ELSEVIER

A Retrospective Pilot Study of Indocyanine Green Enhanced Diode Laser Photocoagulation for Subfoveal Choroidal Neovascularization Associated with Age-Related Macular Degeneration

Akira Obana,* Yuko Gohto,*
Kazuteru Nishiguchi,* Tokuhiko Miki,* Shinichi Nishi† and Akira Asada†

*Departments of *Ophthalmology; †Anesthesiology,*
Osaka City University Medical School, Osaka, Japan

Purpose: The effectiveness and limitations of indocyanine green (ICG) enhanced diode laser photocoagulation in treating subfoveal choroidal neovascularization (CNV) associated with age-related macular degeneration (AMD) were investigated retrospectively.

Methods: Thirty-eight eyes of 37 patients with subfoveal CNV received ICG enhanced diode laser (wavelength, 805 nm) photocoagulation in our preliminary series. Nineteen eyes had classic CNV and the others had occult CNV, which was well-delineated on ICG angiography. The rate of anatomical success and functional outcomes were investigated. Factors prognostic of a final visual acuity of 0.1 or better were analyzed. The follow-up period ranged from 6 to 51 months (mean ± SD = 26.5 ± 14.4 months).

Results: Occlusion of CNV was achieved in 35 of 38 eyes (92%), and 7 eyes (18%) showed recurrence, which was occluded by retreatment in all but 1 eye. Ten eyes (26.3%) showed improvement of visual acuity; 16 (42.1%) showed no change; and in 12 eyes (31.6%) visual acuity deteriorated. Factors prognostic of a final visual acuity of 0.1 or better were good preoperative visual acuity (Mann–Whitney *U*-test, $P = .0028$), and a relatively short distance between the edge of laser burns and the center of the foveal avascular zone (unpaired *t*-test, $P = .0285$).

Conclusion: Indocyanine green enhanced photocoagulation achieved a higher anatomical success rate but functional outcomes equal to those with argon or krypton laser photocoagulation. A controlled prospective study is necessary to prove the efficacy of this treatment.
Jpn J Ophthalmol 2000;44:668–676

Key Words: Age-related macular degeneration, diode laser, indocyanine green enhanced photocoagulation, neovascular occlusion, subfoveal choroidal neovascularization.

Introduction

Subfoveal choroidal neovascularization (CNV) is a major cause of severe visual acuity loss in age-related macular degeneration (AMD). According to the Macular Photocoagulation Study (MPS) Group report, argon or krypton laser photocoagulation has been effective in the therapy of CNV, but the immediate loss of vision following treatment is a major disadvantage of laser photocoagulation in the case of CNV located in the subfoveal region.[1] On the other hand, photocoagulation of CNV feeder vessels, when they can be detected, allows CNV to be occluded without burning the fovea and preserves visual acuity.[2] However, the detection rate of CNV feeder vessels is still low, even with indocyanine green (ICG) angiography. Surgical removal of subfoveal CNV[3,4] and radiation therapy[5] have been reported recently; however, the effectiveness of these

Received: November 26, 1999
Correspondence and reprint requests to: Akira OBANA, MD, Department of Ophthalmology, Osaka City University Medical School, Asahi-machi 1-4-3, Abeno-ku, Osaka 545-8585, Japan

Jpn J Ophthalmol 44, 668–676 (2000)

Published by Elsevier Science Inc.
0021-5155/00/$–see front matter
PII S0021-5155(00)00274-4

techniques remains unclear. Photodynamic therapy seems ideal to preserve visual acuity, but no photosensitizer has been approved yet for clinical treatment of AMD.[6]

Indocyanine green enhanced diode laser photocoagulation was first used by Puliafito et al[7,8] for the treatment of CNV. The photocoagulation effect of an infrared diode laser (805 nm) is enhanced by intravenous injection of ICG prior to laser irradiation, since the peak absorption wavelength of ICG closely matches the emission wavelength of this laser. Reichel et al[9] applied ICG enhanced photocoagulation to 10 cases with poorly defined subfoveal CNV and achieved preservation of visual acuity in 9 of 10 eyes. They suggested the possibility of milder damage to the sensory retina with this method than with conventional laser photocoagulation. Our basic studies showed that coagulation of CNV using a laser irradiance small enough to preclude sensory retinal damage is simply not possible, because the absorption coefficient of ICG is too low.[10] Nevertheless, our experiments demonstrated that this method still has three advantages over argon, krypton, or dye lasers.[10–12] First, infrared diode laser energy transmits readily through turbid retina as well as through retinal and subretinal hemorrhages. Second, this method induces occlusion of relatively deep choroidal vessels, including CNV feeder vessels which are located underneath the CNV. Finally, although in some advanced cases of exudative AMD there is less melanin pigment in the proliferative retinal pigment epithelium (RPE) that covers the CNV[13,14] and little laser light is absorbed by this less pigmented RPE, the therapy is still effective because ICG becomes a new chromophore and absorbs the infrared laser light.

In the present study, we retrospectively investigated the anatomical and functional outcomes of our preliminary series to determine the capability and limitations of this method. The necessity for a controlled prospective study was evaluated.

Materials and Methods

Patients

We reviewed the records of patients who received ICG enhanced photocoagulation for AMD in Osaka City University Hospital between December 1993 and February 1998. Among these patients, 38 eyes of 37 Japanese patients (23 men, 15 women) satisfied the criteria shown in Table 1. Patient ages ranged from 56 to 89 years (mean $\pm$ SD = 71.8 $\pm$ 8.0 years). There were 20 right eyes and 18 left. Fundus examination using a biomicroscope with a Goldmann contact lens showed exudative changes, such as subretinal and/or retinal hemorrhage, serous sensory retinal detachment, and subretinal deposits in all the patients investigated (Figures 1A, 2A, and 3A). Eyes with other disorders affecting visual acuity were excluded. Fluorescein angiography (FAG) and ICG angiography (Topcon IMAGEnet H-1024 Digital Imaging System; Topcon, Tokyo) were performed before treatment. Classification of CNV as “classic” or “occult” and documentation of the location of CNV were in accordance with MPS criteria.[15] Fluorescein angiography clearly showed CNV in 19 eyes (50%) (classic CNV) (Figure 1B), but failed to do so in 19 (50%) (occult CNV) (Figure 2B). Fifteen of 19 occult CNVs had fibrovascular pigment epithelial detachment, two showed late-phase choroidal fluorescein leakage of an undetermined source and two had blocked fluorescence due to a thick hemorrhage. ICG angiography delineated the CNV in these 19 occult cases (Figures 2C and 3B). Indocyanine green angiography defined CNV in 35 eyes (92%) in total (Figure 1C). The size of CNV was measured using the MPS ring software in the Topcon IMAGEnet System.

ICG Administration

Indocyanine green was infused continuously in order to achieve a steady plasma concentration during laser irradiation. Intravenous injection of 5 mL of 5 mg/mL ICG solution was administrated as a bolus, followed by continuous infusion of ICG at 10 mg/min for 5 minutes using an infusion pump. The plasma ICG concentration was monitored during infusion using a finger-tip probe connected to an ICG clearance meter (RK 1000; Sumitomo Denko, Tokyo). Because optical density (OD) data from the ICG clearance meter correlated significantly (R =

Table 1. Principal Eligibility Criteria

Age: ≥ 50 years
Patients received indocyanine green enhanced laser photocoagulation at Osaka City University Hospital between December 1993 and February 1998.
Having:
Subfoveal choroidal neovascularization (classic type) well-defined by fluorescein angiography taken at least 1 week before treatment.
Subfoveal choroidal neovascularization (occult type) poorly defined by fluorescein angiography, but well-defined by indocyanine green angiography taken at least 1 week before treatment.
No other eye disease that could compromise visual acuity.
Follow-up examinations for more than 6 months.
Signed informed consent.

Jpn J Ophthalmol
Vol 44: 668–676, 2000

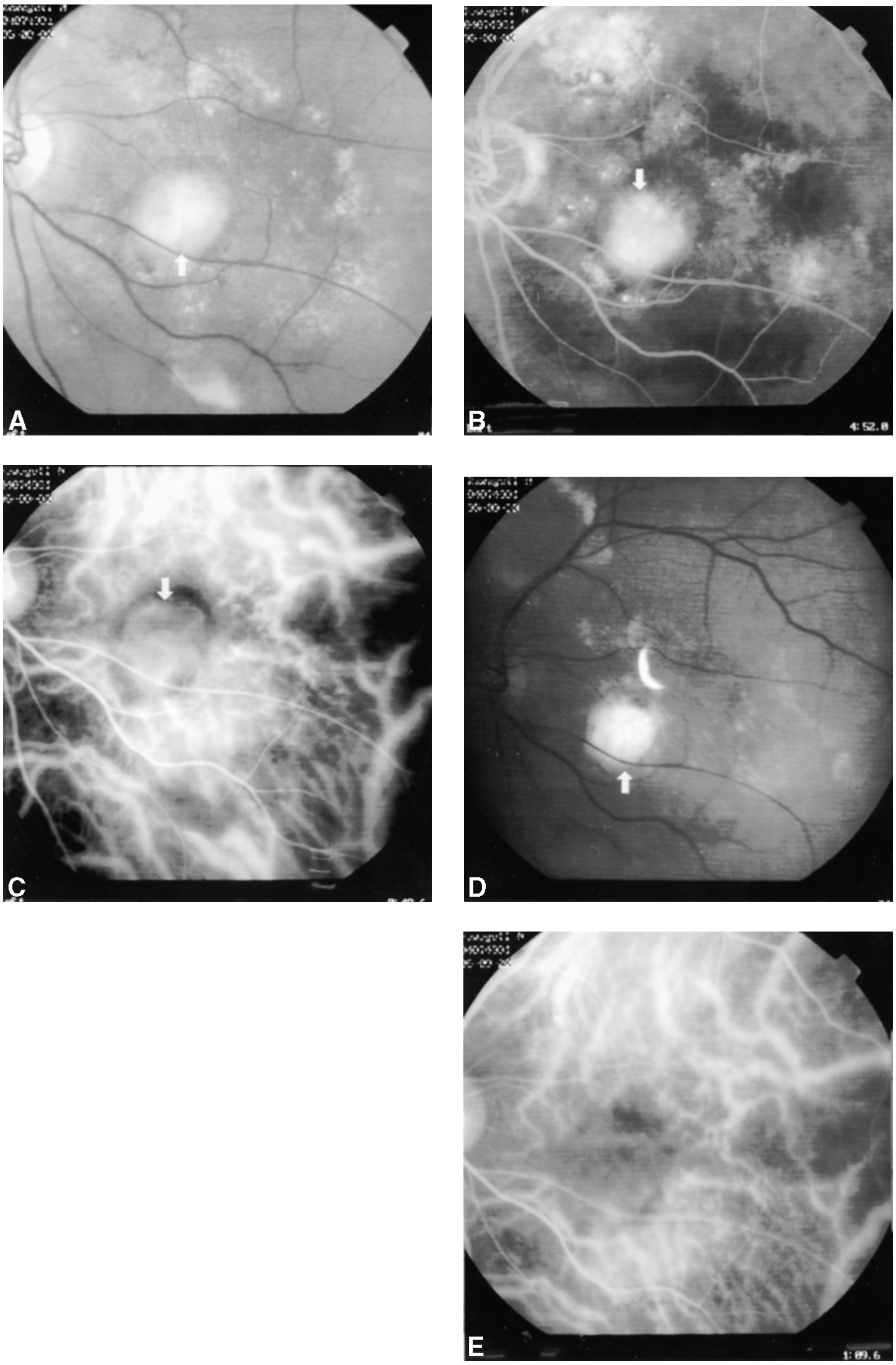

Figure 1. Left eye of 75-year-old man (eye no.14 in Table 2). Pretreatment visual acuity was 0.01. (**A**) Pretreatment red-free fundus photograph. Subretinal proliferative tissue with serous retinal detachment and exudates is noted (arrow). (**B**) Fluorescein angiogram obtained 5 minutes after dye injection shows subfoveal neovascularization (arrow). (**C**) Indocyanine green angiogram obtained 48 seconds after dye injection shows choroidal new vessels (arrow). (**D**) Red-free fundus photograph 2 weeks after treatment. Fibrous change of proliferative tissue (arrow) progressed and serous retinal detachment was resolved. (**E**) Indocyanine green angiogram 2 weeks after treatment revealed no neovascular net. Postoperative visual acuity was 0.01.

0.957) with the concentration obtained by high-performance liquid chromatography (HPLC), and because both values conformed to the formula: HPLC $= 3.56 \times$ OD $- 0.411$, the ICG concentration in each patient was calculated using this formula.[16] During infusion of ICG, the ICG concentration increased rapidly immediately after injection and reached a plateau approximately 3 minutes later. A steady state was maintained for approximately 5 minutes. The mean concentration for all patients investigated over the 5 minutes of this steady state was 11.0 ± 2.4 μg/mL.

ICG Enhanced Photocoagulation and Follow-up Examination

Diode laser irradiation (DC-3000, wavelength = 805 nm; Nidek, Gamagori) was begun when the ICG

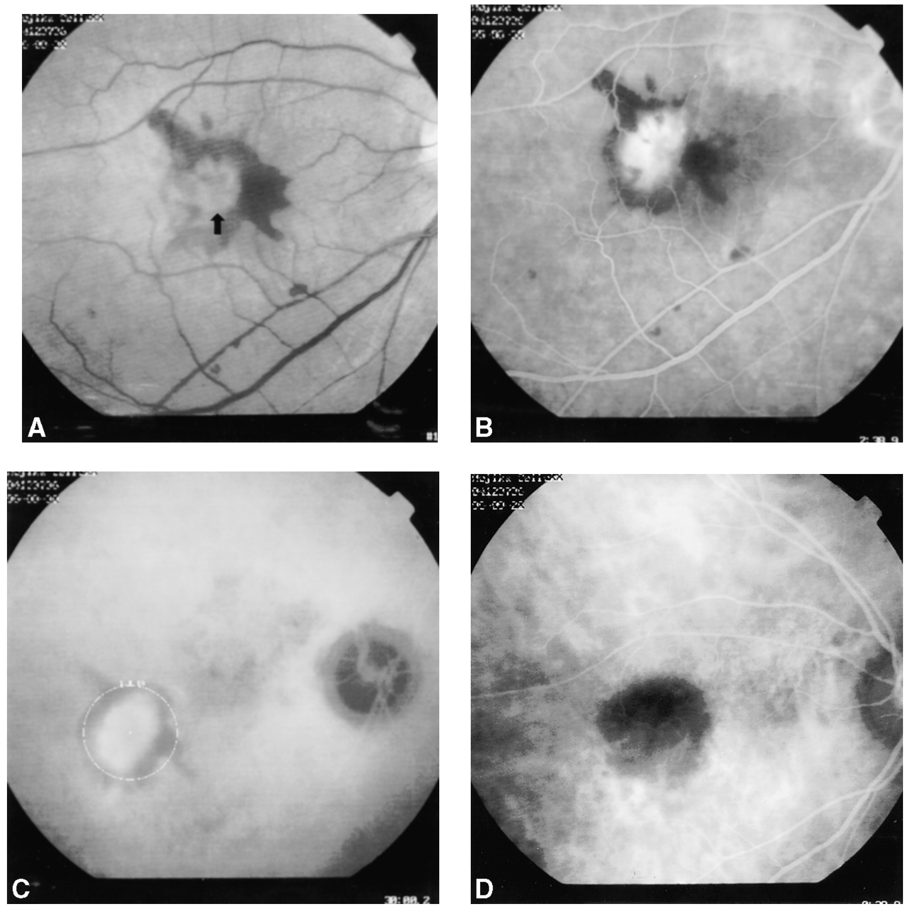

Figure 2. Right eye of 68-year-old man (eye no. 22 in Table 2). Pretreatment visual acuity was 0.2. (**A**) Pretreatment red-free fundus photograph. Subretinal proliferative tissue with serous retinal detachment and subretinal hemorrhage is noted (arrow). (**B**) Fluorescein angiogram obtained 2.5 minutes after dye injection shows subretinal blood obscuring boundaries of subfoveal neovascular tissue. (**C**) Indocyanine green angiogram obtained 30 minutes after dye injection shows subfoveal choroidal neovascularization. Size of neovascularization was smaller than the one disc diameter of the Macular Photocoagulation Study ring (circle). (**D**) Indocyanine green angiogram 2 weeks after treatment shows hypofluorescence of treated lesion. Visual acuity improved to 0.4 in 6 months.

plasma concentration reached a steady-state level. The exposure time was 0.4 or 0.5 seconds and the spot size was between 200 and 300 μm. The entire CNV was irradiated by laser, and the exposure power was gradually increased from 250 mW up to the point at which a faint grayish change of the deep retina (usually $<$650 mW) was observed. Immediately after treatment, ICG angiography was conducted without further ICG administration, and the photocoagulation effect was confirmed when hypofluorescence of the treated area was observed (Figure 3C). The shortest distance between the edge of hypofluorescence on ICG angiography, representing the edge of the laser burns, and the center of the foveal avascular zone was measured using line measurement software in the Topcon IMAGEnet System. The location of the center of the foveal avascular zone was determined from the fluorescein angiogram, which was overlayed onto the ICG angiogram.

Fluorescein angiography and ICG angiography were performed within 4 weeks of treatment (Figures 1E and 2D), and if persistence of the CNV was confirmed, treatment was repeated until complete closure was achieved. After that, fundus examination was performed periodically and FAG and ICG angiography were repeated as necessary. Choroidal neovascularization that developed more than 4 weeks after treatment was considered recurrent, and retreatment was performed. The follow-up period, defined as extending from the time that treatment achieved CNV closure until the time of final examination, ranged from 6 to 51 months (mean $\pm$ SD, 26.5 $\pm$ 14.4 months). The experimental nature of the treatment was fully explained to the patients in accordance with the standards of the Ethics Committee of Osaka City University Medical School and the Declaration of Helsinki (1964), and informed consent was obtained.

Main Outcome Evaluations and Statistical Analysis

The occlusion rate of the CNV and changes in visual acuity were evaluated. Visual acuity was measured by a lantern-type visual acuity test chart and recorded with decimal notation. Decimal visual acu-

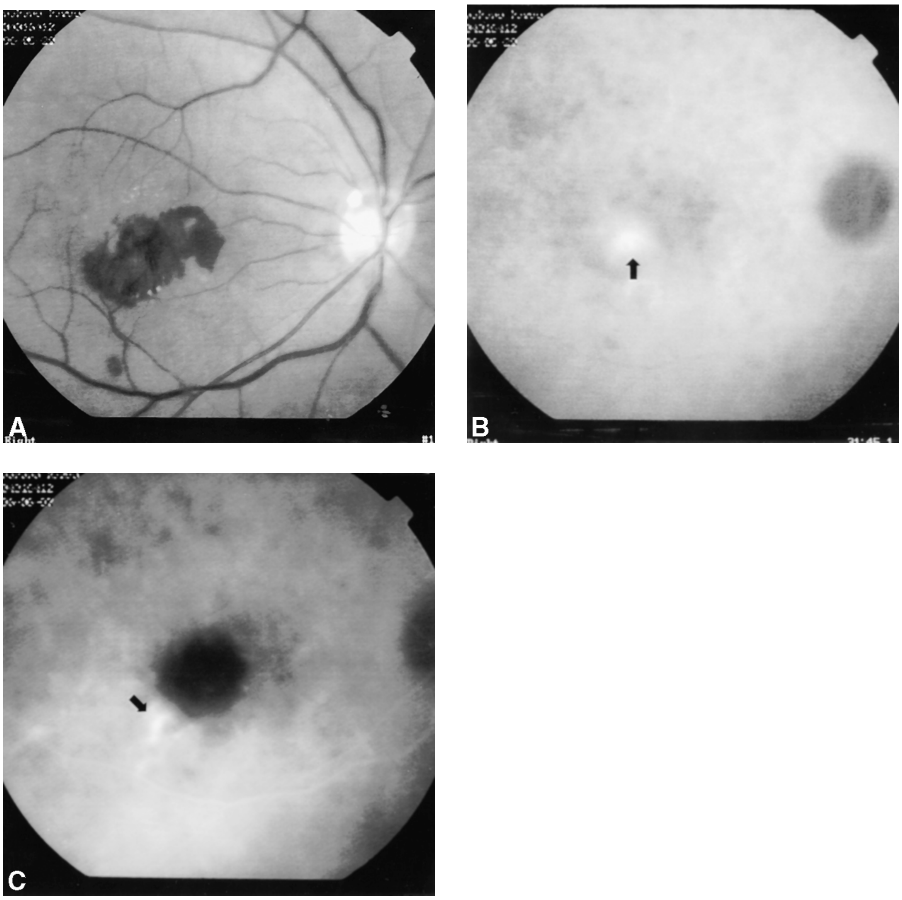

Figure 3. Right eye of 84-year-old man (eye no. 32 in Table 2). Pretreatment visual acuity was 0.05. (**A**) Pretreatment red-free fundus photograph. Subretinal hemorrhage is noted. (**B**) Pretreatment indocyanine green angiogram obtained 31 minutes after dye injection shows hyperfluorescence of choroidal neovascularization (arrow). (**C**) Indocyanine green (ICG) angiogram obtained immediately after treatment shows treated lesion with hypofluorescence. Bright fluorescence at inferotemporal margin of treated area (arrow) represents large choroidal vessels damaged by photocoagulation. Angiogram was taken without further injection of ICG following ICG enhanced photocoagulation. Visual acuity improved to 0.09 in 9 months.

ities were converted to fractional values in order to compare with data in the MPS1 and other reports.[17,18] Change in lines was determined according to the line classification of the Snellen chart. Factors prognostic of postoperative visual acuity of 0.1 or better were evaluated using Fisher's exact probability test, an unpaired *t*-test or the Mann–Whitney *U*-test. The following factors were analyzed: patient age, follow-up period, type of CNV (classic or occult), size of CNV (one disc area or smaller vs. more than one disc area), preoperative visual acuity, the shortest distance between the edge of laser burns and the center of the foveal avascular zone, and number of treatments (once vs. twice or more).

Results

Patient age, sex, type and size of CNV, anatomic outcome, and preoperative and final visual acuity are summarized in Table 2.

Anatomical Outcome

Twenty-four eyes received treatment once; 10, twice; 3, three times; and 1, four times. The mean number of treatments was 1.5. Occlusion of CNV was confirmed in 18 of 19 eyes (94.7%) with classic CNV, and in 17 of 19 eyes (89.5%) with occult CNV, and in total in 35 of 38 eyes (92%) by FAG and ICG angiography conducted within 4 weeks of treatment. Exudative changes were resolved in these 35 eyes. The difference in occlusion rate between eyes with classic CNV and occult CNV was not significant (P = .615, Fisher's exact probability test). In 3 eyes, CNV occlusion was not achieved and residual CNV grew after treatment resulting in disciform scar formation. Insufficient irradiation intensity most likely was the reason occlusion failed in these eyes. No severe complications occurred during treatment except in 2 eyes that suffered mild subretinal hemorrhage, which was absorbed in a few weeks.

Recurrence of CNV occurred in 6 of 18 eyes (33.3%) with classic CNV, and in 1 of 17 eyes (5.9%) with occult CNV, and in 7 of 35 eyes (20%) in total, although in 1 with classic CNV, recurrent CNV could not be seen due to a vitreous hemorrhage that developed 7 months after successful treatment. The recurrence rate between eyes with classic and occult CNV was not significant (P = .088, Fisher's exact

Table 2. Anatomic and Visual Outcomes of Indocyanine Green Enhanced Photocoagulation for Subfoveal Choroidal Neovascularization

Eye No.	Age	Sex	Eye	FAG	Size of CNV	Occlusion of CNV	Recurrence	Initial VA	Final VA
1	70	F	R	Classic	1	Y	N	0.6	0.2
2	85	M	L	Classic	2	Y	N	0.3	0.06
3	59	M	L	Classic	1	Y	Y	0.2	0.05
4	73	M	L	Classic	1	Y	N	0.2	0.2
5	72	M	R	Classic	1	Y	N	0.2	0.5
6	66	F	R	Classic	1	Y	Y	0.2	0.02
7	68	M	R	Classic	3	Y	N	0.08	0.03
8	88	F	L	Classic	3	Y	N	0.06	0.06
9	77	F	R	Classic	2	Y	Y	0.04	0.03
10	85	M	R	Classic	2	Y	Y	0.03	0.08
11	89	M	R	Classic	3	Y	N	0.03	0.02
12	79	M	L	Classic	4	N	N	0.02	cf
13	75	F	R	Classic	1	Y	Y	0.02	hm
14	75	M	L	Classic	2	Y	N	0.01	0.01
15	72	M	R	Classic	2	Y	Y	0.01	0.01
16	68	M	L	Classic	2	Y	N	0.01	0.02
17	66	F	L	Classic	2	Y	N	cf	0.06
18	58	M	L	Classic	3	Y	N	cf	cf
19	70	M	R	Classic	3	Y	N	cf	cf
20	70	F	L	FPED	1	N	N	0.6	0.05
21	60	F	L	FPED	1	Y	N	0.2	0.02
22	68	M	R	FPED	1	Y	N	0.2	0.4
23	76	M	L	FPED	1	Y	Y	0.2	0.4
24	69	M	R	FPED	2	Y	N	0.2	0.1
25	73	F	L	FPED	1	Y	N	0.1	0.01
26	81	M	L	FPED	2	Y	N	0.1	0.1
27	73	M	L	FPED	2	Y	N	0.1	0.2
28	63	F	L	FPED	2	Y	N	0.1	0.09
29	72	M	R	FPED	3	Y	N	0.1	0.06
30	56	F	R	FPED	1	Y	N	0.06	0.02
31	84	M	R	FPED	1	Y	N	0.05	0.09
32	64	M	R	FPED	2	Y	N	0.05	0.6
33	76	M	L	FPED	2	N	N	0.04	0.01
34	71	F	R	FPED	4	Y	N	0.03	0.03
35	80	F	R	FRPE	2	Y	N	0.06	0.05
36	65	M	R	FRPE	4	Y	N	0.02	0.09
37	65	F	R	blood	1	Y	N	0.1	0.6
38	69	F	L	blood	2	Y	N	0.02	0.02

FAG: Fluorescein angiography; CNV: Choroidal neovascularization; VA: Visual acuity; cf: counting fingers; hm: hand movements; FPED: fibrovascular pigment epithelial detachment; FRPE: late-phase fluorescein leakage of undetermined source; blood: blood that is thick enough to obscure the choroidal fluorescence.

probability test). In 5 eyes with classic CNV, recurrence was found at 2, 2, 6, 6, and 10 months after treatment, respectively. In 2 eyes, recurrence occurred in a different area than in the initial classic CNV, and in 3 the recurrence was at the margin of the initial classic CNV. One eye with occult CNV had recurrence at the margin of the treated lesion at 36 months after treatment. Recurrent CNV was occluded by retreatment in all eyes except the eye with the vitreous hemorrhage.

Functional Outcomes

Preoperative visual acuity ranged from 0.6 to counting fingers (geometric mean = 0.058). Postoperative visual acuity at the final follow-up examination ranged from 0.6 to hand motion (geometric mean = 0.042). Acuity improved in 3 eyes (15.8%) with classic CNV by more than two lines of Snellen chart classification, remained the same in 10 (52.6%), and deteriorated by more than two lines in 6 (31.6%). The average change of visual acuity in eyes with classic CNV was a decrease of 1.1 lines from baseline. Acuity improved in 7 eyes (36.8%) with occult CNV, remained the same in 6 (31.6%), and deteriorated in 6 (31.6%). The average change in eyes with occult CNV was an increase of 0.2 lines from baseline. There was no significant difference in change of visual acuity between eyes with classic and occult CNV (P = .273, chi-square test).

Acuity declined in 7 of 11 eyes with a preoperative visual acuity of 0.2 or better; the mean at the final visit was a 3.5 lines decrease. In contrast, acuity declined in 5 of 27 eyes with a preoperative acuity of 0.1 or worse, and the acuity of these eyes improved a mean of 0.8 lines. The ratio of eyes showing visual acuity loss tended to be higher among those with a preoperative acuity of 0.2 or better than in those with a preoperative acuity of 0.1 or worse (P = .089, Fisher's exact probability test).

A statistical analysis of factors predicting postoperative visual acuity is summarized in Table 3. Ten eyes had postoperative visual acuity of 0.1 or better and 28 eyes, that of worse than 0.1. Significant factors predicting a visual acuity of 0.1 or better were: good preoperative visual acuity, and having a relatively short distance between the edge of laser burns and the center of the foveal avascular zone.

Discussion

The occlusion rate of classic CNV was 94.7%, and that of occult CNV 89.5%. The MPS studies[1] found that the occlusion rate of subfoveal classic CNV treated by krypton laser was 76%. The favorable anatomic result in the present study may be attributed to the three advantages of ICG enhanced photocoagulation, as described in the introduction. Another advantage of this method is that ICG angiography could be conducted immediately after photocoagulation without further injection of ICG as shown in Figure 3. We could confirm the absence of CNV by observing the hypofluorescence of the treated area. If persistent hyperfluorescence was noted, we could add photocoagulation immediately. The recurrence rate of classic CNV was 33%, and that of occult CNV was 6% in the present follow-up period (mean ± SD = 26.5 ± 14.4 months). In the MPS report,[1] recurrence occurred in 27% of classic CNV within 2 years, almost the same percentage as in the present study. There are no reported data on the recurrence rate for occult CNV; however, the rate we found is encouraging.

The MPS group[1] reported that after 24-month follow-up, visual acuity decreased in 68% of the treated eyes, and the average decrease was 3.0 lines from baseline. In contrast, visual acuity decreased in 82% of the untreated eyes (natural course), and the average decrease was 4.4 lines. In the present study, the visual acuity of the eyes that met the MPS eligibility criteria, ie, classic CNV with visual acuity ranging from 20/40 to 20/320, decreased in 4 of 7 eyes (57%), and the average decrease was 2.9 lines. These results indicated that, in the present study, functional outcomes for eyes with classic CNV were almost the same as those treated with krypton laser. We suppose that the damage to the retinal pigment epithelial cells and choroid by ICG enhanced photocoagulation induces secondary damage to the neurosensory retina and functional disturbance at the treated lesion.

Bressler et al[17] and Soubrane et al[18] reported that 70% or 56% of eyes with occult CNV lost more than three lines, respectively, in the follow-up time of more than 2 years in the natural course of the disease. No valid data have been reported on visual outcomes of laser treatment in eyes with occult CNV involving the foveal center, but the present results compare favorably with those in other cases as disease progressed.

We found that the factors prognostic of visual acuity of 0.1 or better were a relatively short distance between the edge of the laser burns and the center of the foveal avascular zone and good preoperative visual acuity. The mean of the shortest distance between the edge of laser burns and the center of the foveal avascular zone in eyes with a final visual acuity of 0.1 or better was 490 μm. Yuzawa et al[19] reported that treatment of lesions no more than 500 μm from the foveal center using an argon dye laser allowed recovery of visual acuity to 0.1 or better. Therefore, it is suggested that good visual acuity may be achieved if the integrity of the sensory retina remains at least in some parts within 500 μm from the center of the foveal avascular zone. However, the exact distance to preserve good postoperative visual acuity in case of ICG enhanced photocoagulation should be investigated further. Good preoperative visual acuity was shown as another factor prognostic of a favorable visual outcome. This is because severely damaged retina with poor preoperative visual acuity could not be repaired. However, the proportion of eyes showing visual acuity loss was higher among those with a preoperative acuity of 0.2 or better than in those with a preoperative acuity of 0.1or worse. Therefore, ICG enhanced photocoagulation is indicated for eyes with a preoperative visual acuity of <0.2.

Our preliminary study measuring ICG concentration showed that the ICG concentration increased

Table 3. Factors Prognostic of Visual Acuity After Indocyanine Green Enhanced Photocoagulation of Subfoveal Choroidal Neovascularization

Factor	Final Visual Acuity		P
	20/200 or Better	Worse than 20/200	
Age (yrs) mean ± SD	71.1 ± 5.1	72.1 ± 9.1	.8034*
Follow-up period (months)	29.4	25.4	.4661†
Type of CNV‡			
Classic	3	16	.2691§
Occult	7	12	
Size of CNV‡			
≤1 disc area	6	8	.1269§
>1 disc area	4	20	
Preoperative visual acuity (mean)	20/45	20/80	.0028*
Smallest distance between edge of laser burns and center of FAZ (mm) mean ± SD	0.49 ± 0.23	0.78 ± 0.38	.0285†
Number of treatments‡			
Once	9	15	.0594§
More than twice	1	13	

CNV: Choroidal neovascularization, FAZ: foveal avascular zone.
*Mann–Whitney *U*-test.
†Unpaired *t*-test.
‡Values are number of eyes.
§Fisher's exact probability test.

immediately after the bolus injection and then decreased rapidly.[10] The first half-life time was approximately 4 minutes. In addition, the inter-individual differences in ICG concentration were rather wide. Therefore, we concluded that the variance in ICG concentration after bolus injection resulted in disparate enhancement of laser photocoagulation. However, the continuous infusion of ICG maintained a steady plasma concentration for approximately 5 minutes, which was considered sufficient for laser treatment. The total dose of ICG used was 75 mg per person, which we considered safe based on our experience with ICG angiography.[20]

Indocyanine green angiographic feaures of CNV were classified into several types[21]; for example, some CNV showed bright fluorescence by late ICG dye leakage, and others showed weak fluorescence. There may be different enhancement effects among these various ICG angiographic features. The enhancement effect for each angiographic feature has yet to be determined.

The present study was retrospective and no controls were used. However, this preliminary series of 38 eyes gave some idea of potential benefits and limitations. The procedure clearly can achieve a higher CNV occlusion rate than conventional argon or krypton lasers; however, it has a limitation in functional results that are equal to those with conventional modalities in lesions of predominantly classic CNV. Eyes with a preoperative visual acuity of <0.2 and in which the distance between the laser burns and center of the foveal avascular zone is relatively small appear to be candidates for this treatment. A controlled prospective study is necessary to prove the efficacy of ICG enhanced photocoagulation for these candidates.

Presented in part at The Second International Symposium on Indocyanine Green Angiography at Nara, Japan, April 7,1995, and at The Annual Meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, May 15, 1995, and at The 5th International Congress of Laser Technology in Ophthalmology, Lugano, Switzerland, June 28, 1996.

This study was supported by Grant-in-Aid for Scientific Research C2 of the Ministry of Education, Science, Sports and Culture, Japan (No. 09671812).

References

1. Macular Photocoagulation Study Group. Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. Results of a randomized clinical trial. Arch Ophthalmol 1990;108:816–24.
2. Shiraga F, Ojima Y, Matsuo T, Takasu I, Matsuo N. Feeder vessel photocoagulation of subfoveal choroidal neovascularization secondary to age-related macular degeneration. Ophthalmology 1998;105:662–9.
3. Thomas MA, Grand G, Williams DF, et al. Surgical management of subfoveal choroidal neovascularization. Ophthalmology 1992;99:952–68.
4. Gass JDM. Biomicroscopic and histopathologic considerations regarding the feasibility of surgical excision of subfoveal neovascular membranes. Am J Ophthalmol 1994;118:285–98.

5. Chakravarthy U, Houston RF, Archer DB. Treatment of age-related subfoveal neovascular membranes by teletherapy. Br J Ophthalmol 1993;77:265–73.
6. Treatment of Age-related Macular Degeneration With Photodynamic Therapy Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin. One-year results of 2 randomized clinical trials-TAP report 1. Arch Ophthalmol 1999; 117:1329–45.
7. Puliafito CA, Destro M, To K, Dobi E. Dye-enhanced photocoagulation of choroidal neovascularization. Invest Ophthalmol Vis Sci 1988;29(Suppl):414.
8. Puliafito CA, Guyer DR, Mones JM, Weaver Y. Indocyanine-green digital angiography and dye-enhanced diode laser photocoagulation of choroidal neovascularization. Invest Ophthalmol Vis Sci 1991;32(Suppl):712.
9. Reichel E, Puliafito CA, Duker JS, Guyer DR. Indocyanine green dye-enhanced diode laser photocoagulation of poorly defined subfoveal choroidal neovascularization. Ophthalmic Surg 1994;25:195–201.
10. Obana A, Matsumoto M, Miki T, et al. Quantification of indocyanine-green enhancement of diode laser photocoagulation. Acta Soc Ophthalmol Jpn 1993;97:581–6.
11. Suh J-H, Miki T, Obana A, et al. Effects of indocyanine green dye enhanced diode laser photocoagulation in non-pigmented rabbit eyes. Osaka City Med J 1991;37:89–106.
12. Matsumoto M, Miki T, Obana A, et al. Choroidal damage in dye-enhanced photocoagulation. Lasers Light Ophthalmol 1993;5:157–65.
13. Kornzweig AL. Aging of the retinal pigment epithelium In: Zinn KM, Marmor MF, eds. The retinal pigment epithelium. Cambridge: Harvard University Press, 1979:478–95.
14. Morris DA, Henkind P. Pathological responses of the human retinal pigment epithelium. In: Zinn KM, Marmor MF, eds. The retinal pigment epithelium. Cambridge: Harvard University Press, 1979:247–66.
15. Macular Photocoagulation Study Group. Subfoveal neovascular lesions in age-related macular degeneration: guidelines for evaluation and treatment. Arch Ophthalmol 1991; 109: 1242–58.
16. Nishi S, Asada A, Abe J, Fujimori M. Usefulness of ICG kinetics using ICG clearance meter in ICU. ICU CCU 1992;16:1197–203.
17. Bressler NM, Frost LA, Bressler S, et al. Natural course of poorly defined choroidal neovascularization associated with macular degeneration. Arch Ophthalmol 1988;106:1537–42.
18. Soubrane G, Coscas G, Francais C, Koenig F. Occult subretinal new vessels in age-related macular degeneration. Natural history and early laser treatment. Ophthalmology 1990;97:649–57.
19. Yuzawa M, Tamakoshi A, Ueda M, Kawakubo H, Nakajima M. Factors influencing visual acuity after photocoagulation for subfoveal choroidal neovascularization of exudative age-related macular degeneration. Ophthalmology 1996;103: 2037–41.
20. Obana A, Miki T, Hayashi K, et al. Survey of complications of indocyanine green angiography in Japan. Am J Ophthalmol 1994;118:749–53.
21. Obana A, Gohto Y, Matsumoto M, Miki T, Nishiguti K. Indocyanine green angiographic features prognostic of visual outcome in the natural course of patients with age related macular degeneration. Br J Ophthalmol 1999;83:429–37.