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PASCAL Pre-Clinical Articles


PASCAL Clinical Articles

PASCAL Experience


Comparison of PASCAL with Conventional Laser


48. Paulo Stanga, MD “Subthreshold retinal treatment with yellow 577-nm PASCAL Laser” P77-80 January/February 2013 RETINA TODAY


### Comparison of PASCAL with Conventional Laser

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### Future Directions

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Introduction:
We reasoned that greater precision and safety in retinal photocoagulation might be achieved by delivering a multiplicity of spots in a pattern created by a scanner rather than a series of individually placed lesions. We also wondered whether the pattern application time and patient discomfort could be further reduced by using shorter pulses than the conventional 100 milliseconds to 200 milliseconds recommended in the DRS and ETDRS.

Materials and Method:
Standard Zeiss SL 130 slit lamp, 514 nm argon ion laser, Pentium III PC running under MS Windows 2000 coordinated pulse duration; safety shutter control; scanner positioning; pattern geometry and aiming beam intensity. Scanning was achieved by mirrors mounted on a two-axis galvanometric scanner. Ten New Zealand Red/Hybrid rabbits anesthetized using ketamine, hydrochloride, xylazine, and glycopyrrolate, administered 30 minutes prior to procedure. Pupillary dilation achieved with one drop of 1% tropicamide and one drop of 2.5% phenylephrine hydrochloride. Single spots with pulse durations of 10ms, 20ms, 50ms, 100ms were used to determine threshold power levels required to achieve clinically acceptable standard lesion. Mainster contact lens was used. Spot diameter (in air) = 200 μm with top-hat beam profile. Spot size on retina ≈ 130 μm.

Patterns used:
4x4 array delivered. Post tx: sections of 1 μm in thickness were stained with toluidine blue and examined by light microscopy.

Conclusion:
Patterned photocoagulation with shorter pulses offers the following potential advantages compared with conventional manual application of single spots: (a) significantly improved efficiency, (b) increased safety with a central fixation spot and foveal exclusion zone, (c) increased uniformity and precision of spot placement, (d) more accurate placement of “subthreshold” lesions in a grid pattern, and (d) possible reduced pain and visual field defects due to reduced heat diffusion toward the choroid and inner retina.

Significance:
This pre-Pascal launch in vivo study forms the basis of the Pascal Method of pattern scanning & short pulse duration. The study demonstrated the efficacy, safety & accuracy of the Pascal Method parameters.
The First Truly Pattern Scanning Laser-Evolved

Abstracts


Objective:
Evaluate laser beam size, power and pulse duration of 1 to 100 ms on the characteristics of ophthalmoscopically visible retinal coagulation lesions.

Methods:
A 532-nm Nd:YAG laser was used to irradiate 36 retinas in Dutch Belt rabbits with retinal beam sizes of 66, 132 and 330 µm. Lesions were clinically graded 1 minute after placement, their size measured by digital imaging and their depth assessed histologically at different time points.

Conclusions:
At shorter pulse durations, the width and axial extent of the retinal lesions are smaller and less dependent on variations in laser power than at longer durations. The width of the therapeutic window, a measure of relative safety, increases with the beam size.

Significance:
Pulse durations of approximately 20 ms represent a optimal compromise between the favorable impact of speed, higher spatial localization and reduced collateral damage on one hand, and sufficient width of the therapeutic window (>3) on the other.


Objective:
To systematically asses the changes in retinal morphology during the healing of retinal photocoagulation lesions of various clinical grades.

Methods:
Rabbits were irradiated with a 532-nm Nd:YAG laser with a beam diameter of 330 µm at the retinal surface, a power of 175 mW, and pulse durations between 5 an 100 ms. Retinal lesions were clinically graded 1 minute after placement as invisible, barely visible, light, moderate, intense, very intense and rupture and were assessed histologically at six time points from 1 hour to 4 months.

Conclusions:
The decreasing width of the retinal damage zone suggests that photoreceptors migrating from unaffected areas fill in the gap in the photoreceptor layer. Laser photocoagulation parameters can be specified to avoid not only the inner retinal damage, but also permanent disorganization and scarring in the photoreceptor layer. These data may facilitate studies to determine those aspects of laser treatment necessary for beneficial clinical response and those that result in extraneous retinal damage.

Significance:
This study showed that by altering the pulse duration it is possible to alter the healing characteristics of the retina tissues, whereby shorter pulse duration limits collateral damage as well as encourage photoreceptor cell migration to lesion areas.


Background:
The Pascal is a semiautomated photocoagulator that delivers a pattern array of multiple burns in a rapid predetermined sequence with a single foot pedal depression. Each burn is reduced to 10 or 20 ms to achieve this. The authors report their early experience with the system.

Methods:
75 procedures done in 60 patients divided into four groups – group A, patients undergoing panretinal photocoagulation (PRP); group B, patients undergoing focal or modified grid macular laser; group C, patients undergoing macular grid and group D, patients undergoing retinopexy – were retrospectively studied.

Conclusions:
Although the shorter pulse duration of the Pascal necessitates the use of a higher power, it is not associated with adverse effects. The results here suggest that the Pascal photocoagulator is safe and effective, and offer several potential advantages related to the brief exposure time. No adverse effects noted when patterns were fired upon blood vessels or old laser burns.

Significance:
This first published study on experience with Pascal demonstrated the potential to reduce overall treatment duration, thereby reducing cost to hospital and patient, while at the same time, offering precision, safety, comfort and efficiency.


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This first published study on experience with Pascal demonstrated the potential to reduce overall treatment duration, thereby reducing cost to hospital and patient, while at the same time, offering precision, safety, comfort and efficiency.
The First Truly Pattern Scanning Laser-Evolved

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Purpose:
To analyze the benefits, efficacy, and complications of the PASCAL photocoagulation laser system (OptiMedica, Santa Clara, CA, USA) in patients treated at our institution.

Methods:
We conducted a retrospective chart review of 19 patients (28 eyes) who underwent laser treatment using the PASCAL photocoagulation system from November 2006 to November 2007. These 28 eyes were divided into two groups; group 1 eyes underwent macular grid laser and group 2 eyes underwent panretinal photocoagulation. Treatment was performed for macular edema or for iris or retinal neovascularization. Outcomes measured included best-corrected visual acuity (BCVA), efficacy of laser treatment, complications, duration of the procedure, and pain perception, which were noted in the charts for panretinal treatments.

Conclusions:
Retinal photocoagulation by the PASCAL laser has comparable efficacy to historical results with conventional laser for the treatment of macular edema and retinal neovascularization. Treatment was performed quicker with less discomfort for patients.

Significance:
Another Pascal study demonstrating similar efficacy to conventional laser while being less painful for patients.

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Purpose:
To establish safe laser parameter standards for 10–30 ms Pascal laser in clinical practice and to evaluate clinical and visual outcomes using this 532-nm multi-spot photocoagulation system.

Methods:
Retrospective observational case series of 313 patients treated between 2006 and 2008. Evaluation of eight different pathologies using a Pattern Scan Laser (PASCAL) system and its modified settings.

Results:
There were 1301 consecutive cases. Complications included 17 cases of retinal bleeding (1.3%), two cases of choroidal detachment (0.15%) and one case of exudative retinal detachment (0.07%). There was no statistical difference between the laser parameters used in patients with or without complications.

Conclusions:
The laser parameters for PASCAL are safe. The complications and adverse effects encountered in this series are similar to those reported in other studies.

Significance:
Another study showing that the laser parameters for PASCAL are safe, with the rate of complications and adverse effects similar to those reported in other studies.
The First Truly Pattern Scanning Laser-Evolved Photocoagulation Unit

Aim: To systematically refine and recommend parameter settings of spot size, power, and treatment duration using the PASCAL photocoagulator, a multi-spot, semi-automated, short-duration laser system.

Materials and Methods: A retrospective consecutive series with 752 Caucasian eyes and 1242 laser procedures over two years were grouped into, (1) 374 macular focal / grid photocoagulation (FP), (2), 666 panretinal photocoagulation (PRP), and (3) 202 barrage photocoagulation (BP). Parameters for power, duration, spot number, and spot size were recorded for every group.

Results: Power parameters for all groups showed a non-gaussian distribution; FP group, median 190 mW, range 100 - 950 mW, and PRP group, median 600 mW, range 100 - 2000 mW. On subgroup comparison, for similar spot size, as treatment duration decreased, the power required increased, albeit in a much lesser proportion than that given by energy = power x time. Most frequently used patterns were single spot (89% of cases) in FP, 5 X 5 box (72%) in PRP, and 2 X 2 box (78%) in BP. Spot diameters as high as = 700 μm on retina were given in the PRP group. Single session PRP was attempted in six eyes with a median spot count of 3500.

Conclusion: Overall, due to the small duration of its pulse, the PASCAL photocoagulator tends to use higher powers, although much lower cumulative energies, than those used in a conventional laser. The consequent lesser heat dissipation, especially lateral, can allow one to use relatively larger spot sizes and give more closely spaced burns, without incurring significant side effects.

Significance: Paper demonstrating Pascal parameters causes less collateral damage compared to conventional laser.

Abstracts


Aim: To evaluate the visual acuity (VA) and optical coherence tomography thickness results of short-duration pattern scanning laser macular photocoagulation in the treatment of clinically significant macular edema because of diabetics.

Methods: Consecutive retrospective analysis of VA and optical coherence tomography data from eyes treated in a modified Early Treatment Diabetic Retinopathy Study style using a short-duration pattern scanning laser.

Results: A total of 100 eyes from 70 patients met study criteria. All subjects were treated with the same PASCAL (pattern scanning laser) photocoagulation unit. Parameters varied according to media and pigmentation status, but typical settings were 100-mm spot size, 10-millisecond pulse duration, 225-mW power, and 29 J/cm^2 fluence to give a pale but visible lesion. At 4 months posttreatment, there was an average improvement in VA of 0.060 logMAR (an improvement from 20/45 to 20/40, or approximately 3 Early Treatment Diabetic Retinopathy Study letters; P = 0.0007) and a reduction of central optical coherence tomographic thickness of 40 mm and 37 mm (spectral domain and time domain optical coherence tomography groups, respectively), both of which were statistically significant (P = 0.0049 and 0.012, respectively).

Conclusion: Short-duration PASCAL macular photocoagulation has a biological treatment effect at 4 months for the treatment of clinically significant macular edema. While caution must be used when converting between different VA measurement methods and when using literature-based controls, the observed VA improvement seems equivalent to 3 Early Treatment Diabetic Retinopathy Study letters. These findings are similar to the recently published results from the diabetic retinopathy clinical research network cohort. PASCAL laser photocoagulation for clinically significant macular edema appears safe and effective in the short term and may have significant long-term advantages.


Purpose: To correlate in vivo spatial and spectral morphologic changes of short- to long-pulse 532 nm Nd:YAG retinal laser lesions using Fourier-domain optical coherence tomography (FD OCT), autofluorescence (AF), fluorescein angiography (FA), and multispectral imaging.

Methods: Ten eyes with treatment-naive preproliferative or proliferative diabetic retinopathy were studied. A titration grid of laser burns at 20, 100, and 200 milliseconds was applied to the nasal retina and laser fluence titrated to produce four grades of laser lesion visibility: subvisible (SV), barely visible (BV, light-gray), threshold (TH, gray-white), and suprathreshold (ST, white). The AF, FA, FD-OCT, and multispectral imaging were performed 1 week before laser, and 1 hour, 4 weeks, and 3 and 6 months post-laser. Multispectral imaging measured relative tissue oxygen concentration.

Results: Laser burn visibility and lesion size increased in a linear relationship according to fixed fluence levels. At fixed pulse durations, there was a semilogarithmic increase in lesion size over 6 months. At 20 milliseconds, all grades of laser lesion were reduced significantly in size after 6 months: SV, 51%; BV, 54%; TH, 49%; and ST, 50% (P<0.001), with retinal pigment epithelial proliferation and photoreceptor infilling. At 20 milliseconds, there was healing of photoreceptor inner segment/outer segment junction layers compared with 100- and 200-millisecond lesions. Significant increases in mean tissue oxygenation (range, four to six units) within the laser titration area and in oxygen concentration across the laser lesions (P<0.01) were detected at 6 months.

Conclusions: For patients undergoing therapeutic laser, there may be improved tissue oxygenation, higher predictability of burn morphology, and more spatial localization of healing responses of burns at 20 milliseconds compared with longer pulse durations over time.
The First Truly Pattern Scanning Laser-Evolved


**Purpose:**
The purpose of this study was to compare the efficacy, collateral damage, and convenience of panretinal photocoagulation for proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy using a 532-nm solid-state green laser (GLX) versus a multiphoton 532-nm pattern scan laser (PASCAL).

**Methods:**
This study was a prospective randomized clinical trial. Sixty patients with bilateral symmetrical proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy participated. Each patient underwent panretinal photocoagulation: one eye with GLX and the other with PASCAL, two sittings per eye. Grade 3 burns with a 200-μm spot size were placed with both modalities. The fluence, pain using the visual analog scale, time, laser spot spread with infrared images, and retinal sensitivity were compared.

**Results:**
Pattern scan laser and GLX required an average fluence of 40.33 vs 191 J/cm², respectively. Average time required per sitting was 1.43 minutes with PASCAL and 4.53 minutes with GLX. Average visual analog scale reading for GLX was 4.8, whereas that for PASCAL was 0.33. Heidelberg retinal angiography images showed the spot spread as being 430 versus 310 μm at 3 months with GLX and PASCAL. The eyes treated with PASCAL showed higher average retinal sensitivity in the central 15 ° and 15 ° to 30 ° zones (25.08 and 22.08 dB, respectively) than the eyes treated with GLX (23.16 and 17.14 dB), respectively.

**Conclusion:**
Pattern scan laser showed lesser collateral damage and similar regression of retinopathy compared with GLX. Pattern scan laser treatment was less time consuming and less painful for the patient compared with GLX.

**Significance:**
This is the first published peer-reviewed prospective randomized study comparing PASCAL with conventional laser (GLX). The results showed that PASCAL results in similar retinopathy regression while causing less collateral damage, less pain and less time compared to GLX.


**Purpose:**
To investigate the effects of Pascal multi-spot panretinal photocoagulation given in a single-session (SS-PRP) vs single-spot multiple-session PRP (MS-PRP) on proliferative diabetic retinopathy (PDR).

**Methods:**
Single-center, randomized clinical trial of 40 eyes. Proliferative diabetic retinopathy was treated with a 400-μm spot size in 1500 burns given either as Pascal in 20-millisecond SS-PRP or in 3 sessions (100-millisecond MS-PRP) during a 4-week period. Visual acuity, central subfield retinal thickness (CRT), and 24-2 Swedish interactive threshold algorithm visual fields were recorded at baseline and 4 and 12 weeks. MAIN OUTCOME MEASURES: Central subfield retinal thickness, mean deviation.

**Results:**
There was a significant increase in mean CRT with MS-PRP (22 mum at 4 weeks, 95% CI, -32.25 to -10.75; 20 mum at 12 weeks, 95% CI, -28.75 to -10.82; P < .001) and no significant increase in the SS-PRP group. The mean deviation increased significantly in the SS-PRP group after 4 weeks (0.73 dB, P = .048), with no significant changes in either group at other points. A positive effect on PDR was observed in 74% of eyes in the SS-PRP group vs 53% in the MS-PRP group (P = .31). Mean treatment time for SS-PRP was 5.04 minutes (SD, 1.5 minutes) compared with 59.3 (SD, 12.7 minutes) in the MS-PRP group (P < .001).

**Conclusions:**
There were no adverse outcomes (CRT, visual acuity, or visual field) from using multi-spot SS-PRP vs single-spot MS-PRP at 12 weeks post laser, and treatment times were significantly shorter for multi-spot SS-PRP. Pascal SS-PRP was as effective as MS-PRP in the treatment of PDR.

**Significance:**
SS-PRP may be performed safely and rapidly with same efficacy as MS-PRP with the advantage of significantly shorter treatment time and no increase in mean CRT compared to MS-PRP.


**Purpose:**
To evaluate pain responses following Pascal 20 ms multi-spot and 100 ms single-spot panretinal photocoagulation (PRP).

**Methods:**
Single-centre randomised clinical trial. 40 eyes of 24 patients with treatment-naïve proliferative diabetic retinopathy randomised to 20 and 100 ms PRP under topical 0.4% oxybuprocaine. A masked grader used a pain questionnaire within 1 h (numerical pain score (NPS)) and 1 month after treatment (numerical headache score (NHS)). Primary outcome measure was NPS immediately post-PRP. Secondary outcome measures were mean NHS scores and levels of photophobia reported within 4 weeks of primary PRP.

**Results:**
Mean laser fluence was significantly lower using 20 ms PRP (4.8 J/cm²) compared to 100 ms PRP (11.8 J/cm², p<0.001). Mean NPS scores for treatment were 2.4 (2.3) (mild) for 20 ms PRP group compared to 4.9 (3.3) (moderate) in 100 ms PRP group- a significant difference (95% CI 4.3 to 6.8; p=0.006). Mean NHS score within 1 month was 1.5 (2.7) in 20 ms PRP group compared to 3.2 (3.5) in the 100 ms PRP group (p<0.05). The median duration of photophobia after 20 ms PRP was 3 h, and significantly less compared to 100 ms PRP after which 72 h of photophobia was reported (p<0.001).

**Conclusions:**
Multi-spot 20 ms PRP was associated with significantly lower levels of anxiety, headache, and photophobia compared to 100 ms single-spot PRP treatment. Possible reasons include lower fluence, shorter-pulse duration, and spatial summation of laser nociception with multi-spot Pascal technique.

**Significance:**
20 ms multi-spot single session Pascal PRP is associated with significantly less pain, headaches & photophobia compared to conventional 100-ms single-spot multiple session PRP.
Purpose: To compare the safety and efficacy of Pascal laser photoagulation in comparison with the conventional laser photoagulation in the treatment of diabetic retinopathy.

Patients and methods:
A prospective randomized case series study was done on 120 procedures done in 120 patients divided into two main groups, group A, patients undergoing focal or modified grid macular laser and group B, patients undergoing panretinal photoagulation (PRP). Each of the two groups were subdivided into two subgroups randomly in the first we used conventional laser photoagulation (groups A1 and B1) and in the other we used Pascal laser photoagulation (groups A2 and B2).

Results:
Procedures in groups A1,2 and in groups B1,2 had successful outcomes. Significantly higher powers were required with the Pascal (groups A2 and B2) than with conventional laser (groups A1 and B1) (p<0.001) in eyes that underwent PRP and focal/modified grid macular treatment with both systems. No adverse events were noted in all groups.

Conclusion:
The Pascal photoagulator is safe, rapid, effective, with rapid learning and had short exposure time. Although the shorter pulse duration of the Pascal necessitates the use of a higher power, it is not associated with adverse effects.

Significance:
Another study showing that Pascal parameters are safe & effective for PRP and macula laser.

Abstracts

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Mahul M. K. Muqit, FRCoOphth, George R. Marcellino, PhD, David B. Henson, PhD, Cecilia H. Fenerty, FRCoOphth, Paulo E. Stanga, MD. "Randomized clinical trial to evaluate the effects of Pascal panretinal photoagulation on macular nerve fiber layer: Manchester Pascal Study report 3."

Conclusion:
Complications and the associated pain are less; thus, the patient’s acceptance of PASCAL was high, and single session was well tolerated with topical anesthesia alone.

Significance:
Study shows that Pascal’s single session PRP obtained better results (less pain, better patient acceptance, less complications) compared to multiple session conventional laser PRP.

Methods:
Single-center, randomized clinical trial (n = 40 eyes). Proliferative diabetic retinopathy as treated with 1,500 burns given as Pascal 20-millisecond single-session PRP (SS-PRP) or as multiple-session PRP (100 milliseconds, MS-PRP) over a 4-week period. The main outcome measures included optical coherence tomography measurements of total retinal thickness and nerve fiber layer at the macula, visual acuity, and proliferative diabetic retinopathy regression and were recorded at baseline, 4 weeks, and 12 weeks. Optic disk photographs were graded by masked a glaucoma specialist.

Results:
At 12 weeks, in the SS-PRP group, there was no significant change in total nerve fiber layer thickness from baseline (4 weeks: +7.2 μm, P = 0.78; 12 weeks, −1.8 μm, P = 0.95). There was a significant increase in total retinal thickness for the MS-PRP group at 4 weeks from baseline (96 ± 17 μm, P < 0.001) and at 12 weeks (56 ± 21 μm, P = 0.0167). After 4 weeks in the MS-PRP group, total nerve fiber layer thickness increased significantly by 31 ± 54 μm (P = 0.025) from baseline, with a significant reduction at 12 weeks from baseline (35 ± 63 μm, P = 0.034). There was no change among groups for optic nerve appearance postlaser. At 12 weeks, the mean visual acuity was 81 ± 6 letters (SS-PRP group), compared with 77 ± 15 letters in the MS-PRP group (95% confidence interval, 5.2 to 9 letters; P = 0.286). For the SS-PRP group, a positive effect on proliferative diabetic retinopathy regression was observed in 74% of eyes compared with 53% of the eyes in the MS-PRP group (P = 0.31).

Conclusion:
Compared with 20-millisecond SS-PRP, eyes treated with conventional 100-millisecond single-spot delivered over multiple sessions showed increased total macular thickness at 4 weeks, with a thinning of macular nerve fiber layer at 12 weeks.
Aims: To quantify the 20-ms Pattern Scan Laser (Pascal) panretinal laser photoablation (PRP) ablation dosage required for regression of proliferative diabetic retinopathy (PDR), and to explore factors related to long-term regression.

Methods: We retrospectively studied a cohort of patients who participated in a randomised clinical trial, the Manchester Pascal Study. In all, 36 eyes of 22 patients were investigated over a follow-up period of 18 months. Primary outcome measures included visual acuity (VA) and complete PDR regression. Secondary outcomes included laser burn dosimetry, calculation of retinal PRP ablation areas, and effect of patient-related factors on disease regression. A PDR subgroup analysis was undertaken to assess all factors related to PDR regression according to disease severity.

Results: There were no significant changes in logMAR VA for any group over time. In total, 10 eyes (28%) regressed after a single PRP. Following top-up PRP treatment, regression rates varied according to severity: 75% for mild PDR (n=6), 67% for moderate PDR (n=14), and 43% in severe PDR (n=3). To achieve complete disease regression, mild PDR required a mean of 2187 PRP burns and 264 mm² ablation area, moderate PDR required 3998 PRP burns and area 456 mm², and severe PDR needed 6924 PRP laser burns (836 mm²; P<0.05).

Conclusion: Multiple 20-ms PRP treatments applied over time does not adversely affect visual outcomes, with favourable PDR regression rates and minimal laser burn expansion over 18 months. The average laser dosimetry and retinal ablation areas to achieve complete regression increased significantly with worsening PDR.

Purpose: To investigate the short-term effects of high-density 20-ms laser on macular thickness using Pascaltargeted retinal photoablation (TRP) and reduced fluence/minimally-traumatic panretinal photoablation (MT-PRP) compared to standard-intensity PRP (SI-PRP) in proliferative diabetic retinopathy (PDR).

Methods: Prospective randomised clinical trial. Treatment-naive PDR was treated with single-session 20-ms Pascal 2500 burns photoablation randomised to one of three treatment arms (TRP:MT-PRP:SI-PRP). Primary outcome measure was change in central retinal thickness (CRT) on OCT. Secondary outcomes at 4 and 12 weeks post-laser included: OCT peripapillary nerve fibre layer (NFL) thickness; PDR disease regression on Optos angiography; SITA-Std visual fields (VF); and visual acuity (VA).

Results: 30 eyes of 24 patients were studied, ten eyes/arm. At 12 weeks, there were significant reductions in CRT after TRP (9.6 mm; 95% CI, 1.84 to 17.36; p=0.001) and MT-PRP (7.1 mm; 95% CI, 1.37 to 12.83; p=0.001), versus SI-PRP (+5.9 mm; 95% CI, 7.57 to 18.55; p=0.32). PDR regression was similar between groups (TRP 70%; MT-PRP 70%; SI-PRP 90%; >0.76). No significant changes in VA and NFL thickness developed between groups. The VF mean deviation scores increased significantly in all groups at 12 weeks (TRP, 0.70 dB; 95% CI, 0.07 to 1.48; p=0.07; MT-PRP, +0.63 dB; 95% CI, 0.12 to 1.15; p=0.02; SI-PRP, +1.06 dB; 95% CI, 0.19 to 1.74; p=0.02). There were no laser-related ocular complications.

Conclusions: This pilot study reports that high-density 20-ms Pascal TRP and MT-PRP using 2500 burns did not produce increased macular thickness or any ocular adverse events during the short-term.
Abstracts

49 Katharina Kriechbaum, MD, Matthias Bolz, MD, Gabor G. Deak, MD, Sorja Prager, MD, Christoph Scholda, MD, Ursula Schmidt-Erfurth, MD “High-Resolution Imaging of the Human Retina In Vivo after Scatter Photocoagulation Treatment Using a Semiautomated Laser System” Ophthalmology 2010;117:545–561

Purpose:
To image the ultrastructural morphology of retinal laser effects and their healing response in vivo using spectral domain optical coherence tomography (SD-OCT).

Design:
Prospective, interventional study.

Methods:
All eyes treated for ME from diabetic retinopathy (diabetic ME) and branch retinal vein occlusion between April 2000 and January 2010 were reviewed for subvisible diode micropulse laser-induced retinal damage. Therapeutic outcomes were reviewed for a subgroup treated for diabetic ME with pre- and postoperative spectral-domain optical coherence tomography. Laser-induced retinal thermal effects were modeled computationally using Arrhenius formalism.

Results:
Ten patients undergoing panretinal photocoagulation for proliferative diabetic retinopathy.

Participants:
Subvisible diode micropulse can effectively treat retinovascular ME without laser-induced retinal damage, consistent with Arrhenius modeling of pulsed hyperthermia.

Methods:
Panretinal photocoagulation (PRP) was performed using a semiautomated patterned scanning laser system providing a raster of effects with homogenous intensity. Retinal morphology and localization of effects owing to laser–tissue interaction were imaged at 1 day, 1 week, and at monthly intervals for 6 months. The characteristic, specific structural changes during the healing process were followed over time using an SD-OCT device (Spectralis OCT) allowing for high-resolution raster scanning of the entire lesion pattern with identification of identical retinal sites (tracking modality).

Main Outcome Measures:
Retinal morphology and localization of effects of photocoagulation on SD-OCT images.

Results:
At day 1 after PRP, the photocoagulation effects were sharply delineated from the surrounding unaffected retina and all spots seemed to be identical in size and location. The area of tissue destruction was confined to the outer retinal layers, extending from the outer nuclear layer (ONL) to the retinal pigment epithelium (RPE). At 1 week, images showed a progressive loss of the affected outer retinal layers, namely, the ONL and the outer plexiform layer. Concomitant distortion of the inner nuclear and plexiform layers generated a pattern of “archways” between adjacent laser spots. The photoreceptor layers (PRL) seemed to be eliminated in the photocooagulated area, particularly at the borders of each lesion. The lesion center contained a condensed RPE and PRL segment. The ONL recovered partially, but the PRL inner and outer segments remained absent. During the long-term follow-up, RPE cells migrated to the center of the lesion, forming a hyperplastic scar.

Conclusions:
The characteristic morphology of retinal photocoagulation effects in vivo and over time was identified for the first time in human eyes using SD-OCT. The OCT imaging demonstrated a well-defined reproducible area of destruction confined to the outer retinal layers. Healing proceeded as the condensation of the RPE and PRL in the lesion center.


Objective:
To report the evolution of pattern scanning laser (PASCAL) photocoagulation burns in the treatment of diabetic retinopathy, using Fourier-Domain optical coherence tomography (FD-OCT) and fundus autofluorescence (AF), and to evaluate these characteristics with clinically visible alterations in outer retina (OR) and retinal pigment epithelium (RPE).

Methods:
Standard red-free and colour fundus photography (FP), FD-OCT, and fundus camera-based AF were performed in 17 eyes of 11 patients following macular and panretinal photocoagulation (PRP).

Conclusions:
Using high-resolution FD-OCT and AF, ophthalmoscopically invisible and threshold PASCAL burns within outer retina and RPE may be accurately localized and mapped by AF and FD-OCT.

Significance:
Another study showing limited collateral damage with Pascal burns while even invisible burns were easily located with AF & FD-OCT.
Purpose:
To analyze immediate in vivo intraretinal morphologic changes secondary to standardized grid photocoagulation using spectral domain optical coherence tomography (SD OCT).

Participants:
13 consecutive patients with treatment-naïve clinically significant diabetic macular edema (DME).

Methods:
Before and 1 day after standardized grid photocoagulation using the PASCAL system, Spectralis OCT examinations based on an eye-tracking system, infrared fundus imaging, color fundus photography, and biomicroscopy were performed. A standardized visual acuity assessment (ETDRS protocol) and fluorescein angiography were performed at baseline.

Main Outcome Measures:
Morphologic changes secondary to grid laser treatment.

Results:
One day after laser therapy, immediate morphologic alterations of only the retinal pigment epithelium (RPE), the photoreceptor layer (PRL), and the outer nuclear layer (ONL), were observed. The shape of the laser-induced lesions did not show a sagittal alteration pattern throughout all 3 of the layers, however, but rather seemed to follow an oblique pathway throughout the ONL, changing direction at the level of the external limiting membrane and proceeding sagittally through the PRL and RPE. These morphologic changes also induced biometric changes, such as a decrease in central retinal thickness combined with local thickening at the lesion site, especially in the PRL.

Conclusions:
Spectral domain optical coherence tomography provides new insight into the immediate morphologic changes after laser treatment using the PASCAL laser system. Standardized grid photocoagulation induces characteristic homogenous alteration in the neurosensoric retinal layers. Biometric changes, indicating an immediate effect, were observed within 1 day after treatment.

Significance:
This is the first study that analyse the immediate in vivo morphologic retinal changes secondary to standardized grid photocoagulation using SD-OCT. This is also a first study to show the unique burns morphology post-grid photocoagulation with the PASCAL grid arrays patterns.
**Objectives:**
To compare in vivo burn morphologic features and healing responses of Pascal 20- and 100-millisecond panretinal photocoagulation (PRP) burns in proliferative diabetic retinopathy.

**Design:**
Prospective randomized controlled trial with 24 eyes assigned to either 20- or 100-millisecond Pascal PRP. Fundus autofluorescence and Fourier domain coherence tomography (FD-OCT) were performed 1 hour and 2 and 4 weeks after treatment. Main outcome measures included burn morphologic features on FD-OCT and greatest linear diameter (GLD) of laser burns as evaluated in 6 standard ETDRS photographic field using autofluorescence.

**Results:**
The contemporaneous increase in autofluorescence is observed with increasing pulse duration. Differences in mean GLD between 100- and 20-millisecond burns were 63µm at 1 hour and 198µm at 4 weeks (P<0.001 for both). At 4 weeks, all burns corresponded to defects at the junction of inner and outer segments of photoreceptors (JI/OSP) and apical retinal pigment epithelium. After 4 weeks, the GLD of 20-millisecond burns reduced significantly by 35% (P<0.001), with no changes in the 100-millisecond burns.

**Conclusions:**
All burns initially appear as equivalent square-edged, columnar foci of hyper reflectivity in the outer retina. Pascal 20-millisecond burns progressively reduce in size, and this suggests a novel healing response localized to the JI/OSP and apical retinal pigment epithelium. The higher fluence 100-millisecond burns developed larger defects due to thermal blooming and collateral damage.

**Significance:**
This is the first time a study show that PASCAL’s parameters allow retinal tissue healing with reduction in laser lesion (up to 35%) which may not occur with conventional laser burns.

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**Purpose:**
To investigate the clinical effects and safety of targeted pattern scan laser (Pascal) retinal photocoagulation in proliferative diabetic retinopathy (PDR).

**Methods:**
Prospective and non-randomized study of 28 eyes with treatment-naive proliferative diabetic retinopathy (PDR). Single-session 20-ms-Pascal TRP strategy applied 1500 burns to zones of retinal capillary non-perfusion and intermediate retinal ischaemia guided by wide-field fluorescein angiography (Optos). Main outcome measures at 12 and 24 weeks included; PDR grade (assessed by two masked retina specialists); central retinal thickness (CRT); mean deviation (MD) using 24-2 Swedish interactive threshold algorithm (SITA)-standard visual fields (VF); and ETDRS visual acuity (VA).

**Results:**
Following primary TRP, there was PDR regression in 76% of patients at 12 weeks (k = 0.70; p < 0.001). No laser re-treatment was required at 4 weeks, and 10 eyes underwent repeat TRP at 12 weeks. Wide-field Optos angiography at 24 weeks showed complete disease regression in 37% and partial regression in 33%. Additional panretinal laser photocoagulation (PRP) was planned for active PDR in 30%. There were significant reductions in CRT over time (10.4 µm at 12-weeks, p=0.007; 12.1 µm at 24-weeks, p=0.0003). The MD on VFs improved after 12 weeks (+1.25 dB; p=0.015) and 24 weeks (+1.26 dB; p=0.01). The VA increased by +3 letters at 24 weeks (95% CI, 1.74–5.01; p<0.0001).

**Conclusions:**
This pilot study reports that Optos-guided Pascal 20-ms TRP using 1500 burns for treatment-naive PDR is a promising procedure with favourable safety profile.
The First Truly Pattern Scanning Laser-Evolved

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

Methods:
Forty-seven eyes of 24 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 ± 1.4 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 ablation of the patterns, exhibiting a 24% reduction in intraocular pressure during 6 months of follow-up (P < .01).

Significance:
First PLT study demonstrating IOP reduction similar to SLT.

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Daniel Palanker, Ph.D, Daniel Lavinsky, MD, Mark Scott Blumenkrantz, MD, George Marcellino, Ph.D. “The Impact of Pulse Duration and Burn Grade on Size of Retinal Photocoagulation Lesion Implications for Pattern Density” RETINA31:1664–1669, 2011

Purpose:
Shorter pulses used in pattern scanning photocoagulation (10–20 milliseconds [ms]) tend to produce lighter and smaller lesions than the Early Treatment Diabetic Retinopathy Study standard 100-ms exposures. Smaller lesions result in fewer complications but may potentially reduce clinical efficacy. It is worthwhile to reevaluate existing standards for the number and size of lesions needed.

Methods:
A prospective randomised pilot clinical trial in which 29 eyes of 24 diabetic patients with mild to moderate The width of the coagulated zone in patients undergoing retinal photocoagulation was measured using optical coherence tomography. Lesions of “moderate,” “light,” and “barely visible” clinical grades were compared for 100, 200, and 400mm spot sizes and pulse durations of 20 ms and 100 ms.

Results:
To maintain the same total area as in 1,000 standard burns (100 ms, moderate) with a 400-mm beam, a larger number of 20-ms lesions are required: 1,464, 1,979, and 3,520 for moderate, light, and barely visible grades, respectively. Because of stronger relative effect of heat diffusion with a smaller beam, with 200mm this ratio increases: 1,932, 2,783, and 5,017 lesions of 20 ms with moderate, light, and barely visible grades correspond to the area of 1,000 standard burns.
Introduction:
We performed a study of laser panretinal photocoagulation in 20 patients with proliferative retinopathy. We compared short exposure, high-energy laser settings with conventional settings, using a 532 nm, frequency doubled, Neodymium–Yag laser and assessed the patients in terms of pain experienced and effectiveness of treatment.

Method:
Twenty patients having panretinal photocoagulation for the first time underwent random allocation to treatment of the superior and inferior hemi-retina. Treatment A used ‘conventional’ parameters: exposure time 0.1 s, power sufficient to produce visible grey-white burns, spot size 300 μm. The other hemiretina was treated with treatment B using exposure 0.02 s, 300 μm and sufficient power to have similar endpoint. All patients were asked to evaluate severity of pain on a visual analogue scale. (0 = no pain, 10 = most severe pain). All patients were masked as to the type of treatment and the order of carrying out the treatment on each patient was randomised. Patients underwent fundus photography and were followed up for 6–45 months.

Conclusion:
Shortening exposure time of retinal laser is significantly less painful but equally effective as conventional parameters.

Significance:
Study using 20 ms pulse duration showed significantly less pain compared to conventional laser’ s 100 ms pulse duration.

Background and Objective:
The 577-nm (yellow) laser provides an alternative to the 532-nm (green) laser in retinal photocoagulation, with potential benefits in macular treatment and through ocular opacities. To assess relative risk of thermomechanical rupture of Bruch’ s membrane with yellow laser in photocoagulation, the therapeutic window, the ratio of threshold powers for mild coagulation and rupture, was measured.

Materials and Methods
Retinal coagulation and rupture thresholds, visualized ophthalmoscopically, were measured with 577- and 532-nm lasers using 10- to 100-ms pulses in 34 rabbit eyes. Lesions at 1 and 7 days were assessed histologically.

Results:
Coagulation threshold with yellow laser was 26% lower than with green laser. The therapeutic window increased linearly with log-duration for both wavelengths with a difference in parallel-slope intercept of 0.36 ± 0.20, corresponding to 8% to 15% wider therapeutic window for yellow wavelength.

Conclusions:
The therapeutic window of retinal photocoagulation in rabbits at 577 nm is slightly wider than at 532 nm, whereas histologically the lesions are similar.

Purpose:
To determine the long-term safety of high-density subvisible diode micropulse photocoagulation (810 nm), compare the clinical findings with computational modeling of tissue hyperthermia and to report results for a subset of eyes treated for diabetic macular edema (ME) documented pre- and postoperatively by spectral-domain optical coherence tomography.

Methods:
All eyes treated for ME from diabetic retinopathy (diabetic ME) and branch retinal vein occlusion between April 2000 and January 2010 were reviewed for subvisible diode micropulse laser-induced retinal damage. Therapeutic outcomes were reviewed for a subgroup treated for diabetic ME with pre- and postoperative spectral-domain optical coherence tomography. Laser-induced retinal thermal effects were modeled computationally using Arrhenius formalism.

Results:
A total of 252 eyes (212 diabetic ME, 40 branch retinal vein occlusion) of 181 patients qualified. None of the 168 eyes treated at irradiance, 350 W/cm² and 7 of 84 eyes at ≥ 580 W/cm² had retinal damage (P= 0.0001) (follow-up 3–120 months, median, 47). Sixty-two eyes of 48 patients treated for diabetic ME with pre- and postoperative spectral-domain optical coherence tomography with median 12 months follow-up had no retinal injury by infrared, red-free, or fundus autofluorescence photos, fluorescein angiography or indocyanine green angiography; or spectral-domain optical coherence tomography. Central foveal thickness (P= 0.04) and maximum macular thickness decreased (P < 0.0001). Modeling of retinal hyperthermia demonstrates that the sublethal clinical regimen corresponds to Arrhenius integral > 0.05, while damage is likely to occur if it exceeds 1.

Conclusion:
Subversible diode micropulse can effectively treat retinovascular ME without laser-induced retinal damage, consistent with Arrhenius modeling of pulsed hyperthermia.
Purpose: Laser therapy for diabetic macular edema and other retinal diseases has been used within a wide range of laser settings: from intense burns to nondamaging exposures. However, there has been no algorithm for laser dosimetry that could determine laser parameters yielding a predictable extent of tissue damage. This multimodal imaging and structural correlation study aimed to verify and calibrate a computational model-based titration algorithm for predictable laser dosimetry ranging from nondamaging to intense coagulative tissue effects.

Methods: Endpoint Management, an algorithm based on a computational model of retinal photothermal damage, was used to set laser parameters for various levels of tissue effect. The algorithm adjusts both power and pulse duration to vary the expected level of thermal damage at different percentages of a reference titration energy dose. Experimental verification was conducted in Dutch Belted rabbits using a PASCAL Streamline 577 laser system. Titration was performed by adjusting laser power to produce a barely visible lesion at 20 ms pulse duration, which is defined as the nominal (100%) energy level. Tissue effects were then determined for energy levels of 170, 120, 100, 75, 50, and 30% of the nominal energy at 1 hour and 3, 7, 30, and 60 days after treatment. In vivo imaging included fundus autofluorescence, fluorescein angiography, and spectral-domain optical coherence tomography. Morphologic changes in tissue were analyzed using light microscopy, as well as scanning and transmission electron microscopy.

Results: One hundred and seventy percent and 120% levels corresponded to moderate and light burns, respectively, with damage to retinal pigment epithelium, photoreceptors, and at highest settings, to the inner retina. 50% to 75% lesions were typically subvisible ophthalmoscopically but detectable with fluorescein angiography and optical coherence tomography. Histology in these lesions demonstrated some selective damage to retinal pigment epithelium and photoreceptors. The 30% to 50% lesions were visible with in vivo multimodal imaging, and damage was limited primarily to retinal pigment epithelium, visible best with scanning electron microscopy. Over time, photoreceptors shifted into the coagulated zone, reestablishing normal retinal anatomy in lesions ≤ 100%, as seen in optical coherence tomography and light microscopy. Transmission electron microscopy at 2 months demonstrated restoration of synapses between shifted-in photoreceptors and bipolar cells in these lesions. Retinal pigment epithelium monolayer restored its continuity after 1 week in all lesions. No damage could be seen <30% level.

Conclusions: A retinal laser dosimetry protocol based on the Endpoint Management algorithm provides reproducible changes in retinal morphology in animals with various levels of pigmentation. This algorithm opens doors to clinical trials of well-defined subvisible and nondestructive regimes of retinal therapy, especially important for treatment of macular disorders.

Abstracts


Objective: To compare the effectiveness of "light" versus “classic” laser photocoagulation in diabetic patients with clinically significant macular oedema (CSMO).

Methods: A prospective randomised pilot clinical trial in which 29 eyes of 24 diabetic patients with mild to moderate non-proliferative diabetic retinopathy (NPDR) and CSMO were randomised to either “classic” or “light” Nd:YAG 532 nm (frequency doubled) green laser. “Light” laser treatment differed from conventional (“classic”) photocoagulation in that the energy employed was the lowest capable to produce barely visible burns at the level of the retinal pigment epithelium. Primary outcome measure was the change in foveal retinal thickness as measured by optical coherence tomography (OCT); secondary outcomes were the reduction/elimination of macular oedema on contact lens biomicroscopy and fluorescein angiography, change in visual acuity, contrast sensitivity, and mean deviation in the central 10˚ visual field. Examiners were masked to patients’ treatment.

Conclusions: "Light" photocoagulation for CSMO may be as effective as “classic” laser treatment.


Objective: We wanted to verify whether a panretinal photocoagulation (PRP) performed using low levels of ARGON laser energy (light PRP) has the same efficacy as a PRP performed in a conventional fashion using argon green wavelengths (classic PRP) in eyes with high-risk proliferative diabetic retinopathy (HRPDR). Furthermore, we wanted to compare the session number performed and the side effects produced by the two techniques.

Methods: Sixty-five eyes with HRPDR of 50 consecutive patients were enrolled in a prospective randomized controlled trial. In eyes selected for light PRP, a very light biomicroscopic effect on the retina was obtained for each spot. In eyes assigned to classic PRP, each spot produced a white yellow biomicroscopic effect. Mean follow-up was 22.4 months ±9.7 in the light PRP and 21.6 months ±9.3 in the classic PRP group (p = 0.727).

Conclusions: The efficacy of Light PRP is similar to that of classic Light PRP in eyes with HRPDR. Light PRP is associated with fewer complications and allows the reduction of the number of treatment sessions.

Significance: "Light" PRP has same efficacy in HPDR compared to heavier “classic” PRP burns.
Purpose:
Subthreshold retinal phototherapy demonstrated clinical efficacy for the treatment of diabetic macular edema without visible signs of retinal damage. To assess the range of cellular responses to sublethal hyperthermia, expression of the gene encoding a 70 kDa heat shock protein (HSP70) was evaluated after laser irradiation using a transgenic reporter mouse.

Methods:
One hundred millisecond, 532 nm laser exposures with 400 mW beam diameter were applied to the retina surrounding the optic nerve in 32 mice. Transcription from the HSP70 promoter was assessed relative to the control eye using a bioluminescence assay at 7 hours after laser application. The retinal pigmented epithelium (RPE) viability threshold was determined with a fluorescence assay. A computational model was developed to estimate temperature and the extent of cell damage.

Results:
A significant increase in HSP70 transcription was found at exposures over 20 mW, half the threshold power for RPE cell death. Computational modeling estimated peak temperature \( T = 49\, ^\circ\, C \) at HSP70 expression threshold. At RPE viability threshold, \( T = 57\, ^\circ\, C \). Similar temperatures and damage indices were calculated for clinical subvisible retinal treatment parameters.

Conclusions:
Beneficial effects of laser therapy have been previously shown to extend beyond those resulting from destruction of tissue. One hundred millisecond laser exposures at approximately half the threshold power of RPE damage induced transcription of HSP70, an indication of cellular response to sublethal thermal stress. A computational model of retinal hyperthermia can guide further optimization of laser parameters for nondamaging phototherapy. (Invest Ophthalmol Vis Sci. 2011;52:1780–1787) DOI:10.1167/iovs.10-5917

Background:
To compare the effects of single-sitting vs 4-sitting panretinal photocoagulation (PRP) on macular edema in subjects with severe nonproliferative or early proliferative diabetic retinopathy with relatively good visual acuity and no or mild center-involved macular edema.

Methods:
Subjects were treated with 1 sitting or 4 sittings of PRP in a nonrandomized, prospective, multicentered clinical trial.

Conclusions:
Our results suggest that clinically meaningful differences are unlikely in OCT thickness or visual acuity following application of PRP in 1 sitting compared with 4 sittings in subjects in this cohort. More definitive results would require a large randomized trial.

Significance:
These results suggest PRP costs to some patients in terms of travel and lost productivity as well as to eye care providers could be reduced with single session treatment.