Argon laser photocoagulation of the human retina. I. Histopathologic correlation of chorioretinal lesions in the region of the maculopapilar bundle

Thomas A. Weingeist

Argon laser burns of varying intensity (50 mW./0.2 sec./50 μ, 100 mW./0.1 sec./100 μ, 100 mW./0.2 sec./200 μ, and 100 mW./0.2 sec./400 μ) were made in the region of the maculopapilar bundle of four human eyes 24 hours prior to enucleation for malignant melanoma of the choroid. Light and electron microscopic observations revealed that it is possible to produce chorioretinal lesions between the disc and the macula without damaging the nerve fiber layer of the maculopapilar bundle. In order for this to be accomplished blood vessels should be avoided and the intensity of the argon laser should not exceed 50 mW./0.2 sec./50 μ. These small lesions may be of benefit in the treatment of conditions like central serous retinopathy, histoplasmosis, and senile macular degeneration and deserve further clinical investigation.

Key words: photocoagulation, argon laser, pathology, transmission electron microscopy, retina, nerve fiber layer, maculopapilar bundle, human.

Argon laser photocoagulation has been chiefly used for the treatment of neovascular diseases such as diabetic retinopathy. Recently, photocoagulation therapy with the argon laser has also been advocated for the treatment of macular diseases such as central serous retinopathy, ocular histoplasmosis, and senile macular degeneration. The effectiveness of such treatment is dependent, in part, on the ability to produce chorioretinal lesions without destroying the overlying nerve fiber layer.

Prior to this study there has only been one detailed report on the histopathologic and ultrastructural changes resulting from argon laser burns in man.1 According to these authors, chorioretinal lesions could not be produced in the region of the maculopapilar bundle without destruction of the nerve fiber layer. Studies using experimental animals have expressed conflicting views.2-4 In some instances laser lesions were confined to the outer retina while in others alterations occurred in all layers including the maculopapilar bundle.

From the Department of Ophthalmology, University of Iowa, Iowa City, Iowa.
Supported in part by Neurosensory Center Program Project Grant NS 03354 from the National Institute of Neurological Diseases and Stroke, Neurosensory publication No. 319.
Submitted for publication May 21, 1974.
Reprint requests: Dr. Thomas A. Weingeist, Department of Ophthalmology, University of Iowa, Iowa City, Iowa 52242.
Some conflicting observations are undoubtedly due to species differences such as ocular size and pigmentation. Others are probably due to the method used to produce lesions.

The present study was undertaken to assess acute pathologic changes caused by "mild" argon laser burns. The objective was to produce chorioretinal lesions between the fovea and the optic disc without damaging the nerve fiber layer in the maculopapillar bundle of man.

Material and methods

This study is based on the examination of four eyes obtained from three women and a man. The patients were 36, 48, 52, and 63 years of age, respectively. Each subject had a peripherally located malignant melanoma of the choroid and a normal posterior fundus. The central visual acuity of all patients was correctable to 6/6 and each had a normal intraocular pressure by appplanation and a normal Goldmann field with the I isopter. Prior to enucleation, permission was obtained to administer several argon laser burns to the posterior pole. Fundus photographs were taken before and after laser treatment. All argon laser (Coherent Radiation) burns were produced 24 hours prior to enucleation. The lesions consisted of one application at each site. Rows of individual lesions were made perpendicular to the horizontal raphe (Fig. 1). Care was taken to avoid blood vessels. Four modalities were studied: (1) 50 mW./0.2 sec./50 μ; (2) 100 mW./0.1 sec./100 μ; (3) 100 mW./0.2 sec./200 μ; and (4) 100 mW./0.2 sec./400 μ.

Immediately after enucleation, each globe was immersed in cold 4 per cent glutaraldehyde, buffered in 0.15 M sodium cacodylate at pH 7.3. Thirty minutes later the anterior segment was removed. Individual lesions were dissected from the posterior pole with the aid of a stereomicroscope. Adjacent retina served as a control. Polaroid fundus photographs were invaluable in locating and classifying laser burns. Each specimen was postfixed in 1 per cent osmium tetroxide in cacodylate buffer, dehydrated in alcohol, and embedded in epoxy resin. Thick (1.0 μ) sections were stained with Azure II. Light microscopic serial sections were made of each type of lesion. Thin sections for electron microscopy were doubly stained with uranyl acetate and lead citrate.

Results

Light microscopy. Fifty mW./0.2 sec. per 50 μ argon laser lesions in the region of the maculopapillar bundle are barely visible clinically (Fig. 1). By light microscopy the damage produced by such lesions appears to be confined to the outer retina and choroid. Serial sections of these lesions consistently revealed alterations in the outer nuclear layer of the retina, the photoreceptors, the retinal pigment epithelium, and the superficial choroid (Fig. 2). In every instance the inner nuclear layer of the retina and the maculopapillar bundle appeared to be intact. The changes in the retina are characterized by pyknosis of the nuclei in the outer nuclear layer and disruption of the photoreceptor cells. There was marked coagulation necrosis and pigment dispersion involving the retinal pigment epithelium. The choriocapillaris was congested (Fig. 3) compared with normal and in many areas the vessels appeared occluded.

In 100 mW./0.1 sec./100 μ burns there was minimal damage to the inner portion of the retina (Fig. 4). The alterations in the outer retina and choroid were similar to those observed in 50 mW./0.2 sec./50 μ lesion, but greater in magnitude. One hundred mW./0.2 sec./200 μ argon laser photocoagulation resulted in damage to all retinal layers, but was most extensive from the inner nuclear layer to the retinal pigment epithelium (Fig. 5). The most severe damage to the retina occurred following 100 mW./0.2 sec./400 μ argon laser
Fig. 2. Center of 50 mW./0.2 sec./50 μ argon laser lesion. The maculopapillary bundle remains intact throughout. Pyknotic changes occur in the outer nuclear layer (ONL) and there are alterations in the outer segments (OS), retinal pigment epithelium (PE), and choriocapillaris (CC). (Azure II, ×300.)

burns (Fig. 6). These lesions tended to be pyramidal in shape whether or not a retinal vessel was struck by the laser beam. The apex of the pyramid was located at the inner surface of the retina and the base occurred parallel to the retinal pigment epithelium and choriocapillaris. Serial sections of these retinal lesions demonstrated that even extensive burns could be misinterpreted as being smaller than they really are. In the far periphery of even large burns only the outer retina and choroid were affected.

**Electron microscopy.** Examination of 50 mW./0.2 sec./50 μ argon laser lesions by electron microscopy revealed disruption of the outer segments of the rods and cones and dispersion of melanosomes from the retinal pigment epithelium (Fig. 7). The pigment epithelium was filled with vacuoles which arose from dilation of the endoplasmic reticulum and swollen mitochondria. The characteristic basal infoldings and apical projections of these cells were absent. In addition the normal attachments between adjacent epithelial cells and the epithelium and basal lamina were disrupted. In some areas the vessels in the choriocapillaris were occluded by cellular debris and blood clot. In other segments of the lesion the choriocapillaris appeared normal. Bruch's membrane was always found to be intact.

The inner portion of the retina overlying 50 mW./0.2 sec./50 μ lesions could not be distinguished from control sites. The internal limiting membrane appeared normal and there were no structural changes in the nerve fiber layer in cross or longitudinal sections (Figs. 8 and 9). Myelin
Fig. 3. Retinal pigment epithelium (PE) and choriocapillaris (CC) within a 50 mW./0.2 sec./50 μ argon laser lesion. Note occlusion of vessels within the choriocapillaris (CC). (Azure II, ×900.)

Fig. 4. Center of 100 mW./0.1 sec./100 μ argon laser lesion. Minimal changes are visible by light microscopy in the nerve fiber layer (NFL). (Azure, ×300.)
figures were occasionally visible in the nerve layer of the control eyes and the treated retina. When large retinal blood vessels were inadvertently struck by the laser beam some swelling occurred in the adjacent nerve fiber layer.

In 100 mW./0.1 sec./100 μ laser burns the internal limiting membrane remained intact, but the nerve fiber layer was disrupted (Fig. 10). The axons were swollen and fragmentated and the Müller cells appeared to contain greater amounts of glycogen particles (Fig. 11). These alterations were most prominent adjacent to the inner nuclear layer. In larger burns damage occurred throughout the nerve fiber layer in the region of the maculopapillary bundle.

Discussion

Light and electron microscopic observations in this study reveal that it is possible to produce acute (24 hour) chorioretinal lesions between the fovea and optic disc of man without altering the structure of the maculopapillary bundle. Serial sections of "mild" argon burns repeatedly substantiated this fact. These lesions were barely visible clinically and were in the order of 50 mW./0.2 sec./50 μ. The effectiveness of 25 to 75 mW. lesions is now being evaluated for the treatment of central serous retinopathy. Extreme care should be taken to avoid retinal blood vessels, since the blue-green (5,145 to 4,880 Å) argon laser beam is very well absorbed by hemoglobin. The transformation of this radiant energy into thermal energy may result in damage to adjacent nerve fibers. Theoretically, the ruby laser which emits light in the red portion of the visible spectrum (6,943 Å) would be safer to use in making chorioretinal lesions since little if any of this wavelength is absorbed by hemoglobin. Unfortunately, certain disadvantages in the design of the ruby laser negate this apparent advantage.

The structural changes described in the outer retina and choroid in this study were similar to those reported by other investigators. No attempt was made to establish
Fig. 6. Center of 100 mW./0.2 sec./400 μ argon laser lesion. The laser burn has affected all layers of the retina as well as the superficial choroid. This lesion is temporal to the fovea and is not visible in the fundus photograph (Fig. 1). (Azure II, ×200.)

Fig. 7. A 50 mW./0.2 sec./50 μ argon laser lesion involving retinal pigment epithelium (PE) and outer segments (OS). (×6,300.)
Following a 50 mW./0.2 sec./50 μ argon laser burn the inner retina, including the nerve fiber layer (NFL), Müller's cells, and the internal limiting membrane (ILM), appear normal. (×21,000.)

The nerve fiber layer within the maculopapillary bundle remains intact following a 50 mW./0.2 sec./50 μ argon laser burn. (×21,000.)
Fig. 10. A 100 mW./0.1 sec./100 μ argon laser photocoagulation results in disruption of the nerve fiber layer (NFL) but the internal limiting membrane (ILM) remains intact. (x36,350.)

Fig. 11. Extensive disruption of inner retina following 100 mW./0.1 sec./100 μ argon laser photocoagulation. (x16,000.)
whether there exists a differential susceptibility of rod and cone cells to argon laser radiation.

Because of normal variations in retinal thickness and pigmentation, it is not possible to extrapolate observations concerning laser burns from experimental animals to man or probably from one portion of the retina to another. The response of the retina and choroid to laser treatment probably varies with each location. It seems clear from this and other studies that argon laser photocoagulation of neovascular lesions in the maculopapillar bundle cannot be achieved without damaging the nerve fiber layer of the retina. This layer seems to be spared if "mild" burns (50 mW./0.2 sec./50 μ or less) are made away from retinal vessels. Because of this, this therapeutic modality may be of value in the treatment of conditions such as central serous retinopathy, ocular histoplasmosis, and senile macular degeneration.

Since all the observations in this study were based on acute (24 hour) lesions it was not possible to evaluate the effect of any reparative process. Further clinical studies should be directed toward possible physiologic changes associated with argon laser therapy in the region of the maculopapillar bundle.

The author thanks Dr. Robert C. Watzke for his help and suggestions during the course of this study, Mrs. Vergene Gregory for her technical assistance, and Mrs. Maria Warbasse for typing the manuscript.

REFERENCES