# COMPARISON OF LASER PHOTOCOAGULATION FOR DIABETIC RETINOPATHY USING 532-NM STANDARD LASER VERSUS MULTISPOT PATTERN SCAN LASER

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**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-$\mu$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/cm$^2$, 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 $\mu$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.

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The advent of retinal laser photocoagulation in the early 1970s provided a noninvasive modality for treatment of proliferative retinal conditions. The significant degree of success and low complication rates of this procedure led to its widespread acceptance. This was furthered with the support of the Diabetic Retinopathy Study[1] and the Early Treatment Diabetic Retinopathy Study,[2] which were large multicenter trials, to evaluate the effects of laser treatment on diabetic retinopathy.

Panretinal photocoagulation (PRP) involves applying laser burns over the entire retina while sparing the central macular area. This may be performed using one of the several available laser delivery systems, slit lamp- and indirect ophthalmoscope-based systems being the most prevalent for outpatient indications. Application starts in a circumference of 500 $\mu$m from the disk and 2 disk diameters from the fovea to the wall of the central retina. Moderate-intensity burns of 200 $\mu$m to 500 $\mu$m (gray-white burns) are placed 1 spot size apart, except in areas of neovascularization, where the

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entire frond is treated. This procedure is continued peripherally to achieve a total of 1,200 to 1,600 applications over 2 or 3 sessions.[3]

Contemporary laser delivery systems produce a single laser spot on a single foot switch depression. Sequential spots are laid down by moving the aiming beam. The time required to deliver the total PRP treatment depends on features of the system and the surgeon's skill, as do laying down of a uniform pattern and interspacing of laser spots. Attempts have been made to reduce the inconvenience of multiple, interrupted laser applications placed one at a time and the constraint of operator dexterity. Multiple spot laser modality using beam splitters, multipliers, or preconfigured fiber bundles for simultaneous projection proved impractical because of the difficulty in varying the size and spacing of lesions.[4,5] Fully automated systems with retinal stabilization based on complex tracking and confocal reflectance systems were proposed to control lesion parameters dynamically.[6–10] However, these techniques required prior acquisition of the retinal image and alignment of all treatment locations with reference to retinal images. Such cumbersome requirements barred the introduction of these devices into active clinical use.[11]

Recently, a semiautomated, fully integrated, slit lamp-based pattern scan retinal photocoagulator (Optimedica Corp., Santa Clara, CA) has been introduced into clinical use. It uses frequency-doubled neodymium-doped yttrium aluminum garnet solid-state laser with a wavelength of 532 nm. Scanning function in this modality is achieved by a microprocessor-driven scanner that produces a variety of patterns viewable on a computer screen. Up to 56 (the smallest number being 1) laser spots can be delivered by a single foot pedal depression. The surgeon can select one of the several adjustable predetermined patterns, shapes, and sizes, including lines, squares, and circular arcs, and a "foveal exclusion zone." Pulse durations are in the 10-millisecond to 20-millisecond range. It has been claimed that these features would cut down the time required for PRP. Reduced pulse duration (10- or 20-millisecond in the pattern scan laser [PASCAL] vs 100–500-millisecond duration in the conventional systems) may be associated with less pain, because of decreased thermal diffusion into the choroid, which is rich in sensory nerves. A shorter pulse duration has also been conjectured to lessen the spread of laser burns, resulting in lesser collateral retinal damage and better preservation of retinal sensitivity.[11]

In this study,[12] we sought to compare the PASCAL with a conventional, single-spot slit-lamp delivery, 532-nm solid-state green laser (GLX) (Iridex Corp., Mountain View, CA) system. The parameters that we wanted to evaluate included regression of retinopathy and complications of PRP, change in laser spot size from day of treatment to 3 months, retinal sensitivity with the help of full threshold 30-2 Humphrey visual field examination, total time required for complete PRP, and the patient's pain perception while undergoing PRP.

## Materials and Methods

This was a prospective randomized clinical trial. After we obtained approval from our institutional ethics committee, 60 patients with bilaterally symmetrical proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy were enrolled. After informed consent was obtained, one eye of each patient was randomized to undergo PRP with the GLX and other eye with the PASCAL. We excluded patients with a history of previous laser treatments and/or intravitreal injections in either eye. Eyes with a pretreatment best-corrected visual acuity of $<6/24$ were excluded. Patients with media opacities such as significant cataract, corneal opacity, or vitreous hemorrhage obscuring fundus details in either eye were not included. Eyes with diabetic maculopathy were excluded. Other coincidental ocular disorders, such as glaucoma, uveitis, retinitis pigmentosa, myopia $>-6$ diopters, retinal degenerations and dystrophies, and optic disk pathologies, present or past, were considered to be exclusion factors.

### *Prelaser Examination*

All patients underwent best-corrected Snellen visual acuity examination. Intraocular pressure was measured with Goldman applanation tonometer. Each eye underwent detailed slit-lamp examination of the anterior segment. Posterior segment examination was performed using the indirect ophthalmoscope and slit-lamp biomicroscopy. Baseline fundus photographs were taken for each patient using either the Topcon TRC-50DX (Topcon Optical Company, Tokyo, Japan) or the Visucam (Carl Zeiss Meditec, Jena, Germany). Baseline macular thickness was evaluated using Stratus OCT 3 (Carl Zeiss Meditec, Dublin, CA).

### *Panretinal Photocoagulation Parameters*

One eye of each patient was randomized to undergo treatment with the GLX and the other with the PASCAL. Whatever the modality, PRP was always completed in two sittings in each eye. Therefore, each patient had an experience with both modalities on the

same day, during the first and the second sitting. A time interval of 7 days was maintained between the 2 sittings. All PRP sittings were performed by the same surgeon (M.N.). A total of 500 to 700 laser spots were required with the GLX and 950 to 1100 spots with the PASCAL for each sitting. A spot size of 200 $\mu$m was used in both modalities. A pulse duration of 20 milliseconds was used with the PASCAL and 200 milliseconds with the GLX. The power was adjusted to achieve grade 3 burns. Spots were placed at 1 spot distance with a Mainster 165 PRP lens. Topical anesthesia was used in all eyes. With the PASCAL, we used a 5 $\times$ 5 square grid, thereby applying 25 spots simultaneously. After each session, the required average laser energy density (i.e., the fluence of the system) was calculated using the following formula: power (millijoules) $\times$ duration (milliseconds) $\div$ spot size microns.[13]

We used the visual analog scale (VAS) to compare each patient's pain perception of the GLX and PASCAL sittings.[14–16] The VAS consists of a 10-cm line, with 0 on one end representing no pain and 10 on the other representing the worst pain ever experienced. A subject marks on this line to indicate the severity of his or her pain experience. Patients were seated comfortably after the PRP session. The VAS was filled up by the patient 5 minutes after each procedure; separate forms were filled for each eye. To eliminate potential bias, we randomly selected an equal number of patients to receive each treatment first, that is, in the first sitting. This order was reversed for the second sitting for each patient. The time required for each PRP sitting was measured.

*Follow-Up Procedures*

After completion of PRP, each patient was examined at months 1, 3, and 6 ($\pm$7 days). At each follow-up, complete ophthalmic examination was performed as detailed above. Regression of neovascularization was noted clinically[17] and documented with the help of fundus photographs. At 3 and 6 months, macular thickness was measured by optical coherence tomography.

The effect of PRP on retinal sensitivity was measured using the full threshold, central 30-2 test on the Humphrey visual field analyzer II at 1-month follow-up.[18–20] The measured values of the retinal sensitivity, in decibels (dB), were read in a numeric format from the raw data on the printout. For the purpose of analysis, the raw data were divided into 2 parts, the 16 points within central 15° (zone A) and the 60 points representing 15° to 30° (zone B). The mean retinal sensitivity values of both zones, A and B, were calculated by averaging the threshold values. The mean retinal sensitivity values of the two zones in eyes that underwent PRP with GLX and PASCAL were compared.

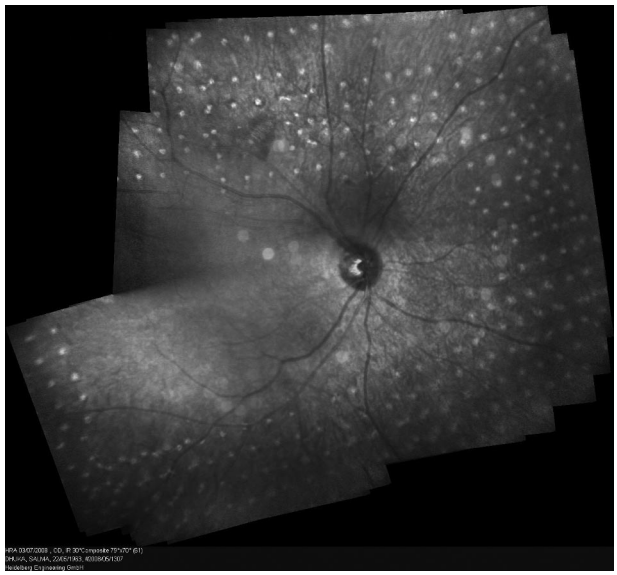

**Fig. 1.** Infrared image at 3 months with PASCAL.

The confocal infrared (810 nm) mode of the Heidelberg retinal angiography system (Heidelberg Instruments, Germany)[21–23] was used to study laser burn images on the same day of treatment and after 3 months to see spot spread (Figures 1 and 2). Infrared images of 10 laser scars from each quadrant on a 30° field of view (image size 512 $\times$ 512 pixels) were studied. Diameters of these laser spots were measured by the reticle of

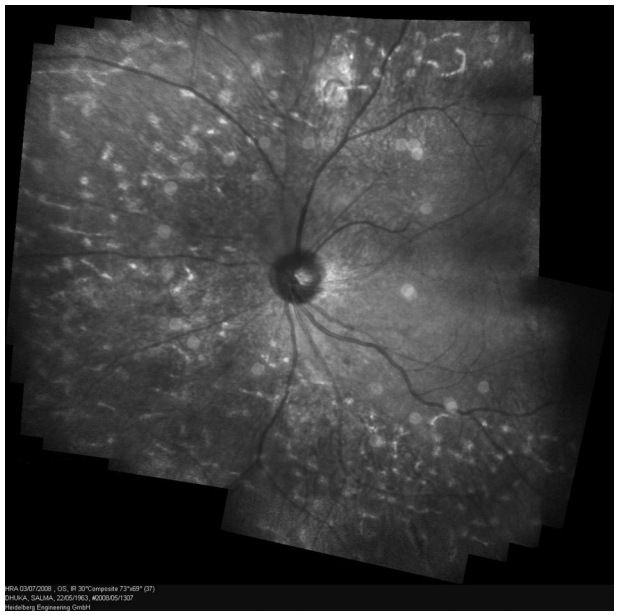

**Fig. 2.** Infrared image at 3 months with GLX.

Heidelberg retinal angiography machine. A mean was obtained, and values at 3 months were compared with those obtained immediately after treatment.

For statistical analysis of the data, relevant statistical tests such as the Mann–Whitney U test, chi-square test, Wilcoxon signed-rank test, and independent *t*-test were used. Snellen visual acuity was converted to decimals for analysis.

## Results

### *Patient Demographics*

This prospective study consisted of 60 eyes of 60 patients, 26 women and 34 men. The age range of these patients was 45 years to 61 years (mean age, 52 years). Duration of diagnosed diabetes ranged from 20 days to 30 years, the mean duration being 14.78 years. Thirty-one patients had proliferative diabetic retinopathy, and 29 had severe nonproliferative diabetic retinopathy.

### *Panretinal Photocoagulation Parameters*

To achieve grade 3 burns, the PASCAL system required an average power of 630 mW, whereas the GLX needed 288 mW (Table 1). The PASCAL and GLX systems showed average fluences of 191 and 40.33 J/cm$^2$, respectively. This difference was statistically significant with a $P$ value of 0.008 (Wilcoxon signed-rank test). The PASCAL required an average of 1.43 minutes per sitting of the PRP, which was significantly less than GLX, which took an average of 4.53 minutes per sitting. This difference was also statistically significant ($P = 0.008$, Wilcoxon signed-rank test). An average of 1,093 spots (range, 950–1,100) were delivered with the PASCAL per sitting to cover a half quadrant of the retina. However, an average of 575 spots (range, 500–700) were required per sitting with the GLX.

Table 1. Laser Parameters for Grade 3 Burns

| | GLX | PASCAL |
|---|---|---|
| Spot size ($\mu$m) | 200 | 200 |
| Duration (milliseconds) | 200 | 20 |
| Spots | | |
| Range | 500–700 | 950–1,100 |
| Average | 575 | 1093 |
| Power (mW) | | |
| Range | 200–400 | 400–1,000 |
| Average | 288 | 630 |
| Fluence (J/cm$^2$) | | |
| Range | 127–255 | 25–64 |
| Average | 40.33 | 191 |
| Time (minute) | | |
| Range | 2.45–5.45 | 1–2.35 |
| Average | 4.53 | 1.43 |
| VAS | | |
| Range | 3–9 | 0–1 |
| Average | 4.6 | 0.33 |

Table 2. Pre- and Postlaser BCVA (at 6 Months)

| Laser | 6/6–6/12 | 6/18–6/24 |
|---|---|---|
| GLX (no. of subjects) | | |
| Prelaser | 27 | 33 |
| Postlaser | 31 | 29 |
| PASCAL (no. of subjects) | | |
| Prelaser | 28 | 32 |
| Postlaser | 34 | 26 |

BCVA, best-corrected visual acuity.

### *Pain*

Patients' pain perception during the PRP procedure was calibrated using the VAS (Table 1). The VAS readings for the GLX were consistently higher than those for the PASCAL, with ranges of 3 to 9 and 0 to 1, respectively. The mean values showed statistically significant less discomfort with the PASCAL compared with the GLX ($P = 0.007$, Wilcoxon signed-rank test). A minimum difference of 3 and a maximum difference of 7.5 were noted in individual patients between the eye treated with GLX and the eye treated with PASCAL, respectively.

### *Visual Acuity*

Mean pre-GLX visual acuity was 6/10.3, and mean post-GLX visual acuity was 6/9.34. Mean pre-PASCAL visual acuity was 6/10.8, and mean post-PASCAL visual acuity was 6/9.3.

The difference between posttreatment visual acuities between the 2 groups was not statistically significant (Table 2). The change in visual acuity was not statistically significant ($P = 0.508$, chi-square test).

### *Regression*

Clinically and on fundus photographs, comparable regression was observed in eyes treated with either modality. None of the eyes developed any complication as a result of the PRP procedure. The eyes treated with PASCAL showed greater uniformity in burn spacing, with hardly any coalescing of laser compared with the eyes treated with GLX. No evidence of change in macular thickness was seen in any of the eyes. Six patients required laser augmentation because

Table 3. Laser Spot Size (Infrared Images Taken on the Heidelberg Retinal Angiography Instrument)

| | Time | Range ($\mu$m) | Average ($\mu$m) |
|---|---|---|---|
| GLX | 0 days | 290–420 | 338 |
| | 3 months | 320–510 | 430 |
| PASCAL | 0 days | 220–280 | 272 |
| | 3 months | 240–340 | 310 |

of fresh neovascularization (NVE) fronds, four from the GLX group and two from the PASCAL group.

*Infrared Images*

Values of laser spot size calculated on the basis of infrared images on the day of treatment and after 3 months are given in Table 3. The GLX spots were found to have spread more than the PASCAL spots. Average size at 3 months was 430 versus 310 $\mu$m in the GLX and PASCAL groups, respectively. This difference was highly statistically significant ($P$ = 0.000, Mann–Whitney U test).

*Retinal Sensitivity*

Both (treated with PASCAL and GLX) eyes of 27 patients underwent a full threshold, central 30-2 test on the Humphrey visual field analyzer II at the 1-month follow-up. In the eyes treated with PASCAL, average retinal sensitivity in central 15° (zone A) was 25.08 dB (range, 20.56–27.62 dB). Average zone A value for the eyes treated with GLX was 23.16 dB (range, 19.31–27.37 dB). Values of 15° to 30° (zone B) values among the eyes treated with PASCAL and GLX were 22.08 dB (range, 8.25–23.88 dB) and 17.14 dB (range, 6.93–23.25 dB), respectively (Table 4). This difference was not statistically significant as calculated by the Wilcoxon signed-rank test (zone A, $P$ = 0.26 and zone B, $P$ = 0.09).

## Discussion

Laser light is absorbed by the melanin of the retinal pigment epithelium, leading to destruction of adjacent mitochondria-rich and, therefore, oxygen-demanding photoreceptors. These are replaced by mitochondria-poor glial scars. This facilitates oxygen diffusion directly from the choroid to the inner retina by reducing the oxygen consumption of the outer retina. Inner retinal hypoxia is relieved, reducing production of angiogenic factors such as vascular endothelial growth factor receptor. Therefore, neovascularization is reduced or stopped.[24] Hemodynamics of the retinal circulation is altered with decreased viable retinal tissue and improvement in retinal oxygenation after PRP.[25]

Table 4. Post-PRP Retinal Sensitivity Values

| | Central 15° (dB) | 15–30° (dB) |
|---|---|---|
| GLX | 23.16 | 17.14 |
| PASCAL | 25.08 | 22.08 |

However, intentional laser-induced therapeutic destruction of isolated retinal areas is accompanied by unavoidable destruction of adjacent normal retinal tissue.[26–28] It has been shown that lasering at least half the retina leads to significant deficits in outer retinal functions over a 2-month period.[29] 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. Pulse durations of ~20 milliseconds have been proposed to represent an optimal compromise between the favorable impact of speed, higher spatial localization, and reduced collateral damage.[30]

Our study comprised 60 eyes of 60 patients with bilaterally symmetrical proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy. Both eyes underwent PRP in two sittings each, one eye with the GLX and the other with the PASCAL. We required greater power with the PASCAL system than with the GLX (630 vs 288 mW) to achieve grade 3 burns. Other authors have also reported requirement of similar higher power parameters.[13]

At the same time, we found that the laser fluence showed by the PASCAL was significantly less (40.33 vs 191 J/cm$^2$) compared with the GLX. This can be explained on the basis of pulse duration. The PASCAL uses an exposure time of 20 milliseconds (as opposed to 200 milliseconds for the GLX) for PRP spots. Thus, for the same burn intensity and same spot size, the fluence (power × time/area) is significantly reduced. In other words, because of the shorter pulse duration, there is reduced laser energy per burn on the retina. An average of 1,093 versus 575 spots were delivered with the PASCAL versus the GLX, respectively, per sitting to cover a half quadrant of the retina.

We studied the infrared images of laser marks on the day of treatment and 3 months after the procedures. At both times, the GLX laser spots were bigger than the PASCAL spots. At 3 months, the GLX and PASCAL spot sizes had increased to 430 and 310 $\mu$m, respectively, a difference that was highly statistically significant. Furthermore, although both eyes had comparable regression, better preservation of visual fields was obtained with the PASCAL compared with the GLX on the basis of retinal sensitivities. Eyes treated with PASCAL showed better average retinal sensitivity, both within the central 15° zone and in the 15° to

30° zone, although this difference was not statistically significant. Uniform spacing of the burns with hardly any coalescing of laser spots may also have a role in better retention of retinal sensitivity in these patients. Furthermore, the higher power used with the PASCAL system was not found to be associated with increased incidence of complications. We noted no evidence of precipitated macular edema in either of the groups.

Reduction in the total time required for the PRP procedure by the PASCAL compared with the GLX was a major advantage noted in our series. Averages of 1.43 and 4.53 minutes were required per sitting for the PASCAL and GLX, respectively. This difference was statistically significant. Although all patients in this study completed the PRP in two sessions, there have been reports of the procedure being successfully completed in a single session.[13]

It has been shown that shortening exposure time of retinal laser is significantly less painful but equally effective as conventional laser parameters.[16] Longer burns may cause greater thermal diffusion, whereas short pulse durations give rise to minimal diffusion of heat to adjacent areas, resulting in localized homogeneous burns and less discomfort.[11] We also found such a difference in the VAS rating between the two groups, with the eyes treated with PASCAL experiencing statistically significant lesser pain during the procedure. On the whole, we believed that the PRP procedure using PASCAL was made less tedious for the patient by both shortening of the total procedure time and decreased patient discomfort compared with a spot-by-spot treatment with GLX.

The current PASCAL system is not designed for portability. Furthermore, it does not support endolaser delivery, which is needed intraoperatively. These aspects provide limitations to the PASCAL compared with the versatility of conventional laser systems. Nonetheless, from a surgeon's outlook, the ability to reduce PRP time is well appreciated. Combined with similar efficacy, decreased patient discomfort, and lesser collateral damage, this represents a significant enhancement in PRP treatments. It may be reasonable to conclude that PASCAL has ushered in a paradigm shift in PRP delivery systems.

**Key words:** PASCAL photocoagulator, panretinal photocoagulation, proliferative diabetic retinopathy, infrared images, retinal sensitivity.

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