of Menoufia faculty of medicine.
Inclusion criteria: Age: 49±15, no sex predilection and patients with myopic choroidal neovascularization.
Exclusion criteria: Opaque refractive medium, such as severe cataract or vitreous hemorrhage and large amount of fundus hemorrhage and any other causes of secondary CNV other than myopia.
All patients were subjected to the following: Initially patients were undergoing a detailed ophthalmological examination at baseline including:The best-corrected visual acuity (BCVA) of Snellen chart, dilated fundus examination by indirect ophthalmoscope, Color fundus photography. Best-corrected visual acuity was converted to the logarithm of the minimum angle of resolution (log MAR). Central macular thickness (CMT), greatest linear dimension (GLD) of CNV, subretinal fluid (SRF), and intraretinal fluid (IRF) was measured using a 10-mm length OCT B-scan and the retinal map was constructed using RTVue XR Avanti with Angio Vue.
Every patient was examined 3 times by OCTA: the first visit will be up to 3 days before treatment with intravitreal ranibizumab (0.5 mg/0.05 mL), and subsequently at 7 days and 1 month after treatment as follow-up. Optical Coherence Tomography Angiography was conducted using RTVue XR Avanti with AngioVue at 70,000 A-scans per second containing 304 · 304 A-scans in approximately 2.6 seconds. The 6 · 6-mm scanning area focused on the macula and was acquired using the split-spectrum amplitude decorrelation angiography technique, and if the former showed no exact CNV or incomplete CNV borders, a 3 · 3-mm scan was necessary for the entire CNV.Each of them consisted of two orthogonal images for motion correction. Optical coherence tomography angiography images were automatically divided into four layers: superficial, deep, outer retina, and choroid capillaries.
Using Angio Analytics software, the CNV areas on the outer retina was selected manually by two qualified technicians independently. The selected CNV area values were the data that will be collected according to the chosen CNV size and the flow area value was automatically measured as just the detected flow signals within the selected area of the CNV.

Statistical Analysis: Results were tabulated and statistically analyzed using standard computer program using MICROSOFT EXCEL 2019 and SPSS V.25 program for MICROSOFT WINDOWS 10 **(Park et al., 2016).**The description of data was in the form of mean (±) SD for quantitively data, and frequency and proportion for qualitative data, The mean is the sum of all observations by the number of observations. While the standard deviation is a measure the degree of scatter of individual varieties around their mean.Analytical statistics: that includes the following test: Standard student-t test (t), Cutoff values.P value <0.05 was considered statistically significant.

III. Results

Age of the studied patients ranged from 20-76 years with mean 52.53± 19.32 years and females were the most common among the studied patients (55%), **(Table1).**Medusa found in 8 patients (40%), sea fan found in 10 patients (50%), Indistinct found in 10 patients (50%) and dark halo found in 3 patients (15%).There were not significantly differences among the studied groups regarding best-corrected visual acuity before and after Treatment with intravitreal ranibizumab (P=0.162), **(Table 2).**

Central macular thickness was significantly decreased after treatment with intravitreal ranibizumab than before treatment, with mean difference 45.55±71.27 (9.62%), (P=0.010), **(Table 3).**Intraretinal fluid, subretinal fluid were significantly decreased after treatment with intravitreal ranibizumab than before treatment with changes 22.11% and 16.21%, respectively (P<0.05), **(Table 4).**Greatest linear dimension did not show any significant differences before and after treatment with intravitreal ranibizumab (P=0.524), **(Table 5).**Flow area did not show any significant differences before and after treatment with intravitreal ranibizumab (P>0.05),

(Table 6).INJNo of the studied patients ranged from 1-5 with mean 2.89 ±1.10 and FAZ was decreased at final (243.9 / 489.5) as compared initial (265.6/504.3), **(Table 7).**

IV. Discussion

High myopia is one of the leading causes of visual impairment in many developed countries. Pathological myopia is defined by an axial length of the eye greater than 26 mm and by a refractive error of −6 dioptres (D) or more, associated with complications of the posterior segment due to progressive and excessive elongation of the globe. Progressive posterior segment elongation is accompanied by degenerative changes, including the sclera, optic disc, choroid, Bruch's membrane, retinal pigment epithelium (RPE) and neural retina. These degenerative changes may lead to the development of macular lesions, such as myopic choroidal neovascularization (CNV), **(Ohno-Matsui et al., 2016).**

Our result showed that, there were no significantly differences among the studied groups regarding best-corrected visual acuity before and after Treatment with intravitreal ranibizumab (P=0.162).In the same way, **Silva et al., (2010)**found mean visual gain was +8 letters, with 24% gaining ≥3 lines of vision and 21% showing a worse visual acuity. Both naïve and previously PDT-treated eyes responded to treatment. The mean number of treatments was 3.6, like the number of injections given at 12 months to our patients, though the mean BCVA (best-corrected visual acuity) recorded at this time point was higher in our patient series and persisted beyond 12 months. Also, **Lalloum et al., (2010)** showed that, no difference in visual outcome was detected between treatment naïve and previously treated patients, although the P value of .08 obtained indicates a need to increase the number of eyes to confirm the differences detected between these 2 group by other authors. Although results obtained so far in the different studies on the use of ranibizumab to treat myopic CNV are not really comparable because of the different patient numbers, times of follow-up, or treatment regimens, our findings do confirm the good visual and anatomic outcomes described by others for ranibizumab **(Lai et al., 2009).**

The present study showed that, central macular thickness was significantly decreased after treatment with intravitreal ranibizumab than before treatment, with mean difference 45.55±71.27 (9.62%). In this concern,**Lalloum et al., (2010)** examined 32 eyes treated with anon loading dosing regimen of ranibizumab. BCVA improved from a baseline value of 0.2 to a final of 0.4, and 46.8% of eyes gained ≥3 lines of vision. Naïve patients gained more vision than those previously treated by PDT (P > .05). The mean reduction in CMT was 92 μm. The mean number of injections given was ≥3, and mean follow-up was 17 months. Our visual and OCT results recorded over a similar follow-up period are consistent with those of them.In addition to, **Silvaet al., (2010)** data revealed an inverse relationship between BCVA and CMT up until 24 months, with maximum inverse correlation produced at 6 months. Also, **Perente et al., (2018)** found that,in study of 32 eyes showed that, the mean CMT was 301.4±11.7 μm at baseline, 264.7±10.9μm at 6 months, 260.7±13.9 μm at 12 months, 258.4±11.5 μmat 18 months, 258.6±10.9 μm at 24 months, 258.6±10.1 μmat 30 months, and 258.8±12.5 μm at 36 months (p<0.005;baseline vs 6, 12, 18, 24, and 36 months). The mean number of injections administered was 3.5±1.1,2.3±0.9, and 1.7±0.8 at the first, second, and third year.

The current study showed that, intraretinal fluid, subretinal fluid were significantly decreased after treatment with intravitreal ranibizumab than before treatment with changes 22.11% and 16.21%, respectively. Our result in agreement with the result of **Talisa et al., (2015)** who found that,anti-VEGF treatment was shown to be effective to treat mCNV. The BCVA improved significantly, accompanied by decreased CMT, GLD, IRF, and/or SRF at 7 days and 1 month after treatment. In this concern **Moon et al., (2017),** larger baseline FA-evaluated CNV lesion size was a negative predictor for VA at month 12. But, although FA remained the gold standard in the evaluation of retinal damage and leakage for a long time, SD-OCT has attracted more attention in the last years and replaced FA in the follow-up of various retinal diseases. As a consequence, there is growing interest in the use of SD-OCT in the management of mCNV (**Introini et al., 2012)** and evaluation of outcome predictors. Within these SD-OCT features, quantitative parameters like absolute CRT seemed not to be correlated to visual outcomes in previous studies (**Introini et al., 2012)** as well as ours. However, we found that less fluctuation in CRT during the maintenance phase indicated better visual outcome at month 12 as a new aspect. This might reflect that eyes with less severe or no recurrence tend to show a better visual outcome. As described by **Introini et al., (2012),** subretinal fluid and intraretinal fluid are markers of less relevance regarding mCNV activity. This is also reflected in our study with only about half of the lesions showing intra- or subretinal fluid at baseline, and no effect of the presence of baseline sub- or intraretinal fluid on visual outcome after 12 months.

In the present study, flow area did not show any significant differences before and after treatment with intravitreal ranibizumab (P>0.05). Furthermore, **Mao et al., (2019)** reported that, the mean flow area of CNV lesion was 0.494±0.556 mm^2 at baseline and 0.264±0.306 mm^2, 0.255±0.293 mm^2, 0.261±0.313 $mm^2$and 0.234±0.295 mm^2 at 1-, 2-, 3- and 6-months' follow-up, respectively. There was no difference between 1-, 2-, 3- and 6-months' follow-up. Although the area of the CNV lesion reduced after injection, in most patients

(95.12%), it didn't disappear even when its activity had been controlled. The mean reduction ratio of lesions was 50.32% (7.07% to 100%). In only two cases, 100% lesion regression was observed (4.88%).

In the era of OCT B-scan, CMT and GLD were considered indicators to evaluate the treatment effect on CNV (**Huang et al., 2015),** which included effects on CNV lesions, SRF, IRF, and/or SRF, and retinal edema. In this study, the average CMT and GLD had decreased at 7 days and 1 month after treatment but showed no significant difference when compared with the first visit. However, the selected CNV and flow areas in the mCNV eyes were significantly smaller on the OCTA images. The outer retina was reported to be short of blood supply in normal conditions, which is the anatomical element in which CNV occurs (**Coscas et al., 2015; Tano, 2002)**.

OCTA finding provided imaging features that confirmed this statement. In the past, CNV activity was judged according to fundus photography and OCT B-scan images. The active CNV, with or without pigment epithelial detachment and ISF/SRF, was found to be more sensitive to anti-VEGF treatment. Some CNV lesions were observed as scars and fibrosis on the fundus photography, with persistent macular edema, which was probably caused by the impaired function of the retinal barrier. These lesions should not be regarded as recurrent. The shapes of mCNV on the OCTA images were irregular, or nearly round closed masses, with internal absorbent capillaries(**Liu et al., 2016)**. Hence, the conversion and representation of this flow to a hyperdense frame was impeded, and some signal interference in the OCTA images might originate from this.

Our study had some limitations includedthe series we analyzed was relatively small and the follow-up period was short. In addition, some limitations were raised from the OCTA hardware and software. Some patients with poor fixation had difficulty in cooperating with the examinations, resulting in noisy images with potentially significant motion artifacts. The axial length of the pathologic myopia eyeballs is relative long and affects the accuracy of the layer divided by OCTA automatically. Selection of the CNV area was performed manually with software provided by OCTA, which probably affected the measurement accuracy.

V. Conclusions

OCTA, which simultaneously provides functional (optical coherence tomography angiograms) and morphological (OCT B-scans and en face) information, is a promising imaging modality that facilitates physicians to characterize mCNV lesion, assess, and predict therapeutic response, and plan the follow-up treatment and we applied semiautomated postprocessing approach to obtain binarized and skeletonized OCTA images of mCNV lesion for fully quantitative analysis to elucidate the morphological changes of mCNV after anti-VEGF therapy. Vessel junction was regarded as the most sensitive indicator of the mCNV activity.

References

[1]. **Ruiz-Medrano J, Montero JA, Flores-Moreno I, Arias L, García-Layana A, Ruiz-Moreno JM.** Myopic maculopathy: status and proposal for a new classification and grading system (ATN). Progress in retinal and eye research. 2019 Mar 1; 69:80-115.

[2]. **Grzybowski A, Kanclerz P, Tsubota K, Lanca C, Saw SM.** A review on the epidemiology of myopia in school children worldwide. BMC ophthalmology. 2020 Dec;20(1):1-1.

[3]. **De Jong PT.** Myopia: its historical contexts. British Journal of Ophthalmology. 2018 Aug 1;102(8):1021-7.

[4]. **Ruan Z, Qian ZM, Guo Y, Zhou J, Yang Y, Acharya BK, Guo S, Zheng Y, Cummings-Vaughn LA, Rigdon SE, Vaughn MG.** Ambient fine particulate matter and ozone higher than certain thresholds associated with myopia in the elderly aged 50 years and above. Environmental research. 2019 Oct 1;177: 108581.

[5]. **Ohno-Matsui K.** Pathologic myopia. The Asia-Pacific Journal of Ophthalmology. 2016 Nov 1;5(6):415-23.

[6]. **Ohno-Matsui, K., Ikuno, Y., Lai, T. Y., & Cheung, C. M. G. (2018).** Diagnosis and treatment guideline for myopic choroidal neovascularization due to pathologic myopia. Progress in retinal and eye research, 63, 92-106.

[7]. **Asahara T, Masuda H.** Endothelial Progenitor Cells for Ischemic Diseases. InTherapeutic Angiogenesis 2017 (pp. 45-66). Springer, Singapore.

[8]. **Ferrara N, Adamis AP.** Ten years of anti-vascular endothelial growth factor therapy. Nature reviews Drug discovery. 2016 Jun;15(6):385-403.

[9]. **Freiberg, F. J., Pfau, M., Wons, J., Wirth, M. A., Becker, M. D., & Michels, S. (2016).**Optical coherence tomography angiography of the foveal avascular zone in diabetic retinopathy. Graefe's Archive for Clinical and Experimental Ophthalmology, 254(6), 1051-1058.

[10]. **Savastano MC, Rispoli M, Lumbroso B.** The incidence of neovascularization in central serous chorioretinopathy by optical coherence tomography angiography. Retina (Philadelphia, Pa.). 2021 Feb;41(2):302.

[11]. **Al-Sheikh M, Phasukkijwatana N, Dolz-Marco R, Rahimi M, Iafe NA, Freund KB, Sadda SR, Sarraf D**. Quantitative OCT angiography of the retinal microvasculature and the choriocapillaris in myopic eyes. Investigative ophthalmology & visual science. 2017 Apr 1;58(4):2063-9

[12]. **Silva RM, Ruiz-Moreno JM, Rosa P, Carneiro A, Nascimento J, Rito LF, Cachulo ML, Carvalheira F, Murta JN.** Intravitreal ranibizumab for myopic choroidal neovascularization: 12-month results. Retina. 2010 Mar 1;30(3):407-12.

[13]. **Lalloum F, Souied EH, Bastuji-Garin S, Puche N, Querques G, Glacet-Bernard A, Coscas G, Soubrane G, Leveziel N.** Intravitreal ranibizumab for choroidal neovascularization complicating pathologic myopia. Retina. 2010 Mar 1;30(3):399-406.

[14]. **Lai TY, Chan WM, Liu DT, Lam DS.** Intravitreal ranibizumab for the primary treatment of choroidal neovascularization secondary to pathologic myopia. Retina. 2009 Jun 1;29(6):750-6.

[15]. **Perente I, Artunay O, Sengul A.** Intravitreal Ranibizumab Therapy for Choroidal Neovascularization Secondary to Pathological Myopia: 3-Year Outcomes. Age (years). 2018;57:14-6.

[16]. **Talisa E, Bonini Filho MA, Chin AT, Adhi M, Ferrara D, Baumal CR, Witkin AJ, Reichel E, Duker JS, Waheed NK.** Spectral-domain optical coherence tomography angiography of choroidal neovascularization. Ophthalmology. 2015 Jun 1;122(6):1228-38.
[17]. **Moon BG, Cho AR, Lee J, Kim YJ, Lee JY, Kim JG, Yoon YH.** Improved visual outcome and low recurrence with early treatment with intravitreal anti-vascular endothelial growth factor in myopic choroidal neovascularization. Ophthalmologica. 2017;237(3):128-38.
[18]. **Introini U, Casalino G, Querques G, Gimeno AT, Scotti F, Bandello F.** Spectral-domain OCT in anti-VEGF treatment of myopic choroidal neovascularization. Eye. 2012 Jul;26(7):976-82.
[19]. **Mao J, Shao Y, Liu C, Zhang C, Chen Y, Zhang Y, Xu Z, Shen L.** Optical coherence tomography angiography of myopic choroidal neovascularization treated by anti-VEGF therapy, 2019.
[20]. **Huang D, Jia Y, Rispoli M, Tan O, Lumbroso B.** OCT angiography of time course of choroidal neovascularization in response to anti-angiogenic treatment. Retina (Philadelphia, Pa.). 2015 Nov;35(11):2260
[21]. **Coscas G, Lupidi M, Coscas F, Français C, Cagini C, Souied EH.** Optical coherence tomography angiography during follow-up: qualitative and quantitative analysis of mixed type I and II choroidal neovascularization after vascular endothelial growth factor trap therapy. Ophthalmic research. 2015;54(2):57-63.
[22]. **Tano Y.** Pathologic myopia: where are we now. American journal of ophthalmology. 2002 Nov 1;134(5):645-60
[23]. **Liu B, Bao L, Zhang J.** Optical coherence tomography angiography of pathological myopia sourced and idiopathic choroidal neovascularization with follow-up. Medicine. 2016 Apr;95(14).

Table 1. Demographic data and Optical coherence tomography angiography results of the studied patients (N=20).

Variable	No.	%
Age/year Mean ± SD Median (range)	52.53±19.32 52(20-76)	
Gender Male Female	9 11	45.00 55.00
Eye Left Right	11 9	55.00 45.00
Medusa No Yes	12 8	60.00 40.00
Sea fan No Yes	10 10	50.00 50.00
Indistinct No Yes	10 10	50.00 50.00
Dark halo No Yes	17 3	85.00 15.00

Table 2. Best-corrected visual acuity before and after treatment with intravitreal ranibizumab (N=20).

Variable	Treatment with intravitreal ranibizumab		Paired t test	P-value	95% CI	
	Before	After			Lower	Upper
BCVA						
Mean ±SD	0.28±0.27	0.39±0.48	1.455	0.162	-0.45	0.081
Median (range)	0.2(0.03-0.90)	0.20(0.05-2.00)				
Mean changes (%)	-0.19 ±0.57 39.29%					

BCVA: Best-corrected visual acuity. **t**: Independent t-test. *****Significant.

Table 3. Central macular thickness before and after treatment with intravitreal ranibizumab (N=20).

Variable	Treatment with intravitreal ranibizumab		Paired t test	P-value	95% CI	
	Before	After			Lower	Upper
CMT						
Mean ±SD	415.68±189.91	375.68±153.28	2.858	**0.010***	12.19	78.91
Median (range)	365(252-976)	321(235-885)				
Mean changes (%)	45.55±71.27 9.62%					

CMT: Central macular thickness. **t**: Independent t-test. *****Significant.

Table 4. Intraretinal fluid and subretinal fluid before and after treatment with intravitreal ranibizumab (N=20).

Variable	Treatment with intravitreal ranibizumab		Paired t test	P-value	95% CI	
	Before	After			Lower	Upper
IRF						
Mean ±SD	218.95±189.76	170.53±158.62	3.024	**0.007***	14.62	80.38
Median (range)	190(30-770)	140(10-630)				
Mean changes (%)	47.50±70.25 22.11%					
SRF						
Mean ±SD	247.05±190.38	207.16±155.93	3.042	**0.007***	12.34	67.45
Median (range)	210(97-920)	188(50-720)				
Mean changes (%)	39.89±57.16 16.21%					

IRF: Intraretinal fluid. **SRF**: Subretinal fluid. **t**: Independent t-test. *****Significant.

Table 5. Greatest linear dimension before and after treatment with intravitreal ranibizumab (N=20).

Variable	Treatment with intravitreal ranibizumab		Paired t test	P-value	95% CI	
	Before	After			Lower	Upper
GLD						
Mean ±SD	615.79±374.19	615.42±372.74	0.649	0.524	-21.93	41.63
Median (range)	500(200-1600)	500(200-1600)				
Mean changes (%)	9.85±67.90 0.06%					

GLD: Greatest linear dimension. **t**: Independent t-test.

Table 6. Flow area before and after treatment with intravitreal ranibizumab (N=20).

Variable	Treatment with intravitreal ranibizumab				Paired t test	P-value	95% CI	
	Before		After				Lower	Upper
Flow area, n%								
Increased	20	100%	7	35.00%	1.422	0.171	-0.12	0.62
Decreased	---	---	9	45.00%				
Stable	---	---	4	20.00%				
Mean ±SD	0.58±0.46		0.53±0.44		1.094	0.288	-0.05	0.16
Median (range)	0.40(0.1-1.44)		0.39(0.1-1.46)					
Mean changes (%)	0.06±0.23 8.62%							

t: Independent t-test.

Table 7. INJNo and FAZ before and after treatment with intravitreal ranibizumab (N=20).

Variable	Studied patients (N=20)
INJNo	
Mean ±SD	2.89 ±1.10
Median (range)	3(1-5)
FAZ	
Initial	265.6 /504.3
Final	243.9 /489.5