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Retinal Photocoagulation Density in the Treatment of Neovascular Glaucoma due to Diabetic Retinopathy

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Abstract

Purpose: The risk factors for pan-retinal photocoagulation (PRP) failure and the efficacy of achieving a PRP burn density of ≥ 40% in the mid-periphery against diabetic neovascular glaucoma (NVG) were retrospectively evaluated.

Methods: All eyes were treated in order to exceed more than 40% PRP density by fluorescein fundus angiography before and after PRP. Risk factors for failed IOP control (≦22 mmHg or baseline) were evaluated by dividing into two groups; eyes received previous retinal photocoagulation (RP) before NVG (group I) and eyes with no RP before NVG (group II).

Results: Thirty one eyes of 25 patients were used (group I: 12 eyes, group II: 19 eyes).RP density before NVG in all eyes in group I was less than 40%. Risk factors for failed IOP control were prolonged PRP treatment of more than 12 months in group I (p=0.00053), and higher IOP at the diagnosis of NVG (p=0.01157), preexisting glaucoma or ocular hypertension (OH) (p=0.04664) and the persistence of optic disc neovascularization (NVD) in group II (p=0.01766).

Conclusion: Eyes with RP density of less than 40% may have a risk for later development of NVG. The prompt initiation of PRP, a PRP burn density of greater than 40%, and the completion of PRP within 6 months are strongly recommended for the treatment of NVG. Special care should be taken in NVG-affected eyes with small pupils, preexisting glaucoma or OH, or persistent NVD as well as those that are subjected to PRP for more than 12 months.

Keywords: Neovascular glaucoma; Retinal photocoagulation density

Introduction

PRP is considered standard treatment for NVG due to diabetic retinopathy [1-5]. It is suggested that PRP in diabetic patients may prevent the later development of rubeosis iridis, angle neovascularization, and NVG [6]. According to the guidelines issued by the Diabetic Retinopathy Study (DRS) Research Group, a total of 1,200 to 1,600 spots of 500 µm burns should be applied randomly over the peripheral retina [7]. On the other hand, it is reported that the number of spots recommended by the DRS. Research Group is insufficient, and 2,500 to 3,000 spots or more of 500 µm burns are necessary to reduce the incidence of severe visual loss [8]. NVG is one of the most serious complications of diabetic retinopathy and it is very important to give sufficient PRP to treat NVG. Augmentation of PRP after initial treatment failure achieves faster regression of diabetic retinopathy in eyes with proliferative disease when compared to those with no additional PRP [9] and may reduce the elevated IOP in NVG due to diabetic retinopathy. However, it has not yet been clarified what is sufficient PRP for the treatment or prevention of NVG. In this study, we retrospectively reviewed whether a PRP burn density of 40% or more in the mid-periphery and extreme periphery is able to prevent NVG or reduce IOP during the treatment of NVG and also assessed the risk factors for PRP failure.

Methods

Seventy-two eyes of 58 consecutive Japanese patients with NVG due to diabetic retinopathy, who visited three clinics between October, 2004 and September, 2007 were retrospectively reviewed for this study. NVG patients were divided into two groups, group I: eyes which received retinal photocoagulation before the occurrence of NVG and group II: eyes which received retinal photocoagulation after the occurrence of NVG. The institutional Review Board/Ethics Committee judged that this retrospective study had no ethical issues. Diagnosis of NVG was made if IOP was equal to or more than 22 mmHg with angle neovascularization detected by gonioscopy before pupil dilatation. The referred patients in which NVG had been diagnosed at another hospital were included if the occurrence of NVG was traceable and fluorescein fundus angiography (FFA) was available at the diagnosis of NVG. Fluorescein gonio angiography (FGA) and fluorescein iris angiography (FIA) were used in some of the referred patients and the eyes with ocular hypertension and primary open angle glaucoma to detect iris and angle rubeosis if angle neovascularization was not visible. The exclusion criteria for eyes or patients in this study were eyes for which panoramic photographs were not available, previous ocular surgery including vitrectomy, cataract surgery within 6 months before the diagnosis of NVG and serious vitreous loss at cataract surgery, more than 50% peripheral anterior synechia (PAS), retinal detachment, serious anterior chamber hemorrhage, serious vitreous hemorrhage, carotid artery occlusion on the same side (Table 1).

Focal retinal photocoagulation (RP) or PRP density was calculated

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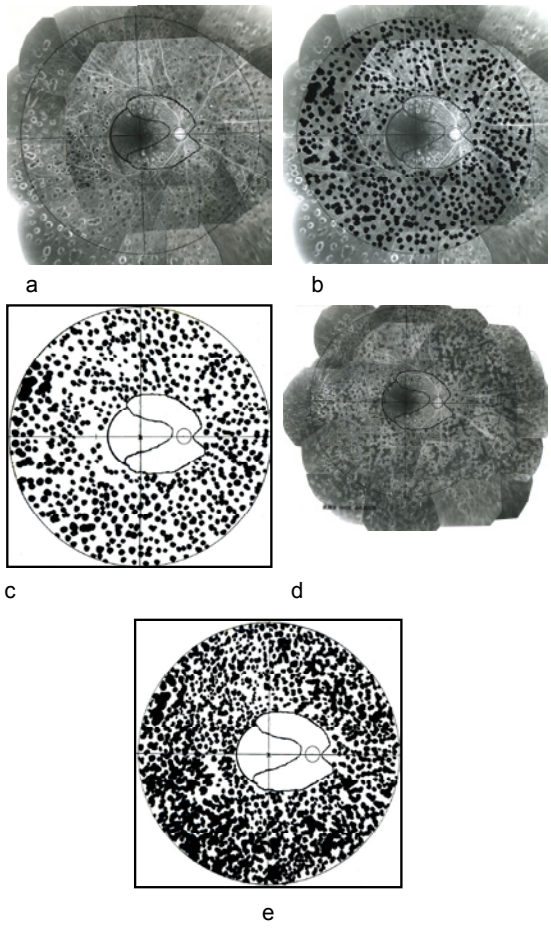
as follows: transparent sheets [10] were first placed on FFA panoramic photographs (Figure 1a), then RP or PRP spots in the mid-periphery were traced digitally along the light margin of the spots and painted black (Figure 1b), and the total area of the black spots was expressed with pixels using SCION IMAGE Beta 4.02 on a computer (Figure 1c). The results of IOP control were judged successful six months after the final PRP if the IOP was less than 21 mmHg or less than the baseline before the diagnosis of NVG. Failed IOP was defined if IOP with or without glaucoma medication after achieving PRP did not return below 21 mm Hg or the baseline before the diagnosis of NVG. Statistical evaluation was performed by $\chi 2$ test and one-factor ANOVA.

Results

Seventy-two eyes of 58 Japanese patients diagnosed with NVG due to diabetic retinopathy were treated in this period. Vitreous hemorrhage (15 eyes), more than half-peripheral anterior synechia (PAS) (17 eyes) and vitrectomy (15 eyes) were the most common excluded items. Both groups were composed of 12 eyes in group I (Table 2) and 19 eyes in group II (Table 3). All eyes included in this study had no PAS or less than 25% after achieving PRP. The missing area of the mid-periphery panoramic photographs within an 8.2 optic disc diameter in the FFA of both groups I and II ranged between 0% and 29.2%. In most patients, except a few eyes from each group (Table 2 and 3) (group I: Patients 7-9, group II: Patients 1-3), serial PRP was started within a month after the diagnosis of NVG and was completed within 6 months. The aim of PRP in all eyes in both groups was to achieve a PRP burn density of greater than 40% in the mid-periphery and to coagulate more than 40% of the extreme peripheral part of the retina (Figure 2a and 2b). The coagulation of the retina was assessed by comparing it with a schematic picture of a 40% PRP burn distribution in the mid-periphery (Figure 1d). PRP burn density and the presence of optic disc neovascularization (NVD) and neovascularization elsewhere (NVE) were evaluated on the second FFA, which was performed within six months after the completion of PRP.



Figures 1:
a: Panoramic FFA of the right eye of Patient 7 in group I before treatment with additional PRP. A transparent sheet on which was drawn radial peripapillary capillaries, optic papilla, temporal raphe, and mid-periphery (8.2 optic disc diameter) indicated by a large circle and the extreme periphery beyond the large circle [12], was placed on the photograph.
b: PRP spots were traced digitally along the right margin and painted black on the sheet.
c: schematic image of PRP density in the mid periphery (30.0%).
d: Panoramic FFA of the same eye after completion of PRP. PRP density exceeded more than 40 % in the mid-periphery and extremely periphery.
e: Schematic picture of PRP density in the mid-periphery after completion of PRP (56.6%).

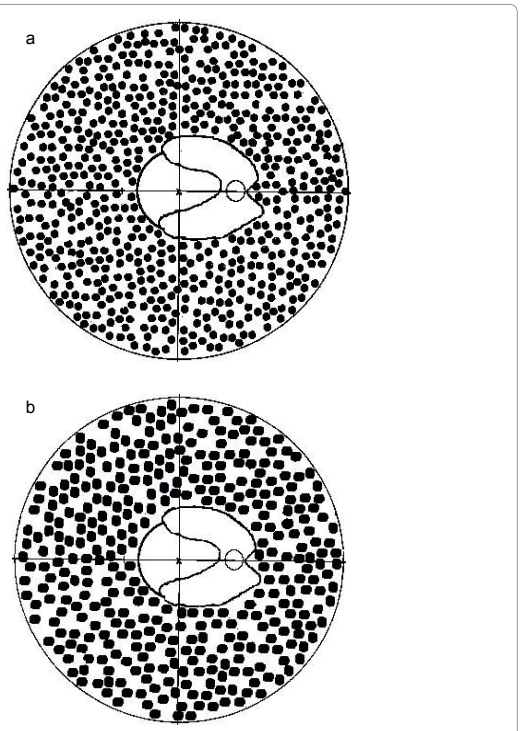


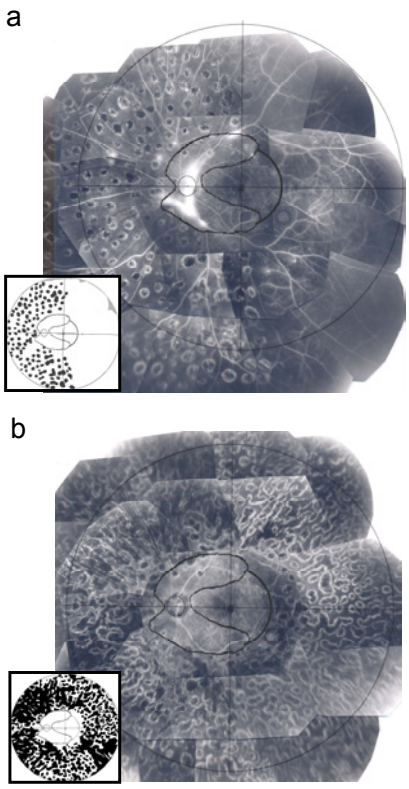
Figure 2: a-b Schematic pictures of 40 % PRP density in the mid-periphery. a: 300μm spot size. b: 500μm spot size.

	Characteristics of the excluded eyes (number of eyes)
a	Panoramic photographs were not available (6)
b	Vitrectomy (15),
c	Serious vitreous loss at cataract surgery (3), cataract surgery within 6 months (4)
d	Eyes with more than 50% peripheral anterior synechia (17)
e	Retinal detachment (8), serious anterior chamber hemorrhage (3), serious viterous hemorrhage(15), carotid artery occlusion on the same side (4)

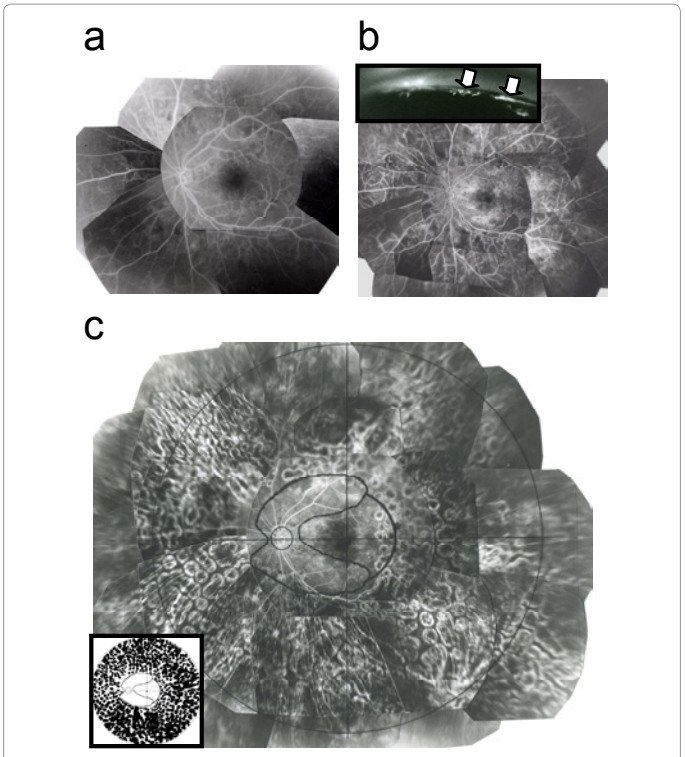
Table1: The content of patients used in this study

Eyes used in this study; 72 eyes of 58 patients (mean age: 58.93±0.94 year) Eyes which fixed the criteria; 31 eyes of 25 patients (mean age: 59.28±9.56 year) Excluded patients in this study; 41 eyes of 33 patients (mean age: 58.67±12.01 year) No significance between included and excluded group in age (T test=0.835)

Among groups I and II, there were 6 eyes that failed to achieve IOP control, and hence, underwent trabeculectomy or glaucoma drainage implantation within six months after the last PRP (Tables 2 and 3). In group I, all patients except Patient 9 were followed-up for between three and six months before the diagnosis of NVG. The pre-NVG IOP was less than 21mmHg in all eyes. The period between the first PRP and the diagnosis of NVG ranged from 7 to 64 months, and the IOP at the diagnosis of NVG ranged from 24 to 41 mmHg (Table 2). There was no statistical significance regarding the level of IOP at the diagnosis of NVG between eyes with successful and unsuccessful PRP treatment (p=0.89468, Table 4a). The density of previous RP before NVG ranged between 2.3% and 37.3%. Ten eyes with successful IOP control in group I received additional PRP within eight months. On the other hand, in the two eyes that failed IOP control, it took more than 12 months to achieve more than 40% PRP density (Figure 3a and 3b, Table 2). Statistical significance was shown in controlling IOP between eyes with a gap between the diagnosis of NVG and accomplishment PRP of less than 12 months and those with more than 12 months (p=0.00053, Table 4b). NVD and NVE were observed in 5 eyes and 11 eyes at the diagnosis of NVG, respectively, but disappeared after PRP treatment in all eyes, except in Patient 6 (Table 2). Patients in group II were followed up for between three to 12 months. Two patients (Patients no 9 and 10) were not followed up by an ophthalmologist before the diagnosis of NVG. Ten eyes of seven patients achieved IOP control



Figures 3: a-b Panoramic FFA of the left eye of Patient 9 with a long duration between the diagnosis of NVG and achievement of PRP (33 months) in group I. He was referred to our hospital because of uncontrolled IOP in the left eye 31 months after the diagnosis of NVG. PRP density was increased by additional PRP from 20.0% (Figure 3a) to 61.1% (figure 3b), but IOP did not change before (41 mmHg) and after additional PRP (38 mmHg). Peripheral anterior synechia was not observed before and
after achieving PRP. Insets of Figures 3a and b indicate schematic images of PRP densities. Defect areas of the mid periphery (colored grey) in Figure 3a and b insets are 1.98% and 0.21%, respectively.



Figures 4: a-c Panoramic FFA of the left eye of Patient 13 with ocular hypertension in group II before (Figure 4a), at the diagnosis of NVG (Figure 4b), and after PRP (Figure 4c).
A slight non-perfusion area (Figure 4a) was observed before the diagnosis of NVG, and IOP fluctuated between 21-23 mmHg. No angle NV or iris rubeosis was observed at this time. Nine months later, the non-perfusion area had increased (Figure 4b) and IOP had increased to 38 mmHg. Faint angle NV was observed by gonioscopy, but FGA clearly demonstrated angle NV (Figure 4b inset, arrows). IOP after PRP (Figure 4c) was 26-27mmHg, although the PRP density was 62.8% (Figure 4c inset).

and nine eyes of nine patients failed to achieve IOP control (Table 3). One patient had preexisting ocular hypertension and two patients had glaucomatous cupping of more than 0.7 before the diagnosis of NVG. All three eyes failed IOP control after PRP (Figure 4). In Patients 6 and 13, IOP increased to a very high level despite slight angle NV, which was difficult to recognize by gonioscopy (Figure 4b). There was statistical significance regarding the success in IOP control (p=0.042929, $\chi 2$ test Table 5a) between eyes with preexisting ocular hypertension or POAG (success: 0 eyes, fail: 3 eyes) and eyes free from preexisting ocular hypertension or POAG (success: 9 eyes, fail: 5 eyes). There was also statistical significance regarding the level of IOP before PRP treatment between eyes with successful and unsuccessful PRP treatment (p=0.01157, Table 3). IOP control after PRP treatment in Group II (Table 3, 52.3%) was worse when compared to that of Group I (Table 2, 83.3%). There was no statistical difference between eyes which achieved PRP within 12 months and eyes which needed more than 12 months to achieve PRP in Group II (p=0.90557, Table 5). However, IOP control failed in the eyes in which PRP took longer than 12 months to complete or NVD persisted (Figure 5). The PRP density in Patient 12 and 15 was more than 40% in the mid-periphery, but the extreme periphery retina could not be coagulated because of small pupils. NVE decreased or disappeared in most of the eyes after PRP, except Patients 1, 9 and 11 (Table 3). All eyes with persistent NVD even after achieving PRP failed to achieve IOP control (Table 3). There was a significant difference regarding the success in IOP control (p=0.017659, $\chi 2$ test Table 5b)

patient no & affected eye	age, sex	IOP at NVG (IOP before NVG) ※1	OH or POAG ※2	NVE & NVD ※3	PRP density at the diagnosis of NVG	Period between the first RP or PRP and NVG※4	Period between NVG and PRP ※5	IOP of 6 months after accomplishment of PRP, ※6
1 R	63, M	25 (15)	-	II→0, -	24.2	20 m	6 m	15, +
L		35 (14)	-	I→0,	19.8	28 m	6 m	15, +
				+→-				
2 R	48, M	26 (14)	-	I→0, -	23.6	9 m	4 m	15, +
L		29 (14)	-	0→0, -	37.3	7 m	4 m	13, +
3 L	65, F	34 (12, 14)	-	I→0, -	16.2	18 m	6 m	12, -
4 R	65, F	28 (18, 18)	-	I→0,	2.3	48 m	3 m	18, +
				+→-				
5 L	70, M	37 (12, 14)	-	I→0, -	19.7	38 m	6 m	12, -
6 L	64, F	36 (14, 13)	-	II→II,	3.9	10 m	4 m	12, -
				+→-				
7 R	49, F	33 (16)	-	I→0,	30.0	7 m	8 m	17, +
				+→-				
L		36 (14)	-	I→0, -	28.4	7 m	8 m	16, +
8 R	76, F	24 (18, 18)	-	II→0,	22.8	16 m	15 m	23, +
				+→-				
9 L	61, M	41 (17, 16)	-	I→0,	20.0	64 m	33 m	38, +, GDI ※7
				+→-				

GDI: glaucoma drainage implant, NVD: optic disc neovascularization, NVG: neovascular glaucoma, PRP: pan-retinal photocoagulation, RP: retinal photocoagulation,

※ 1: Values in ( ) indicate IOP before the occurrence of neovascular glaucoma (NVG). Values in (,) indicate IOP of R & L eyes before the occurrence of NVG.

※ 2: Existence of ocular hypertension (OH) or primary open angle glaucoma (POAG) before occurrence of neovascular glaucoma.

※ 3: Neovascularization elsewhere (NVE) and optic disc neovascularization (NVD) before and after accomplishment of pan-retinal photocoagulation Number of NVE: 0=0, I=1-3, II=4>

※ 4: Period between the first RP or PRP and diagnosis of NVG

※ 5: Period between the diagnosis of neovascular glaucoma and achievement of PRP.

※ 6: +- indicates with or without topical anti-glaucoma medication.

※ 7: Glaucoma drainage surgery was performed for the left eye of Patient 9 within six months after the achievement of PRP

Table 2: Group I: Eyes which received retinal photocoagulation before the occurrence of neovascular glaucoma
Twelve eyes of 9 patients. Grey line indicates the eyes that failed to achieve IOP control (21 or <21 mmHg) after achieving PRP

patient no & affected eye	age, sex	IOP at NVG (IOP before NVG) ※1	OH or POAG ※2	NVE & NVD※ 3	Period between NVG and PRP ※4	IOP of 6 months after accomplishment of PRP, ※5
1 R	44, M	40 (12, 12)	-	II→II, +→+	14 m	28, +
2 R	59, M	34 (16, 16)	-	I→0, +→+	20 m	25, +
3 R	61, F	27 (18)	-	I→0, -	15 m	20, +
L		26 (18)	-	I→0, -	18 m	20, +
4 R	60, M	22 (16, 16)	-	II→0, -	3 m	18, +
5 L	43, M	39 (10,10)	-	II→I, +→-	4 m	17, +
6 R	68, M	42 (23, 28)	+ (0.8, 1.0)	II→I, -	3 m	26, +, TLE ※6
7 R	65, F	28 (14)	-	II→0, -	4 m	18, +
L		28 (14)	-	II→0, +→-	4 m	20, +
8 R	52, M	25 (11)	-	II→I, -	3 m	18, +
L		26 (13)	-	II→0, -	3 m	18, +
9 L	56, F	36 (/) ※2	-	I→I, +→-	2 m	18, +
10 L	55, M	54 (/) ※2	-	II→I, +→+	2 m	26, +, TLE ※6
11 L	62, M	50 (18, 18)	-	I→I, +→-	4 m	30, +, TLE ※6
12 R	69, M	30 (16,15)	-	I→0, -	4 m	26, +, TLE ※6
13 L	71, F	38 (24,23)	+(0.2, 0,2)	0→0, +→+	4 m	27, +
14 L	60, M	27 (18,18)	+(0.8, 0.7)	I→0, -	3 m	23, +
15 L	71, M	27 (17,18)	-	I→0, -	3 m	25, +, TLE ※6
16 L	42, M	23 (10, 10)	-	I→0, +→-	4 m	16, +

NVD: optic disc neovascularization, NVG: neovascular glaucoma, PRP: pan-retinal photocoagulation, TLE: trabeculectomy

※ 1: Values in ( ) indicate IOP before the occurrence of neovascular glaucoma (NVG). Values in (,) indicate IOP of R & L eyes before the occurrence of NVG.

※ 2: Existence of ocular hypertension (OH) or primary open angle glaucoma (POAG) before the occurrence of neovascular glaucoma. () indicate cup/disc ratio in the right and left eyes before the occurrence of NVG. IOPs in Patients 6, 13 and 14 indicate under the topical glaucoma medication.

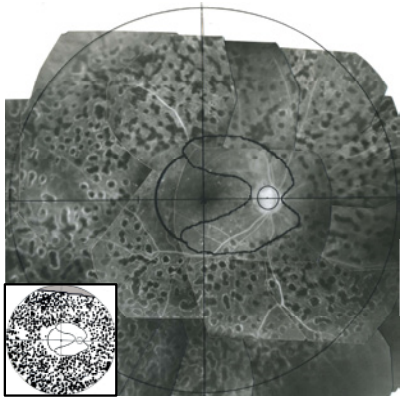
※ 3: 3: Neovascularization elsewhere (NVE) and optic disc neovascularization (NVD) before and after accomplishment of pan-retinal photocoagulation Number of NVE: 0=0, I=1-3, II=4>

※ 4: Period between the diagnosis of neovascular glaucoma and achievement of PRP.

※ 5: +- indicates with or without topical anti-glaucoma medication.

※ 6: Trabeculectomy was performed within six months after achieving PRP

Table 3: Group I I: Eyes which received retinal photocoagulation after the occurrence of neovascular glaucoma
Nineteen eyes of 16 patients. Grey line indicates the eyes that failed to achieve IOP control (≤21 mmHg or below base line) after achieving PRP



Figures 5: Panoramic FFA of the right eye of Patient 2 in group II with a long duration before PRP. PRP was performed according to the protocol, but actually the density was 36.0% (inset). IOP temporally decreased from 34 mmHg to 18 mmHg, but increased again to 25 mmHg. IOP did not return to the normal level despite additional PRP to more than 40%, which was achieved 18 months after the diagnosis of NVG. Note the persistence of optic disc neovascularization, which did not disappear, even after the accomplishment of PRP. The missing area of the panoramic photographs (painted grey) in Figure 5 inset is 4.16%.

Group I			
		eyes	average of IOP
	success ※	10	31.9
	failure ※	2	32.5
p=0.8946 (One-factor ANOVA)			
Group II			
		eyes	average of IOP
	success ※	10	28.0
	failure ※	9	38.0
p=0.0115702 (One-factor ANOVA)			

Table 4a: Influence of elevated IOP level at diagnosis of neovascular glaucoma on the result of IOP control after achieving pan-retinal photocoagulation (PRP).

Group I			
		success ※	fail ※
	12 months>	10	0
	12 months<	0	2
p=0.00053201(χ^2 test)			
Group II			
		success ※	fail ※
	12 months>	8	7
	12 months<	2	2
p=0.90556517(χ^2 test)			

※ Success: less than 21mmHg at six months after achieving PRP.
※ Failure: 21mmHg or more than 21mmHg at six months after achieving PRP.

Table 4b: Comparison of the period between the diagnosis of neovascular glaucoma and achievement of pan-retinal photocoagulation (PRP) between the eyes of successful IOP and those of failed IOP.

between eyes with persistent NVD after PRP treatment (success: no eye, fail: 4 eyes) and eyes with no, or disappeared, NVD after PRP (success: 10 eyes, fail: 5 eyes).

Discussion

A large number of eyes with serious anterior or posterior segment disease, such as anterior chamber or vitreous hemorrhaging or retinal detachment due to proliferative vitreoretinopathy, were excluded (Table 1) because these conditions could have influenced our assessment of the effects of PRP. For example, eye which has received vitrectomy should be excluded because vitrectomy itself causes IOP elevation [11]. Eyes with more than 50% PAS should also be excluded because PAS of more than 50% is believed to cause IOP elevation; however, all eyes used in this study showed less than 25% PAS after achieving PRP. There is no optimal method for evaluating PRP in the treatment of NVG; however, using panoramic photographs of the FFA seems to be a useful method. In this study, we tried to coagulate the retina to more than 40% density (Figure 1e) by using a schematic picture of 40 % PRP distribution in the mid (Figure 2a and 2b) and extreme periphery (Figures 1d, 3b and 4c). PRP density may change during the time course because of the expansion of laser spots in the later period [12]. FFA within 6 months after the completion of PRP may not affect the result of PRP density. All patients in group I with less than 40% PRP density had developed NVG. This indicates that a PRP density less than 40% has no effect in preventing NVG. Prolonged PRP treatment of more than 12 months resulted in worse IOP control in group I (p=0.00053, Table 4b). In the eyes of the failed IOP control which received prolonged PRP treatment of more than 12 months both in group I and II (Patients 8 and 9 in group I, and Patients 1, 2 in group II), irreversible changes in the trabecular meshwork or the Schlemm canal may have occurred because PAS was not observed in those eyes after achieving PRP. Delayed assessment of the PRP burn density might also lead to delays in the accomplishment of PRP, as was seen in Patient 2 (Figure 5), which resulted in IOP control failure. Therefore, achieving a PRP burn density of greater than 50% might be a safe target for the initial treatment of NVG. The success rate of IOP in group II (52.3%) was lower than that of group I (83.3%). This may be because of multifactorial reasons for the failure of IOP control in group II. First, a longer follow-up period and no visit to the ophthalmologist before the diagnosis of NVG (Patients 9 and 10) may be reasons for the delayed start of PRP. In this study, it was impossible to prove the actual onset of NVG because the follow-up period differed among patients. We therefore decided to use the time of NVG diagnosis and achievement of PRP. Second, preexisting POAG or ocular hypertension included in group II and it seemed to be less responsible for the lowering effect of IOP by PRP in these eyes (p=0.04293 Table 5a). A third reason is that group II included patients (Patients 12 and 15) with small pupils. PRP in these eyes might have not covered the non-perfusion area in the extreme periphery, regardless of sufficient PRP in the mid-periphery; therefore, care should be taken when evaluating RP density using only the mid-periphery on a panoramic FFA photograph. The fourth reason is that NVD persisted in four eyes in group II because all eyes with persistent NVD after PRP showed failed IOP control (p=0.01766 Table 5b). In group II, the IOP level of successful eyes before PRP treatment was significantly lower than in unsuccessful eyes (p=0.01157, Table 4a), while there was no significance in group I (p=0.8946, Table 4a). The higher the IOP, the lower the success rate for IOP control in group II may be because of the delayed start of PRP, as mentioned above. The reason for the lack of significance in group I may be that neovascular tissues in the trabecular meshwork did not respond in the same way as those in group II. One possible reason for the reduced response to PRP in group I is that PRP completion might have taken more than 12 months because the period between the first focal RP or PRP and the diagnosis of NVG was only 7-10 months in 5 eyes (Table 2). A temporarily high IOP or angle neovascularization might have been overlooked at the start of the first RP or PRP in these eyes. Therefore, thorough evaluations of the risk of angle neovascularization using FFA [10] at the start of the first PRP might be very important. In addition, unfinished or insufficient PRP causes invisible rubeosis, which can only be visualized by fluorescein gonioangiography [10].

	success ※	fail ※
normal IOP	9	5
OH or POAG	0	3
P=0.042929 (χ^2 test)		

※ Patients 9 and 10 were not included in this table because the IOP before the diagnosis of NVG was not known.

Table 5a: In group II, comparison of the presence of ocular hypertension (OH) or primary
open angle glaucoma (POAG) before the occurrence of neovascular glaucoma (NVG)
between the eyes of successful IOP and those of failed IOP after achieving pan-retinal
photocoagulation (PRP)

	success ※	fail ※
NVD (-)	10	5
NVD (+)	0	4
P=0.017659 (χ^2 test)		

※ Success: less than 21mmHg at six months after achieving PRP.
※ Failure: 21mmHg or more than 21mmHg at six months after achieving PRP.

Table 5b: In group II, persistence of optic disc neovascularization (NVD) before and after PRP.

In summary, from the results of this study, we cannot postulate that all proliferative diabetic retinopathy should be treated at more than 40% PRP density, however, it should be kept in mind that some eyes will develop NVG if the PRP density in the mid-periphery is less than 40%. Although the risk factors for controlling IOP were different between group I and II, care should be taken with these eyes, as listed below: eyes with prolonged PRP treatment of more than 12 months, persistence of NVD after PRP treatment, small pupils, and pre-existing ocular hypertension or POAG. Further investigations are needed to assess whether a PRP burn density of greater than 40% produces acceptable long-term results.

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b. Financial disclosure: none to declare

c. Contribution of authors in each area: Design and conduct of this study, collection, management, analysis, and interpretation of the data (TH); preparation (TH, TO, NA, TY, NI), review (TH, TO).

d. Statement of conformity with author information: IRB of the Japanese Red Cross Medical Centre judged that the methods of this study were appropriate.

e. We appreciate the assistance of Dr. Tatsuo Tsuboi, Green Project Coop, in testing statistical hypotheses.

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