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The Effect of Micropulse Laser in Treatment of Diabetic Macular Edema

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Abstract

Background: In the industrialized world, diabetic macular edema (DME) is the leading cause of blindness in those under the age of 50. Diabetic retinopathy may begin to manifest in patients with type I (insulin-dependent) DM within 3–5 years after disease initiation. Nearly all diabetics will develop retinopathy by the age of twenty.

Aim of the work: Is to evaluate the effect of subthreshold micropulse laser (SMPL) in treatment of DME with central macular thickness less than 400 μ .

Patients and methods: A Prospective, interventional comparative study was done at the Ophthalmology department and clinic of EL Zahraa and Bab EL-Shariya University Hospitals, Cairo, Egypt.

Results: There was no clinically significant difference between both groups as regard (BCVA, CMT and AMT) prelaser and after various period of follow-up. Among group I there were no statistically significant changes regarding AMT and BCVA after 6 months except CMT which shows statistically clinically significant changes denoting a high incidence of reduction of CMT. There were no statistically significant clinical changes in group II regarding AMT, CMT and BCVA after 6 months of follow-up.

Conclusion: SMPL laser 532 nm is an alternative as primary treatment for DME and can substitute intravitreal injection and conventional laser photocoagulation. No visible or invisible retinal scar seen clinical or by OCT after SMPL, so it is a safe procedure and can be repeated.

Keywords: Diabetic macular edema, Micropulse laser, Treatment

1. Introduction

In the industrialized world, diabetic macular edema (DME) is the leading cause of blindness in those under the age of 50. Persons with type I (insulin-dependent) DM may develop diabetic retinopathy as early as 3–5 years after the onset of diabetes. Nearly all diabetics will develop retinopathy by the age of 20. Diabetic retinopathy is more common as diabetes progresses, however, it can be mitigated with long-term strict glycemic management. Between 14% and 25% of patients will have DME at the end of the projection period. Untreated, 32% of individuals with ‘clinically substantial’ DME may experience potentially disabling ‘moderate’ vision loss within 3 years.¹

Eyes affected by mild to moderate non-proliferative diabetic retinopathy and ‘clinically significant macular edema’ (DME) responded well to argon laser macular photocoagulation, as shown by the Early Treatment of Diabetic Retinopathy Study (ETDRS). Iatrogenic multifocal chorioretinitis was associated with several major risks and adverse effects, including the creation of full-thickness retinal laser burns in the areas of retinal pathology, which were visible at the time of treatment as white or light grey retinal lesions (‘supra threshold’ retinal photocoagulation). Inadvertent foveal photocoagulation causes early and late visual loss, treatment-associated inflammation worsens macular edema (ME), pre- and sub-retinal fibrosis, choroidal neovascularization, visual field loss, color vision loss,

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metamorphopsia, and laser scars expand into the fovea, causing permanent vision loss.²

Patient outcomes have improved and the progression of DME in many diabetics has been slowed by the development of anti-VEGF medication. However, anti-VEGF medication should be used with caution in patients who may already have systemic impairments. However, intravitreal anti-VEGFs are costly and necessitate regular injections to preserve the optical and anatomic improvement. It is possible for endophthalmitis to develop after any intravitreal injection.³

In 1990, Pankratov⁴ stated creation of a novel laser that, rather than emitting laser light in one continuous wave, emits it in rapid bursts (called 'micro pulses'). Retinal thermal lesion size from micro pulsed laser photocoagulation was found to be determined primarily by the duty cycle (frequency of the train of micro pulses) and, by extension, the length of the thermal relaxation time between consecutive pulses, given constant retinal spot size, pulse energy, and pulse duration. By decreasing the repetition rate and increasing the off time between pulses (duty cycle), thermal effects can be delivered preferentially to the retinal pigment epithelium (RPE), which produces a powerful extracellular factor serving as a disease mediator, while causing less thermal retinal damage.

Inducing RPE hyperthermia below the threshold for cell death is hypothesized as the mechanism of action of a non-damaging laser. Accordingly, it has a stimulating effect on RPE metabolism and aids regeneration in one of numerous ways.⁵

Safer than anti-VEGF treatment alone or with Continuous wave (CW) laser, DME can now be treated with Subthreshold Micropulse Laser Therapy (MPLT) using the IQ 532 laser.⁶ It can be administered directly over the fovea or any other location of edema using a Micropulse laser Iridex IQ 532. Laser treatment may take many months to show results, longer than anti-VEGF therapy. The MPLT seems to have more long-term effects than anti-VEGF therapy alone. Thus, the treatment of DME is now safer and more effective than anti-VEGF treatment alone or with CW laser thanks to MPLT with the Iridex IQ 532 laser. When it comes to treating DME, MLT Iridex IQ 532 is a viable and efficient first-line treatment option.^{7,8}

2. Aim of the work

Is to evaluate the effect of subthreshold micropulse laser 532 nm in treatment of DME with central macular thickness less than 400 μ .

3. Patients and methods

3.1. Study design

Ophthalmologists from EL Zahraa and Bab EL-Shariya Al-Azhar University Hospitals in Cairo, Egypt, participated in a prospective, interventional comparative study. Forty eyes were involved in the study, each of which had CMT and AMT values below 400 μ , and the participants were split into two groups. The 1st group included 20 eyes with diabetic macular edema, without previous retinal laser or anti-VEGF therapy. The 2nd group included 20 eyes with DME, that received anti- VEGF therapy 6 months before laser treatment.

3.2. Study population

3.2.1. Inclusion criteria: included

Patients with diabetic macular edema with average macular thickness <400 μ measured by optical coherence tomography. Diabetic cases without previous retinal laser or Anti-VEGF therapy, diabetic patient with previous Anti-VEGF for more than 6 months.

3.2.2. Exclusion criteria

Patients with the following were excluded from the study: history of pervious surgery or laser therapy, history of pervious intravitreal injection within the previous 6 month, presence of other diseases affecting macula e.g.: retinal vein occlusion.

3.3. Methods

3.3.1. Each patient underwent the following

Full history taking, general and Local examination, laboratory investigations, visual acuity (log-Mar), biomicroscopic slit limp eye examination using 90 diopter lens, optical Coherence Tomography (OCT): to measure central (subfoveal) and average macular thicknesses. Under a dilated pupil,

Table 1. Baseline characteristics of the patients.

Groups variables	Group I Number = 20 Mean \pm SD		Group II Number = 20 Mean \pm SD	
	Age	50.90 \pm 12.662		61 \pm 10.477
DM duration (years)	13.80 \pm 6.443		14.50 \pm 5.169	
HbA1c	6.11 \pm 0.390		6.80 \pm 0.891	
Sex	Frequency	Percent	Frequency	Percent
Male	16	80%	2	10%
Female	4	20%	18	90%

Table 2. Clinical changes within groups with pre and post-operative mean CMT, AMT, BCVA.

Groups Variables	Group 1 Number = 20 Mean ± SD	Significance test		Group 2 Number = 20 Mean ± SD	Significance test	
		t-test	P value		t-test	P value
Central Macular Thickness (CMT)						
Prelaser -1 st month	8.867 ± 32.872	1.045	0.314	-5.067 ± 37.475	-0.524	0.609
post laser						
Prelaser-2 nd month	17.800 ± 51.04	1.350	0.198	0.733 ± 65.058	0.044	0.966
post laser						
Prelaser-3 rd month	26.333 ± 47.04	2.168	0.048	21.600 ± 70.300	1.190	0.254
post laser						
Prelaser-6 th month	42.267 ± 73.06	2.241	0.042	20.533 ± 89.457	0.889	0.389
post laser						
Average Macular Thickness (AMT)						
Prelaser-6 th month	5.933 ± 32.88	0.699	0.496	-9.000 ± 36.403	-0.958	0.355
post laser						
Best Corrected Visual Acuity (BCVA)						
Prelaser-1 st month	0.000 ± 0.038	0.000	1.000	0.000 ± 0.038	0.000	1.000
post laser						
Prelaser-2 nd month	-0.013 ± 0.064	-0.807	0.433	0.000 ± 0.085	0.000	1.000
post laser						
Prelaser-3 rd month	-0.033 ± 0.07237	-1.784	0.096	-0.013 ± 0.01869	-0.521	0.610
post laser						
Prelaser-6 th month	-0.060 ± 0.09103	-2.553	0.023	-0.027 ± 0.12799	-0.807	0.433
post laser						

six radial scans were carried out, each one measuring 6 mm in length and centred on the fixation point. The macula was segmented into nine regions for quantitative analysis, with the central disc having a diameter of 1000 m and the inner and outer rings having sizes of 3000 and 6000 m, respectively, and each having four quadrants. AMT (mean optical thickness) was determined.

3.3.2. Follow-up

Follow-up examinations were performed at 1st, 2nd 3rd, and 6th month after laser treatment for

central macular (foveal) thickness (CMT) and after 6th month for average macular thickness (AMT). At each visit, a complete examination was performed with recording of the BCVA.

3.3.3. Procedures

All diabetic eyes were subjected to a session of low intensity high density confluent micropulse green laser 532 nm with power 400 mW, pulse duration 0.2 s and duty cycle 5% and 200 µm spot size, applied on the edematous retina.

Table 3. Comparison of clinical changes within the group I at 6th month.

Groups variables	Group I Number = 20		Significance tests	
	Frequency	%	Chi-sq (x ²)	P value
CMT				
Improved	14	70%	6.200	0.045
Unchanged (stability)	2	10%		
Worsened	4	20%		
AMT				
Improved	8	40%	0.200	0.905
Unchanged (stability)	6	30%		
Worsened	6	30%		
BCVA				
Improved	10	50%	0.000	1000
Unchanged (stability)	10	50%		
Worsened	0	0.0%		

Table 4. Comparison of clinical changes within the group II at 6th month.

Groups variables	Group II Number = 20		Significance tests	
	Frequency	%	Chi-sq (x ²)	P value
CMT				
Improved	12	60%	3.800	0.150
Unchanged (stability)	2	10%		
Worsened	6	30%		
AMT				
Improved	12	60%	3.800	0.150
Unchanged (stability)	2	10%		
Worsened	6	30%		
BCVA				
Improved	12	60%	0.400	0.527
Unchanged (stability)	8	40%		
Worsened	0	0.0%		

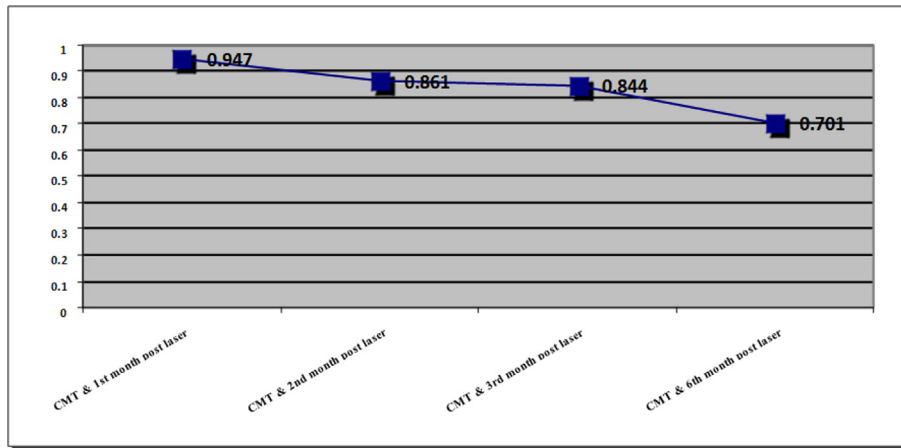


Fig. 1. Correlation between CMT pre laser and various period of follow-up.

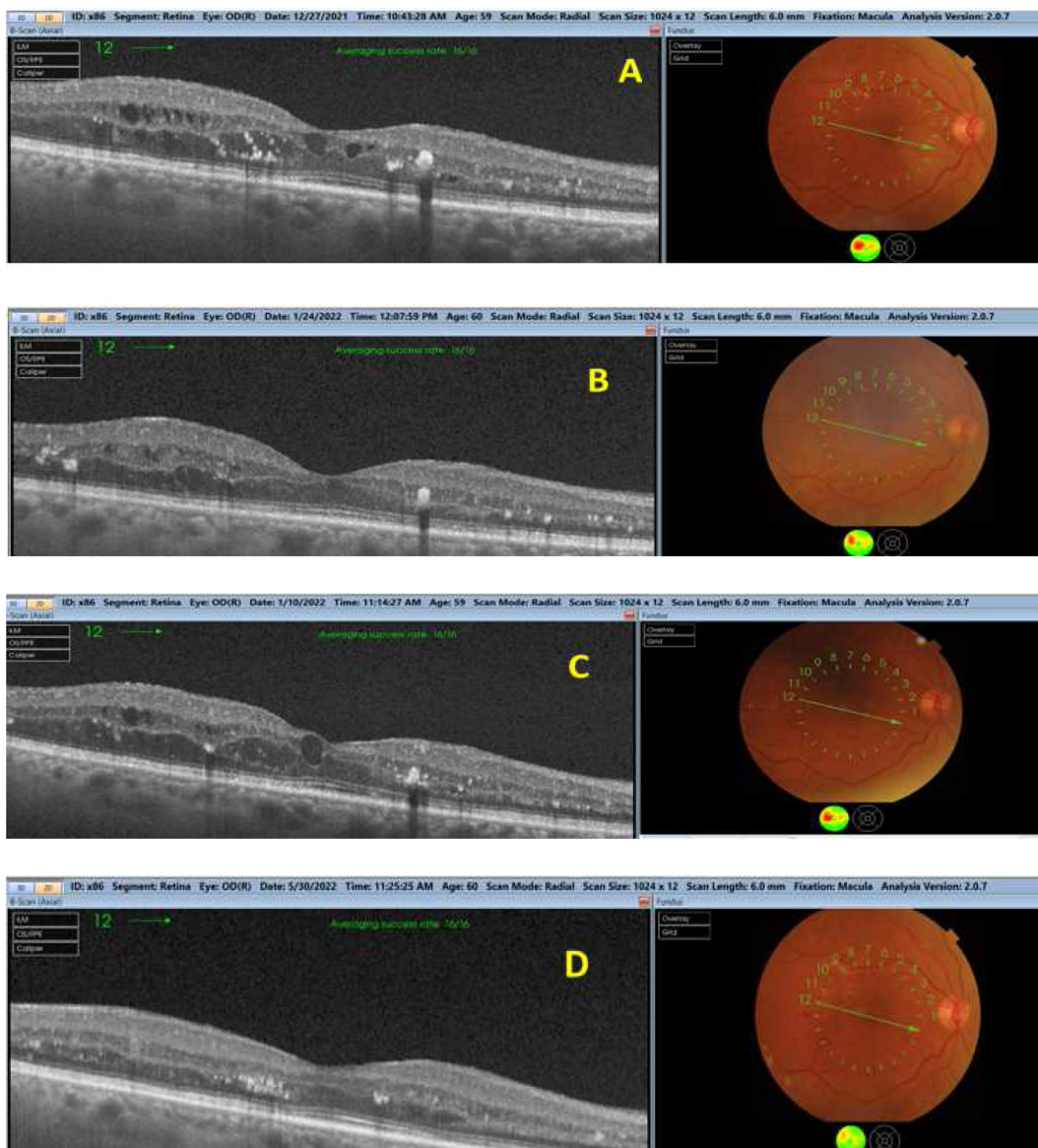


Fig. 2. Cases No. (1): A = prelaser B = 1st month C = 2nd month D = 6th month improvement.

3.3.4. Outcome

Outcome measures included: BCVA: Either: improvement (>one line), unimprovement (stability) or worsened (loss > more than one line on the visual acuity chart), Central macular thickness and Average macular thickness (by OCT): improvement (decrease of retinal thickness), unimprovement (stability) or worsening (increase of the retinal thickness).

3.4. Statistical analysis

SPSS (version 20; SPSS Inc., Chicago, Illinois, USA) was used to analyse the data. The *t*-test was performed to compare each follow-up time point to the initial sample. The significance threshold was set at 0.05.

4. Results

The study included 40 eyes divided into two groups. mean age: 50.90 ± 12.662 years for group I

and 61 ± 10.477 for group I, and the mean duration of diabetes mellitus in group II is 13.80 ± 6.443 years and for group II is 14.50 ± 5.169 years. **Table 1** summarizes the baseline characteristics of the patients.

Table 2 shows There was no statistically significant difference between the two groups in terms of baseline and follow-up BCVA, CMT, or AMT.

Table 3 shows a no statistically significant changes regarding AMT and BCVA at 6th month within the group I except CMT which shows a statistically clinically significant changes denoting high incidence of reduction of CMT.

Table 4 shows no statistically significant clinical changes in group II regarding AMT, CMT and BCVA at 6th month.

There were no macula scars, apparent or otherwise, after SMPL in either group.

There is a negative correlation between the mean pre laser CMT and various period of follow-up. The line is straight denoting regular reduction in mean CMT (**Fig. 1**).

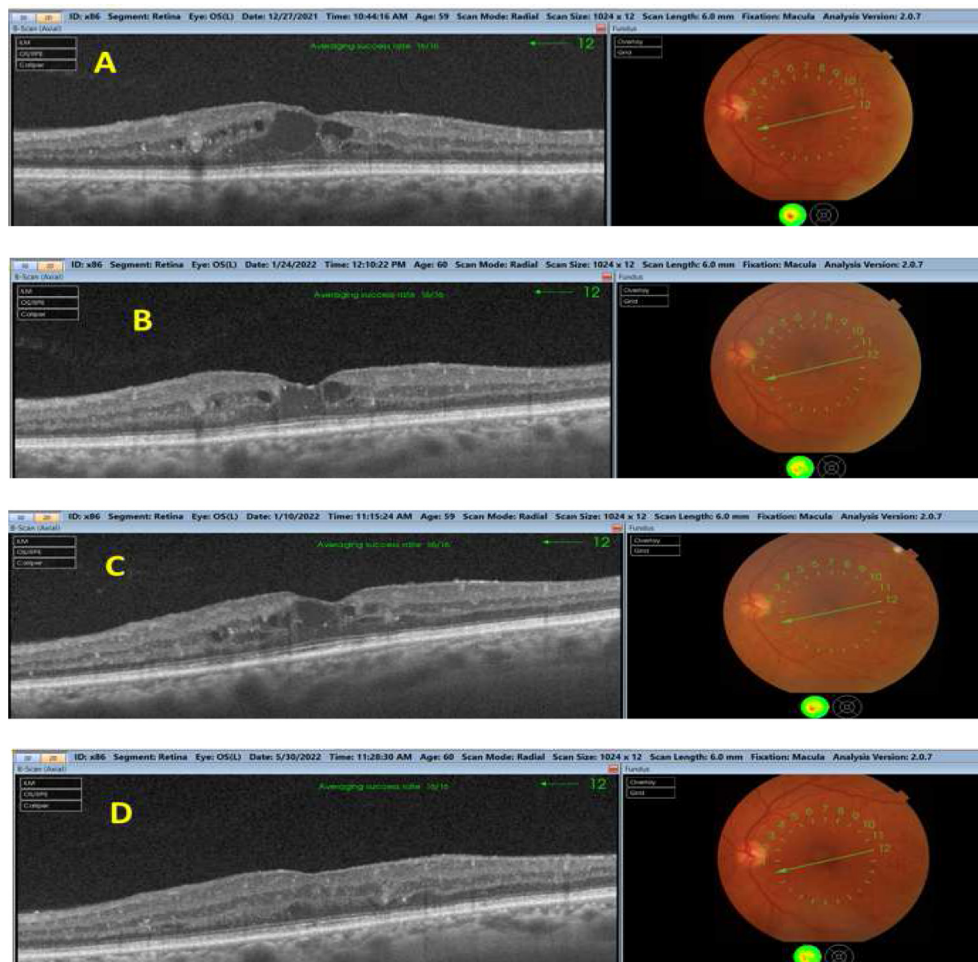


Fig. 3. Cases No. (2): A = prelaser B = 1st month C = 2nd month D = 6th month improvement.

5. Discussion

The ETDRS found that patients whose CSME was treated with laser had better visual acuity, less risk of vision loss, and almost no loss of visual field.⁹ Chorio-retinal scarring, macular hemorrhage, choroidal neovascularization, decreased visual acuity and contrast sensitivity, and visual field abnormalities are all side effects of traditional photocoagulation.¹⁰ Mainster¹¹ tried to minimize the chorio-retinal damage by adjusting the parameters of the laser and the clinical endpoints. By reducing the laser's wavelength, spot size, and exposure time, and by using threshold or subthreshold therapy methods, he said, the effects can be contained to a specific area. Repetitively pulsed laser photocoagulations are an effective method for avoiding the complications of short-pulse therapy protocols.

The present study also agrees with the study of Frizziero *et al.*¹² who analysed 134 eyes with untreated, mild, central DME (CMT 400 μm) that were

treated with 577-nm SMPL under constant conditions. In the event of persistent retinal thickness, retreatment was conducted 3 months after the initial procedure. The average time between visits was 16.6 months, with a standard deviation of 6.5 months (within 2 years study). Without achieving statistical significance, they did observe a decrease in both the CMT and the AMT.

In a study by Passos *et al.*¹³ upon 23 eyes with DME who treated with 577 SMPL and followed up only for 3 months. Not statistically significant, but they did find a decrease in CMT. Similar findings were found in their studies, which corroborate the findings of the current investigation.

In this trial, BCVA improved visual acuity in both groups, however the difference between groups at 6 months post-baseline was not statistically significant. CMT for group II showed reduction at 6th month follow-up compared to pre laser CMT (Figs. 2–5), this result also was not statistically significant. These results are similar to that obtained by Pei-pei *et al.*¹⁴

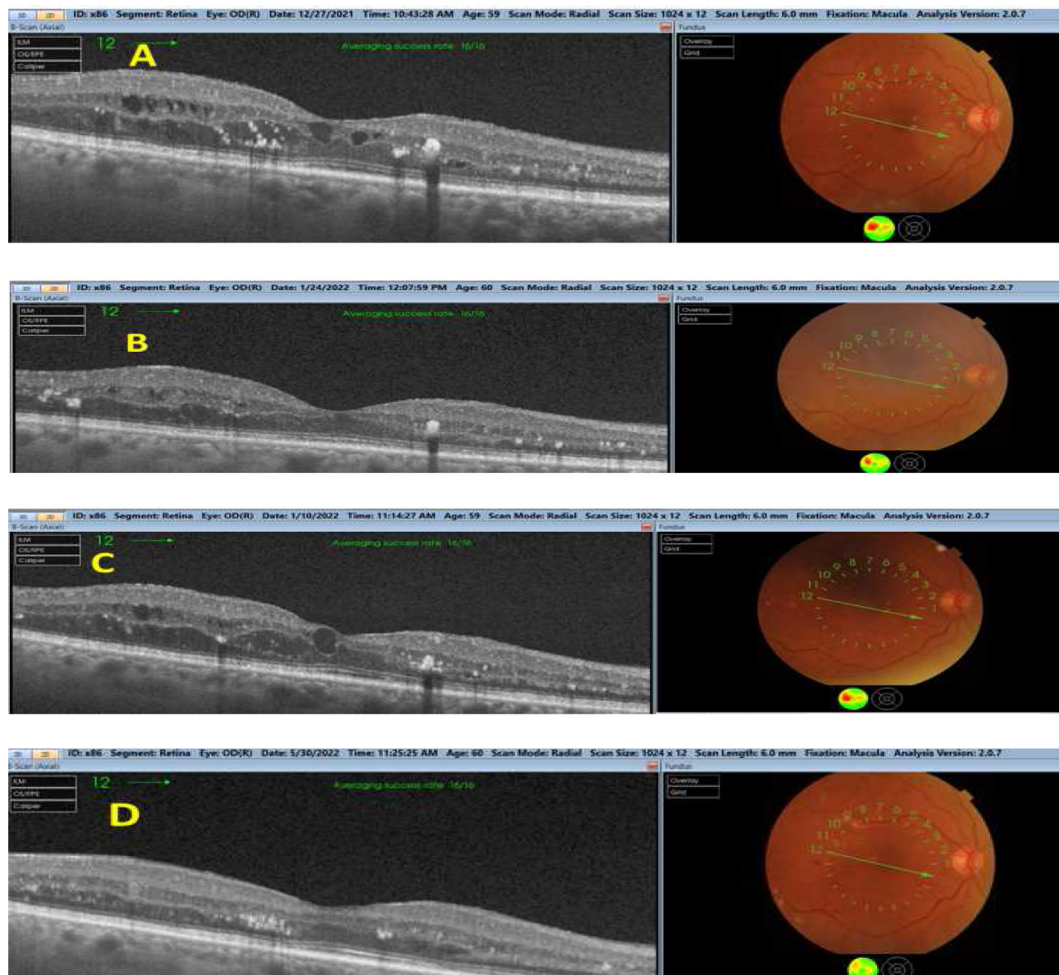


Fig. 4. Cases No. (3): A = prelaser B = 1st month C = 2nd month D = 6th month improvement.

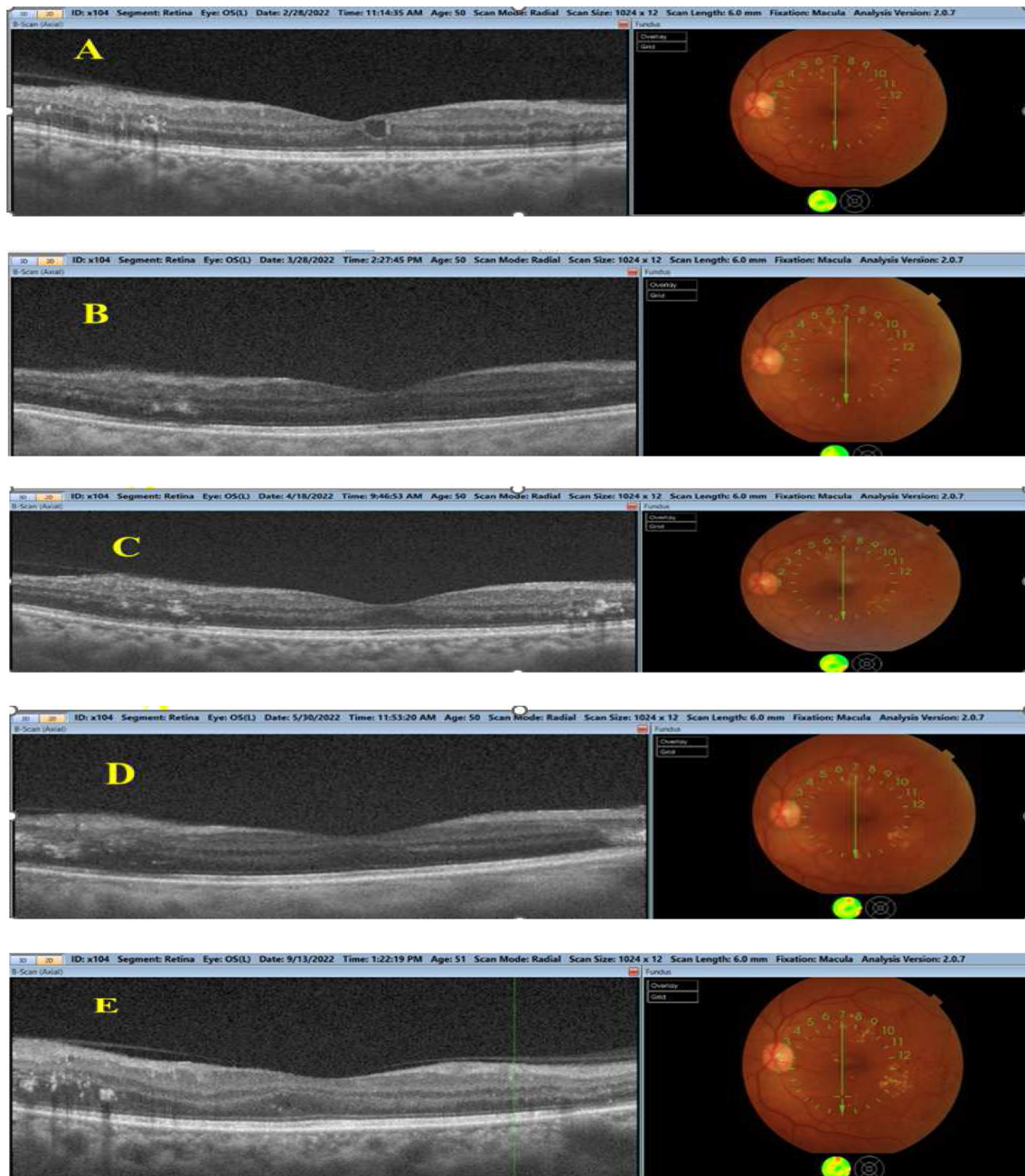


Fig. 5. Cases No. (4): A = prelaser B = 1st month C = 2nd month D = 3rd month E = 6th month improvement.

His study included 23 eyes with $>300 \mu$ DME that were treated with 532 subthreshold micropulse laser and followed for 6 months.

In the present study the patient of group I who did not receive anti VEGF before laser treatment (primary cases) showed a statistically significant improvement of CMT while group II did not. Thus SMPL as a primary therapy in DME should be the first line of treatment for DME replacing anti-VEGF.

In the present study it is found that CMT is continuously improved (reduced) with the time of

follow-up reaching the maximum at the 6th month (last follow-up) of laser treatment, this finding agrees with the study of *Vujosevic et al.*¹⁵ who found that Over a 12-month follow-up period, the morphological and functional aspects of the SMPL effect on the retinal layers of the macula improved. Consistent with the results of the study by *Frizziero et al.*¹² that demonstrated an increase in visual acuity and a decrease in the mean retinal thickness after at least a year of follow-up compared to the initial measurements.

6. Conclusion

Green laser 532 nm is an alternative as a primary treatment for DME and can substitute intravitreal injection, conventional laser photocoagulation. No visible or invisible retinal scar or any damage seen clinical or by OCT after SMPL. SMPL is a safe procedure can be repeated and should replace conventional laser for treatment of DME. SMPL can be applied directly to the fovea even people with good visual acuity can have less serious complications from laser photocoagulation and intravitreal injections. SMPL should be a primary treatment for all cases with DME but not anti-VEGF nor conventional laser. SMPL treatment in primary cases with DME (without previous anti-VEGF) gave better results than those previously received anti-VEGF.

Disclosure

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

Authorship

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Conflict of Interest

The authors declared that there were NO conflicts of Interest.

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