

Retinal thermal damage threshold dependence on exposure duration for the transitional near-infrared laser radiation at 1319 nm

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Abstract: The retinal damage effects induced by transitional near-infrared (NIR) lasers have been investigated for years. However, the damage threshold dependence on exposure duration has not been revealed. In this paper, the *in-vivo* retinal damage ED₅₀ thresholds were determined in chinchilla grey rabbits for 1319 nm laser radiation for exposure durations from 0.1 s to 10 s. The incident corneal irradiance diameter was fixed at 5 mm. The ED₅₀ thresholds given in terms of the total intraocular energy (TIE) for exposure durations of 0.1, 1 and 10 s were 1.36, 6.33 and 28.6 J respectively. The ED₅₀ thresholds were correlated by a power law equation, $ED_{50} = 6.31t^{0.66}$ [J] where t is time [s], with correlation coefficient $R = 0.9999$. There exists a sufficient safety margin (factor of 28~60) between the human ED₅₀ thresholds derived from the rabbit and the maximum permissible exposure (MPE) values in the current laser safety standards.

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OCIS codes: (140.3360) Laser safety and eye protection; (350.6830) Thermal lensing; (350.5340) Photothermal effects.

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1. Introduction

The transitional infrared wavelength range refers to the wavelength band from 1.3 μm to 1.4 μm [1–3]. With the wavelength increase in this region, the most sensitive tissue changes gradually from the retina to the cornea. Some unique ocular injury characteristics have been revealed in the past two decades. Firstly, the absorption of incident laser energy in this region is more evenly distributed across the ocular media [4,5]. Damage may be induced in one or more of the cornea, lens, and retina/choroid, depending on the precise exposure parameters [1–3,6,7]. Secondly, strong spot size dependence exists for this wavelength range. Threshold-level damage occurs at the retina for relatively large corneal beam spot while occurs at the cornea for relatively small spot [3]. Thirdly, retinal or corneal threshold lesion involves full thickness of that layer [8,9]. These characteristics are remarkably different from the ocular damage induced by other wavelength range and receive increasing concern.

For the setting of ocular MPEs in laser safety standards, the dependence of damage threshold on exposure duration is a critical issue, especially for the thermal-damage-dominated time region. For retinal damage induced by visible and short IR-A (0.7 ~1.4 μm) lasers [10,11] and corneal damage induced by IR-B (1.4 ~3.0 μm) [12,13] and IR-C (3.0 ~1000 μm) lasers [14,15], the damage threshold dependences on exposure duration have been determined. For the unique transitional NIR lasers, the corneal damage threshold dependence on exposure duration has been established at 1319 nm [16]. However, the retinal damage threshold dependence on exposure duration has not been made clear, although some damage thresholds have been determined for different animal species and diverse exposure conditions [1–3,17,18].

The rhesus is the most widely used animal model for the study of retinal damage threshold. For transitional NIR wavelengths, thermal mechanism dominated retinal damage

thresholds have been determined for rhesus at exposure durations of 350 μ s, 650 μ s and 80 ms [2,3,6]. Experiments at longer exposure duration up to 10 s were also conducted but no retinal damage were found [1,3]. The rabbit is also used for retinal damage threshold study in this wavelength range. The rabbit retinal damage threshold has been determined only for 0.4 s exposure duration [17]. For 10 s exposure duration, the rabbit retinal damage was observed but the threshold was not exactly determined [1,3]. From the existing threshold data, the dependence of retinal damage threshold on exposure duration cannot be reasonably established. One important fact should be noted that the volumetric absorption of refractive media has great influence on the retinal damage induced by transitional NIR lasers [4–7,19]. The higher absorption of pre-retinal ocular media allows less energy arriving at the retina, which decreases the retinal exposure. Moreover, thermal lensing effect induced by the heating of ocular media will lead to enlarged retinal spot size [6,20]. This effect is more obvious at longer exposure duration, which might further protect the retina against laser damage. Compared with the rhesus, the rabbit has a shorter ocular axis [21,22] and thus the retina is more sensitive to laser damage. From this point of view, the rabbit is more proper for the study on the dependence of retinal damage threshold on the exposure duration. Furthermore, for the transitional NIR lasers, retinal damage is mainly dominated by the water absorption, and the absorption of the retinal pigmented epithelium layer has relatively little effect [17]. From this perspective, it can be thought that the rabbit and the rhesus have similar retinal structure. In this paper we determined the retinal damage ED₅₀ thresholds for exposure durations from 0.1 s to 10 s and their dependence on exposure duration in a rabbit model.

2. Materials and methods

2.1 Experimental set-up

The experimental set-up was shown in Fig. 1. Retinal exposures were conducted with a diode pumped continuous wave (CW) Nd:YAG laser (Fujian Institute of Research on the Structure of Matter, Chinese Academy of Science, Fujian, China) at 1319 nm. The maximum output of the CW 1319 nm laser was ~50 W, with power stability within $\pm 2\%$ for 1 hour operating time. The intensity of the incident radiation was nearly “top hat” distributed which was provided by the laser manufactures and verified through the exposure of photosensitive paper. A beam splitter placed slightly off the axis reflected a small portion of the laser beam to a power meter (3A, Ophir, Jerusalem, Israel) for monitoring the laser power incident on the cornea. Another power meter (30A, Ophir, Jerusalem, Israel) was placed at the animal eye’s position to measure the power arriving at the cornea. An electronically controlled mechanical shutter was employed to control the exposure duration for the CW 1319 nm laser. A low-power 633 nm He-Ne laser, coaxial with the 1319 nm laser, was used as a pointer for retinal exposure position. A 5 mm circular aperture was positioned to select the central portion of the beam and control the corneal spot diameter. The animal was placed such that its fundus could be observed through a direct ophthalmoscope by the investigator with a 1319 nm mirror placed just between the ophthalmoscope and the animal. This mirror was highly transmissive in the visible allowing for a clear fundus image even during laser exposure. In order to avoid corneal and/or lens damage that might result from energy accumulation of repeated exposure, only five to six exposures for 0.1 s and 1 s, and two to three exposures for 10 s exposure duration, were delivered to each eye fundus. The time interval between the exposures was 3~5 seconds for 0.1 and 1 s exposure durations, and 1~2 min for 10 s exposure duration.

2.2 Animals and laser damage

The animals involved in this study included 30 chinchilla grey rabbits (2.5 ~3 kg). The animals were procured, maintained in the Center for Laboratory Animal Medicine and Care, Beijing, China and used in accordance with the institutional guidelines of the Animal Care and Use Committee; and the ARVO Resolution on the Use of Animals in Research. Subjects

were pre-exposure examined by a slit-lamp to insure clear ocular media and normal fundus. To ensure the subjects did not experience pain and distress, all animals were anesthetized with an intramuscular injection of a mixture of ketamine hydrochloride (40 mg/kg) and xylazine (12 mg/kg). Full pupil dilation was performed with two drops each of proparacaine hydrochloride 0.5%, phenylephrine hydrochloride 2.5% and tropicamide 1% at a 5-minute interval. The anesthetized animals were placed in a conventional holder where they were positioned with the aid of the He-Ne laser. The overlapping of retinal lesions was avoided by changing the incident beam angle.

Following each exposure session, lesion/no lesion determinations were made for each exposure site by two experienced investigators for each irradiation site at 1- and 24-hour post-exposure. Retinal lesions were examined with an ophthalmoscope. Corneal and lens were examined with a slit-lamp microscopy. The lesion/no lesion data were collected and analyzed using the SAS statistical package (version 6.12, SAS Institute, Inc., Cary, NC). Bliss probit analysis was performed to determine the ED₅₀ thresholds, fiducial limits at the 95% confidence level and probit slope (ED₈₄/ED₅₀). The ED₅₀ refers to the effective dose corresponding to 50% damage probability. The dependence of ED₅₀ on exposure duration was determined through regression analysis.

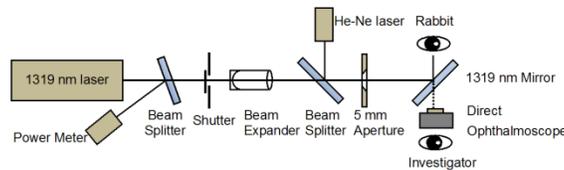


Fig. 1. Experimental set-up for rabbit retina exposure.

3. Results

Retinal lesion induced by 1319 nm laser appeared as circular, well-demarcated, white, opaque lesions. Under threshold radiant exposure condition, some lesions that were indiscernible immediately or within 1-hour post-exposure were readily detected by 24-hour post-exposure. No retinal hemorrhage, corneal and lenticular lesion was observed through the experiment. One interesting phenomena was that for the 10 s exposure duration, the dilated pupil retracted seriously after two or three exposures at all of the four laser doses (24.0, 30.0, 38.1, and 47.1 J), which prevented the delivery of more exposures to the retina.

Table 1. Retinal damage thresholds induced by 1319 nm laser at different exposure durations

Exposure duration (s)	Number of eyes	Number of exposures	1-hour post exposure		24-hour post exposure	
			ED ₅₀ in TIE (95% fiducial limits) (J)	Probit slope	ED ₅₀ in TIE (95% fiducial limits) (J)	Probit slope
0.1	20	116	1.53 (1.25, 2.37)	1.22	1.36 (0.84, 1.79)	1.28
1	20	114	7.51 (7.02, 8.07)	1.26	6.33 (5.70, 6.80)	1.30
10	20	48	38.0 (33.3, 44.3)	1.27	28.6(24.5, 32.2)	1.24

A total of 278 data points were obtained at 0.1 s, 1 s and 10 s exposure durations. All the experimental results, including the ED₅₀ thresholds termed in total intraocular energy (TIE), the 95% fiducial limits and the probit slopes were summarized in Table 1. The ED₅₀ thresholds determined at 24-hour check point were lower than those at 1-hour, therefore were chosen as damage thresholds and plotted in Fig. 2. It could be seen that these three data points followed a linear function. Through regression analysis, the dependence of damage threshold

on exposure duration was determined, i.e., $ED_{50} = 6.31t^{0.66}$ [J] where t is time [s], with the correlation coefficient 0.9999. The existing retinal damage thresholds for $\sim 1.32 \mu\text{m}$ [1–3,6,17], 1060 nm [23] and 514 nm [24] were also plotted in Fig. 2 for further discussion.

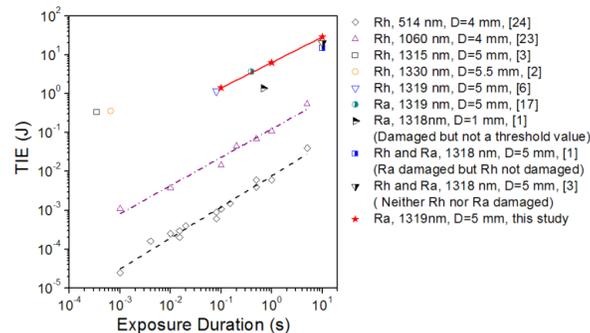


Fig. 2. Retinal damage threshold (ED_{50}) in terms of TIE. The parameters following the symbols denoted the animal species (Rh: Rhesus; Ra: Rabbit), the laser wavelength and the corneal spot diameter. The fitted line was the least square fit to ED_{50} thresholds: $ED_{50} = 6.31t^{0.66}$ ($R = 0.9999$).

4. Discussion

Laser-induced ocular damage mainly depends on the wavelength and exposure duration. For visible or IR-A lasers with CW or long-pulse output, the ocular damage is thermal-dominated [25]. The retinal damage threshold follows a power function law: $ED_{50} \propto t^k$, where k is the slope of the fitted line in the log-log space [24]. Previous investigations show that the values of k are about $2/3 \sim 3/4$, as shown by the 514 nm [24] and 1060 nm [23] data points in Fig. 2. For transitional NIR lasers, the unique thermal lensing effect was believed to enlarge retinal spot size and thus increase retinal damage thresholds, especially at longer exposure durations [7,20], which may obviously alter the k value. However, our study showed that the k value for 1319 nm was 0.66, not obviously different from those for other wavelengths. This could be explained by following possible mechanisms. Firstly, the thermal lensing effect requires a Gaussian beam profile, since an axial gradient index causes the lensing [7]. However, our study uses a top hat beam profile. The thermal lensing effect may be very weak. Additionally, as the 1319 nm wavelength is far from the visible region, the chromatic dispersion of ocular media causes the laser beam to focus at a more posterior retinal location and makes the retinal spot size enlarged greatly [4,7]. Although thermal lensing would further shift the beam focus posteriorly, we thought this probably has limited impact on the expansion of the retinal spot size. Previous retinal damage thresholds for transitional NIR lasers were also summarized in Fig. 2. For the rabbit, the reported thresholds showed good accordance with our results, except for the 0.69 s data point. The discrepancy could be explained as follows. Firstly, the 0.69 s data point was not a damage threshold actually. In Ref [1], for the 0.69 s exposure duration, the estimated retinal damage threshold was larger than 1.37 J. Secondly, the ocular axial length is a key influence factor to the damage threshold. The experimental subject of Ref [1] was Dutch Belted rabbits and our subject was chinchilla grey rabbits. Maybe obvious difference existed between these two kinds of subjects regard to the ocular axial length. For the rhesus, the 80 ms point also showed good accordance, while the 350 μs and 650 μs points obviously departed from the trend of the fitted line.

The transitional NIR region is unique in terms of potential ocular hazards, i.e. multiple ocular tissues are sensitive to laser damage, different from other spectrum region where only one ocular media (cornea or retina) is the most sensitive tissue [1–3,8]. Therefore, retinal and corneal injury risks should be simultaneously evaluated in relation to the laser safety standard. There exists a safety margin between ED_{50} and the corresponding MPE, which is defined as the ED_{50}/MPE ratio and generally preferred to be at least 2 for cornea and ~ 10 for retina

[26,27]. In Fig. 3 the ocular MPEs (“dual limit”) for 1319 nm proposed by ICNIRP-2013 guideline [27] and specified by ANSI Z136.1-2014 [26] were presented. In addition, the retinal damage thresholds in this work and corneal damage thresholds from our previous experiment [16] were also plotted for comparison. When assessing the human retinal damage risks, one critical issue should be noted is that for transitional NIR lasers the pre-retinal light absorption affects the retinal damage thresholds significantly. The average ocular axial length of rabbit measured by A-scan ultrasonic system in our experiment was 16.6 mm. Based on the ocular axial length of adult human (24.2 mm [28]) and the absorption coefficient of pure water at 1319 nm (1.79 cm^{-1} [4]), the retinal damage thresholds for human were estimated to be about 3.9 times of those for rabbit, assuming that equal energy results in the same degree damage. Accordingly, the retinal damage thresholds for human were plotted by shifting those for rabbit, as shown by the red dash line in Fig. 3. It could be readily seen that the lines for corneal and retinal damage thresholds crossed at about 1 s, implying that for human the most sensitive tissue to laser damage would shift from the retina to the cornea as the increase of exposure duration. This tendency was also reflected by the dual-limit MPEs in ANSI Z136.1 and ICNIRP guideline. Additionally, it also could be seen that the ANSI Z136.1 provided a much conserved safety margin at longer exposure durations and the ICNIRP guideline seemed to more closely follow the trend of retinal damage as shown in this study. The factor between the human ED_{50} thresholds and the maximum permissible exposure (MPE) values in the current laser safety standards ranged from 28 to 60.

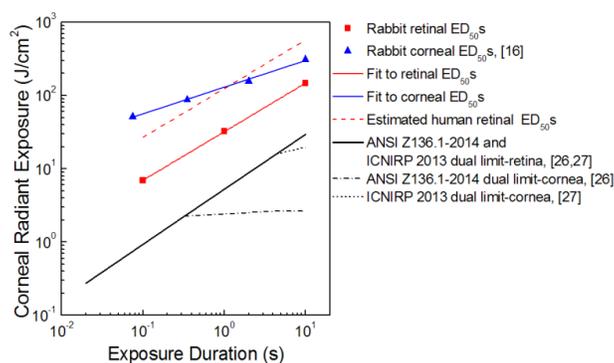


Fig. 3. Retinal ED_{50} thresholds determined in our experiment, corneal ED_{50} thresholds reported by our previous investigation [16], and MPEs from ANSI Z136.1-2014 [26] and ICNIRP-2013 for 1319 nm [27]. Estimated human retinal damage thresholds were derived from the rabbit ED_{50} thresholds.

5. Conclusion

The rabbit retinal ED_{50} thresholds given in terms of the TIE for 1319 nm at exposure durations of 0.1 s, 1 s and 10 s were 1.36, 6.33 and 28.6 J respectively. The ED_{50} thresholds were correlated by a power law equation, $ED_{50} = 6.31t^{0.66}$ [J] where t is time [s], with correlation coefficient 0.999, which was similar to those for other wavelengths. Enough safe margins existed between the ED_{50} thresholds and the MPEs from both ANSI Z136.1-2014 and ICNIRP-2013 guideline. The obtained results could be used for the refinement of the safety standards for transitional NIR lasers.

Acknowledgments

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