Retinal injury from simultaneous exposure to 532 nm and 860 nm laser irradiation

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ABSTRACT

To properly assess the retinal hazards from several lasers using multiple wavelengths, the retinal effects of 10-second laser irradiation from 532 and 860 nm were determined in non-human primates for several different power combinations of these wavelengths. A total of 12 eyes were exposed using four different ratios of power levels to determine the contribution to the damage levels from each wavelength. The data are compared to the calculations resulting from use of the currently accepted method of predicting hazards from simultaneous lasing. The ANSI-Z136 – 2000 standard was used to calculate the combined maximum permissible exposure (MPE) and for comparison with the measured visible lesion thresholds, i.e., ED_{50}s.

INTRODUCTION

This study was designed to investigate the retinal effects of two lasers being used to simultaneously expose the retina and determine the minimum visible lesion (MVL) thresholds for different ratios of powers from these two lasers. The ANSI standard, ANSI-Z136.1-2000[1] (*American National Standard for Safe Use of Lasers)*, for multiple wavelengths was based on very little data reported in the literature using multiple wavelengths. Since two widely separated wavelengths were used in our experimental setup, caution had to be used in deriving the rules for these exposure situations and calculations for the MPE are complex as stated by the ANSI standard. It states that the effects of simultaneous exposure of pulsed and CW laser radiation may act synergistically. For multiple-wavelength laser emissions, the MPE must first be determined for each wavelength separately. Exposures from several wavelengths in the same time domain are additive on a proportional basis of spectral effectiveness with due allowance for all correction factors. The goal of this study was to provide additional data to support this additivety for lasers when exposure durations are longer than the aversion response time (0.25 sec) and to insure that the MPEs as determined by the ANSI standards are well below the MVL thresholds. Thus, 10-second exposure durations were used for these measurements.

Also, exposure duration for these two wavelengths must be considered as purposeful staring into the beam and the aversion response time (0.25 sec) to visible light is not allowable under these circumstances when performing safety analysis.

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METHODS

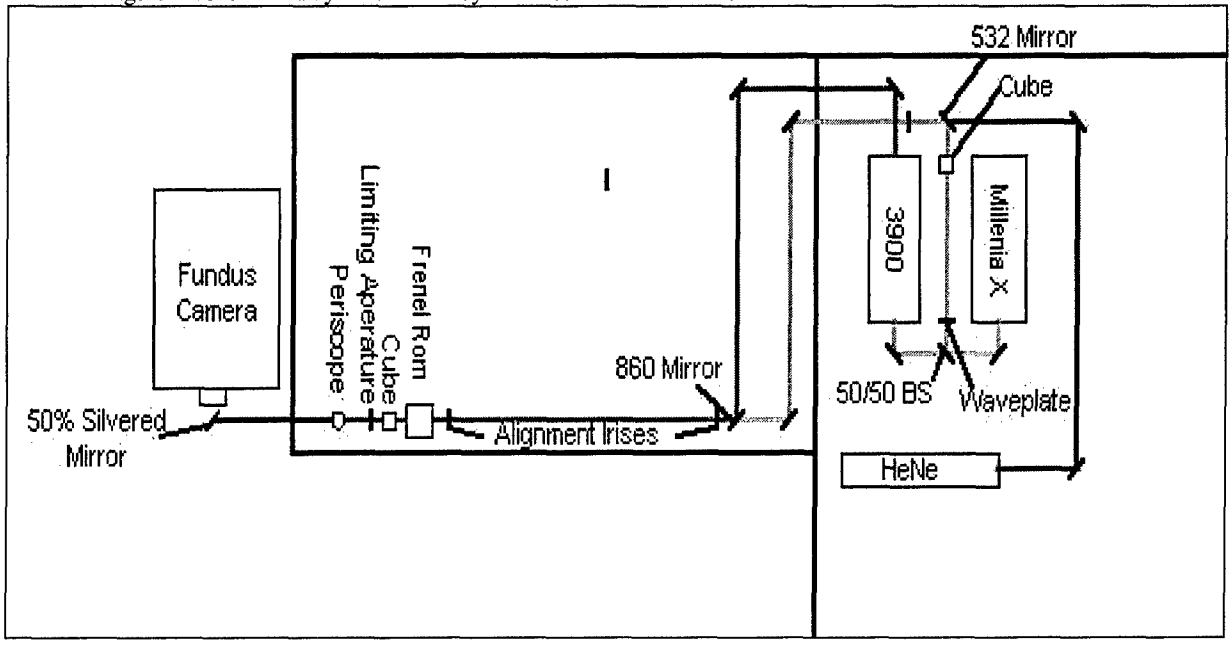
Experimental Laser Setup

The equipment used in our setup (Figure 1) starts out with a Spectra Physics Millennia X, 10-W, 532-nm laser. The beam is split into two beams with a 50/50 532-nm beam-splitter. (BS-1) The transmitted part of the beam is then directed into a Spectra Physics Model 3900, Ti-Sapphire laser as the pump source and provides an output tuned to 860 nm. The reflected part of the 532 nm beam is directed through a cube and waveplate combination to independently vary the power without affecting the tuning of the Model 3900 Ti:Sapphire. This beam is then combined with a helium-neon beam (632 nm) for alignment as shown in the diagram below. The 860-nm beam from the Model 3900 is then combined with 532/632 nm beam and aligned coaxially through a set of irises. The combined beams are then passed through a Fresnel Rhomb and cube to vary the power equally for both the 532-nm and 860-nm beams. The beams then pass through a limiting aperture and a controlling shutter (not shown) before being reflected through the periscope. After the beams are raised to the height of the fundus camera, they are directed past the front lens of the camera to be split again by a 50% silvered mirror. (BS-2) The reflected beam was directed into the subject's eye, and the transmitted portion is directed into a reference detector. The RM6600 radiometer and RKP575 detector heads monitored and measured the reference beam through the 50% silvered mirror.

The subject was positioned with the cornea approximately one centimeter from BS-2 so that the reflected portion of the beam entered the eye co-linear with the optical axis of the fundus camera (see Fig. 1). The fundus camera was used to directly view the retina through BS-2. Prior to subject placement, the ratio of average power delivered to the eye to the amount measured at the monitor detector at the beam splitter marked BS-2 (see Fig. 1) was recorded. Each day the ratio of reflected and transmitted portions of the beam was measured and recorded for visible and infrared beams. The ratio did not change as a function of power delivered. All detectors were independently calibrated to NIST-traceable standards. Laser power was delivered to the corneal surface without a contact lens or other device to control the image size on the retina.

There were four sets of independent measurements of the minimum visible lesion (MVL) thresholds taken. A ratio of 7/1 for the powers generated by the two lasers for 532/860 was used in the first set of measurements. In addition to this ratio, three other ratios were used for the measurement of the MVL thresholds: 1/1, 1/3, and 0/1 for the 532/860 powers.

Figure 1 Schematic Layout of Laser System Used for Measurements.



MVL study

Mature *Macaca mulatta* primates from 3 to 8 kg were maintained under standard laboratory conditions (12 hours light, 12 hours dark). The subjects were screened before exposure to ensure that no eye was more than 0.5 diopter from being emmetropic. Procedures were performed during the light cycle. Animals involved in this study were procured, maintained, and used in accordance with the Federal Animal Welfare Act, the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources, National Research Council, and the ARVO Resolution for the Use of Animals in Ophthalmic and Vision Research.

Subjects had food withheld for 12 hours prior to procedure and were chemically restrained using 10 milligrams (mg)/kg ketamine hydrochloride (HCl) intramuscularly by veterinary staff. Once restrained, 0.16 mg atropine sulfate was administered subcutaneously. Two drops of proparacaine HCl 0.5%, phenylephrine HCl 2.5%, and tropicamide 1% were each administered to both eyes to allow cycloplegia as well as dilation for fundus photography. Gauze pads were taped over both eyes to protect the eyes and to keep them moistened during transport. The subject was evaluated immediately after arrival at laboratory facility for level of anesthesia and ketamine HCl was re-administered IM as indicated. Under ketamine restraint, the subject's arm hair was clipped and area over and surrounding the superficial saphenous veins was cleansed with a betadine scrub and solution followed with an isopropyl alcohol rinse. A 22 gauge intravenous catheter was placed and securely taped in each arm for administration of warmed NaCl 0.9% or Lactated Ringers solution [10 milliliters (ml)/kg/hour flow rate] and for administration of propofol. An initial induction (bolus) dose of propofol (2 - 10 mg/kg) was administered to effect. The state of anesthesia was maintained using 0.2 – 1.0 mg/kg/min of propofol via syringe pump. The subject was intubated with a cuffed endotracheal tube sized appropriate for the subject. A peribulbar injection of either 4% lidocaine or cocktail mix of equal amounts of 2% lidocaine/bupivacaine 0.75% (with 0.1ml hyaluronidase to improve tissue perfusion) was administered with a 25 gauge 0.5 – 0.75" needle, to reduce extra-ocular muscular movement during exposure. The subject was securely restrained in a prone position on an adjustable stage for fundus photography, laser exposure, and fluorescein angiography (FA). The eye was kept open with an ophthalmic speculum and rinsed frequently with 0.9% saline solution to maintain moisture during procedure. Ten to 15 minutes prior to Fluorescite administration, acepromezine (0.5-1.0 mg/kg) was administered intravenously as an antiemetic. Immediately prior to FA, 0.6 ml of Fluorescite 10% was administered as an intravenous bolus followed by a NaCL flush or Lactated Ringers IV push. The subject's heart rate, oxygen saturation and respiratory rate were continuously monitored throughout the experimental protocol using a pulse oximeter. Normal body temperature was maintained by the use of circulating warm water blankets. After completion of procedure, subject was transported back to prep room where it was monitored until initial indications of recovery from the anesthetic agents, usually cough or pulling of endotracheal tube. Upon arousal, subject was extubated, recovered from anesthesia and promply transported back to the animal housing area.

The retina was viewed with a fundus camera and all laser exposures were delivered to the eye in the macular region. Marker lesions were created with approximately 60-mW, 50-ms, single-pulse exposures at 832 nm to define one margin of the grid rows and columns. These marker lesions allowed precise placement of experimental lesions in a pre-defined grid. These lesions were created approximately 10 minutes before experimental exposures were placed. Exposures were placed laterally, temporal to the macula in a five-by-five grid. The subject was maintained under anesthesia throughout the one-hour post-laser evaluation. At 24 hours after laser treatment the subject was anesthetized following the protocol above but without peribulbar injection. Eyes were evaluated at 1 hr and 24 hr postexposure and visible lesions at a given exposure site were reported as a "yes" only if at least two examiners identified a lesion.

Energy delivered, along with a "yes" or "no" value, was recorded if a lesion was or was not observed on the retina at each laser delivery site. A probit data analysis technique [2] was applied to the "yes" or "no" recorded as a one or zero, respectively, for each dosage applied. This analysis provides the estimated dosage to cause a MVL with 50% probability (ED_{50}) and confidence intervals (fiducial limits at the 95% confidence level). Color fundus photographs were taken at 1 hr and 24 hr postexposure along with black-and-white photographs of the fluorescein angiography.

RESULTS

All minimum visible lesion thresholds measured in the laboratory are presented in Table 1 for 1- hour post exposures along with their fiducial limits (FL) calculated at their 95% confidence level. This table provides additional data such as the number of subjects, eyes, exposures, etc and the slope of the probit line. All powers calculated in Table 1 are the total intraocular powers entering the eye for a 2.5 mm diameter beam for both co-axial wavelengths.

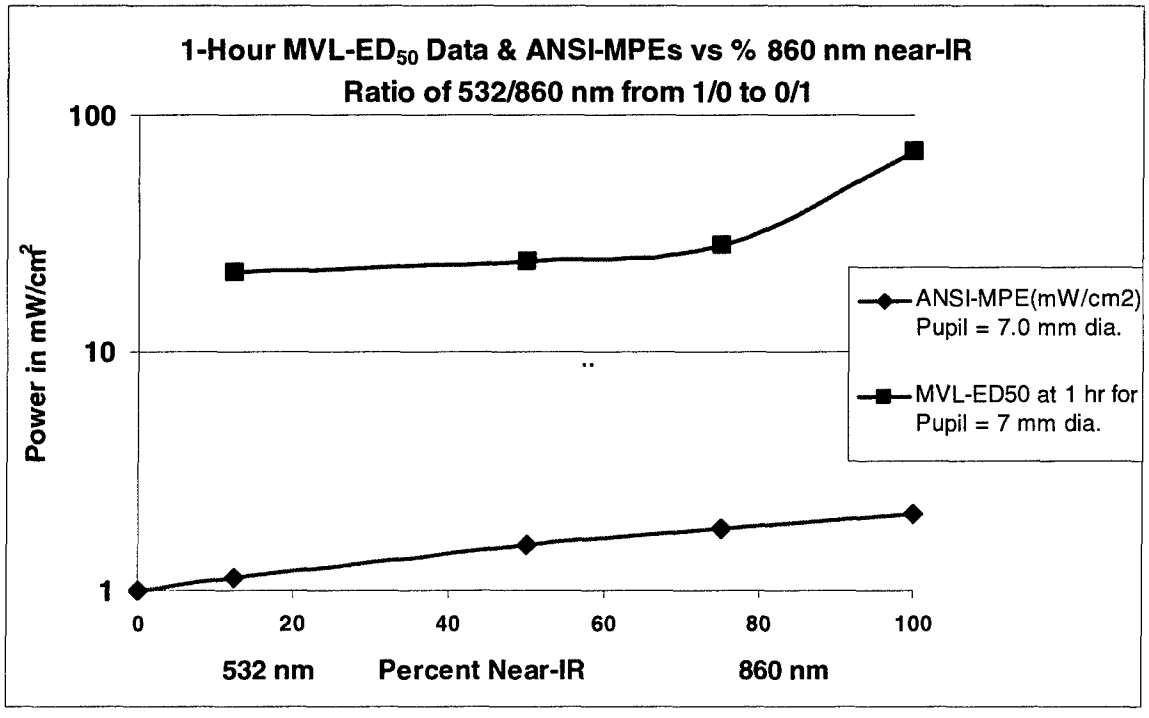
Table 1 Minimum Visible Lesions Thresholds in Milliwatts

Experimental Setup Number of Subjects & Shots	MVL-ED_{50} 1 Hour Reading
Eye with 532/860 = 7/1 3 Subjects, 3 Eyes, 70 Exposures	8.4(6.8 – 10.6) mW
Eye with 532/860 = 1/1 3 Subjects, 3 Eyes, 70 Exposures	9.2(6.4 – 13.1) mW
Eye with 532/860 = 1/3 2 Subjects, 2 Eyes, 50 Exposures	10.8(8.1 – 15.1) mW
Eye with 532/860 = 0/1 2 Subjects, 4 Eyes, 100 Exposures	27.0(21.6– 39.7) mW

Fiducial Limits at the 95% confidence level are in parenthesis

Since the ANSI standards provide for the corneal irradiance for the MPE values, the results in Table 1 were converted to this irradiance using a 7-mm diameter pupil for comparisons to the MPEs. These results are plotted in Figure 2. From the data plotted in this figure, the MVL-ED50 threshold values surpass the ANSI-MPE values by over a factor of 10.

Figure 2 MPEs and MVL-ED50s for 532 & 860 nm



DISCUSSION

Table 2 lists and summarizes the previous MVL studies, including the researcher, wavelength, image size, and ED_{50} values. Threshold values have not been reported for long exposure times (>1 msec to 10 sec) for 532 nm wavelength studies. This is due to the fact that until recently, there were no CW lasers capable of producing 532 nm wavelengths. ED_{50} values were reported for a 514 nm wavelength, which is generated from an argon laser. From this table, we see that reported ED_{50} data is 5.6 mW and 4.2 mW for small spot sizes and exposure durations of 5sec and 1 sec, respectively. Data collected during this experiment with a power ratio of 7/1 for 532/860 nm had an ED_{50} of 8.4 mW at 1 hour post-exposure for a 10 sec exposure duration. Other comparable data at 623 nm wavelength for 7.5 and 10 sec exposure durations and ED_{50} values for 6.4 mW and 16 mW respectively. The reason we are able to compare these two values is because is has been reported that there is no wavelength dependence on the retinal injury thresholds between the 514 and 632 nm wavelengths [3].

Table 2 MVL Thresholds Reported in the Literature

Author, et al	Wavelength	Image size	ED50
Gibbons [4]	514 nm	small	5.6 mW
Ham [5]	514 nm	500 μm	11.6 mW
Onda [6]	514 nm	small	4.2 mW
Lappin [7]	632 nm	small	6.4 mW
Ham [5]	632 nm	500 μm	16 mW
Gallagher [8]	860 nm	476 μm	27.6 mW
Lund [9]	860 nm	small	19.4 mW
Ham [10]	860 nm	500 μm	44.3 mW

For the other wavelength, 860 nm, three exposure times (5 – 10 sec) have been reported as also shown in Table 2. These ED_{50} thresholds vary between 19.4 and 44 mW depending on the retinal image size. Data show that the ED_{50} threshold for the small retinal spot size is 19.4 mW at 8 sec exposure durations. This value compares well to our threshold at 10 sec of 27 mW, for 1-hour post exposure ED_{50}.

CONCLUSIONS

From the measurements reported herein and the ANSI standard referenced, there is the required safety margin between the MPEs as defined by the standards and the minimum visible lesion thresholds measured and reported by other research groups in the literature. Threshold data also show that there is at least a factor of 12 difference between the MPE and the MVL-ED_{50} in live rhesus eyes and this ratio increases as the percentage of 860 nm increases to 100%. This leads to a slightly higher safety margin for 860 nm radiation than there is for 532 nm radiation.

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