

Sub-Threshold Laser Therapies using the PASCAL Laser System

Clinical and Scientific Dossier



YOUR VISION.
OUR FOCUS.

Table of Contents

Section 1: Introduction

Introduction to PASCAL and Sub-Threshold Therapies **1**

Section 2: Physician White Papers

The Scientific Rationale for Non-Damaging Retinal Laser Therapy Endpoint Management **2**

PSLT Offers Benefits Over SLT For Glaucoma Patients **4**

Section 3: Selected Peer-Reviewed Abstracts

Retina

Nondamaging Retinal Laser Therapy: Rationale and Applications to the Macula **7**

Nondamaging photothermal therapy for the retina: Initial clinical experience with chronic central serous retinopathy. **8**

Nondamaging retinal laser therapy for treatment of central serous chorioretinopathy: What is the evidence? **9**

Randomised clinical trial evaluating best-corrected visual acuity and central macular thickness after 532-nm subthreshold laser grid photocoagulation treatment in diabetic macular oedema. **10**

Glaucoma

Comparing Pattern Scanning Laser Trabeculoplasty to Selective Laser Trabeculoplasty: A Randomized Controlled Trial **11**

Patterned laser trabeculoplasty. **12**

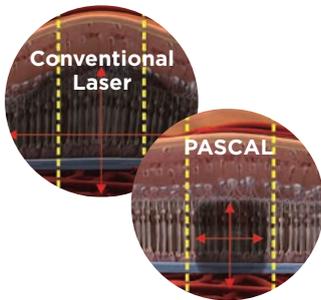
Short-Term Clinical Outcomes of Laser Trabeculoplasty Using a 577-nm Wavelength Laser **13**

Topcon's PAttern SCAnning Laser (PASCAL®) technology has been offered to customers for over a decade with an installed base of over 2000 lasers worldwide. Developed in partnership with Stanford University, the PASCAL technology revolutionized ophthalmic laser photocoagulation by introducing a new concept widely accepted as standard of care, known as the PASCAL Method. Today, physicians continue to partner with Topcon by choosing PASCAL because of the advanced technology, ease of use, and superior clinical outcomes.

As we move into a new era of treatment approaches, more physicians are trending towards protocols that cause less damage while delivering clinically effective therapeutic results for their patients.

In response to this trend, Topcon has introduced treatment options that, in conjunction with the PASCAL laser system, go many steps further to minimize laser damage in both Retina and Glaucoma Disorders. Endpoint Management (for Retina) and Pattern Scanning Laser Trabeculoplasty (for Glaucoma) have been clinically shown to be as effective and in some cases provide a greater advantage over other sub-visible technologies, such as micropulse.

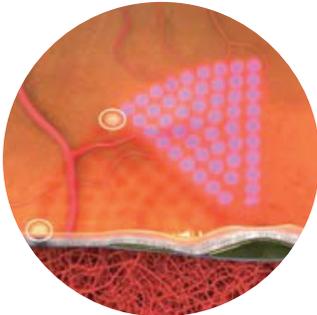
A robust and growing body of evidence continues to show that PASCAL® Sub-Threshold Laser Therapies, together with appropriate dosimetry, provide unparalleled rapid and precise laser treatments from Retina to Glaucoma.



What is the PASCAL Method?

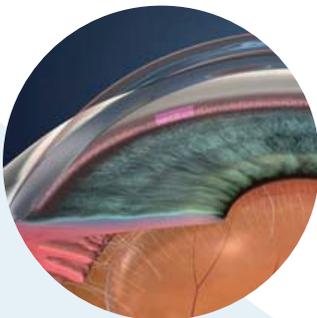
Over the past 10 years, research studies on Pattern Scanning Lasers and specifically PASCAL Laser Systems have shown that the PASCAL Method of treatment provides faster treatments, greater patient comfort and less pain.^{1,2,3}

Using PASCAL's shorter pulse duration (10 ms), less heat is diffused to the retinal nerve fibers and choroid which results in faster procedures with less collateral damage and scarring for your patients.



What is Endpoint Management (EpM)?

EpM is a proprietary feature that uses a process to control power and duration more precisely, specifically at non-visible treatment levels. With EpM, you can adjust the treatment from barely visible down to various sub-threshold levels, even down to completely non-detectable points while maintaining clinical efficacy.



What is Pattern Scanning Laser Trabeculoplasty (PSLT)?

PSLT is a computer-guided therapy that provides precise placement of laser patterns along the trabecular meshwork, independent of visibility of the lesions. PSLT provides rapid, precise, and sub-visible computer-guided treatment with exact placement of the patterns. This allows for faster and easier applications compared to other laser modalities such as ALT.

1. Al-Hussainy S, Dodson PM, Gibson JM. Pain response and follow-up of patients undergoing panretinal laser photocoagulation with reduced exposure times. *Eye (London)*. 2008 Jan;22(1):96-9.

2. Muqit MM, Marcellino GR, Gray JC, McLauchlan R, Henson DB, Young LB, et al. Pain responses of Pascal 20 ms multi-spot and 100 ms single-spot panretinal photocoagulation: Manchester Pascal Study, MAPASS report 2. *British Journal of Ophthalmology*. 2010 Nov;94(11):1493-8

3. Sheth S, Lanzetta P, Veritti D, Zucchiatti I, Savorgnani C, Bandello F. Experience with the Pascal® photocoagulator: an analysis of over 1,200 laser procedures with regard to parameter refinement. *Indian Journal of Ophthalmology*. 2011 Mar-Apr;59(2):87-91.

For a complete list of PASCAL's Clinical Evidence, please visit www.pascalvision.com

The Scientific Rationale for Non-Damaging Retinal Laser Therapy

BY Daniel Palanker, PhD; Stanford University, Palo Alto, CA | Nov/Dec 2015 Insert to Retina Today

INTRODUCTION

Light falling on the retina is absorbed primarily by melanin and blood. For yellow and green wavelengths, about 5% of the energy is absorbed in the nearly-transparent neural retina, about 45% in the retinal pigment epithelium (RPE), and the rest in the choroid. Therefore, retinal heating and coagulation is governed primarily by heat diffusion from the pigmented layers, which absorb laser energy. Duration of the laser exposure defines how deep the heat wave will penetrate into the retina during the laser pulse. Thus, the size of the affected zone is a function of not only the laser spot micropulse exposure width, but also the power and pulse duration.

Heating of biomolecules leads to their denaturation, which, above a certain threshold, can result in cellular necrosis and coagulation. Dynamics of denaturation can be described as a chemical reaction, with its rate scaling as an exponential function of temperature (Arrhenius equation). The total amount of thermal damage at every point in the tissue can then be calculated as an integral, known as the Arrhenius integral, of the denaturation rate over the duration of hyperthermia in that point. The Arrhenius integral is typically normalized to unity at the cellular damage threshold (exposures with Arrhenius integral W less than 1 are sublethal). Different clinical grades of retinal lesions correspond to different levels of Arrhenius integral: in barely visible lesions, W reaches approximately 1000, in lesions visible only in OCT the W peaks at about 100, etc.

THE ENDPOINT MANAGEMENT ALGORITHM

Conventional retinal burns damage RPE cells, coagulate photoreceptors, and intense burns even damage the inner retina. Such burns typically result in retinal scarring, and preclude retreatments.

Endpoint Management (EpM, Topcon) technology was developed to enable delivery of the well-defined thermal effects to the retina even below the threshold of visible changes in the tissue. EpM converts the highly nonlinear scale of Arrhenius integral into linear steps of pulse energy by adjusting laser power and duration such that a 20% change in pulse energy corresponds to a factor of 10 change in Arrhenius integral, as shown in Figure 1. To ensure precise dosing in every patient, despite variation in pigmentation and tissue transparency, EpM

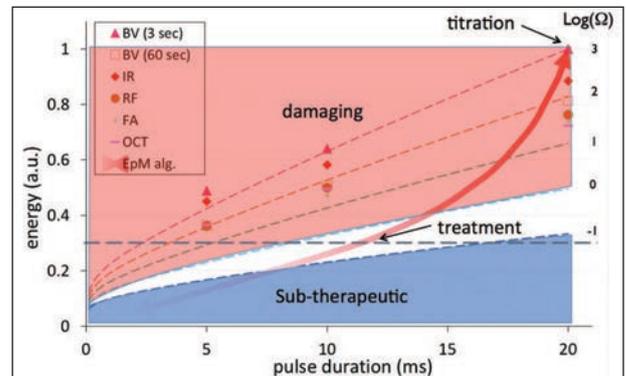


Figure 1. Endpoint Management is a non-damaging retinal laser therapy that uses the Arrhenius integral algorithm to control laser power and pulse duration, optimizing the therapeutic effect of the laser at sub-visible levels. Laser settings above the Arrhenius integral of 1 ($\log(\Omega)=0$) correspond to tissue damage. Laser settings below the $\Omega=0.1$ ($\log(\Omega)=-1$) are sub-therapeutic.

algorithm begins with titration of the laser power to produce barely visible burns in the retina outside the arcade using 15 or 20 ms pulse duration. Laser energy corresponding to this power is then defined as 100%.

At 75% laser energy, the lesions are not visible ophthalmoscopically, but photoreceptors damage can be seen in OCT. At 50% energy, they might not be visible in OCT, but are still visible in histology, and RPE damage is detectable using fluorescein angiography (FA). However, at 30% energy, there is no damage detectable on histology, nor on FA or OCT (Figure 2).¹

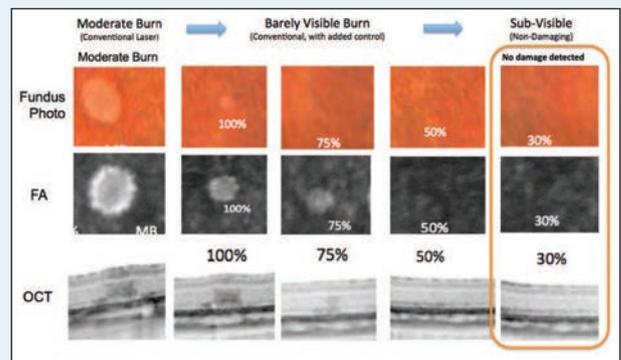


Figure 2. There is no damage detectable on histology, nor on FA or OCT when using EpM.

TISSUE RESPONSE BELOW DAMAGE THRESHOLD

To explore whether retinal cells respond to thermal stress below the damage threshold, we first used transgenic mice, which express bioluminescent marker attached to the heat shock protein 70 (HSP-70). We discovered that HSP-70 was upregulated even below the damage threshold, down to Arrhenius integral of $\Omega = 0.1$. Using immunohistochemistry, we observed expression of HSP-70 in the RPE at energy levels of 30% and 25%, with very little response at 20%. With conventional photocoagulation burns, HSP-70 is detectable in the ring of cells surrounding the damage zone, whereas in nondamaging exposures produced at 30% energy and below, HSP-70 is detectable in the middle of the spot, with no evidence of cell death (Figure 3).²

HEAT SHOCK PROTEINS

Misfolding and aggregation of proteins in cell is a fundamental component of aging. As chaperones, heat shock proteins normally refold the damaged proteins and thereby protect cells from protein aggregation and associated toxicity. However, transcriptional pathways decline with aging, leading to protein aggregation, commonly observed in neurodegenerative diseases. Induction of HSP in aging cells promotes longevity and rejuvenates cellular functions. In addition, molecular chaperones, such as HSP27 and HSP70, have antiapoptotic functions. Therefore, enhanced synthesis of HSP and co-chaperones in response to laser-induced thermal stress in RPE can normalize physiology of these cells in aging and disease, including enhanced capability of fluid pumping from the retina and control of choroidal permeability.

RATIONAL FOR NONDAMAGING RETINAL LASER THERAPY

Mechanisms leading to therapeutic benefits of the laser photocoagulation in the macula have never been established. If we hypothesize that the benefits originate from the response of cells surviving the hyperthermia at the edges of the damage zone, such response could be replicated without tissue damage. This can be accomplished by titrating the laser energy into the range of cellular response to thermal stress below the damage threshold, which is at 30% on the EpM scale.

To ensure efficient tissue response, the treatment should be applied in a dense pattern, with laser spots separated by about one-quarter of the spot diameter. EpM was developed with retinal laser spot diameter of 200 μm , currently being used clinically. Smaller spot sizes are not recommended since (a) EpM is not calibrated for smaller spots, and (b) smaller, barely visible lesions are hard to detect. Even with 200 μm spots, typical macular treatment requires about 400 to 500 exposures. With 100 μm

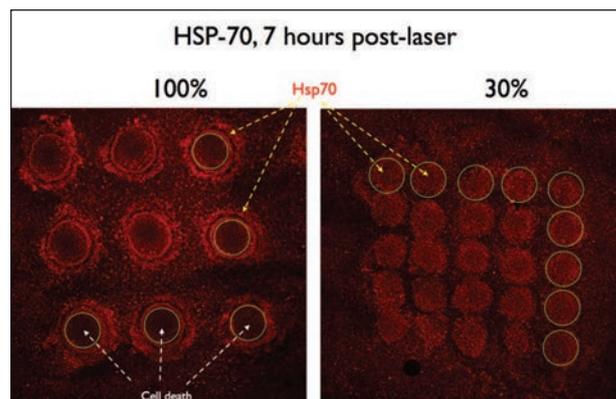


Figure 3. HSP-70 expression in laser spots with 100% energy (barely visible burns) on the left and with 30% energy on the right. Note the presence of HSP-70 at the periphery of traditional laser burns (surrounding the areas of cell death) but in the center of those produced with non-damaging exposures.

spots, it would require four times larger the number of pulses, which would be difficult to deliver within a few minutes of treatment.

Treatment of the patients with chronic central serous chorioretinopathy using EpM demonstrated that 30% energy does not produce any signs of damage on the retina or RPE. Subretinal fluid was resolved completely in 81% of patients, and partially in 19% of the patients, without any nonresponders. Choroidal and retinal thickness decreased to normal levels and visual acuity improved by 12 ETDRS letters within 2 months of the treatment.³ Importantly, lack of tissue damage allows high density treatment to boost therapeutic response and periodic retreatments, which are essential in management of chronic diseases.

CONCLUSIONS

Initial clinical experience with non-damaging retinal laser therapy enabled by EpM confirms that the therapeutic window defined in preclinical experiments is indeed below the damage threshold and within the range of therapeutic response in human patients. A nondamaging approach to retinal laser therapy provides an exciting opportunity of treating macular diseases without retinal scarring and other side effects of conventional photocoagulation. This allows for periodic retreatment, which is essential in the management of chronic diseases. Clinical trials continue with chronic central serous chorioretinopathy, diabetic macular edema, edema secondary to BRVO and other retinal diseases.

1. Lavinsky D, Sramek C, Wang J, et al. Subvisible Retinal Laser Therapy: Titration Algorithm and Tissue Response. *Retina*. 2014; 34(1):87-97.
2. Sramek C, Mackanos M, Spittler R, et al. Non-damaging retinal phototherapy: dynamic range of heat shock protein expression. *Invest Ophthalmol Vis Sci*. 2011;52(3):1780-1787.
3. Lavinsky D, Palanker D. NonDamaging photothermal therapy for the retina: initial clinical experience with chronic central serous retinopathy. *Retina*. 2015;35(2):213-22.

PSLT Offers Benefits Over SLT For Glaucoma Patients

By Miho Nozaki, MD, PHD, and Kaweh Mansouri, MD, MPH | Nov/Dec 2015 Insert to Glaucoma Today

INTRODUCTION

PASCAL Pattern Scanning Laser Trabeculoplasty, PSLT, (Topcon) is an important breakthrough in laser treatment. It has been shown to have several benefits for treating patients with retinal conditions; for example, short pulse durations result in less heat diffusion to the inner retina and choroid, yielding less pain for patients, less lateral expansion, and less damage to the inner retina. This technology may also be of benefit in treating patients with glaucoma. A new computer-guided treatment algorithm, PSLT, applies a sequence of laser pulses to the trabecular meshwork using the PASCAL laser with yellow (577 nm) wavelength light.

USING LASERS TO TREAT GLAUCOMA

The working mechanism of retinal phototherapy is PSLT is an advanced tissue-sparing laser treatment for open-angle glaucoma. PSLT provides a rapid, precise, and minimally traumatic (subvisible) computer-guided treatment by applying a sequence of laser patterns to the trabecular meshwork (Figure 1). Calculated alignment of each pattern ensures that consecutive treatment steps are pieced together around the trabecular meshwork without overlap or excessive gaps. Using a Gonio lens, treatment is administered in 32 steps for 360° of the trabecular meshwork with three rows of 13 spots each. The laser automatically rotates the aiming beam, allowing for precise and accurate pattern treatment of the trabecular meshwork. Laser energy delivered is under the threshold necessary to create coagulative damage but within the therapeutic boundary to disrupt the trabecula resulting in the reduction of IOP.

PSLT is similar to selective laser trabeculoplasty (SLT) in principle but with some important differences in the treatment parameters. Notably, the pulse energy is higher with PSLT (3.4 mJ) compared to the 0.8 mJ used in SLT, and pulse energy for both are considerably lower than for argon laser trabeculoplasty (ALT), which is typically 33 mJ. With PSLT, the spot size is 100 μm. There are 13 spots in each row, and 3 rows of spots are placed with spots spaced as close together as possible.

During PSLT, the physician titrates laser power using a single spot to achieve light blanching of the trabecular meshwork, with 10 ms laser pulses applied to the inferior segment of the eye, where pigmentation is often most densely concentrated (Figure 2). After titration, power is maintained and

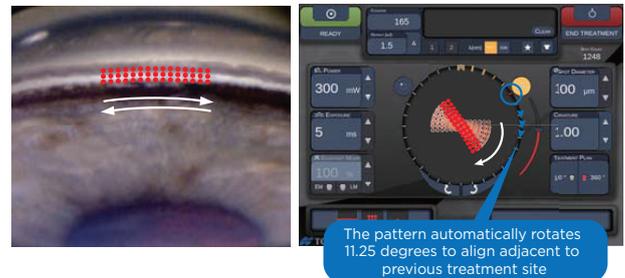


Figure 1. Calculated alignment of each pattern allows for consecutive treatment steps pieced together around the trabecular meshwork without overlap or excessive gaps.

the pulse duration is reduced to 5 ms. The pulse energy is cut in half, which makes the treatment outcome ophthalmoscopically invisible. The surgeon then selects treatment of onehalf (180°) or the total area (360°) for treatment. The aiming beam will automatically rotate during the treatment process to address the treatment area selected.

A CLOSER LOOK: PSLT STUDIES

A study of 47 eyes of 25 patients with primary open angle glaucoma evaluated the effectiveness of PSLT using 532 nm wavelength light.¹ After 1 month, average IOP was reduced from 21.9 mmHg to 16.0 mmHg; at 6 months, the average IOP was 15.5 mm Hg. Overall, IOP was reduced by 24% at the end of the study.

Recently, a retrospective chart review was performed looking at 24 eyes of 21 patients with open-angle glaucoma comparing PSLT using a yellow wavelength (577 nm) light and SLT.² All cases were treated for 360°, and the average follow-up was 11 months in the PSLT group and 18 months in the SLT group. There were no significant differences in baseline characteristics between the groups of patients.

The PSLT group was treated with the PASCAL Streamline 577 (Topcon) using the following parameters:

- Wavelength: 577 nm (yellow)
- Average number of spots (360°): 1277
- Exposure energy: 1.5 to 2.3 mJ (average: 1.7 mJ)

The SLT group was treated with the Tango Ophthalmic Laser (Ellex) using the following parameters:

- Wavelength: 532 nm (green)
- Average number of spots (360°): 88
- Exposure energy: 0.5 to 0.9 mJ (average: 0.8 mJ)

PSLT is not currently available in the US.

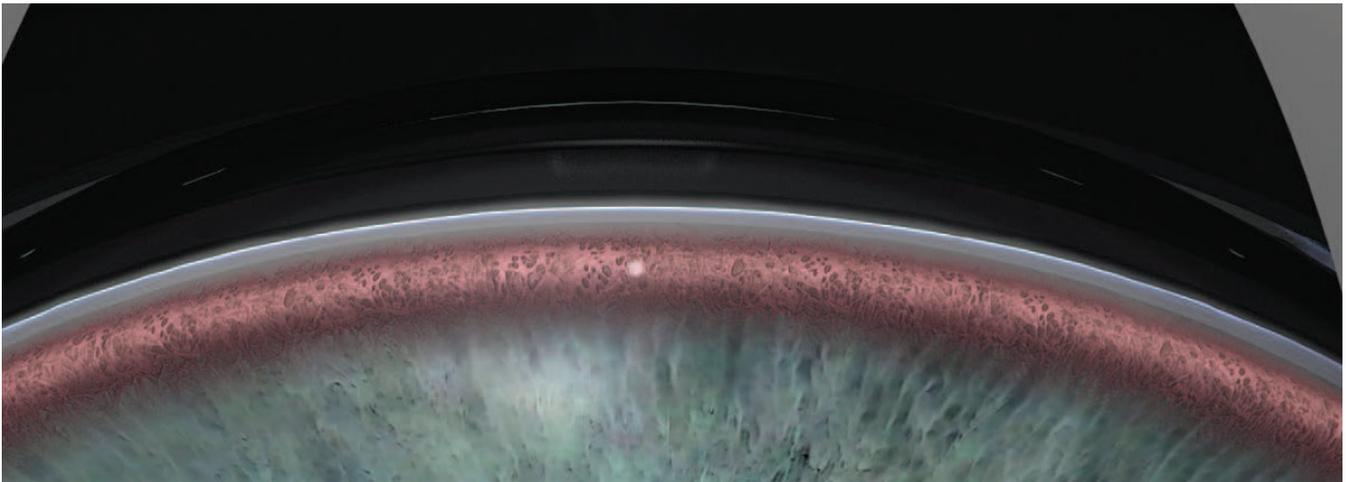


Figure 2. Laser power is titrated using a single spot to achieve light blanching of the trabecular meshwork.

The investigators concluded that PSLT was as effective as SLT in lowering IOP over a 6-month period.

IOP significantly decreased from 1 month to 6 months in both groups, and both exhibited greater than 20% reduction in IOP. In the PSLT group, the reduction was greater than 30% (Figure 3). The medication score (topical antiglaucoma drops and fixed-combination glaucoma agents were given a score of 2) was slightly increased in both groups. Kaplan-Meier survival curves were similar for both PSLT and SLT, and cumulative survival rate (failure rate defined as IOP reduction rate <20) at 6 months was 0.80 for the PSLT group and 0.67 for the SLT group. Three eyes in the SLT group required additional glaucoma surgery 7 months after SLT. One patient in each group experienced a transient IOP elevation of more than 5 mmHg after treatment.

In the PSLT group, the mean IOP was 21.8 mmHg at baseline and 14.3 mmHg at 6 months. In the SLT group, the mean IOP was 23.8 mmHg at baseline and 17.3 mmHg at 6 months. There was no significant difference in average reduction in IOP from baseline between the groups (33% for PSLT and 22% for SLT). The investigators concluded that PSLT was as effective as SLT in lowering IOP over a 6-month period.

STUDY COMPARING SLT TO PSLT

A study conducted by Dr. Kaweh Mansouri at the University of Geneva, Switzerland compared SLT in one eye with PSLT performed in the fellow eye.³ The researchers recorded 24-hour IOP measurements before and after the procedure. The objective was to

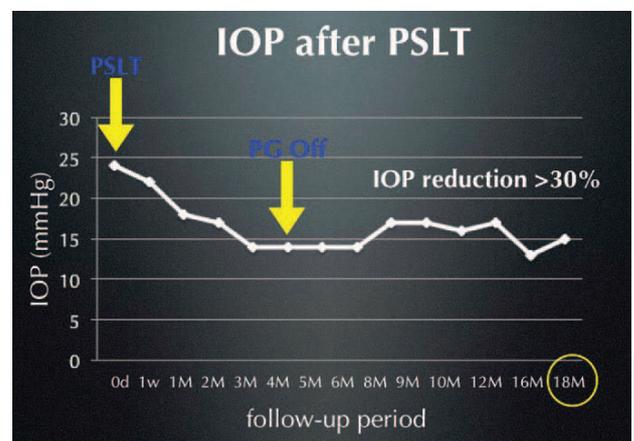


Figure 3. IOP reduction of >30% was maintained through 18 months.

compare the safety, tolerability, and 24-hour IOP-lowering efficacy of the two treatment modalities.

The study included 60 eyes of 30 patients with primary open-angle or pseudoexfoliative glaucoma. Patients underwent 24 hours of monitoring with a contact lens sensor that monitors IOP indirectly.

For the eyes randomized to SLT, the Ellex Tango SLT/ YAG device was used. All four quadrants were treated in a single session. On average, there were 92 pulses, and the average energy level was 1.1 mJ. Average total procedure time, including placement of patients at the laser device and adjustment of the Gonio lens, was 9.4 minutes. For the eyes randomized to PSLT, the PASCAL Streamline 577 laser was used. Again, all four quadrants were treated in a single session. On average, there were 1,248 pulses (32 x 39 spots). The average energy level was 2.8 mJ. This procedure time was significantly shorter compared with SLT (average 4.5 minutes).

There were no serious adverse events reported in either group among these initial cases. Two eyes treated with SLT and one eye treated with PSLT experienced an IOP spike of more than 10 mmHg, but in all cases, the spike resolved after 24 hours. Using a visual analog scale, patients reported their comfort level after the procedure; the average value for SLT eyes was 49 mmHg, which is in the moderate pain range. The average value for PSLT eyes was 25 mmHg ($P = 0.0001$), indicating a significantly lower level of patient discomfort.

The preprocedure IOPs were similar between treatment groups: 20.9 mm Hg versus 20.3 mmHg for the SLT and PSLT groups, respectively. One month after laser treatment, there was a reduction to 14.9 mmHg among eyes treated with SLT (-28%) compared with 15.4 mm Hg among eyes randomized to PSLT (-24%); however, the difference was not statistically significant.

PSLT is a safe and effective treatment for glaucoma in certain patients.

The study employed the use of a Triggerfish sensor, a contact lens device that measures expansion of the ocular circumference as a biomechanical measure of pressure changes (this device is not cleared for use by the US Food and Drug Administration but is cleared for use in Europe). The sensor provides a curve showing IOP changes over a 24-hour period, producing a pattern corresponding to pressure diurnal pressure fluctuations. In the study, prior to treatment, there was good correlation in pressure patterns between the two eyes. One month after the procedures, among eyes in the SLT group, the daytime rhythm did not change much; however, at night, there was a slight flattening of the curve. Among eyes in the PSLT group, there was a similar effect on the nighttime IOP profile.

CASE PRESENTATION

Miho Nozaki, MD, PhD

A 52-year-old woman with primary open-angle glaucoma presented to our clinic. The IOP in her right eye was 26 to 30 mmHg while on timolol/dorzolamide (Cosopt; Oak Pharms). Prior to consultation, her medication was changed to travoprost/timolol (DuoTrav), which is not approved for use in the United States, and brinzolamide (Azopt; Alcon), but the IOP in her right eye remained at 24 to 26 mmHg. At the time of referral, her IOP

was 24 mmHg and visual acuity in her right eye was 20/20; central corneal thickness was 483 μm .

This patient was relatively young, and she did not want to use a prostaglandin analog. Her cornea was thin, so we could have performed a trabeculectomy, but her fellow eye showed no evidence of glaucoma. Therefore, we opted to treat with PSLT. After PSLT, her IOP dropped to less than 15 mmHg. Four months later, her medication was changed from DuoTrav and Azopt to Cosopt and brimonidine. Her lower IOP was maintained for more than a year and there was no change in visual field.

CONCLUSION

These studies and case presentations demonstrate that PSLT is a safe and effective treatment for glaucoma in certain patients. It is faster and more comfortable for patients than SLT. Efficacy of PSLT is similar to SLT, both in daytime and nighttime IOP. Additional studies are needed to confirm these findings; however, PSLT seems to be a potentially intriguing option for treating glaucoma.

1. Turati M, Gil-Carrasco F, Morales A, et al. Patterned laser trabeculectomy. *Ophthalmic Surg Lasers Imaging*. 2010;41(5):538-545.

2. Nozaki M, Yoshida M, Ogura Y. Outcomes of Patterned Laser Trabeculectomy versus Selective Laser Trabeculectomy in Open-Angle Glaucoma. Poster #4529. Presented at ASCRS 2014; April 25-29, 2014; Boston, MA.

3. Mansouri K, Shaarawy T. Randomized, controlled trial to compare safety, tolerability and efficacy of pattern scanning laser trabeculectomy (PSLT) to selective laser trabeculectomy (SLT). Presented at: American Glaucoma Society Annual Meeting; March 1-3, 2015; Coronado, CA..

Investigative Ophthalmology & Visual Science

Nondamaging Retinal Laser Therapy: Rationale and Applications to the Macula

Daniel Lavinsky, Jenny Wang, Philip Huie, Roopa Dalal, Seung Jun Lee, Dae Yeong Lee, and Daniel Palanker

PURPOSE

Retinal photocoagulation and nondamaging laser therapy are used for treatment of macular disorders, without understanding of the response mechanism and with no rationale for dosimetry. To establish a proper titration algorithm, we measured the range of tissue response and damage threshold. We then evaluated safety and efficacy of nondamaging retinal therapy (NRT) based on this algorithm for chronic central serous chorioretinopathy (CSCR) and macular telangiectasia (MacTel).

METHOD

Retinal response to laser treatment below damage threshold was assessed in pigmented rabbits by expression of the heat shock protein HSP70 and glial fibrillary acidic protein (GFAP). Energy was adjusted relative to visible titration using the Endpoint Management (EpM) algorithm. In clinical studies, 21 eyes with CSCR and 10 eyes with MacTel were treated at 30% EpM energy with high spot density (0.25-diameter spacing). Visual acuity, retinal and choroidal thickness, and subretinal fluid were monitored for 1 year.

RESULTS

At 25% EpM energy and higher, HSP70 was expressed acutely in RPE, and GFAP upregulation in Müller cells was observed at 1 month. Damage appeared starting at 40% setting. Subretinal fluid resolved completely in 81% and partially in 19% of the CSCR patients, and visual acuity improved by 12 ± 3 letters. Lacunae in the majority of MacTel patients decreased while preserving the retinal thickness, and vision improved by 10 letters.

CONCLUSIONS

Heat shock protein expression in response to hyperthermia helps define the therapeutic window for NRT. Lack of tissue damage enables high-density treatment to boost clinical efficacy, therapy in the fovea, and retreatments to manage chronic diseases.

ABSTRACT HIGHLIGHTS

In summary, 1 year results with choronic CSCR and MacTel demonstrated that Nondamaging Retinal Therapy (NRT) is efficient and safe for treatment of macula. Success in treatment of two disparate disorders by activation of endogenous repair pathways, indicated by upregulation of HSP in RPE and GFAP expression in Muller cells, suggest that NRT might also be beneficial for treatment of other outer retinal diseases with different pathology including macula edema and disease associated with RPE deficiency such as drusen in dry AMD. Lack of tissue damage allows for application of high-density treatment patterns to increase therapeutic response.

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/pubmed/27159441>

REFERENCE

Lavinsky D, Wang J, Huie P, et al. Nondamaging Retinal Laser Therapy: Rationale and Applications to the Macula. *Invest Ophthalmol Vis Sci*. 2016;57:2488–2500

Retina, The Journal of Retinal and Vitreous Diseases

Nondamaging photothermal therapy for the retina: Initial clinical experience with chronic central serous retinopathy.

Daniel Lavinsky & Daniel Palanker

PURPOSE

To assess safety and clinical efficacy of the nondamaging photothermal therapy for the macula for the treatment of chronic central serous retinopathy.

METHOD

Sixteen eyes of 16 patients with persistent central serous retinopathy (>4 months of duration) were treated with the PASCAL Streamline) at 577-nm wavelength, using 200- μm retinal spot sizes. Using Endpoint Management Software, the laser power was first titrated for a barely visible burn with 15-ms pulses, which was defined as 100% pulse energy. Treatment was then applied over the area of serous retinal detachment and adjacent nonthickened retina, using 30% pulse energy with the spot spacing of 0.25 beam diameter. Changes in subretinal fluid, Early Treatment Diabetic Retinopathy Study best-corrected visual acuity, and central macular thickness were measured over 6 months of follow-up. Pretreatment and posttreatment fluorescein angiography and fundus autofluorescence were also assessed.

RESULTS

On average, 532 spots have been applied per treatment. No visible laser marks could be detected by clinical observation, optical coherence tomography, fundus autofluorescence, or fluorescein angiography. On average, 12 Early Treatment Diabetic Retinopathy Study letters gain was achieved at 2 months and was sustained by 6 months ($P < 0.001$). Central macular thickness decreased from 350 μm to 282 μm ($P = 0.004$). Subretinal fluid completely resolved in 37% of the patients after first treatment, whereas 44% of the patients required retreatment after 3 months because of recurrent fluid or incomplete resolution. The remaining 19% of the patients received a second retreatment. By 6 months, in 75% of the patients, the subretinal fluid was completely resolved, whereas in 25%, there was some minimal fluid left.

CONCLUSIONS

Photothermal therapy using 577-nm PASCAL laser with Endpoint Management graphic user interface was safe, and it improved visual acuity and resolution of subretinal fluid in chronic central serous retinopathy. Lack of tissue damage allows periodic retreatment without cumulative scarring, characteristic to conventional photocoagulation. This technique should be tested in the treatment of other macular disorders and may offer an alternative to conventional laser coagulation of the macula and to anti-vascular endothelial growth factor pharmacological treatments of macular diseases.

ABSTRACT HIGHLIGHTS

Previous studies using subvisible micropulse laser treatment demonstrated a success rate of approximately 70% in patients with chronic CSR, and retreatment rate of approximately 50%. Using Endpoint Management software has many advantages compared to micropulse laser treatment: 1 - proper titration protocol provides appropriate energy to stimulate RPE, 2 - shorter pulse and use of patterns allow faster and more reproducible treatment and 3 - option of placing barely visible landmark helps with documentation of the treatment location.

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/pubmed/25158944>

REFERENCE

Lavinsky D, Palanker, D. Nondamaging photothermal therapy for the retina: initial clinical experience with chronic central serous retinopathy. *Retina, The Journal of Retinal and Vitreous Diseases*. 2014;1-10

Retina, The Journal of Retinal and Vitreous Diseases

Nondamaging retinal laser therapy for treatment of central serous chorioretinopathy: What is the evidence?

Edward H. Wood, Peter A. Karth, Steven R. Sanislo, Darius M. Moshfeghi, Daniel V. Palanker

PURPOSE

To summarize the literature addressing subthreshold or nondamaging retinal laser therapy (NRT) for central serous chorioretinopathy (CSCR) and to discuss results and trends that provoke further investigation.

METHOD

Analysis of current literature evaluating NRT with micropulse or continuous wave lasers for CSCR.

RESULTS

Sixteen studies including 398 patients consisted of retrospective case series, prospective nonrandomized interventional case series, and prospective randomized clinical trials. All studies but one evaluated chronic CSCR, and laser parameters varied greatly between studies. Mean central macular thickness decreased, on average, by 80 μm by 3 months. Mean best-corrected visual acuity increased, on average, by about 9 letters by 3 months, and no study reported a decrease in acuity below presentation. No retinal complications were observed with the various forms of NRT used, but six patients in two studies with micropulse laser experienced pigmentary changes in the retinal pigment epithelium attributed to excessive laser settings.

CONCLUSIONS

Based on the current evidence, NRT demonstrates efficacy and safety in 12-month follow-up in patients with chronic and possibly acute CSCR. The NRT would benefit from better standardization of the laser settings and understanding of mechanisms of action, as well as further prospective randomized clinical trials.

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/pubmed/27841848>

REFERENCE

Wood E, Karth P, Sanislo S, et al. Nondamaging retinal laser therapy for treatment of central serous chorioretinopathy: What is the evidence? *Retina, The Journal of Retinal and Vitreous Diseases*. 2016;1-13

Eye

Randomised clinical trial evaluating best-corrected visual acuity and central macular thickness after 532-nm subthreshold laser grid photocoagulation treatment in diabetic macular oedema.

W Pei-pei, H Shi-zhou, T Zhen, L Lin, L Ying, O Jiexiong, Z Wen-bo and J Chen-jin

PURPOSE

To compare best-corrected visual acuity (BCVA) and central macular thickness (CMT) after 532-nm subthreshold laser grid photocoagulation and threshold laser grid photocoagulation for the treatment of diabetic macular oedema (DME).

METHOD

Twenty-three patients (46 eyes) with binocular DME were enrolled in this study. The two eyes of each patient were divided into a subthreshold photocoagulation group and a threshold photocoagulation group. The eyes of the subthreshold group underwent 532-nm pattern scan laser system (PASCAL) 50% end point subthreshold laser grid photocoagulation therapy, whereas the threshold photocoagulation group underwent short-pulse grid photocoagulation with a 532-nm PASCAL system. BCVA and CMT were assessed in all patients before treatment, 7 days after treatment, and 1, 3, and 6 months after treatment.

RESULTS

After grid photocoagulation, the mean BCVA improved in both the subthreshold group, and the threshold group, and the two groups did not differ statistically significantly from each other. Similarly, the macular oedema diminished in both groups after treatment, and the two groups did not differ statistically significantly from each other with regard to CMT.

CONCLUSIONS

Both 532-nm subthreshold laser grid photocoagulation and threshold laser grid photocoagulation can improve the visual acuity and reduce CMT in DME patients.

ABSTRACT HIGHLIGHTS

Our preliminary study suggests that subthreshold photocoagulation enhance visual acuity and alleviate macular oedema. Invisible laser spots after therapy means subthreshold photocoagulation causes a relatively low level of damage to the RNFL and lower inflammatory reactions which preserves DR patient's visual function.

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/pubmed/25697457>

REFERENCE

Pei-pei W, Shi-zhou H, Zhen T, et al. Randomised clinical trial evaluating best-corrected visual acuity and central macular thickness after 532-nm subthreshold laser grid photocoagulation treatment in diabetic macular oedema. *Eye*. 2015;29:313-22

Acta Ophthalmologica

Comparing Pattern Scanning Laser Trabeculoplasty to Selective Laser Trabeculoplasty: A Randomized Controlled Trial

Kaweh Mansouri & Tarek Shaarawy

PURPOSE

To compare safety, tolerability and intraocular pressure (IOP)-lowering efficacy of pattern scanning laser trabeculoplasty (PSLT) with selective laser trabeculoplasty (SLT) in fellow eyes of untreated patients with glaucoma.

METHOD

Pattern scanning laser trabeculoplasty was performed using the PASCAL laser (PASCAL Streamline 577; Topcon Inc., Tokyo, Japan). Patients' comfort level to treatment was assessed using a visual analogue scale (VAS). Follow-up visits were at week 1, month 1, 3 and 6. Success was defined as IOP reduction $\geq 20\%$.

RESULTS

The mean age of patients was 54.1 ± 15.5 years. Baseline IOP was similar between both groups (PSLT, 17.3 ± 4.0 mmHg; SLT, 16.8 ± 3.6 mmHg, $p > 0.05$). In the PSLT group, the mean IOP at 1, 3 and 6 months was 14.2 ± 3.5 , 13.9 ± 2.6 and 14.0 ± 2.7 mmHg, respectively. In the SLT group, the mean IOP at 1, 3 and 6 months was 14.4 ± 4.1 , 13.7 ± 3.2 and 13.7 ± 3.1 mmHg, respectively. The IOP reduction in the PSLT group was greater than the SLT group at 1 month ($p < 0.01$) and 3 months ($p < 0.01$). VAS score was better in PSLT eyes: 23.9 ± 20.5 (range, 0-82) than in SLT eyes: 50.4 ± 25.3 (range, 0-98) ($p < 0.001$). No serious adverse events were recorded.

CONCLUSIONS

Both laser modalities had similar safety and efficacy profiles while PSLT was better tolerated by patients.

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/labs/articles/27778483/>

REFERENCE

Mansouri K, Shaarawy T. Comparing Pattern Scanning Laser Trabeculoplasty to Selective Laser Trabeculoplasty: A Randomized Controlled Trial. *Acta Ophthalmologica*. 2016:1-3

Ophthalmic Lasers, Surgery & Imaging

Patterned Laser Trabeculoplasty.

Carrasco, Adolfo Morales, Hugo Quiroz-Mercado, Dan Andersen, George Marcellino, Georg Schuele, Daniel Palanker

PURPOSE

A novel computer-guided laser treatment for open-angle glaucoma, called patterned laser trabeculoplasty, and its preliminary clinical evaluation is described.

METHOD

Forty-seven eyes of 25 patients with open-angle glaucoma received 532-nm laser treatment with 100- μ m spots. Power was titrated for trabecular meshwork blanching at 10 ms and sub-visible treatment was applied with 5-ms pulses. The arc patterns of 66 spots rotated automatically after each laser application so that the new pattern was applied at an untreated position.

RESULTS

Approximately 1,100 laser spots were placed per eye in 16 steps, covering 360° of trabecular meshwork. The intraocular pressure decreased from the pretreatment level of 21.9 ± 4.1 to 16.0 ± 2.3 mm Hg at 1 month ($n = 41$) and remained stable around 15.5 ± 2.7 mm Hg during 6 months of follow-up ($n = 30$).

CONCLUSIONS

Patterned laser trabeculoplasty provides rapid, precise, and minimally traumatic (sub-visible) computer-guided treatment with exact abutment of the patterns, exhibiting a 24% reduction in intraocular pressure during 6 months of follow-up ($P < .01$).

LINK TO ABSTRACT

<https://www.ncbi.nlm.nih.gov/pubmed/20968276>

REFERENCE

Turati M, Morales A, Anderson D, et al. Patterned laser trabeculoplasty. *Ophthalmic Surgery, Lasers & Imaging*. 2010 Jun;41(5):538-545

Journal of the Korean Ophthalmological Society

Short-Term Clinical Outcomes of Laser Trabeculoplasty Using a 577-nm Wavelength Laser

Jong Min Kim, Kyong Jin Cho, Sung Eun Kyung, and Moo Hwan Chang

PURPOSE

To evaluate the pressure-lowering effects of single-spot laser trabeculoplasty and patterned laser trabeculoplasty using a 577-nm wavelength laser.

METHOD

A total 35 eyes of 35 patients with primary open-angle glaucoma were enrolled in this study. Eighteen eyes of 18 patients were treated with 360° single-spot laser trabeculoplasty and 17 eyes of 17 patients were treated with 360° patterned laser trabeculoplasty. All patients were evaluated after laser trabeculoplasty at 1 week, 1 month, 3 months, and 6 months using slit lamp examination and Goldmann applanation tonometry.

RESULTS

A total 35 eyes of 35 patients with primary open-angle glaucoma were enrolled in this study. Eighteen eyes of 18 patients were treated with 360° single-spot laser trabeculoplasty and 17 eyes of 17 patients were treated with 360° patterned laser trabeculoplasty. All patients were evaluated after laser trabeculoplasty at 1 week, 1 month, 3 months, and 6 months using slit lamp examination and Goldmann applanation tonometry.

CONCLUSIONS

Laser trabeculoplasty with a 577-nm optically pumped semiconductor laser was safe and demonstrated an IOP lowering effect. There were no significant differences in the IOP lowering effects between the single-spot laser trabeculoplasty and the patterned laser trabeculoplasty.

LINK TO ABSTRACT

<https://synapse.koreamed.org/DOIx.php?id=10.3341/jkos.2014.55.4.563&vmode=PUBREADER>

REFERENCE

Jong Min Kim, Kyong Jin Cho, Sung Eun Kyung et al. *Journal of the Korean Ophthalmological Society*. 2014 Apr;55(4):563-569.

Patient cases, parameters and techniques provided by the physician/author.

Abstracts are collected from Pubmed and includes study information approved and published by the author.

Topcon assumes no responsibility for patient outcome or for physician oversight.

Endpoint Management is an optional accessory for PASCAL Streamline and Synthesis laser systems.
Contact your local Topcon representative for information about system upgrade requirements.



TOPCON CORPORATION

75-1 Hasunuma-cho, Itabashi-ku, Tokyo 174-8580, Japan. Phone:+81-(0)3-3558-2522/2502 Fax:+81-(0)3-3965-6898 www.topcon.co.jp

TOPCON MEDICAL SYSTEMS, INC.

111 Bauer Drive, Oakland, NJ 07436, U.S.A.
Phone:+1-201-599-5100 Fax:+1-201-599-5250 www.topconmedical.com

TOPCON CANADA INC.

110 Provencher Avenue, Boisbriand, QC J7G 1N1 CANADA
Phone:+1-450-430-7771 Fax:+1-450-430-6457 www.topcon.ca

TOPCON EUROPE MEDICAL B.V.

Essebaan 11, 2908 LJ Capelle a/d IJssel, P.O.Box145;
2900 AC Capelle a/d IJssel, THE NETHERLANDS
Phone:+31-(0)10-4585077 Fax:+31-(0)10-4585045
E-mail: medical@topcon.eu; www.topcon-medical.eu

ITALY OFFICE

Viale dell' Industria 60; 20037 Paderno Dugnano; (Milano), ITALY
Phone:+39-02-9186671 Fax:+39-02-91081091 E-mail: info@topcon.it; www.topcon.it

DANMARK OFFICE

Praestemarksvej 25; 4000 Roskilde, DANMARK
Phone:+45-46-327500 Fax:+45-46-327555
E-mail: topcon@topcondanmark.dk www.topcondanmark.dk

IRELAND OFFICE

Unit 276, Blanchardstown; Corporate Park 2 Ballycoolin Dublin 15, IRELAND
Phone:+353-18975900 Fax:+353-18923915 E-mail: medical@topcon.ie; www.topcon.ie

TOPCON S.A.R.L.

BAT A1 3 route de la révolte 93206 SAINT DENIS CEDEX
Phone:+33-1-49-21-23-23 Fax: +33-1-49-21-23-24 E-mail:topcon@topcon.fr; www.topcon.fr

TOPCON DEUTSCHLAND MEDICAL G.m.b.H.

Hanns-Martin-Schleyer Strasse 41; D-47877 Willich, GERMANY
Phone:+49-(0)2154-8850 Fax:+49-(0)2154-885177 E-mail:med@topcon.de; www.topcon.de

TOPCON SCANDINAVIA A.B.

Neongatan 2; P.O.Box 25; 43151 Mölndal, SWEDEN
Phone:+46-(0)31-7109200 Fax:+46-(0)31-7109249 E-mail:medical@topcon.se; www.topcon.se

TOPCON ESPAÑA S.A.

Frederic Mompou 4 Esc. A Bajos 3, 08960 Sant Just Desvern Barcelona, SPAIN
Phone:+34-93-4734057 Fax:+34-93-4733932 E-mail: medica@topcon.es; www.topcon.es

TOPCON (GREAT BRITAIN) LTD.

Topcon House,Kennet Side,Bone Lane,Newbury,Berkshire RG14 5PX United Kingdom
Phone:+44-(0)1635-55120 Fax:+44-(0)1635-551170 E-mail:medical@topcon.co.uk; www.topcon.co.uk

TOPCON POLSKA Sp. z o. o.

ul. Warszawska 23; 42-470 Stewierz, POLAND
Phone:+48-(0)32-6705045 Fax:+48-(0)32-6713405 www.topcon-polska.pl

TOPCON SINGAPORE MEDICAL PTE. LTD.

1 JALAN KILANG TIMOR #09-01 PACIFIC TECH CENTRE SINGAPORE 159303
Phone:+65-68720606 Fax:+65-67736150
E-mail:medical_sales@topcon.com.sg www.topcon.com.sg

REPRESENTATIVE OFFICE IN INDONESIA

Level 38, Tower A, Kota Kasablanka unit GH-04, Jl.
Casablanca, Kav 88, Jakarta, Indonesia 12870
Phone:+62-21-2963-8004

TOPCON INSTRUMENTS (MALAYSIA) SDN.BHD.

No. D1, (Ground Floor), Jalan Excella 2, Off Jalan Ampang Putra,
Taman Ampang Hilir, 55100 Kuala Lumpur,MALAYSIA
Phone:+60-(0)3-42709866 Fax:+60-(0)3-42709766

TOPCON INSTRUMENTS (THAILAND) CO.,LTD.

77/162 Sinnsathorn Tower, 37th Floor,Krunghthoburi Rd.,Klongtongnai,
Klongsarn, Bangkok 10600,THAILAND
Phone:+66(0)2-440-1152-7 Fax:+66-(0)2-440-1158

Mehra Eyetech Private Limited

801 B Wing, Lotus Corporate Park, Graham Firth Steel Compound Goregaon (East)
Mumbai 400063 Maharashtra, INDIA
Phone:+91-22-61285455 www.mehraeyetech.in

© TOPCON MEDICAL LASER SYSTEMS, INC.
PASCAL and PASCAL Streamline are registered trademarks
of TOPCON MEDICAL LASER SYSTEMS, INC.

Patented 7766903 (USA); 4377405 (Japan) and other patents pending
E167-1