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# Assessment of Retinal Microvascular Changes by Oct Angiography after use of Argon Micropulse Laser Versus Traditional Argon Laser for Treatment of Diabetic Macular Edema

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## Abstract

*Background: Diabetic macular edema (DME) is the main factor causing diabetic patients' eyesight impairment around the world. One novel non-invasive technique for imaging and monitoring DME is optical coherence tomography angiography (OCTA). The study aims to compare retinal microvascular changes by OCTA after the use of argon micropulse laser versus traditional argon laser in order to treat diabetic macular edema.*

*Patients and methods: The research was performed on 50 eyes of 34 diabetic macular edema patients. After clinical assessment and imaging by OCTA, 25 eyes were treated by conventional argon laser and included in group A, while another 25 eyes were treated by micropulse argon laser and included in group B.*

*Results: OCTA metrics regarding FAZ enlargement, decrease in vessel density, and increase in areas of non-perfusion showed more detectable changes after four months than one month. The parameters did not change significantly after four months, with slightly less progression with MPLT. The conventional laser treatment group showed slightly more effective results than the MPLT group regarding functional parameters.*

*Conclusion: MPL and conventional laser have slightly similar results as regards OCTA metrics after four months.*

**Keywords:** ME, OCTA, FAZ, VD

## 1. Introduction

In DME, an increase in extracellular fluid originating from hyperpermeable retinal capillaries causes the thickening of the macula.<sup>1</sup>

An array of DR morphological characteristics are detectable with OCTA. It possesses a number of benefits with respect to conventional FA. First, it is non-invasive. Without the need for dye injection, OCTA techniques enable the visualization and thorough evaluation of modifications in the retinal microvasculature. This is crucial, as OCTA is obtainable more often than FA for longitudinal management of patients' eyes. Additionally,

OCTA acquires data at a faster rate than FA. Moreover, OCTA data is depth-resolved and three-dimensional. Capillary plexuses at the individual level are visible and testable.<sup>2</sup>

In contrast to conventional retinal photocoagulation, micropulse laser treatment (MPLT) is a non-invasive therapeutic modality that targets the retinal pigment epithelium (RPE) specifically, thereby reducing the extent of chorioretinal scarring.<sup>3</sup>

This work aims to compare retinal microvascular changes by OCT angiography after the use of an argon micropulse laser versus a traditional argon laser to treat diabetic macular edema.

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## 2. Patients and methods

The research was performed on 50 eyes of 34 diabetic macular edema patients. Patients comprised in this research were split into two main groups {A and B} according to the type of laser photocoagulation used. Twenty-five eyes were treated by conventional argon laser and included in group A. Another 25 eyes were treated by micropulse argon laser and included in group B.

### Inclusion criteria:

Patients with diabetic macular edema were ascertained by slit lamp biomicroscopy and confirmed by OCT Angiography.

### EXCLUSION CRITERIA

Patients who previously had laser photocoagulation, nondiabetic macular edema, ischemic maculopathy, tractional DME, Previous intravitreal injection, or elevated HA1C

### ASSESSMENT

Detailed workup, history taking including medical and surgical history, complete ophthalmological examination including detailed fundus examination and HA1C assessment.

### INVESTIGATION

The patient was informed about the steps of the procedure, and the pupil was dilated. OCTA was executed by (DRI Triton Plus, Topcon Systems, Tokyo, Japan). The patient was briefed on the technique. A rough position was approximated by adjusting the chin height, imaging instrument, and chin rest. A circular scan 6x6 with a 320x320 mm diameter circle was performed, with the subject gazing at the internal fixation target while the subject's macula was centered. Retinal experts of two distinct masked readers conducted a quantitative and qualitative analysis of images taken from the IMAGE Net Six database. The evaluation of macular perfusion was conducted in accordance with the ETDRS classification. En-face, SS-OCTA pictures of the superficial and deep capillary plexuses were produced. For each scan, manual segmentation was carried out.

### PROCEDURE

Using an IQ532 Laser system ( IRIDEX, USA ), a Green Laser is set on micropulse mode. In our research, the subthreshold micropulse laser was used on 25 patients, using a Mainster focal grid contact lens ( $\times 1.05$  magnification).

In every instance, the following fixed treatment parameters were implemented: 200 ms of exposure time, 200  $\mu\text{m}$  spot size, 400 mW of power, and a 5 % duty cycle. There was a 10 ms "on" and 190 ms "off" laser pulse to provide sufficient time for the surrounding tissues to cool and prevent thermal damage to the inner retina. Two sets were performed with a one-week break in between.

25 more eyes were laser-treated with argon

blue/green (488/514 nm). The entire region of retinal thickness was treated with a photocoagulation laser, with the exception of the middle 500 microns at the fovea. One spot width separated 200-micron spots for 0.1 seconds while applying adequate force to generate a burn that was instantly apparent following treatment. There was no endeavor to employ direct photocoagulation as a treatment method for the leaking capillary segments and microaneurysms. Unless there was concomitant edema, specialized treatment was not administered to regions affected by ischemia. All patients were followed up by clinical assessment and OCT Angiography one month after and four months following laser therapy. The statistical methods were executed utilizing version 15.0 of the Statistical Package for the Social Sciences (SPSS® for Windows®) and version 22 of Microsoft® Excel®. Following the t-test, continuous data were displayed as range, mean, and SD (if parametric). For dichotomous or categorical data, number and percentage, the Chi-squared test and McNemar's test were utilized (for categorical variables). Assigning a significance threshold of 0.05.

## 3. Results

At the four-month mark, the mean BCVA for group A was 0.30, with a SD of 0.17, which varied from 0.083 to 0.6. This difference was found to be statistically significant from the baseline. Similarly, for group B, the BCVA was 0.36, with a SD of 0.14, varying from 0.08 to 0.6. While the variation between the two groups was insignificant ( $p=0.137$ ), as illustrated in the table

Table 1. Best Corrected Visual Acuity (BCVA)

BCVA	GROUP A	GROUP B
BASELINE		
MEAN $\pm$ SD	0.21 $\pm$ 0.13	0.26 $\pm$ 0.12
RANGE	0.1–0.5	0.1–0.5
AFTER 1 MONTH		
MEAN $\pm$ SD	0.21 $\pm$ 0.14	0.26 $\pm$ 0.14
RANGE	0.1–0.7	0.1–0.6
AFTER 4 MONTHS		
MEAN $\pm$ SD	0.30 $\pm$ 0.17	0.36 $\pm$ 0.14
RANGE	0.083–0.7	0.08–0.8

At the four-month mark, the average CMT in group A was 322.48  $\mu\text{m}$ , with a SD of 53.36  $\mu\text{m}$ , spanning from 213 to 431  $\mu\text{m}$ . This variation was found to be statistically significant from the baseline. In group B, the CMT was 315.48  $\mu\text{m}$ , with a SD of 48.70  $\mu\text{m}$ , varying from 240 to 400  $\mu\text{m}$ . Neither group differed significantly from the baseline, and there was no significant variation between the two groups ( $p\text{-value}=0.115$ ).

Table 2. Central Macular Thickness CMT

CMT	GROUP A	GROUP B
BASELINE		
MEAN $\pm$ SD	347.84 $\pm$ 34.95	333.04 $\pm$ 37.85
RANGE	269–390	264–391
AFTER 1 MONTH		
MEAN $\pm$ SD	342.48 $\pm$ 39.63	329.44 $\pm$ 39.45

RANGE	257-427	260-398
AFTER 4 MONTHS		
MEAN±SD	322.48±53.36#	315.48±48.70#
RANGE	213-431	240-390

At four months, the mean FAZ area was 0.39 mm<sup>2</sup> with SD ±0.09 mm<sup>2</sup> varying between 0.16 to 0.93 mm<sup>2</sup> in SCP and 0.49 mm<sup>2</sup> with SD ±0.01mm<sup>2</sup> ranging from 0.19 to 1.06 mm<sup>2</sup> in DCP in group A with non significant variation from baseline. The mean FAZ area was 0.40 mm<sup>2</sup> with SD ±0.06 mm<sup>2</sup> varying between 0.15 to 0.89 mm<sup>2</sup> in SCP and 0.50 mm<sup>2</sup> with SD ±0.08 mm<sup>2</sup> ranging from 0.18 to 1.06 mm<sup>2</sup> in DCP in group B with non significant variation from baseline and non significant variation between both groups with ( p-value 0.197).

Table 3. Mean FAZ Area

	SCP		DCP	
	Group A	Group B	Group A	Group B
BASELINE				
MEAN±SD	0.37 ± 0.07	0.39 ± 0.07	0.47 ± 0.06	0.49 ± 0.04
RANGE	0.17 to 0.81	0.14 to 0.74	0.21 to 1.01	0.23 to 1.07
AFTER 1 MONTH				
MEAN±SD	0.37 ± 0.07	0.39 ± 0.07	0.47 ± 0.06	0.49 ± 0.04
RANGE	0.16 to 0.86	0.15 to 0.78	0.22 to 1.03	0.24 to 1.09
AFTER 4 MONTHS				
MEAN±SD	0.39 ± 0.09	0.40 ± 0.06	0.49 ± 0.08	0.50±0.07
RANGE	0.16 to 0.93	0.15 to 0.89	0.19 to 1.06	0.18 to 1.06

Table 4: Change in the mean FAZ area

	SCP		DCP	
	Group A	Group B	Group A	Group B
AFTER 4 MONTHS				
MEAN DIFF.±SD	0.021 (±0.003)	0.016 (±0.006)	0.011 (±0.002)	0.009 (±0.007)
CHANGE%	0.42%	0.28%	0.29%	0.18%

At four months, the mean Vessel Density% was 42.01 % with SD ±4.78 ranging from 36.91% to 48.13 % in SCP and 43.57 % with SD ±2.68 ranging from 40.75 % to 51.23 % in DCP in group A with non significant variation from baseline. The mean Vessel Density was 43.48% with SD ±4.70 varying between 37.72% to 48.63 % in SCP and 43.88 % with SD ±3.08 ranging from 40.36% to 50.83% in DCP in group B with non significant variation from baseline and non significant variation between both groups with ( p-value 0.276)

Table 5. Vessel Density VD

	SCP		DCP	
	Group A	Group B	Group A	Group B
BASELINE				
MEAN±SD	42.89±4.49	43.03±3.79	44.07±2.36	44.25±2.44
RANGE	37.7 - 47.41	38.48 - 47.16	41.52 - 53.83	40.81-55.73
AFTER 1 MONTH				
MEAN±SD	42.36±4.39	43.42±3.77	44.03±2.42	44.20±2.63
RANGE	37.5 - 47.71	40.7 - 47.84	41.59 - 53.25	40.75 -55.84
AFTER 4 MONTHS				
MEAN±SD	42.01±4.78	42.48±4.70	43.57±2.68	43.88±3.08
RANGE	36.91 - 48.13	37.72 - 48.63	40.75 - 51.23	40.36-50.83

Table 6. Change in the Vessel Density%

SCP	GROUP A (N=25)	GROUP B (N=25)
AFTER 4 MONTHS		
MEAN DIFF.±SD	-0.023 (±0.007)	-0.015 (±0.007)
CHANGE%	-0.39%	-0.32%
DCP		
AFTER 4 MONTHS		
MEAN DIFF.±SD	-0.017 (±0.004)	-0.011 (±0.006)
CHANGE%	-0.23%	-0.17%

A mild positive correlation was existed between BCVA(decimal) and FAZ area(microns) (SCP r= 0.255, p=0.03 & DCP r= 0.215, p=0.036) in group A and (r= 0.220, p=0.033& DCP r= 0.205, p=0.04) in group B with statistically insignificant variation between both groups 4 months after laser treatment in relation to baseline. A mild negative correlation was found between BCVA(decimal) and VD % (SCP r= -0.315, p=0.027 & DCP r= -0.242, p=0.036) in group A and (r= 0.235, p=0.031& DCP r= 0.217, p=0.042) in group B with non significant variation between both groups 4 months after laser treatment in relation to baseline

Table 7 . Correlation between FAZ area &VD and BCVA

	BCVA (DECIMAL)			
	Group A		Group B	
	r	p	r	p
FAZ AREA (MM 2 ):				
SCP	0.255	0.03	0.22	0.033
DCP	0.215	0.036	0.205	0.04
VD %				
SCP	-0.315	0.027	-0.235	0.031
DCP	-0.242	0.036	-0.217	0.042

P: p value

r: Pearson coefficient

CASES

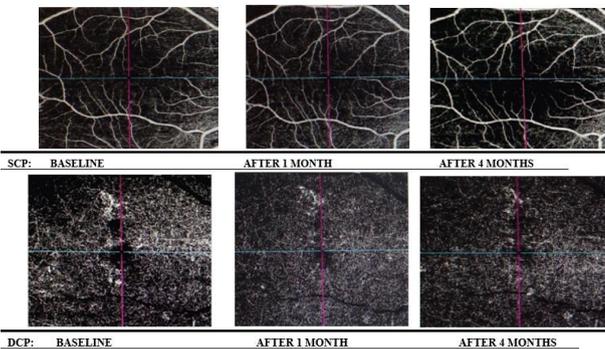
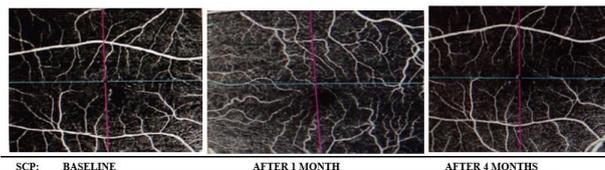


Figure 1 . 45 years old diabetic female for 9 years diagnosed NPDR with DME clinically and confirmed by OCTA. She was treated by conventional Argon laser and followed up by OCTA 1 month and 4 months after treatment



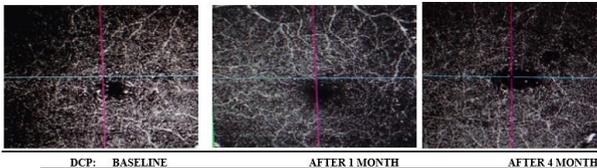


Figure 2 . 58 years old diabetic female for 19 years diagnosed NPDR with DME clinically and confirmed by OCTA. She was treated by Micropulse Argon laser and followed up by OCTA 1 month and 4 months after treatment

#### 4. Discussion

Microaneurysm-induced leakage, capillary hyperpermeability, and blood-retinal barrier impairment resulting in elevated levels of inflammatory cytokines and vascular endothelial growth factors (VEGF) and capillary drop-out all appear to contribute to a rise in macular thickness observed in DME.<sup>4</sup>

An innovative, non-invasive method, optical coherence tomography angiography (OCTA), permits the examination of microstructure anomalies and retinal vascular layers (superficial and deep capillary plexuses) without the need for dye injection. On OCTA, identification of vascular abnormalities in diabetic retinopathy (DR), such as microaneurysms, regions of capillary non-perfusion, foveal avascular zone (FAZ) degradation, and neovessels has been assessed.<sup>5</sup>

Nakamura et al. demonstrated that the extent of functional improvement following MPLT was restricted to enhanced visual acuity. The investigation yielded comparable findings.<sup>6</sup>

The research by Vujosevic et al. demonstrated that the chorioretinal perfusion parameters remained unchanged following the implementation of the MPLT.<sup>7,8</sup>

Mansouri et al. found that MPLT is a safe and effective treatment for mild to moderate DMEs based on a comparison of its efficacy with the anatomical severity of the edema.<sup>9</sup>

Lavinsky et al. showed that, after a year of follow-up, the morphological and functional outcomes of a high-density, confluent micropulse treatment were superior. On the other hand, following the normal-density treatment (two burn widths apart), no progress was observed.<sup>10</sup> In our study, a few cases showed improvement regarding BCVA and CMT one month after treatment, while the majority of improvement was after four months.

Othman et al. evaluated MPLT three months following conventional macular photocoagulation in individuals with recurrent or persistent DME vs those who had not received any therapy. Both groups received equal levels of benefit from the therapy; more patients, however, comprised the secondary group. needed intravitreal steroid

rescue therapy. During one and four months of our study, the group receiving conventional laser treatment performed marginally better than the MPLT group in terms of structural and functional aspects related to BCVA and CRT.<sup>11</sup>

In alignment with this, Fazel et al. found that MPLT considerably enhanced BCVA and CRT parameters in mild DME eyes that had not been treated before. The study demonstrated that, in the concise term, MPLT was more successful than continuous-wave therapy (4 months).<sup>12</sup>

In the same way, Bougatsou et al. affirmed that in cases of clinically significant macular edema that were not center-related, MPLT was more effective than a conventional laser. whereas Al-Barky et al. noticed a marginal improvement in functional results following MPLT.<sup>13,14</sup>

Lois et al. recently released the results of a multicenter clinical trial. Despite not receiving direct treatment from SMPL, The quantity of MAs declined dramatically in both the SCP and the DCP, according to the findings.<sup>15</sup> The DCP showed a more rapid decline in MA, which began in the third month following therapy and persisted for the duration of the follow-up (12 months).

Research by Parravano et al. showed that the MAs seen in DCP on OCTA might be hyper-reflective MAs on structural OCT, which might be understood as leaky MAs with a high blood flow rate.<sup>16</sup>

According to a prior study assessing alterations in the single retinal layer following SMPL, the most significant decrease in thickness was observed at the level of INL at 12 months.<sup>17</sup> In the current study, improvements were noted after four months, but no significant decrease in CMT was found after one month.

#### 4. Conclusion

MPL and conventional laser have slightly similar results as regards OCTA metrics after four months.

#### Disclosure

The authors have no financial interest to declare in relation to the content of this article.

#### Authorship

All authors have a substantial contribution to the article

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#### Conflicts of interest

There are no conflicts of interest.

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