Sub-Threshold Laser Therapies using the PASCAL Laser System

Clinical and Scientific Dossier
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.

**INTRODUCTION**

**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. 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.

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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 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 tissue damage. Laser settings below the 1=01 (log=1) are sub-therapeutic. The algorithm begins with titration of the laser power to produce visible burns in the retina outside the arcades 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 fluorescence angiography (FA). However, at 30% energy, there is no damage detectable on histology, nor on FA or OCT (Figure 2).

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 requires about 400 to 500 exposures. With 100 µm 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 choroids. This energy 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. 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 photoagulation. 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.

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 (Zeepcon) 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 phototheraphy 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 trabeculoplaspy (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 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. 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. 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 ST7 (Zeepcon) using the following parameters:
- Wavelength: 577 nm (yellow)
- Average number of spots (360°): 127
- Exposure energy: 1.5 to 2.3 μJ (average: 1.7 μJ)

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 μJ (average: 0.8 μJ)

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 25.3 mmHg at baseline and 17.3 mm Hg at 6 months. There was no significant difference in average reduction in IOP from baseline, the rate of 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 25.3 mmHg at baseline and 17.3 mm Hg 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 primary open-angle or pseudoexfoliative glaucoma. Patients under 70 received concurrent monitoring with a contact lens sensor that monitors IOP indirectly. The study included 60 eyes of 30 patients with primary open-angle or pseudoexfoliative glaucoma. Patients underwent 24 hours of monitoring with a 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 11 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).

The investigators concluded that PSLT was as effective as SLT in lowering IOP over a 6-month period.
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 procedures: 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 mm Hg 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 (P = 0.0001). The average value for PSLT eyes was 25 mmHg (P = 0.0001), indicating a significantly lower level of patient discomfort.

At the time of referral, her IOP for use in the United States, and brinzolamide travoprost/timolol (DuoTrav), which is not approved consult, her medication was changed to right eye was 26 to 30 mmHg while on timolol/glaucoma presented to our clinic. The IOP in her A 52-year-old woman with primary open-angle Miho Nozaki, MD, PhD

**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.

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 scaring, 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
- 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.
- 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
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.
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 Jie-xiong, 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 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 inflammation reactions which preserves DR patient’s visual function.

REFERENCE

ABSTRACTS — GLAUCOMA

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 ≥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 ± 3.6, 13.9 ± 3.6 and 14.0 ± 2.7 mmHg, respectively. In the SLT group, the mean IOP at 1, 3 and 6 months was 14.4 ± 3.6, 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.

REFERENCE
ABSTRACTS — GLAUCOMA

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-μm 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).

REFERENCE

ABSTRACTS — GLAUCOMA

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.

REFERENCE
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.**