NEW APPROACHES TO SELECTIVE LASER TRABECULOPLASTY

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Abstract

Selective laser trabeculoplasty (SLT) is the "golden standard" of laser glaucoma surgery. Its efficacy can be compared to pharmacological therapy, while in some cases its advantages may even lead to a more stable hypotensive effect. SLT may be used as a primary treatment for primary open-angle glaucoma patients and patients with ocular hypertension, while also considered safe and effective in cases when a repeat procedure is required. SLT may potentially decrease the demand for antiglaucoma drugs, improve patient's response to treatment, make the treatment more comfortable and overall increase the patient's quality of life. New modifications of standard laser treatment procedures have been emerging lately. This article summarizes scientific data on the efficacy and safety of the new generation of laser trabeculoplasty. It specifies the charateristics of micropulse laser trabeculoplasty (MLT), pattern-scanning laser trabeculoplasty (PLT) and titanium-sapphire laser trabeculoplasty (TSLT) and recounts the latest research dedicated to them.

Keywords: glaucoma, selective laser trabeculoplasty, micropulse laser trabeculoplasty, pattern-scanning trabeculoplasty, titanium-sapphire laser trabeculoplasty.

For citations: Petrov S.Yu., Poleva R.P. New approaches to selective laser trabeculoplasty, *Biomedical photonics,* 2018, T. 7, No. 3, pp. 47-56 (in Russian). doi: 10.24931/2413–9432–2018–7–3–47–56.

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НОВЫЕ ПОДХОДЫ К СЕЛЕКТИВНОЙ ЛАЗЕРНОЙ ТРАБЕКУЛОПЛАСТИКЕ

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Резюме

Селективная лазерная трабекулопластика (СЛТ) является «золотым стандартом» лазерной хирургии глаукомы. Её эффективность сопоставима с медикаментозной терапией; в отдельных случаях она обладает рядом преимуществ, способствующих созданию более стойкого гипотензивного эффекта, и может рассматриваться в качестве стартовой терапии первичной открытоугольной глаукомы и офтальмогипертензии. СЛТ безопасна и эффективна при повторном проведении процедуры. Потенциально СЛТ способна снизить потребность в антиглаукомных препаратах, повысить приверженность лечению и сделать его более комфортным, что в конечном итоге может улучшить качество жизни. В последние годы завоевывают популярность новые модификации стандартных лазерных технологий. В приводимом ниже обзоре суммированы данные научной литературы о безопасности и эффективности лазерной трабекулопластики нового поколения. Приведены характеристики микроимпульсной лазерной трабекулопластики, паттерн-сканирующей лазерной трабекулопластики и титан-сапфировой лазерной трабекулопластики и описаны посвященные им исследования последних лет.

Ключевые слова: глаукома, селективная лазерная трабекулопластика, микроимпульсная лазерная трабекулопластика, паттерн-сканирующая лазерная трабекулопластика, титан-сапфировая лазерная трабекулопластика.

Для цитирования: Петров С.Ю., Полева Р.П. Новые подходы к селективной лазерной трабекулопластике // Biomedical photonics. – 2018. – Т. 7, № 3. – С. 47-56. doi: 10.24931/2413–9432–2018–7–3–47–56.

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Introduction

The widespread use of laser technology in the surgical treatment of glaucoma to reduce intraocular pressure began in the 1970s, with argon laser trabeculoplasty (ALT). The efficacy and safety of ALT was demonstrated during a large multicenter prospective clinical study on the use of lasers for the treatment of glaucoma (Glau-

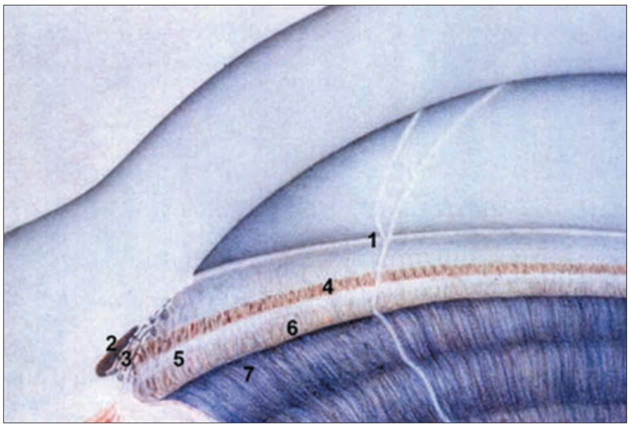

Рис. 1. Строение угла передней камеры глаза:
1 – переднее пограничное кольцо Швальбе, 2 – вырезка,
3 – трабекула, 4 – Шлеммов канал, 5 – склеральная шпора,
6 – цилиарное тело, 7 – периферия корня радужки
Fig. 1. Anterior chamber angle anatomy:
1 – anterior Schwalbe's annular line, 2 – incisura, 3 – trabecular meshwork, 4 – Schlemm's canal, 5 – scleral spur, 6 – ciliary body, 7 – peripheral part of the iris root

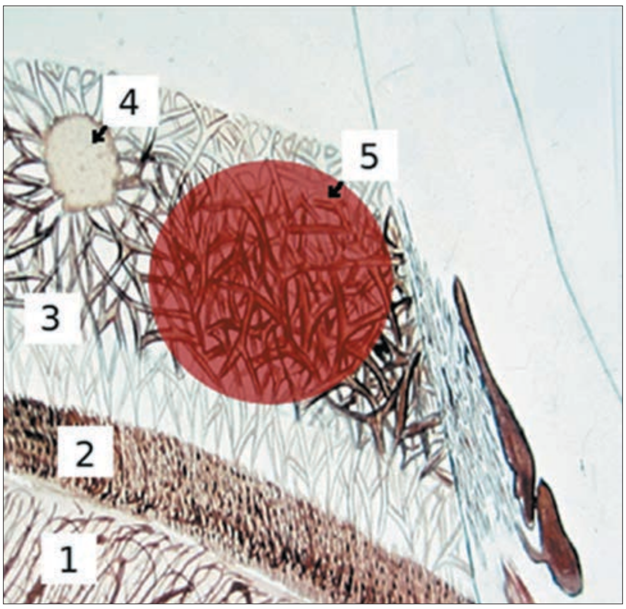

Рис. 2. Схема нанесения лазерных коагулятов при трабекулопластике:
1 – радужка, 2 – цилиарное тело, 3 – трабекулярная сеть,
4 – лазеркоагулят после аргон-лазерной трабекулопластики (коагулирующее поражение трабекулы после термического ожога),
5 – воздействие при СЛТ (селективное воздействие на пигментированные меланинсодержащие клетки без последующих дефектов трабекулы)
Fig. 2. Scheme of applying laser coagulation in trabeculoplasty:
1 – iris, 2 – ciliary body, 3 – trabecular meshwork, 4 – laser burn after ALT (trabecular coagulation defect after the thermic burn),
5 – SLT laser exposure zone (selective action on the melaniferous cells without any subsequent visual or structural damage)

coma Laser Trial) [1], and ALT remained the method of choice for open-angle glaucoma for a long time [2, 3].

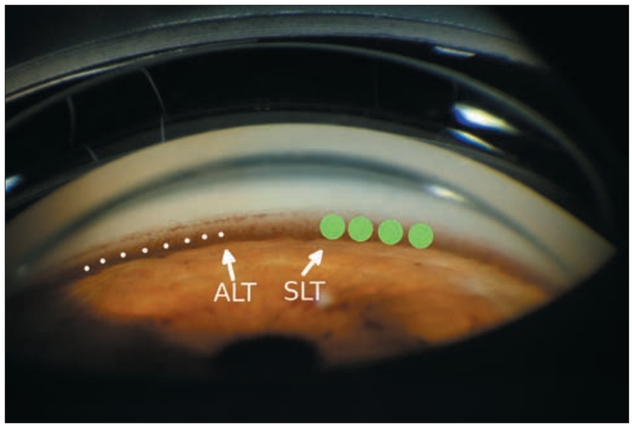

Рис. 3. Сравнение размеров светового пятна при АЛТ и СЛТ
Fig. 3. Comparison of the ALT and SLT light spot sizes

However, despite the positive results of studies, this technique has not replaced the instillation of antihypertensive drugs as a starting treatment for primary open-angle glaucoma (POAG), which was associated with the emergence of more modern and effective means of drug therapy and with a number of shortcomings of ALT itself. Interest in laser treatment has increased again in recent years with the advent of new techniques that do not have the disadvantages of ALT, such as selective laser trabeculoplasty (SLT) [4]. With the same hypotensive effect of SLT at 360° and ALT at 180°, SLT only minimally injures endothelial cells and leaves the trabecular meshwork intact, which, in turn, leads to less severe inflammation in the anterior chamber after the procedure, while ALT in some cases can lead to the formation of peripheral anterior synechia and scarring of the trabecular meshwork [5–7]. The schemes showing the location of the eye angle structures, the application of laser coagulates during trabeculoplasty and a comparison of the sizes of the light spot are provided in Fig. 1, 2 and 3, respectively.

With efficacy similar to that of drug therapy and SLT [8–11], laser intervention has several advantages, such as the absence of problems associated with adherence to treatment or being unable to purchase drugs in a timely manner, and thus contributes to a more stable hypotensive effect. Moreover, in recent years, SLT is often considered as the first line of treatment for POAG and ophthalmic hypertension [12-14]. The comparability of the results of the use of drug and laser techniques has been repeatedly proven in studies such as the Glaucoma Laser Trial and Ocular Hypertension Treatment Study, as well as in numerous research papers by a number of foreign and

Russian scientists. Moreover, in the studies of J. Tsai and R. Lee, laser trabeculoplasty made it possible to achieve a more stable decrease in intraocular pressure (IOP) [10, 15].

Despite somewhat limited data regarding repeated SLT with a decrease in the antihypertensive effect in the long term, it is believed that the procedure can be repeated annually, being a safe and effective option for maintenance therapy [16–18]. Potentially, SLT can reduce the need for anti-glaucoma drugs, increase treatment adherence and make it more comfortable, which can ultimately improve the quality of life. In recent years, a wide variety of studies have been conducted on the safety and efficacy of SLT in various types of glaucoma in order to study the possible ways of using the treatment with the most beneficial effect by optimizing the level of laser energy, identifying prognostic factors for a successful outcome, determining the nature of the correlation of IOP if the procedure is performed in both eyes and assessment of the impact on other glaucoma progress risk factors (for example, IOP fluctuations) [19–28].

The introduction of minimally invasive glaucoma surgery into clinical practice has not led to a gradual decrease in the frequency of trabeculoplasty. Although the indications for these procedures are partially the same, laser trabeculoplasty has several advantages: it is less invasive, being an extraocular manipulation, is not combined with cataract extraction and is a cheaper treatment option. Trabeculoplasty still plays an important role in various glaucoma treatment strategies, and thanks to the achievements of modern science, its efficacy and safety continue to grow.

New generation laser trabeculoplasty procedures that help reduce IOP and drug demand include micropulse laser trabeculoplasty (MLT), pattern-scanning laser trabeculoplasty (PLT), and titanium-sapphire laser trabeculoplasty (TSLT). The review below summarizes the scientific literature data on the safety and efficacy of new generation laser trabeculoplasty.

Micropulse laser trabeculoplasty

The technology of micropulse laser trabeculoplasty (MLT) involves the supply of energy in the form of repeating subthreshold micropulses with interruptions between them. Such a scheme can reduce the accumulation of thermal energy, control the temperature increase and avoid cicatricial damage to eye tissue [29, 30]. The effect from the use of a new generation of laser trabeculoplasty is generated due to stimulation of the cell biochemical cascade mediated by cytokines, which ultimately helps to increase the aqueous outflow with less tissue damage [31]. According to scanning electron microscopy, MLT does not cause coagulation damage to the trabecular meshwork [32], which is the advantage of MLT compared to continuous-wave laser technologies such as ALT, which lead to mechanical damage and scarring of trabecular structures [33]. Moreover, despite the fact that SLT also does not lead to scarring, it is still inferior to MLT in terms of safety, since the latter does not damage pigment cells of the trabecular meshwork [34].

For MLT, there is no mandatory endpoint for treatment in the form of tissue blanching at the site of exposure or the formation of a gas-vapor bubble in the trabecula structure. Since the inflammatory process is minimal or absent, anti-inflammatory drugs after MLT are not necessary [35].

The advantages of MLT over SLT are especially pronounced in patients with an increased risk of IOP elevation after the laser procedure, in particular, those with pronounced pigmentation of the trabecular meshwork. In the first studies, MLT showed promising results for open-angle glaucoma. It is rightfully suggested that, based on the results of large-scale multicenter studies currently being conducted, MLT will prove to be just as effective as SLT, but safer [35–36].

MLT is normally performed with the following laser settings: spot diameter: 300 μm (with SLT, spot diameter is 400 μm), exposure: 300 ms, power: 1000 mW, fill factor: 15%. The fill factor is a value that characterizes the degree of laser use in the treatment process. N.M. Radcliffe recommends application of 100 individual coagulates around the circumference (360°), while I.K. Ahmed suggests making them confluent [37, 38]. Like other types of laser trabeculoplasty, MLT requires only local anesthesia. If the patient experiences pain during the procedure, the laser energy is gradually reduced.

The efficacy of MLT is confirmed by the results of various studies. In a study by A. M. Fea et al. with the involvement of 20 patients, the application of confluent coagulates was carried out with a subthreshold micropulse laser exposure (laser wavelength: 810 nm) in the lower segment of the trabecular meshwork anterior section at 180°. The laser characteristics were the following: spot diameter 200 μm, power 2000 mW, exposure 200 ms, fill factor: 15%, number of cauterizations: 70–84. In 15 patients (75%), MLT was successful, as within 12 months the IOP level decreased by about 20%. In 5 cases (25%), MLT was found to be unsuccessful, in 4 patients during the first week and in 1 patient within 6 months [39].

D. Gossage et al. presented biennial results of MLT (wavelength 532 nm) performed on 18 eyes with POAG. The laser power was 300 mW, 700 mW and 1000 mW. In the group which had MLT, conducted with laser power of 1000 mW, the results were statistically significantly better: after 24 months, the IOP decreased by 24% [40].

According to preliminary data obtained by P. Coombs in his comparison of MLT and SLT, the efficacy of the techniques is similar. In 12 eyes, MLT was performed, and SLT in 14 eyes. In both groups, a significant decrease in IOP was observed, by an average of 3.9 mm Hg and 2.6 mm Hg, respectively. After MLT, the need for medications decreased slightly more than after SLT (by 0.6 and 0.1, respectively) [41].

In Abuja, a study of E. Olufemi was held, which involved 34 cycles of laser therapy performed on 30 eyes of 16 patients. The main selection criterion was failure to compensate IOP with maximum antihypertensive therapy. One hour after the completion of the procedure, the IOP decreased by an average of 3.2 mm Hg. and subsequently remained at a steady level reliably decreased by 17.2% compared to the base level of IOP [42].

There are also reports in the literature about the efficacy of MLT performed after SLT [43].

During a short-term prospective controlled pilot study D. Ingvoldstad compared the efficacy and safety of MLT and ALT performed after randomization in 21 eyes. MLT was performed with the following laser settings: spot diameter 300 µm, power 2000 mW, fill factor; 15%, number of cauterizations: 66 (applied at 180° from the nasal side). After 3 months, the IOP in both groups decreased by 20%, there were no statistically significant differences between the groups. Pain during the procedure and the inflammatory process in the postoperative period (cell suspension or opalescence of the anterior chamber moisture) are expressed insignificantly, and it was noted that after MLT these phenomena were much less common [44].

A study by E. Rantala suggests that 180° MLT may not be effective in open-angle glaucoma. According to the data obtained in this retrospective study, a decrease in IOP by ≥20% was observed only in 1 out of 40 cases (2.5%), and over the 19 months of observation IOP decreased by ≥ 3 mm Hg only in 3 people (7.5%). The final conclusion about the lack of effect from MLT was made after approximately 3 months. In the sample described, the initial mean IOP level was relatively low (21.8 ± 4.9 mm Hg, with the range of 14–34 mm Hg), with patients using an average of 2.0 ± 1.3 drugs. MLT was performed with the following laser settings: spot diameter 300 µm, power 2000 mW, exposure 200 ms, fill factor: 15%, number of cauterizations: 60–66 (applied at 180°) [45].

In general, researchers agree on the safety of MLT in patients with open-angle glaucoma. A. M. Fea et al. report an increase in IOP and opalescence of moisture in the anterior chamber after MLT for pigmented glaucoma; IOP levels returned to normal after 3 days with the use of systemic drugs. MLT is well tolerated, with the exception of a burning or heating sensation during the procedure, which was experienced by 4 patients (20% of cases) [39]. No data is found in the scientific literature in respect of late postoperative complications of MLT.

Pattern-scanning laser trabeculoplasty

The process of pattern-scanning laser trabeculoplasty (PLT) involves applying laser coagulates to the trabecular meshwork according to a predefined pattern under computer control. Today, PLT is most commonly used for massive laser fundus interventions, such as pan-retinal laser coagulation (PRLC). In recent years, its use in the treatment of patients with POAG has also become popular, since the complete treatment of the trabecular meshwork with the calculated alignment of each pattern and automated rotation makes it possible to avoid both overlapping of coagulates and the formation of excessively wide gaps between them [46]. It is suggested that the cellular response to PLT is accompanied by less severe scarring and coagulation damage. With PLT, the pulse duration is much shorter compared to ALT, which reduces the degree of thermal damage. The efficacy of the procedure is due to the fact that approximately 10 times more laser coagulates are applied to the area of the trabecular meshwork [47].

PASCAL semi-automated pattern-scanning system (Optimedica Corp, USA) is based on a doubled frequency Nd-YAG laser (continuous exposure to a green beam with a wavelength of 532 nm or a yellow beam with a wavelength of 577 nm). The spot diameter is 100 µm, the exposure is 5–10 ms, and the power is calibrated until at 10 ms trabecular meshwork blanching occurs in the lower segment of the eye, where the laser permeability is the highest. Tissue blanching occurs within 10 ms at a power level of less than 1 W. The exposure time is then reduced to 5ms, so sub-visible treatment spots are produced. Next, a computer-controlled pattern scanning algorithm is used. Each pattern includes two or three rows (24–66 coagulates) of arcuate coagulates and has a length of 22.5°. After the pattern is completed, the beam automatically rotates by 22.5°. 8 adjacent coagulation segments correspond to 180° of the trabecular meshwork, and 16 segments correspond to 360° [48].

In a prospective pilot study conducted by M. Turati, 360° PLT (16 segments, wavelength 532 nm) was performed in 47 eyes of 25 patients. During the 6 months of observation, the mean IOP decreased from 21.9±4.1 to 15.5±2.7 mm Hg. However, 17 eyes were excluded from the study due to the development of viral conjunctivitis or the need for additional anti-glaucoma therapy in connection with an increase in IOP after the treatment. In 20 of 30 eyes (67%), the average IOP level decreased by 24% [49].

The results of several studies have been published, in which the efficacy of ALT and PLT is compared. According to a retrospective study by C. Barbu, after a PLT performed in 20 eyes of 20 patients, over 8 weeks, the average IOP decreased from 20.2±1.1 to 15.6±0.8 mm Hg ($p < 0.001$). There was no statistically significant difference between the results of PLT and ALT ($p = 0.26$) [46]. According to the study by J. Kim, after 6 months, PLT reduces the mean IOP by 27.1%, from 24.1 ± 4.2 to 17.6 ± 2.6 mm Hg. ($p = 0.03$). There was no statistically significant difference found between the results of PLT and ALT [50]. A study by K. Mansouri and T. Shaarawy, performed on 58 eyes with primary and secondary glaucoma, showed similar efficacy and safety profiles of PLT and SLT with a slightly more pronounced antihypertensive effect of PLT 1 month and 3 months after the treatment, as well as with better tolerability of the PLT procedure by patients [51].

T. Turati et al., it was been demonstrated that PLT did not lead to IOP increase or inflammation [49]. The results of a retrospective study of a series of clinical cases (9 patients, 11 eyes) show that IOP decreased by 31% within 6 months after PMT (wavelength 577 nm). There was no statistically significant difference between the number of drugs used before and after the procedure (2.6 and 2.8, respectively). In one case, there was a transient rise in IOP after the performance of PLT. No cases of the formation of peripheral anterior synechia or damage to the corneal endothelium have been reported [47].

Thus, PLT is an effective method of reducing IOP. The positive results of the first studies will give rise to larger-scale controlled studies of its safety, efficacy and the long-term stability of the antihypertensive effect.

Titanium-sapphire laser trabeculoplasty

The advantage of TSLT is a deeper (about 200 µm) penetration of laser radiation due to the wavelength used (790 nm, i. e., a spectrum close to infrared radiation), while the energy comes in the form of pulses with a duration of 5 to 10 ms . Such characteristics make it possible to reach the juxtacanalicular meshwork and the inner wall of the Schlemm's canal. Then, the laser is selectively absorbed by pigmented phagocytic cells, which protects the trabecular meshwork from damage [52].

The laser beam is focused on the pigmented trabecular meshwork and produces 50 separate (not overlapping) coagulates at 180° on the meshwork. The diameter of the spot at a depth of 200 µm is smaller than in the case of SLT or MLT. The laser energy is 50 mJ, but, if necessary, it can be reduced to 30 mJ. The treatment endpoint of treatment is the formation of mini-bubbles or a visible burn of the pigment of the trabecular meshwork [52, 53].

In 2009, M. Goldenfeld et al. published the data obtained during the pilot study lasting 15 months, which was aimed at comparing the efficacy of TSLT and ALT. It was shown that after TSLT, the IOP level decreases on average by 8 mm Hg. (32%), and after ALT, by 6.5 mm Hg (25%). No statistically significant difference between the groups wqas found. The number of drugs used after trabeculoplasty decreased, albeit not significantly (from 1.4 ± 1.0 to 1.3 ± 1.0 in the TSLT group and from 2.1 ± 0.8 to 2.0 ± 0.8 in the ALT group) [52].

An increase in IOP after TSLT was observed in one patient. No cases of the formation of peripheral anterior synechia in the postoperative period are reported. No long-term complications (within 2 years after TSLT) were recorded [53, 54].

The results of histological studies of G. Simon on donor eyes indicate insignificant anatomical changes in the trabecular meshwork due to laser exposure when thermal damage is excluded, which suggests the possibility of multiple repeated TSLT procedures if the hypotensive effect decreases [55].

Since TSLT is a relatively new technology, only limited amount of information can be found in its respect

Таблица
Сравнение характеристик модификаций лазерной трабекулопластики
Table
Comparison of the characteristics of laser trabeculoplasty modifications

	АЛТ ALT	СЛТ SLT	МЛТ MLT	ПЛТ PLT	ТСЛТ TSLT
Длина волны **Wavelength**	488–512 нм 488–512 nm	532 нм 532 nm	532, 577 или 810 нм 532, 577 or 810 nm	532 или 577 нм 532 or 577 nm	790 нм 790 nm
Продолжительность импульса **Pulse duration**	0,1 с 0.1 s	3x10^{-9} с 3x10^{-9} s	200–300x10^{-3} с 200–300x10^{-3} s	5–10x10^{-3} с 5–10x10^{-3} s	5–10x10^{-3} с 5–10x10^{-3} s
Мощность импульса (мВт) или количество энергии на 1 импульс (мДж) **Pulse power (mW) or pulse energy (mJ)**	400–1200 мВт 400–1200 mW	0,1–2,0 мДж 0.1–2.0 mJ	1000–2000 мВт 1000–2000 mW	500–1000 мВт 500–1000 mW	30–50 мДж 30–50 mJ
Размер лазеркоагулята **Laser coagulant size**	50 мкм 50 µm	400 мкм 400 µm	200–300 мкм 200–300 µm	100 мкм 100 µm	200 мкм 200 µm
Рекомендуемое количество лазеркоагулятов **Recommended number of laser coagulants**	50–100 равномерно рассредоточенных коагулятов 50–100 uniformly spread coagulants	50 или 100 сливных лазеркоагулятов 50 or 100 merging laser coagulants	60–100 одиночных или сливных коагулятов 60–100 independent or merged coagulants	8 или 16 сегментов 8 or 16 segments	50 граничащих, но не сливающихся коагулятов 50 bordering but not merging coagulants
Величина угла воздействия на трабекулярную сеть **Angle of effect on the trabecular network**	180–360°	180° или 360° 180° or 360°	180° или 360° 180° or 360°	180° или 360° 180° or 360°	180°
Реакция тканей **Tissue reaction**	Очаговая депигментация, возможно образование пузырьков газа («эффект попкорна») Focal depigmentation, possible formation of gas bubbles ("popcorn effect")	Небольшие пузырьки. Мощность воздействия калибруется до появления пузырьков в точке воздействия, затем мощность поступательно снижается с шагом 0,1 мДж до порога отсутствия реакции Small bubbles. The affecting power is calibrated until the appearance of bubbles at the affected point, then the energy is gradually decreased in steps of 0.1 mJ until a threshold of no reaction	Видимая реакция тканей отсутствует No visible tissue reaction	После калибровки мощности видимая реакция тканей отсутствует No visible tissue reaction after power calibration	Образование мини-пузырьков или видимого ожога пигмента трабекулярной сети Formation of mini-bubbles or visible burn of the trabecular network pigment

Реакция/ Осложнения **Reaction / Complications**	Офтальмогипертензия, воспаление в передней камере, в отдельных случаях возможно повреждение эндотелия, образование периферических передних синехий и рубцевание трабекулярной сети Ocular hypertension, inflammation in the anterior chamber, in some cases, damage to the endothelium, the formation of peripheral anterior synechiae and scarring of the trabecular network	Офтальмогипертензия, воспаление в передней камере Ocular hypertension, inflammation in the anterior chamber	Жжение. Редко – офтальмогипертензия, воспаление в передней камере Burning sensation. Rarely – ocular hypertension, inflammation in the anterior chamber	Возможна транзиторная реактивная офтальмогипертензия Possible transient reactive ocular hypertension	Возможна реактивная офтальмогипертензия Possible reactive ocular hypertension

in the scientific literature, and, therefore, large-scale randomized trials are necessary to make meaningful conclusions about its efficacy and safety, including in the long term.

Conclusion

Selective laser trabeculoplasty once revived the interest in laser methods of treating open-angle glaucoma and today is the gold standard of laser surgery. According to the first studies, the developing new technologies such as MLT, PLT and TSLT reduce the IOP level with comparable efficacy, often have better tolerance and are less likely to provoke complications including postoperative inflammation and IOP increase. A comparison of the characteristics of the listed laser trabeculoplasty modifications is privided in table.

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