LOW-INTENSITY/HIGH-DENSITY SUBTHRESHOLD DIODE MICROPULSE LASER FOR CENTRAL SEROUS CHORIORETINOPATHY

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Purpose: To review the results of low-intensity/high-density subthreshold micropulse laser (SDM) for treatment of central serous chorioretinopathy.

Method: The records of all patients treated in a retinal subspecialty practice with SDM for central serous chorioretinopathy were reviewed.

Results: Eleven consecutive eyes of 11 patients treated between October 2011 and April 2014 were identified for study, 9 men and 2 women, aged 30 to 55 (mean = 46). Symptom duration before treatment ranged 1 month to 7 months (mean = 3.6 months) and after treatment with SDM laser, follow-up ranged 1 month to 45 months (mean = 14). Preoperative visual acuities ranged 20/20 to 20/100 (mean = 20/37) and postoperative visual acuities were 20/15 to 20/40 (mean = 20/24) (P = 0.01, paired t-test). Maximum retinal thickness ranged 314 μm to 893 μm (mean = 508) preoperatively and 222 μm to 365 μm (mean = 250) postoperatively for an average 258 μm reduction in retinal thickness (P = 0.002, paired t-test). Subretinal fluid was eliminated in all eyes by 3 months after treatment (mean = 1.3 months). The number of SDM laser spot applications ranged 295 to 1431 per treatment session (mean = 772). One eye required retreatment, but for a new leakage locus 4 months after initial treatment. There were no adverse treatment effects.

Conclusion: An SDM laser seems to be safe and effective for the treatment of central serous chorioretinopathy. As advocated in the literature, a higher treatment density and larger treatment area, as reported in this article, may improve clinical results.

RETINA 0:1–6, 2016

Evidenced by the number of recent reports, there is growing interest in subthreshold laser treatment, particularly using micropulsed lasers (MPLs), for treatment of idiopathic central serous chorioretinopathy (CSR). Subthreshold diode micropulse (SDM) laser treatment refers to using a micropulsed laser in a low-intensity/high-density treatment application paradigm. In this report, the results of SDM for CSR in a retina subspecialty practice are reviewed.

Methods

This study adhered to the tenets of the Declaration of Helsinki. The records of all patients treated in a retinal subspecialty practice with SDM for simple CSR were reviewed. Each of these cases was defined as "simple" CSR, because it was characterized by the presence of subretinal fluid and the absence of retinal edema, with active subretinal leakage due to focal/local retinal pigment epithelial (RPE) decompensation demonstrated by intravenous fundus fluorescein angiography, characteristics generally associated with a favorable therapeutic response. Applying traditional classification based on historical duration of disease, those eyes with disease for 4 months or more could be considered as "chronic," and those less than 4 months as "acute" (Table 1).[1,2]

The indications for treatment included visual need, chronicity, or retinal damage from previous episodes of exudation.

Treatment With Subthreshold Micropulse Laser

After obtaining informed consent and performing pupillary dilation, topical proparacaine was applied to

Private Practice, Ventura, California.

The author has no financial/conflicting interests to disclose.

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Table 1. Demographics and Results of Low-Intensity/High-Density Subthreshold Diode Micropulse Laser (SDM) for Idiopathic Central Serous Chorioretinopathy

Pt	Age	Sex	PreD	PreVA	PostVA	PreT	PostT	LS	Recur?	Dry	Time	F/U
1	50	M	7	100	40	407	365	453	No	Yes	1	45
2	39	M	6*	40	20	554	296	907	Yes‡	Yes	3	38
3	39	M	3	20	20	458	303	1,290	No	Yes	1	21
4	55	F	1	25	25	314	231	295	No	Yes	1	12
5	47	F	2	20	20	489	258	484	No	Yes	1	3
6	52	M	2	30	25	647	248	822	No	Yes	1	5
7	52	M	4	30	20	327	251	893	No	Yes	1	10
8	30	M	6	25	15	457	268	478	No	Yes	1	1
9	51	M	2	20	20	893	222	584	No	Yes	2	2
10	42	M	1	50	15	699	262	1,431	No	Yes	1	14
11	49	M	6†	50	40	341	248	857	No	Yes	1	1

*History of recurrent disease for 10 years, with previous photocoagulation 5 years before SDM.

†History of recurrent disease for 10 years, with previous photocoagulation on 3 occasions, last 1 year previous to SDM.

‡Initial resolution with recurrence after 3 months. Intravenous fundus fluorescein angiography at 3 months after first SDM revealed cessation of leakage from original focus, with new area of leakage. Subthreshold micropulse laser repeated 4 months after initial treatment with complete resolution of subretinal fluid in 3 months.

Pt, patient number; PreD, duration of recent symptoms before SDM treatment; PreVA, pretreatment visual acuity as 20/X; PostVA, final visual acuity after treatment as 20/X; PreT, maximum retinal thickness, in microns, before treatment; PostT, retinal thickness, in microns, after treatment measured at same location as pretreatment maximal retinal thickness; LS, Number of SDM laser spot applications; Recur?, Recurrence of subretinal fluid; Dry, Complete resolution of subretinal fluid after treatment; Time, Time, in months, to complete resolution of subretinal fluid; F/U, length of follow-up, in months, after SDM treatment.

the cornea. A Mainster macular contact lens (Ocular Instruments, Mentor, OH, magnification factor ×1.05) was then applied to the cornea with viscoelastic contact solution. Contiguous spot applications of SDM laser treatment, 810 nm wavelength, 200 μm spot size, 5% duty cycle, 1.4 Watt power, 0.15 seconds duration, were applied over the area of RPE leakage and all areas of pigmentary abnormality, including the fovea if indicated, directed by the preoperative fundus fluorescein angiogram projected beside the patient (Figures 1–3).

All patients were evaluated by clinical examination, fundus fluorescein angiography, and spectral-domain optical coherence tomography (OCT) before treatment to confirm active disease and characterize the leakage

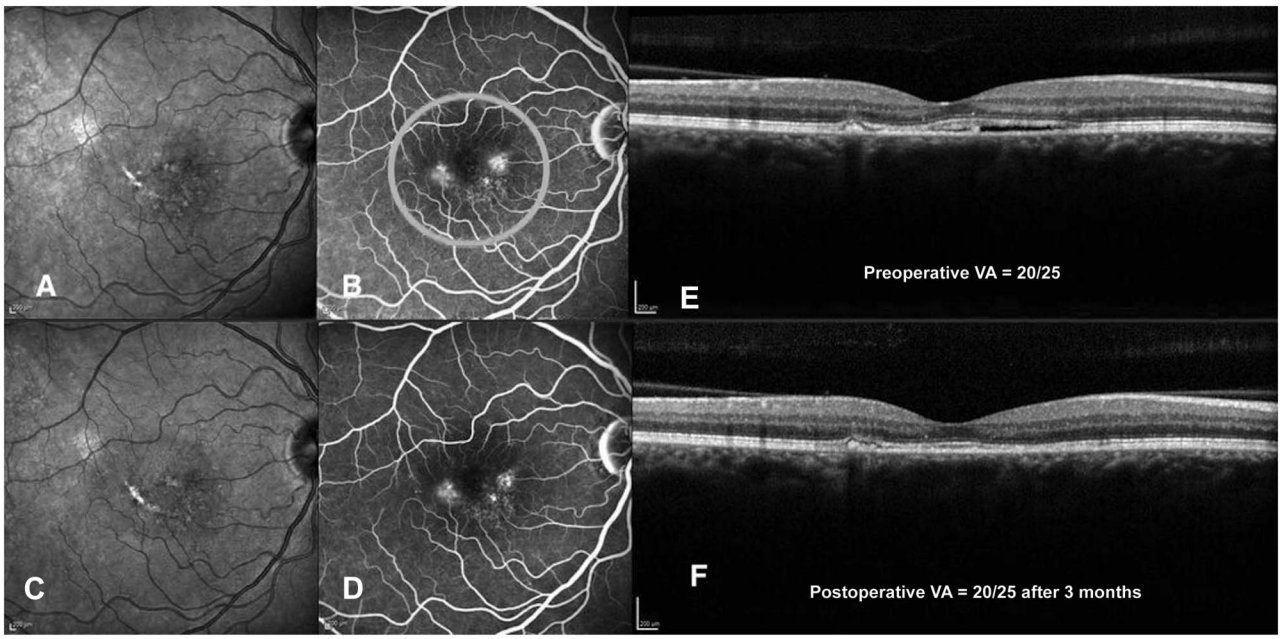

Fig. 1. Preoperative fundus photograph (**A**), and late-phase intravenous fundus fluorescein angiogram (**B**) of an eye with active CSR. The superimposed circle approximates the area of confluent SDM spot application at the time of treatment. Postoperative fundus photograph (**C**) and late phase fundus fluorescein angiography (**D**). Note absence of leakage and absence of laser-induced retinal damage. Optical coherence tomograms of the same eye (**E**) before and (**F**) after SDM treatment. Note resolution of subretinal fluid and absence of laser-induced retinal damage.

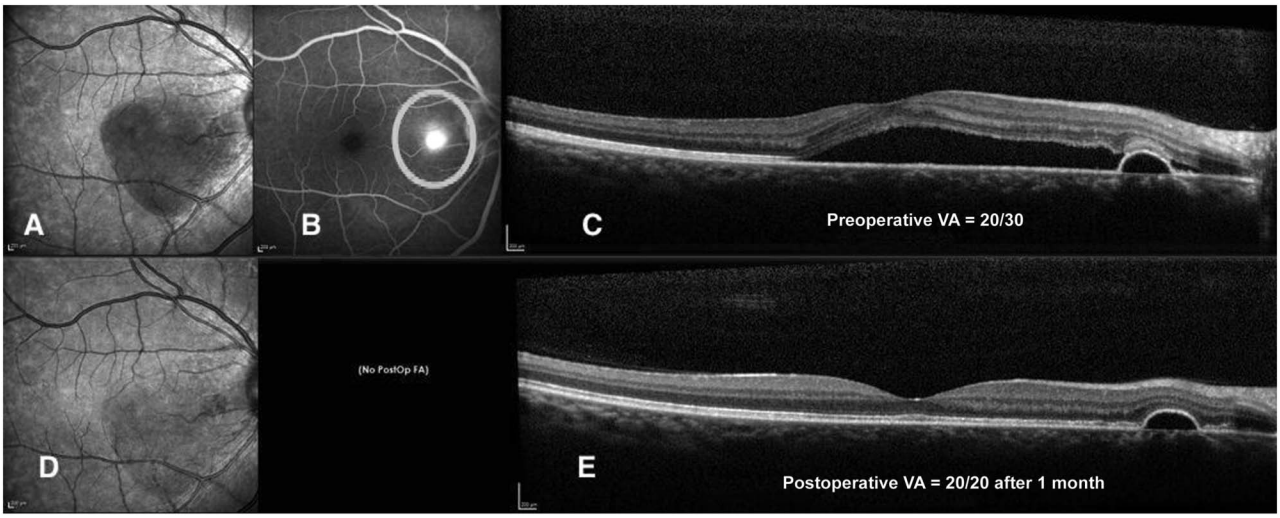

Fig. 2. Preoperative fundus photographs (**A**) and late-phase fundus fluorescein angiograms (**B**) of eye with active CSR. The superimposed circles approximate the areas of confluent SDM spot application at the time of treatment. Postoperative fundus photographs showing resolution of exudation without laser-induced retinal damage (**C**). Pretreatment OCTs of the same eye before (**D**) and after (**E**) SDM treatment. Note the resolution of subretinal fluid and absence of laser-induced retinal damage.

pattern. "Enhanced depth OCT imaging" to characterize choroidal thickness was unavailable and thus not performed.[3] All treated patients underwent clinical examination and OCT at 1 month after treatment, and at various times thereafter. Repeat fundus fluorescein angiography was performed if the subretinal fluid was unimproved by 6 weeks after SDM treatment.

Results

Eleven consecutive eyes of 11 patients treated with SDM for CSR were identified for study and treated between October 2011 and April 2014 (Table 1). They are 9 men and 2 women aged 30 years to 55 years (mean = 46). Historically, these 5 eyes could be considered chronic and 6 acute CSR.[1,2] Preoperative visual acuities ranged 20/20 to 20/100 (mean = 20/37) and preoperative maximum retinal thickness ranged 314 μm to 893 μm (mean = 508). Two eyes had previous conventional laser treatment of CSR, most recently 2 years and 5 years before SDM. Symptomatic visual loss ranged from 1 month to 7 months (mean = 3.6) before SDM treatment. The number of SDM laser spot

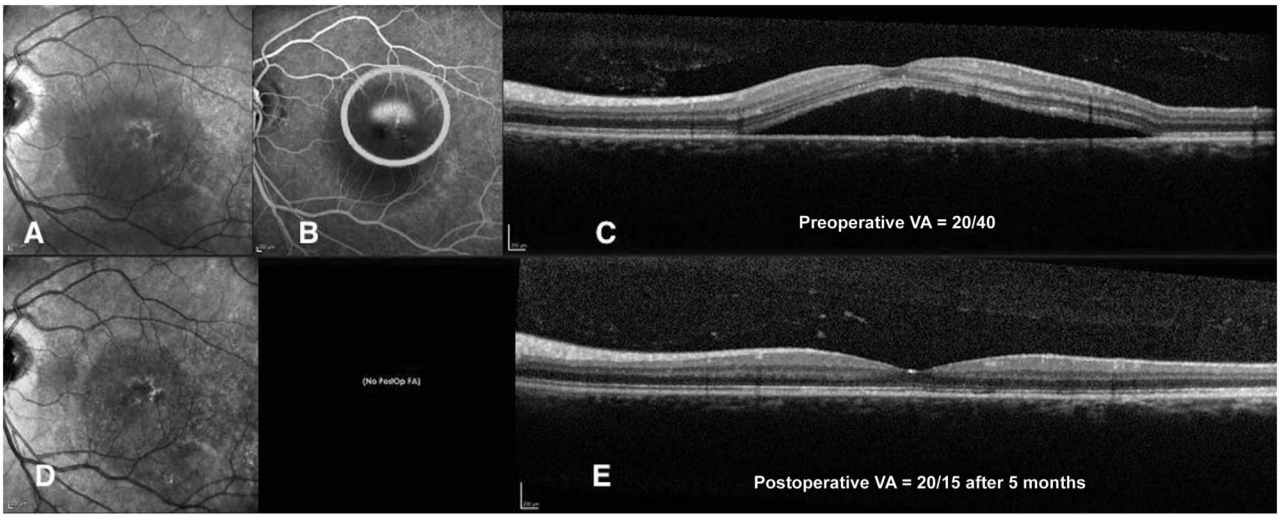

Fig. 3. Preoperative fundus photographs (**A**) and late-phase fundus fluorescein angiograms (**B**) of eye with active CSR. The superimposed circles approximate the areas of confluent SDM spot application at the time of treatment. Postoperative fundus photographs showing resolution of exudation without laser-induced retinal damage (**C**). Pretreatment OCTs of the same eye (**D**) before, and (**E**) after SDM treatment. Note resolution of subretinal fluid and absence of laser-induced retinal damage.

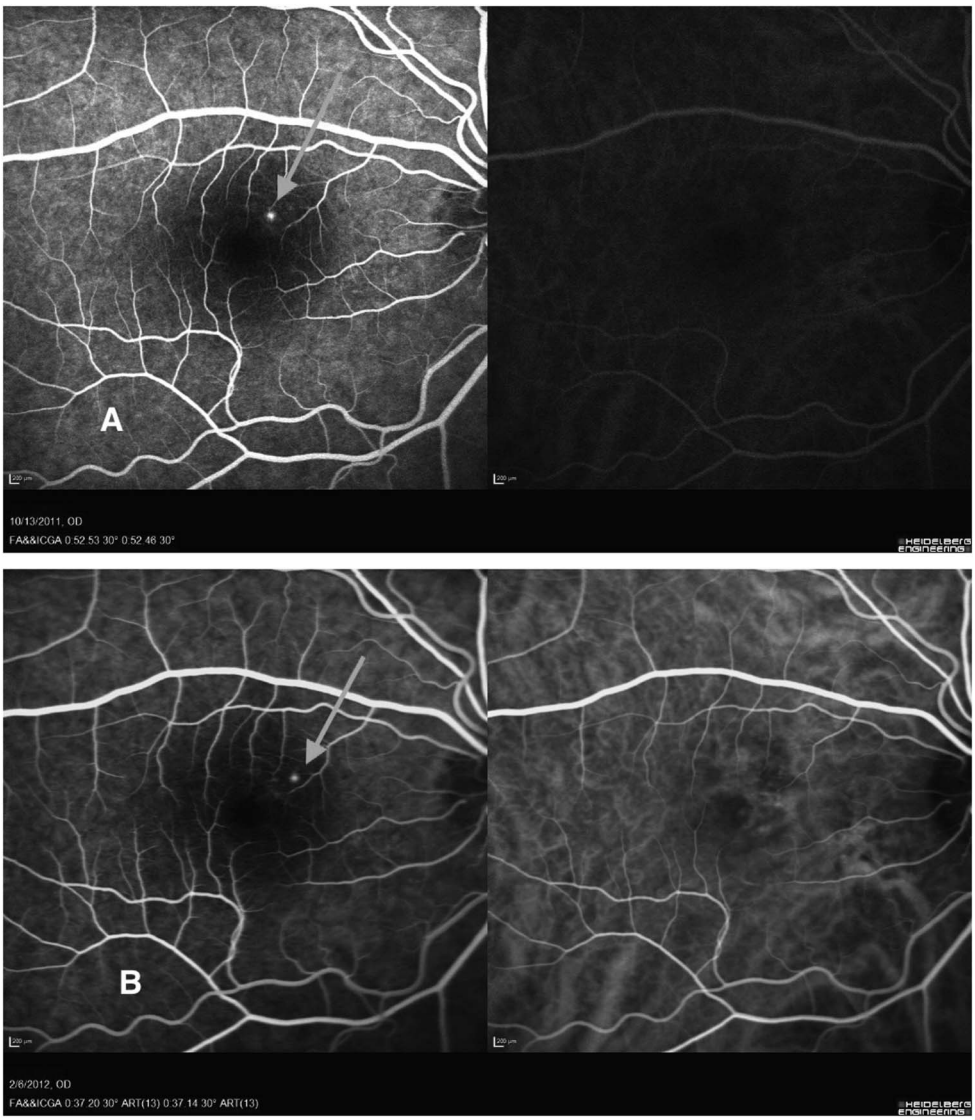

Fig. 4. Intravenous fundus fluorescein angiogram of eye with active CSR on presentation (**A**), and 4 months after initial SDM treatment (**B**, arrows). Note the absence of laser-induced retinal damage, resolution of the initial locus of leakage, with a new point of leakage in a different location. Repeat SDM treatment was performed and subretinal fluid resolved 3 months later. No further recurrence was noted in 35 months of follow-up.

applications ranged 295 to 1,431 per treatment session (mean = 772).

Complete resolution of subretinal fluid after SDM was documented by OCT in all eyes. The duration from treatment to resolution of subretinal fluid ranged from 1 month to 3 months (mean = 1.3 months). One eye had recurrent leakage from a new focus of RPE decompensation at 3 months after initial SDM treatment (Figure 4). One month later SDM was repeated, with complete resolution of subretinal fluid 3 months later. No further recurrence was noted in this eye for 35 months. In the remaining 10 eyes, a single SDM treatment was required.

Postoperative visual acuity ranged 20/15 to 20/40 (mean = 20/24), with improved visual acuity in 10 of 11 eyes ($P = 0.01$, paired t-test). Postoperative maximum macular thickness ranged from 222 μm to 365 μm (mean = 250) for an average 258 μm reduction in retinal thickness ($P = 0.002$, paired t-test). Postoperative follow-up ranged 1 month to 45 months (mean = 14). There were no adverse effects due to treatment. In particular, there was no evidence of laser-induced retinal damage on high-resolution retinal imaging.

Discussion

Central serous chorioretinopathy is a common condition of unknown etiology affecting men primarily during midlife. Usually clinically unilateral, it may be episodic, with evidence of previous subclinical disease often noted in both the affected and fellow eyes. Treatment of CSR is seldom necessary, as most cases resolve spontaneously with return of normal or

near-normal visual acuity within a few weeks. In rare cases, due to visual need or accumulated damage due to previous episodes, treatment may be indicated for speedy recovery and/or minimize the risk of further macular damage that might be visually limiting and irreversible.[1,2]

In this small retrospective review of SDM for CSR, subretinal fluid resolved in all eyes with significant improvements in visual acuity and retinal thickness. Only one eye required a second treatment and this was because of recurrent exudation from a new locus of RPE leakage. There were no adverse treatment effects. Of 11 eyes, 5 eyes in this study could be considered chronic by history, and thus more resistant to treatment. However, there did not seem to be any difference in treatment response between historically acute and chronic cases in this series. This may reflect the small size of this study, the effectiveness of SDM, and/or the usefulness of the anatomical classification used in this study, compared to traditional classification based on historical chronicity.[1,2] Increased choroidal thickness by OCT enhanced depth imaging in CSR has been observed.[3] The clinical relevance of this finding remains unclear, as underscored by results of this study for which enhanced depth imaging was unavailable[3] (Table 1; Figures 1–4).

A number of different effective treatments of CSR have been reported.[1] Historically, light retinal photocoagulation has been the preferred treatment, found to speed resolution of the exudative macular detachment. However, retinal photocoagulation has two principal drawbacks that have led to continued investigation of alternatives, such as scotomata resulting from the retinal damage inherent even in low-intensity retinal photocoagulation (which may also increase the risk of secondary choroidal neovascularization), and the inability to safely treat leaks near or within the fovea.[4–9]

Thus, other approaches have been investigated with the hope of avoiding the adverse effects of retinal photocoagulation, including transpupillary thermotherapy, full-fluence and reduced-fluence photodynamic therapy, and MPL. Transpupillary thermotherapy, operating at the edge of the lethal thermal threshold of the RPE, has lost favor for macular treatment because of the risk of unexpected macular infarction.[8] Full-fluence photodynamic therapy has been found to be effective for CSR, but also with a significant risk of unexpected visual loss due to macular atrophy. Reducing photodynamic therapy fluence may reduce the risk of treatment-associated visual loss, and also treatment effectiveness. Photodynamic therapy is also more invasive than other laser treatments, requiring intravenous infusion of an expensive drug contraindicated in patients with liver disease, and avoidance of sun exposure for several days.[1,10,11] Anti–vascular endothelial growth factor drugs have also been investigated. As one might expect in light of the mechanistic theories of CSR; and despite the expense, adverse effects (such as pain, anxiety), frequency, and risks (including endophthalmitis), only modest effectiveness of vascular endothelial growth factor inhibitors has been reported in uncomplicated CSR.[1,2,7,12]

In recent years, a number of studies, both retrospective and randomized, have reported use of MPLs for subthreshold treatment of CSR. These studies vary in size, laser wavelength, treatment technique (focal/local application vs. low-intensity/high-density application), and laser parameters, and in one report, a combination with indocyanine green dye infusion as an adjuvant is shown. Despite these differences, without adverse treatment effects, elimination of exudation was achieved in most cases. In controlled studies, MPL has been found to be comparable to half-fluence photodynamic therapy, superior to bevacizumab, and superior to sham in the treatment of CSR.[12–19]

This study is distinguished by the high number of laser spot applications per treatment session (mean = 772), and a high success rate. In previous studies, including the one previous report of SDM for CSR by Malik et al,[12–18] unsuccessful treatment was associated with fewer MPL spot applications. These observations support the theory of SDM, that a high treatment density and large coverage area maximizes the therapeutic benefits of low-intensity laser treatment and improves clinical outcomes.[20–22]

The safety and effectiveness of low-intensity/high-density MPL laser (SDM) in a number of disorders has led to interest in attempting similar effects with a short-pulsed continuous wave laser. In the one report thus far, an algorithm was used to titrate short-pulse 577 nm continuous wave laser applications to a non-damaging intensity, then applied in high-density to treat 16 eyes with CSR for 4 or more months in duration with clinical characteristics similar to those reported in this report. This low-power short-pulse continuous wave laser approach reported a lower 37% rate of single treatment success, higher 63% rate of retreatment, and lower final success rate (achieving complete resolution of subretinal fluid) of 75%.[23] Homeotrophic normalization of RPE function and retinal autoregulation by means of sublethal RPE heat-shock protein (HSP) activation (reset to default theory) has been postulated as the primary mode of action of retinal lasers.[20,21,24–27] These findings support the hypothesis that MPL may be a more effective activator of heat-shock proteins than low-power continuous wave lasers at sublethal levels.[21]

This study is limited by the small size, short follow-up, retrospective data collection, and single treatment center. However, the results are uniform and consistent with all previous reports of MPL for CSR. The safety, effectiveness, brevity, simplicity, repeatability, and low cost of SDM suggest SDM should be considered for treatment of CSR. The findings reported in this report suggest that treatment effectiveness may be improved by using the high-density SDM treatment paradigm. The safety of SDM allows treatment of eyes with preexisting pigment damage or laser scarring without adverse effects, unlimited retreatment, and, if necessary, direct treatment of leaks within the fovea.[20,21,24–27] These unique facilities, the results reported previously, and those reported in this report suggest that further study of SDM laser for CSR is warranted.

Key words: subthreshold, diode laser, micropulse, low-intensity, high-density, central, serous, chorioretinopathy, reset, heat-shock proteins, photocoagulation.

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