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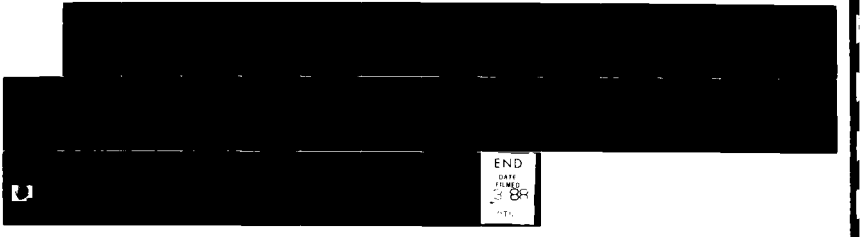

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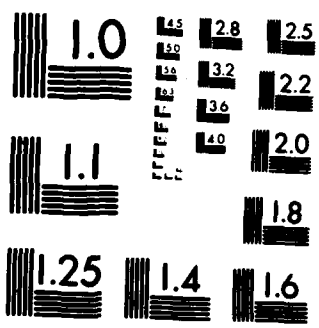

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FUNCTIONAL ASSESSMENT OF HIGH LEVEL LASER IRRADIATION

ANNUAL PROGRESS REPORT

DAVID O. ROBBINS, PH.D.

NOVEMBER 1985

Supported by

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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Small foveal lesions produced by single, Q-switched (532 nm) pulses were difficult to detect both morphologically and behaviorally. These lesions were produced by pulses significantly above the ED_{50} and their effects changed over time as perhaps edema and repair mechanisms proceeded. The initial deficits in visual function were often slight and variable. As additional pulses were presented, the variability decreased while the visual deficit increased. Computer analyses of fundus changes in grey scale taken from exposed retinae also change over time and correspond to our behavioral data.

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FOREWORD

In conducting the research described in this report, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (DHEW Publication No. (NIH) 78-23, Revised 1978).

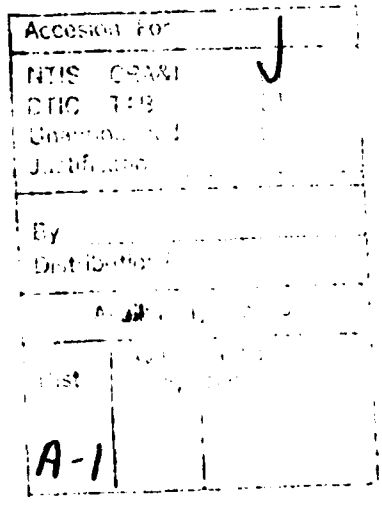


TABLE OF CONTENTS

LIST OF ILLUSTRATIONS

INTRODUCTION

The conversion of light energy into alternate energy forms within the outer segments of photoreceptors can temporarily or permanently change the natural transduction process. Normally, the absorption of light within the system's physiological operating limits changes the polarizing currents of the photoreceptor leading to the initiation of electrochemical events that may ultimately results in a visual sensation. A natural consequence of this process is to temporarily change the absorption characteristics of individual receptors to further light absorptions and thereby change the overall visual sensitivity of the organism. This change is dependent upon the degree, number and retinal location of bleached photoreceptors. The regeneration of bleached pigments within each receptor is relatively rapid as are the normal changes in sensitivity resulting from light aborption.

A completely different process can occur when the retina is exposed to intense levels of light that are beyond the system's physiological operating limits. Depending upon the wavelength, coherency, and duration of light exposure, gross pathological damage has been reported to exist in the cornea, pigment epithelium, and in the outer segments of photoreceptors (1-4). Several different damage mechanisms have been proposed to explain the observed pathology. Generally, a thermal model has been attributed to those changes resulting from relatively long duration, low energy exposures to long wavelength light (5) while mechanical damage mechanisms have typically been associated with extremely high-energy, short duration (Q-switched) exposures. For visible wavelengths, Q-switched pulses may initiate an acoustic explosion in addition to a mechanical disruption and thermal burn. Data from both morphological and behavioral studies, however, have shown changes in the

retina at power levels well below those where these types of damage mechanisms (thermal, acoustic and mechanical) could be predicted (6, 7). In these instances, actinic insult may produce either transient or permanent changes in the natural cyclic mechanisms within the photoreceptor which then can ultimately affect the receptor viability.

While incoherent sources such as the sun are capable of producing various types of retinitis, especially of concern today is the emplcyment of lasers since these devices are capable of producing ultrashort pulses of highly collimated light in both the visible and invisible regions of the spectrum. The output power densities of many of these lasers are sufficient to produce damage after only incidental viewing. Devices such as laser range finders and designators are currently being used in the modern battlefield and along with the increasing possibilities of the deployment of laser weapons, create unique problems for military medicine and strategic planners.

Ocular hazards from laser exposure can be assessed in several different ways. The most popular approach has been to assess the gross morphological changes using clinical fundoscopy. Using this criterion, the retina is exposed to relatively intense irradiation above the MPE and changes in fundus examined over the course of time. In more recent years, however, morphological techniques have been refined to include scanning electron-microscopy which has led to a significant reduction in the presumed energy necessary to elicit structure change within the retina. Associated with these refined analytical tools has been a shift in the site of primary anatomical alteration from the pigment epithelial layer to the outer segments of the photoreceptors (7, 8) when lower exposure energies are employed. The consequences of these structural alterations and especially those of a minor and/or transient nature can only be implied from these morphological studies.

Less numerous are those studies that have attempted to explain the

effects of laser irradiation by examining changes in the electrical properties of the eye or brain. Long term changes in these electrical potentials should reflect morphological alterations and can be used as an explanation for obvious shifts in visual sensitivity. Low-level exposures of long-wavelength, coherent light in the turtle retina, for example, have been shown to produce irreversible changes in the spectral sensitivity and receptive fields of cells in the optic tectum (9). This study also demonstrated some unique aspects of coherent (laser) light as opposed to incoherent light. Passing a laser beam through a vibrating (60 Hz) diffuser to reduce the typical speckle pattern greatly attenuated the more permanent effects observed for equivalent energy that is not time-averaged. The range of overall retinal irradiances used in this study were well below those where any morphological disruptions could be directly attributed to thermal changes in the retina. It was proposed that the high spatial frequencies of the speckle pattern might be manifested at the retina by very small spots of extremely high monochromaticity, contrast, and peak irradiances which could either adversely effect the retina's fine morphological ultrastructure and/or electrical properties (i.e. excitatory and inhibitory processes). A similar situation does not exist in a typical incoherent pattern and this form of energy was also less effective in producing electrical changes.

A limitation of both the morphological and electrophysiological approaches is that neither approach can directly predict the changes in visual performance that might be expected and especially those immediate changes that might occur following laser exposure. For instance, the functional consequences resulting from thermal and mechanical insult should be almost immediate while those resulting from actinic reactions may develop more slowly (10, 11). From a military perspective, any alteration in the ability of a

soldier to complete an assigned mission requiring visually guided behavior may be of greater immediate importance than any morphological damage or actinic insult that may also co-exist with the change in visual function.

Early behavioral studies which examined the effects of laser irradiation on visual sensitivity employed relatively intense power densities which produced irreversible decrements in visual acuity ranging from 40 to 80% of the animal's pre-exposure level (12, 13, 14). Unfortunately, in virtually all of the previous functional studies, the postexposure measurements had to be delayed at least 24 hours because anesthesia was required to properly position the laser beam on the fovea. The development of a behavioral technique to expose awake, task-oriented animals has been developed (15). Critical for this technique was the ability to determine the animal's exact fixation point so that the laser beam could be positioned onto the central fovea and a punctate lesion made. The employment of Landolt rings which require an animal to use its fovea for resolution of the critical feature of the target (the break in a "C") has produced predictable and reliable shifts in photopic acuity immediately after exposure. With large beam diameters (>150 microns), postexposure acuity dropped 40 - 60% from its pre-exposure level in over 80% of the exposures (15). This shift in acuity presumably reflected foveal involvement. The magnitude of the initial deficit was shown to vary systematically with beam diameter; the larger the area of involvement, the larger the observed acuity deficit. The energy of the flash, on the other hand, directly affected recovery time and had no influence on the magnitude of the deficit for those energy densities below the ED_{50} (16 - 19).

Our original studies explored energy densities at or below the ED_{50} in what we have defined as the transition zone between temporary and permanent changes in visual acuity. These studies were primarily directed toward long and intermediate wavelength laser exposures of relatively long duration (100

msec) and large beam diameters. More recently we have begun studying the effects of Q-switched 532 nm pulses at power densities significantly above the ED_{50}. The recent development and employment of Q-switched lasers bring new problems to the field of eye safety. These lasers are capable of presenting extremely intense pulses of very short (10-20 nsec) duration which can create a series of punctate lesions and hemorrhages. In our last annual report (1983/84 USAMRDC Annual Report for Contract #DAMD17-83-C-3172) we described some of the preliminary results from these types of exposures and problems associated within their functional assessment. In this report additional behavioral data is presented along with some preliminary data using computer image analysis of fundoscopic changes that exist in these animals' eye following Q-switched pulses of the type used in our behavioral studies.

METHODS

Basic procedures used during this effort, such as the optical system, means of delivering laser exposures, and means for assessing visual function, are essentially the same as those reported earlier and will only be briefly described here.

Subjects: six, adolescent rhesus monkeys (Macaca mulatta) have served as subjects during portions of this effort. Two of these have been in the training and baseline assessment portion of the paradigm while the remaining animals have been exposed to various Q-switched pulses from a Nd:YAG laser.

These animals were housed in standard primate cages and removed and temporarily restrained only during the actual test session. These test sessions lasted approximately 1 hour per day. The restraint device, along with the procedure for transfer, has been described elsewhere (20). Briefly, the device is a portable cage similar to a tranfer cage that might be used in any animal facility to remove or transfer an awake animal from its home environment.

Apparatus and Procedure. The animal's head movements were immoblized by a custom fitted helmet that was positioned over the animal's head. Animals were conditioned to voluntarily position their head into this device and to align their pupils with a small, adjustable iris diaphragm in the front of an opaque facemask that accompanied the animal's helmet. This apparatus was necessary to help maintain the animal's line of sight and distance from the viewing screen.

Animals were tested under monocular viewing conditions in a light-tight, sound attenuated chamber. On the far wall of the chamber was a rear-projection screen subtending 4 deg at a distance of 1 m from the subject's pupil. Two programmable carousel slide projectors with code slide controls were used to present the discriminanda and control it's size, wavelength, intensity, and contrast. The timing and order of slide presentations were computer controlled as were data analyses and storage.

Discrimination Task. The animal's task was to discriminate the presence of a Landolt ring ("C") from among a series of gapless rings ("O") of equal dimensions. Threshold acuity was derived by a computer activated, tracking technique which allowed the subject to adjust the size of the test targets about its threshold for the different background wavelength, intensity and contrast conditions examined. Prior to any exposure, complete monocular baseline spectral and contrast sensitivity curves were derived for both eyes.

Immediately after exposure and for several months thereafter, postexposure visual sensitivity was derived under a variety of viewing conditions and comparisons made to the animal's pre-exposure baseline in the exposed eye and postexposure baseline in his unexposed (control) eye.

Laser System. A diagram of the optical system is presented in Figure 1. A Nd:YAG laser (Molectron MY32-20) served as the primary laser device. A small HeNe laser was used for aligning purposes and a 4 W CW Argon laser (Spectra Physics Model 165/265) was also available for exposure under different flash conditions. The output of the Nd:YAG laser was set at 532 nm; the invisible lines from this laser were physically blocked internally from exiting the laser. The power density of the laser beam was controlled by adjustments at the laser head and by neutral density filters placed in the beam pathway. All power densities were measured both at the artificial pupil and at the laser head with a volume absorbing disc calorimeter (Scientech, Model 362) according to a procedure developed by J. Lund of LAIR. The power

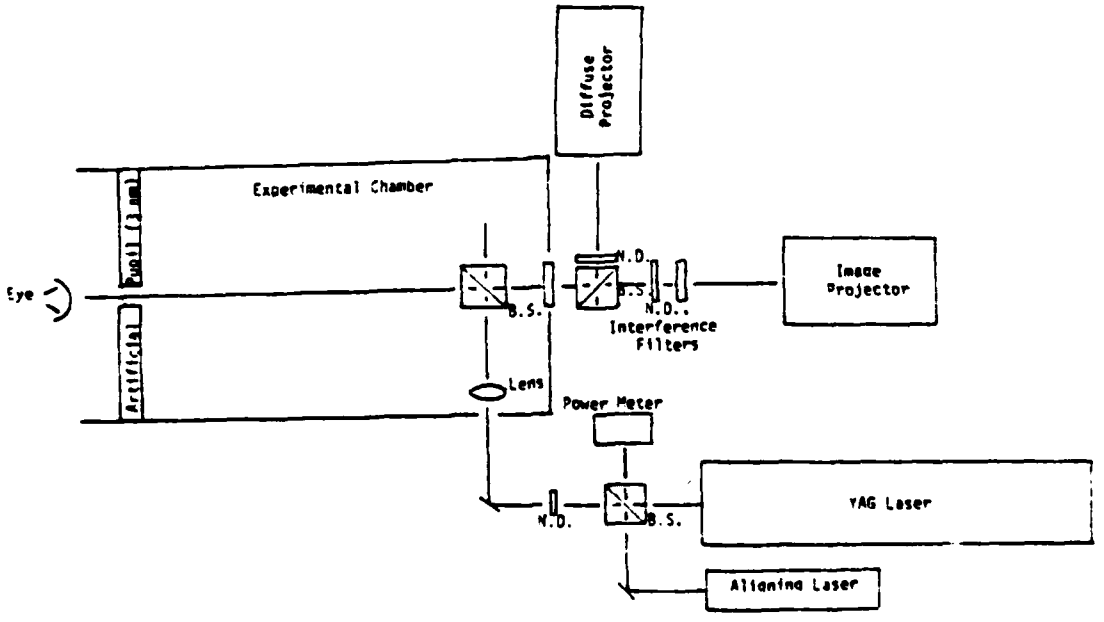


Figure 1 Diagram of the laser optical system used.

level of individual pulses were expressed in uJ at the cornea and were calibrated immediately prior to and after laser exposure.

The laser beam was aligned for on-axis (foveal) exposures such that it was coaxial with a line between an artificial pupil and the gap in a specified Landolt ring subtending less than 1 min of arc. The beam passed through a converging lens positioned so that the cornea was in the focal plane of the lens. A manual and electronic safety shutter was positioned between the first beam splitter and the converging lens to protect against accidental exposure. When properly aligned, the beam entered the animal's eye co-axial with the gap in a predetermined Landolt ring to which the animal was centrally fixating at the moment of exposure. Either a single or repetitive pulse, separated in time from several msec to minutes, was presented to the animal at 2, 10, 50, or 100 uJ per pulse. In the case of multiple pulses separated in time by greater than 100 msec, each individual pulse was presented in the manner described below for the single pulse condition.

Exposures were triggered by the animal's correct detection of its threshold Landolt ring, while the subject was viewing a high contrast target on either a chromatic or achromatic background. In the past it has been determined that animals in this task maintain central fixation for several seconds after responding while awaiting some form of reinforcement (discriminable tone or avoidance of a mildly annoying shock). Immediately after each exposure, visual acuity was measured. If the subject failed to return to its pre-exposure acuity level within the session, further exposures on subsequent days were suspended and daily baseline measures of spectral and contrast sensitivity were obtained. If recovery to baseline occurred, the animal was re-exposed as before. Long-term changes in chromatic and contrast sensitivity were followed with daily test sessions for over 6 months following each exposure that produced a permanent acuity shift.

RESULTS

Four animals have received single and repetitive Q-switched pulses at levels significantly above the ED_{50}. Sample data from an animal exposed to a single 50 uJ, Q-switched pulse is presented in Figure 2. In this case, as with all exposures, the animal's baseline acuity was within ± 1 SD of its predetermined baseline prior to exposure. Typically, animals plotted very stable pre-exposure baselines over relatively long periods of time (45 minutes). In this figure, upward excursions represent correct detections of Landolt rings and the presentation of smaller overall rings while downward excursions represent missed Landolt rings and the presentation of larger test targets. The presentation of any specific size target, in terms of visual angle, was entirely dependent upon the animal's response to preceding targets. Only responses to the Landolt rings ("C"), not the gapless rings, controlled the size of targets to be presented. The number of false positive responses to gapless rings was always low ($< 10\%$ at threshold) indicating that the reinforcement contingencies used in our paradigm discouraged guessing. The occurrence of a 50 uJ pulsed exposure is indicated in the figure by an arrow and corresponds to the zero point on the time abscissa. This was the fourth such Q-switched pulse that this animal had received over a period of several months. In each case, following an initial transient deficit of approximately 30% (from the animal's pre-exposure acuity level), the animal gradually returned to a level slightly below its pre-exposure baseline. In the days following this exposure, the animal continued to plot an acuity slightly below, but not significantly different from, its pre-exposure level. A major difference, however, was a marked increase in the variability both within and across postexposure sessions.

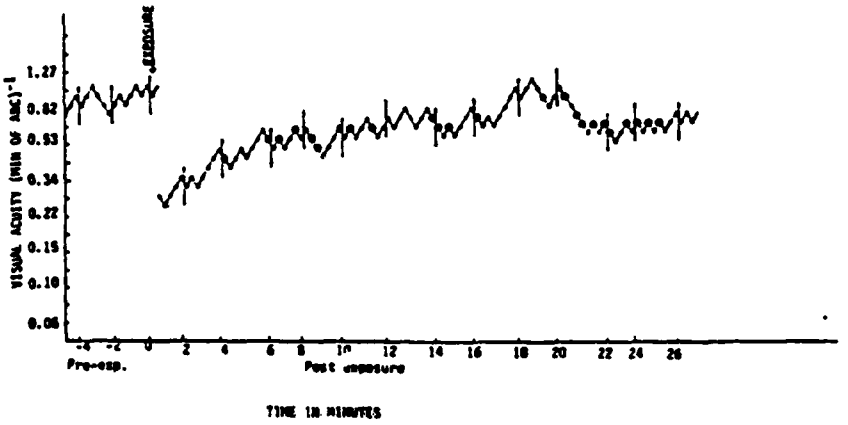


Figure 2. Sample data of threshold acuity following a single, 50 uJ pulse of 532 nm laser light. The vertical lines through the data represent 2 minute time marks. Beam diameter on the retina represented less than 50 microns.

The energy of the flash (50 uJ) used in the above figure was significantly above the ED_{50} for this condition. Much more severe initial deficits in acuity and equally long-lasting recoveries have been observed using exposures of lesser energies (below the ED_{50}) but which were presented for a much longer duration (100 msec) and involved a larger retinal area. In Figure 3, recovery from a 7 mW, 100 msec flash to a 632.8 nm laser is shown. With this type of exposure, immediate postexposure acuity decreased to 0.51 $(\text{min of arc})^{-1}$, which corresponded to an acuity deficit of 59% relative to pre-exposure acuity. This visual deficit lasted 9 minutes before acuity gradually returned

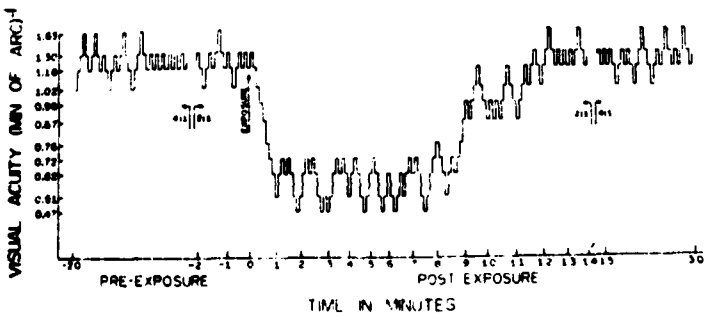


Figure 3. Sample data of threshold acuity prior to and immediately following a 7 mW, 100 msec flash from a HeNe laser. Beam diameter on the retina was approximately 150 microns.

to the S mean pre-exposure level. Total recovery from the initial deficit was complete within approximately 13 minutes. Unlike the situation for the Q-switched exposure shown in Figure 2, however, this animal's postexposure acuity returned to normal and on subsequent days remained within the mean baseline level without any increased variability as was noted above. In other cases of exposure to relatively long duration flashes (>50 msec), similar recovery functions were derived although the exact duration of the function was directly dependent upon the energy of the flash; the higher the exposure energy, the longer the time for recovery. The magnitude of the deficit, however, remained invariant with changes in exposure energy and appeared to be affected only by the diameter of the laser beam on the retina.

An example of the increased variability following exposure to Q-switched pulses at power densities significantly above the ED_{50} is shown in Figure 4. In this case, the animal was exposed to several single 50 uJ pulses from a

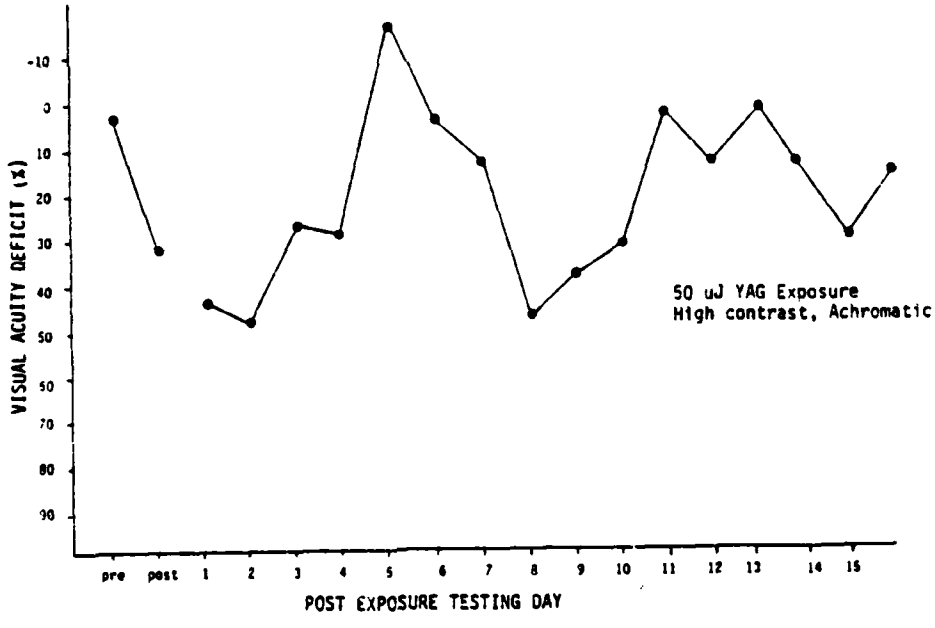


Figure 4. Daily mean postexposure acuities in one animal exposed to several 50 uJ, 532 nm pulses separated in time by days. The beam represented <50 microns in diameter on the retina.

Nd:YAG laser over several months, the first three to which the animal returned to his pre-exposure acuity level within 20 minutes of exposure. With each subsequent exposure, however, the animal's mean daily acuity level demonstrated increased variability within and between sessions. In this figure, each data point represents the mean acuity level, expressed as a percent of this animal's pre-exposure baseline acuity. These mean deficits were calculated from a minimum of 15 minutes of threshold tracking which was equivalent to the presentation of approximately 60 threshold Landolt rings.

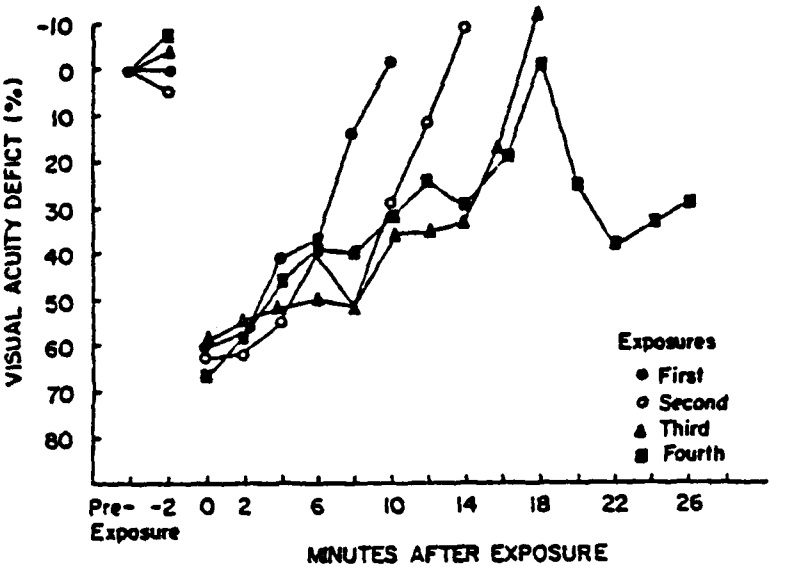


Figure 5 Percent visual acuity deficit following each of four 50 uJ, 532 nm Q-switched pulses presented over a period of several weeks for one subject. No more than one exposure was presented per session (day).

This animal had shown progressively longer recovery durations for each 50 uJ exposure. The recovery functions, plotted in percent deficit for each running 2 minutes following exposure is shown in the following figure (Figure 5). For the initial 50 uJ pulse, recovery was complete within 10 minutes but with each addition pulse, total recovery time increased by approximately 4 minutes. By the fourth exposure, full recovery was not obtained during the test session

but did occur within the next several days although as previously mentioned (Figure 4), the animal's day to day variability increased significantly.

A second animal exposed to four, 100 uJ Q-switched pulses under a similar exposure paradigm is shown in Figure 6. Increasing the energy of individual pulses by twofold did not significantly increase either the initial deficit or total recovery time for the first three exposures although it must be pointed out that after each exposure, the animal's postexposure baseline decreased and remained depressed for several weeks (see Figure 7). Additional exposures were made at these depressed acuity levels and may not be immediately obvious since the data in Figure 6 is plotted as a percent of the

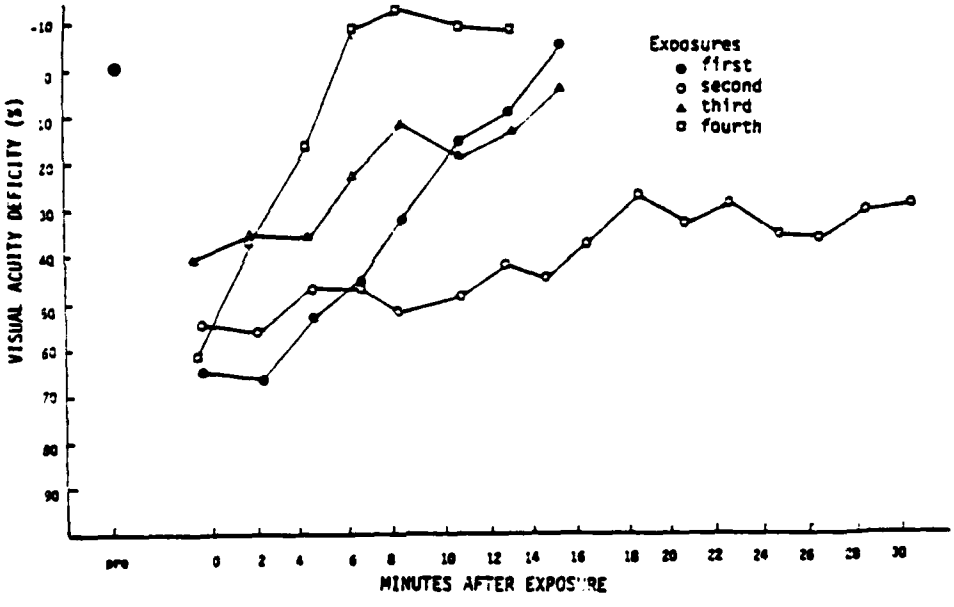


Figure 6 Percent visual acuity deficit following each of four 100 uJ, 532 nm Q-switched pulses presented over a period of several months for one subject. No more than one pulse was presented per session (day) and acuity was derived daily between each exposure.

immediate pre-exposure level. Similar to the example used for multiple, 50 uJ pulses, the fourth exposure, which occurred several weeks after the initial exposure, produced a longer duration deficit which did not recover

significantly during the remaining 30 minutes of the session.

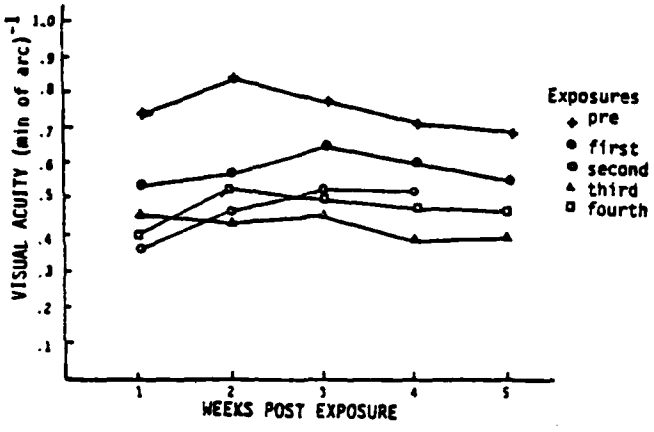


Figure 7. Mean weekly acuity following each of four 100 uJ pulses. This is the same subject shown in Figure 6 and represents the progressive downward shift in acuity following each of the individual pulses. What is not shown in these figures is the greatly increased daily variability in post exposure baselines that occurred. On a weekly average, however, the animal's postexposure baseline appeared relatively invariant.

In each of the above examples, only one exposure was presented per session (day) and multiple pulses were separated from each other by as long as several weeks. While each exposure was significantly above the ED_{50}, the total area of retinal involvement was relatively small due to the short duration of the pulse (10 -20 nsec) and its small beam diameter (<50 microns). In two other animals, repetitive pulses at slightly lower energy per pulse (10 uJ) were presented within a single test session. The purpose of these repetitive pulses was to test for any cumulative effects that might occur when an animal was exposed to several pulses close in time. The initial effects of a single 10 uJ pulse are shown for one animal in Figure 8. This figure is similar in design to Figures 2 and 3 and represents the raw acuity data prior to and immediately following exposure as derived from our self-

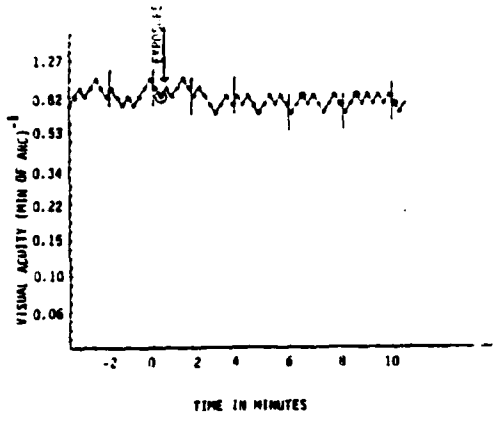


Figure 8 Sample data of threshold acuity prior to and immediately following a single, 10 uJ pulse of 532 nm laser light. The vertical lines through the data represent 2 minute time marks. Beam diameter on the retina represented less than 50 microns.

adjusting procedure. No immediate shift in baseline acuity was obvious with this exposure even though the energy of the single pulse was slightly above the ED_{50}. There was a gradual downward shift in baseline acuity with prolonged testing although the effect was extremely weak and statistically insignificant. Daily exposure to single, 10 uJ pulses, however, did increase the magnitude of the immediate acuity deficit although no systematic changes as a function of multiple pulses were evident in the two animals tested thus far (see Figure 9). As can be seen in the recovery functions plotted in Figure 9, for the first animal (left) immediate postexposure acuity following the second and sixth pulse produced a signficant decrease in acuity which lasted for 6 to 8 minutes before leveling off and remaining depressed for the duration of the test session. For the other exposures in this animal (first, third, fourth, and fifth), no such downward shift in acuity was evident although as previously mentioned for other Q-switched pulses, the animal's

variability increased significantly. A similar situation was evident for the second animal (right) although in this animal no large deficits in acuity were noted in any of the first six exposures.

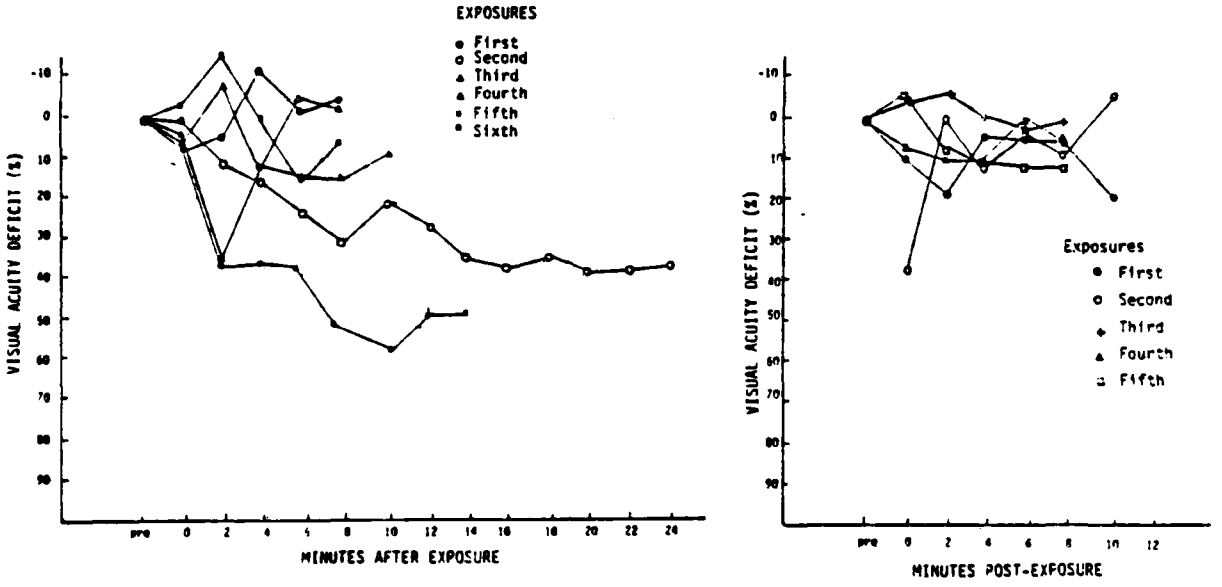


Figure 9. Recovery functions for two different animals exposed to multiple, 10 uJ pulses of 532 nm light over a series of six consecutive sessions (days). Acuity is plotted in terms of percentage deficit from the animal's immediate pre-exposure baseline.

The recovery functions shown in the previous figure were derived from plots of acuity under achromatic, high contrast background conditions. Contrast sensitivity functions were derived for each animal after the sixth and final exposure session. In Figure 10 is shown abbreviated curves for both animals prior to any exposure and following the final, 10 uJ pulse. The differences between the pre- and postexposure sensitivity functions were quite small and because of the variability previously mentioned any observed differences in these plots were statistically insignificant. Similar

functions were derived for spectral acuity in these two animals (see Figure 11) and again the differences while somewhat larger were extremely difficult to interpret because of the animals' increased postexposure variability.

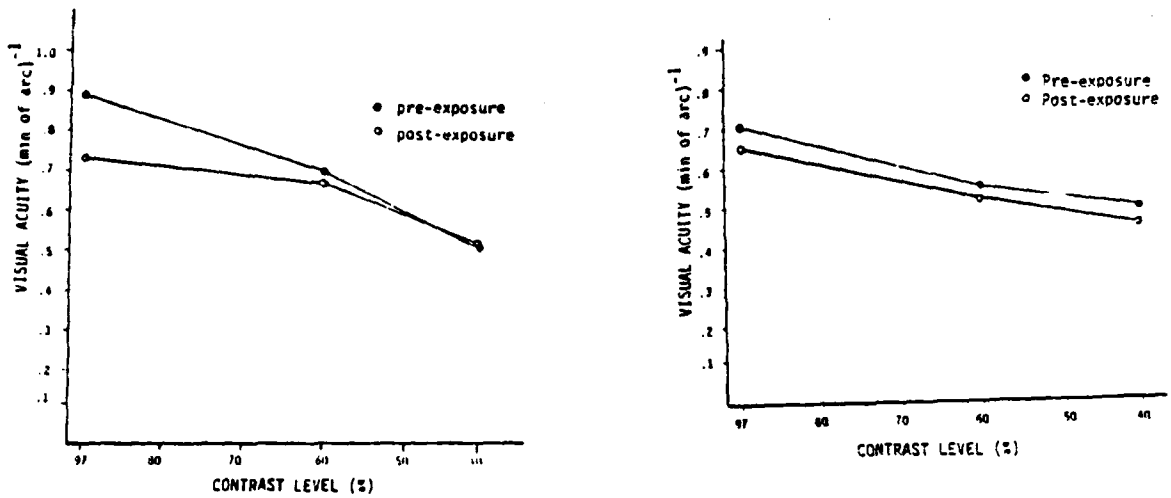


Figure 10. Contrast sensitivity curves (abbreviated) in two animals prior to and following the last of a series of repeated exposures to single, 532 nm Q-switched pulses. Only one pulse was presented per session (day).

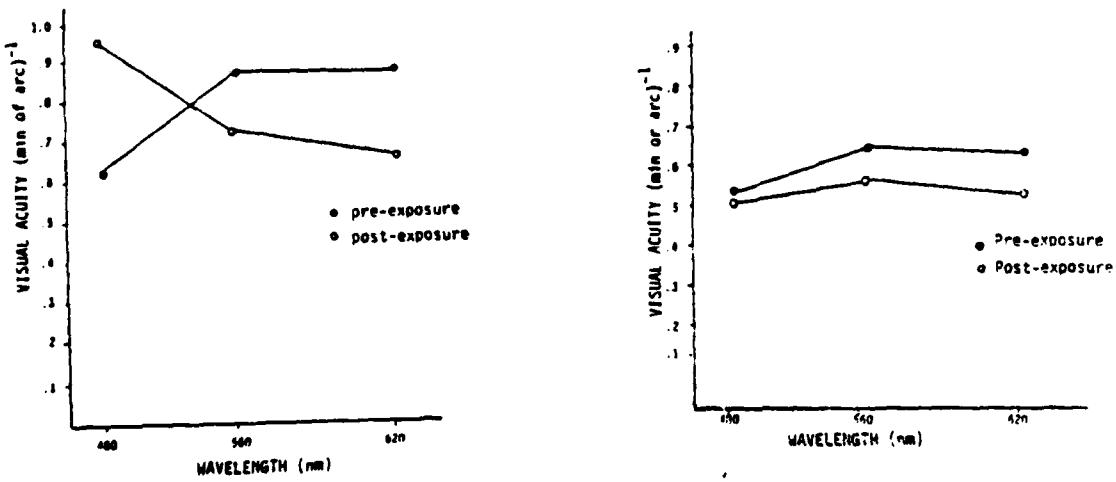


Figure 11. Spectral acuity pre- and postexposure for the same two animals shown in the previous figures. Acuity was derived using different monochromatic backgrounds equated for equal numbers of quanta.

Repeated Q-switched pulses at energy densities above the ED_{50} and presented within the same test session (day) are shown in Figure 12. In this example, single, 2 uJ pulses were presented approximately 10 minutes apart to one while the animal was discriminating threshold targets. In this figure representing the raw data of the up-down procedure, the arrows represent the time of exposure; the vertical lines through the data representing running 2 minute interval marks. The breaks in the figure represent 5 minute rest periods between conditions. The animal's visual acuity before, during, and

Figure 12. Raw data derived directly from our computer printout of the up-down procedure for deriving threshold visual acuity. In these plots, the animal was repeatedly exposed to 2 uJ pulses of 532 nm laser light.

24 hours following exposure shown in Figure 12 are presented in Figure 13. In this figure the data has been plotted both as a function of visual acuity (left) and as a function of percent deficit from its pre-exposure level (right). Regardless of the way it is plotted, it is evident that although immediate postexposure acuity was not affected, postexposure acuity 24 hours later was significantly depressed. This condition of depressed acuity remained for several weeks along with increased within session variability before the animal gradually returned to a baseline level not significantly different from either its unexposed eye or its pre-exposure baseline. A similar exposure paradigm is shown for a second animal at a somewhat higher exposure power (see Figure 14). In this case single, 10 uJ, 532 nm pulses were presented approximately 8 minutes apart while the subject was making threshold discriminations to Landolt rings presented on high contrast,

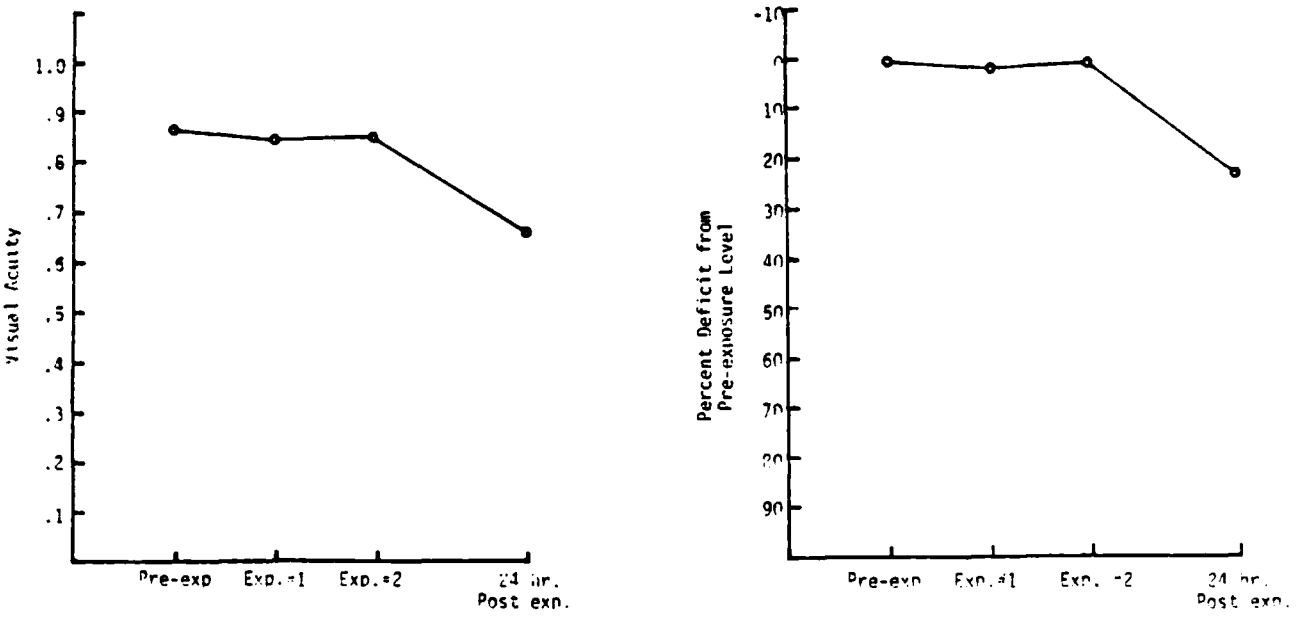


Figure 13. Plots of the visual acuity (left) and percent deficit in acuity following two 532 nm, Q-switched pules of 10 uJ each. The data points represent the animal's mean acuity for an approximate 10 minute period before, immediately after, and 24 hours following exposure.

achromatic backgrounds. The two arrows (one at time zero and the second at minute eight) represent the presentation of a Q-switched pulse triggered by the animal's correct detection of a threshold Landolt ring. All changes in postexposure acuity are plotted in terms of percent deficit from the animal's pre-exposure level. The curve plotted with closed circles represents the first such exposure session while the curve plotted with open circles represents a second exposure session several weeks later. In both sessions the animal was exposed to two, Q-switched, 10 uJ pulses within the test session.

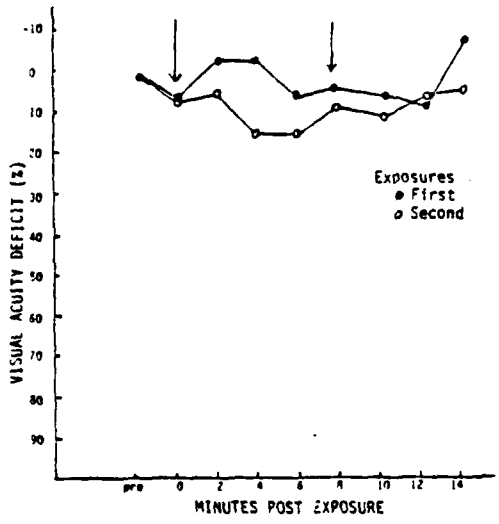


Figure 14. Recovery functions for two different test sessions where an animal was exposed to two Q-switched, 10 uJ pulses within 8 minutes of each other in the same test session.

Of some importance in resolving some of the questions that could be raised regarding our behavioral data is the nature of the ocular media and the retina itself. For example, while the energies employed in this study were above the ED_{50}, were these energy densities signficant enough to produce widespread retinal bleeding and hence clouding of the ocular media? Also, were these exposures of sufficient magnitude to produce damage beyond the minimum extent of the beam on the retina (< 50 microns)? Any additional regions affected could incapacitate a large enough region within the central fovea to disrupt the fine resolving power of the eye. In collaboration with the Division of Biorheology at Letterman Army Institute of Research, we have begun to explore the nature of changes in the fundus at various time intervals after exposure. Using their computer assisted, image analysis equipment we have begun a joint effort to study the changes in the grey scale of recorded fundus photographs taken from irradiated retinae. In Figure 15 is shown a fundus photograph and computer analysis of a rhesus retina exposed to single, Q-switched Nd:YAG laser pulses. The marked boxes located within the animal's

macula indicate the region where the retinal image was digitized by a Robot 650 video frame grabber and analyzed for grey scale content (64 shades over a 256 x 256 grid) by a DEC PDP 11/70 minicomputer. In the top box, a single pulse comparable to those used in our behavioral study was presented and produced a fundoscopically visible lesion. In the second box, a lesser energy exposure was presented which was barely visible upon visual examination. The third box represents a control area of the macula which was not exposed to laser light. Grey scale analyses using the computer method described above is shown to the right of the fundus photograph. This plot demonstrates a lightening of the region around where the suprathreshold, Q-switched pulse was presented over that observed in the other two regions.

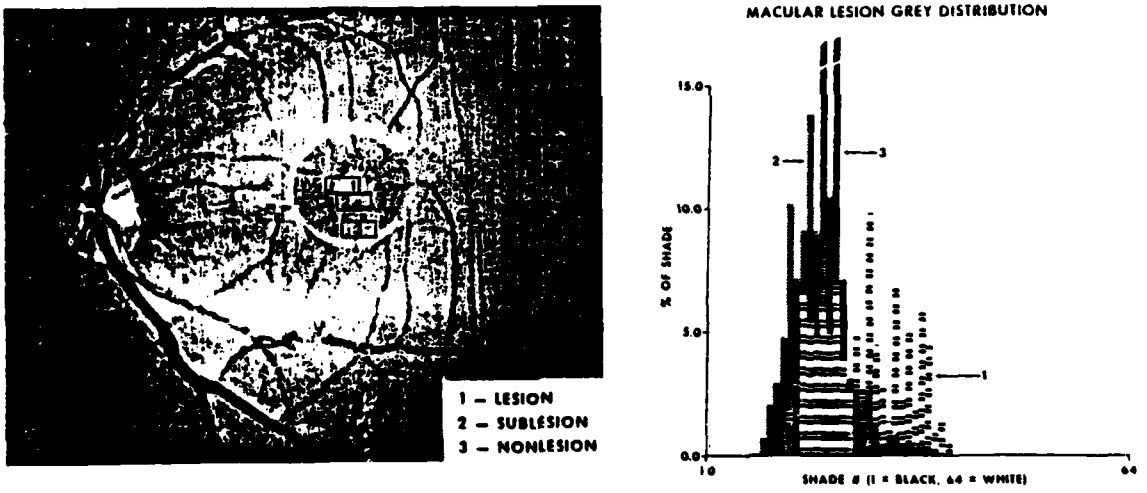


Figure 15. In the left portion is shown a fundus photograph taken from a rhesus monkey retina exposed to two, single Q-switched pulses from a Nd:YAG laser at energies above and below that necessary to produce a visible lesion. In the right portion is shown the grey scale analysis of three regions (lesion, sublesion, nonlesion) in the macula.

The foveal grey scale content across several different lesion sites are shown in the next series of figures. These figures were derived by moving a computer cursor horizontally across different regions of the lesion site (256 x 256) and determining for each location the grey scale content (64 units from light to dark). In Figure 16, the grey scale analysis across a region of the fovea is shown prior to exposure, immediately after exposure to a single Q-switched pulse, and 1 hour after the exposure. As can be seen in this figure, a region of the exposed retina first darkened immediately after exposure and then lightened by 1 hour after exposure. The long-term changes in an

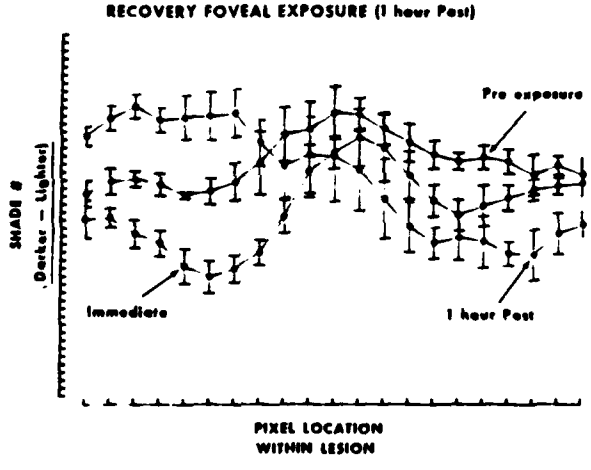


Figure 16. Computer-assisted, grey scale analyses of the foveal region of an exposed rhesus retina prior to and immediately after a single Q-switched Nd:YAG pulse.

exposed retina using the same analyses is shown in Figure 17. As evident in both this figure and the previous one, the lesion site goes through a number of changes in grey scale as a function of time following laser exposure. These changes appear to last for some time and could reflect changes in this region's ability to adequately process light absorption.

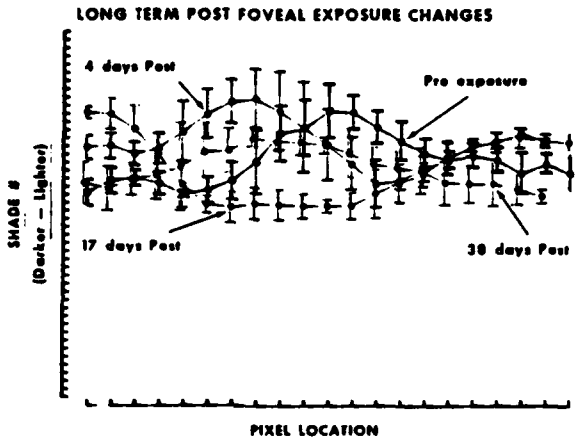


Figure 17. Long-term changes in the grey scale of the fovea following exposure to a Q-switched,Nd:YAG pulse.

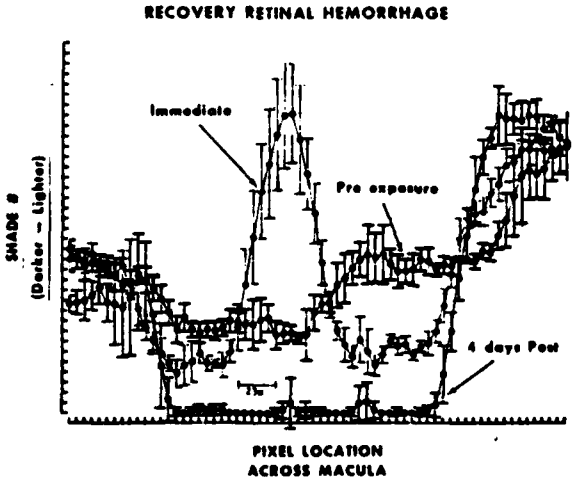


Figure 18. Grey scale analysis of a Q-switched, Nd:YAG exposure which produced a hemorrhage in the exposed macula.

Exposure of the retina to extremely intense, Q-switched pulses not only can create a visible lesion indicating destruction of retinal tissue but also can cause severe bleeding due to hemorrhaging of retinal blood vessels. Any significant retinal hemorrhaging can lead to the clouding of the ocular media which can itself lead to temporary losses in visual sensitivity. Figure 18 shows a lesion which also was accompanied by severe bleeding. The grey scale analysis of the lesion site was enhanced by the hemorrhage creating an increased lightening and darkening around the site of the lesion immediately following exposure. This enhancement was followed by a severe darkening of the entire exposed area after about 4 days which replaced the original lightened area as well as surrounding areas.

DISCUSSION

Small lesions produced by single, Q-switched pulses from a Nd:YAG laser tuned to the 532 nm line are difficult to detect both morphologically and behaviorally and seem to change over time as recovery mechanisms proceed. Unlike exposures where the exposure duration was longer (100 msec), the immediate and long-term postexposure consequences of Q-switched pulses were lesser in magnitude and more variable in nature. This result appeared regardless of the greatly increased energies densities employed in the current study as opposed to the lesser densities previously used. These results suggest that small isolated lesions within the central fovea may not totally disrupt the fine resolution capability of the fovea when single resolution, high contrast targets are used to assess visual function and the subject is given the necessary time to scan the object across the entire fovea. The use

of more complex visual targets, targets briefer in duration, and/or different contrast and spectral conditions may be important in future studies to further delineate the consequences of this type of damage.

In the past, we have examined the immediate and long-term changes in visual acuity following exposures to various wavelength CW lasers (11, 15 20). In these experiments, all exposures were made at or below the ED_{50} and the immediate behavioral consequences were dramatic - a reduction in threshold acuity by as much as 80% from the subject's pre-exposure level. While many of these changes were only transient in nature, their recovery was quite predictable and invariant across either repeated exposures or in different animals. A major difference between these studies and the current one is in the amount of tissue exposed. In previous studies we varied the diameter of the beam on the retina from > 350 microns to < 50 microns. We found in these experiments that the diameter of the incident beam directly affected the magnitude of the initial deficit without significantly altering either the likelihood of full recovery or the total time for whatever recovery was possible. It must be pointed out, however, that in these exposures the duration of exposure was quite long (100 msec) and because of continuous, involuntary eye movements, the tissue actually exposed was always significantly larger than simply the diameter of the laser beam on the retina. Since the eye is always in constant, random movements about a fixation point, this washing effect occurred regardless of beam diameter and therefore resulted in a larger area of exposure than would otherwise be expected. In the current study, however, the duration of exposure was significantly less (approximately 15 nsec) and little washing effect could be expected with such short-duration exposures. Individual laser pulses, of minimal retinal diameter, resulted in more punctate lesions of much smaller diameter than were previously produced by our other exposure paradigm. While the energies were

significantly higher and above the ED_{50}, enough remaining foveal areas were still available to resolve the targets used in the current study.

The increased variability observed in all of our animals immediately following exposure and for some time thereafter does suggest that these small lesions may have made central fixation more difficult. Initial clouding of the ocular media due to localized hemorrhages would result in a blurring of the retinal image making fine resolution difficult but not necessarily impossible in highly motivated animals such as ours. Long term, the hemorrhages should cease and media clear, but the existing small punctate lesions produced by the intense power of a Q-switched pulse could also increase the likelihood that at any given moment a small target presented for only a brief period of time may fall on an affected region making the required discrimination still difficult or impossible.

In these preliminary studies of postexposure sensitivity, chromatic acuity targets appeared to be more sensitive in assessing the long-term changes in visual functioning than did achromatic targets. This result is similar to what we observed for larger diameter exposures and should be more fully explored in future studies. Initial examination of variations in target contrast, however, had little impact on the results, although due to the nature of background, all targets employed were of relatively high contrast. In future studies we hope to test at lesser contrast levels than those currently employed.

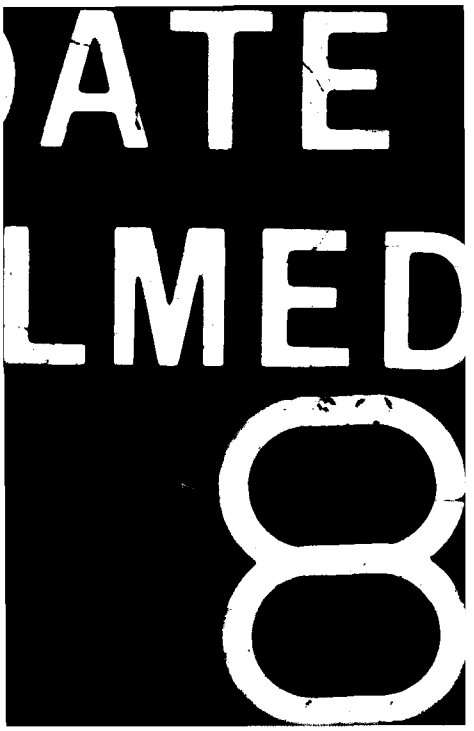
Preliminary examination of repetitive pulse exposures suggest, as might be expected, that multiple exposures are more effective in reducing visual sensitivity than is the single pulse condition. While the actual number of repetitive pulse conditions explored was quite limited, these results suggest that repetitive pulses above the ED_{50} presented within seconds, minutes, or

days of one another create multiple lesions and thereby make visual functioning much more difficult than would any single lesion. The additivity of these exposures over both time and space and the possibility of additional retinal hemorrhaging and ocular clouding has not been investigated in the current study and needs further delineation. It is the repetitive pulse condition that may more likely be the type of exposure condition found on the battlefield and the one that will create the greatest threat to continued optimal visual functioning.

The morphological interface to our behavioral data is still in its infancy. The development at LAIR of a computer image analysis of grey scale content that can be taken directly from fundus photographs of exposed retina is a positive step in combining our behavioral data with a morphological correlate. Currently, we are taking fundus photographs of our animals prior to and at intervals following exposure and these will be analyzed in terms of any changes in grey scale content across the exposure (lesion) site. Initial data incorporated into the current report suggest that this technique is quite sensitive. When necessary to increase the resolution power of the technique, it is possible to enhance the contrast of the digitized image by fast fourier analysis which will enhance the grey scale analysis. This procedure also provides for a quantitative description of previous qualitative data and this will make direct comparisons with our behavioral data easier. The initial results of grey scale analysis is consistent with our behavioral data in that the gross morphology of the fundus appeared to undergo continuous change over the course of several weeks following exposure. Our behavioral data likewise showed changes in both average acuity and in session variability as a function of time following exposure. The changes observed in the fundus over time may reflect changes in pigment migration, hemorrhages, and the presence of repair mechanisms at work. Any of these factors should, of course, effect light

absorption and visual function.

The behavioral changes associated with laser irradition continue to be an important tool in assessment of the ocular hazards of lasers. For wide-field stimulation of the retina, the changes in visual performance of an exposed organism are a good determinant for revisions in the MPE. The possibility still exists that subthreshold burn levels may produce permanent changes in visual function . This method may still be one of the most sensitive measures available since visual function and performance can be altered without obvious evidence of morphological disruptions. The examination of the effects of laser irradiation below the MPE is still given only limited attention but may be just as important as suprathreshold burn studies for the development of adequate laser ocular protection systems in the military. When smaller or more limited exposure sites and lesions are examined, the nature of the behavioral tasks becomes more critical. Measurements of spatial and spectral vision under a wider range of viewing conditions are necessary to delineate even the smallest possible disruption in the retina. While these measurements may be more time consuming, they can provide the information necessary to predict what changes in visual capabilities can be expected in persons either accidentally or intentionally exposed. Other conventional analyses may be capable of detecting a small, isolated lesion but in these types of studies the behavioral implications can only be inferred.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