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Clinical Validation of PASCAL

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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.

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.

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4 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; 2:1061 - 1064.

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6 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.

7 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.

8 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.

9 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.

10 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.

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Reduced Exposure Time:

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44 Christopher K. Sramek, PhD; Loh-Shan B. Leung, MD; Yannis M. Paulus, MD; Daniel V. Palanker, PhD “Therapeutic Window of Retinal Photocoagulation With Green (532-nm) and Yellow (577-nm) Lasers” OphthalmicSurgery, laSerS& imaging, 2012

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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 bydrochloride. 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.

Abstracts

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 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.

4

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.

5

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.

Abstracts

6

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.

7

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.

8

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.

Abstracts

9

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 ≈ 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.

10

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 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.

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Mahiul M. K. Muqit, Jonathan Denniss, Vincent Nourrit, George R. Marcellino, David B. Henson, Ingo Schiessl, and Paulo E. Stanga "Spatial and Spectral Imaging of Retinal Laser Photocoagulation Burns" Ophthalmol Vis Sci. 2011; 52:994 –1002) DOI:10.1167/iovs.10-6309

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% (P0.001), 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.

Abstracts

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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-!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 4.53minutes 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 !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.

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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.

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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.

Abstracts

14 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.

15 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.

16 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 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 = 0.029) 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.

Abstracts

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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 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.

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AIMEE V. CHAPPELOW, KEVIN TAN, NADIA K. WAHEED, AND PETER K. KAISER “Panretinal Photocoagulation for Proliferative Diabetic Retinopathy: Pattern Scan Laser Versus Argon Laser” Am J Ophthalmol 2012;153:137–142.(AMERICAN JOURNAL OF OPHTHALMOLOGY JANUARY 2012)

Purpose:
To evaluate the efficacy of the pattern scan laser (PASCAL) in treating newly diagnosed high-risk proliferative diabetic retinopathy (PDR).

Design:
Retrospective comparative case series.

Methods:
SETTING: Institutional. STUDY POPULATION: Eighty-two consecutive eyes of the same number of patients with newly diagnosed high-risk PDR treated with panretinal photocoagulation (PRP) using either argon green laser (41 eyes treated before February 2007) or PASCAL (41 eyes treated February 2007 or thereafter), then followed for at least 6 months. PROCEDURE: Retrospective chart review with attention to main outcome measures, age, sex, race, follow-up interval, insulin dependence, hemoglobin A1c, and total number of lasers
spots. MAIN OUTCOME MEASURES: Persistence or recurrence of neovascularization, incidence of vitreous hemorrhage (VH), neovascularization of the iris (NVI), neovascular glaucoma (NVG), and need for vitrectomy.

Results:
Patients treated with the PASCAL and argon laser received a similar number of spots (1438 vs 1386; P=.59). Patients treated with the PASCAL were more likely to experience persistence or recurrence of neovascularization within 6 months of initial treatment (73% vs 34%; P < .0008). The study was not adequately powered to detect a significant difference in incidence of vitreous hemorrhage, NVI, NVG, or need for vitrectomy.

Conclusions:
When using traditional laser settings, PRP performed with the PASCAL is less effective than that performed with traditional argon laser in effecting
lasting regression of retinal neovascularization in the setting of previously untreated high-risk PDR. Physicians may need to change treatment parameters when
using PASCAL pattern laser therapy for high-risk PDR.

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Mahiul M K Muqit, Lorna B Young, Rod McKenzie, Binu John, George R Marcellino, David B Henson, George S Turner, Paulo E Stanga “Pilot randomised clinical trial of Pascal TargETEd Retinal versus variablefluence PANretinal 20 ms laser in diabetic retinopathy: PETER PAN study” Br J Ophthalmol 2013 97: 220-227 originally published online November 24, 2012 doi: 10.1136/bjophthalmol-2012-302189laser in diabetic retinopathy: PETER PAN study

Purpose:
To investigate the short-term effects of highdensity 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.vTreatment-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%; κ=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 didvnot produce increased macular thickness or any ocularvadverse events during the short-term.

Abstracts

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Katharina Kriechbaum, MD, Matthias Bolz, MD, Gabor G. Deak, MD, Sonja 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;117:545–551

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 photocoagulated 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.

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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.

Abstracts

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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.

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Matthias Bolz, Katharina Kriechbaum, Christian Simader, Gabor Deak, Jan Lammer, Clara Treu, Christoph Scholda, Christian Prünte, 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 (ETDRSprotocol) 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.

Abstracts

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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.

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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.

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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-naive PDR is a promising procedure with favourable safety profile.

Abstracts

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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-µm spots. Power was titrated for trabecular meshwork blanching at 10 ms and sub-visible treatment was applied with 5-ms pulses. The arc patterns of 66 spots rotated automatically after each laser application so that the new pattern was applied at an untreated position.

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

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

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

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DANIEL PALANKER, PHD, DANIEL LAVINSKY, MD, MARK SCOTT BLUMENKRANZ, MD, GEORGE MARCELLINO, PHD “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.

Conclusion:
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.

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Yannis M. Paulus, Atul Jain, Hiroyuki Nomoto, Christopher Sramek, Ray F. Gariano, Dan Anderson, George Schuele, Loh-Shan Leung, Theodore Leng, Daniel Palanker. “Selective Retinal Therapy with Microsecond Exposure using Continuous Line Scanning Laser.” Retina 2011 Feb; 31(2): 380-388

Purpose:
To evaluate the safety, selectivity, and healing of retinal lesions created using a continuous line scanning laser.

Methods:
A 532 nm Nd:YAG laser (PASCAL) with retinal beam diameters of 40 and 66 µm was applied to 60 eyes of 30 Dutch-Belted rabbits. Retinal exposure duration varied from 15 to 60 µs. Lesions were acutely assessed by ophthalmoscopy and fluorescein angiography (FA). RPE flatmounts were evaluated with live-dead fluorescent assay (LD). Histological analysis was performed at 7 time points from 1 hour to 2 months.

Results:
The ratios of the threshold of rupture and of OV to FA visibility (measures of safety and selectivity) increased with decreasing duration and beam diameter. FA and LD yielded similar thresholds of RPE damage. Above the OV threshold, histology showed focal RPE damage and photoreceptor loss at one day, without inner retinal effects. By one week, photoreceptor andRPE continuity was restored. By 1 month, photoreceptors appeared normal.

Conclusions:
Retinal therapy with a fast scanning continuous laser achieves selective targeting of the RPE and, at higher power, of the photoreceptors without permanent scarring or inner retinal damage. Continuous scanning laser can treat large retinal areas within standard eye fixation time.

Significance:
Experimental study using Pascal to achieve microsecond pulse burns by fast scanning continuous line scanning method resulting in selective targeting of RPE & photoreceptors while leaving no permanent scarring & intact inner retinal layers.

Abstracts

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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 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.

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Christopher K. Sramek, PhD; Loh-Shan B. Leung, MD; Yannis M. Paulus, MD; Daniel V. Palanker, PhD “Therapeutic Window of Retinal Photocoagulation With Green (532-nm) and Yellow (577-nm) Lasers” OphthalmicSurgery, laSerS& imaging, 2012

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

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JEFFREY K. LUTTRULL, MD, CHRISTOPHER SRAMEK, PHD, DANIEL PALANKER, PHD, CHARLES J. SPINK, MA, DAVID C. MUSCH, PHD, MPH “LONG-TERM SAFETY, HIGH-RESOLUTION IMAGING, AND TISSUE TEMPERATURE MODELING OF SUBVISIBLE DIODE MICROPULSE PHOTOCOAGULATION FOR RETINOVASCULAR MACULAR EDEMA” RETINA32:375–386, 2012

Purpose:
To determine the long-term safety of high-density subvisible diode micropulse photocoagulation (810 nm), compare the clinicalfindings 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 ≥ 590 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 spectraldomain 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:
Subvisible diode micropulse can effectively treat retinovascular ME without laser-induced retinal damage, consistent with Arrhenius modeling of pulsed hyperthermia.

Abstracts

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DANIEL LAVINSKY, MD, PHD, CHRISTOPHER SRAMEK, PHD, JENNY WANG, BSC, PHILIP HUIE, MSC, ROOPA DALAL, MSC, YOSSI MANDEL, MD, PHD, DANIEL PALANKER, PHD
"SUBVISIBLE RETINAL LASER THERAPY Titration Algorithm and Tissue Response" RETINA0:1–11, 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 withfluorescein 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.

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.

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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 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.

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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 ±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.

Abstracts

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Christopher Sramek, Mark Mackanos, Ryan Spitler, Loh-Shan Leung, Hiroyuki Nomoto, Christopher H. Contag, and Daniel Palanker “Non-damaging Retinal Phototherapy: Dynamic Range of Heat Shock Protein Expression” Investigative Ophthalmology & Visual Science, March 2011, Vol. 52, No. 3

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 m 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 ° C at HSP70 expression threshold. At RPE viability threshold, T=57 ° 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

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Alexander J Brucker, Haijing Qin. “Observational Study of the Development of Diabetic Macular Edema Following Panretinal (Scatter) Photocoagulation Given in 1 or 4 Sittings.” 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.

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Mahiul M. K. Muqit, MRCOphth; George R. Marcellino, PhD; David B. Henson, PhD; Lorna B. Young, MBChB; Niall Patton, FRCOphth; Stephen J. Charles, FRCOphth; George S. Turner, FRCOphth; Paulo E. Stanga, MD “Single-Session vs Multiple-Session Pattern Scanning Laser Panretinal Photocoagulation in Proliferative Diabetic Retinopathy” The Manchester Pascal Study, ARCH OPHTHALMOL / VOL 128 (NO. 5), MAY 2010 (Arch Ophthalmol. 2010;128(5):525-533)

Objective:
To investigate the effects of pattern scanning laser (Pascal; OptiMedica, Santa Clara, California) multispot panretinal photocoagulation given in a singlesession (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 thresholding algorithm visual fields were recorded at baseline and 4 and 12 weeks.

Main Outcome Measures:
Central subfield retinal thickness, mean deviation, and PDR grade at 12 weeks.

Results:
There was a significant increase in mean CRT with MS-PRP (22 µm at 4 weeks, 95% CI, −32.25 to −10.75; 20 µm 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 SSPRP 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 MSPRP group (P < .001).

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

Application to Clinical Practice:
Twenty-millisecond Pascal SS-PRP may be safely and rapidly performed in 1500 burns with a similar efficacy to conventional MS-PRP.

Trial Identifier:
Research and Development Office PIN R00037, Central Manchester University Hospitals Foundation Trust.