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ORIGINAL RESEARCH

Acute Structural Effects of Novel Endoscopic Cyclophotocoagulation versus Standard Endoscopic and Transscleral Cyclophotocoagulation

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Purpose: To compare the acute structural changes of standard endoscopic cyclophotocoagulation (ECP), a novel ECP device (Leos™), and transscleral cyclophotocoagulation (TCP) on the ciliary processes and surrounding structures in human cadaveric eyes using scanning electron microscopy (SEM).

Patients and Methods: Three human cadaveric eyes were treated with standard ECP, Leos ECP, or TCP. Untreated areas served as controls. Tissues were prepared for SEM to evaluate microarchitectural changes in the ciliary processes and adjacent structures.

Results: SEM imaging revealed that both standard and Leos ECP resulted in blunting of the ciliary processes without injury to collateral tissues. In contrast, TCP-treated tissues showed significant structural disorganization extending to the iris and pars plana.

Conclusion: In this study, we demonstrate that both standard and novel Leos ECP techniques produce significantly less structural disruption to the ciliary processes compared to TCP. The Leos ECP system, with its enhanced imaging and automation features, may offer more clinical value through ease-of-use and improved consistency while still generating similar tissue effects to standard ECP. Additionally, these findings further validate the more targeted approach that ECP offers compared to TCP. However, no clinical outcomes were evaluated in this study, and further investigation is needed to determine how these findings translate to patient care.

Keywords: aqueous humor, ciliary body, transscleral cyclophotocoagulation, endoscopic cyclophotocoagulation, intraocular pressure, electron microscopy

Introduction

Glaucoma is a leading cause of irreversible blindness worldwide, and is characterized by optic neuropathy with associated visual field damage.[1,2] Intraocular pressure (IOP) control is the gold-standard method of slowing the progression of glaucoma, which can be achieved through various means, including pharmacotherapy, laser, and surgery.[3] Transscleral cyclophotocoagulation (TCP) and endoscopic cyclophotocoagulation (ECP) are two laser-based cycloablative techniques that are commonly used to treat mild to end-stage glaucomatous disease.[4–7]

TCP is a laser-based procedure designed to reduce IOP by indirectly targeting the ciliary processes.[4] Accurate targeting in TCP is critical, as deviations can lead to suboptimal results and damage to surrounding ocular tissues. Complications of TCP include prolonged inflammation, pain, hyphema, and hypotony.[5] While evolutions in TCP have led to improved safety, this technique still lacks the ability to treat with a targeted approach. ECP is a relatively newer technique, offering a more targeted and controlled method of cycloablation.[6] Previous literature has demonstrated that ECP effectively reduces IOP with lower risk of collateral damage to surrounding tissue.[7,8] Unlike TCP, ECP involves direct visualization of the ciliary processes via an endoscope.

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Previous histological and acute structural analyses have demonstrated clear differences in tissue effects between TCP and ECP.[7,9] TCP induces widespread disruption of the ciliary body, including coagulative necrosis of the stroma often with extension into adjacent structures like the pars plana. In contrast, ECP produces more localized alterations, primarily affecting the ciliary epithelium. These differences can be observed under both light and scanning electron microscopy (SEM), further validating that ECP is a more tissue-sparing approach.

A newly developed ECP system (Leos™ BVI Medical Waltham, MA, USA) features enhanced imaging capabilities through a high-resolution camera and customized LED illumination, offering over twice the pixel density of traditional systems (40,000 vs 17,000 pixels). Using a single-use 19-gauge endoscope, laser delivery is integrated with real-time projections of intraocular images onto a large display allowing for a more detailed view. During treatment, a red aiming beam ensures precise targeting of the ciliary processes, much like standard ECP. Unlike standard ECP setups that require manual adjustment by an assistant, the Leos system automates parameters such as image focus, illumination, and orientation. The introduction of this system—with enhanced resolution and automated imaging capabilities—may further refine the precision of ECP.

This study aims to extend prior findings by comparing the acute structural changes induced by standard ECP, Leos ECP, and TCP on the ciliary body and surrounding structures in human cadaveric eyes.

Materials and Methods

No living human subjects or identifiable private information were involved in this study. As such, this study was exempted for IRB review by the Colorado Multiple Institutional Review Board under institutional policy.

This study was designed to compare acute structural changes induced by standard ECP, the investigational Leos ECP system, and TCP using SEM on three human cadaveric eyes. Human eyes were obtained within 24 hours of death from the Lions World Vision Institute (Tampa, Florida). Eyes had no prior history of glaucoma, intraocular surgery (excluding lens implantation), or laser intervention. Institutional review board waiver was obtained for this tissue-based laboratory analysis, and this study was performed in accordance with the latest declaration of Helsinki.

Each globe was inflated to physiologic intraocular pressure using balanced salt solution injected via a 25-gauge needle through the optic nerve. This facilitated optimal internal tension and consistent external placement of the TCP probe. Two eyes were divided into three 120° sections—one untreated segment served as a control, while the remaining two-thirds received Leos ECP (0.25W) and either the standard ECP (0.25W) or TCP (2.5W, 2–4 seconds), respectively. In a third eye, the globe was hemisected; one half was treated with Leos ECP (0.25W) and the other half with TCP (2.5W, 2–4 seconds). Treated areas were demarcated with permanent ink to help with subsequent sectioning and orientation.

A 2.4 mm corneal incision was made and the anterior chamber and ciliary sulcus were deepened with viscoelastic (Healon, Advanced Medical Optics, Santa Ana, CA, USA) to visualize the ciliary processes. Endoscopic treatments were delivered using either a reusable 19-gauge laser microendoscope (EndoOptiks®, BVI Medical Waltham, MA) or a single-use 19-gauge Leos ECP device (BVI Medical, Waltham, MA), both of which delivered continuous-wave 810 nm diode laser energy with a 640 nm red aiming beam. ECP was applied until visible whitening and shrinkage of the processes was observed.

For TCP, a G-probe was connected to an Iridex 810nm diode laser (Mountain Vew, CA, SLx diode laser photocoagulation system). The probe was positioned 1.2 mm posterior to the limbus and aligned perpendicularly to the limbus externally on the sclera. Energy was delivered in pulses of ~2.5W for 2 to 4-second duration, targeting the pars plicata region. Laser treatment was titrated as needed to minimize audible "pops" which indicated tissue over-treatment.

Following treatment, all eyes were sectioned at the level of the pars plana and divided into control and treatment segments. Each section was fixed in 10% Neutral buffered formalin (Sigma-Aldrich, St. Louis, MO, USA) and stored on wet ice for transfer to the electron microscopy facility.

The tissues designated for acute structural evaluation were initially fixed in 2.5% glutaraldehyde at 4°C for 24 hours. The samples were then rinsed in 0.1 M phosphate-buffered saline, followed by secondary soaking in 1% osmium tetroxide. Subsequently, the specimens underwent graded ethanol dehydration and were kept in acetone. They were then critical point dried, ion coated, and then imaged using SEM to assess microarchitectural changes in the ciliary body and adjacent ocular structures.

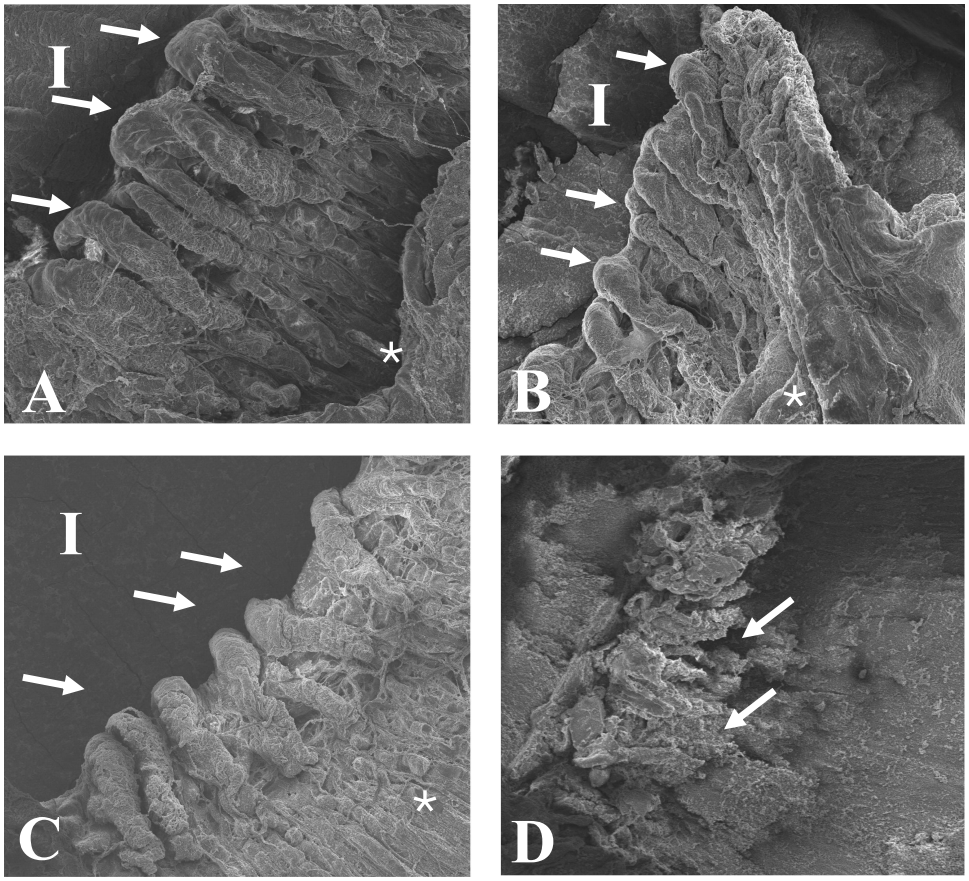

Figure 1 (**A**) Scanning electron microscopy of normal ciliary processes (arrows) with adjacent pars plana (asterisk) and iris stroma (I). (**B**) Scanning electron microscopy of standard endoscopic cyclophotocoagulation-treated ciliary processes showing shrinking of the processes with blunting of their tips (arrows). The adjacent pars plana (asterisk) and iris stroma (I) are unaffected. (**C**) Scanning electron microscopy of the LEOS endoscopic cyclophotocoagulation-treated ciliary processes showing shrinking of the processes with blunting of their tips (arrows). The adjacent pars plana (asterisk) and iris stroma (I) are unaffected. (**D**) Scanning electron microscopy of transscleral cyclophotocoagulation-treated ciliary processes showing extensive architectural destruction (straight arrows).

All SEM images were analyzed by a single observer with extensive experience (MYK). Particular focus was paid to the ciliary processes and changes to the ciliary epithelium after treatment. Further observations were made on any tissue disorganization and extension of damage into the pars plana and iris stroma. The observer was not masked to the treatment modality. Statistical methods were not applicable due to the qualitative nature of SEM image comparisons.

Results

Electron microscopic analysis revealed distinct acute structural alterations among the different treatment modalities. In untreated control samples, the ciliary processes exhibited well-preserved architecture with intact epithelial surfaces and regularly arranged longitudinal ridges (Figure 1A). Tissues treated with the standard ECP and Leos ECP method demonstrated moderate ciliary epithelial disruption, including blunting and partial flattening of the ciliary processes (Figure 1B and C). There was minimal damage to the pars plana. TCP treated tissues displayed extensive tissue disorganization, including destruction of ciliary processes that extended into the iris and pars plana (Figure 1D). These acute structural patterns were consistently observed across all treated sections from each eye. None of the laser treatment modalities resulted in detectable damage to the adjacent scleral tissue in any of the specimens.

Discussion

This study provides new insights into the acute structural impact of different cyclophotocoagulation modalities on the ciliary processes. Both the novel Leos ECP and standard ECP demonstrated more targeted tissue destruction without the

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collateral tissue damage seen with TCP. These findings further validate results from previous literature by confirming SEM patterns and by introducing comparable histologic outcomes with a novel ECP platform.[7–11]

The significance of minimizing collateral damage during cyclophotocoagulation rests in its clinical implications. Namely, excessive destruction of the ciliary body, stroma, and adjacent iris tissue has been associated with complications such as phthisis, hypotony, and prolonged inflammation.[5]

SEM has been used in prior studies to assess structural changes[7,8,10,12] and laser-induced injury patterns[13] with exquisite resolution, making it a valuable tool for evaluating the effects of glaucoma and laser treatment. These views offer insights into laser-induced cellular disruption, stromal damage, and epithelial integrity beyond what is visible with light microscopy. Incorporation of electron microscopic analysis in the current study allows for a more refined analysis of tissue alterations across different cycloablation modalities.

Cyclophotocoagulation is the only surgical modality that targets aqueous production; ECP is the only micro-invasive surgery to do so.[14–16] Therefore, both surgical techniques are important parts of a glaucoma surgeon's armamentarium. Compared to TCP, the safety profile of ECP has been demonstrated to be more favorable in both prospective and retrospective studies.[16,17] Though conventional ECP outcomes are good, improvements in device design may further reduce clinical variability and ensure safety. Importantly, the consistency in histologic findings between the two ECP modalities evaluated here suggest the Leos system is similar in tissue impact. However, the Leos system may offer the additional benefit of simpler and more consistent operation through its enhanced imaging capabilities, more detailed view, its larger, more ergonomic screen and standardized settings, which limit risk of human error in manual setting adjustments.

Attempts have also been made to modify TCP to mitigate complications with MicroPulse CPC, which cycles laser energy off/on to allow cooling of tissue during transscleral laser therapy.[18,19] With MicroPulse there is still extensive histological and structural damage, through a recent meta-analysis found a more favorable side-effect profile versus traditional TCP.[20] MicroPulse, like TCP, lacks direct visualization of ciliary tissue and variations in anatomy.[21]

Limitations

Despite these promising results, there are limitations inherent to this study. First, the analysis was performed by a single, unmasked observer, which introduces the potential for interpretation bias. Human cadaveric eyes cannot replicate the dynamic biological processes of live tissue, such as inflammation, wound healing, and aqueous humor flow. Thus, it is unclear how these findings will translate into clinical outcomes. Additionally, the number of eyes studied was small with only three cadaveric globes evaluated. This limited size restricts generalizability. As such, findings should be interpreted as preliminary rather than conclusive. Further research could be aimed at correlating these structural findings with functional data such as aqueous production rates. Future studies are also needed to validate these results using multiple, masked observers, a rigorous quantitative scoring system, and a larger sample size. It would also be valuable to investigate whether the other advances in the Leos ECP system lead to improved surgeon and surgical staff satisfaction, ergonomics, shortened learning curve for new surgeons and improved operative efficiency all of which are incredibly important in our current climate.

Conclusions

In this study, we demonstrate that both standard ECP and the novel Leos ECP produce significantly less acute structural disruption to the ciliary body compared to TCP. While the Leos ECP system yielded tissue effects similar to standard ECP, its enhanced imaging and automated features may translate into greater clinical consistency and usability across operators. However, this remains a hypothesis and requires confirmation through clinical trials. These findings also further validate the more targeted approach that ECP offers compared to TCP.

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Disclosure

Malik Y. Kahook: Consultant to FCI, New World Medical, and SpyGlass Pharma, Ownership of SpyGlass Pharma, Patent Royalties from Alcon, New World Medical, FCI, and SpyGlass Pharma. Leonard Seibold: Consultant to New World Medical, Thea, and Abbvie/Allergan. The authors report no other conflicts of interest in this work.

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