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Evaluation of retinal blood flow before and after panretinal photocoagulation using pattern scan laser for diabetic retinopathy

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ABSTRACT

Purpose: Laser speckle flowgraphy (LSFG) can measure blood flow in the ocular fundus. We analyzed the relationship between retinal blood flow and panretinal photocoagulation (PRP) in diabetic retinopathy.
Methods: This retrospective observational study examined the eyes of 35 patients with proliferative diabetic retinopathy (PDR) or non-PDR (NPDR). PRP was performed using a pattern scan laser. Using LSFG, blood flow was evaluated as the mean blur rate (MBR) or the relative flow volume (RFV). We also evaluated MBR in the vessels of the optic nerve head (MBR-V), RFV at the first retinal artery (RFV-A), and RFV at the first retinal vein (RFV-V) before bifurcation. Blood flows were measured prior to treatment initiation, during each PRP session, and after PRP.
Results: The total number of laser spots created was 4258 ± 461. Regression of neovascular activity at 6 months after PRP occurred in 29 (82.85%) eyes. MBR-V significantly decreased to 83.9 ± 16% (p = .0039), 79.3 ± 21% (p = .0001), and 73.5 ± 26% (p = .0001) after the first, second, and third PRP treatment sessions. MBR-V was also reduced to 75.0 ± 25% (p = .0001), 75.0 ± 25% (p = .0001), and 80.3 ± 22% (p = .0001) at 1, 3, and 6 months following PRP. During and at 6 months after the PRP treatments, RFV-A and RFV-V were also significantly reduced (p< .01).
Conclusions: During and after PRP treatments using pattern scan laser, retinal blood flow was reduced. Retinal blood flow may be an auxiliary measurement for effectively evaluating PRP or PDR.

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diabetic retinopathy; laser speckle flowgraphy; pattern scan laser; photocoagulation; retinal blood flow

Introduction

Diabetic retinopathy (DR) is a leading cause of blindness in the industrialized world. Panretinal photocoagulation (PRP) therapy has been shown to reduce the progression of neovascularization and the incidence of blindness in patients with proliferative diabetic retinopathy (PDR).[1,2]

PRP induces regression of retinal neovascularization, which leads to a reduction in the incidence of blindness in PDR.[3] Despite the widespread clinical use of PRP, the mechanisms mediating its effects remain unknown. A number of authors have reported a significant decrease in the retinal blood flow following PRP in eyes affected by PDR.[4–7] Using bidirectional laser Doppler velocimetry and photographic measurements of the vessel caliber, Grunwald et al. demonstrated there was decreased venous diameter, flow velocity, and total blood flow following PRP.[4,5] Fujio et al. demonstrated that after PRP treatment of half of the fundus, there were statistically significant regional decreases in the retinal blood flow (50–78%) and decreased vessel diameters, ranging from 1% to 9%.[6]

Previous studies have evaluated the utility of pattern scan laser in treating PDR.[8–10] The use of a pattern scan laser in PDR cases makes it possible to provide less-painful laser treatments.[8,9] Muraly et al. reported that a pattern scan laser was effective and even better than conventional laser with regard to the effectiveness of the treatment.[8]

Laser speckle flowgraphy (LSFG) performs repeated measurements of defined retinal regions, which makes it possible to quantitatively estimate blood flow changes in the optic nerve head (ONH), choroid, retina, and iris, in vivo. LSFG, which utilizes the laser speckle phenomenon, was developed to facilitate the noncontact analysis of ocular blood flow in living eyes.[11]

Blood flow can be quantified as the mean blur rate (MBR) through the use of the LSFG-NAVI instrument (Softcare Ltd., Fukuoka, Japan). Recent studies have reported the utility of the MBR measurement in the evaluation of blood flow.[12–15] Recently, Iwase et al. used LSFG to demonstrate that the blood flow in severe nonproliferative diabetic retinopathy (NPDR) with PRP was significantly lower than that of NPDR without PRP.[7]

In the present study, after performing PRP with a pattern scan laser to treat PDR in diabetic patients, we used LSFG to evaluate the retinal blood flow changes. The evaluation of retinal blood flow before and during the PRP treatment of PDR with a pattern scan laser may provide valuable insights into DR and contribute to the development of future treatment options.

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Methods

Patients

We retrospectively reviewed clinical data for type 1 and type 2 diabetic patients who had been newly treated by PRP for PDR or severe NPDR at the Department of Ophthalmology, Nagasaki University, Japan. A total of 35 eyes of 26 consecutive patients were included in this study. All patients underwent slit-lamp examination, intraocular pressure measurement, dilated fundus examination, fluorescein angiography (FA), fundus photography, optical coherence tomography (OCT), LSFG, and blood pressure measurements at baseline prior to the laser treatment.

The exclusion criteria were as follows: corneal opacity, cataract, or vitreous hemorrhage that potentially could influence vision and digital photography; previous vitreous surgery or photocoagulation treatment of the study eye; any history of ocular conditions associated with a risk of macular edema; planned intraocular surgery within 6 months; OCT evidence of vitreomacular traction or epiretinal membranes; and a history of chronic renal failure or renal transplantation for diabetic nephropathy.

The present study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Nagasaki University College of Medicine.

Pattern scan laser

PRP was performed by using a pattern scan laser photocoagulation system. Diabetic retinopathy was treated with three sessions of PRP. All photocoagulation sessions were performed at 1-week intervals. The pattern scan laser photocoagulation system uses a frequency-doubled 532 nm wavelength neodymium:yttrium aluminum garnet solid-state laser (PASCAL®, Topcon Medical Laser Systems, Santa Clara, CA). PRP treatments with the pattern scan laser were performed using an Ocular Mainster wide-field contact lens (1.5× magnification, Ocular Instruments, Bellevue, WA) with a 200 µm spot size, 0.75 burn width, and laser powers of 250–600 mW for 0.02–0.03 s. PASCAL® 4 × 4 arrays with topical 0.4% oxybuprocaine hydrochloride were used.

The PRP treatment burn distribution extended from outside of the retinal arcades to more than two disc diameters temporal to the fovea and as close to the ora serrata as possible. The primary efficacy endpoint was the proportion of eyes demonstrating maintenance of the regression at 6 months after the PDR treatment compared with the baseline. Multiple reviewers graded the FA evaluation of the retinal neovascularization regression at 3 and 6 months after the final PRP session.

In accordance with ethical and good clinical practice, all serious adverse events, whether deemed related to the treatment or not, were recorded.

Retinal blood flow measurements

The LSFG-NAVI system uses a fundus camera equipped with a diode laser (wavelength = 830 nm) and a highly sensitive charge-coupled device (CCD) camera (750 × 360 pixels) with a scanning speed of 30 frames per second. To observe the fundal blood flow, the area of interest was illuminated using a wide laser spot created with a back scattered laser in a speckled pattern in the image plane of the fundus. The intensity variation of the pattern was detected by the CCD camera.

Pupils were dilated with 0.5% tropicamide and 0.5% phenylephrine hydrochloride. LSFG and blood pressure measurements were conducted after subjects had rested for 10 min in a darkened room. Patients were asked to gaze at the fixation point of the device, which was at the center of their visual field, with the investigator then able to control the eye position by moving the fixation point. The center of the captured image was set at a point midway between the optic disc and the macula. The position of the subject's eye was then saved, which enabled the same area to be captured in each of the subsequent examinations. When the images were insufficiently focused, dark vertical lines were used instead on the live images. The principles of the LSFG technique and its application in the measurement of the blood flow of the ONH have previously been described in detail.[13] We used a round band to help us manually identify the margin of the ONH, with the software then separating out the vessels by utilizing an automated definitive threshold. We also evaluated the MBR parameter in the vessels of the ONH (MBR-V). The software saved all of the positions for the regions of interest according to the vascular pattern so that they could be reused during any subsequent analyses in the same patient.

The relative flow volume (RFV), which is a novel LSFG measurement parameter, is produced by subtracting the background choroidal blood flow from the overall blood flow value of a region of interest that is centered on a retinal vessel. This measurement reflects the retinal flow velocity and the vascular diameter.[15] We additionally evaluated the MBR-V, the RFV at the first retinal artery (RFV-A), and the RFV at the first retinal vein (RFV-V) before the bifurcation Figure 1. To evaluate the changes in the retinal blood flow that occurred before and after the PRP treatment of PDR with the pattern scan laser, we measured the MBR-V, RFV-A, and RFV-V prior to the initiation of the treatment; during each PRP session; and at 1, 3, and 6 months after the final PRP treatment session. Values were calculated as a percentage of the pretreatment value (100%).

Blood pressure, mean arterial pressure, ocular perfusion pressure, and intraocular pressure were also measured prior to the PRP treatment and at 1, 3, and 6 months after the PRP treatment. Figure 2 shows a typical blood flow pattern that was observed following the PRP treatment.

Statistical analysis

All the results are expressed as means ± standard deviations. Retinal blood flow changes were evaluated using Dunnett's test. Values with $p < 0.05$ compared with the pretreatment values were considered statistically significant. The paired *t*-test was used to compare the systolic and diastolic blood pressures, mean arterial pressure, ocular perfusion pressure, and intraocular pressure values before and after the PRP

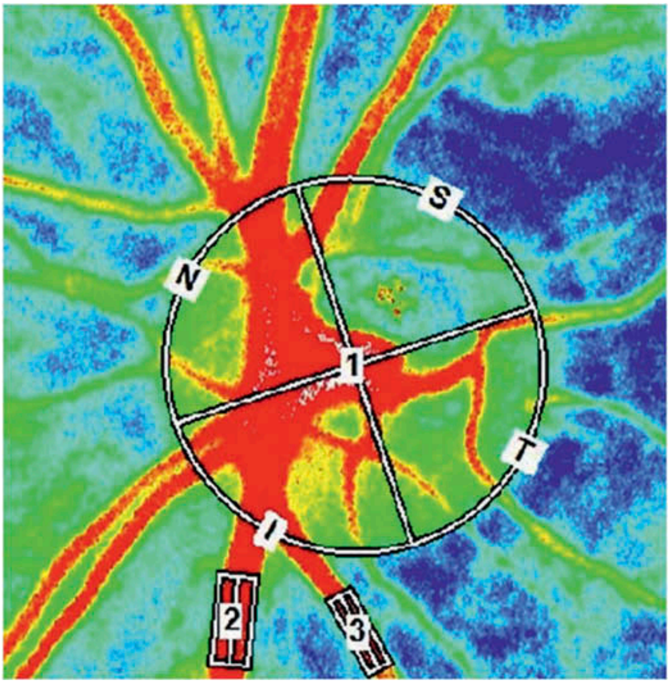

Figure 1. A composite map of the optic nerve head. The optic nerve head (1), the first retinal vein before bifurcation (2), and the first retinal artery before bifurcation (3) were analyzed using laser speckle flowgraphy. Since the distinction between the retinal vein and artery can be difficult, these were identified using the fundal photograph. Red indicates a faster vessel blood flow, while blue indicates a slower blood flow. S, N, I, and T in the figure stand for superior part, nasal part, inferior part, and temporal part, respectively, and are not related to the current study.

treatment. Statistical analysis was performed using StatFlex ver. 5.0 software (Artech Inc., Osaka, Japan).

Results

Patient demographics

Mean patient age was 56 ± 13 years (range 30–79 years), with the study group consisting of 18 males (25 eyes) and 8 females (10 eyes). Severe NPDR was found in 7 (20%) eyes, while 28 (80%) eyes had PDR. There were 17 (65.4%) patients with hypertension.

Pattern scan laser treatment parameters

PRP with the pattern scan laser was performed in three sessions at 1-week intervals. The total number of laser spots created over the three sessions was 4258 ± 461. Table 1 shows the mean number and standard deviation of the laser spots created during the three sessions.

After 3 months of the PRP sessions, our results showed that regression was maintained in 29 (82.85%) eyes at 6 months after the final PRP session, thereby demonstrating the efficacy of PRP with the pattern scan laser procedure. Regression of neovascular activity was detected with FA in 22 (78.5%) of 28 eyes with PDR at 3 months. This regression was maintained at 6 months after the final PRP session.

Complications

No unexpected or serious adverse events were reported in any of the patients during the study period. There were no signs of intra-retinal or sub-retinal hemorrhage or blood vessel damage from the 20-ms PRP burns observed directly after the treatment or during the follow-up period. There were also no indirect laser-related ocular complications reported.

Blood flow changes

There was a significant decrease of MBR-V to 83.9 ± 16% (p = .0039), 79.3 ± 21% (p = .0001), and 73.5 ± 26% (p = .0001) at the first, second, and third sessions of the PRP treatment with the pattern scan laser, respectively. MBR-V was also reduced to 75.0 ± 25% (p = .0001), 75.0 ± 25% (p = .0001), and 80.3 ± 22% (p = .0001) at 1, 3, and 6 months following the PRP, respectively Table 2. Figure 2 shows a typical case of MBR-V that was treated with PRP.

As seen in Table 2, there was a significant decrease of RFV-A to 82.1 ± 21% (p = .0056), 75.9 ± 28% (p = .0095), and 71.3 ± 21% (p = .0001) at the first, second, and third sessions of the PRP treatment with the pattern scan laser, with a further reduction to 75.7 ± 24% (p = .002), 73.9 ± 24% (p = .0009), and 80.1 ± 27% (p = .0022) at 1, 3, and 6 months following the PRP treatment, respectively.

RFV-V significantly decreased to 77.1 ± 22% (p = .0056), 78.7 ± 27% (p = .0095), and 68.8 ± 26% (p = .0001) at the first, second, and third sessions of the PRP treatment with the pattern scan laser, and was reduced to 77.2 ± 29% (p = .002), 75.6 ± 24% (p = .0009), and 77.1 ± 27% (p = .0022) at 1, 3, and 6 months following the PRP treatment, respectively Table 2.

MBR-V, RFV-A, and RFV-V were comparable during and after the PRP treatment, with no significant differences observed (p = .1859, Table 3).

Blood and perfusion pressures

There were no significant differences following the PRP treatment in the systolic and diastolic blood pressures, mean arterial pressure, ocular perfusion pressure, or intraocular pressure compared with the pretreatment values Table 3.

Discussion

MBR represents the blood velocity as relative values of the blurring of the speckled pattern caused by the blood flow. However, it has been shown that the measured MBR values correlate well with the absolute blood flow values that have been measured by hydrogen gas clearance and microsphere methods.[16,17] While it is possible that the MBR-V may reflect the entire circulation, we believe that it is better to separately measure the blood velocity of the artery and vein. Therefore, we evaluated both the RFV-A and RFV-V. As previously reported, the RFV values can be considered to be an accurate and reliable index of the relative blood flow.[15]

In the current study, we confirmed that there were significant reductions in MBR-V, RFV-A, and RFV-V when

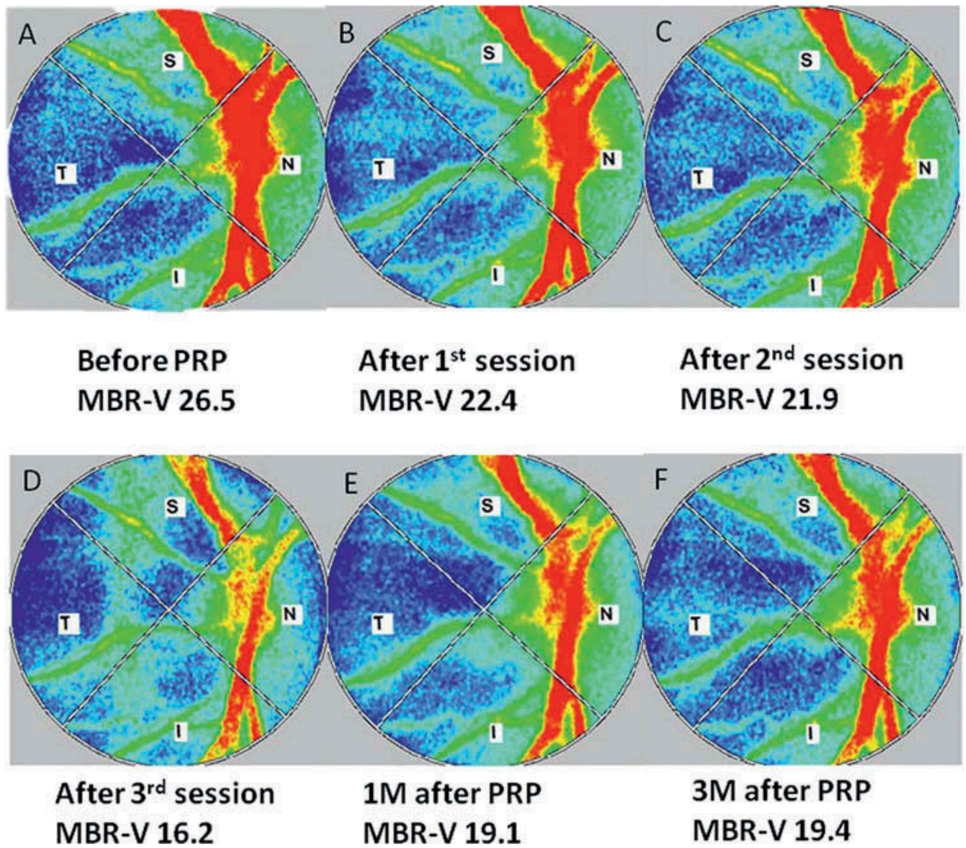

Figure 2. A typical blood flow change following treatment with panretinal photocoagulation (PRP). A) A composite map within the optic disc with an initial optic disc blood flow (MBR-V) value of 26.5. B) The MBR-V value, which was measured after the first PRP session, was 22.4. This was a decrease to 84.5% of the initial value. C) After the second session, the MBR-V value was 21.9. This was a decrease to 82.6% of the initial value. D) After the third PRP session, the MBR-V value was 16.2. This was a decrease to 61.1% of the initial value. E) At 1 month after the PRP treatment, the MBR-V value was 19.1. This was a decrease to 72.1% of the initial value. F) At 3 months after PRP treatment, the MBR-V was 19.4. This was a decrease to 73.2% of the initial value. S, N, I, and T in the figure stand for superior part, nasal part, inferior part, and temporal part, respectively, and are not related to the current study.

Table 1. PRP treatment parameters.

Number of sessions	3
First session (mean ± SD)	1367 ± 459
Second session (mean ± SD)	1471 ± 473
Third session (mean ± SD)	1420 ± 451
Total number of burns (mean ± SD)	4258 ± 461

SD = standard deviation; PASCAL = pattern scan laser.

using pattern scan laser PRP. We also demonstrated that these reductions were maintained for up to 6 months after the final treatment session. Another study has also reported that after PRP for PDR, there was a significant decrease in the blood flow in the retinal vein.[4] The reasons for the reduced blood flow may be as follows. Laser photocoagula-

Table 3. Blood and ocular perfusion pressures.

	Before PRP*	1 month after PRP*	3 months after PRP*	6 months after PRP*
Systolic blood pressure (mmHg)	149 ± 26	136 ± 22	140 ± 20	137 ± 23
Diastolic blood pressure (mmHg)	85 ± 16	78 ± 14	82 ± 15	81 ± 16
Mean arterial pressure (mmHg)	107 ± 17	97 ± 15	102 ± 15	100 ± 16
Ocular perfusion pressure (mmHg)	55 ± 11	48 ± 11	51 ± 11	51 ± 10

PRP = panretinal photocoagulation
*Values are expressed as the mean ± standard deviation.

Table 2. Changes in MBR value before and after PRP.

	Before PRP	First PC*	Second PC*	Third PC*	1 month after PRP*	3 months after PRP*	6 months after PRP*
MBR-V (%)	100	83.9 ± 16	79.3 ± 21	73.5 ± 26	75.0 ± 25	75.0 ± 25	80.3 ± 22
RFV-A (%)	100	82.1 ± 21	75.9 ± 28	71.3 ± 21	75.7 ± 24	73.9 ± 24	80.1 ± 27
RFV-V (%)	100	77.1 ± 22	78.8 ± 27	68.8 ± 26	77.2 ± 29	75.6 ± 24	77.1 ± 27

MBR = mean blur rate; PRP = panretinal photocoagulation; PC = photocoagulation; MBR-V = mean blur rate in the vessels of the optic nerve head; RFV-A = relative flow volume at the first retinal artery before bifurcation; RFV-V = relative flow volume at the first retinal vein before bifurcation
*Values are expressed as the mean ± standard deviation.

tion reduces both the oxygen consumption of the outer retina and the oxygen that normally diffuses from the choriocapillaris into the retina. When the changes in the oxygen flux reach the inner retina, the retinal arteries constrict, causing a decrease in the blood flow. It has been previously reported that hypoxia relief reduces the production of growth factors, including vascular endothelial growth factors, and reduces or terminates neovascularization.[18] An animal study has also demonstrated that there is increased oxygen delivery to the inner retina following photocoagulation.[19] In our current study, we were not able to determine a suitable ocular blood flow that would elevate the oxygen tension in the inner retina or the appropriate number of laser burns. We detected that the RFV-V was reduced by 77.1 ± 27% at 6 months after the PRP treatment. Together with the study by Grunwald et al., which showed a significant decrease in the blood flow in the retinal vein from 11.5 ± 3.8 μL/min to 8.4 ± 3.3 μL/min (73%),[4] our data indicate that a reduced blood flow of between 70% and 80% with PRP may be an appropriate level. Fujio et al. previously suggested that retinal blood flow and vessel diameter could represent potential surrogate markers for the laser response.[6] Grunwald et al. suggested that the restored response to a hyperoxic challenge can be used as a tool to gauge the success of the laser therapy.[4] Recently, Okamoto et al. demonstrated that the sub-foveal choroidal thickness and sub-foveal choroidal blood flow significantly decreased after PRP in eyes with severe NPDR, which suggests that these parameters may be helpful in assessing the effectiveness of treatment with PRP for NPDR.[20] Additionally, Iwase et al. used LSFG to demonstrate that the blood flow in severe NPDR with PRP on the ONH and choroid was significantly lower than that of severe NPDR without PRP.[7] The present investigation was a longitudinal study that used the LSFG design to examine reductions in blood flow after PRP for PDR or NPDR as opposed to the cross-sectional study of Iwase et al. However, since the optimal amount of PRP treatment and the end-points for laser treatment have yet to be established, in part due to the variable individual responses to PRP, the success of PRP therapy is usually characterized by the regression of neovascularization.

Although there was no significant difference between the ocular blood flow at 3 and 6 months after the PRP in the current study, we found a slight increase in all values such as the MBR-V, RFV-A, and RFV-V at 6 months after PRP. Muqit et al. have reported that the 20-ms laser burns were significantly reduced in size at 6 months after the laser treatment.[21,22] This finding suggests that increased ocular blood flow might be related to reductions in the size of the laser burns. Unfortunately, our current study did not evaluate the lesion size of the laser burns. Thus, if further LSFG measurements of the ocular blood flow are able to demonstrate that PRP treatments are effective, this would indicate that laser treatments could be added to a procedure when necessary.

Our study also showed that after PRP treatment, there were no significant differences in the systolic or diastolic blood pressures, mean arterial pressure, ocular perfusion pressure, or intraocular pressure. Therefore, reductions in the retinal blood flow are almost certainly due to the curative effect of the PRP treatment.

The main limitations of this retrospective study were the small sample size and the short follow-up period. Prospective studies that assess the long-term benefits of PRP and the relationship between the severity of PDR and the ocular blood flow will need to be undertaken in the future. Another limitation of this study was that we did not compare the retinal blood flow in accordance with the type of diabetes millitus or the severity of DR. In addition, this study did not analyze the relationship between the non-perfusion area and the blood flow results.

In conclusion, this study demonstrated the clinical utility and short-term safety profile of PRP with the pattern scan laser in the treatment of PDR. Our results also showed the utility of LSFG as a simple method for detecting retinal blood flow changes following PRP during the follow-up of patients with DR. LSFG may serve as an auxiliary measurement that can be used to evaluate the effectiveness of PRP. Further measurements and examinations of the ocular blood flow in future studies may be able to determine the appropriate number of laser burns that are required during these types of treatments.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. The Diabetic Retinopathy Study Research Group. Preliminary report on effects of photocoagulation therapy. Am J Ophthalmol. 1976;81:383–96. 10.1016/0002-9394(76)90292-0.
2. Photocoagulation treatment of proliferative diabetic retinopathy. Clinical application of Diabetic Retinopathy Study (DRS) findings, DRS Report Number 8. Diabetic Retinopathy Stud Res Group Ophthalmol. 1981;88:583–600.
3. Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy: the second report of Diabetic Retinopathy Study findings. Ophthalmology. 1978;85:82–106. 10.1016/S0161-6420(78)35693-1.
4. Grunwald JE, Riva CE, Brucker AJ, Sinclair SH, Petrig BL. Effect of panretinal photocoagulation on retinal blood flow in proliferative diabetic retinopathy. Ophthalmology. 1986;93:590–95. 10.1016/S0161-6420(86)33691-1.
5. Grunwald JE, Brucker AJ, Petrig BL, Riva CE. Retinal blood flow regulation and the clinical response to panretinal photocoagulation in proliferative diabetic retinopathy. Ophthalmology. 1989;96:1518–22. 10.1016/S0161-6420(89)32697-2.
6. Fujio N, Feke GT, Goger DG, McMeel JW. Regional retinal blood flow reduction following half fundus photocoagulation treatment. Br J Ophthalmol. 1994;78:335–38. 10.1136/bjo.78.5.335.
7. Iwase T, Kobayashi M, Yamamoto K, Ra E, Terasaki H. Effects of photocoagulation on ocular blood flow in patients with severe non-proliferative diabetic retinopathy. PLoS One. 2017;12: e0174427. 10.1371/journal.pone.0174427.
8. 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;31:1359–65. 10.1097/IAE.0b013e318203c140.

9. Al-Hussainy S, Dodson PM, Gibson JM. Pain response and follow-up of patients undergoing panretinal laser photocoagulation with reduced exposure times. Eye. 2008;22:96–99. 10.1038/sj.eye.6703026.
10. Muqit MM, Marcellino GR, Henson DB, Young LB, Patton N, Charles SJ, et al. Single-session vs multiple-session pattern scanning laser panretinal photocoagulation in proliferative diabetic retinopathy: the Manchester Pascal Study. Arch Ophthalmol. 2010;128:525–33. 10.1001/archophthalmol.2010.60.
11. Sugiyama T, Araie M, Riva CE, Schmetterer L, Orgul S. Use of laser speckle flowgraphy in ocular blood flow research. Acta Ophthalmol. 2010;88:723–29. 10.1111/j.1755-3768.2009.01586.x.
12. Watanabe G, Fujii H, Kishi S. Imaging of choroidal hemodynamics in eyes with polypoidal choroidal vasculopathy using laser speckle phenomenon. Jpn J Ophthalmol. 2008;52:175–81. 10.1007/s10384-007-0521-7.
13. Liang Y, Downs JC, Fortune B, Cull G, Cioffi GA, Wang L. Impact of systemic blood pressure on the relationship between intraocular pressure and blood flow in the optic nerve head of nonhuman primates. Invest Ophthalmol Vis Sci. 2009;50:2154–60. 10.1167/iovs.08-2882.
14. Ubuka M, Sugiyama T, Onoda Y, Shiba T, Hori Y, Maeno T. Changes in the blood flow of the optic nerve head induced by different concentrations of epinephrine in intravitreal infusion during vitreous surgery. Invest Ophthalmol Vis Sci. 2014;55:1625–29. 10.1167/iovs.13-13801.
15. Shiga Y, Asano T, Kunikata H, Nitta F, Sato H, Nakazawa T, et al. Relative flow volume, a novel blood flow index in the human retina derived from laser speckle flowgraphy. Invest Ophthalmol Vis Sci. 2014;55:3899–904. 10.1167/iovs.14-14116.
16. Takahashi H, Sugiyama T, Tokushige H, Maeno T, Nakazawa T, Ikeda T, et al. Comparison of CCD-equipped laser speckle flowgraphy with hydrogen gas clearance method in the measurement of optic nerve head microcirculation in rabbits. Exp Eye Res. 2013;108:10–15. 10.1016/j.exer.2012.12.003.
17. Wang L, Cull GA, Piper C, Burgoyne CF, Fortune B. Anterior and posterior optic nerve head blood flow in nonhuman primate experimental glaucoma model measured by laser speckle imaging technique and microsphere method. Invest Ophthalmol Vis Sci. 2012;53:8303–09. 10.1167/iovs.12-10911.
18. Stefánsson E. The therapeutic effects of retinal laser treatment and vitrectomy. A theory based on oxygen and vascular physiology. Acta Ophthalmol Scand. 2001;79:435–40. 10.1034/j.1600-0420.2001.790502.x.
19. Budzynski E, Smith JH, Bryar P, Birol G, Linsenmeier RA. Effects of photocoagulation on intraretinal PO_2 in cat. Invest Ophthalmol Vis Sci. 2008;49:380–89. 10.1167/iovs.07-0065.
20. Okamoto M, Matsuura T, Ogata N. Effects of panretinal photocoagulation on choroidal thickness and choroidal blood flow in patients with severe nonproliferative diabetic retinopathy. Retina. 2016;36:805–11. 10.1097/IAE.0000000000000800.
21. Muqit MM, Gray JC, Marcellino GR, Henson DB, Young LB, Patton N, et al. In vivo laser–tissue interactions and healing responses from 20- vs 100-millisecond pulse Pascal photocoagulation burns. Arch Ophthalmol. 2010;128:448–55. 10.1001/archophthalmol.2010.36.
22. Muqit MM, Denniss J, Nourrit V, Marcellino GR, Henson DB, Schiessl I, et al. Spatial and spectral imaging of retinal laser photocoagulation burns. Invest Ophthalmol Vis Sci. 2011;52:994–1002. 10.1167/iovs.10-6309.