

Title	Tab Number
PASCAL Pre-Clinical Articles	
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Dimple Modi, Paulpoj Chiranand, Levent Akduman. "Efficacy of patterned scan laser in treatment of macular edema and retinal neovascularization". <i>Clinical Ophthalmology</i> 2009;3 465-470.	6
Mahiul M.K. Muqit, Chintan Sanghvi, Rita McLauchlan, Christine Delgado, Lorna B. Young, Stephen J. Charles, George R. Marcellino and Paulo E. Stanga. "Study of clinical applications and safety for Pascal® laser photocoagulation in retinal vascular disorders". <i>Acta Ophthalmologica</i> 2010 ePublication	7
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Saumil Sheth, Paolo Lanzetta, Daniele Veritti, Ilaria Zucchiatti, Carola Savorgnani, Francesco Bandello. «Experience with the Pascal photocoagulator: An analysis of over 1200 laser procedures with regard to parameter refinement" <i>Indian Journal of Ophthalmology</i> 2011; 59 (20): 87-91.	9

Title	Tab Number
<p>Atul Jain, MD, James Collen, BS, Andrew Kaines, MD, Jean-Pierre Hubschman, MD, Steven Schwartz, MD. "Short-duration focal pattern grid macular photocoagulation for diabetic macular edema: four-month outcomes". <i>Retina</i> 2010 Nov-Dec; 30(10) :1622-1626.</p>	10
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PASCAL Clinical and Pre-Clinical Article Abstracts

1

Mark S Blumenkranz, Daniel Yellachich, Dan E Andersen, Michael W Wiltberger, David Mordaunt, George R Marcellino, Daniel Palanker. "Semiautomated Patterned Scanning Laser for Retinal Photocoagulation." *Retina* 2006; 26(3): 370-376.

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 \approx 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.

2

Atul Jain, Mark S. Blumenkranz, Yannis Paulus, Michael W. Wiltberger, Dan E. Andersen, Phil Huie, Daniel Palanker. "Effect of Pulse Duration on Size and Character of the Lesion in Retinal Photocoagulation." *Archives in Ophthalmology* 2008; 126 (1):78-85.

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.

3

Yannis M. Paulus, Atul Jain, Ray F. Gariano, Boris V. Stanzel, Michael Marmor, Mark S. Blumenkranz, Daniel Palanker. "Healing of Retinal Photocoagulation Lesions." *Investigative Ophthalmology and Clinical Science* 2008; 49 (12):5540-5.

Objective: To systematically assess 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 and 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.

C Sanghvi, R McLauchlan, C Delgado, L Young, SJ Charles, GR Marcellino, PE Stanga. "Initial experience with the PASCAL® Photocoagulator- a pilot study of 75 procedures." *British Journal of Ophthalmology* 2008; 92:1061-1064.

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.

AV Bol'shunov. "The first experience in clinically using a PASCAL laser photocoagulator." [Article in Russian]. *Vestn Oftalmol.* 2009 Jul-Aug;125(4):37-8.

Conclusions: A new PASCAL laser photocoagulator (OptiMedica, USA) was clinically tested. A total of 38 laser interventions were performed in 38 eyes with diabetic retinopathy (n = 25), peripheral retinal dystrophy (n = 2), retinal ruptures (n = 2), hemophthalmos (n = 3), primary open-angle glaucoma (n = 5), and ectopic pupil (n = 1). An example of successful use of the new laser unit for pupilloplasty for the ectopic pupil is given.

Dimple Modi, Paulpoj Chiranand, Levent Akduman. “Efficacy of patterned scan laser in treatment of macular edema and retinal neovascularization.” *Clinical Ophthalmology* 2009;3 465-470.

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 retinal photocoagulation in short-term follow-up. PASCAL® photocoagulation can be performed quicker with less discomfort for patients.

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

Mahiul M.K. Muqit, Chintan Sanghvi, Rita McLauchlan, Christine Delgado, Lorna B. Young, Stephen J. Charles, George R. Marcellino and Paulo E. Stanga. “Study of clinical applications and safety for Pascal® laser photocoagulation in retinal vascular disorders.” *Acta Ophthalmologica* 2010 Epublication

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 groups: A – panretinal photocoagulation (PRP) for proliferative diabetic retinopathy (PDR); B – focal laser treatment for clinically significant diabetic macular oedema; C – grid laser for diffuse diabetic macular oedema; D – sector PRP for ischaemic branch retinal vein occlusions (I-BRVO); E – full PRP for ischaemic central retinal vein occlusions (I-CRVO); F – macular laser treatment for macular oedema secondary to non-ischaemic BRVO; G – full PRP for rubeosis iridis and / or neovascular glaucoma (NVG) secondary to I-BRVO, I – CRVO or PDR; H – laser retinopexy for retinal breaks / degenerations.

Results: Mean LogMAR visual acuity for all procedures improved postlaser ($p = 0.065$), and laser prevented visual loss in 85% eyes. Topical anaesthesia was only required. At mean follow-up of 5 months, 72% procedures had a successful clinical outcome. Significantly higher powers were required for PRP using Pascal compared to conventional laser ($p = 0.001$) in PDR, I-BRVO, I-CRVO and NVG. Sixty-seven per cent of patients (15 / 20) were successfully treated with single-session 20-ms PRP using a mean 1952 burns. There were no laser-associated adverse effects or ocular complications associated with multi-spot PRP or macular Pascal arrays.

Conclusions: The clinical efficacy using 10- to 30-ms pulse duration Pascal laser is comparable to conventional standard protocols used for the treatment of vascular retinal disorders. Higher power, 10- to 30-ms pulse duration laser may be safely and effectively used in clinical practice.

Significance: This retrospective observational study demonstrates the clinical efficacy & safety of Pascal's shorter pulse duration & higher power compared to conventional standard protocols used for treatment of various retinal vascular disorders. This study also shows the safety of Pascal's macula grid pattern.

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E. Romo-Garcia, R. Velez-Montoya, J. Guerrero-Naranjo, J. Jimenez-Sierra, J. Fromow-Guerra, H. Quiroz-Mercado, V. Morales-Cantón. "Pattern Scan Laser Photocoagulation: Safety and Complications, Experience After 1301 Consecutive Cases." *British Journal of Ophthalmology* 2010; 94:720-724.

Purpose: To report the safety and incidence of adverse effects, during and after a successful photocoagulation for different pathologies using a Pattern Scan Laser (PASCAL) system and its modified settings.

Methods: This was a retrospective study. We reviewed the clinical records of all laser sessions performed with PASCAL from November 2007 to July 2008. Where there were any complications, we recorded the laser parameters, type, affected retina region, postoperative interval and treatment if required.

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.

Saumil Sheth, Paolo Lanzetta, Daniele Veritti, Ilaria Zucchiatti, Carola Savorgnani, Francesco Bandello. «Experience with the Pascal photocoagulator: An analysis of over 1200 laser procedures with regard to parameter refinement” *Indian Journal of Ophthalmology* 2011; 59 (20): 87-91.

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 800 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 $\approx 700 \mu\text{m}$ 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.

Atul Jain, MD, James Collen, BS, Andrew Kaines, MD, Jean-Pierre Hubschman, MD, Steven Schwartz, MD. “Short-duration focal pattern grid macular photocoagulation for diabetic macular edema: four-month outcomes”. *Retina* 2010 Nov-Dec; 30(10) :1622-1626.

Purpose: 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 diabetes.

Methods: Consecutive retrospective analysis of VA and optical coherence tomographic 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/cm² 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 μ m and 37 μ m (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.

Manish Nagpal, Sangita Marlecha, Kamal Nagpal. "Comparison of Laser Photocoagulation for Diabetic Retinopathy using 532-nm Standard Laser versus multispot Pattern Scan Laser." *Retina* 2010; 30(3): 453-458.

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 multispot 532-nm pattern scan laser (PASCAL).

Methods: This study was a prospective randomized clinical trial. Sixty patients with bilaterally 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- μ m 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 4.6, whereas that for PASCAL was 0.33. Heidelberg retinal angiography images showed the spot spread as being 430 versus 310 μ m 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 randomised 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.

Mahiul M.K. Muqit, George R. Marcellino, David B. Henson, Lorna B. Young, Niall Patton, Stephen J. Charles, George S. Turner and Paulo E. Stanga. "Single-session vs multiple-session pattern scanning laser panretinal photocoagulation in proliferative diabetic retinopathy: The Manchester Pascal Study." *Arch Ophthalmology* 2010 May; 128(5):525-33.

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-mum 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.

Mahiul M.K. Muqit, George R. Marcellino, Jane C.B. Gray, Rita McLauchlan, David B. Henson, Lorna B. Young, Niall Patton, Stephen J. Charles, George S. Turner and Paulo E. Stanga. "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): 1493-1498.

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-naive 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 0.68; $p=0.006$). 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, pain 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.

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Abdelrahman Gaber Salman. "Pascal laser versus conventional laser for treatment of diabetic retinopathy." *Saudi Journal of Ophthalmology* 2011 Apr; 25 (2): 175-179.

Purpose: To compare the safety and efficacy of Pascal laser photocoagulation in comparison with the conventional laser photocoagulation 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 photocoagulation (PRP). Each of the two groups were subdivided into two subgroups randomly in the first we used conventional laser photocoagulation (groups A1 and B1) and in the other we used Pascal laser photocoagulation (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 photocoagulator 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.

Muraly P, Limbad P, Srinivasan K, Ramasamy K. "Single session of Pascal versus multiple sessions of Conventional Laser for Panretinal Photocoagulation in proliferative diabetic retinopathy: A Comparative Study." *Retina* 2011 March ePublication.

Background: Panretinal photocoagulation remains the gold standard for treatment of proliferative diabetic retinopathy, which can be done in a single session or in multiple sessions. However, because of different reasons, single session is less frequently practiced. We describe the results of a single session of pattern scan laser versus multiple sessions of conventional laser in cases of proliferative diabetic retinopathy.

Methods: A prospective study was performed on 50 patients (100 eyes), in whom proliferative diabetic retinopathy was diagnosed recently. Two eyes of an individual patient were randomly assigned, one for a single session of panretinal photocoagulation using pattern scan laser and the other for multiple sessions of conventional laser.

Results: Our study confirms that single session is effective and even better than conventional laser in relation to the effect of treatment.

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.

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

Purpose: To investigate the effects of panretinal photocoagulation (PRP) on macular thickness and macular nerve fiber layer thickness in eyes with proliferative diabetic retinopathy.

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; $+7.2 \mu\text{m}$, $P = 0.78$; 12 weeks, $-1.8 \mu\text{m}$, $P = 0.95$). There was a significant increase in total retinal thickness for the MS-PRP group at 4 weeks from baseline ($96 \pm 17 \mu\text{m}$; $P < 0.001$) and at 12 weeks ($56 \pm 21 \mu\text{m}$; $P = 0.0167$). After 4 weeks in the MS-PRP group, total nerve fiber layer thickness increased significantly by $31 \pm 54 \mu\text{m}$ ($P = 0.029$) from baseline, with a significant reduction at 12 weeks from baseline ($35 \pm 63 \mu\text{m}$; $P = 0.034$). 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.

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Mahiul M. K. Muqit, George R. Marcellino, David B. Henson, Louna B. Young, George S. Turner Paulo E. Stanga. "Pascal panretinal laser ablation and regression analysis in proliferative diabetic retinopathy: Manchester Pascal Study Report 4". *Eye* 2011; 25(11): 1447-1456.

Aims To quantify the 20-ms Pattern Scan Laser (Pascal) panretinal laser photocoagulation (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 mm^2 ablation area, moderate PDR required 3998 PRP burns and area 456 mm^2 , and severe PDR needed 6924 PRP laser burns (836 mm^2 ; $P < 0.05$).

Conclusions 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.

Mahiul MK Muqit, Jonathan Denniss, Vincent Nourrit, George R Marcellino, David Henson, Paulo E Stanga. "Spatial and Spectral Imaging of Retinal Laser Photocoagulation Burns", Invest Ophthalmol Vis Sci. 2011; 52:994-1002)

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-naïve 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

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.

Mahiul MK Muqit, Jane CB Gray, George R Marcellino, David Henson, Lorna B Young, Stephen J Charles, George S Turner, Paulo E Stanga. "Fundus Autofluorescence and Fourier-Domain Optical Coherence Tomography Imaging of 10 and 20 millisecond PASCAL Retinal Photocoagulation Treatment." *British Journal of Ophthalmology* 2009 Apr; 93:518-525.

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.

Gábor Gy Deák, Matthias Bolz, Katharina Kriechbaum, Sonja Prager, Georgios Mylonas, Christoph Scholda, Ursula Schmidt-Erfurth. "Effect of Retinal Photocoagulation on Intraretinal Lipid Exudates in Diabetic Macular Edema documented by Optical Coherence Tomography." *Ophthalmology* 2010; 117(4): 773-779.

Purpose: To study the changes in the distribution and morphologic features of intraretinal microexudates after macular photocoagulation.

Participants: Thirteen treatment-naïve patients with clinically significant macular edema in type 2 diabetes.

Methods: Patients were treated with focal macular photocoagulation. Changes in the localization of hyperreflective foci were analyzed by spectral domain (SD) optical coherence tomography (OCT) during follow-up at day 1, week 1, and months 1, 2, 3, and 4 in defined areas. Further, fundus photography and infrared imaging were performed at all visits and findings were correlated to OCT results.

Main Outcome Measures: Changes in retinal morphologic features detected in OCT.

Results: A dynamic change in the distribution pattern of hyperreflective foci was observed over 4 months after the photocoagulation. With the decrease of retinal thickness, the dots either resolved completely or became confluent at the apical border of the outer nuclear layer, and finally formed ophthalmoscopically detectable hard exudates during extended follow-up. In the event of retinal thickening despite laser treatment, the hyperreflective dots maintained their previous distribution throughout all retinal layers. As a fourth response, dissemination of plaques of hard exudates into multiple, separate, hyperreflective foci were detected.

Conclusions: Hyperreflective foci in the retina seem to represent precursors or components of hard exudates. Their specific localization depends greatly on the presence of microvascular extravasation and intraretinal fluid accumulation. Retinal photocoagulation has a major impact on retinal edema and subsequently on the distribution of intraretinal lipid deposits.

Significance: Study using SD-OCT showed impact of Pascal lasering on lipid exudates in diabetic macular edema patients.

Matthias Bolz, Katharina Kriechbaum, Christian Simader, Gabor Deak, Jan Lammer, Clara Treu, Christoph Scholda, Christian Prünke, Ursula Schmidt-Erfurth. "In vivo retinal morphology after grid laser treatment in diabetic macular edema." *Ophthalmology* 2010; 117(3): 538-544.

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.

Mahiul M.K. Muqit, Jane C.B. Gray, George R. Marcellino, David B. Henson, Lorna B. Young, Niall Patton, Stephen J. Charles, George S. Turner, Andrew D. Dick, Paulo E. Stanga. "In vivo Laser-Tissue Interactions and Healing Responses From 20- vs 100-Millisecond Pulse Photocoagulation Burns." *Acta Ophthalmologica* 201; 128(4): 448-455.

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 liner 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 63um at 1 hour and 198um 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 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.

Mahiul M.K. Muqit, Jane C.B. Gray, George R. Marcellino, David B. Henson, Lorna B. Young, Niall Patton, Stephen J. Charles, George S. Turner and Paulo E. Stanga. "Barely Visible 10-Millisecond Pascal Laser Photocoagulation for Diabetic Macular Edema: Observations of Clinical Effect and Burn Localization." *American Journal of Ophthalmology* 2010; 149: 979-986.

Purpose: To investigate the morphologic features and clinical efficacy of barely visible Pascal (Optimedica Corporation) photocoagulation burns in diabetic macular edema (DME) using Fourier-domain optical coherence tomography (FD OCT) and fundus autofluorescence (AF).

Methods: Retrospective evaluation of 10 eyes with newly diagnosed DME that underwent barely visible Pascal photocoagulation using an array of 10-um, 10-millisecond photocoagulation burns. FD OCT and camera-based AF was performed at baseline and at 1 hour, 2 weeks, 4 weeks, and 12 weeks after laser. Changes in retinal thickening after laser treatment were measured using retinal thickness maps within the treated sector and the central foveal subfield.

Results: At 1 hour after treatment, burns were visualized partially with clinical biomicroscopy. AF demonstrated spots lacking autofluorescence that confirmed effective laser uptake within the Pascal arrays. Sequential changes in hyperreflectivity on FD OCT correlated with morphologic alterations seen on AF. Burns became increasingly hyperautofluorescent between 2 and 4 weeks. There were significant reductions in the retinal thickness within treated sectors on FD OCT at 2 weeks (26 + 32 um; P = .012) and 3 months after laser (20 + 21 um; P = .02) compared with baseline. Clinical biomicroscopic reduction of DME was the most common finding in 80%.

Conclusions: Barely visible 10-millisecond Pascal laser seems to produce an effect at the level of the inner and outer photoreceptor segments and apical retinal pigment epithelium, with minimal axial and lateral spread of burns. FD OCT confirmed spatial localization of AF signal changes that correlated with laser burn-tissue interactions over 3 months. The technique of lower fluence barely visible 10-millisecond laser may reduce retinal edema within affected sectors and effectively treat DME with minimization of scar formation.

Significance: Barely visible burns with Pascal produced highly localised lesions while retaining effective treatment outcomes for DME patients.

Mahiul M. K. Muqit, George R. Marcellino, David B. Henson, Lorna B. Young, Niall Patton, Stephen J. Charles, George S. Turner and Paulo E. Stanga. "Optos-guided pattern scan laser (Pascal)-targeted retinal photocoagulation in proliferative diabetic retinopathy".

Purpose: To investigate the clinical effects and safety of targeted pattern scan laser (Pascal) retinal photocoagulation (TRP) 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 ($\kappa = 0.70$; $p < 0.001$). 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-naïve PDR is a promising procedure with favourable safety profile.

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Yanfeng Wang, Mahiul M.K. Muqit, Paulo E. Stanga, Lorna B. Young, and David B. Henson, "Spatial Changes of Central Field Loss in Diabetic Retinopathy After Laser"

Optom Vis Sci 2014;**91**:111Y120

Purpose. To explore the spatial distribution of central visual field loss in untreated proliferative diabetic retinopathy (PDR) and to quantify the effect of medium-pulse Optos-guided 20-millisecond Pascal laser treatment on the central field.

Methods. Visual field data (Swedish Interactive Threshold Algorithm 24-2) from 99 eyes (66 patients) with treatment-naïve PDR were used to train a self-organizing map (SOM) that classified the defects into nine patterns. Twenty-eight eyes of 23 patients treated with 20-millisecond Pascal retinal laser photocoagulation underwent Optos widefield fundus fluorescein angiography (WF-FFA) at baseline and 3 months after treatment. Postlaser changes in SOM patterns and global indices were analyzed. Visual field defect changes (Total Deviation [TD]) with eccentricity and extent of initial loss were analyzed. Grading of WF-FFA after laser was undertaken by two masked retina specialists.

Results. At baseline, 44.4% of PDR eyes showed early visual field loss patterns (1 to 3), with 23.2% classified into the advanced patterns (7 to 9). Mild SOM patterns had more superior hemifield field defects, whereas advanced patterns involved both superior and inferior hemifield field loss. After laser, a significant shift to early SOM patterns were observed ($p = 0.02$), as well as improvement of Mean Deviation and Pattern Standard Deviation ($p = 0.003$ and $p = 0.06$, respectively). Improvement of TD was commonly observed in test locations of 0 to 10, 10 to 20, and 20 to 30 degrees. Greater improvement was observed with deeper baseline TD ($p < 0.001$). Masked WF-FFA image grading showed 78.6% PDR regression.

Conclusions. The SOM method is a promising technique to classify and monitor over time PDR-associated visual field defects. Medium-pulse Optos-guided 20-millisecond Pascal laser treatment improved the spatial patterns and global parameters of central field defects.

Mahiul MK Muqit, George R Marcellino, David Henson, Lorna B Young, George S Turner, Paulo E Stanga. *“Pilot randomised clinical trial of Pascal TargetED Retinal versus variable fluence PANretinal 20ms laser in diabetic retinopathy: PETER PAN study”*. *British Journal of Ophthalmology* 2013; 97: 220-227.

Purpose To investigate the short-term effects of high-density 20-ms laser on macular thickness using Pascaltargeted retinal photocoagulation (TRP) and reduced fluence/minimally-traumatic panretinal photocoagulation (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 photocoagulation 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=0.021) and MT-PRP (17.1 mm; 95% CI, 11 to 23.2; p=0.001), versus SI-PRP (+5.9 mm; 95% CI, -6.75 to 18.55; p=0.32). PDR regression was similar between groups (TRP 70%; MT-PRP 70%; SI-PRP 90%; $\kappa=0.76$).

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, +0.70dB; 95% CI, 0.07 to 1.48; p=0.07], [MTPRP, +0.63dB; 95% CI, 0.12 to 1.15; p=0.02], [SI-PRP, +1.0dB; 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.

Daniel Lavinsky, Jose A. Cardillo, Yossi Mandel, Rubens Belfort and Daniel Palanker, *“Restoration of retinal morphology and residual scarring after photocoagulation”*, *Acta Ophthalmologica* doi: 10.1111/aos.12045

Purpose: To study healing of retinal laser lesions in patients undergoing PRP using SD-OCT. **Methods:** Moderate, light and barely visible retinal burns were produced in patients with proliferative diabetic retinopathy scheduled for PRP using 100-, 20- and 10-ms pulses of 532-nm laser, with retinal spot sizes of 100, 200 and 400 μm . Lesions were measured with OCT at 1 hr, 1 week, 1, 2, 4, 6, 9 and 12 months. OCT imaging was correlated with histology in a separate study in rabbits.

Results: Lesions produced by the standard 100-ms exposures exhibited steady scarring, with the damage zone stabilized after 2 months. For 400- and 200-lm spots and 100-ms pulses, the residual scar area at 12 months was approximately 50% of the initial lesion size for moderate, light and barely visible burns. In contrast, lesions produced by shorter exposures demonstrated enhanced restoration of the photoreceptor layer, especially in smaller burns. With 20-ms pulses, the damage zone decreased to 32%, 24% and 20% for moderate, light and barely visible burns of 400 lm, respectively, and down to 12% for barely visible burns of 200 lm. In the 100-lm spots, the residual scar area of the moderate 100-ms burns was 41% of the initial lesion, while barely visible 10-ms burns contracted to 6% of the initial size. Histological observations in rabbits were useful for proper interpretation of the damage zone boundaries in OCT.

Conclusions: Traditional photocoagulation parameters (400 lm, 100 ms and moderate burn) result in a stable scar similar in size to the beam diameter. Restoration of the damaged photoreceptor layer in lighter lesions produced by shorter pulses should allow reducing the common side-effects of photocoagulation such as scotoma and scarring.

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HIROYUKI NOMOTO, DANIEL LAVINSKY, YANNIS M. PAULUS, LOH-SHAN LEUNG, MARK S. BLUMENKRANZ, DANIEL PALANKER, "EFFECT OF INTRAVITREAL TRIAMCINOLONE ACETONIDE ON HEALING OF RETINAL PHOTOCOAGULATION LESIONS", RETINA 33:63–70, 2013

Purpose: To evaluate the effect of intravitreal triamcinolone acetonide (TA) on healing of retinal photocoagulation lesions using drug and laser dosing typically employed in clinical practice.

Methods: Laser burns with a 267-mm retinal beam size at 532-nm wavelength were applied to 40 eyes of Dutch belted rabbits. Barely visible to intense lesions were produced with pulses of 5, 10, 20, and 50 milliseconds and power of 175 mW. Eyes received intravitreal injections of either 2 mg TA/50 mL or balanced salt solution administered either 1 week before or immediately after laser treatment. Lesion grades were assessed acutely ophthalmoscopically and by a masked observer histologically at 1, 3, 7, 30, and 60 days.

Results: Both TA groups demonstrated significant reduction in retinal thickness throughout follow-up compared with balanced salt solution groups ($P < 0.001$). The width of the lesions at 1 day after injection was not significantly different between groups. However, by 7 days, the lesions in balanced salt solution groups contracted much more than in the TA groups, especially the more intense burns, and this difference persisted to 2 months. The healing rate of the barely visible burns was not significantly affected by TA compared with the balanced salt solution control eyes.

Conclusion: Triamcinolone acetonide injection previously or concurrently with photocoagulation significantly decreases laser-induced edema but interferes with lesions healing, thereby leaving wider residual scarring, especially persistent in more intense burns.

RETINA 33:63–70, 2013

DANIEL LAVINSKY, MD, CHRISTOPHER SRAMEK, JENNY WANG, PHILIP HUIE, YOSSI MANDEL, DANIEL PALANKER, “SUBVISIBLE RETINAL LASER THERAPY Titration Algorithm and Tissue Response”, RETINA 0:1–11, 2013

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 invisible 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.

Conclusion: 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

Mauricio Turati, Felix Gil-Carrasco, Adolfo Morales, Hugo Quiroz-Mercado, Dan Anderson, George Marcellino, Georg Schuele, Daniel Palanker. "Patterned Laser Trabeculoplasty." *Ophthalmic Surg Lasers Imaging* 2010;41: 538-545.

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 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 \pm 4.1 to 16.0 \pm 2.3 mm Hg at 1 month (n = 41) and remained stable around 15.5 \pm 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).

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

PASCAL – Related Articles Abstracts

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

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 μ m. The other hemiretina was treated with treatment B using exposure 0.02 s, 300 μ m 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.

Francesco Bandello, Rosario Brancato, Ugo Menchini, Gianni Virgili, Paolo Lanzetta, Ettore Ferrari, Carlo Incorvaia. "Light versus classic laser treatment for clinically significant diabetic macular oedema." *British Journal of Ophthalmology* 2005 Jul; 89(7):864-870.

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

F Bandello, A Polito, M Del Borrello, N Zemella, M Isola. "Light panretinal photocoagulation (LPRP) versus classic Panretinal photocoagulation (CPRP) in proliferative diabetic retinopathy." *Seminars in Ophthalmology* 2001 Mar; 16 (1):12-8.

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 \pm 9.7 in the light PRP and 21.6 months \pm 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.

Alexander J Brucker, Haijing Qin. "Observational Study of the Development of Diabetic Macular Edema Following Panretinal (Scatter) Photocoagulation Given in 1 or 4 Sitzings." *Archives of Ophthalmology* 2009; 127(2): 132-140.

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.

STAVROS N. MOYSIDIS, LEJLA VAJZOVIC, GIOVANNI GREGORI, JEFFREY L. GOLDBERG. "ACUTE RETINAL PIGMENT EPITHELIUM DETACHMENTS AFTER PHOTOCOAGULATION". *RETINA* 34:749–760, 2014

Purpose: To characterize the morphology of patterned scanning laser (PASCAL) panretinal photocoagulation.

Methods: In this prospective cohort study, patients with proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy with high-risk characteristics, who were treated with PASCAL panretinal photocoagulation as part of their indicated clinical course, were serially imaged with spectral domain optical coherence tomography. Thirty eyes of 25 patients were studied from 1 hour to 21 weeks after laser treatment.

Results: Over a quarter (26.1%) of all treatment spots were imaged by spectral domain optical coherence tomography 1 hour after PASCAL panretinal photocoagulation. At 1 hour (± 30 minutes) after PASCAL treatment, spectral domain optical coherence tomography demonstrated retinal pigment epithelium detachment in 23 of 27 eyes (85.2%) and in 36.1% of all imaged laser spots. Detachments occurred preferentially at the photocoagulation edges in 48.4% of pigment epithelium detachments (PEDs). Linear regression analysis revealed that average laser power (Pearson's $r = 0.671$, $P = 0.001$) and average laser energy (Pearson's $r = 0.588$, $P = 0.001$) were significantly associated with PEDs observed 1 hour after treatment. Pigment epithelium detachments occurred at a rate of $9.2\% \pm 4.9\%$ at an average power of 0 mW to 400 mW, $37.8\% \pm 9.5\%$ at 401 mW to 800 mW, $42.1\% \pm 5.6\%$ at 801 mW to 1,200 mW, and $53.6\% \pm 5.7\%$ at 1,200 mW. By a 1-week follow-up, no PEDs were observed, and the retinal pigment epithelium appeared morphologically similar to its preoperative structure by 3 weeks. Patient characteristics (study eye, sex, race, diagnosis, age, preoperative blood glucose, hemoglobin A1C, duration of diabetes, and body mass index) and other PASCAL parameters (number of laser applications, spot size, pulse duration, and average laser fluence) were not significantly associated with PEDs.

Conclusion: Retinal pigment epithelium detachment occurs 1 hour after PASCAL treatment over a wide range of laser settings. Laser power and energy are positively correlated with the occurrence of PEDs, which are no longer observed by 1-week follow-up. Future studies might examine various acute post treatment time points and directly compare the morphology of PASCAL burns with that of longer pulse–duration laser modalities.

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Daniel Lavinsky, Thomas W. Chalberg, Yossi Mandel, Philip Huie, Roopa Dalal, Daniel Palanker, “Modulation of transgene Expression in Retinal Gene Therapy by Selective Laser Treatment”, Invest Ophthalmol Vis Sci. 2013;54:1873-1880)

PURPOSE. To develop a method for modulation of transgene expression in retinal pigment epithelium (RPE) using scanning laser that spares neurosensory retina.

METHODS. Fifteen pigmented rabbits received subretinal injection of recombinant adeno-associated virus (rAAV-2) encoding green fluorescent protein (GFP). GFP expression was measured using confocal scanning laser ophthalmoscopy (cSLO) fluorescence imaging and immunohistochemistry. To reduce the total expression in RPE by half, 50% of the transfected RPE cells were selectively destroyed by microsecond exposures to scanning laser with 50% pattern density. The selectivity of RPE destruction and its migration and proliferation were monitored using fluorescein angiography, spectral-domain optical coherence tomography (SD-OCT), and light transmission, and scanning electron microscopy. 5-Bromo-2'-deoxyuridine (BrdU) assay was performed to evaluate proliferation of RPE cells.

RESULTS. RPE cells were selectively destroyed by the line scanning laser with 15 ls exposures, without damage to the photoreceptors or Bruch's membrane. RPE cells started migrating after the first day, and in 1 week there was complete restoration of RPE monolayer. Selective laser treatment decreased the GFP fluorescence by 54% as compared to control areas; this was further decreased by an additional 48% following a second treatment 1 month later. BrdU assay demonstrated proliferation in approximately half of the RPE cells in treatment areas.

CONCLUSIONS. Microsecond exposures produced by scanning laser destroyed RPE cells selectively, without damage to neural retina. Continuity of RPE layer is restored within days by migration and proliferation, but transgene not integrated into the nucleus is not replicated. Therefore, gene expression can be modulated in a precise manner by controlling the laser pattern density and further adjusted using repeated applications. (Invest Ophthalmol Vis Sci. 2013;54:1873–1880)