

# Nonvisible subthreshold micropulse diode laser (810 nm) treatment of central serous chorioretinopathy: A pilot study

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**PURPOSE.** To verify the efficacy of nonvisible micropulse diode laser irradiation in the treatment of central serous chorioretinopathy (CSC).

**METHODS.** Twenty-two patients with CSC for a total of 24 eyes with a disease duration longer than 3 months were included in a prospective study. Patients underwent Early Treatment Diabetic Retinopathy Study visual acuity (VA) examination, dilated ophthalmoscopy, fluorescein angiography, and optical coherence tomography before treatment and during follow-up. Treatment with a micropulse diode laser was given with a duty cycle of 15%. Multiple spots were placed over and adjacent to the area of retinal pigment epithelium leak or decompensation.

**RESULTS.** Mean follow-up was 14 months (range 3–36 months). Powers used ranged from 1 to 2 W (mean 1.35 W). Mean number of spots was 215 (range 90–400). Fourteen eyes were treated once, nine eyes received two to three treatments, and one eye had five treatments during a follow-up of 3 years. Subretinal fluid was resolved or improved in two third of cases 1 month after laser treatment, and in three-quarters at the end of follow-up. Mean retinal thickness was 328  $\mu\text{m}$ , 197  $\mu\text{m}$ , and 168  $\mu\text{m}$  before, 1 month after irradiation, and at the end of follow-up, respectively. No evidence of RPE or retinal changes due to laser treatment were discernible in most of the eyes. Median VA was 20/32 (range 20/100–20/20) before treatment and 20/25 (range 20/200–20/20) at the end of the follow-up.

**CONCLUSIONS.** Nonvisible micropulse diode laser may have efficacy in the treatment of CSC. A randomized study with larger series is needed. (*Eur J Ophthalmol* 2008; 18: 934-40)

**KEY WORDS.** Nonvisible micropulse laser, Central serous chorioretinopathy

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## INTRODUCTION

Central serous chorioretinopathy (CSC) is defined as the idiopathic serous detachment of the neurosensory macula secondary to leakage at the level of the retinal pigment epithelium (RPE) (1). CSC may present with a number of other degenerative and exudative changes, including diffuse decompensation of the RPE, choroidal neovascularization (CNV) with associated serosanguineous complications, descending atrophic pigment epithelial tracts, dependent retinal detachments, and retinal vascular microangiopathy (2). CSC is usually a self-limited disease

with a good prognosis for visual recovery (1, 3-5). However, some patients with prolonged or recurrent episodes develop some degree of permanent reduction of visual acuity (1-8). The pathogenesis of the disease seems to be related to an increased permeability of the choriocapillaris and subsequent metabolic impairment of the RPE (5). The rationale of laser treatment of CSC is to debride the RPE in the area of the leakage, permitting ingrowth of surrounding RPE and subsequent resolution of the detachment. Focal laser photocoagulation to an RPE leak or scatter laser treatment to areas of RPE decompensation can shorten the duration of the serous detachment (9).

However, their efficacy in improving the final visual acuity and decreasing the incidence of recurrences is controversial. Laser photocoagulation may be also associated to accidental burn of the foveola, retinal distortion, CNV, and paracentral scotoma (5). Therefore, laser treatment of CSC has doubtful indications and is usually deferred (2, 9-11).

A number of experimental findings postulated that a selective photocoagulation aimed at the RPE layer alone might be enough to mediate a biologic response in the treatment of retinal diseases (12). Also, such treatment may result in fewer side effects and complications (12).

The aim of this study was to report a new method of treatment for patients with CSC using nonvisible micropulse diode infrared laser photocoagulation (810 nm) to resolve macular detachment. Optical coherence tomography (OCT) was used to document the presence and change of neurosensory detachments.

## METHODS

A consecutive series of patients with CSC was prospectively studied. Diagnosis of CSC was based on clinical and angiographic patterns. Patients were considered to have CSC when presenting with idiopathic detachment of the neurosensory macula with focal leak at the level of the RPE or areas of decompensating RPE with gradual, indistinct RPE leakage at fluorescein angiography (FA). Inclusion criterion for treatment was a disease duration of at least 3 months as documented by clinical examination, FA, and OCT. Patients were excluded if they had other associated ocular and macular conditions that compromised visual acuity, previous laser treatment, intraocular surgery within 6 months of the clinical diagnosis, inability to obtain photographs, known adverse reaction to fluorescein dye, and pregnancy. The local review board approved the study, and informed consent was obtained.

Patient examination included ETDRS visual acuity measurement, dilated ophthalmoscopy, FA using the Topcon fundus camera ImageNet System (Topcon), and OCT. FA was obtained to identify the presence of acute RPE leaks and areas of late hyperfluorescence, which indicated decompensation of the RPE. OCT images were obtained using the Zeiss OCT-2 or the Zeiss OCT-3 Stratus (Zeiss Humphrey). OCT was essential for documenting macular detachments and retinal thickness and evaluating the outcome after treatment. Each patient was re-examined 1

month and then every 3 months after treatment. Additional visits were scheduled on a patient-by-patient basis. Each follow-up evaluation included visual acuity, dilated ophthalmoscopy, FA, and OCT.

Treatment was delivered through a three mirror Goldmann lens following mydriasis with tropicamide 1% and topical anesthesia with benoxinate 0.4% eyedrops. Irradiation with a micropulse diode infrared laser (Iris Medical Oculight SLx) was applied to RPE leaks or zones of RPE decompensation. A continuous wave test spot of 200  $\mu$ m and 0.2 seconds exposure time with such power that mild retinal whitening was obtained was placed at the posterior pole. Subsequently, treatment was given with a duty cycle of 15% and the same parameters used for the test spot. Multiple overlapping spots were placed over and adjacent to the area of RPE leak or decompensation. No visible change at the retina level was evident during and after irradiation when powers below 2 W were applied. Two subjects treated with maximum power (2 W) showed some subtle color change at the level of the RPE during irradiation.

Data obtained were analyzed with frequency and descriptive statistics. Visual acuity was converted to logarithm of the minimum angle of resolution (logMAR) for analysis. The Wilcoxon signed rank test was performed to assess change in visual acuity and retinal thickness from baseline to the interval examination 1 month and the longest follow-up available after treatment.

## RESULTS

Twenty-four eyes of 22 subjects with the diagnosis of CSC were recruited and treated with nonvisible micropulse diode infrared laser irradiation. The mean age of the patients was 47 years (range, 38-64 years). Eighteen patients were men. All patients had a history of CSC for more than 3 months (mean, 3 years; range, 3 months-10 years) and none had been treated with laser photocoagulation or other therapies in the past. Table I summarizes visual acuity and morphologic outcomes. Initial median visual acuity was 20/32 (range, 20/100-20/20). There were 19 cases of RPE leaks causing the macular detachment and five cases with areas of RPE decompensation. One eye presented with serous pigment epithelium detachment (PED).

Treatment powers ranged from 1 to 2 W (mean, 1.35 W). Mean number of spots applied was 215 (range, 90-400).

Fourteen eyes were treated once, nine eyes received two to three treatments, and one eye had five treatments during a follow-up of 3 years.

The mean follow-up period was 14 months (range, 3–36 months). One month after laser treatment, nine eyes had complete anatomic resolution of the subretinal fluid in the central macula, and seven had incomplete resolution of the exudative detachment, confirmed by OCT. Median visual acuity at 1 month was 20/25 ( $p=0.64$ ) (range, 20/100–20/20). At the end of follow-up, 17 eyes manifested complete absorption of fluid and one eye had incomplete resolution. The only eye with serous PED did not respond to treatment. At final visit, median visual acuity was 20/25 ( $p=0.062$ ) (range 20/200–20/20). Visual acuity improved by two or more lines in six eyes and by one line in four eyes. Two eyes worsened by one and five lines, respectively. Visual acuity did not show any change in 12 eyes. Mean retinal thickness at the fovea was 328  $\mu\text{m}$

(range, 162–702  $\mu\text{m}$ ) before treatment, 197  $\mu\text{m}$  ( $p=0.0003$ ) (range, 93–403  $\mu\text{m}$ ) 1 month after irradiation, and reduced to 168  $\mu\text{m}$  ( $p<0.0001$ ) (range 107–340  $\mu\text{m}$ ) at the end of follow-up. Pigmentary changes at the level of the RPE were seen at the site of micropulse laser application in five eyes during follow-up. No patients had any complications from the treatment (Figs. 1 and 2).

## DISCUSSION

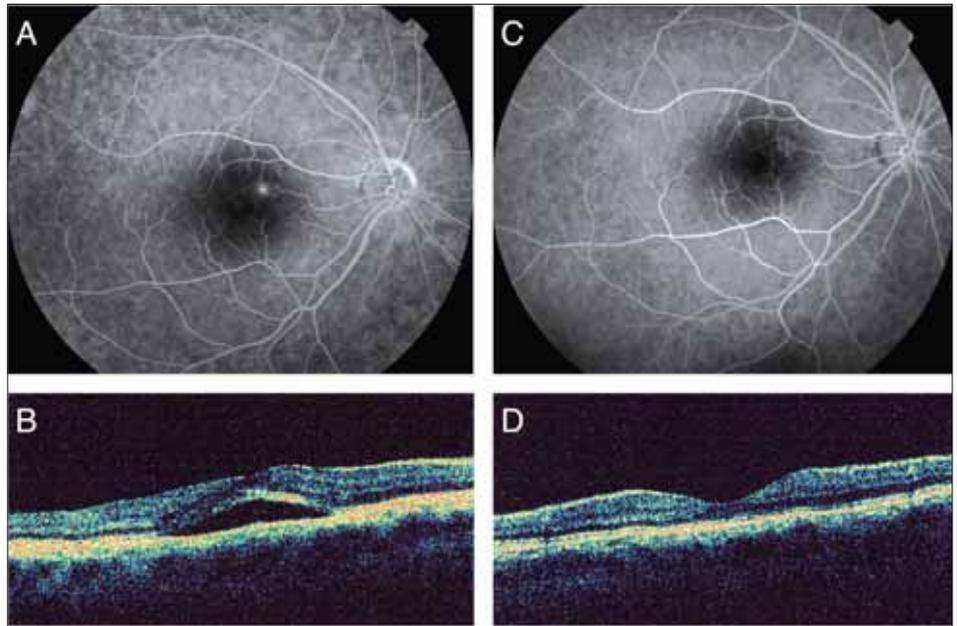
The cause of CSC is not known. The exact pathophysiologic alterations that occur to produce the characteristic RPE leak associated with CSC are not clear. Hyperpermeable choroid has been shown with indocyanine green angiography (13, 14). Chronic exudation in the inner choroid in CSC can lead to serous PED, and focal leak in the RPE with subsequent serous leakage beneath the neurosenso-

TABLE I - SUMMARY OF PATIENT CHARACTERISTICS

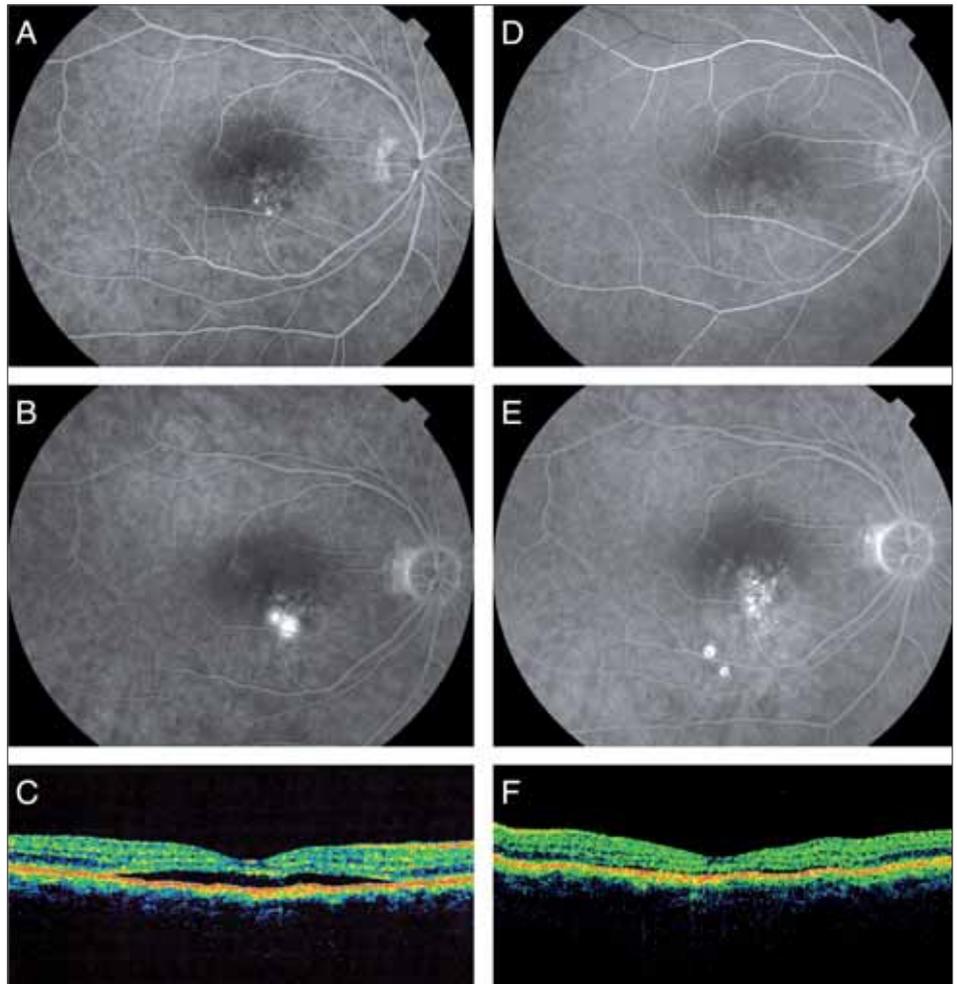
Patient no.	Age, yrs	Gender	Eye	Episode duration before treatment, mo	VA before treatment (LogMAR)	VA at final follow-up (LogMAR)	RT before treatment ( $\mu\text{m}$ )	RT at final follow-up ( $\mu\text{m}$ )	Follow-up mo	Laser sessions, n
1	38	M	L	83	0.2	0.0	400	191	3	1
2	46	M	R	60	0.4	0.1	265	199	27	1
3	42	M	R	18	0.5	0.5	423	214	15	3
4	49	M	L	8	0.3	0.0	324	156	21	1
5	64	F	R	3	0.1	0.0	367	154	27	1
6	52	M	L	6	0.5	1.0	150	160	30	1
7	38	M	L	3	0.2	0.1	446	157	18	3
8	54	F	L	12	0.1	0.1	359	107	27	1
9	39	M	L	3	0.3	0.1	702	142	3	1
10	42	F	L	120	0.2	0.0	405	149	27	1
11	58	M	R	4	0.1	0.0	328	274	36	5
12	47	M	L	7	0.0	0.0	263	133	18	3
			R	3	0.0	0.0	195	165	6	1
13	61	M	R	3	0.3	0.3	224	107	9	2
14	35	M	R	12	0.0	0.0	514	181	3	1
15	43	M	R	30	0.0	0.0	170	160	3	3
16	46	M	R	3	0.7	0.7	355	165	3	1
17	42	M	R	47	0.1	0.2	353	116	9	3
18	47	M	R	83	0.2	0.2	171	182	6	1
19	54	M	R	117	0.4	0.2	162	127	15	3
			L	3	0.0	0.0	185	116	15	2
20	54	F	L	12	0.2	0.1	348	224	3	1
21	33	M	R	7	0.0	0.0	390	340	6	1
22	37	M	R	120	0.3	0.3	367	116	9	2

VA = Visual acuity; RT = Retinal thickness

**Fig. 1 - Fluorescein angiography (FA)** (A) shows a focal leak of dye. Subretinal fluid is visible at optical coherence tomography (OCT) scan (B). The patient received one single treatment and at month 6 FA (C) and OCT (D) confirm resolution of leakage and neuroretinal detachment.



**Fig. 2 - Mid- (A) and late-phase (B) fluorescein angiography (FA)** showing two spots of fluorescein leakage within an area of retinal pigment epithelium (RPE) mottling. Optical coherence tomography (OCT) scan (C) shows the neurosensory detachment of the macular region. Fifteen months later, after three laser sessions, early (D) and late-phase (E) FA exhibit resolution of leakage, two test spots along the inferior vascular arcades, and reactive RPE changes. OCT scan (F) documents resolution of subretinal fluid.



ry retina. With persistent or recurrent detachment, progressive atrophic degeneration of the RPE in a multizoned distribution evolves, leading to decompensation of the posterior blood–retina barrier and slow and indistinct leakage with FA (15). Persistent subretinal fluid is associated with reduced visual acuity in CSC (8). Particularly, progressive chorioretinal deterioration with areas of RPE decompensation can produce severe and irreversible visual loss (6, 7).

The self-limited nature and the good visual prognosis of CSC usually inhibit the use of laser photocoagulation unless a retinal detachment has been present for 10 to 12 weeks (16). In the case of persistent CSC, laser photocoagulation aimed at sealing focal sites of RPE leakage can shorten the duration of the serous detachment, improve final visual acuity, and decrease the incidence of recurrence (17–20). However, Khosla et al reported that laser treatment is associated with significant loss and slower recovery of contrast sensitivity (21). Moreover, treatment may carry an increased risk of subsequent CNV development. For these reasons, laser photocoagulation with retinal whitening is usually delayed until the advanced stages of the disease are reached. The aim of laser treatment is to repair the leaking RPE layer and restore a new RPE barrier. Unfortunately, standard laser photocoagulation is accompanied by severe destruction of photoreceptors and choriocapillaris that may lead to the cited side effects.

Recently, some case series have been reported on the use of photodynamic therapy to treat chronic CSC with diffuse decompensation of the RPE (15, 22, 23) or CSC with focal retinal pigment epithelial leaks (24). The rationale for applying photodynamic therapy to chronic or acute CSC is to decrease choroidal hyperpermeability through a photochemical mechanism, leading to reduction of choroidal exudation. However, the use of photodynamic therapy is not without complications such as RPE atrophy and CNV (15, 22–25).

A selective photocoagulation aimed to the RPE layer alone, without destroying the photoreceptors and without any visible whitening of the retina, theoretically might be enough to mediate a biologic response in the treatment of CSC. Diode laser micropulse photocoagulation represents a viable modality for the precise control and spatial confinement of laser lesions to the RPE cells (12). We delivered multiple and overlapping nonvisible spots to the areas of diseased RPE with the aim of stimulating the recovery of the outer blood–retinal barrier. It has been

shown that retinochoroidal temperature elevation with diode laser irradiation is associated with heat shock protein hyperexpression (26, 27). Heat shock proteins could have an important role in the protection of RPE cells against different stimuli and they represent an interesting target in the development of therapeutic strategies attempting to stimulate endogenous protective mechanisms. It could be conceived that heat shock proteins might reduce RPE injury, accelerate functional recovery of the RPE cells, and improve survival of retinal neuronal cells in RPE degenerative processes (28). The hypothesis is that a confined and moderate thermal elevation at the level of the RPE layer may stimulate such repair. Our study shows that nonvisible micropulse treatment of CSC may lead to prompt resolution of subretinal fluid in most patients, therefore to recovery of the blood–retinal barrier. Treatment was indicated based on the clinical and angiographic diagnosis even in the presence of good visual acuity. OCT was helpful in monitoring the change of retinal fluid before and after laser irradiation and may become an additional tool to identify the need of therapy and to evaluate its efficacy.

The treatment was not visible at ophthalmoscopy and fluorescein angiography during its administration and along the whole follow-up in patients treated with powers below 2 W. In those subjects during treatment the retina did not lose its transparency nor did the RPE show any color change or mottling secondary to laser irradiation. At the time of treatment, two eyes irradiated with maximum power showed some subtle color change at the level of the RPE which did not involve any whitening of the neural retina. After treatment, five eyes showed minimal pigmentary changes where the laser spots were placed which were detectable both at ophthalmoscopy and fluorescein angiography. Four of them had received maximum power. At the end of a follow-up of 30 months, the only patient with PED experienced five-line visual loss. The extent of the juxtafoveal PED was unchanged; however, the underlying choriocapillaris was extensively atrophic.

The absence of any visible treatment sign raises questions on the uncertainty of a biophysiological reaction after our treatment modality. Prompt response to treatment—i.e., resolution of subretinal fluid—may be due to the improved metabolic health of the RPE cells. On the other hand, a placebo effect secondary to subclinical irradiation should be considered (29). The temporal course of our series suggests that the improvement is likely due to laser irradiation. However, this is a pilot study and the lack of

matched controls does not allow any definitive conclusion. Similar concerns are raised by other recent reports on the treatment of CSC with photodynamic therapy in which a control group was absent (15, 22-25). Moreover, in order to show limited photoreceptor damage with this subthreshold irradiation as compared to standard laser photocoagulation, additional functional tests such as microperimetry and multifocal electroretinography would be helpful.

Despite the limitations related to the inherent methodology in the study design, there were anatomic and functional improvements in the treated eyes. Therefore, we view the proposed concept as a new and promising method

for treating a previously untreatable disorder. Moreover, a minimally invasive and retina sparing treatment may allow the cure of CSC at its earlier stages when irreversible visual loss has not occurred.

*The authors declare no conflicts of interest.*

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