RESEARCH ON THE OCULAR EFFECTS OF LASER RADIATION

Executive Summary

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NOTICES

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The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources-National Research Council.

The voluntary fully informed consent of the subjects used in this research was obtained in accordance with AFR 169-3.

The Office of Public Affairs has reviewed this report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

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Research on the Ocular Effects of Laser Radiation: Executive Summary

This Executive Summary is an overview of the research accomplishments of KRUG International Technology Services Division under contract F33615-84-C-0600 with the United States Air Force School of Aerospace Medicine, Radiation Sciences Division, Vulnerability Assessment Branch (RZV). The objective of the research was to evaluate the bioeffects of laser radiation in order to quantify threats, primarily losses of visual function (transient or permanent), which might affect performance during critical phases of military operations. The results of this research have also been applied to evaluating current laser safety standards and identifying the need for additional safety criteria.

The Executive Summary is presented in seven parts dealing with the effects of laser exposures on vision via one or more of the following approaches: electrophysiological measures of visual function degradation (Parts I and II); psychophysical measures of visual function degradation (Parts III, IV, and VI); quantitative evaluation of observable ocular damage (Part V); and predictive modeling of laser radiation interactions with the eye and with visual (cont'd.)
18. SUBJECT TERMS (Cont'd.)

Thermal model

19. ABSTRACT (Cont'd.)

Performance (Parts V - VII). Also included is an Appendix which lists the publications and presentations generated as a result of this contract.
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RESEARCH ON THE OCULAR EFFECTS OF LASER RADIATION

Executive Summary

INTRODUCTION

Under contract with the United States Air Force School of Aerospace Medicine (USAFSAM), KRUG International, Technology Services Division, has conducted research on the ocular effects of laser radiation. The specific objectives of the research have been to evaluate the bioeffects of laser radiation in order to quantify threats and to establish the characteristics needed for protective materials and equipment. The loss of useful vision, for even short periods of time during critical phases of air operations, could be catastrophic to mission completion. Thus, this research effort has been primarily concerned with describing the effects of laser exposures on visual function. The results of these studies will aid the Air Force in evaluating current laser safety standards and in identifying the need for additional safety criteria.

The Executive Summary is divided into seven parts, dealing with laser-induced visual function degradation via one or more of the following measures: electrophysiologic effects in animal subjects; psychophysical effects in human subjects; quantitative determinations of thresholds and degree of observable ocular damage in animal subjects; and predictive modeling of laser radiation interactions with the eye.

In Part I are presented the results of electrophysiologic measurements in rhesus subjects exposed to laser radiation. Visual function was assessed by the recording of the visual evoked potential (VEP) from either gold-cup scalp electrodes or bipolar electrodes implanted in the visual cortex; and of both the focal electroretinogram (ERG) and the pattern electroretinogram (PERG) from contact lens electrodes. Effects on these measures of laser lesions, ranging in severity from punctate ophthalmoscopic lesions to those producing a spreading hemorrhage, were also assessed. Evaluated, in addition, were the effects of multiple-lesion grids typical of clinical photocoagulation treatments.

In Part II are discussed the results of a feasibility study on pharmacological protection of the retina against potentially damaging laser exposures. The investigation determined the degree to which pharmacological pre-treatments could protect a model retina (a perfused rabbit eyecup preparation) agains a visible-wavelength laser. Among the pharmacological agents examined were an anti-inflammatory steroid hormone, a chelating agent, and three anti-oxidants. The measure of retinal response was the transretinal ERG elicited by a white test light.
In Part III, the effect of laser-induced veiling glare on the visibility of targets is examined. In Part III-A is discussed the visibility of heads-up display (HUD) symbology in the presence of laser glare sources. Obscuration thresholds from six human subjects were collected, and the dependence on wavelength of the glare source was determined by using five wavelengths from argon and krypton lasers. The effects on HUD symbology visibility were separated into wavelength-dependent and wavelength-independent components—the former being correlated with the wavelength dependence of human luminous efficiency, and the latter, in part, with subject age.

In Part III-B is described the obscuration of visual field resulting from laser radiation striking an aircraft canopy. Measurements were made on human subjects' ability to detect targets of varying brightness while looking through a canopy irradiated by a laser beam emanating from the opposite end of the laser range.* The size of the field of view obscured was measured as a function of laser intensity and target brightness for experiments conducted under both nighttime and daylight conditions.

In Part IV are summarized human psychophysical measurements of flashblindness recovery to moving targets. Most of what is known about flashblindness recovery times following bright flashes comes from laboratory studies employing stationary targets. This study compares flashblindness recovery times for moving (temporally modulated, spatial sine-wave gratings) and stationary gratings. Contrast sensitivity to both moving and stationary targets was measured as well.

A quantitative study of the cumulative nature of multiple-pulse or repeated retinal exposures is described in Part V. Retinal damage thresholds were collected from rhesus subjects who received multiple exposures to krypton laser radiation. The variations of multiple-pulse threshold with number of pulses, with interpulse interval, and with retinal image size were systematically examined. Experimental data from this study and other studies of multiple-pulse thresholds were compared to predicted thresholds obtained from thermal model calculations, and to the predictions of an empirical model relating multiple-pulse thresholds to the corresponding single-pulse threshold.

The progress of a newly developed image-processing facility is presented in Part VI. The image-processing facility is designed to augment the experimental psychophysical capabilities and to facilitate investigations of laser effects on aircrew performance, where concerns with complex visual tasks and stimuli are not easily related to fundamental processes. The image-processing capabilities were designed to support psychophysical experiments which bear a meaningful relationship to operational problems. The facility allows the means for creating complex images and stimuli, simulating laser-induced visual degradation and monitoring subjects' performance on complex visual tasks during and after simulated laser exposures.

*At the USAFSAM Vulnerability Assessment Branch (RZV).
Discussed in Part VII is the development of a computer model designed to predict the retinal distribution of lesions induced by multiple-pulse lasers. This preliminary version of the model considers a pilot's exposure to a multiple-pulse, doubled (532-nm) neodymium:yttrium-aluminum-garnet (Nd:YAG) laser and the distribution of retinal lesions which could result from the following potential responses to the laser: the pilot closes his eyes; the pilot foveates the laser with an acquisition saccade; the pilot executes an avoidance saccade; the pilot's eyes remain stationary relative to the laser (the beam may not be visible); and the pilot continues to track a moving object despite the laser exposures. Using data for eye movement velocities and latencies, the model predicts the probable distribution of retinal lesions as apportioned between concentric zones.

As a result of the experimental and/or theoretical research projects described in Parts I-VII, contract personnel have authored over 50 papers for publication in the open literature or for presentation at scientific conferences. A list of contract-generated publications and presentations is given in the Appendix.* Technical details of the research discussed in this Executive Summary are available in the listed references.

**PART I: VISUAL FUNCTION IN THE PRESENCE OF LASER LESIONS**

**A. Single-Pulse Exposures**

Although considerable research has been conducted on visual function after exposure to coherent and noncoherent light flashes at flashblinding intensities, only limited studies have been made of the functional effects of lesion-producing exposures, especially those producing retinal hemorrhages. This investigation examined retinal output in the presence of laser lesions which ranged in severity from non-hemorrhagic to those producing a spreading hemorrhage. Lesions were placed in the fovea, parafovea, and perifovea, in order for the effects of lesions on and off the visual axis to be studied. The subjects were five adult rhesus monkeys, without ocular abnormalities or refractive errors exceeding 1.0 spherical or cylindrical diopter. Visual function was assessed electrophysiologically by simultaneously recording the VEP and the PERG.

VEPs were recorded through bipolar electrodes implanted in the visual cortex in the foveal projection area, and at cortical locations receiving input from visual field loci of 3-4° (parafovea) and 6-8° (perifovea) eccentricity. One tip of each electrode rested on the cortical surface, while the other was 3 mm beneath. These electrodes typically responded to visual input over a 1-2° diameter receptive field. Each individual bipolar electrode therefore yielded a measure of local retinal function. Since the electrodes were so placed as to record from retinal locations about 3-4° apart, the electrode array gave an indication of the spread of the effect.

*This report does not contain any sensitive information from referenced limited distribution publications or presentations.*
if any, of a localized lesion. Lesions were placed in the receptive fields of the VEP electrodes: first, in the most peripheral location (perifovea); and then, in subsequent experimental sessions, in the more central locations (parafovea and fovea).

The PERGs were recorded with a corneal contact-lens electrode designed and manufactured in this laboratory. The electrode consisted of a gold annulus vacuum-deposited on the interior surface of the contact lens. A lead-off wire made contact with this ring through a fenestration in the lens. The PERG, which gives a good measure of the overall output of the retina, especially reflects the activity of the central 80. The PERG was used as an indicator of the overall effect of the laser insult on macular function.

Experiments were conducted while the animals were maintained at a surgical plane of anesthesia with sodium barbiturate. The animals viewed a CRT on which counterphased, square-wave luminance gratings were presented. These visual stimuli elicited the VEPs and PERGs, which were then amplified and digitized by a MicroVAX-based data acquisition and display system. The baseline responses of the animals were characterized before the laser exposures. On the day that a lesion was to be made, VEPs and PERGs were recorded simultaneously before, during, and after the lesion placement. Retinal lesions were produced by a focused beam from a doubled, Q-switched Nd:YAG laser (532 nm), with a 15-ns pulsewidth.

The intensity of the laser exposures ranged from 10- to 92-μJ total intraocular energy (50 to 460 times the MPE). Generally, exposures that exceeded 40 μJ produced a hemorrhage; but the severity of the resulting hemorrhage varied considerably, depending on lesion location and individual susceptibility.

For those exposures depositing less than 40 μJ, the resulting lesions ranged from a minimal lesion to a local hemorrhage (no apparent spreading of blood away from lesion site). One exposure depositing 40 μJ in the para-macular region resulted in a spreading hemorrhage into the fovea. More intense exposures generally produced contained hemorrhages (bleeding entirely sub- or intra-retinal), or spreading hemorrhages (frank bleeding into the vitreous and away from the lesion site).

When an exposure producing either non-hemorrhagic or local hemorrhagic lesions was made in the fovea, the PERG exhibited a rapid decline in amplitude, and then recovered at a rather monotonic rate within one minute to the pre-flash level. When the laser exposure occurred at more eccentric sites, the PERG was much less affected. VEPs recorded from electrodes whose receptive fields lay under the site of laser impact were suppressed for up to 60 s. When the receptive field was 40 or more from the exposure site, however, the VEP was suppressed for only 1-5 s. These transient effects probably reflect the flashblindness associated with the exposures. A notable finding regarding lesions with only localized hemorrhages was that such lesions failed to produce any permanent losses in either the PERG or the VEP, even in the VEP recorded from the electrode whose receptive field contained the respective lesions.
The results obtained after the production of spreading hemorrhagic lesions were quite different. Two monkeys sustained severe foveal and parafoveal hemorrhagic lesions. In both cases, the VEP from the lesion site was abolished for periods ranging from several days to several weeks. The PERG was reduced in amplitude. Only partial recovery of function occurred, and may have been correlated with the resorption of the retinal hemorrhage. Activity recorded from electrodes other than those whose receptive field overlapped the foveal lesion indicated that the effect of such lesions was attenuated by about 50% at a distance of 40. At a displacement of 6-80 from the lesion site, an essentially normal VEP was recorded.

The loss of foveal function appears to be correlated with the severity of the foveal lesion. Non-hemorrhagic lesions, or those producing only localized hemorrhages, transiently suppress foveal output for periods up to 1 min through flashblindness effects. Consequently, the spread-of-effect of laser exposures of this magnitude can be predicted in the same manner as strictly flashblinding exposures. In contrast, lesions producing hemorrhages spreading into the vitreous or into the retina (e.g., along the fiber tracts of Henle leading out of the fovea) can result in permanent losses of function. During the first several days after these laser exposures, the loss can be total, at least as far as can be assessed by electrophysiological measures. Although hemorrhage-producing exposures do not appear to cause a global spreading depression that markedly supresses distant retinal function, the retina immediately adjacent to the limits of the lesion and its hemorrhage may be partially affected. This zone of intermediate impairment extends out at least 40 (~1000 μm) in the monkey. Thus, lesions more than 40 off the visual axis, that do not produce a spreading hemorrhage, would not be expected to produce permanent losses in foveal function.

B. Multiple-Pulse Exposures

Currently, laser photocoagulation of the retina is a common treatment modality for various retinopathies. While beneficial effects of the laser treatments have been demonstrated, particularly in stabilization of diabetic retinopathy, visual acuity in photocoagulated eyes often is unimproved. Visual acuity immediately after photocoagulation may even be less than that of untreated eyes, according to several clinical studies. Over the long term, however, the acuity of the untreated eyes generally becomes worse. This worsening probably reflects the progress of the underlying disease process. The initial visual loss in the treated group, therefore, may reflect the effect of the laser exposure itself.

In order to study the effects not only of photocoagulation without the complication of additional retinal pathology, but also of off-axis (paramacular) laser lesions on central retinal function, we examined the effects of two types of laser photocoagulation protocols on retinal function in normal rhesus monkey eyes. The VEP and the PERG were used to assess retinal function after the laser exposures.

Because of its widespread clinical application, we examined the retinal effects of pan-retinal photocoagulation (PRP), which may comprise as many as 3,000 laser burns placed outside the central venous arcade; i.e., covering
the retina, starting at about 20° from the foveola and continuing out to the retinal periphery. We also examined the effects of so-called "macular grid" photocoagulation, experimentally used to treat diffuse macular edema. This procedure consisted of a grid of 56 burns, 200 μm or less in diameter, spaced one burn diameter apart, with no lesion placed within 500 μm of the foveola. Only six lesions were allowed over the papillo-macular fiber bundle.

The adult male rhesus subjects received thorough ocular examinations, including baseline records of VEPs, flash ERGs, and PERGs. Each of two animals received PRP therapy in one eye: one animal had 459, and one had 620 500-μm-diameter lesions placed in the retinal periphery. Each of two other animals received, in one eye, macular grid photocoagulation (as just described). Photocoagulations were performed with the 514.5-nm output of an ophthalmic, argon laser. Retinal function in each animal was determined electrophysiologically before and after laser treatment, with periodic follow-up testing for over 8 months after photocoagulation.

PERGs and VEPs were recorded as described in Part I-A. Physiological signals were subjected to discrete Fourier analysis; and the rms voltages of the fundamental through the fourth harmonic components of the stimulus temporal frequency were extracted. These amplitudes were used to construct tuning curves for stimulus spatial frequency, temporal frequency, and contrast dependence. Focal ERGs and dark-adapted flash ERGs completed the electrophysiological battery of tests.

Electrophysiological evaluation commenced the day after laser exposures for animals receiving the macular grid photocoagulation, and 3 days after treatment for those receiving PRP. PRP did not produce any long-term changes in central retinal function, as manifested in the shape of the VEP and PERG response functions. After a transient drop in response amplitude, the VEP recovered and was then stable over time. The amplitude of the PERG recorded from one animal had increased at 2 months after PRP, but the significance of this increase is not yet known. The stable shape of the stimulus-response curves throughout the post-treatment course is probably a more reliable indicator of normal retinal function. The focal ERG was unaffected by PRP, but the dark-adapted flash ERG was reduced to about half amplitude. Partial recovery of the flash ERG amplitude occurred over the course of 2 months.

In contrast, the animals receiving the macular grid photocoagulation exhibited VEPs and PERGs that were both depressed in amplitude and changed in tuning characteristics, although flash and focal ERGs were not affected. The responses in these animals followed a variable recovery. During the first two months after the treatment, the response amplitudes of both VEP and PERG began to recover, particularly for spatial frequencies less than 3 cpd. One animal continued to recover more or less to normal. In the other "grid" animal, however, at about 3 months post-photocoagulation, central retinal function deteriorated so that the VEP and PERG showed a differential loss in response to spatial frequencies above 3 cpd. No obvious explanation for this change has become apparent. The fundus developed pigmentary changes under the site of the laser lesions; but marked hyperpigmentation was seen in the other animal, without comparable degeneration.
of retinal responses. Refractive changes in the ocular media have been ruled out. The difference in the two animals' responses may be due to the spacing between the burns comprising the grid. By means of fluorescein angiography, the lesions were visualized and the inter-lesion spacing was determined. The average spacing between lesions in the animal experiencing loss in visual acuity proved to be 62% less than in the other animal.

The present study indicates that parafoveal grid coagulation can, in some cases, permanently reduce central retinal function. The permanent nature of these changes rules out transient mechanisms, such as spreading depression or lateral neural effects. The degradation of foveal function must be due to structural changes in the retina. In the case of the animal with the "tight" macular grid, enough damage may have been done to the nerve fibers and receptor axons (fibers of Henle) to functionally disconnect the fovea. Because of these observations, future investigations involving lesion-producing laser exposures in the parafovea and fovea should determine if functional effects resulting from these lesions are wavelength-dependent in a manner consistent with the topographical variation of the retinal and choroidal absorption coefficients.

PART II: PHARMACOLOGICAL PROTECTION OF THE RETINA AGAINST DAMAGING LASER EXPOSURES

Light damage to the eye, whether produced by laser exposures or by non-coherent sources, occurs through at least three mechanisms--thermal, photochemical, or mechanical (photoacoustic). These processes may act singly or in combination, depending on the intensity, wavelength, and temporal parameters of the damaging light exposure. Currently, most modalities of protection against laser threats involve physical barriers (e.g., filters) to block or attenuate the laser energy entering the eye. Increasing sophistication and flexibility of laser systems, however, make infeasible the provision of complete eye protection with a transmission barrier alone. It may be possible to provide enhanced protection by blocking some of the light-damage mechanisms through pharmacological means. While purely mechanical damage will probably prove to be refractory to pharmacological treatments, the other two mechanisms (thermal and photochemical) might respond to pharmacological or biochemical intervention.

The present project was designed to examine the feasibility of protecting the retina from the damaging effects of a laser exposure with pharmacological pretreatments. Five agents were tested for protective activity. These agents included: three anti-oxidants (ascorbic acid, d-alpha-tocopherol, and 3-aminotyrosine); a chelator (EGTA); and an anti-inflammatory steroid hormone (dexamethasone). The experiments were conducted in the perfused, isolated rabbit eyecup. This system was selected because it was a mammalian retina which could be maintained in vitro for many hours while being treated with pharmacological agents in the perfusion bath. Retinal function was monitored via the ERG. Laser exposures were made with the 530.9-nm output of a krypton continuous-wave (cw) laser, with exposure durations ranging from 0.5 s up to several seconds. The protection conferred by the various pharmacological treatments was measured by the
degree to which they prevented a change in the ERG stimulus-response curve after the laser exposure.

After the eyecup had dark adapted and its baseline intensity-response curve had been measured, the eyecup either received a laser exposure (laser/without protective agent), or was treated with the protective agent and then exposed (laser/with protective agent). In the latter case, the agent was introduced into the perfusion fluid and allowed to circulate over the retina for 20-30 min. None of the five tested agents had deleterious effects on retinal response. In the absence of any protective treatments, single laser exposures at 1-3 times the ED50 intensity produced an average decrement of 42% relative to baseline in the ERG intensity-response function. With low-intensity stimuli, the post-laser ERG amplitude was 38% of control (62% reduction), but, with brighter stimuli, was 74% of control (26% reduction). These data provided the basis for comparison to the ERG decrement in laser-exposed, treated retinas.

Intensity-response curves were obtained from retinas that had been treated for at least 20 min with the protective agent, and were then exposed to the krypton laser radiation at the criterion intensity. Pretreating the retinas with any of the following agents—ascorbate (78-88 μg/ml), dexamethasone (8-9 μg/ml), or d-alpha-tocopherol (0.06-0.13 I.U./ml)—did not afford any apparent protective effect against laser insult at any stimulus intensity. EGTA (38 μg/ml) afforded marginal protection (with borderline statistical significance) at two intermediate stimulus intensities. The experimental anti-oxidant, 3-aminotyrosine (67-135 μg/ml), provided up to 90% protection at the four highest stimulus intensities after criterion laser exposure. The effect of combining two of the agents (dexamethasone and EGTA) was also tested in two experiments; but no additional protective effect was observed.

By fitting a regression curve to the post-flash data, both in the presence and absence of protective agents, the time to recover half-maximal ERG amplitude was obtained. With the exception of those retinas treated with ascorbate, the recovery rates of treated and untreated retinas were very similar—all required about 3 min after laser exposure to reach 50% recovery. After ascorbate treatment, the time to half-maximal recovery was delayed to nearly 6 min.

The ERG is an evoked potential reflecting activity over the entire stimulated portion of retina. In this investigation, the area of retina actually exposed to the laser represented less than 0.5% of the total area of the stimulated retina in the perfusion chamber, yet the ERG amplitude was typically reduced over 50%. This reduction indicated that the laser exposure triggered some global process which affected the ERG. According to considerable evidence in the biological literature, light and chemical stress initiate peroxidation reactions in the retina with damaging effects.

The decline in the ERG amplitude after acute laser injury may result from widespread peroxidation reactions, or from loss of RPE integrity. The efficacy of anti-oxidant therapies reported here and in other studies points to the former mechanism. Too, the rapid onset of the ERG deterioration is
consistent with a biochemical involvement; for other mechanisms proposed for light damage often require hours or days to develop. While future investigations should incorporate histological and biochemical probes to determine the actual mechanisms involved in light damage, the present study has indicated that a pharmacological treatment can provide a significant degree of prophylaxis against the acute effects of at least some types of laser exposures.

PART III: GLARE INDUCED BY CONTINUOUS-WAVE LASER RADIATION

A. The Effect of Laser Glare Source Wavelength on the Visibility of HUD Symbology

Among the many external hazards and stressors that pilots may encounter are laser beams of high intensity. At long range, cw lasers can create significant glare that can obscure a pilot's instruments and interfere with the mission. The purpose of this study is to investigate, under conditions similar to a pilot's operating environment, one aspect of glare produced by lasers.

An important factor in the analysis of glare is the point-spread function (PSF) of the human eye. Every optical system has a characteristic PSF which indicates the way that the system images the light from an ideal point source. In the case of the human eye, the PSF may be generalized to include intraocular scatter and spatial vision effects, resulting in what may be called a "glare-spread function" (GSF). These functions may be used to predict visual sensitivity to any target by means of the convolution theorem and the equivalent background assumption.

A recent report* has tested whether wavelength must be included as a parameter of the GSF because of differential scattering by the ocular media. The authors of the report concluded that no wavelength effects were due to scatter, and that the GSF need only include a term for source luminous flux density at the cornea. However, these authors used spatially extended sources and not point sources in their study. We extended the results of that paper in an increment threshold experiment that employed intense, monochromatic point sources (cw argon and krypton lasers) to produce eye-safe veiling glare. Our results are consistent with those of the previously published report.

Six volunteers took part in the study in accordance with a human use protocol. Their vision was examined by Air Force ophthalmologists before and after experimentation. All had 6/6 or corrected 6/6 visual acuity. Five subjects were male, and one was female. They ranged in age from 27 to 47 years, with a mean of 37.2 years.

A frame apparatus was constructed as a cockpit mockup and covered by an aircraft canopy. A pre-production HUD, manufactured by General Dynamics, was placed within the frame in proper relation to the canopy. Experimental

Subjects were seated on an adjustable aircraft seat so that their heads were at the design eye position of the HUD. In this position, the subjects looked through the HUD and saw its symbology superimposed on their fields of view.

Subjects were required to detect a symbol produced by the heads-up display. A glare source was produced by routing laser light through a fiber-optic cable, and by having the subjects view the output of the fiber-optic cable from a distance of 3 meters. The fiber-optic cable removed the beam collimation and caused it to spread at about a 30-deg angle. The output of the fiber-optic cable subtended less than a minute in arc; and so its image (and hence, the image of the glare source) was limited by the GSF of the eye. The fiber optic was placed so that its output appeared at the same point in the visual field as did the HUD symbol. Two lasers and five wavelengths were used (488 and 514 nm from argon; 531, 568, and 647 nm from krypton). Both lasers were run with an output of 1 W for each wavelength. The HUD color was broad-band green.

The threshold laser irradiance at which the glare obscured the HUD symbol was measured for a fixed symbol luminance of 175 cd/m². For each wavelength, 36 thresholds were measured, and were collected in three sessions of 12 thresholds per session.

The HUD symbology was obscured by low-power, cw lasers when the line of sight to the laser was the same as that to the symbology. Threshold irradiances were less than 5% of the MPE for every wavelength. A wavelength dependence exists for radiometric thresholds, with minimum thresholds in the green and maximum thresholds in the red (sensitivity relations are inverse with threshold). The ratio of this difference can be as high as 50 to 1, and averages 19 to 1. When the inherent luminous efficiency as a function of wavelength is factored out by plotting thresholds in luminance units, the ratio of threshold differences is reduced to an average factor of 4.5, and is statistically significant for only one wavelength. None of the wavelengths differ significantly from the across-wavelength grand mean.

Large individual differences are present in sensitivity to glare, but most of these differences are independent of wavelength. The cause of the wavelength-independent variability is not known; but a significant rank order negative correlation exists between subject age and across-wavelength threshold for wavelengths other than 647 nm. Age effects have been demonstrated previously in glare studies. The correlation suggests that age effects should be investigated further.

B. Laser Range Measurements of Veiling Glare

"Veiling glare," "veiling luminance," and "disability glare" are terms used synonymously to describe the loss of visual detectability of objects when a bright light source is present in the visual field. This is the effect experienced in trying to see objects near a bright source, such as the sun, or when confronted by oncoming headlights at night. Nighttime irradiation of an aircraft canopy with low laser energy levels (well below maximum permissible exposure limits) can produce a veiling glare which causes significant visual impairment.
The glare effect is due to a scattering of light both inside and outside the eye. The glare reduces vision most for targets which are the closest in the visual field to the glare source. The scattered light affects vision by reducing the image contrast in the eye, and by reducing visual sensitivity to light by the normal physiological process of light adaptation. The size of the visual field affected by laser glare depends on a number of factors, including the intensity of the glare source, the size and brightness of the target, and the target's brightness contrast with respect to its surrounding or background. Also critical is the amount of forward light scattering in the atmosphere, the windscreen, and the eye.

Veiling glare is distinguished from "discomfort glare," which is the sensation resulting from the strong reflex constriction of the eye's pupil in response to a bright light.

During the contract period, behavioral studies with volunteer subjects were begun at the USAFSAM/RZV laser range to measure the extent of the visual field obscured by the veiling glare produced by direct (intrabeam) viewing of a laser source. The purpose of the experiments was to estimate the ability of a laser to hide or obscure visual targets. For the operational conditions of interest, it was important to measure the glare effect when the laser light was scattered by the atmosphere, an aircraft canopy, and the eye.

The experiments were performed on an outdoor laser range which permitted the laser beam to be propagated over a 1.5-km path. The psychophysical technique used to measure glare was a variant of the standard clinical kinetic perimetry used for measuring visual fields. Subjects viewed an illuminated visual "target" while sitting behind an aircraft canopy irradiated by the laser beam. At the range distance, 1.5 km, the beam diameter was ~1 m, so the entire canopy was irradiated.

The target moved back and forth across the subjects' field of view. The subjects' task was to press a hand-held button when the target disappeared from view, and to release the button when the target reappeared. From the data of the time during which the target was invisible, the angular size of the visual field obscured by the laser could be calculated for the specified target distance and velocity.

The effects of laser irradiance and target brightness were measured in a series of day and night trials for several subjects. All trials were performed at eye-safe levels of laser exposure, with the expectation that the results could also be used to predict effects at higher levels of laser exposure.

The results showed that the size of the obscured field of view increased with increasing laser intensity and decreasing target brightness. The size of the effects varied from subject to subject.

The results will be used to make laser vulnerability assessments, and will be compared with the results of ongoing indoor studies of glare (refer to Part III-A) which do not involve atmospheric effects.
PART IV: FLASHBLINDNESS RECOVERY TO MOVING SPATIAL SINE-WAVE GRATINGS

Brief, high-intensity flashes can produce a temporary impairment in the ability to detect visual targets (flashblindness). Although vision rapidly recovers from a non-damaging flash, even a short period of blindness could be crucial in a combat environment. Much of what is known about recovery from bright flashes comes from laboratory studies that employ stationary targets. One potential limitation of these studies is that, in operational settings, targets of interest may be moving.

A basic finding in studies of flashblindness is that recovery time follows the contrast sensitivity function. Recovery is faster for medium-sized targets (i.e., middle spatial frequencies) than for either small or large targets (i.e., low or high spatial frequencies). Since recovery from flashblindness is dependent on contrast sensitivity, motion might influence recovery—because motion also influences sensitivity.

This proposition was tested by comparing flashblindness recovery times for moving and stationary gratings to determine if flashblindness recovery to moving gratings could be predicted from contrast sensitivity measures of temporally modulated (i.e., moving) targets. If target motion decreases sensitivity, then recovery from flashblindness to a moving target should take longer than to a stationary one. Similarly, if target motion increases sensitivity, then a moving target should decrease the flashblindness recovery time. Because the relationship between temporal modulation and spatial frequency is complex and not fully understood, experiments measured both flashblindness recovery and contrast sensitivity to moving and stationary targets.

Recovery time from flashblindness was measured using two spatial and two temporal modulation frequencies. The two spatial frequencies were 1 and 12 cpd. Motion was achieved by square-wave counterphasing the grating at either 0 Hz (stationary grating) or 3 Hz. Square-wave counterphasing alternately switched the luminance of adjacent bars in the grating, and thereby induced a powerful apparent motion percept in which the grating appeared to move in a direction orthogonal to the orientation of the bars. All gratings were presented at a low contrast level (10%) around a low photopic mean luminance of 10 cd/m².

Each of two observers received one flash per trial from a filtered xenon arc lamp. The 6° diameter flash, presented in Maxwellian view, was 7.2 log Troland-s in luminous energy, and 200 ms in duration, and centered on the fovea of the observer's right eye. After a flash presentation, the observer's task was to determine the orientation (horizontal or vertical) of a grating displayed on a green phosphor video monitor.

The results showed that motion influenced recovery time, but the effect was not strong. Both observers showed 20% faster recovery when the low spatial frequency grating was moving rather than stationary. However, this improvement was statistically significant for only one observer. Motion did not influence recovery time to the high spatial frequency target.
As expected, contrast sensitivity measures were consistent with the recovery data. The observer who demonstrated the statistically significant enhanced recovery to the moving, low spatial frequency grating was also more sensitive to this stimulus, as compared with the stationary grating. In contrast, no differential sensitivity to motion was found for the observer who showed no motion effect to flashblindness recovery. Finally, both observers showed little change in their sensitivity to moving high spatial frequency gratings, an effect that paralleled their recovery times to this stimulus.

Although the effect of motion on recovery time was small, these results should not be construed as meaning that motion is a trivial factor in flashblindness recovery. Rather, motion is expected to influence flashblindness recovery when the motion induces a substantial change in sensitivity, relative to a stationary target. Since the stimulus conditions created a negligible sensitivity difference between moving and static targets, the results did not disprove the hypothesis. A more definitive test of the hypothesis would compare recovery functions of stimuli demonstrating a marked motion effect. An advantage for motion might be expected when the target must be detected against a complex background rather than a uniform background, such as the one employed in this study.

PART V: ADDITIVITY OF RETINAL DAMAGE FOR MULTIPLE-PULSE LASER EXPOSURES

Repetitively pulsed laser sources with pulse-repetition frequencies (PRFs) ranging from 10 Hz to greater than 1 MHz are becoming relatively commonplace in military applications. With such high PRF systems, accidental or deliberate exposures of personnel to laser beams could result in a few, or many, pulses striking the retina with each exposure episode. Further, as long as the mission requires that military personnel remain in an environment where they continue to be vulnerable to laser radiation, additional exposure episodes may occur. Thus, significance is attached to evaluating potential ocular effects of laser radiation, in order to achieve an understanding of the cumulative effects of repeated exposures.

The objective of this research effort is to provide a quantitative basis for evaluating the cumulative nature of multiple-pulse or repeated retinal exposures for the various exposure conditions which may be anticipated with existing laser systems. The effort is concerned with exposure conditions where laser-induced retinal damage would result from a thermal damage mechanism—and not with ultrashort pulse cases where photoacoustic or mechanical shock mechanisms may be dominant, nor with ultraviolet or long (>1-s) blue-light exposures where photochemical mechanisms may prevail. To this end, three sets of experiments were conducted to determine: (1) the variation of multiple-pulse threshold with the interval between pulses; (2) the variation of threshold with number of pulses in the exposure train when the PRF is held constant; and (3) the variation of threshold with the retinal image size, when both the number of pulses and the PRF are invariant.

For all three sets of experiments, the wavelength used was the 647-nm output from a krypton laser, and the pulsewidth was 100 ms. For experiment (1), the interpulse interval was varied over seven values from 10 ms to
24 hr, and the threshold for each case was determined for 2-pulse exposures. For experiment (2), the number of pulses varied from 1 to 50, while the PRF was kept at 6.25 Hz. For experiment (3), PRF was again held at 6.25 Hz; and the variation of threshold with retinal image size was examined for both single-pulse and 2-pulse exposures.

In addition to the experimental threshold determinations, thermal model predictions were generated for the exposure conditions associated with each of the experiments just mentioned. Tripartite comparisons were then conducted among the experimental data, the thermal model predictions, and the predictions of a previously proposed empirical model for multiple-pulse threshold as a function of the corresponding single-pulse threshold. In general, both the thermal model and the empirical model predictions provided acceptable fits to the experimental threshold data generated by this study and other studies.

The following conclusions were drawn from the experimental data and the model predictions:

1. The threshold for an exposure to a periodic train of \( n \) identical pulses \((ED_{50})\) is related, by a function of the number of pulses, to the threshold for a single pulse in that train \((ED_{50})\)--but is independent of PRF and pulse train length. This observation is in general accordance with both the thermal model predictions and the empirical model. The functional dependence is expressed by:

\[
ED_{50}^n = (n)^x ED_{50},
\]

in which \( x \) is equal to 0.75 according to the empirical model, and equal to \(-0.90\) according to thermal model predictions. Experimental multiple-pulse threshold data from several sources are best fitted by Equation 1 with values of \( x \) ranging from 0.70 to 0.92.

2. The additivity of multiple pulses is quantitatively similar for collimated and expanded laser beams incident at the cornea.

3. The repair or recovery of laser-induced reversible retinal damage (i.e., retinal disruptions which are subthreshold with respect to the ophthalmoscopic lesion endpoint) is slow, having a time constant of the order of days. Thus, the cumulative nature of multiple-pulse or repeated exposures within a 24-hr period is relatively unaffected by the ongoing repair process; and only when repeated daily exposures are of concern does the repair process become a factor.

4. Thermal model calculations indicate a divergence between its predictions and those of the empirical model when PRF exceeds 1 kHz. Thus, under high PRF conditions, the simple empirical predictor for multiple-pulse thresholds might yield a poor estimate of threshold and, thereby, compromise safety considerations. Thermal model calculations and comparisons to experimental threshold data for high PRF lasers are continuing.
PART VI: IMAGE-PROCESSING LABORATORY: SIMULATING LASER BIOEFFECTS, CREATING COMPLEX STIMULI, AND SUPPORTING PSYCHOPHYSICS EXPERIMENTS

Modern psychophysical experiments rely on precisely calibrated visual stimuli. Many of these stimuli are simple patterns, such as spots or gratings, that probe fundamental visual function. Investigators of laser effects on aircrew performance are concerned with complex visual tasks and stimuli that are not easily related to fundamental processes. The image-processing facility, developed as part of the contract effort, supplies stimuli that are complex and yet have precise mathematical descriptions. With such stimuli, quantitative psychophysical experiments can be designed that bear a meaningful relationship to operational problems. This facility supports creating and filtering targets, embedding such targets in real world scenes, and tracking experimental subjects' responses to them. Simulations have also been implemented in order to assess the effects of flashblindness on complex visual tasks. The objective is to produce whatever images are necessary for controlled, mission-relevant psychophysical experiments. Using a Digital Equipment Corporation MicroVAX computer and a Parallax frame buffer, the image-processing laboratory has developed capabilities which support this objective.

Software written in-house was combined with purchased software packages to create a user interface and a library of image-processing functions. The HIPS image-processing package was purchased from New York University. That package consists of a number of standard image-processing utilities and source code (written in the C programming language). A second software package, UNITY, was purchased to provide the user with a UNIX operating environment (required by HIPS) running as a VMS job. UNITY also includes a C compiler. Software developed in-house was integrated with that provided by HIPS and modified HIPS programs to produce a customized environment. HIPS file formats and operations were integrated with operations performed by the Parallax frame buffer via a driver program written for the Parallax. A user interface program was also written that provided the user with a set of menus for operating on images. The result of these software efforts is that images can be acquired, manipulated, displayed, and put into experimental procedures. They are easy to use, and can be exported to other machines.

Specific accomplishments include:

Software was written to digitize images acquired with a video camera and a Parallax frame buffer.

Software written in-house can be used to display complex images.

Standard image-processing operations have been performed, such as 2-D Fourier analysis, Fourier filtering, convolution, and image reduction or expansion. Hard-copy images have been generated, text added, and sequences of images ("movies") produced. Pan, tilt, and zoom display modes have been added with software developed in-house.
Software written in-house was used to add HUD symbology to digitized aerial photographs. This symbology will be used in future psychophysical experiments. The symbology stays centered as the image is moved, and so simulates a pilot's-eye view.

Simulations have been produced of flashblinding laser exposures. The simulated flashes reduced contrast across the scene and decayed with the same time course as an actual flash.

Finally, Gabor stimuli have been embedded in complex digitized scenes. A Gabor stimulus is a bit of sinusoidal grating in a Gaussian window. It also is modulated slowly with a smooth Gaussian time course. The Gabor stimulus is an important psychophysical probe stimulus, because it has a definite location and spatial frequency content. The local, point-to-point contrast is easily calculated, but is dependent on the scene content. Thus, a scene with an embedded Gabor represents a complex stimulus which has a precise mathematical description.

PART VII: A PRELIMINARY MODEL OF THE RETINAL DISTRIBUTION OF LESIONS INDUCED BY MULTIPLE-PULSE LASERS

Multiple-pulse lasers generating high peak power levels are becoming widely deployed in military operations, increasing the aircrew's risk of ocular damage. One implication of this development is that eye movements become a relevant variable in the damage potential equation. The moving eye will influence the distribution of the laser pulses on the retina. Thus, the aircrew's reaction must now be considered in models that attempt to predict visual loss from laser exposures.

This study devised a computer simulation to analyze the interplay between a laser and a pilot, in order to estimate the laser's potential threat to vision. Specifically, a computer simulation was developed to estimate the distribution of retinal lesions resulting from exposure to a repetitively pulsed laser, while a pilot engaged in various visual tasks. These visual tasks require specific eye and head movements which would, in turn, influence the number and distribution of lesions delivered to the retina.

Five different eye movement responses or scenarios were considered in the model. In three scenarios, the assumption was that the pilot saw and responded to the laser. These scenarios were: (1) The pilot closed his eyes in response to the laser; (2) the pilot foveated the laser with an acquisition saccade; and (3) the pilot looked away from the laser by executing an avoidance saccade. In scenarios (4) and (5), it was assumed that the pilot did not respond to the laser, but continued to perform the ongoing visual task (the beam may or may not be a visible wavelength). These scenarios included: (4) the pilot's eyes were stationary relative to the laser throughout the exposure period; and (5) the pilot tracked a moving object during the laser exposure.
In all of the scenarios, the pilot was assumed to be exposed to a Nd:YAG laser with a 532-nm wavelength. The laser generated 1-s trains of 10-\(\mu\)s pulses with PRF equal to 5, 15, or 30 Hz. The beam incident at the cornea was either coincident with the visual axis, or 10\(^\circ\), 20\(^\circ\), or 30\(^\circ\) off axis. A further assumption was that on-axis and off-axis exposures required the same amount of energy to produce a lesion.

The simulation output described the probable distribution of lesions delivered to the retina for each combination of PRF and beam eccentricity. For purposes of describing the lesion pattern, the retina was divided into four concentric zones or rings: The first zone, representing Snellen acuity of at least 20/20, was a circular area 0.40 in radius measured from the foveal center. The other three zones comprised annular rings concentric with the first zone, had outside radii of 10, 20, and 50, and supported minimum acuities of 20/30, 20/40, and 20/80, respectively. The region extending beyond 50\(^\circ\) was called the extra-macular region, and supported less than 20/80 acuity levels. The model estimated the number of laser pulses falling within each of these zones as well as other parameters. For instance, the outputs of the tracking and saccadic eye movement scenarios listed the separation distance between lesions on the retina, and the number of pulses delivered before the pilot could respond. A description of the results by scenario is presented below.

Closing the eyes in response to the laser proved to be an effective means of minimizing retinal damage. By closing his eyes, the pilot could avoid 80-87% of the laser pulses. Although the reaction time of a lid closure increases with beam eccentricity, the longer reaction time for eccentric beam angles added only a small number of lesions to the total.

In the avoidance scenario, the pilot attempted to avoid the laser beam by executing a combined saccade and head movement. The eye movement directed the laser beam away from the fovea. For on-axis viewing of the laser, the avoidance saccade was effective in displacing 60-77% of the laser pulses away from the fovea (Zone 1). Because of the high velocity of the gaze displacement, the residual exposures were displaced at least 120\(^\circ\) from the fovea, affecting acuity levels less than 20/80.

When the eyes are held steady, as when fixating an object, the retinal lesions would be expected to have a restricted distribution. Despite steady fixation, the laser image moves on the retina because the eye is never completely still. Estimates of the dispersion of the lesions due to fixational eye movements were computed.

Other responses tended to increase the risk of eye injury. Saccade latency and velocity were relevant factors in determining the distribution of lesions for a saccade that brought the laser beam toward the fovea. For off-axis beam angles, 30-40% of the exposures were delivered before an acquisition saccade was initiated. However, the saccade was effective in causing the remaining exposures to fall on the fovea (Zone 1). Between 40% and 67% of the total was delivered there. As beam eccentricity increased, fewer of the exposures fell on the central fovea, and more fell in the outer zones.
The tracking scenario yielded a different pattern of retinal lesions. In this scenario, the pilot tracked an object moving at a constant velocity of 1, 5, 15, or 30° per second. It was assumed that the eye movement direction moved the laser beam toward the fovea. Nevertheless, the majority of lesions fell in the extra-macular region under most conditions of beam eccentricity, repetition rate, and tracking velocity, thereby affecting visual acuities of 20/80 or less. Only when the beam was located initially on the visual axis did a substantial number of exposures fall in the first two zones, thus affecting acuity levels of 20/30 and better.

At this stage of development, the simulation predicts the distribution of lesions on the retina for a given set of eye movement responses. In order to assess more quantitatively the degree of visual loss associated with these responses, however, lesion size must be incorporated into the model. The size of a lesion from a laser pulse depends on a number of factors—including wavelength, pulsewidth, pulse energy, angle of the incident beam, and beam divergence—as well as on the lesion threshold of the retinal patch irradiated. The next phase of this simulation will incorporate these factors by introducing a thermal model that provides quantitative information regarding the extent of retinal damage from laser exposures.
APPENDIX

PUBLICATIONS AND PRESENTATIONS*


*Arranged in the order in which they were submitted to the Air Force as contract deliverables.


38. Glickman, R.D. Activity of retinal ganglion cells following intense, nanosecond laser flashes. Accepted for publication in Clin Vis Sci.


47. Glickman, R.D. Retinal function in the presence of multiple laser lesions. Submitted as USAFSAM-TR.


