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CORNEAL DAMAGE THRESHOLDS FOR HYDROGEN FLUORIDE AND DEUTERIUM FLUORIDE CHEMICAL LASERS

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A series of biomedical experiments was performed by the USAF School of Aerospace Medicine personnel using the Aerospace Corporation HF/DF chemical lasers to establish corneal damage threshold levels. Threshold levels for visible corneal damage to the rhesus monkey eye due to exposure to HF and DF wavelengths were determined for exposure times of about 10^{-7}, 10^{-2}, 2.5×10^{-2}, 10^{-1} and 5×10^{-1} sec duration. The DF corneal damage thresholds are higher than the HF thresholds for all conditions tested. Resultant

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50%-probability-of-damage values (ED_{50}) for pulsed and CW HF and DF lasers, having specified spectral and pulse characteristics, are expressed with theoretical and safety implications.

NOTICES

This final report was submitted by personnel of the Laser Effects Branch, Radiobiology Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 6301-05-28. The work was performed in the Aerodynamics and Propulsion Research Laboratory, Aerospace Corporation, El Segundo, California, by personnel of the Laser Effects Branch.

The animals involved in this study were maintained and used in accordance with the Animal Welfare Act of 1970 and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences - National Research Council.

This technical report has been reviewed and is approved for publication.

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PREFACE

The authors acknowledge the personnel of the Laser Effects Branch, Radiobiology Division, for their support of the field team at Aerospace Corporation. Special mention is given to Captain Peter C. Laudieri, Technical Sergeant Ralph G. Keller, and Staff Sergeant Carroll W. Houser for their support in physics, electronics, animal preparations and in the animal holding facilities while at Aerospace Corporation.

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Special thanks are extended to the professional, technical, administrative, and support personnel of Aerospace Corporation for their many services performed to complete this project.

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CORNEAL DAMAGE THRESHOLDS FOR HYDROGEN FLUORIDE AND DEUTERIUM FLUORIDE CHEMICAL LASERS

INTRODUCTION

Coherent laser radiation in the near infrared and visible region of the spectrum is capable of producing irreversible injury to the retina (1, 2, 3). However, lasers emitting in the mid-infrared region (1.5 - 13 μm) produce injury primarily in the cornea of the eye.

Extensive data for corneal injury following continuous wave (CW) CO_2 (10.6 μm) laser irradiation have been reported (4-8, 15). The most complete corneal threshold study to date for the CO_2 laser is that of Vassiliadis et al. (5) and his coworkers Peppers et al. (6) and Peabody et al. (7). They determined the 50%-probability-of-damage value as a function of incident power density for pulse widths of 3.5 to 5.5 msec. Leibowitz and Peacock (8) investigated corneal lesions from a CO_2 laser for 0.07 to 1 sec pulse widths. The irradiance and pulse duration were both varied; consequently, there were not enough exposures at any given pulse duration to obtain a reliable threshold.

Limited data also exist on the ocular effects of the erbium laser (1.54 μm) (9). However, no threshold data exist for the hydrogen fluoride (HF) and deuterium fluoride (DF) lasers (2.6 - 4 μm).

This report describes a series of experiments to determine corneal damage thresholds for HF/DF lasers operating under specified spectral and pulse characteristics, and compares the results with thresholds from other infrared laser sources. These experiments were performed in the Aerodynamics and Propulsion Research Laboratory, Aerospace Corporation, El Segundo, California between 7 February and 30 March 1972.

MATERIALS AND METHODS

Two HF/DF chemical lasers were used in these experiments: a CW gas dynamic laser and a pulsed pin discharge laser. Both systems were experimental engineering models built and operated by Aerospace Corporation. In this and the remaining sections of this report, the experiments with the CW HF/DF laser and those with the pulsed HF/DF laser are treated separately.

Continuous Wave HF/DF Laser

System Description--The CW HF/DF laser used in this study combines hydrogen or deuterium with fluorine from dissociated SF_6, to form excited HF or DF molecules as the laser medium. The laser is described in detail in the literature (10-12). This laser, as it was configured for the corneal threshold study, was capable of output powers from 0.05 to 20 watts. The intensity distribution of the laser beam was limited to the TEM_{00} (Gaussian) mode with a 3-mm diameter aperture in the laser cavity. The beam cross-sectional areas at the cornea were 0.64 mm^2 for HF and 0.88 mm^2 for DF with standard deviations of 20%. These areas were calculated from the averages of the beam diameter (1/e intensity level) determined from daily beam scans.

Monochromatic eye exposures to the CW HF laser were made for 10, 100, and 500 msec using the 2.795 μm wavelength, and for 25, 100, and 500 msec using the 2.727 μm wavelength. The CW DF laser beam consisted principally of two wavelengths: 3.698 μm and 3.731 μm; eye exposures were made using this beam for 125 and 500 msec. The total power was distributed between the two lines, with about 30% at 3.698 μm and 70% at 3.731 μm. The CW HF/DF laser exposure parameters are summarized in Table 1.

TABLE 1. CW HF/DF LASER EXPOSURE PARAMETERS

Nominal shutter time (msec)	Wavelength (μm)
10	2.795 (HF)
100	2.795 (HF)
500	2.795 (HF)
25	2.727 (HF)
100	2.727 (HF)
500	2.727 (HF)
125	DF[a]
500	DF[a]

[a]DF beam was composed of two wavelengths, with about 30% of the power at 3.698 μm and 70% at 3.731 μm.

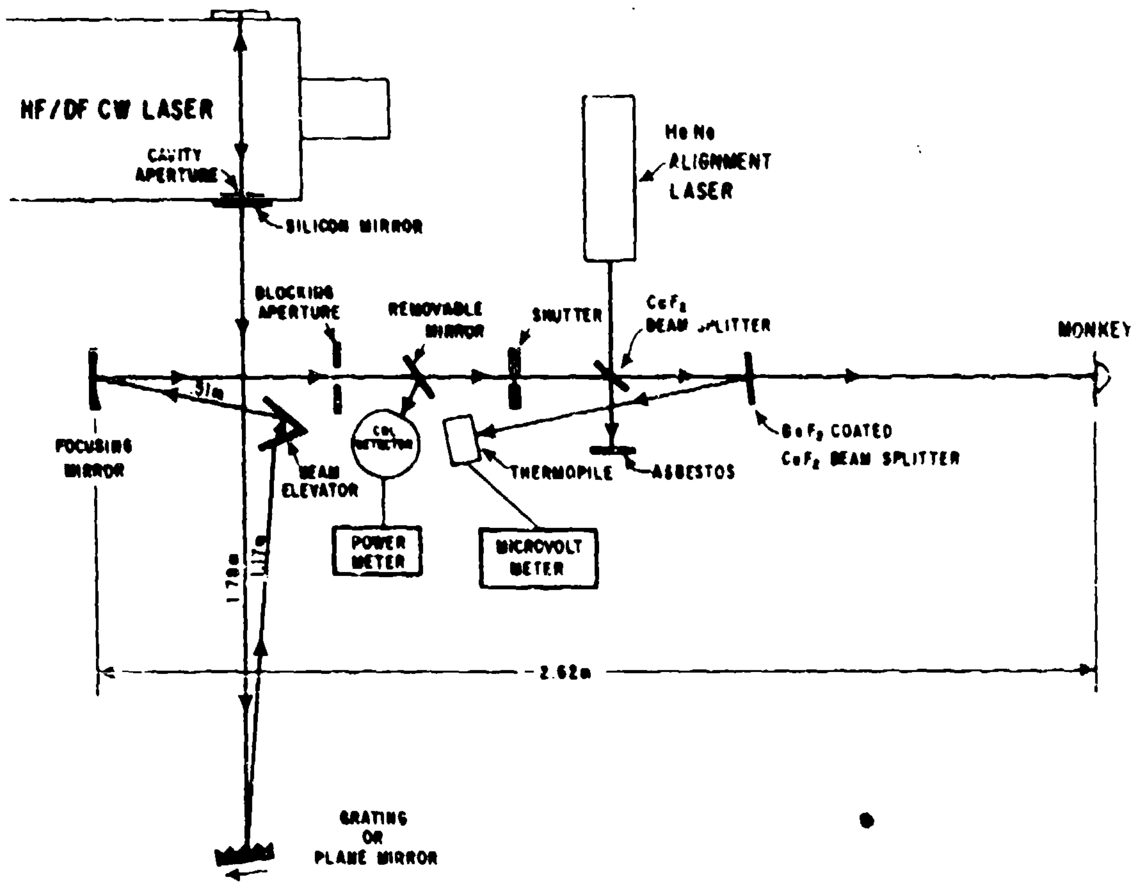

Figure 1. HF/DF CW laser configuration.

The laser and delivery system are depicted in Figure 1. Tracing the HF/DF laser beam from the output mirror, it reflected from a grating (Bausch and Lomb, 300 grooves/mm, blazed for 3 μm) for the HF beam, or a plane mirror for the DF beam, to a beam elevator. (It was necessary to raise the beam about 13 mm to the height of the animal mount.) The beam was then reflected toward a mirror with a 3.05-meter radius of curvature, which focused the laser beam to a spot on the cornea. A 19-mm aperture in a piece of carbon blocked the unwanted HF wavelengths, and a removable mirror prevented the beam from damaging the leaves of the electronic shutter. This mirror also permitted measurement of the total power in the beam before and after an exposure using a Coherent Radiation Laboratory (CRL) model 201 power meter. The mirror was removed during an exposure by activating a solenoid. The duration of the exposure was controlled by a Gerbrands 300 or a Compur II shutter, both of which were accurate to within 5%.

The beam from a 0.3 mW CW HeNe laser was reflected off a CaF_2 beam splitter coaxial with the HF or DF laser beam. The HeNe beam served as an aiming device to place the exposure on the desired area on the cornea. A second beam splitter (BaF_2-coated CaF_2) reflected about 10% of the HF or DF beam to an Eppley thermopile, which was used as a ballistic thermopile. The energy of each exposure was monitored by measuring the thermopile output with a Keithley microvolt ammeter (model 150A). The readings from both the CRL power meter and the Eppley thermopile were calibrated daily with a TRG 100 ballistic thermopile located at the corneal plane. A Keithley millimicrovoltmeter (model 149) measured the TRG 100 output. The TRG 100 calibration was traceable to the National Bureau of Standards.

Animal preparations and exposure procedures--Rhesus monkeys (*Macaca mulatta*) ranging in weight from 2 to 3 kg served as subjects. The animals were air transported to the test site, housed in individual cages in an air-conditioned trailer especially prepared for animal handling, and maintained on a standard laboratory diet. Approximately 50 monkeys were housed in the trailer at one time. Upon arrival of replacements, the animals were returned to Brooks AFB.

Preanesthetic medication was induced by the intramuscular injection of a sedative dose of phencyclidine hydrochloride (Sernylan) of 0.25 mg per kilogram of body weight. Anesthesia was induced by the intravenous administration of sodium pentobarbital (Nembutal) at 20 mg/kg. The pupils were dilated with 10% phenylephrine hydrochloride (Neo-Synephrine hydrochloride) and 1% cyclopentolate (Cyclogyl) about 1 hour prior to exposure. Sutures of 3-0 silk were placed in the upper eyelids to facilitate their manipulation. Corneal drying was prevented by periodic applications of either normal saline or methylcellulose ophthalmic solution and by manual blinking of the lids.

Prior to laser exposure, all animal eyes were carefully examined by slit lamp biomicroscopy, and any animal found to have corneal abnormality in either eye was rejected. The animal was placed in a movable stereotaxic mount on a test stand, which also included the slit lamp for observation and photography of the cornea (Fig. 2). The animal was positioned facing

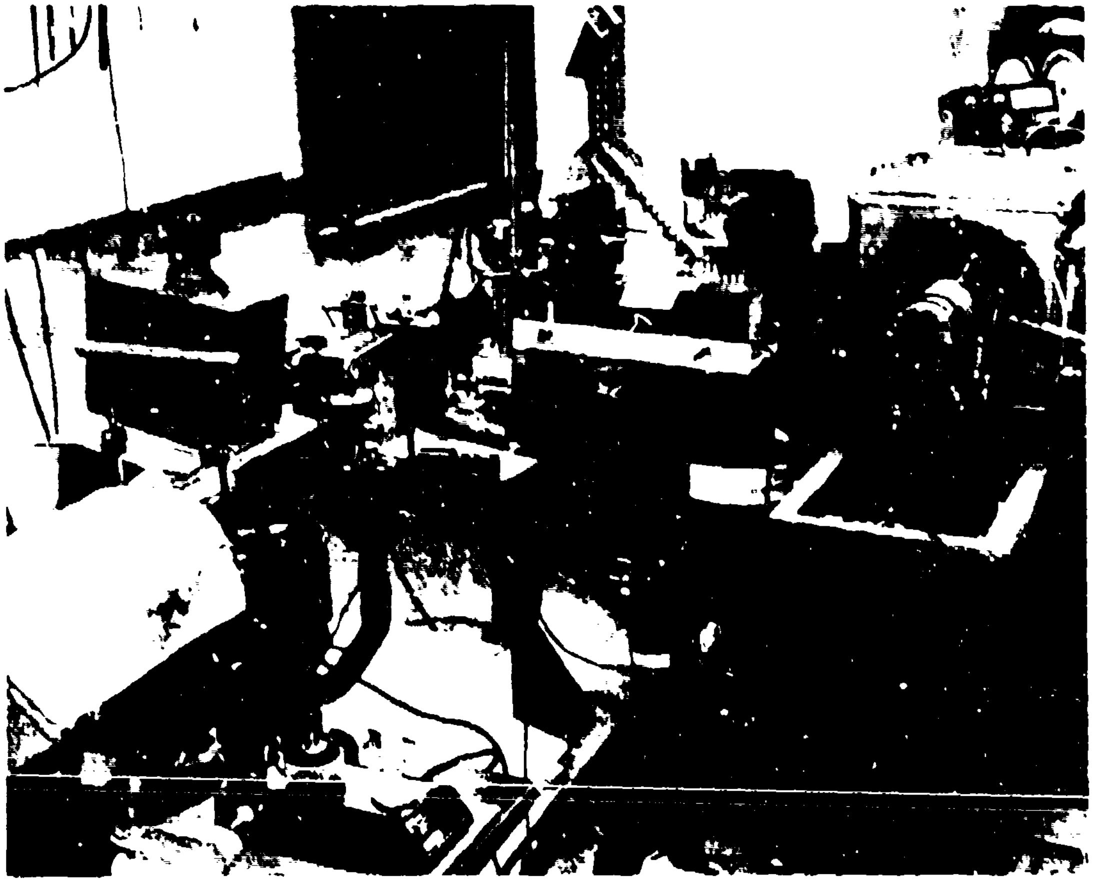

Figure 2. HF/DF test station for CW irradiations.

the HF or DF beam so that the red alignment beam from the helium-neon laser produced a small spot on the cornea. The investigator located the desired exposure area by making micrometer movements of the stereotaxic mount to place the HeNe spot at the desired site. Then the animal's cornea was ready for irradiation.

The gas flow for the laser was adjusted to achieve the desired stable output. The operator then activated the solenoid to remove the blocking mirror and triggered the shutter (set for the desired exposure time). The solenoid was deactivated, which dropped the mirror back into position, after each exposure. The CRL power reading before and after each exposure and the Eppley thermopile reading during each exposure were recorded. No significant differences were found in the power readings before and after exposure. The animal was then repositioned to a new corneal site for the next exposure, and the above procedure was repeated. The following five sites were sequentially exposed on each eye: the center, nasal, temporal, superior, and inferior areas. This procedure enabled each eye to be exposed rapidly and specific exposure sites to be identified later.

The range of power levels used for each exposure time was established by a preliminary study on 4 to 6 eyes, which determined the narrowest practical range of power levels centered about the estimated threshold.

Each corneal exposure site was observed immediately after irradiation of both eyes of the animal. If no effect was noted after 10 minutes, the result was considered negative.

Pulsed HF/DF Laser

System Description--The pulsed HF/DF laser is a high voltage (50-100 kv) transverse discharge laser excited by two helical arrays of 61 electrodes or pins about a Plexiglas cylinder. Because of its construction, the laser is referred to as the "pin" laser. The HF or DF pin laser action occurred as a result of a capacitive discharge through the flowing mixture of SF_6 and H_2 (13), or D_2. The laser was capable of an output of approximately 25 mJ for HF and 18 mJ for DF.

The laser cavity was in an unstable configuration consisting of a convex mirror with a radius of curvature of 24 meters and a flat, partially transmitting silicon mirror. A conical aperture of approximately 20-mm diameter was inside the cavity next to the silicon mirror. The resultant output beam intensity distribution was Gaussian.

Horizontal and vertical spatial beam scans were made before and after the study with an apertured (127 μm) Raytheon (QKN 1563) gold-doped germanium detector at 77° K and an oscilloscope. An average of the estimated diameters (measured at the 1/e points) from the horizontal and vertical scans was used to calculate the beam area. The area for HF and DF was 0.53 mm^2 and 0.72 mm^2, respectively. Figure 3 is a typical beam scan.

The pulse exposures from the HF/DF pin laser were not monochromatic, nor were they simple, regularly shaped pulses; so time-resolved spectral scans were made of both the HF and DF beams at the discharge voltages corresponding to the threshold exposure levels.

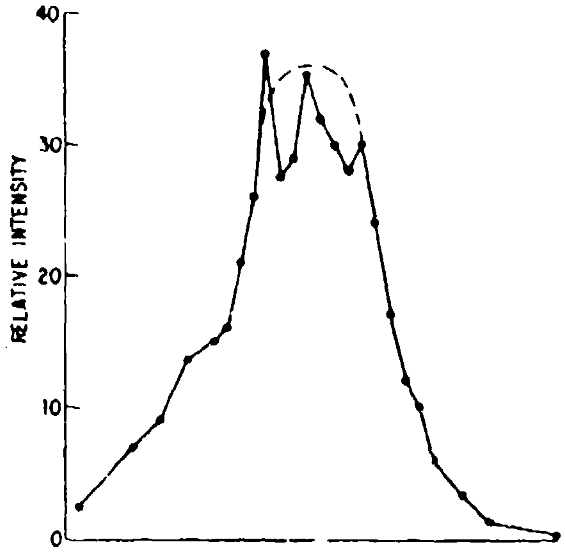

Figure 3. HF pin laser spatial beam scan.

The width of the HF pulse, "full width at half maximum" (FWHM), measured from the total spectral pulse was about 45 nsec. Sixty-one percent of the pulse energy was emitted at the 2.6397, 2.6084, and 2.8705 μm wavelengths (Table 2).

TABLE 2. HF PIN LASER SPECTRAL CONTENT

Fractional total energy	Transition (v,J)	Wavelength (μm)
0.15	(2,7)	2.8705
0.11	(2,6)	2.8319
0.10	(2,5)	2.7952
0.09	(2,4)	2.7604
0.01	(1,7)	2.7440
0.08	(1,6)	2.7074
0.32	(1,4)	2.6397
0.14	(1,3)	2.6084

The DF pulse had three peaks, of which only the second and third pulse were significant (23% and 69% of the total energy respectively). The second pulse had a pulse width (FWHM) of 50 nsec and the third pulse, of 80 nsec. The second and third peaks were about 100 nsec apart. Table 3 presents the spectral content of the DF pulses. The experimental configuration used for the HF/DF pin laser is depicted in Figure 4. The HF or DF beam was incident on a microscope slide beam splitter, which reflected a portion of the total power to a room temperature indium arsenide (InAs) detector (Mullard ORP-10); this signal was displayed on an oscilloscope. Both the detector and oscilloscope were enclosed in a screen box to shield the electronics from radio-frequency noise generated by the high voltage discharge. A helium-neon alignment laser beam was introduced at the microscope-slide beam splitter colinear with the HF or DF beam to provide an aiming device for placing exposures on the desired area of the cornea.

A plane mirror reflected the HF or DF beam to a focusing mirror. Usually a 100% reflecting gold-coated mirror was used for DF exposures and a partially reflecting silicon mirror for HF exposures. The focusing mirror was gold-coated and spherical (204.5 cm radius of curvature), and focused the beams at the corneal plane. A beam splitter (gold-coated CaF_2 for HF or BaF_2-coated CaF_2 for DF exposures) reflected a portion of the beams to an Eppley thermopile which was used as a ballistic thermopile. A Kiethley microvolt ammeter (model 150A) was used to measure the peak output of the Eppley thermopile.

The beams were attenuated with a thin silicon flat for the DF exposures and germanium flats for the HF exposures. The attenuators were placed between the last beam splitter and the corneal plane. The laser energy output was controlled by varying the discharge voltage, the beam splitters, the attenuators, or the plane mirrors. Table 4 summarizes the various optical components used for the HF and DF pin laser exposures.

The Eppley thermopile readings were calibrated each day against a TRG 100 ballistic thermopile at the corneal plane. The TRG 100 output was measured by a Kiethley millimicrovoltmeter (model 149). Calculations were made of the energy of each exposure from the Eppley thermopile readings and attenuator transmission measurements.

Animal preparations and exposure procedures--The animal preparations used in this series of experiments were the same as described previously for the CW laser exposures. The animal was placed in the stereotaxic mount, positioned facing the pin laser beam (Fig. 5), and an exposure site was located with the

TABLE 3. DF PIN LASER SPECTRAL CONTENT

Fraction of energy in the pulse	Transition (v,J)	Wavelength (μm)
Pulse at 0.50 nsec (0.08 of total energy)		
0.0072	(3,7)	3.8903
0.0224	(3,6)	3.8547
0.0352	(3,5)	3.8206
0.0096	(3,4)	3.7878
0.0056	(2,6)	3.7310
Pulse at 50-160 nsec (0.23 of total energy)		
0.0322	(3,7)	3.8903
0.0391	(3,6)	3.8547
0.0621	(3,5)	3.8206
0.0046	(2,8)	3.8007
0.0184	(3,4)	3.7878
0.0069	(2,7)	3.7651
0.0299	(2,6)	3.7310
0.0299	(2,5)	3.6983
0.0069	(2,4)	3.6665
Pulse at 160-360 nsec (0.69 of total energy)		
0.0897	(4,6)	3.9843
0.0138	(4,5)	3.9487
0.0069	(3,8)	3.9272
0.0966	(3,7)	3.8903
0.0966	(3,6)	3.8547
0.0621	(3,5)	3.8206
0.0207	(2,8)	3.8007
0.0069	(3,4)	3.7878
0.0414	(2,7)	3.7651
0.0345	(2,6)	3.7310
0.0276	(2,5)	3.6983
0.0069	(2,4)	3.6665
0.0690	(1,6)	3.6128
0.0759	(1,5)	3.5811
0.0483	(1,4)	3.5507

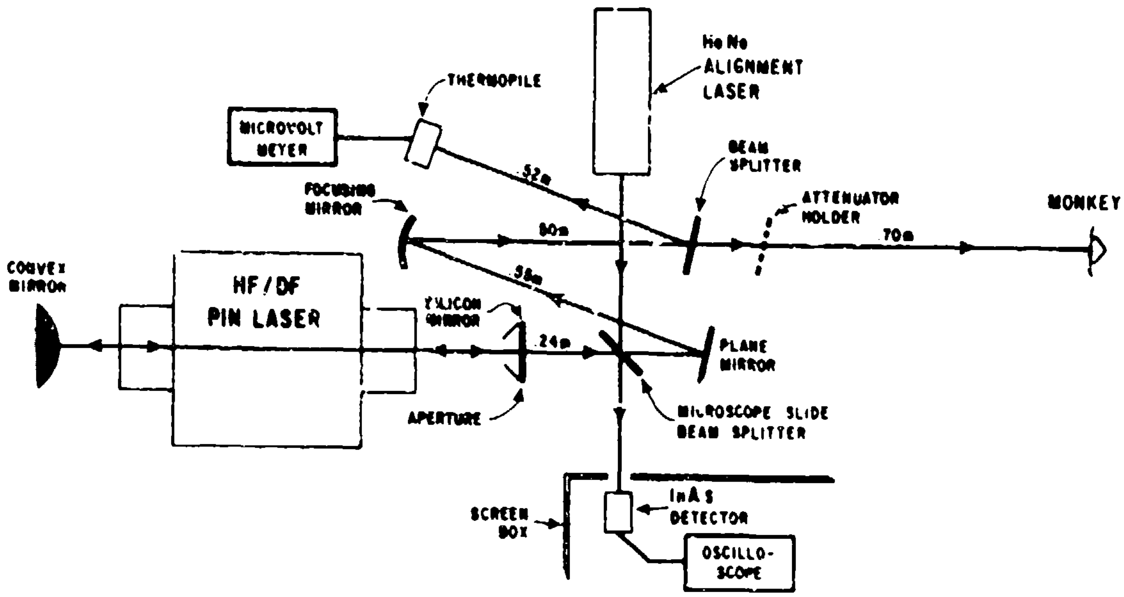

Figure 4. HF/DF pin laser configuration.

TABLE 4. HF/DF PIN LASER SYSTEM OPTICAL COMPONENTS

	Plane mirror	Beam splitter	Attenuator
HF:	silicon	gold-coated CaF_2	None
	gold coated		germanium
DF:	gold coated	BaF_2-coated CaF_2	silicon
	silicon		

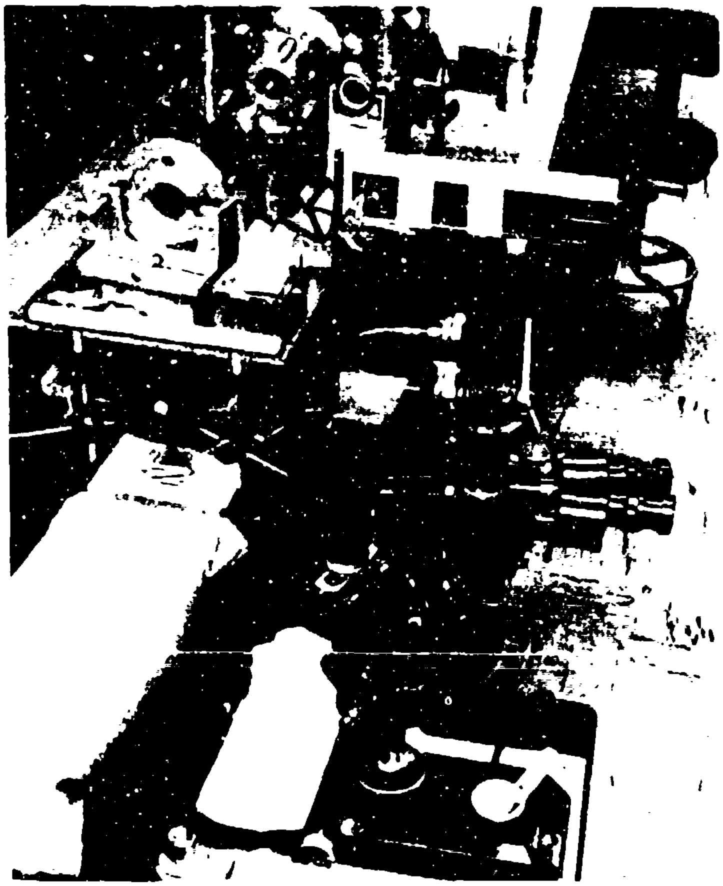

Figure 5. HF/DF pin laser test station.

aid of the HeNe beam as described previously. The discharge voltage was set at the desired value, and the operator triggered the discharge. After each exposure the animal was repositioned to a new exposure site and the procedure repeated.

In the HF or DF pin laser experiment, approximately 6 eyes were used to determine the energy range of "burns" and "no burns." The exposures were placed in a 3 x 3 array centered on the pupil. After both corneas were exposed, each exposure site was examined. If no effect was noted after 10 minutes, the results were considered negative.

In both the CW and pulsed experiments, a randomly selected group of eyes were examined approximately 36-48 hours after exposure. No lesions were observed that were not present within 10 minutes after exposure.

RESULTS

Continuous Wave HF/DF Lasers

Approximately 116 rhesus monkey eyes were irradiated by the continuous wave HF/DF chemical laser; each eye received five exposures. The power levels of the CW DF data ranged from approximately 0.1 to 1.0 W. The results for the CW HF data were determined only from preliminary data collected to establish the general exposure range for threshold values. Shutter difficulties precluded completion of the CW DF experiment.

The minimum criterion for damage was defined as the presence of a corneal lesion seen by slit lamp biomicroscopy at 10 minutes following exposure. As power was decreased, the size of the lesion decreased. Near threshold lesions were typically characterized by a shallow depression of the corneal epithelial surface with localized edema and mild fluorescein staining (Fig. 6). Discrete grayish opacities occurred at

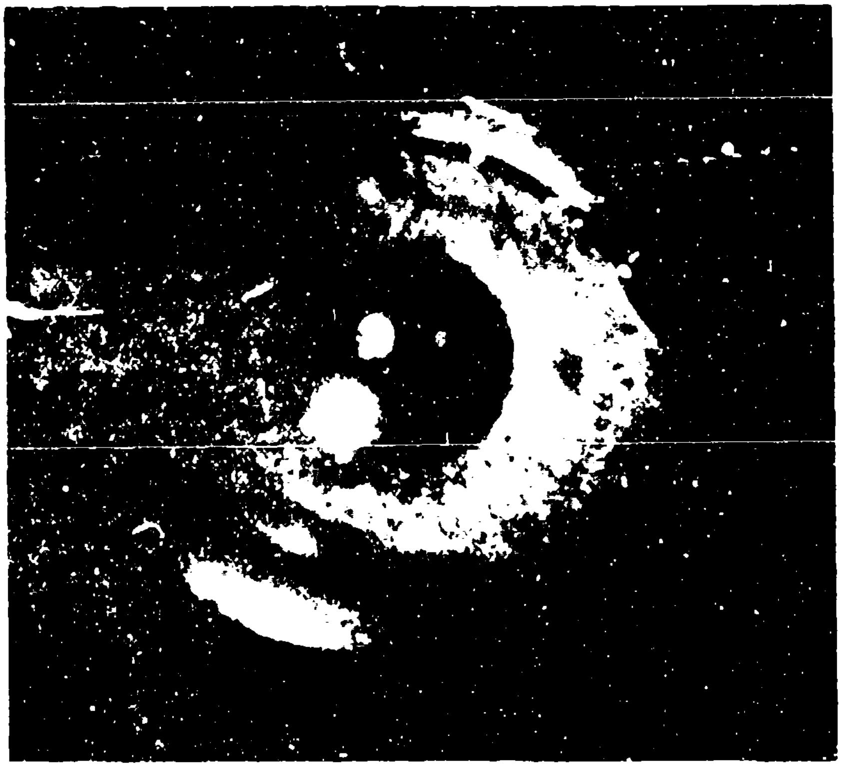

Figure 6. Typical HF/DF CW corneal lesions.

these impact sites. Severe lesions showed opacities in deeper layers. In all cases, the epithelial lesions healed in 1 to 3 days, while the more severe lesions took slightly longer. No evidence of lenticular or retinal damage was found upon careful examination with slit lamp or ophthalmoscope. Samples of the CW HF data from which thresholds were determined are shown in Table 5 for the 100 msec exposure time. The threshold per eye was obtained by calculating the average of the maximum exposure with no burn and the minimum exposure with a burn. Using a logarithmic transformation, means and standard deviations were computed in logarithmic units for each set of data. Ninety-five percent confidence limits were computed for each mean, and these means and confidence limits were then converted back to original units for estimates of the ED_{50} and 95% confidence limits on the ED_{50}. These results are given in Table 6 and plotted in Figure 7. ED_{50} is defined as the effective dose necessary to produce a lesion on 50% of the exposure sites in the eye. The results for the CW DF laser were determined from preliminary data, and caution should be exercised in the use of the data.

Pulsed HF/DF Laser

Thirty-eight eyes, each receiving 9 exposures, were irradiated by the pulsed HF/DF chemical laser, using the same damage criterion as described earlier. The energy levels ranged from approximately 0.77 to 0.92 mJ and 2.2 to 3.5 mJ for HF and DF radiation, respectively.

Under biomicroscopy, all suprathreshold corneal lesions were seen instantaneously after exposure as small, edematous, discrete, grayish spots. As energy was decreased, the size of the lesion decreased. At threshold levels, lesions became small, revealed fluorescein staining, and were located in similar corneal layers to those described in the CW series of experiments.

Table 7 is representative of the data used to determine the threshold values for the pulsed HF/DF laser. The incident energy values shown were converted to energy densities by dividing by the appropriate HF or DF beam area within the 1/e diameter. The method of data analysis was the same as that described previously, and the ED_{50} and 95% confidence limits on the ED_{50} are given in Table 8. Because of the unusual DF pulse shapes, an estimated pulse width of approximately 100 nsec was used for analytical purposes.

TABLE 5. SAMPLE (HF) THRESHOLD DATA (100 MSEC EXPOSURE)

Corneal power density (W/cm^2)	Burn/no burn 10-min. criterion
Animal No. 758	
Left eye (OS)	
19.8	Burn
20.2	Burn
18.4	Burn
17.4	No burn
16.5	No burn
Right eye (OD)	
20.2	Burn
19.8	Burn
17.9	Burn
17.4	Burn
16.5	No burn
Animal No. 678	
Left eye (OS)	
20.2	Burn
18.8	Burn
18.4	No burn
17.4	No burn
16.5	No burn
Right eye (OD)	
20.2	Burn
19.5	Burn
18.4	No burn
17.4	No burn
16.5	No burn

TABLE 6. ED_{50} VALUES AND 95% CONFIDENCE LIMITS ON ED_{50} FOR CW HF/DF

Wavelength (μm)	Exposure time (msec)	Number of eyes	ED_{50} (W/cm^2)	95% CL (W/cm^2)
2.795 (HF)	10	18	85.71	85.14-86.28
2.795 (HF)	100	16	20.57	19.56-21.63
2.795 (HF)	500	22	9.52	9.25- 9.80
2.727 (HF)	25	17	61.93	61.02-62.86
2.727 (HF)	100	16	28.05	27.42-28.70
2.727 (HF)	500	16	13.97	13.11-14.88
Multiline[a] (DF)	125	5	36.88	34.56-39.35
Multiline[a] (DF)	500	6	15.37	14.60-16.18

[a] 30% of the power at 3.698 μm and 70% at 3.731 μm.

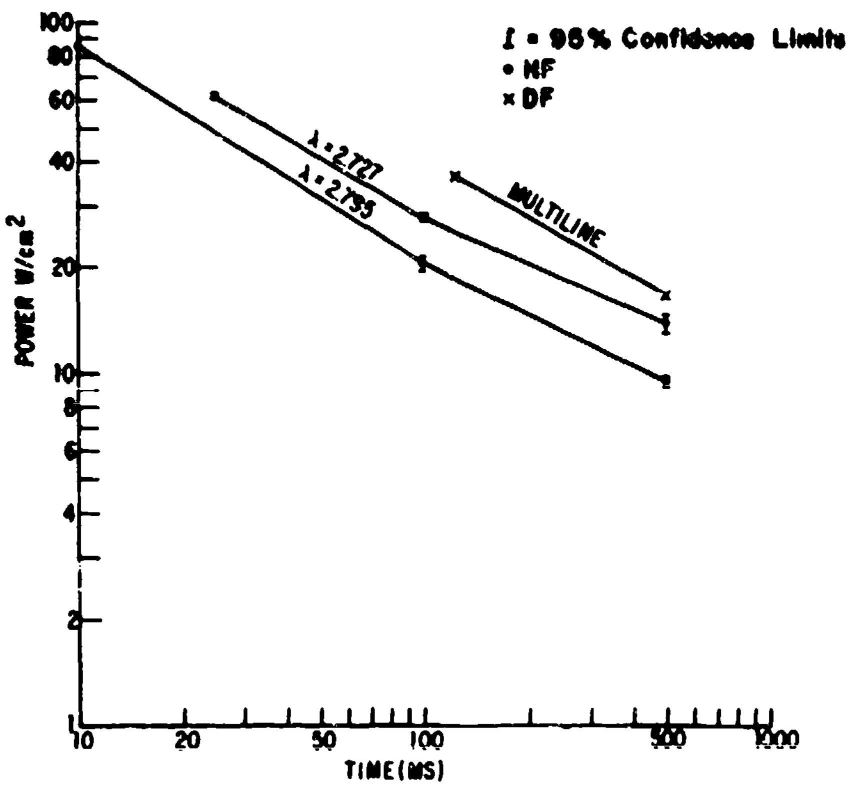

Figure 7. CW plot of ED_{50} values vs. exposure time.

TABLE 7. SAMPLE HF/DF THRESHOLD (PULSED)

Energy (mJ)	Burn/no burn 10-min. criterion
Animal No. 775 (Exposed to HF)	
Left eye (OS)	
0.86	Burn
0.84	Burn
0.83	No burn
0.81	No burn
0.83	Burn
0.86	Burn
0.83	Burn
0.83	No burn
0.82	No burn
Right eye (OD)	
0.85	Burn
0.85	Burn
0.82	No burn
0.81	No burn
0.81	No burn
0.85	Burn
0.85	Burn
0.83	Burn
0.84	Burn
Animal No. 413 (Exposed to DF)	
Left eye (OS)	
3.03	Burn
2.75	Burn
2.81	No burn
2.64	No burn
2.64	No burn
2.53	No burn
2.70	Burn
2.59	Burn
2.53	No burn
Right eye (OD)	
3.22	Burn
2.92	Burn
2.78	Burn
2.67	No burn
2.51	No burn
2.48	No burn
2.97	Burn
2.70	Burn
2.53	No burn

TABLE 8. ED_{50} VALUES AND 95% CONFIDENCE LIMITS ON ED_{50} FOR PULSED HF/DF

Wavelength	Pulse width (nsec)	Number of eyes	ED_{50} (J/cm^2)	95% CL (J/cm^2)
Multiline HF (See Table 2)	45	18	0.156	0.153-0.160
Multiline DF (See Table 3)	100	20	0.377	0.368-0.385

The estimates of the ED_{50} and the standard error of the ED_{50} as derived for the thresholds per eye were compared with the estimates derived from probit analysis of the same experimental data (14). This comparison is shown in Table 9 and indicates reasonable agreement in the two estimates for both the means and the standard errors. The use of multiple exposures on each eye had only a marginal effect on these estimates. It is recommended that only the threshold per eye results be used.

DISCUSSION

This report represents the first published data on the ocular effects of the HF/DF laser. The threshold data collected in this study for the pulsed HF/DF laser are valid only for HF or DF lasers operating under similar conditions (i.e., the same spectral lines and pulse characteristics). However, the data may be considered for guidance purposes. The site of ocular injury at the power or energy densities used in this study appears to be restricted to the cornea. It seems likely that, even at higher exposure levels, no retinal damage would occur because of the attenuation of the HF/DF wavelengths by the ocular media. This is in contrast to lasers operating in the visible and near infrared, where the combined effects of high ocular transmission and focusing by the eye produce intense amplification of the incident energy density at the retina. In this respect, the HF/DF laser seems to be a comparatively "safe" laser.

Corneal threshold lesions from carbon dioxide and Q-switch erbium lasers are qualitatively similar to those produced by the HF/DF laser and have been described by several groups (7, 9, 15). The carbon dioxide research utilized a continuous wave laser to expose rabbit corneas for exposure times from 3.5 to 5.5 msec. The erbium laser experiment utilized a Q-switch laser (50 nsec pulse width) focused onto monkey corneas.

TABLE 9. COMPARISON OF THE TWO ESTIMATES OF MEANS AND STANDARD ERRORS IN LOG UNITS

Wavelength (μm)	Pulse duration	Number of eyes	Mean		Standard error	
			Threshold/Eye	Probit	Threshold/Eye	Probit
CW 2.795(HF)	10 msec	18	1.933	1.933	0.00136	0.00120
CW 2.795(HF)	100 msec	16	1.313	1.313	0.01024	0.00906
CW 2.795(HF)	500 msec	22	0.979	0.980	0.00610	0.00535
CW 2.727(HF)	25 msec	17	1.792	1.792	0.00305	0.00223
CW 2.727(HF)	100 msec	16	1.448	1.447	0.00466	0.00334
CW 2.727(HF)	500 msec	16	1.145	1.143	0.01290	0.01017
Pulsed HF	45 nsec	18	-0.906	-0.820	0.00490	0.00790
Pulsed DF	100 nsec	20	-0.424	-0.420	0.00686	0.00499

The ED_{50} derived from the CW HF/DF data in this study and the CO_2 thresholds cited in the above references have been converted to energy densities and plotted with the pulsed HF/DF and erbium thresholds for comparison purposes (Fig. 8). This figure reveals that a typical direct relationship exists between ED_{50} corneal energy densities and time, that the DF damage threshold values are higher than the HF values, and that the damage thresholds for the two CW HF wavelengths (2.795 and 2.727 μm) are different. These CW HF/DF differences are substantiated by statistical tests at comparable exposure times (Table 6).

The direct relationship seen in Figure 8 indicates that more energy was required to produce threshold damage with long duration pulses than with the very short duration pulses because of the increased thermal relief provided by conduction into the surrounding layers of the cornea with increase in exposure time.

Corneal damage thresholds at specified wavelengths shown in Figure 8 can be related to the absorption coefficients of water at the same wavelengths, assuming the cornea has the spectral properties of water. Table 10 contains the absorption coefficients of water and the respective corneal thresholds for the wavelengths of interest in this study. It also contains the 90% absorption depths ($z_{0.1}$) corresponding to the absorption coefficient (a) at each wavelength. $z_{0.1}$ is defined as that depth at which the relative transmitted intensity I/I_0 has been reduced to 0.1 (i.e., 90% absorption). The calculations were done according to the Lambert absorption law; $I/I_0 = e^{-az}$, hence, $z_{0.1} = \ln(.1)/(-a)$. It can be seen from the table that HF radiation has a higher absorption coefficient than DF. From this result one would expect a greater energy absorption per unit volume of irradiated tissue, and thus a lower corneal damage threshold, for the HF than for the DF radiation for a given exposure time. This reasoning is supported by the data of this study. The biologic data (Fig. 8) also support similar threshold comparisons of pulsed HF with Q-switched erbium; CO_2 with CW DF, and pulsed DF with Q-switched erbium. However, the data do not support the comparison of CW HF with CO_2. The reason for this is not known, other than the variability of the results among different investigators.

Figure 9 is a plot of threshold power density vs. $z_{0.1}$. The corresponding absorption coefficients are also shown. In Figure 9, the comparison of the thresholds for given exposure time (i.e., 0.5, 0.1 or about 10^{-7} sec) shows that the threshold levels increase rapidly with increasing $z_{0.1}$ until they level off at some value. For example, for a 0.5 sec exposure time, the threshold increases with $z_{0.1}$ until it levels off at approximately 15 W/cm^2 at a $z_{0.1}$ of about 12 μm.

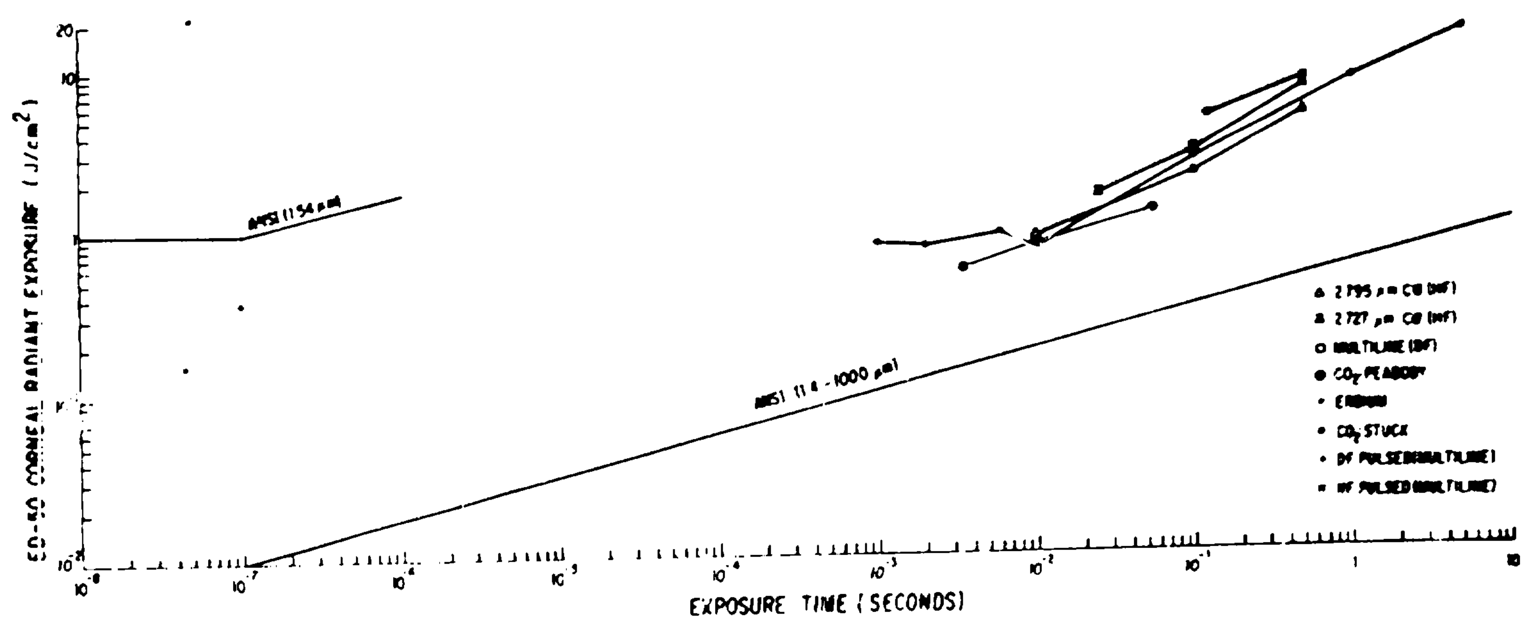

Figure 8. Comparative plot of ED_{50} and safety levels for infrared lasers.

TABLE 10. ABSORPTION COEFFICIENTS OF WATER AND CORNEAL THRESHOLDS

Laser wavelength (µm)	Absorption coefficients[a] cm^{-1}	90% Absorption depth (µm)	ED_{50} (W/cm^2) for exposure times of .5 sec	10^{-1} sec	10^{-2} sec	10^{-7} sec
(ANSI MPE) 1.4-1000			.94	3.2	17.5	10^5
1.54						10^7
Erbium 1.54	19	1212				4.2×10^{8}[d] (2[illegible])
DF (CW) 3.70 & 3.7[illegible]	121	190	15.37 (16)[c]	36.88[d] (11)		
DF (pulsed) 3.55-3.[illegible]	146	158				3.77×10^6 (38)
CO_2[b]	817	28		25 (8)	77 (4)	
HF (CW) 2.727	1740	13	13.97 (15)	26.05 (9)	61.9[d] (7)	
HF (pulsed) 2.64-2.75	3038	7.6				3.48×10^6[d] (19)
HF (CW) 2.795	4920	4.6	9.52 (10)	20.57 (6)	85.7 (5)	
[illegible] 2.95	11,900	1.9				

[a]From references 16 and 17. Those for multiple wavelengths are average values weighted by their relative magnitudes at each wavelength. See Tables 2 and 3.

[b]CO_2 thresholds from reference 15.

[c]Numbers appearing in parentheses are the ratios of ED_{50} to MPE.

[d]Exposure times different than stated, see Tables [illegible] and 8. Safety factors calculated from MPE of actual exposure times.

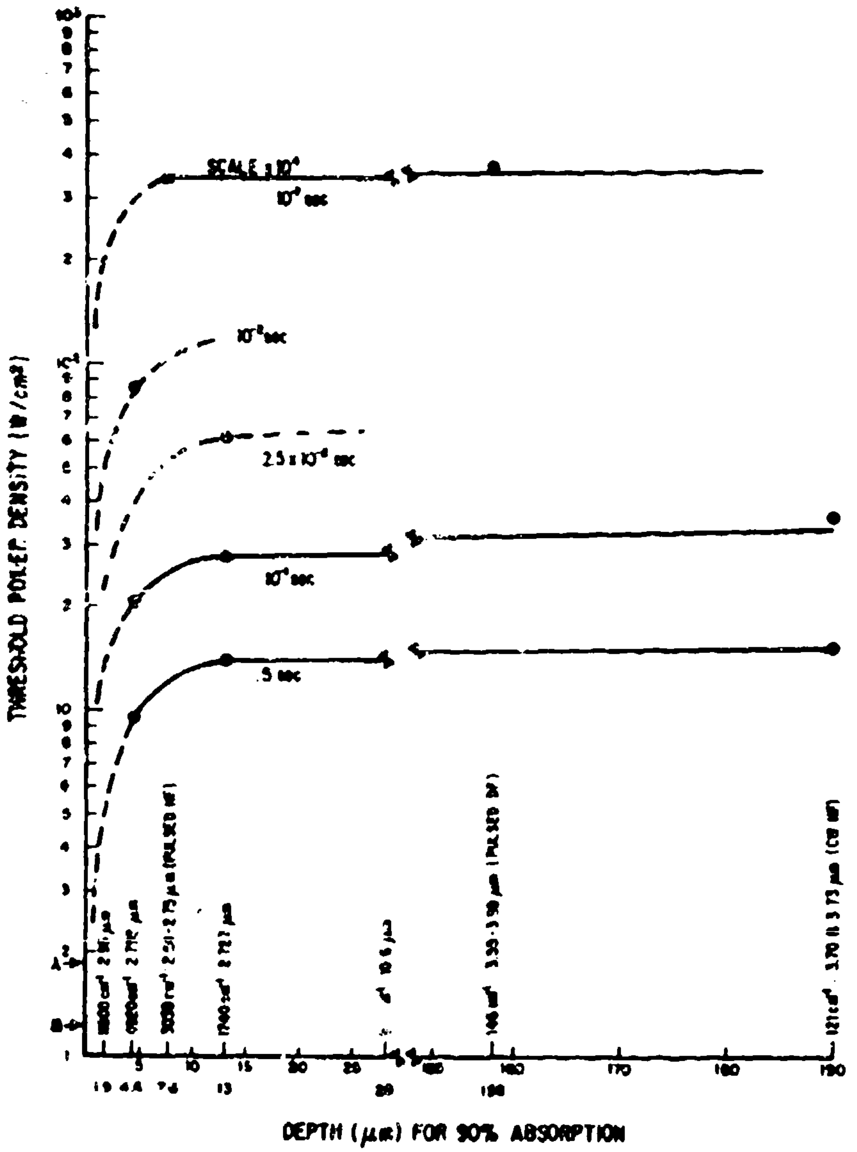

Figure 9. Threshold power density vs. depth for 90% absorption.

This increase in $z_{0.1}$ corresponds to decrease in the absorption coefficient to about 2000 cm^{-1}. For absorption coefficients between 2000 cm^{-1} to 100 cm^{-1} (90% absorption depths 12 to 30 μm) the thresholds increase slowly. However, if erbium data are an indication (Table 10), the thresholds again increase rapidly for a decrease in the absorption coefficients between 100 and 19 cm^{-1} (from 3.5 x 10^6 W/cm; 45 nsec pulse to 4.2 x 10^8 W/cm^2). From our previous rationale relating the absorption law and the expected threshold for a given absorption coefficient, the thresholds should approach infinity as absorption coefficients go to zero.

The American National Standards Institute (ANSI) has recently accepted and approved a standard on the safe use of lasers (19). The maximum permissible exposure (MPE) levels recommended by ANSI for wavelengths from 1.4 to 1000 μm for exposure of 10^{-7} to 10 sec are presented in Figure 9. Comparing the thresholds and associated absorption coefficients from this study with the ANSI MPE, the following observations are made. For absorption coefficients between 100 and 2000 cm^{-1} the lowest safety factor is about 7 (Table 10). For an absorption coefficient equal to 4920 cm (2.795 μm) the safety factor is down to 5. The peak absorption in the 1.4 to 200 μm wavelength region is at a wavelength of about 3 μm (18) with an absorption coefficient of 11,900 + 500 cm^{-1} (16). The 90% absorption depth for 11,900 cm^{-1} is 1.9 μm. From Figure 9, an estimate of the threshold for the 90% absorption depth of 1.9 μm is 40%-60% lower than that at 4.6 μm depth (2.795 μm). Hence, for lasers emitting at 3 μm wavelength the ANSI MPE may have a safety factor of only 2.

The HF/DF ED_{50} values of this study are from 5 to 38 times higher than the ANSI MPE at their respective exposure times. Such high factors may not be warranted based on the 95% confidence limits from this study and assuming that the variability within and among corneas is less than the variability within and among retinas. In this discussion, considering such factors as measurement accuracy, variations in results among investigators and biologic variability, an acceptable safety factor could be as low as 5. If one recalls the estimate made for the 3 μm wavelength exposure, the safety factor may be as low as 2. Considering this variation in safety factor (from 2 to 38), it is recommended that an MPE weighting factor be developed so that this significant wavelength dependence of threshold can be reflected in the ANSI MPE. This would eliminate the necessity of establishing conservative MPE for most infrared wavelengths. It is also recommended that threshold studies be done at the 3 μm wavelength to establish a lower limit to the threshold in the 1.4 to 200 μm region.

This study on the two HF/DF lasers produced the first experimental threshold values for corneal lesions obtained in the wavelength region between 1.54 μm (erbium) and 10.6 μm (CO_2). These threshold data indicate some appreciable dependence on wavelength and support some correlation with the water absorption coefficients.

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