ARTYKUŁ PRZEGLĄDOWY REVIEW ARTICLE
DOI: 10.24292/01.OT.311220.11

Laser trabeculoplasty and subthreshold transscleral cyclophotocoagulation – the new therapeutic options are modifying therapeutic algorithm in glaucoma

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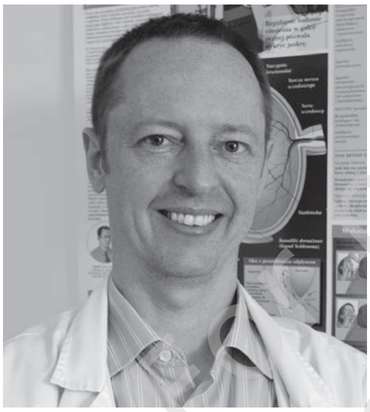


HIGHLIGHTS
Laser trabeculoplasty (SLT and MLT) as well as subthreshold TS-CPC and are new, safe and effective procedures in glaucoma laser therapy being a good alternative for medications and classic surgical methods.

ABSTRACT
Selective laser trabeculoplasty (SLT) and micropulse laser trabeculoplasty (MLT) are well established, non-invasive laser procedures in glaucoma, but their place in the therapeutic algorithm still evolves. Lately published multicenter randomized clinical trials indicate the need to consider laser trabeculoplasty as the first-line treatment before medications in primary open-angle glaucoma an ocular hypertension due to its favorable safety profile, efficacy and cost-effectiveness. Subthreshold transscleral cyclophotocoagulation (present on the market under different brand names: SubCyclo® TS-CPC [Quantel, France] or Cyclo G6® mTS-CPC [Iridex, USA]) is an antiglaucomatous laser procedure, recently arousing more and more interest in ophthalmologists as a new non-invasive method in our therapeutic portfolio. This new device utilizes 810 nm diode laser beam, fractionated into ultra-short pulses, resulting in low energy spots without causing ciliary body coagulation. Subthreshold (or subliminal) energy delivered during the session spares the tissue due to very limited local heat accumulation zone and therefore this procedure may be repeated. Laser energy partially disables aqueous producing ciliary epithelium and opens supraciliary space thus activating the additional outflow facility. Subthreshold TS-CPC in several clinical trials proved to be effective in lowering the intraocular pressure and devoid of significant sight threatening side effects, comparing to the classical thermal diode cyclophotocoagulation method.

Key words: glaucoma, laser trabeculoplasty, subthreshold transscleral cyclophotocoagulation

INTRODUCTION

In recent years, the glaucoma treatment marketplace has been inundated with new laser technologies, which have excited physicians and surgeons as they have completely reinvented and invigorated the glaucoma treatment paradigm. Today, glaucoma is on the rise and continues to be one of the leading causes of blindness and vision loss worldwide. According to the American Academy of Ophthalmology, the estimated number of people with glaucoma around the world will increase to 112 mln by the year 2040 [1].

New glaucoma laser designs were subtle but meaningful. Some focused more on the type of laser (wavelength), while others went further to focus on which tissue was targeted (iris, ciliary body, trabecular meshwork, sclera). Some lasers were developed as non-invasive for use in an outpatient setting, and others were considered incisional requiring traditional surgery. One of the more critical variables was how the targeted tissue was affected and are categorized as causing thermal coagulation or no tissue destruction, the latter allowing for future, repeatable treatments. With new laser options hitting the market, laser treatment is now being considered as a I line level of intervention within the glaucoma treatment decision tree. It is crucial at this point to take a good look at which lasers are most effective toward patient safety and outcome.

As mentioned, lasers were developed for its effects on target tissues. The Nd : YAG laser peripheral iridotomy and the Argon laser peripheral iridoplasty were effective on the iris. For targeting the sclera, laser-assisted filtration surgery, such as non-penetrating deep sclerectomy and trabeculectomy (excimer, erbium, CO_2), were available but not widely used.

LASER TRABECULOPLASTY

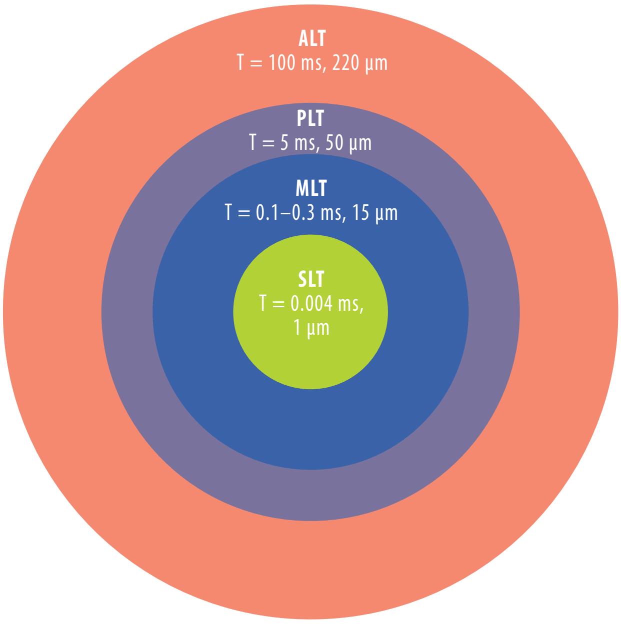
For the most part, lasers were designed to target the TM or ciliary body. The argon laser trabeculoplasty (ALT), pattern laser trabeculoplasty (PLT), micropulse laser trabeculoplasty (MLT), and the selective laser trabeculoplasty (SLT) all target the TM. Subthreshold SLT is widely used today targeting TM. The other targeted tissue of interest with newer lasers is the ciliary body. Endoscopic cyclophotocoagulation and transscleral diode laser are well-known laser methods targeting the ciliary body. A newest method is subthreshold (or subliminal) cyclophotocoagulation (SubCyclo by Quantel or Micropulse TS-CPC by Iridex).

Laser trabeculoplasty has evolved since the 1970s and has varied in laser types and wavelengths with critical differences. The significant difference is the tissue effect and whether the laser energy destroys, stimulates, or preserves the targeted tissue. The effective outcomes are based on spot size, impact energy, total energy, inflammation caused, and if you can repeat similar procedures in the future. What we've learned in laser trabeculoplasty is that the older methods do not offer the flexibility needed for today's glaucoma patient. Inflammation has shown to be clinically significant in both ALT and PLT methods and is not repeatable. The newer SLT or MLT have demonstrated no inflammation and offers repeatability by utilizing larger spot size with less impact and total energy.

Laser-induced collateral thermal effect is a very important issue. One of the most critical elements that affect the tissue during any laser treatment is impact duration. Impact duration is directly responsible for the heat accumulation zone, which is the area around the target treatment spot and how much the thermal effect spreads through the surrounding tissue. Of the methods available today, SLT is the only method that produces a very limited thermal accumulation zone of 1 μm, which is extremely important for the health of the tissue and the possibility of treatment repetitions. Comparatively, PLT produces a thermal accumulation of 50 μm, and ALT produces at 220 μm, which covers the entire TM (fig. 1). The wider the heating zone, the more severe the thermal effect in surrounding tissue which is an unwanted result.

FIGURE 1

Heat accumulation zones in tissue in different laser procedures in glaucoma.



SLT is based on the principle of selective photothermolysis, which relies on selective absorption of a short laser pulse to generate and spatially confine heat to pigmented targets. SLT mechanism causes minimal thermal diffusion and no collateral tissue destruction. Furthermore, it induces cytokine release and macrophages activation, which causes the cleaning of extracellular debris. One of the most important effects of SLT is the stimulation of cell division, increasing and rejuvenating TM and Schlemm's canal porosity. All these factors contribute to increased trabecular outflow and a hypotensive effect. Since its introduction, SLT superseded the other laser trabeculoplasty techniques with fewer adverse events, greater ease of use, and improved repeatability [1]. These indicators lead us to believe that SLT should be considered as an initial treatment for primary open-angle glaucoma, ocular hypertension, and pigmentary glaucoma [2].

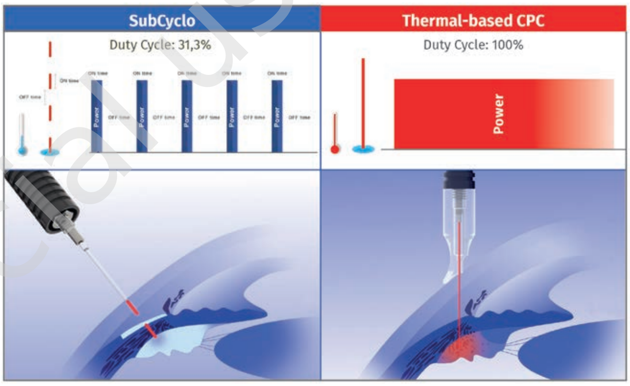
TRANSSCLERAL CYCLOPHOTOCOAGULATION

Transscleral cyclophotocoagulation (TS-CPC) was invented in the early 1970s with the Xe, ruby, and diode lasers. The technology at the time was extraordinarily innovative and succeeded in alleviating pain in the blind or visually impaired eye; it was used after multiple surgical failures or when surgery wasn't possible. TS-CPC was effective in lowering IOP but caused numerous side effects and severe complications, including pain, uveitis, hypotony, permanent decrease in visual acuity, and phthisis bulbi [1]. The procedure was not repeatable due to the thermal tissue destruction and was generally considered as a last resort treatment option.

Subthreshold TS-CPC is the latest technology available, featuring a non-destructive laser procedure that is based on traditional TS-CPC. The new device is a non-destructive 810-nm diode laser used to treat open-angle, angle-closure, and even neovascular glaucoma [3]. The technology is specifically designed to reduce the production of aqueous humour, selectively impairing the pigmented ciliary body epithelium and resulting in minimal coagulative necrosis. Another benefit of the technology is that it undertakes uveoscleral remodeling which increases outflow through the unconventional pathway [3]. Although the device is based on TSCPC principles, the differences are significant. The most crucial difference is the tissue effect the laser produces. Unlike traditional TSCPC, subthreshold laser is based on pulse technology that delivers a continuous wave of repetitive ultra-short pulses with cooling breaks which controls levels of thermal elevation and preserves the structures of the ciliary body. The presence of "cool-off" periods between treating pulses (Duty Cycle), eliminates the risk of overheating (leading to tissue thermal destruction) and minimalizes the likelihood of inflammation and other serious adverse effects (fig. 2). This provides a thermal relaxation time for the TM tissue. The preservation of the ciliary body allows future glaucoma procedures to be repeated. Subthreshold TS-CPC in several clinical trials proved to be effective in lowering the intraocular pressure and devoid of significant sight threatening side effects, comparing to the classical thermal diode cyclcophotocoagulation method [4–12].

FIGURE 2

Different mechanisms of action between subthreshold and thermal TS-CPC.

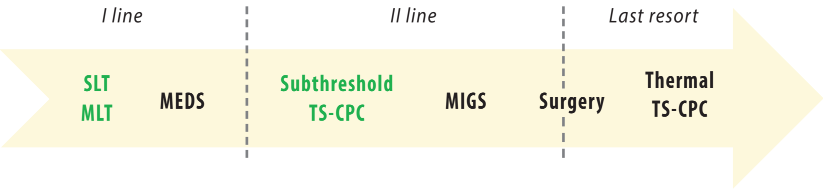


RE-THINKING THE THERAPEUTIC ALGORITHM IN GLAUCOMA

Previously, the I line of treatment for glaucoma involved prescribed prostaglandin analogues (eye drops) in reducing and maintaining IOP. This treatment therapy could last for years until the patient reached critical mass and required surgery, which was thermal TSCPC. That algorithm changed as more lasers were introduced into the field and several minimally invasive glaucoma surgery (MIGS) methods were developed. With the introduction of new laser trabeculoplasty technologies, the therapeutic algorithm changed once again. In a randomized controlled study testing SLT versus eye drops for the I line of treatment of ocular hypertension and glaucoma (LIGHT trial), it was concluded that SLT should be considered as a I line of treatment for open-angle glaucoma and ocular hypertension [3]. We can now consider specific methods of laser trabeculoplasty, such as SLT and subthreshold TS-CPC, in the same category as eye drops when considering I and II line treatment options [3] (fig. 3).

FIGURE 3

Modified glaucoma therapy algorithm



We can offer our patients SLT and MLT treatment parallel to drops or make a shift to laser from medications anytime, but we should consider the fact that trabeculoplasty may work more efficiently in treatment-naïve subjects. Further analysis of LIGHT trial data shows that patients treated first with medications were more prone to undergo rapid visual field progression than those treated first with SLT [3]. Subthreshold TS-CPC as a II line treatment in glaucoma may be paced before the classical surgery methods (trabs, shunts) and be a good to consider alternative to MIGS. Repeatability, cost effectiveness and predictability of the new TS-CPC are the additional benefits which make it superior to incisional procedures

CONCLUSION

As you move through the decision tree of options for glaucoma patients, there are more than enough options to consider, especially in laser treatment, for primary open-angle glaucoma or ocular hypertension, and in some secondary glaucoma pathologies laser trabeculoplasty can be considered as a I and II line of treatment. This includes SLT, MLT and subthreshold TS-CPC. For angle-closure glaucoma, you can choose iridotomy and iridoplasty, and despite having new technology that surpasses in efficacy and outcomes, you can still select thermal TSCPC. How you proceed and the options presented to patients rely on your experience, comfort levels with new technologies, and, ultimately, what is best for your patient.

Figures: from the author's own materials.

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Wkład autorów:
Jaromir Wasyluk: 80%; Ilona Kaczmarek: 10%; Radosław Różycki: 10%.

Konflikt interesów:
Nie występuje.

Finansowanie:
Nie występuje.

Etyka:
Treści przedstawione w artykule są zgodne z zasadami Deklaracji Helsińskiej, dyrektywami EU oraz ujednoliconymi wymaganiami dla czasopism biomedycznych.

Authors' contributions:
Jaromir Wasyluk: 80%; Ilona Kaczmarek: 10%; Radosław Różycki: 10%.

Conflict of interest:
None.

Financial support:
None.

Ethics:
The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.