Journal of Korean Medical Science
Vol. 8, No. 6, 420-430 December 1993

Histopathologic and Ultrastructural Findings of Photocoagulation Lesions Produced by Transpupillary Diode Laser in the Rabbit Retina

Ho Kyun Cho, M.D., Yong Wook Park, M.D.*,
Young Jae Kim, M.D., Kyung Hwan Shyn, M.D.

Department of Ophthalmology and Pathology Collage of Medicine Chung Ang University, Seoul, Korea*

Transpupillary retinal photocoagulations were performed on ten eyes of five pigmented rabbits using a diode laser (Nidek Co., LTD, Aichi, Japan) emitting infrared radiation at 800 nm wavelength. A histological and an ultrastructural study on the treated eyes were done at 1, 3, 5, and 7 days after retinal photocoagulations. The purpose of this study was to observe the sequential changes in the retina and the choroid following transpupillary diode laser retinal photocoagulations at the parameters of laser power which produced a grayish white retinal discoloration with distinct white center. It seemed that the lesion was grade 3 retinal photocoagulation by Tso et al's classification. It appeared that the parameters necessary to produce grade 3 photocoagulation lesions were 160 mW power, and 0.2 second duration at 200 um size. In general, with an agreement to other reports, histologic study of the diode laser lesions showed that the outer retina was damaged more severely than the inner retina. However, on day 1 after laser treatment, the alterations were more profound in the inner retina than in the outer retina and an occasional swelling of the axons in the nerve fiber layer was observed on the ultrastructural study. The results observed have not been found in other previous studies and suggest that the inner retina might be injured directly by 800 nm wavelength diode laser radiations. Thus we could conclude that 800 nm wavelength diode radiation might be absorbed by melanin pigment and also by other chromophores contained in inner retinal tissues. Further studies must follow to verify the laser-tissue interactions in diode laser retinal photocoagulations.

Key Words: *diode laser, histopathologic, photocoagulation lesion, rabbit retina, ultrastructural*

INTRODUCTION

The use of ophthalmic laser radiation in the treatment of some intraocular diseases is well established. Since the clinical application of optical radiation treating eye problems by photocoagulation using solar radiation by G. Meyer-Schwickerath in 1946, several kinds of medical laser systems have been invented. One of them, a semiconductor diode laser system is a recently developed device for retinal photocoagulation. It has been proved by several investigators that transpupillary diode laser photocoagulations were effective in inducing chorioretinal adhesions in experimental models (Duker, 1989; Smiddy, 1992).

The goal of retinal photocoagulations is to pro-

Address for correspondence: *Ho Kyun Cho, Department of Ophthalmology, Chung-Ang University Hospital, 82-1, Pil-Dong 2-Ga, Chung-Gu,Seoul 100-272 Korea (phone: 260-2180)*

This paper was supported by the NON DIRECTED RESEARCH FUND, Korea Research Foundation, 1992.

duce chorioretinal adhesion and to destroy intraocular abnormal tissue.The usual laser sources for retinal photocoagulations are continuous wave ion lasers such as argon blue-green (488- 514 nm) and krypton (647 nm). A solid state diode laser emitting at 808 to 817 nm was used for endophotocoagulations of the rabbit retina by Puliafito et al. in 1987 (Puliafito et al., 1987). Since Puliafito's experimental study several reports have presented favorable results from using diode lasers to treat various ocular disorders (McHugh et al., 1989; Brancato et al., 1990). The clinico-pathological study results with the diode laser system were similar to those produced by argon laser (Noyori et al., 1990). In addition to its clinical benefit the diode laser has several advantages compared to the argon laser system such as; compact sized machine, low price, long durability, and ease of use (Balles MW and Puliafito CA, 1990).

The commercio-clinical benefits of the diode laser systems have expended its uses in the treatment of various ocular disorders since Brancato's clinical application of transpupillary diode laser retinal photocoagulations operating from a Slit-lamp microscope (Brancato et al., 1988). But ocular pain during diode laser photocoagulations limits its use in the panretinal photocoagulation. One clinical study reported a more frequent occurrence of ocular pain in patients when treating with relatively long wavelength krypton laser (647 nm) compared with argon laser photocoagulation (514 nm) (Schlenburg et al., 1979). It may be related with ciliary nerve damage which was observed with high power diode laser irradiation in animal study (Wallow et al., 1991). Theoretically the longer wavelength enables deeper penetration at the retina and the choroid.

Several experimental studies using diode laser retinal photocoagulations has been performed, but those were focused on observing the changes of the outer retina. And also an information about the changes of the inner retina at the usual laser power setting for clinical use is lacking. The purpose of this experimental study is to observe the sequential changes of the retina, choroid, and sclera following transpupillary diode laser retinal photocoagulations at the parameters producing a grayish white retinal discoloration with distinct white center.

MATERIALS AND METHODS

Laser system

A diode laser photocoagulator (DC-3000, Nidek Co., LTD., Aichi, Japan) connected to a Topcon slit-lamp was used in this study. The laser system emits laser beam at 800 nm wavelenth. A 3-mirror Goldman contact lens was used to obtain clear retinal focus.

Transpupillary retinal photocoagulation

Ten eyes of five pigmented rabbits weighing 1.5 to 2.0 Kg were used. The pupils were dilated with 10% phenylephrine hydrochloride. The rabbits were anesthetized with an intramuscular injection of ketamine (60mg/ Kg body weight). The clinical classification of the retinal photocoagulation lesions was based on clinicopathologic findings proposed by Tso et al. (Tso et al., 1977). Lesions consisting of a grayish white retinal discoloration with distinct white center were classified as intensity grade 3 (Fig. 1). In a preliminary trial we were able to induce retinal photocoagulations of grade 3 intensity with 160 mW power, and 0.2 second exposure time at 200 um beam diameter in the retina of pigmented rabbits.

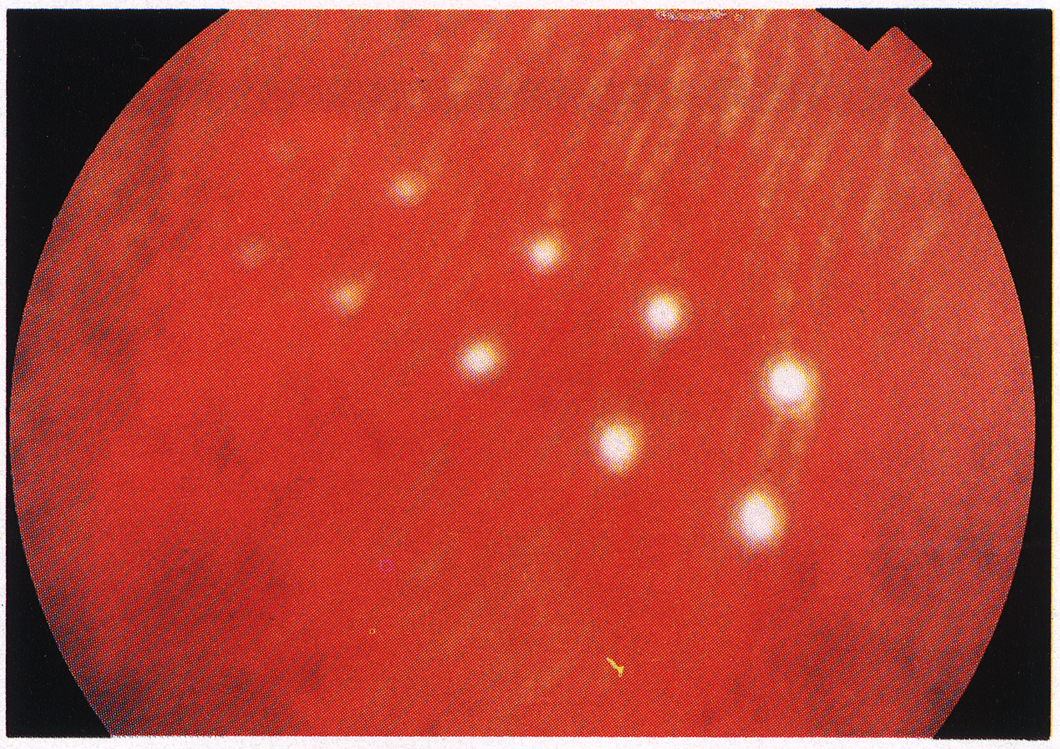

Fig. 1. Fundus photograph: transpupillary diode laser retinal photocoagulation 20 minutes after the irradiation. Power setting of 160-mW power and 0.2-second exposure time at 200 um beam size. Grade 3 lesions showing a grayish white retinal discoloration with distinct white center. An oblique entrance of the laser beam produced less intense laser burns as shown in the left six lesions. The right four photocoagulated lesions were prepared for histologic examination.

The transpupillary diode laser retinal photocoagulations were made in the rabbit retina at the present parameters. The retinal photocoagulations

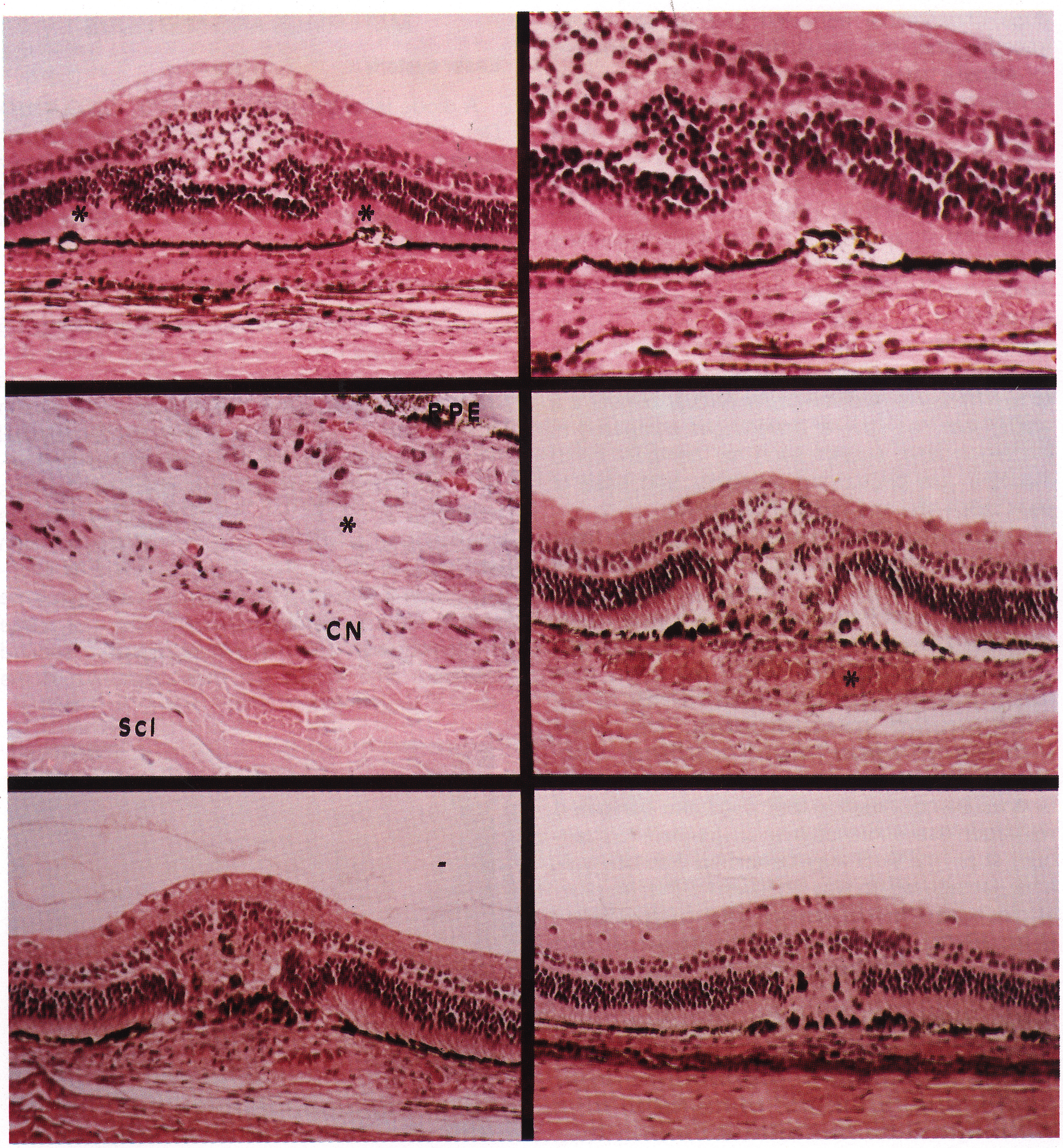

Fig. 2. Light micrographs of the rabbit retina. (Top left, x 200) One day after irradiation. The retina showes dome-shaped elevation within the area of irradiation. The nerve fiber layer and inner plexiform layer show vesicular degeneration. The cells of the inner nuclear layer are arranged sparsely due to an intercellular edema. At the margins of the irradiation the outer nuclear layer shows marginal elevations with a vacuole formation of the underlying retinal pigment epithelium (asterisks). There are significant leukocytes infiltrations in the outer retina and the superficial choroid, especially around the defective areas of the pigment epithelium. (Top right, x 400) Higher magnification of the left figure at the margin of the irradiation. The normal architecture of the inner and outer segments of the photoreceptor cells is destroyed. The pigment epithelium shows vacuolar degeneration. Several polymorphonuclear leukocytes are seen around the vacuolar degeneration. (Middle left, x 400) One day after irradiation. The outer coat of the eyeball beneath the irradiated area. There is significant intercellular edema (asterisk) around the ciliary nerve (CN). RPE; retinal pigment epithelium, Scl; sclera. (Middle right, x 200) Three days after irradiation. The innermost layer of the retina is somewhat

compact compared to that of day 1. There is severe destruction of the photoreceptor cells and dispersion of the pigmented cells in the deep retina. The sensory retina is detached artifactitiously. The choroidal vessels at the center of the irradiation are congested (asterisk). (Low left, x 200) Five days after irradiation. The number of cells of the inner nuclar layer at the area of irradiation are increased compared to the surrounding non-irradiated area. The defective areas of the outer nuclear layer are replaced by regenerating cells intermixed with pigment cells. (Low right, x 200) Seven days after irradiation. The innermost retina is nearly normal in thickness, but the inner nuclear layer is thick compared to the surrounding non-irradiated area. The defective area of the outer retina is replaced by regenerating fibrous tissue. The monolayered retinal pigment epithelium is high. (Hematoxylin-eosin stain)

were arranged in double rows at the inferior peripapillary retina in both eyes. The fundus color photographs were taken with a Topcon fundus camera (Topcon TRC-50, Tokyo, Japan) immediately after and 1, 3, 5, and 7 days after retinal photocoagulations.

Histological and ultrastructural study

The eyeballs were enucleated under general anesthesia with an intramuscular injection of ketamine hydrochloride 1, 3, 5, and 7 days after laser treatment. Immediately after enucleation the animal was sacrificed by intracardiac injection of air. Immediately after enucleation the eyeball was immersed in a fixative solution of 2% glutaraldehyde in 0.1 M phosphate buffer. The enucleated eyeball was opened coronally. The posterior half of the globe was prepared.

For light microscopic examination one eyeball from each rabbit was hemisected and placed in 20 ml solution of 2% glutaraldehyde 4% formaldehyde in 0.1 M phosphate buffer for 24 hours.

For electron microscopic procedure, the other eyeball was bisected and tissue blocks were cut into 2x 3 mm size under an operating microscope. Each block contained the retina with 3 to 4 photocoagulation lesions, the choroid and sclera. The specimens were placed in 2% glutaraldehyde in 0. 1 M phosphate buffer for 90 minutes in cold, and post-fixed in 1% osmium tetraoxide for 90 minutes in cold. After fixation the specimens were dehydrated serially with ethanol, and embedded in epon. All blocks were serially sectioned, and were stained with uranyl acetate and lead citrate. The ultrastructural study was performed with a transmission electron microscope (ISI-LEM 2000, Akashi, Japan).

RESULTS

Histological Findings

A light microscopic finding following transpupillary diode laser retinal photocoagulations in the rabbit retina is shown in fig. 2. At one day after irradiation, damage was clearly demarcated within the irradiated areas, and was centered on the inner retina, with spread of damage to the full-thickness sensory retina, retinal pigment epithelium, and choroid. Although the inner limiting membrane was intact, the whole retina revealed dome-shaped elevation within the areas of irradiation. There were many tiny vaculoes in the inner retina including nerve fiber layer, ganglion cell layer, and inner plexiform layer. The inner nuclear layer showed marked disruption of architecture by intra-and/ or intercellular edema. A few polymorphonuclear leukocytes were seen in the inner retina. The outer plexiform layer and outer nuclear layer showed varying degrees of disruption. The outer nuclear layer was markedly disarranged by intercellular edema, and also showed a marginal elevation, and some degenerative changes in the cells. At the margins of the irradiation, the photoreceptor cells were disrupted and detached from the underlying Bruch's membrane. There was significant infiltration of polymorphonuclear leukocytes in the outer retina and superficial choroid. A liberation of pigment into the subretinal space with occasional vacuolization of the pigment epithelium suggested pigment epithelial damages. The Bruch's membrane appeared relatively intact. The choroid showed an infiltration of polymorphonuclear leukocytes, vascular congestion and an extravasation of the red blood cells, suggesting vascular damage.

On day 3 after irradiation, the number of the vacuole in the inner retina decreased and the inner nuclear cells appeared orderly arranged. On the other hand the outer retina showed more progressed damage including distortion of the outer plexiform layer, decreased number of photoreceptor cells, and shrunken pigment epithelial cells. The retinal pigment epithelial cell layer was discontinued. The polymorphonuclear leukocytes presented on day 1 were not found throughout the whole retina, but several fibroblast-like cells were scattered in the outer retina.

On day 5 after irradiation the nerve fiber layer appeared thin. On the other hand, the inner nucle-

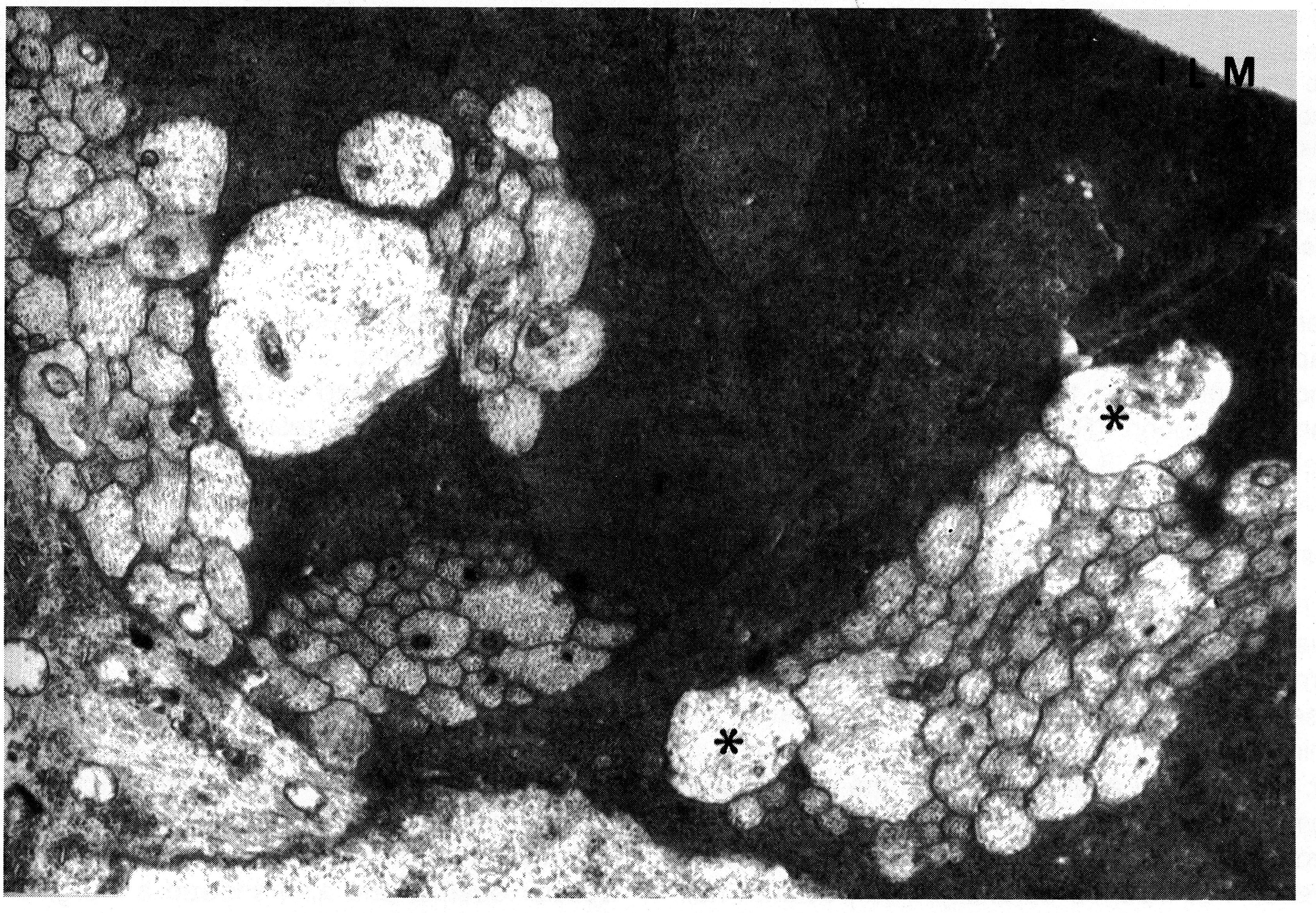

Fig. 3. Transmission electron micrograph of the inner retina in the rabbit retina at the center of irradiation. One day after a diode laser retinal photocoagulation of grade 3 intensity. Well preserved inner limiting membrane (ILM) is visible. There is marked swelling of the axons (asterisks) in the nerve fiber layer. x 8,300.

ar layer was thickened by an increased number of cells, suggesting cellular proliferation, but appeared in a somewhat disorderly arrangement. The outer plexiform layer was obliterated. The photoreceptor cells were lost, resulting in discontinuation of cells. The choroid showed no significant finding.

On day 7 after irradiation, the inner retina showed a thinning of the nerve fiber layer, and multilayered thickened inner nuclear layer. The previously obliterated areas of the outer nuclear layer were replaced by fibrosis. There was proliferation of pigment epithelial cells along the Bruch's membrane.

Ultrastructural Findings

On day 1 after diode laser retinal photocoagulations, the inner limiting membrane was intact. But there were diffuse full-thickness sensory retinal and superficial choroidal changes. The changes in the inner sensory retina were as follows; an axonal swelling of the nerve fiber (Fig. 3), swelling of the synaptic vesicles in the inner and outer plexiform layers with frequent formation of tiny vacuoles, occasional pyknosis of the cells in the inner nuclear layer. Some multinucleated cells containing pigment granules were found in the inner retina. The changes in the outer nuclear layer (Fig. 4) were relatively mild compared to those of the inner layer. There was occasional loss of the outer segments of the photoreceptor cells, however the inner segments were relatively intact. The alterations in the photoreceptor cells were more severe at the margin than at the center of irradiation. Some macrophages engulfed the detached and degenerated outer segments of the photoreceptor cells. The retinal pigment epithelium was shrunken, and detached from the Bruch's membrane. Within the area of irradiation multinucleated cells were found between the shrunken pigment epithelium and underlying Bruch's membrane. The microvilli of the pigmented epithelium were short and decreased in number. Tiny intracytoplasmic vaculoes were observed in the pigment epithelium. There was partial discontinuation of the Bruch's membrane (Fig. 5). In the area of irradiation there was extensive occlusion of the choriocapillaris and marked

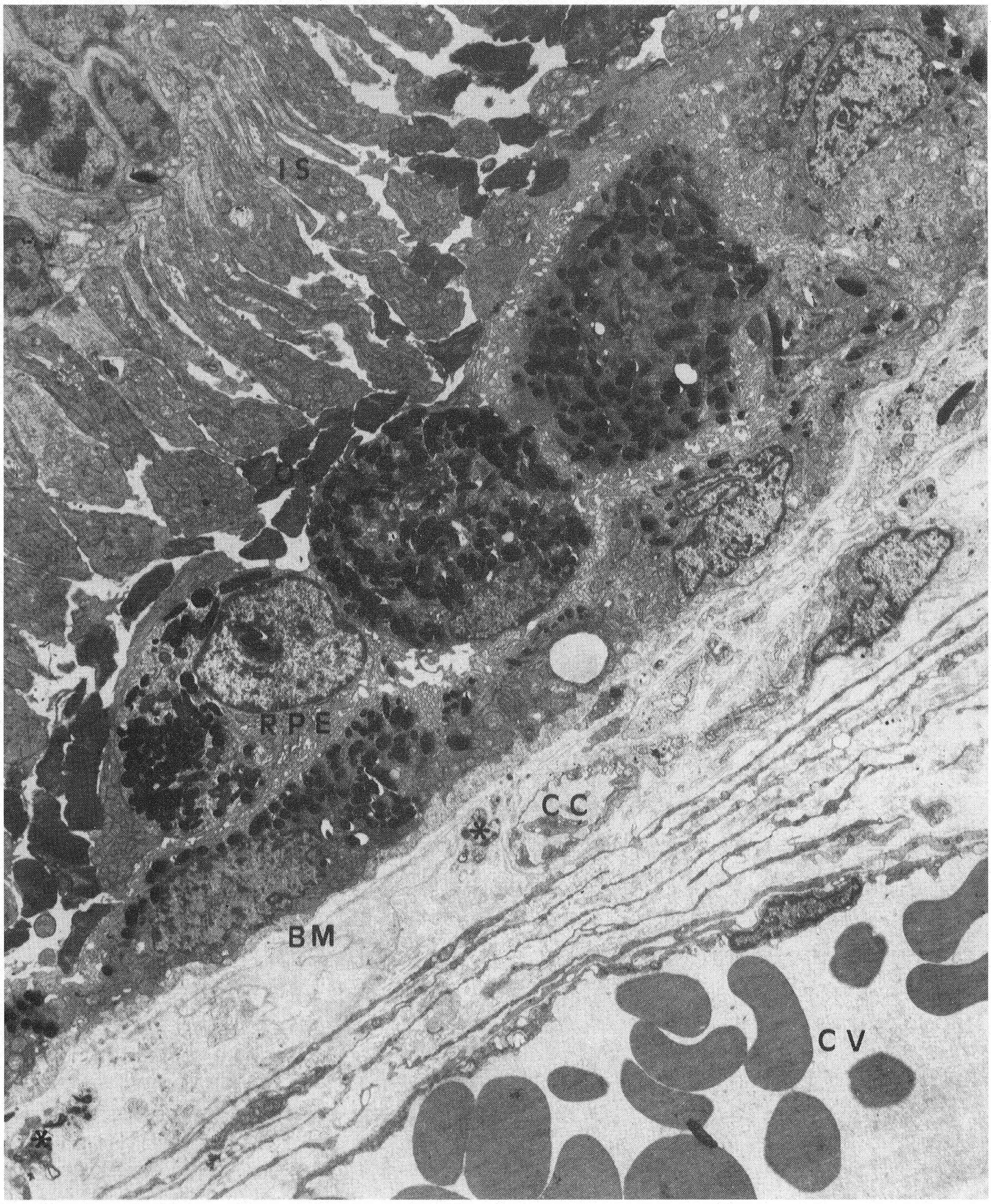

Fig. 4. Transmission electron micrograph of the rabbit outer retina at the margin of the photocoagulated region. One day after diode laser retinal photocoagulations of grade 3 intensity. The inner segments (IS) of the photorecptor cells are intact, while the outer segments (OS) of the photoreceptor cells are almost all destroyed. The retinal pigment epitheliums (RPE) are shrunken, and detached from the Bruch's membrane (BM). The nuclei of the retinal pigment epitheliums show pyknosis. Two multinucleated cells lie between detached retinal pigment epithelium and Bruch's membrane. The Bruch's membrane shows discontinuity. There are occasional occlusions of the choriocapillaris leaving tissue debris (asterisks) in the suprachoroidal space. The endothelium lining the choriocapillaris (CC) shows degenerative changes. There are significant extracellular edema around the choroidal vessel (CV). x 3,300.

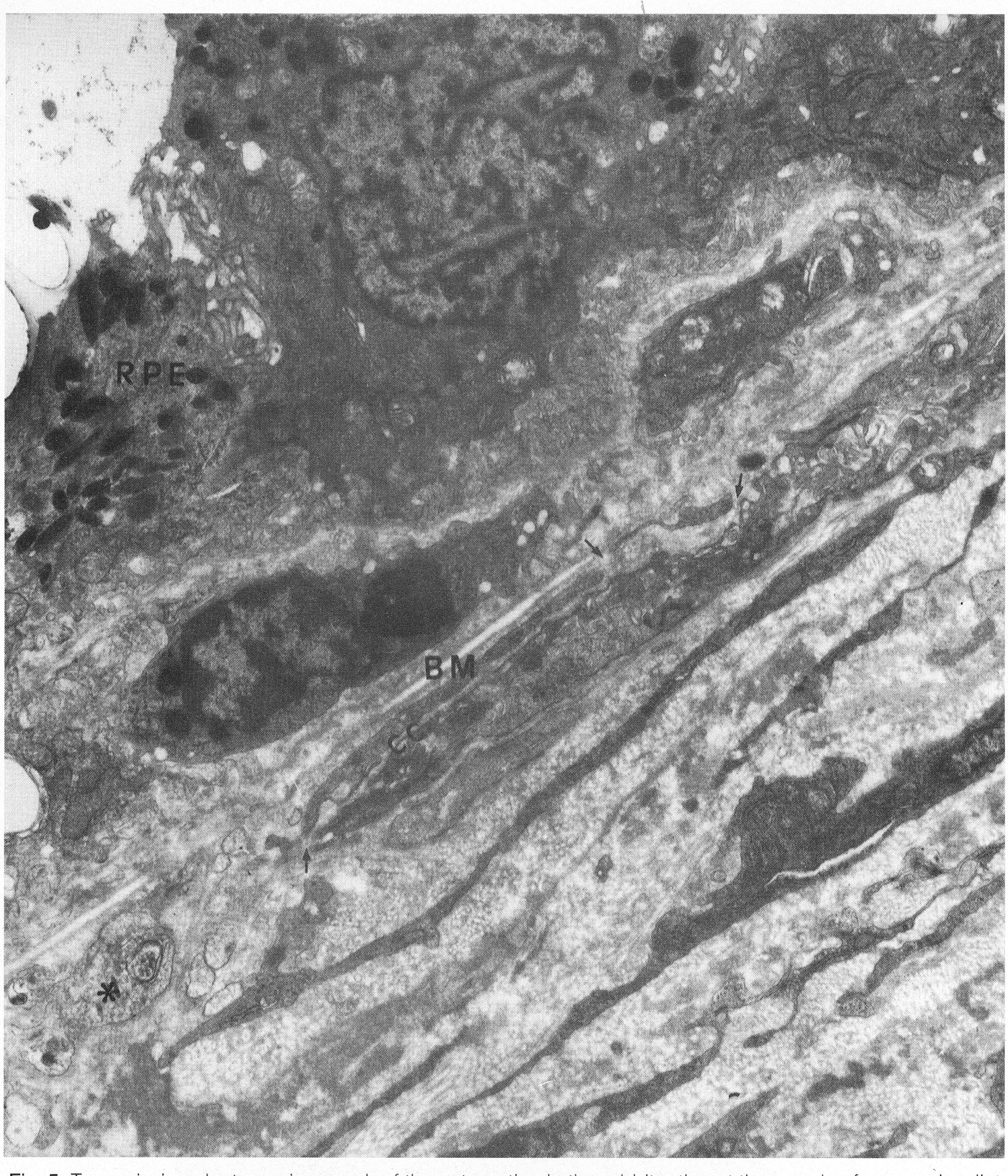

Fig. 5. Transmission electron micrograph of the outer retina in the rabbit retina at the margin of an area irradiated by diode laser. One day after diode laser photocoagulation of grade 3 intensity. A degenerated retinal pigment epithelium (RPE) is detached from the underlying Bruch's membrane (BM). A cell, that seems to have migrated through the disrupted Bruch's membrane, is located in the subretinal space. Degenerative tissue debris is visible in the superficial choroid (asterisk). A slit-lumened choriocapillaris (CC) showing a fenestration (arrows) of the capillary lumen lies just beneath the ruptured Bruch's membrane. x 6,900.

extracellular edema in the superficial choroid. The endothelial cell of the choriocapillaris showed degenerative changes.

On day 3 after diode laser retinal photocoagulations, the changes in the axon and the synaptic vesicles were similar to those seen on day 1. There was total loss of the photoreceptor cells within the area of irradiation. The defective areas

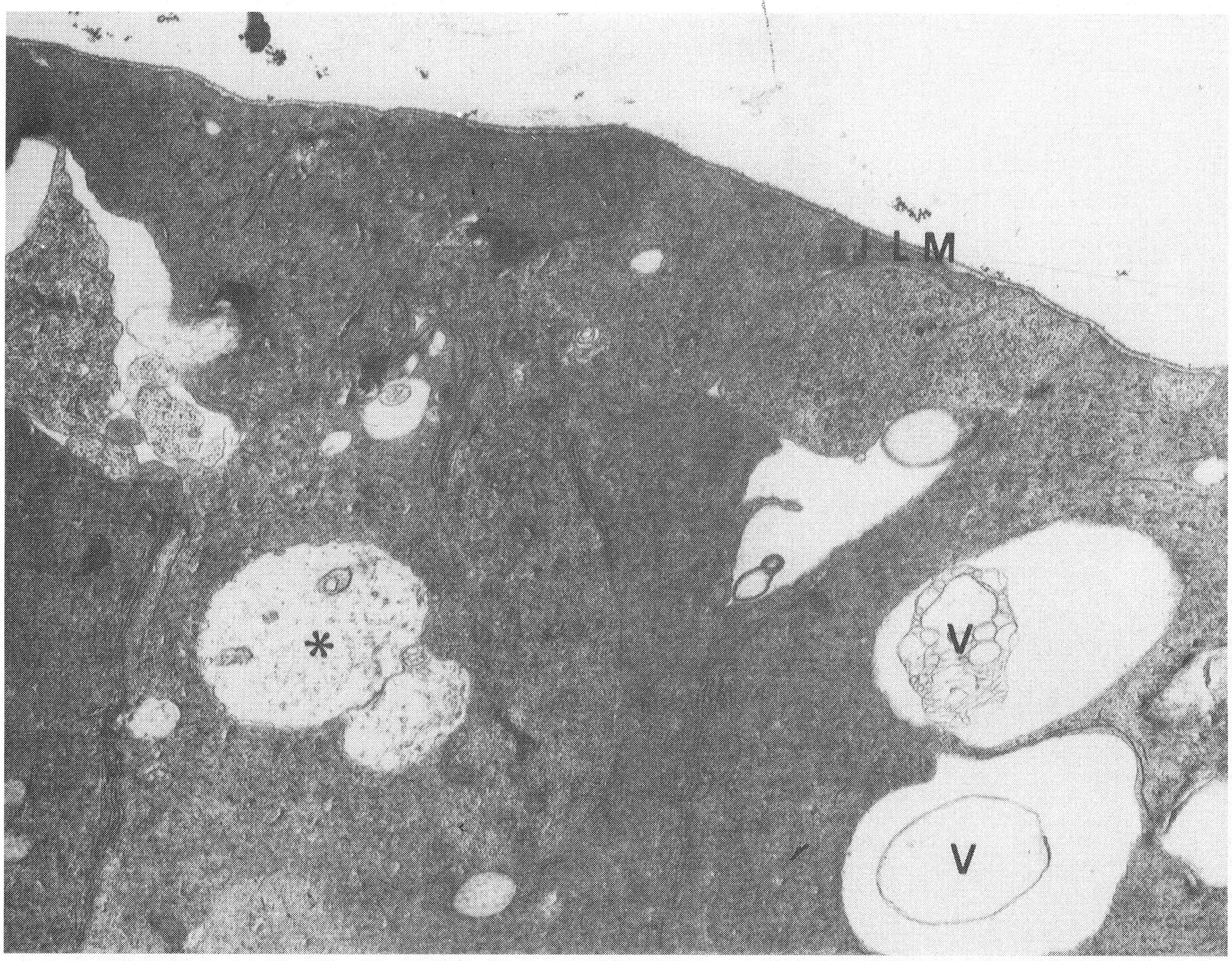

Fig. 6. Transmission electron micrograph of the inner retina in the rabbit retina at the center of irradiation. Seven days after a diode laser retinal photocoagulation of grade 3 intensity. Occasional loss of the axons leaving several vacuoles (V) are seen in the nerve fiber layer. A degenerating axon (asterisk), and debris is also seen in the nerve fiber layer. ILM ; inner limiting membrane. x 9,100.

in the outer nuclear layer were repalced by Müller cells and partly by collagen rich multinucleated cells. The inner and the outer segments of the photoreceptor cells were completely lost within the area of irradiation. The degenerative changes in the retinal pigment epithelium were more severe than those of day 1. There was shrinkage and flattening of the pigment epithelium, fragmentation of intracellular melanin pigments, and liberation of pigments into the subretinal space. Some patent choriocapillaris were seen in the superficial choroid beneath damaged pigment epithelium, that seemed to be recanalised capillary. The changes at day 5 were similar to those at day 3.

On day 7 after diode laser retinal photocoagulations, there was occasional loss of the axon leaving degenerative vacuoles in the nerve fiber layer (Fig. 6). The previousely damaged outer retina was replaced by regenerating cells containing a lot of collagen fibrils, and partly by Müller cells. The damaged pigment epithelial layer was replaced by the proliferating pigment epithelial cells (Fig. 7). The regenerated pigment epithelial cells directly contacted to the underlying choroid. No proliferation of the photoreceptor cells was found. Some fibroblast-like cells containing a lot of collagen fibrils and prominent rough endoplasmic reticulums, were found beneath the area of irradiation.

DISCUSSION

A system of classifying retinal photocoagulation lesions was introduced by Tso et al. in 1977 (Tso et al., 1977). Lesions consisting of faint, grayish white discoloration were referred to as intensity grade 1. Lesions consisting of a whitish retinal discoloration surrounded by a grayish periphery were classified as intensity grade 2, and lesions with a distinct white center were classified as intensity grade 3. In this study we were able to successfully create retinal photocoagulations of grade 3 using a diode laser attached to slit-lamp microscope. The pa-

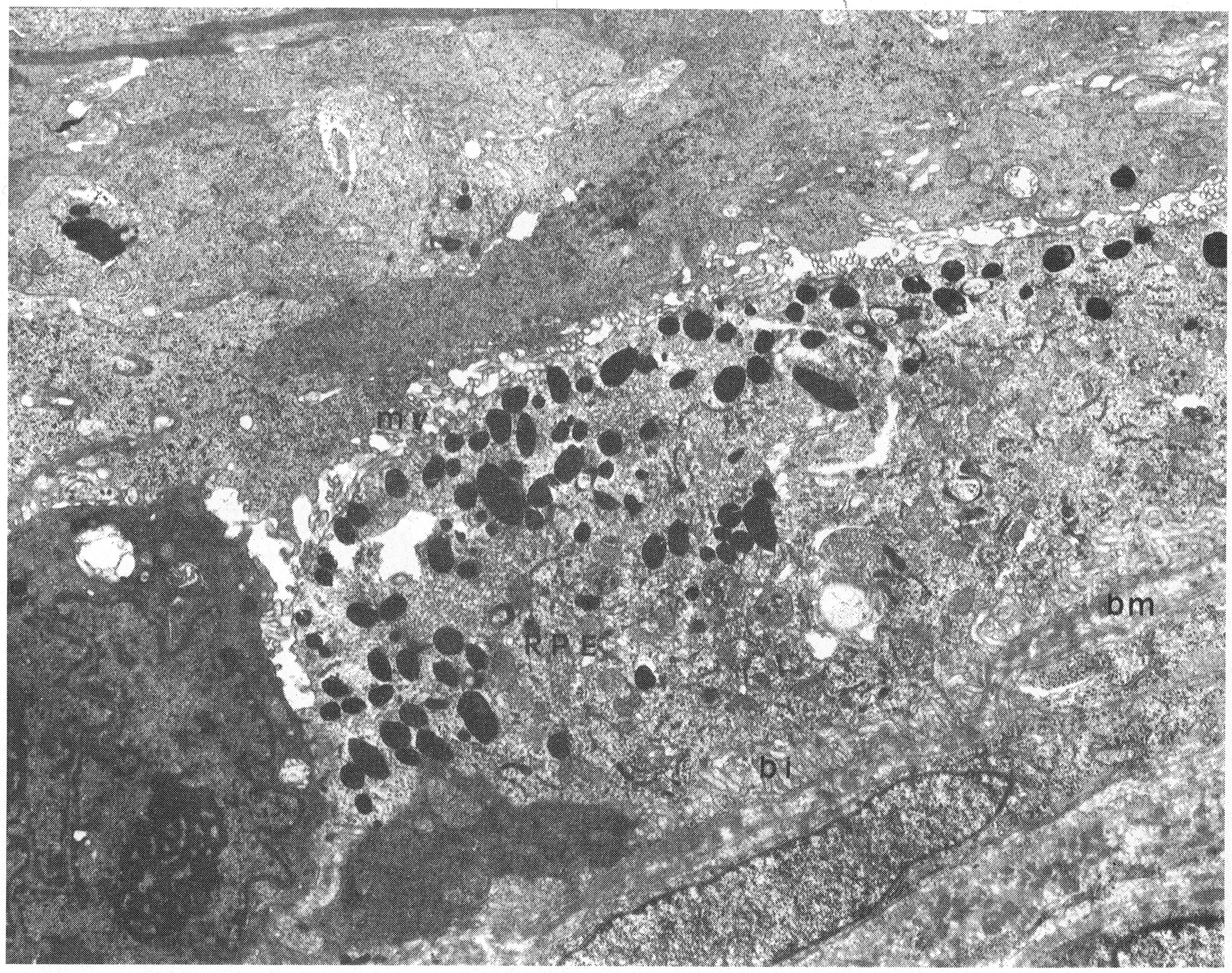

Fig. 7. Transmission electron micrograph of the outer retina in the rabbit retina at the center of irradiation. Seven days after a diode laser retinal photocoagulation of grade 3 intensity. The microvilli (mv) of the regenerated retinal pigment epithelium (RPE), that are relatively short, contact the overlying cell membrane directly. Well developed basal infoldings (bi) of the retinal pigment epithelium are shown. The Bruch's membrane (bm) is irregular in thickness. x 6,900.

rameters required to induce grade 3 photocoagulation lesions were 160 mW and 0.2 second duration at 200-um beam diameter. These parameters were dissimilar to those by Noyori which required greater energy (Noyori, 1990).

One day after diode laser retinal photocoagulations there were full-thickness sensory retinal damage. Although the laser power producing the retinal photocoagulation was not exactly same to those of other reports, these findings seemed to differ from those of other reports, in which no inner retinal damage was observed at the usual power density of argon or diode laser retinal photocoagulations (McHugh et al., 1990; Brancato et al., 1989; Menchini et al., 1992). It has been proved that retinal laser radiation is primarily absorbed by melanin pigments in the deep retina. Therefore, the deep retina is primarily and directly injured from thermal damage, while the inner retina is involved indirectly from a propagation of the primary injury. However, in this study the retinal photocoagulation of grayish white discoloration with distinct white center initially resulted in a full-thickness retinal injury on day 1 after treatment. This provokes a question whether the diode laser radiation emitting at 800 nm might also be absorbed directly by the inner retina and the inner retina would suffer a direct injury, not indirect damage from the radiation. This difference of clinical and histologic correlations from those of the previous reports requires a further verification of justifying that diode laser grade 3 lesion will preserve the inner retina free from radiation injury.

Some nerve fibers revealed an axonal swelling on day 1. This remained unchanged until day 7. An ultrastructural study showed a partial loss of the axons leaving vacuoles in the nerve fiber layer. The presence of the irreversible damage to the nerve fiber following diode laser retinal photocoagulations shown in this study is somewhat dissimilar to those of other reports. Wallow et al. observed an axonal loss almost invariably at the lesions of grade 3 laser burn (Wallow et al., 1991). Although the laser intensity used by them was more intense than ours, the histopathological findings were similar to that of ours. Assumming that the purpose of the laser retinal photocoagulations is to produce a chorioretinal adhesion without damaging the inner retina, our result suggests that the laser power producing a grayish white retinal discoloration with distinct white center is too high to use for laser retinopexy.

Laser retinal photocoagulations damage the retinal pigment epithelium directly by laser radiation itself and/or secondarily by malfunctioning of the surrounding tissues. One day following diode laser retinal photocoagulations there was stasis of the blood column in the choroid, together with occlusion of the choriocapillaris. The retinal pigment epithelium and the Bruch's membrane revealed more severe structural changes on day 3 than those of day 1 following diode laser retinal photocoagulations. As the retinal pigment epitheliums are supplied their nutrients from the choriocapillaris, the direct thermal damages to the choriocapillaris might interfere with the nutritional supply to the retinal pigment epithelium (Cohen AI, 1987). The progressed structural changes of the retinal pigment epithelium on day 3 might also be caused by malfunctioning of the choriocapillaris.

Laser-tissue interactions depend on the amount of light that is transmitted and absorbed by ocular tissue (Ham et al., 1980). They are also determined by many other factors such as wavelength of radiation, amount of tissue pigmentation, clarity of the media, energy density at the target, etc.. The longer the wavelength, the more transmission and the deeper penetration occurs. Melanin is the principal chromophore for any type of laser radiations in the retina and choroid. This is true for both blue-green argon and infrared diode laser radiation. Compared with the 95% absorption of argon green light at 514 nm, only 20% of diode laser light at 800 nm incident on the retina is absorbed by melanin pigment of the retinal pigment epithelium and the choroid (Birngruber et al., 1985). Although total absorption decreases as wavelength increases from 514 to 800 nm , more deep penetration occurs with increased wavelength of the radiation. Clinically the optical characteristic of the diode laser radiation penetrating deep in the ocular tissues, is very useful in the treatment of devastating subretinal neovascularization. Recently, a diode laser together with an injection of indocyanine green has made much advance in the treatment of subretinal new vessels by enhancing laser absorption (Balles et al., 1990). The deep penetration of the diode laser radiation can cause direct thermal injury to the choriocapillaris and also to the deep seated ciliary nerve. On light microscopic study we could find occlusion of the choroicapillaris and significant extracellular edema around the ciliary nerve in the suprachoroidal space. The deep penetration of the diode laser radiation could explain the cause of ocular pain during diode laser retinal photocoagulations. Wallow et al. reported ciliary nerve damage underneath photocoagulated lesions with intensity grade 3 (Wallow et al., 1991). Although we couldn't find an area containing the ciliary nerve damage in ultrastructural study, a significant extracellular edema around the ciliary nerve was observed under the light microscopic examination.

In preliminary trials there was rupture of the choroidal vessels at relatively high laser power (350-mWpower, 0.2-second duration, 200-um size). And also we could observe significant stasis of the blood columns together with denatured blood cells inside the choriodal vessels under the relatively less damaged retinal pigment epithelium at present laser parameters. Since the laser power of 160-mW power and 0.2-second duration at 200-um beam size is 40 mJ (0.2x 200) and the power of 350-mW power and 0.2-second duration in 200-um diameter which caused choroidal rupture is 70 mJ (0.2x 350), the safety zone of the laser power for diode laser retinal photocoagulations was not so wide as thought. This indicates that much careful attention is needed at the time of diode laser retinal photocoagulations.

In conclusion, the results observed demonstrated that diode laser retinal photocoagulation is as capable of producing chorioretinal scars as other lasers. At one day following the diode laser retinal photocoagulations there were diffuse occlusions of the choriocapillaris and stasis of the choroidal vessels. The optical characteristic of the diode laser radiation that penetrates deep into the ocular tissues, reconfirmed the beneficial use of the diode laser for treating the subretinal neovascular disorders. There was full-thickness damage of the entire sensory retina on day 1 following diode laser retinal photocoagulations. But the alterations of the pigment epithelium were mild on day 1 compared to those of consequent days. On ultrastructural study significant axonal damage in the nerve fiber layer was observed on day 1, and that was irreversible on day 7. This disagrees with the results of other reports. The facts suggest that 800 nm wavelength from a diode laser might be absorbed by melanin pigments and also other chromophores. Further studies must follow to clarify laser-tissue interactions in diode laser retinal photocoagulations.

ACKNOWLEGEMENT

The authors would like to thank Mr. Shin Hyung Kang for his technical assistance.

REFERENCES

Balles MW, Puliafito CA, Kliman GH, Elkoumy HA, Reidy WT: *Indocyanine green dye enhanced diode laser photocoagulation of subretinal neovascular membranes. Invest Ophthalmol Vis Sci 31(sup):282, 1990.*

Balles MW, Puliafito CA: *Semiconductor diode lasers: A new laser light source in ophthalmology. International Ophthalmology Clinics 30:77-83, 1990.*

Birngruber R, Hillenkamp F, Gabel VP; *Theoretical investigations of laser thermal retinal injury. Health Phys 48:781-796, 1985.*

Brancato R, Bandello F, Trabucchi G, Leoni G, Lattanzio R: *Argon and diode laser photocoagulation in proliferative diabetic retinopathy: A preliminary report. Laser and Light in Ophthalmology 3:233-237, 1990.*

Brancato R, Pratesi R, Leoni G, Trabucchi G, Vanni U: *Histopathology of diode and argon laser lesions in rabbit retina. Invest Ophthalmol Vis Sci 30:1504-1510, 1989.*

Brancato R, Pratesi R, Leoni G, Trabucchi G: *Retinal photocoagulation with diode laser operating from a slit lamp microscope. Lasers and Light in Ophthalmology 2:73-78, 1988.*

Cohen AI: *The retina In: Moses RA, Hart WM eds. Physiology of the eye. 8th ed, The C.V. Mosby Company, St. Louis. pp458-490, 1987.*

Duker JS, Federman JL, Schubert H, Talbot C: *Semiconductor diode laser endophotocoagulation. Ophthalmic Surgery 20:717-720, 1989.*

Ham WT Jr, Ruffolo JJ Jr, Mueller HA, Guerry D III: *The nature of retinal radiation damage: dependence on wavelength, power level and exposure time. Vision Res 20:1105-1111, 1980.*

McHugh JDA, Marshall J, Ffytche TJ, Hamilton AM, Raven A: *Initial clinical experience using diode laser in the treatment of retinal vascular diseases. Eye 3: 516-527, 1989.*

McHugh JDA, Marshall J, Ffytche TJ, Hamilton AM, Raven A: *Macular photocoagulation of human retina with a diode laser: a comparative histopathologic study. Lasers and Light in Ophthalmology 3:11-28, 1990.*

Menchini U, Trabucchi G, Brancato R: *Can the diode laser (810 nm) effectively produce chorioretinal adhesion?. Retina 12:S80--S86, 1992.*

Noyori K, Noyori S, Ohki R: *Clinical trial of a diode laser photocoagulator- a preliminary report. Laser and Light in Ophthalmology 3:81-87, 1990.*

Puliafito CA, Deutsch TF, Boll J, To K: *Semiconductor laser endophotocoagulation of the retina. Arch Ophthalmol 105:424-427, 1987.*

Schulenburg WE, Hamilton AM, Blach RK: *A comparative study of argon and krypton laser in the treatment of diabetic optic disc neovascularization. Br J Ophthalmol 63:412-417, 1979.*

Smiddy WE, Hernandez E: *Histopathologic characteristics of diode laser-induced chorioretinal adhesions for experimental retinal detachment in rabbit eyes. Arch Ophthalmol 110:1630-1633, 1992.*

Tso MOM, Wallow IHL, Elgin S: *Experimental photocoagulation of the human retina: Correlation of physical, clinical, and pathologic data. Arch Ophthalmol 95: 1035-1040, 1977.*

Wallow IL, Sponsel WE, Stevens TS: *Clinicopathologic correlation of diode laser burns in monkeys. Arch Ophthalmol 109:648-653, 1991.*