DOI: 10.17816/OV11415-20

SUBTHRESHOLD LASERCOAGULATION (810 NM) FOR DIABETIC MACULAR EDEMA

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For citation: Izmaylov AS, Kotsur TV. Subthreshold lasercoagulation (810 nm) for diabetic macular edema. *Ophthalmology Journal*. 2018;11(4):15-20. doi: 10.17816/OV11415-20

Received: 04.09.2018 Revised: 07.12.2018 Accepted: 18.12.2018

✧ ***Introduction.*** The threshold laser coagulation leads to irreversible damage of retinal structures, microscotomata appearance in the central visual field, contrast sensitivity decrease, and color vision impairment, being accompanied as well by the release of proinflammatory cytokines. For diabetic macular edema treatment, a method of high-density subthreshold laser coagulation (810 nm) was first developed, based on individualized choice of subthreshold parameters of laser irradiation, and permitting confluent application of laser impacts to the retina. Using multimodal diagnostic approach to the estimation of anatomic and functional treatment results, a minimally invasive character and safety of this DME treatment method were confirmed. ***Purpose.*** The aim of this study was to comparatively evaluate the efficacy of a diode laser (810 mn) subthreshold laser treatment using high-density laser impact application in diode laser coagulation (DLC) and diode microphotocoagulation (DMP) modes. ***Materials and methods.*** To compare the efficacy of subthreshold laser treatment methods (DLC and DMP), patients were divided into two groups, comparable in macular edema thickness and area. The first group (24 eyes) received a macular laser coagulation in grid pattern and MicroPulse diode laser (810 nm) regimen; biomicroscopically it was predominantly subthreshold high-density application of burns. The second group (29 eyes) received a macular laser coagulation in grid pattern and continuous diode laser (810 nm) regimen; biomicroscopically it was predominantly subthreshold high-density application of burns. ***Results.*** After DLC and DMP, there was no statistically significant difference between compared groups in best corrected visual acuity. There was also no significant difference in retinal edema maximal height dynamics, retinal edema area, and central thickness in 2 and 4 months. ***Conclusion.*** Subthreshold microphotocoagulation and laser coagulation methods at the same average power of laser exposure and other exposure parameters in the shortterm follow-up have comparable efficacy in the treatment of diabetic macular edema.

✧ ***Keywords:*** diabetic macular edema; diabetic retinopathy; diabetes type 2; microphotocoagulation (MicroPulse); subthreshold high-density laser coagulation.

СУБПОРОГОВЫЕ МЕТОДИКИ ЛАЗЕРНОГО ЛЕЧЕНИЯ (810 НМ) ДИАБЕТИЧЕСКОГО МАКУЛЯРНОГО ОТЁКА

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Для цитирования: Измайлов А.С., Коцур Т.В. Субпороговые методики лазерного лечения (810 нм) диабетического макулярного отёка // Офтальмологические ведомости. – 2018. – Т. 11. – № 4. – С. 15–20. doi: 10.17816/OV11415-20

Поступила: 04.09.2018 Одобрена: 07.12.2018 Принята: 18.12.2018

✧ ***Введение.*** Пороговая лазеркоагуляция приводит к необратимому повреждению структур сетчатки, появлению микроскотом в центральном поле зрения, снижению контрастной чувствительности и ухудшению цветового зрения, а также сопровождается выбросом провоспалительных цитокинов. Впервые для лечения диабетического макулярного отёка ДМО разработана методика субпороговой лазеркоагуляции высокой плотности (810 нм), основанная на индивидуальном подборе субпороговых параметров лазерного излучения и допускающая конфлюэнтное (сливное) нанесение лазерных аппликаций на сетчатку. При помощи мультимодального диагностического подхода к оценке анатомо-функциональных результатов лечения подтверждена малая инвазивность и безопасность технологии лазерного лечения ДМО. ***Цель*** — провести сравнительный анализ эффективности субпорогового лечения диодным (810 нм) лазером при высокой плотности нанесения лазерных аппликаций по методике диодной лазеркоагуляции (ДЛК) и диодной микрофотокоагуляции (ДМФ). ***Материалы и методы.*** Для сравнения эффективности субпороговых методов лазерного воздействия (ДЛК и ДМФ) были сформированы две группы исследования, сопоставимые по толщине и протяжённости макулярного отёка. Первая группа (24 глаза) — лазерная коагуляция в макуле по методике «решётки» в режиме MicroPulse диодного лазера (810 нм), биомикроскопически преимущественно субпороговое воздействие при высокой плотности нанесения ожогов. Вторая группа (29 глаз) — лазерная коагуляция в макуле по методике «решётки» в непрерывном режиме диодного лазера (810 нм), биомикроскопически преимущественно субпороговое воздействие при высокой плотности нанесения ожогов. ***Результаты.*** После проведения ДЛК и ДМФ достоверных отличий максимально корригированной остроты зрения между группами сравнения не отмечалось. Также не наблюдалось достоверных различий относительно динамики максимальной высоты отёка сетчатки, площади отёка сетчатки и центральной толщины через 2 и 4 месяца.

✧ ***Ключевые слова:*** диабетический макулярный отёк; диабетическая ретинопатия; сахарный диабет 2-го типа; микрофотокоагуляция (MicroPulse); субпороговая лазерная коагуляция высокой плотности.

INTRODUCTION

Diabetic retinopathy is the leading cause of blindness in economically developed countries, while diabetic macular edema (DME) is one of the primary causes of patient disability.

The efficacy of laser coagulation of the macula performed as a part of DME treatment was confirmed in a multicenter randomized Early Treatment Diabetic Retinopathy Study. Laser coagulation using modified "grid" pattern (mETDRS) is the modern standard for laser treatment of DME.

BACKGROUND

Despite the changes in the DME treatment strategy over the past decade, such as the use of pharmacological approach involving intravitreous administration of anti-angiogenic and anti-inflammatory drugs, laser retinal coagulation has not lost its relevance [1, 2, 6, 8]. The modern standard for laser treatment of DME is represented by laser coagulation along a modified "grid" (mETDRS), which is accompanied in the threshold mode by an increase in the concentration of proinflammatory cytokines, the appearance of microscotomas in the visual field, and a decrease in the contrast sensitivity of the retina [5, 7]. In this regard, there is a growing interest among ophthalmologists to spare subthreshold microphotocoagulation techniques in various modifications and with the use of lasers of different wavelengths [3, 4]. Nevertheless, the use of subthreshold microphotocoagulation technology is associated with several disadvantages, such as the degree of pigmentation of the fundus not being considered, and the requirement of special equipment and trained medical personnel. Another disadvantage of this minimally invasive technique, as well as the traditional laser coagulation along a "grid" of the macula, is the limited number of laser impacts and the insufficient total area of the treated edematous retina.

New high-tech diagnostic instrumental methods, particularly high-resolution optical coherence tomography (OCT), OCT-angiography, and microperimetry have expanded the possibilities for studying structural and functional changes in the retina and chorioretinal complex. Therefore, the nature of tissue changes occurring with the use of minimally invasive laser interventions could be accurately assessed, and the treatment results could also be precisely evaluated.

This study aimed to comparatively analyze the efficacy of subthreshold treatment employing a diode laser (810 nm) with high-density laser impacts using diode laser coagulation (DLC) and diode microphotocoagulation (DMP) methods.

MATERIAL AND METHODS

To compare the efficacies of DLC and DMP, 2 study groups of patients with comparable thickness and length of macular edema were formed (Table 1).

In group 1 (DLC group), patients were treated using high-density subthreshold laser coagulation method, whereas patients in group 2 (DMP group) were treated using high-density microphotocoagulation (Table 2).

The best corrected visual acuity (BCVA) of patients in the DMP group prior to treatment was approximately 0.55 ± 0.05. In the DLC group, the BCVA value was 0.48 ± 0.04.

Patients with uncontrolled arterial hypertension (mean blood pressure >150/90 mmHg), edema of the lower extremities, and high macular edema (>500 μm) were excluded from the study. The follow-up period was 4 months.

Medical equipment included infrared diode ophthalmocoagulator ALOD01 (Alcom Medica, St. Pe-

Table 1 / Таблица 1

ОКТ-морфометрические показатели сетчатки групп сравнения до лазерного лечения
OCT-morphometric retinal parameters of comparison groups before laser treatment

Group of patients	Central retinal thickness ($M \pm m$, μm)	Maximum retinal thickness ($M \pm m$, μm)	Area of edema ($M \pm m$, pix.)
One (diode microphotocoagulation)	258.21 ± 70.3	410.32 ± 63.4	1413.61 ± 177.43
Two (diode laser coagulation)	257.25 ± 74.5	418.32 ± 8.4	1942.42 ± 166.01

Table 2 / Таблица 2

Patients distribution by comparison groups
Распределение пациентов по группам в зависимости от метода лазерного лечения

Group of patients	Laser treatment technique
One (24 eyes) – diode microphotocoagulation	Laser coagulation of the macula by the “grid” method in the MicroPulse mode of a diode laser (810 nm), biomicroscopically primarily subthreshold exposure with high-density burns.
Two (29 eyes) – diode laser coagulation	Laser coagulation of the macula by the “grid” method in the continuous mode of a diode laser (810 nm), biomicroscopically primarily subthreshold exposure with high-density burns.

tersburg) with a wavelength of 810 nm and a continuous mode of operation and microphotocoagulation.

High-density subthreshold laser coagulation and microphotocoagulation were performed over the entire area of the edema with high-density laser pulses (a distance of 0–1 irradiation spot diameter between the laser spots, and confluent nature of laser application were allowed). With microphotocoagulation, 10% of the “duty cycle” was used, the exposure time was 0.3 s, and the spot diameter was 100 μm. High-density subthreshold laser coagulation was performed in a continuous mode using the same procedure.

The main stage of treatment was preceded by a preliminary selection of the energy parameters for laser irradiation. The exposure parameters were considered as conforming ones if a subtle burn of the retina was observed in 1 of the 10 laser applications. The laser radiation power was 200–310 mW for high-density subthreshold laser coagulation and 2100–3000 mW for high-density microphotocoagulation. The number of laser burns was 200–800 per treatment session.

Following laser treatment, OCT was performed (HD-OCT Cirrus 4000, Carl Zeiss Meditec AG) to assess the changes occurring in the macular edema over a period of time. Upon completion of the procedure, fluorescein angiography (FA) of the retina (ImageNet, Topcon) and OCT-angiography (RTVue Xr, OptoVue) were performed.

Statistical analysis was performed with non-parametric data processing methods using the Statistica 6.0 software.

STUDY RESULTS

Following DLC and DMP, there were no significant differences in BCVA between the groups upon comparison after 2 ($p = 0.06$) and 4 months ($p = 0.1$).

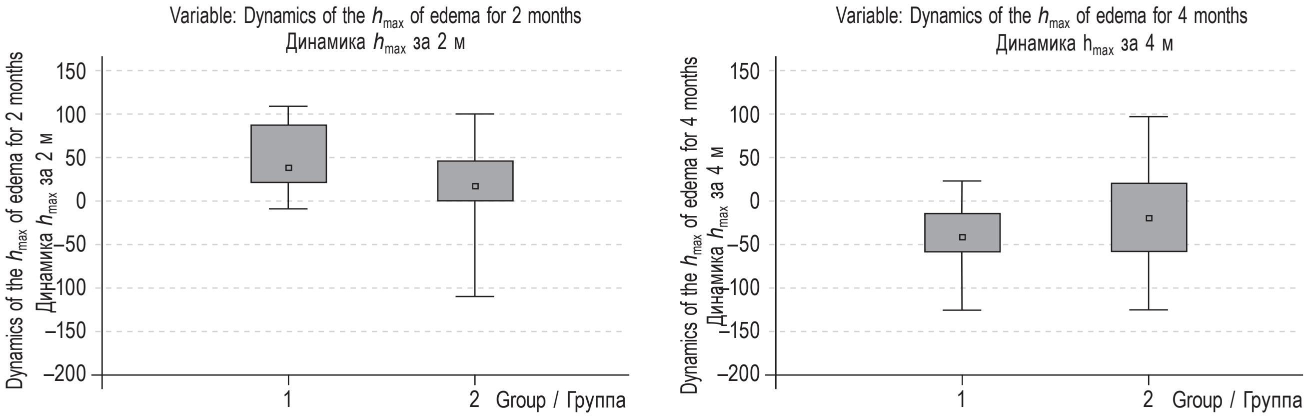
Following treatment consisting of the high-density subthreshold laser coagulation technique, the maximum thickness of retinal edema decreased significantly. Before the treatment, the edema was of 416.79 ± 55.11 μm; after 2 and 4 months, it was reduced to 398.82 ± 57.27 μm ($p = 0.007761$) and 393.85 ± 53.15 ($p = 0.010616$), respectively. A similar effect was observed on the retinal edema area. Before treatment, the area was of 1805.61 ± 917.97 pix.; after 2 and 4 months, the area reduced to 1442.27 ± 825.96 pix. and 1165.42 ± 727.61 pix. ($p = 0.000001$), respectively.

After 2 months, the central retinal thickness significantly decreased from 258.0 ± 70.29 to 242.85 ± 62.71 μm ($p = 0.00248$). However, BCVA following treatment did not change significantly.

Comparative analysis of the OCT morphometric indices of retinal edema, the examination being performed 2 and 4 months following treatment which consisted of high-density subthreshold laser coagulation (810 nm) and high-density microphotocoagulation (810 nm), revealed comparable pretreatment parameters and the absence of changes in the regression of the macular edema between the 2 groups (Figs. 1–3).

FA and OCT-angiography (17 eyes) performed 1 month following subthreshold DLC revealed no atrophic alterations in the pigment epithelium in 14 eyes, and showed a decrease in the number of microaneurysms in 10 eyes (Fig. 4).

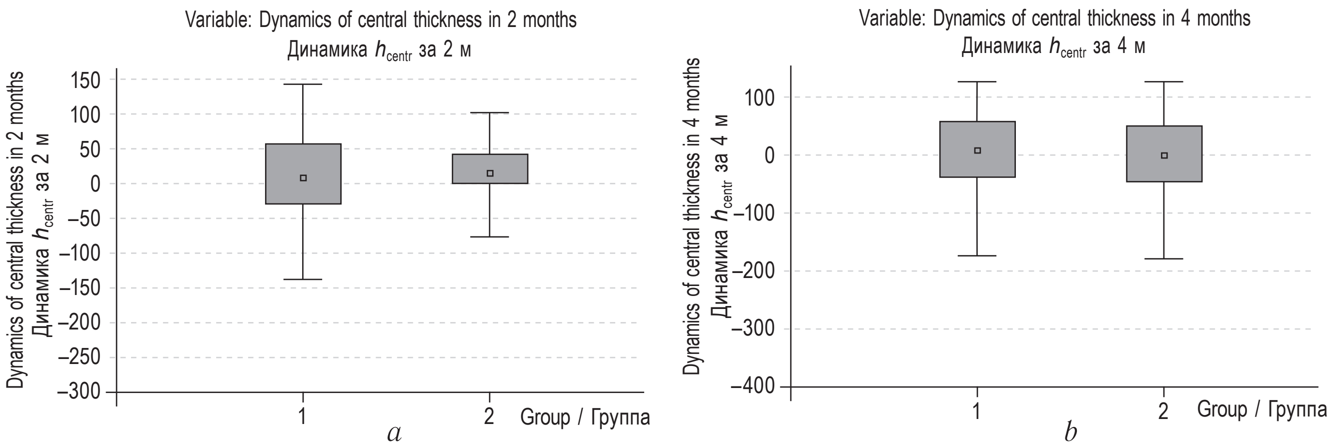
FA performed before and 1 month following subthreshold DLC (7 eyes) revealed the absence of foci of atrophy in the areas of the final test coagulate and retinal edema treated by applying confluent subthreshold coagulates (Fig. 5).



a *b*

Fig. 1. Dynamics of the maximal retinal edema height after high-density microphotocoagulation and after high-density subthreshold laser coagulation: *a* – in 2 months; *b* – in 4 months

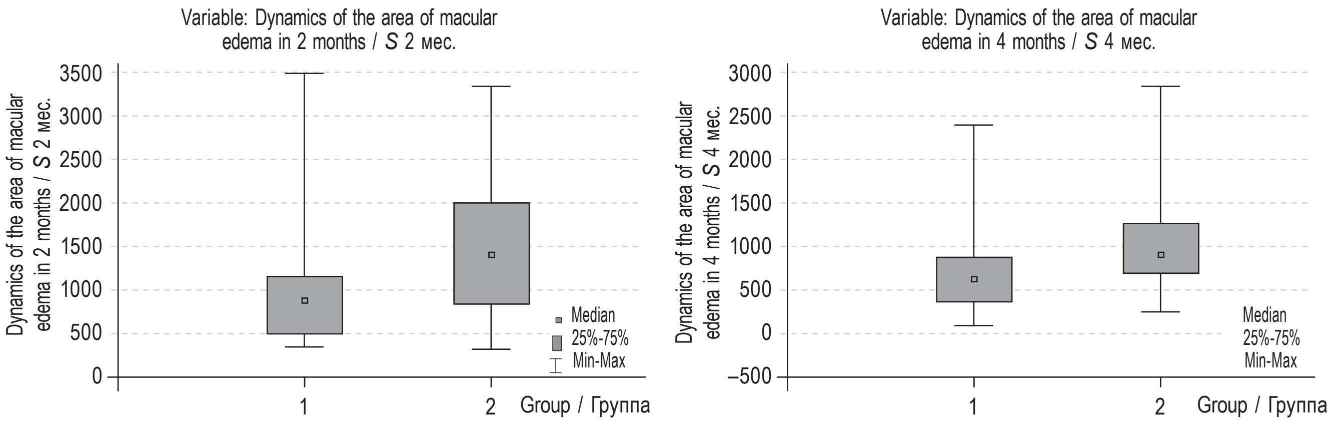
Рис. 1. Динамика максимальной высоты отёка сетчатки после микрофотокоагуляции высокой плотности и субпороговой лазерной коагуляции высокой плотности: *a* — через 2 месяца; *b* — через 4 месяца



a *b*

Fig. 2. Dynamics of the central retinal thickness after high-density microphotocoagulation and after high-density subthreshold laser coagulation: *a* – in 2 months; *b* – in 4 months

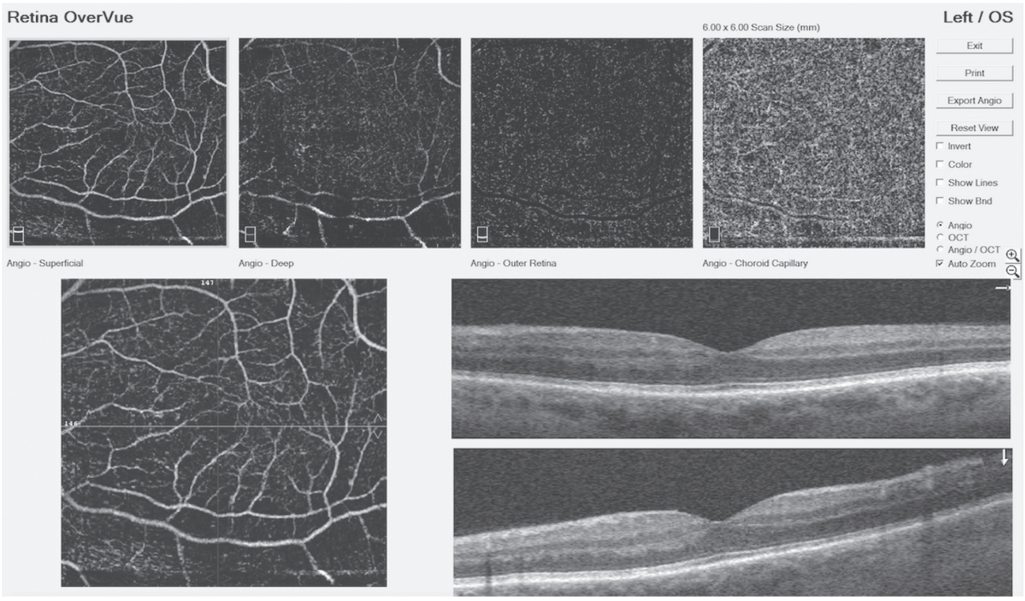
Рис. 2. Динамика центральной толщины сетчатки после микрофотокоагуляции высокой плотности и субпороговой лазерной коагуляции высокой плотности: *a* — через 2 месяца; *b* — через 4 месяца



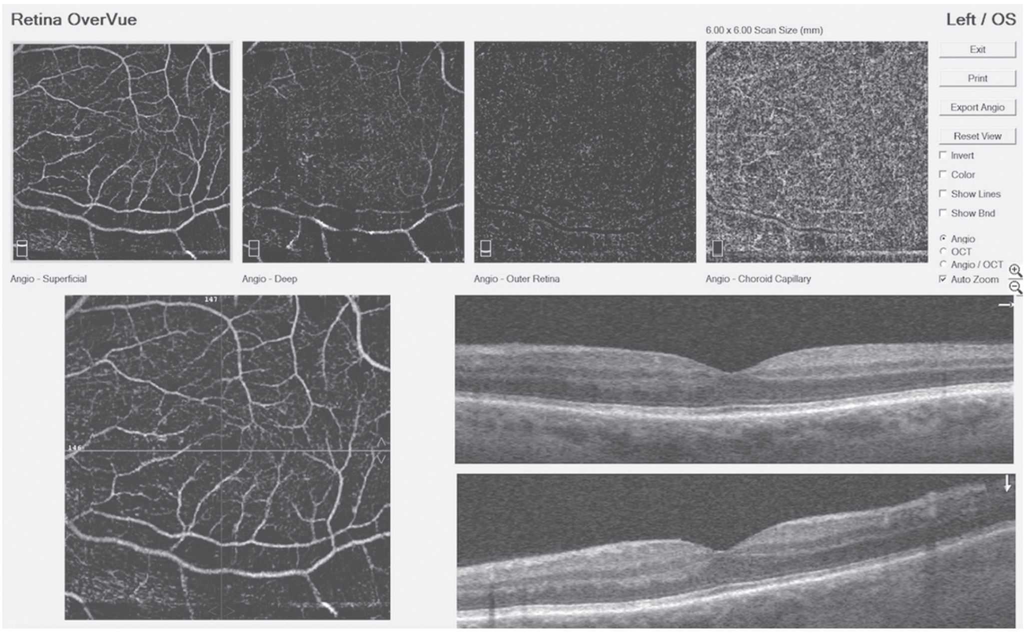
a *b*

Fig. 3. Dynamics of the macular edema area after high-density microphotocoagulation and after high-density subthreshold laser coagulation: *a* – in 2 months; *b* – in 4 months

Рис. 3. Динамика площади макулярного отёка после микрофотокоагуляции высокой плотности и субпороговой лазерной коагуляции высокой плотности: *a* — через 2 месяца; *b* — через 4 месяца



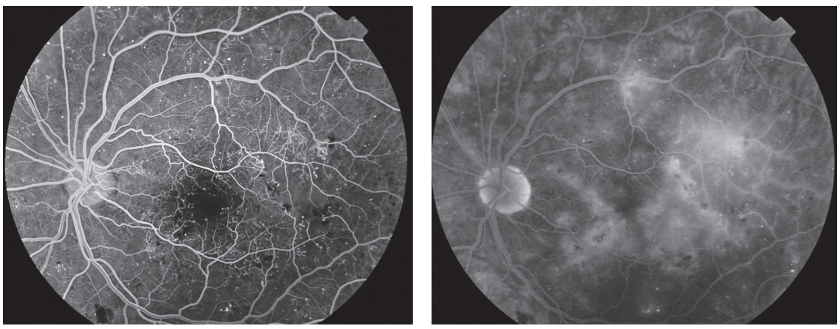
a



b

Fig. 4. Angio-OCT results after high-density subthreshold laser coagulation: *a* – before treatment; *b* – in 1 month after treatment

Рис. 4. Результаты ОКТ-ангиографии после выполнения субпороговой лазерной коагуляции высокой плотности: *a* — до лечения; *b* — через 1 месяц



a *b*

Fig. 5. Fluorescein angiography: *a* – before treatment (arteriovenous and late venous phases); *b* – in 1 month after subthreshold high-density laser coagulation

Рис. 5. Флюоресцентная ангиография: *a* — до лечения (артериовенозная и поздняя венозная фазы исследования); *b* — через 1 месяц после проведения субпороговой лазерной коагуляции высокой плотности

CONCLUSION

High-density subthreshold laser coagulation (810 nm) and high-density microphotocoagulation (810 nm) methods lead to a comparable reduction of DME during the follow-up period of 4 months.

Based on the complex application of modern diagnostic methods (OCT, FA, and angio-OCT), it is established that high-density subthreshold laser coagulation (810 nm) with individual selection of laser power does not have any damaging effect on the chorioretinal complex structures.

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