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**Review of Cornea Laser-Induced Damage
Thresholds from Exposure to UV and IR
Wavelengths**

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The research reviewed and cited in this publication was accomplished in accordance with local requirements regarding proper animal and human use research. The research cited was performed elsewhere, therefore, the publications cited would have statements regarding the type of animal/human research approved, and those policies may be different for each.

1.0 SUMMARY

This report reviews the published literature on corneal damage thresholds for femtosecond pulse durations up to 1 millisecond exposure durations at ultraviolet wavelengths (UV; 100 – 400 nm) and a subset of infrared wavelengths (IR; 800 – 10,600 nm) which were not included in a previous report [1]. It also provides an overview of the absorption properties of the cornea and laser damage mechanisms identified in the available studies in those wavelength ranges. The cornea laser damage thresholds are tabulated for the reader's convenience. This review identifies exposure regimes where data is scarce or lacking.

2.0 BACKGROUND

The human cornea is a ~ 600 μm thick avascular tissue that forms the anterior surface of the eye. It is the clear, protective outer layer of the eye and can be considered as the first line of defense against infection or injury to the eye. It plays a role in vision as it refracts light that enters the eye and, together with the lens, helps determine how well the eye can focus. Starting from the anterior layer, the five layers that comprise the human cornea are: *epithelium* (~ 50 μm thick), *Bowman's layer* (8 -12 μm thick), *stroma* (~ 500 μm thick), *Descemet's membrane* (2 - 10 μm thick), and the *endothelium* (5 μm thick) – see Figure 1a). The corneal epithelium is covered with an acellular tear film approximately 3 – 8 μm thick, which consists of lipid, aqueous, and mucin layers although 98% of its total volume is water [2–4].

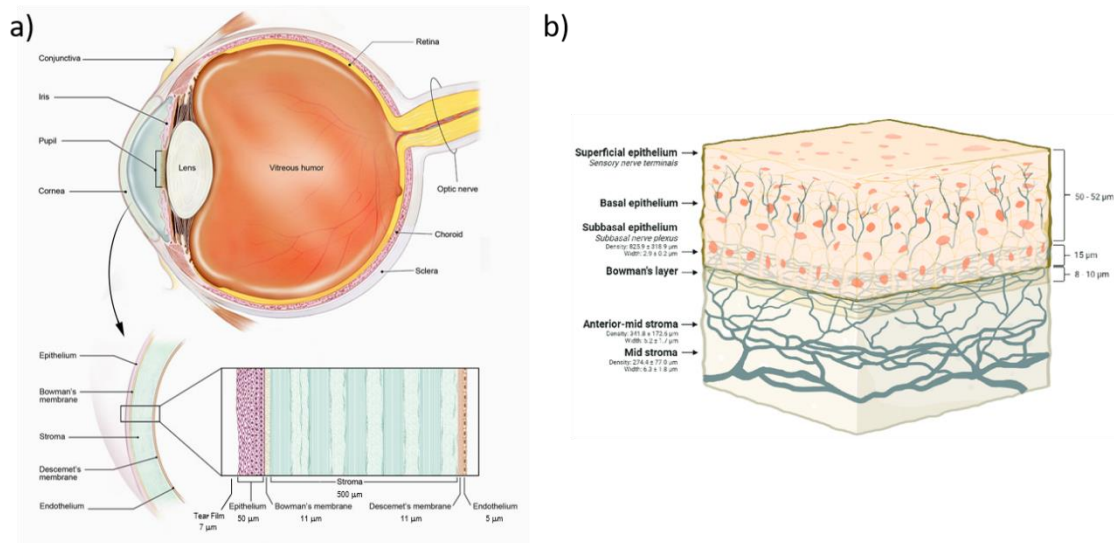


Figure 1. Diagrammatic representation of a human cornea. a) Structural layers with approximate dimensions [5]. Reproduced under the terms and conditions of the Creative Commons Attribution (CC BY-NC 2.0) (<https://creativecommons.org/licenses/by-nc/2.0/>). b) Corneal nerves distribution [6]. Reproduced under the terms and conditions of the Creative Commons Attribution (CC BY) (<http://creativecommons.org/licenses/by/4.0/>).

The *corneal epithelium* consists of three different cell types (squamous, wing, and columnar cells) forming around 6 cell layers. It is a self-renewing tissue such that all the cells turnover

within 7 to 10 days [7,8]. This process occurs as new cells form in the basal cell layer via mitosis and migrate towards the outer surface of the cornea, replacing the squamous cells, which are shed into the tear film. When an injury occurs, this cell turnover accelerates, and the epithelial cell layer heals within 1 to 3 days [9–11]. The *Bowman's layer* consists of a random arrangement of type I and type II collagen fibers but does not regenerate following injury. However, lesions to the Bowman's layer do not appear to affect vision [12–14]. The *stroma* forms the bulk of the cornea and consists of densely packed, parallel laminar collagen fibrils and corneal keratocytes [15]. When a corneal injury occurs, the corneal keratocytes undergo apoptosis or become involved in the healing process [16]. The stroma has a slow and limited repair capacity, and resulting scars may affect the subject's vision [17]. The *Descemet membrane* consists of type VIII collagen produced by the neighboring endothelial cells [18]. It is highly resistant to trauma and can regenerate if damaged [19]. The *endothelium* consists of a single layer of cells separating the cornea from the anterior chamber filled with aqueous humor. The endothelial cells cannot divide so they cannot regenerate when damaged. However, the undamaged cells have some ability to change shape or size to restore the integrity of the endothelium after an injury [20].

The cornea is considered to be the first line of defense against kinetic force or directed energy and intrusion by pathogens or materials. As such, it is the most densely innervated structure in the human body [21] and, consequently, injuries can be very painful. The nerves enter the cornea through the stroma and extend anteriorly, forming a dense network in between the anterior stroma and the Bowman layer known as the subepithelial plexus. Some nerves terminate as free nerve endings while others pierce through the corneal epithelial basement membrane to form the subbasal plexus in between the Bowman layer and the basal cell layer of the corneal epithelium, see Figure 1b). From the subbasal plexus, nerve endings extend to the superficial epithelial layers [21,22], terminating within or in between epithelial cells [23]. These nerve terminals have different pain receptors for chemical, thermal, and mechanical stimuli [6] and are responsible for maintaining the integrity and clarity of the cornea by modulating the blink reflex, wound healing, and the production and secretion of tears [23].

The cornea absorbs light below 380 nm and above 1400 nm [24–29] (see Figure 2) therefore these wavelength regions pose a risk of injury as a laser's energy is increased. The epithelial layer is the outermost layer, and although it accounts for only ~10% of the overall corneal thickness, it is responsible for most of the corneal absorption [30]. The main goal of this overview was to provide data to populate corneal dose response models by documenting known corneal damage thresholds for femtosecond pulse durations up to 1 millisecond exposure durations at ultraviolet wavelengths (UV; 100 – 400 nm) and infrared wavelengths (IR; 800 – 10,000 nm) which were not included in a previous report [1]. The studies covered within this report focused on determining the radiant energy dose that produces a minimum visible lesion (MVL) on the cornea.

Corneal lesions generated by an exposure level that results in a MVL are referred to as threshold lesions and typically appear within 1 hour from exposure [31–33]. Threshold lesions appear as greyish white spots on the cornea, see Figure 3b), and can be detected with a slit lamp down to 100 μ m in diameter [34]. According to Jean *et al.* [33], if the lesion is visible immediately after exposure, that level of exposure is considered a “super-threshold” exposure. The typical procedure used to determine corneal damage thresholds, or ED₅₀, consists of exposures at various radiant exposure levels followed by an examination to determine the presence or absence of an alteration of the cornea. Therefore, most threshold studies include data within the super-threshold, or supra-threshold, exposure regime as defined by Jean *et al.* [33]. Note that as the radiant exposure increases, depending on the wavelength and exposure duration, material may be removed and the endpoints of exposure transition from tissue damage to ablative tissue removal [35] and/or photothermal effects may start to play a more important role [32,36–40].

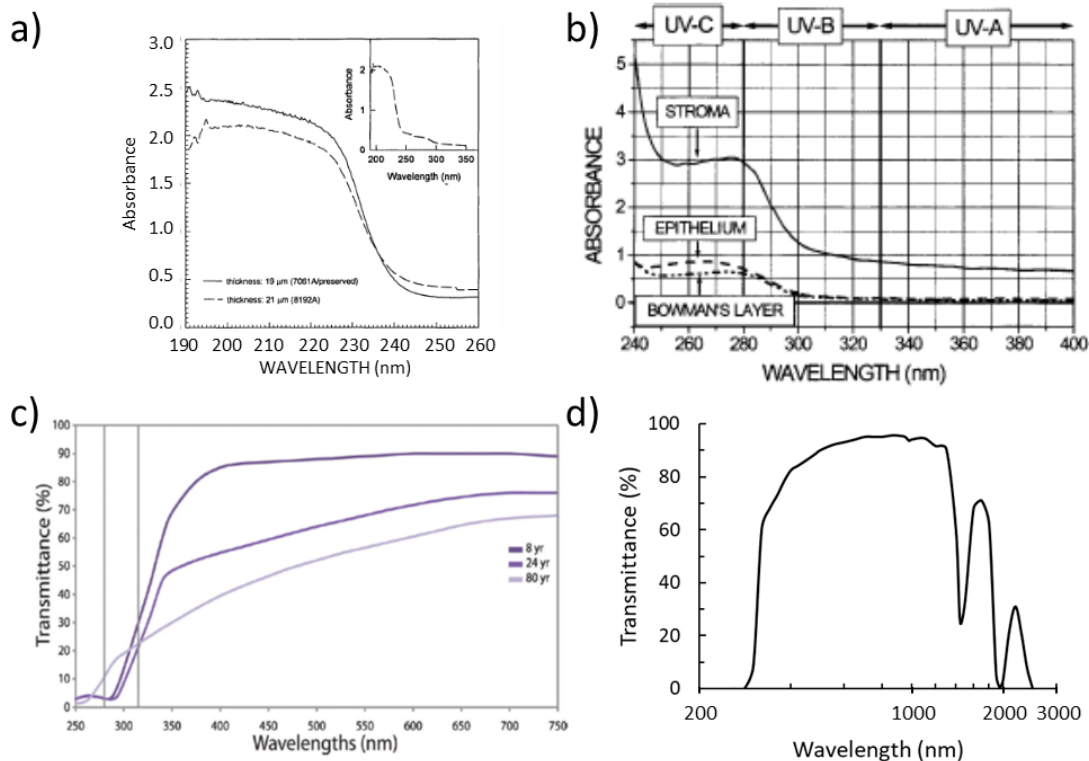


Figure 2. Spectra of human corneas. a) Absorbance spectra from 190 to 260 nm [25]. b) Absorbance spectra of the epithelium, Bowman's layer, and stroma from 240 to 400 nm [26]. c) Transmittance spectra of different age corneas from 250 to 750 nm [27]. Copyright © 2013, Springer Nature. Reprinted by permission as indicated in the Terms and Conditions of the license that you have received ([Rightslink - Springer Nature Terms and Conditions \(copyright.com\)](#)). d) Transmittance spectra of the cornea from 300 to 2800 nm. Plotted using data from [41]. (Awaiting copyright permission for panels a and b)

From a biological or medical perspective, ocular damage from light can occur through an inflammatory response to an initial insult or a photooxidative reaction [42]. In the former, the initial insult triggers a set of cellular events that affect a larger portion of the tissue. In the latter, molecules in the tissue(s) of the eye undergo a chemical change which can lead to the generation of free radicals and reactive oxygen species that ultimately damage the ocular tissues. From a physical standpoint, there are three main mechanisms for laser induced ocular damage: photochemical, photomechanical and thermal [36]. Which one dominates depends on the absorption characteristics of the tissue as well as the wavelength, duration, and fluence of the laser exposure. In general, photothermal damage, or thermal damage, dominates when exposures have long durations with high-peak powers. Photomechanical damage, including photoablation, occurs when short-pulse, high-peak power laser exposures occur. Photochemical reactions dominate at wavelengths close to the absorption lines of the molecular constituents of the tissues occur [30,36]. Photochemical reactions are the primary mechanism for photobiological alterations from exposure to UV radiation and are nominally non-existent for exposure to IR light, therefore, we will expand on their discussion in section 3.1.

Thermal damage occurs when sufficient energy from the incoming light is deposited in the tissue and converted into heat, increasing the temperature of the tissue within the exposed volume. If the temperature increase of the tissue exceeds a certain threshold, thermal damage occurs. The temperature rise is inversely related to the absorption depth since a larger absorption depth means

the energy distributes over a larger volume and consequently there is a smaller temperature rise. Thermal damage is directly related to the absorption characteristic of the tissue, the particular wavelength and pulse duration of exposure [37]. In general, thermal damage dominates for pulse durations longer than around 100 μ s [36,43,44]. Photomechanical damage is a surface phenomenon that occurs for short pulse durations and high-peak powers. In that case, energy from the incoming light is concentrated in space and time [36]. This concentration of energy can create a flux of photons that breaks molecular bonds and results in an explosive dispersion of tissue fragments, or photoablation [30]. If there is strong absorption, the damage is confined to a very small volume of tissue which is ablated with little to no collateral damage. In addition or alternatively, the large concentration of energy can cause optical breakdown or ionization, and may result in cavitation, shock waves, and/or plasma formation [36].

The authors encountered several studies focused on corneal ablation for ophthalmic procedures while reviewing the literature on light induced damage to the cornea. In that body of literature, the goal is to determine the optimal amount of energy deposited on the cornea per unit time that most efficiently removes tissue while minimizing collateral damage. The traditional figure of merit for these types of studies is the rate of ablation. However, although the rate of ablation is related to corneal damage, the authors of the current technical report could not elucidate a straightforward relationship between the corneal damage threshold and the rate of ablation that is applicable at the wavelengths of interest.

3.0 UV WAVELENGTHS

3.1 Interaction of UV Wavelengths with the Cornea

The UV region of the electromagnetic spectrum divides into three spectral regions: UVC (100 – 290 nm), UVB (290 – 320 nm), and UVA (320 – 400 nm). Absorption measurements show that longer wavelengths penetrate tissues more deeply than shorter wavelengths, Figure 2a) and b), such that UVC and UVB wavelengths are mostly absorbed by the corneal epithelium while UVA wavelengths can penetrate the entire thickness of the cornea as schematically represented in Figure 3a) [27,45].

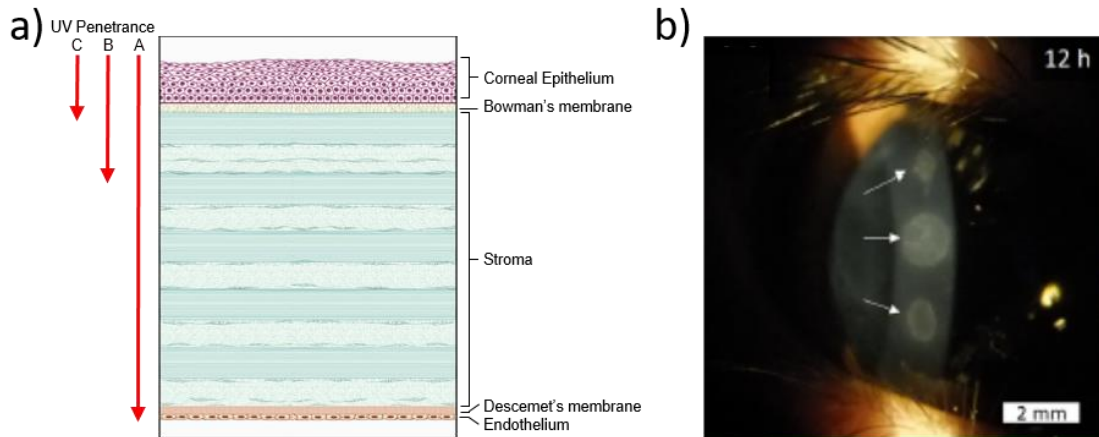


Figure 3. a) Schematic representation of the depth of penetration of the UV bands into the different layers of the cornea - adapted from [5]. Reproduced under the terms and conditions of the Creative Commons Attribution (CC BY-NC 2.0) (<https://creativecommons.org/licenses/by-nc/2.0/>). b) Slit-lamp image of a rabbit eye 12 h after exposure to 355 nm at $1.3 \times ED_{50}$ (top and bottom) and $5.2 \times ED_{50}$ (middle) [46]. Reproduced under the terms and conditions of the Creative Commons Attribution (CC BY 4.0) – Gold Open Access (<https://creativecommons.org/licenses/by/4.0/>).

As shown in Figure 2a) and b), corneal absorption increases rapidly below 300 nm. Since water does not significantly absorb light between 193 nm and 293 nm, the absorption observed for corneal tissue in that wavelength range is due to the solid components of the cornea, particularly in the epithelium [30,36]. The solid components primarily consist of proteins distributed differently throughout the corneal layers. For example, nucleic acids (RNA and DNA), ATP, and ascorbic acids are mostly found in the epithelium, while collagen is the primary component of the stroma. Notably, all of these components have a high absorption below 293 nm, e.g. nucleic acids absorb strongly at 248 nm while ascorbic acid and collagen do so around 250 nm. However, different UV wavelengths can interact and affect the same solid component in different ways. For example, it is thought that UVA light primarily damages the DNA through oxidative stress [47], while UVB and UVC light are directly absorbed by the DNA, generating mutagenic photoproducts [27,48]. Research conducted to identify damage parameters for corneal exposure to UV light note that, although there is a clear relationship between the absorption properties of the cornea's constituents to changes in the cornea as a result of UV exposure, maxima in plots of the damage threshold as a function of wavelength are not directly correlated to the absorption peaks of a particular molecule [36]. In addition, the UV induced corneal damage is restricted to the epithelial and endothelial layers, except for extremely high exposure levels where the stroma is also affected.

The primary mechanism for photobiological alterations of the cornea when exposed to UVA [31,49], UVB and UVC wavelengths [31,36,50] is photochemical reactions. To understand a photochemical reaction, consider a molecule that has absorbed the energy of a photon, raising it to an electronically excited state. This excited-state molecule undergoes an electronic relaxation process, resulting in a different molecule. If during the relaxation process one of the original bonds is broken relative to the ground state, or a new bond is formed, then the excited-state molecule is considered to have undergone a photochemical reaction [36]. Although it is thought that different molecules are involved in the photochemical reactions upon exposure to the different UV bands [49], the temporal development of the effects, general appearance and clinical symptoms associated with the corresponding damage are all similar.

It is generally accepted that for single-photon photochemical mechanisms there is a relationship between the laser intensity and the exposure time such that the total energy dose needed to cause tissue damage remains the same [30], referred to as the principle of reciprocity or the Bunsen-Roscoe reciprocity law [51–53]. Consequently, the threshold for corneal damage does not change with pulse or exposure duration over a relatively large range from nanoseconds to thousands of seconds. Another consequence of having a single-photon photochemical mechanism responsible for damage is that as long as the tissue is not repaired or replaced in between exposures, repeated exposures will have a cumulative effect [30]. However, although the threshold for corneal damage does not change with pulse or exposure duration, there is a strong wavelength dependence on the threshold exposure values as shown in Figure 4.

Another mechanism for photobiological alteration of the cornea when exposed to UV lasers is that of photoablation. There is a large volume of literature primarily focused on photothermal ablation of the cornea for medical purposes. However, given the focus of the current report, we will not include that body of work in this report. For the purposes of this report, we focus on collecting only corneal damage thresholds.

At UV wavelengths, each individual photon may have enough energy to induce a photochemical effect and disrupt the normal functioning of a cell. However, there may be a delay between the UV exposure and the macroscopic observation of any abnormality in the tissue. For the cornea, this delay is built into the modern criteria used to identify a threshold lesion, *i.e.*, 1 hour after exposure, although not all studies follow that criterion. Reports found in the literature utilize a variety of different experimental setups to produce corneal tissue damage as well as a large range

of experimental conditions, including laser sources and exposure parameters, human vs. animal models, live vs. excised corneas, among others. In addition, there is no consensus on the definition for damage, which ranges from a barely visible greyish spot on the cornea to the removal of corneal tissue, or on when to assess the damage, *i.e.* 1 hour versus 24 hours after exposure. These differences need to be taken into consideration when using other studies as a guide and/or when comparing between studies. It is also important to note that laboratory experiments to determine the ED₅₀ typically use small area exposures; therefore, they do not produce any symptoms of eye irritation [31] as seen in whole eye corneal exposures to UV radiation.

Historically, the initial interest in assessing corneal UV exposures was motivated by several medical conditions associated with whole eye corneal exposures to UV radiation [45]. The most well-known is photokeratitis - an acute reaction to UV radiation exposure equivalent to a sunburn. Snow blindness and welder's flash are two layman's terms for photokeratitis where the former is a result of whole-eye exposure to sunlight reflected by snow and ice over a long period of time and the latter is a result of exposure to a welding torch, *i.e.*, a very intense source of light, over short periods of time. The symptoms of photokeratitis usually develop several hours after exposure to UV light, initially starting as a gritty ocular sensation followed by photophobia and tearing. These initial symptoms are a result of loss and damage of the epithelial cells. When there is corneal edema or swelling, the resulting symptoms are haze and vision impairment. Further exposure to UV light results in shedding of the epithelial cells, which exposes the nerve endings and results in agonizing pain. It is thought the main wavelengths responsible for photokeratitis lie within the UVC band and, depending on the severity of the exposure, the symptoms may last a few hours up to 48 h. Exposures that result in photokeratitis are considered supra-threshold level exposures [31].

3.2 Cornea Damage Thresholds at UV Wavelengths

Figure 4 is a plot of the UV corneal damage thresholds or ED₅₀ levels as a function of wavelength compiled from the literature where the sources are referenced in the legend. For completeness and ease of comparison, the plot includes data obtained from different species, live and enucleated eyes, incoherent and coherent (laser) sources, and various exposure durations. Details about the specific exposures can be found in Appendix A. Given the large amount of literature and the availability of reviews on corneal damage thresholds at UV wavelengths, we will address only the most salient features in the data.

From Figure 4, corneal damage thresholds span ~6 orders of magnitude across all the UV range, changing most rapidly between 210 to 220 nm and between 310 to 330 nm. There are only two studies focused on corneal damage thresholds from exposures to 193 nm and their results, although conducted on different species with different number of pulses, are roughly consistent with each other. From Figure 4, there have been many studies to determine the corneal damage threshold between 207 nm and ~400 nm. As detailed in the Appendix A, these studies used widely varying experimental conditions, *i.e.*, animal models, source type, exposure durations, criteria for damage. Despite this variety, most of the data followed a similar trend. The cornea exhibited a maximum sensitivity to UV light at 193 nm and in the 260 – 280 nm range, which is contained in the UVC band [31]. The 260 – 280 nm waveband corresponds to the first absorption bands of aromatic amino acids found in proteins and nucleic acids [54]. From Figure 4, the corneal damage thresholds for the UVA band, or near-UV, were several orders of magnitude larger than the corneal damage thresholds for the UVC band, or far-UV. It has been speculated that the cornea exhibits a larger damage threshold for exposure to light in the UVA band due to evolutionary pressures resulting from the fact that most of the UV light from the Sun reaching the Earth's surface is UVA.

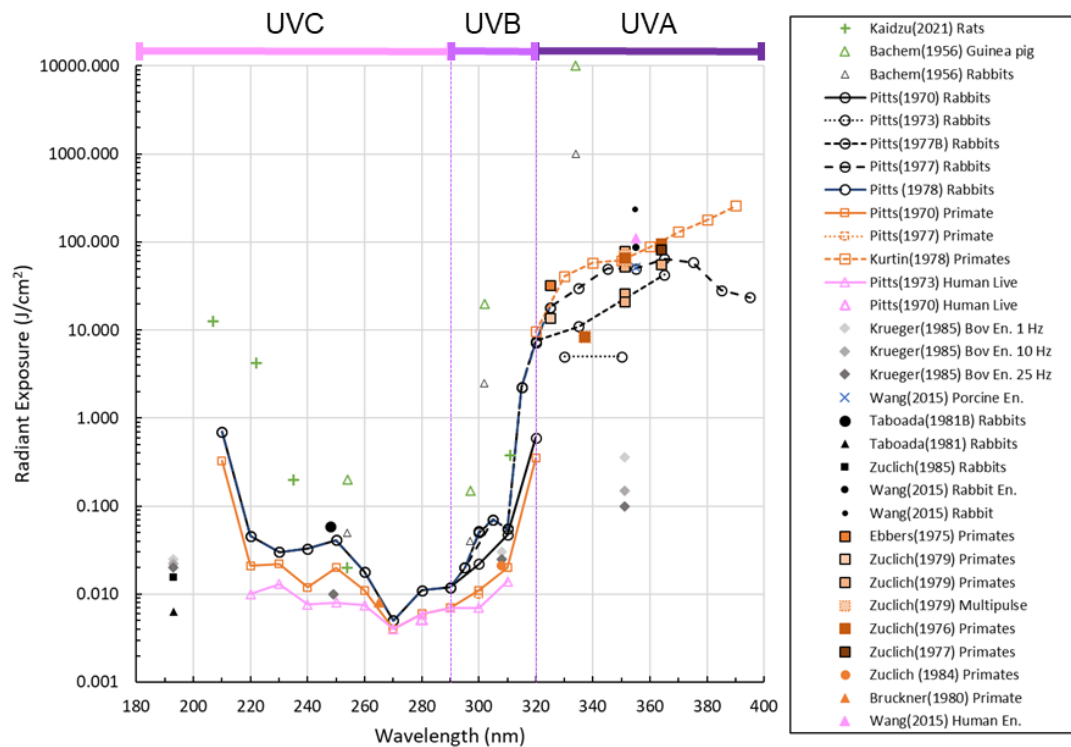


Figure 4. UV Corneal damage thresholds complied from the literature Bar above the graph identifies the three spectral regions referenced in the text. **Legend description:** + and open symbols correspond to incoherent sources; × and solid symbols correspond to short pulsed laser exposures (< 50 ns), while symbols with different colored edges correspond to longer pulse durations (>250 μs). Species are color coded: **green** – rodents, **black** – rabbits, **orange** – primates, **pink** – humans, **gray** – bovine, **blue** – porcine. All data were obtained from live subjects except as noted (En. stands for enucleated).

The majority of the data points presented in Figure 4 were obtained using incoherent sources (+ and open symbols in Figure 4) with exposure durations that varied from ~3 to ~23,000 s. For most studies using incoherent sources, the bandwidth of exposure was limited to 5 or 10 nm. Only one study limited the bandwidth of exposure to 1, 2 and 4 nm depending on the wavelength (+, [55]). The coherent sources used were both pulsed and continuous wave (CW) lasers (× and solid symbols in Figure 4). The exposure durations for the pulsed sources consisted of single pulse exposures to 0.8 – 50 ns pulse durations and multiple pulse exposures lasting between 17 to 3000 s. The exposure durations to CW lasers lasted between 4 and 10,000 s depending on the study. In general, the data obtained from laser exposures agreed with the corneal damage thresholds obtained with the incoherent sources.

Most of the data presented in Figure 4 was obtained from experiments in live subjects, primarily rabbits and primates, although some data was obtained from enucleated eyes from various species (noted by En. in the legend). In general, the data obtained from ex-vivo subjects agreed with the corneal damage thresholds obtained from live subjects. However, the data collected from live rats [55], live guinea pigs [56], bovine enucleated eyes [39], and one study with live rabbits [37], fell outside the range of the other studies. These outliers will be discussed in more detail below.

The corneal damage thresholds at 207, 222, and 235 nm in the study by Kaidzu *et al.* (+ in Figure 4) were higher than those expected by comparing to other studies. This discrepancy may be attributed to the use of rats, which are nocturnal, and the authors reported lowest adverse effect levels instead of actual ED₅₀ levels. However, the damage thresholds for exposures to 254 and 311 nm agreed with data from other studies.

In the study conducted by Bachem *et al.*, the corneal damage thresholds for rabbits (Δ in Figure 4), at 254 and 297 nm agreed with data from other studies. The same study also reported the damage thresholds for guinea pigs (Δ in Figure 4). Damage thresholds for guinea pigs at all wavelengths reported were considerably higher than those expected by comparing to other studies. This discrepancy may be attributed to using corneal blurring as the criteria for damage. The corneal blurring was evaluated using a flashlight and, from similar observations reported in that same study using rabbits, corneal blurring is noticeable at irradiances at least 3 times larger than those found when evaluating the corneal threshold using a slit lamp and fluorescein stain. Taking that observation into account brings the damage thresholds for guinea pigs closer to those reported for rabbits in that same study. Nevertheless, the damage thresholds at 302 and 334 nm were higher than those expected by comparing to other studies. This study utilized three different mercury arc sources with and without filters such that, in some cases, the spectrum of the light used for exposures consisted of a broad band of wavelengths. That is, for the data point labeled 254 nm, the actual spectrum extended from 240 nm into the visible range, although 254 nm was predominant. For the data point labeled 297 nm, the spectrum also contained 289 nm and longer wavelengths, while the data point labeled 302 nm, contained wavelengths longer than 302 nm (<1%) extending into the visible. The data labeled 334 nm represented wavelengths between 334 nm (1%) and 365 nm (2%). Therefore, the corneal damage thresholds presented in Bachem's study are actually the result of exposures to multiple wavelengths, including visible wavelengths in some cases. The bandwidth characteristics of the sources used in this study may be responsible for the higher damage thresholds observed at 302 and 334 nm for both species. Note that in this study the authors also reported lens opacification and cataract formation at 297, 302, and 334 nm for both species.

In the study conducted by Krueger *et al.*, the authors used enucleate bovine eyes and an excimer laser to produce three different wavelengths. They explored the effect of different repetition rates in the context of multiple nanosecond long pulse exposures. The corneal damage thresholds they reported at 193 and 308 nm were comparable to those of other studies. At 254 nm the authors reported the corneal damage threshold as $< 0.010 \text{ J/cm}^2$ independent of the repetition rate, which is also within the values of other studies. However, at 351 nm the corneal damage thresholds were considerably lower than in other studies. The source of this discrepancy with other studies could be the fact that this is the only study that evaluated the effect of the exposures after 2000 to 3000 nanosecond long pulses. This study may be an example of how the cumulative effect from multiple pulses at 351 nm reduced the damage threshold with respect to that from a single pulse although it did not at 193, 254, and 308 nm. This study utilized bovine enucleated eyes, which may also be a contributing factor to the discrepancy with other studies.

4.0 IR WAVELENGTHS

4.1 Interaction of IR Wavelengths with the Cornea

The IR region of the electromagnetic spectrum extends from ~800 nm to 1 mm and in that range the transmission of the cornea varies from being almost 100% transparent to nearly completely opaque at about 3000 nm, see Figure 3d). The IR region divides into three regions; the near-IR (NIR; 780 – 1400 nm), the mid-IR (mid IR; 1400 – 3000 nm), and the far-IR (FIR; 3000 nm – 1 mm). However, this report covers only up to 10,600 nm in the FIR. In the near- and mid-IR

regions, the cornea transitions from allowing most of the light through to becoming more absorptive. The cornea and ocular media transmit wavelengths shorter than ~1000 nm, which can reach the retina and are therefore excluded from this report. Due to the optical properties and absorption characteristics of the ocular tissues, between 1100 nm and 1350 nm there is a gradual transition in which tissue (cornea, lens, or retina) is most sensitive to laser damage. Below 1000 nm the retina is the most sensitive tissue but above 1400 nm, the cornea becomes more absorptive, being the primary ocular element determining the ocular damage thresholds. Wavelengths between 1400 to 1500 nm and 1800 to 2600 nm have moderate penetration into the cornea, therefore it is expected that the damage for short pulse durations would be confined to the epithelium [57–59]. Wavelengths between 1500 and 1800 nm can penetrate the cornea and the aqueous, distributing the energy over a larger volume and raising the damage thresholds. Wavelengths above 2600 nm primarily absorb in the cornea.

Corneal damage mechanisms in the IR region are primarily photothermal although for short pulse durations, thermomechanical mechanisms are also involved. The damage thresholds generally follow the wavelength dependence of the penetration depth into the cornea, which is inversely related to the absorption coefficient of water [24,60], see Figure 3d) and Figure 6. The fact that the damage threshold approximately follows the wavelength dependence of the absorption depth may be related to a thermal damage mechanism where the temperature rise is reduced because the energy transferred is distributed over a larger volume [32]. However, there are also some biological constituents with transmission and absorption peaks in the IR region, *e.g.* collagen and amides, which may affect the absorption characteristics of IR light in the cornea, especially for wavelengths around 3000 nm.

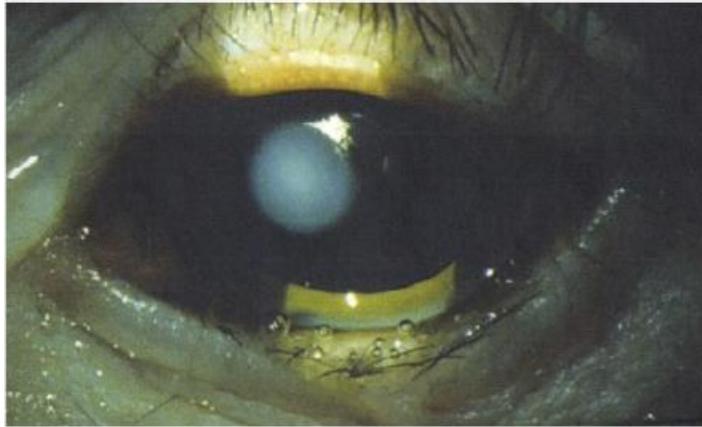


Figure 5. Slit-lamp image of a non-human primate eye 15 min after exposure to 10600 nm at $3 \times \text{ED}_{50}$ [33] (Copyright 2020 Optical Society of America under the terms of the OSA Open Access Publishing Agreement). Exposure duration was 100 ms and 1/e diameter was 2.5 mm.

Similar to UV exposures, threshold lesions may take some time to develop and become macroscopically visible such that the modern standard for evaluating corneal lesions is 1 hour after exposure [31–33]. Threshold lesions appear as a superficial clouding or whitening of the exposed area as observed with a slit lamp, see Figure 5. The current review focused on collecting corneal damage thresholds defined as an MVL with data obtained using a range of experimental conditions, including laser sources and exposure parameters. However, unlike at UV wavelengths, the studies mainly used live rabbit and primate animal models. The definition for damage ranged from a barely visible greyish spot on the cornea to the removal of corneal tissue, and when to assess the damage ranged from immediate up to 24 hours after exposure. Differences

in experimental conditions and evaluation need to be considered when using other studies as a guide and/or when comparing between studies.

Note there are several reviews of damage thresholds in the IR available in the literature [33,61,62]. The current technical note includes all the data from those reviews as well as additional data found in the literature.

4.2 Cornea Damage Thresholds at IR Wavelengths

Figure 6 is a plot of the published IR corneal damage thresholds as a function of wavelength which were not include in the previous report and the absorption coefficient of water (black line, scale not shown). The sources are referenced in the legend. The plot includes data obtained from different species, live and enucleated eyes, incoherent and coherent (laser) sources, and various exposure durations. Details about the studies can be found in the appendices. However, given the large amount of literature, we will address only the most salient features of the data in the following discussion.

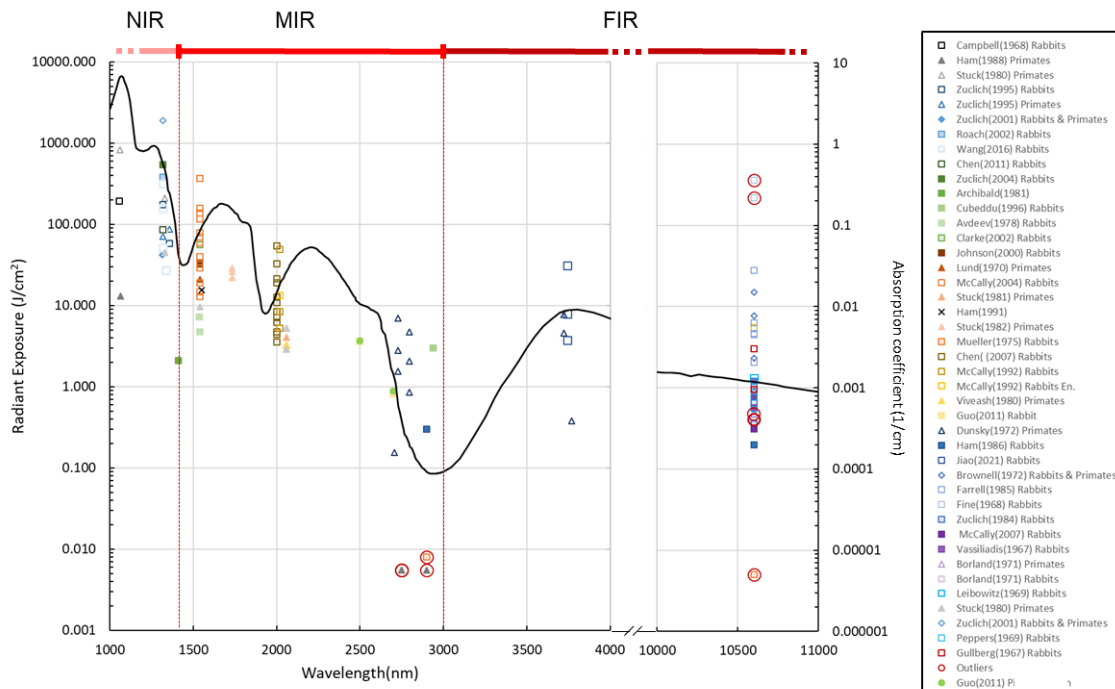


Figure 6. IR Corneal damage thresholds compiled from the literature and absorption coefficient of water (black solid line; right hand axis). Legend: open symbols correspond to CW sources, solid symbols to pulsed sources. Species are color by symbol: square – rabbits, triangle – primates, and rhombus – both rabbits and primates. All data were obtained from live subjects except as noted (En. stands for enucleated). Data within red open circles – see text.

The results reported by some studies [63–65] have come into question resulting in those data points not being considered when determining MPEs [32] or modeling corneal damage thresholds [33]. We briefly describe the shortcoming of those studies and will not consider the corresponding data points in further discussions. Ham and Mueller [63] reported values for 1.4 ns and 100 ns at 2900 nm and 10600 nm. The beam profile of the 2900 nm laser in that study was described as “poorly Gaussian with hot and cold spots” by the authors, rendering the beam profile poorly defined. The values reported in that study for 10,600 nm were considerably lower than damage threshold values reported by other groups for comparable pulse durations [66,67]. Speculation is that those values were affected by the experimental technique and issues with the

energy meter's calibration [32,33]. The damage threshold reported by Borland *et al.* [65] at 10,600 nm for 70 ms pulse durations was lower than damage threshold values reported by other groups for comparable pulse durations [68,69]. The discrepancy was attributed to the beam profile of the laser used [70]. In the study conducted by Fine *et al.* [64], the cornea was not kept moist, therefore the resulting damage thresholds were considerably lower than those from other studies at 10,600 nm and is not considered representative of a live eye. Therefore, the damage thresholds corresponding to references [63–65] (red open circles in Figure 6) are not considered in the following discussions.

Figure 6 summarizes the results of 42 studies. Between 1000 nm and 11,000 nm, corneal damage thresholds have been reported at only 23 different wavelengths, none of which are found between around 3000 – 3600 nm and between ~4000 – 10,400 nm. At four specific wavelengths, *i.e.*, 1319 nm, 1540 nm, 2000 nm, and 10,600 nm, there have been three or more studies to determine the corneal damage threshold. The corneal damage thresholds reported at the other 19 wavelengths were based on only one or two studies. The majority of the studies (60%) utilized live rabbits, 24% utilized live primates and 7% utilized both. Two studies utilized rabbit enucleated eyes while another one utilized both rabbit and pig enucleated eyes. However, in general, the data collected from enucleated eyes was consistent with that collected from live subjects.

Figure 6 shows that the wavelength dependence of the corneal damage thresholds follows the wavelength dependence of the absorption coefficient of water, with the cornea exhibiting a maximum sensitivity to IR radiation between 2500 nm and 3000 nm and at 10,600 nm. Given the variability in the corneal damage thresholds, there are no apparent inconsistencies between the data obtained with CW sources versus pulsed lasers at a given wavelength. At 1319 nm, 1540 nm, 2000 nm, and 10,600 nm, the variability in the damage thresholds reported spans ~2 orders of magnitude. However, to some extent differences in the exposure duration account for this variability, see Figure 7 and related discussion below.

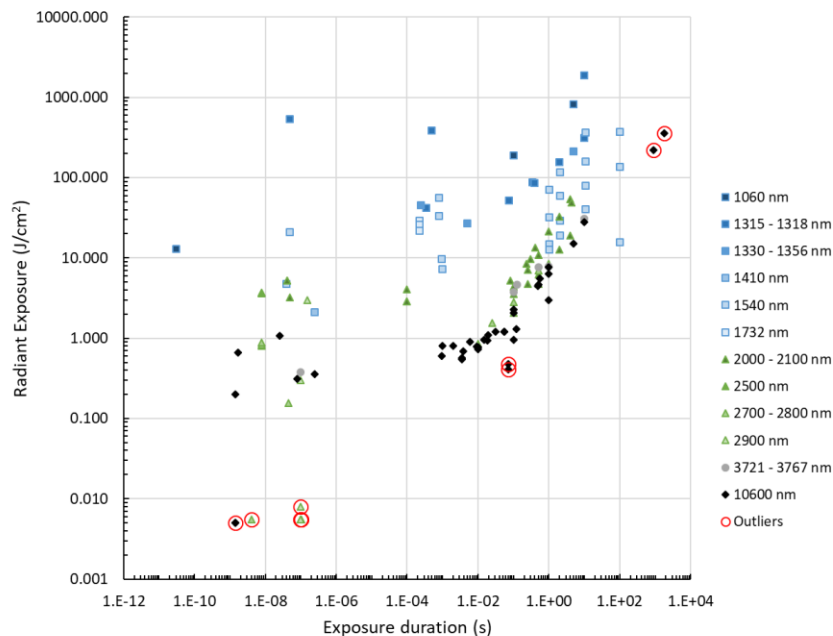


Figure 7. IR Corneal damage threshold as a function of exposure duration.

Figure 7 is a plot of the corneal damage threshold as a function of pulse duration where the blue squares correspond to wavelengths (λ) such that $1000 \text{ nm} < \lambda < 2000 \text{ nm}$, green triangles

correspond to $2000\text{ nm} < \lambda < 3000\text{ nm}$, and the black rhombus correspond to $10,600\text{ nm}$. Data is grouped into those three wavelength ranges to highlight similar trends. From this figure, most exposure durations varied from tens of seconds to milliseconds and from microseconds to nanoseconds. In the longer exposure regime ($> \text{milliseconds}$), the damage thresholds within a specific wavelength range appear to follow a power law relationship. Damage thresholds are consistently higher for wavelengths between 1000 nm and 2000 nm compared to those at the other wavelength ranges, which is consistent with the trend followed by the absorption coefficient of water at those wavelengths, Figure 6. Data at pulse durations shorter than microseconds are much sparser and do not appear to follow the power law trend, which may be a result of not having enough data points to generalize the behavior or having different tissue damage mechanisms.

5.0 DISCUSSION

This document provides an overview of absorption properties of the cornea, as well as laser induced corneal damage thresholds and laser damage mechanisms from exposure to UV wavelengths (100 nm to 400 nm) and IR wavelengths spanning 800 nm to $11,000\text{ nm}$.

The cornea has higher absorption at wavelengths between 100 nm to 320 nm (UVC and UVB) than between 320 nm and 400 nm (UVA) wavelengths. In surveying the corneal damage thresholds data published in the UV range, there are very few studies between 100 nm and 220 nm , possibly due to the lack of sources. However, from 220 nm to 400 nm , there have been many studies to determine the corneal damage threshold which, overall, indicate the cornea is the most sensitive to laser induced damage in the $260 - 280\text{ nm}$ range.

The absorption properties of the cornea vary considerably within the IR region of the electromagnetic spectrum. The cornea is almost completely transparent at 800 nm but transitions to becoming opaque at longer wavelengths, such that wavelengths longer than 2600 nm are primarily absorbed in the cornea. However, this transition is not monotonic. Wavelengths between $1400 - 1500\text{ nm}$ and $1800 - 2600\text{ nm}$ moderately penetrate the cornea, while wavelengths between 1500 and 1800 nm penetrate the cornea and the aqueous. The corneal damage thresholds in the IR range generally follow the wavelength dependence of the penetration depth into the cornea, which is inversely related to the absorption coefficient of water up to around 3000 nm . There is a lack of studies between 3000 and 3500 nm and between ~ 4000 up to $10,600\text{ nm}$, with pulse durations between 1 and $100\text{ }\mu\text{s}$ with limited multi-pulse data. There is a need to obtain data at larger beam diameters in order to establish if, and for what dimensions, the thresholds for corneal damage become constant in terms of radiant exposures.

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APPENDIX A – UV Cornea Laser Damage Threshold Tables

The following tables contain the corneal damage thresholds from the reviewed literature in the three spectral bands: UVC (100 – 290 nm), UVB (290 – 320 nm), and UVA (320 – 400 nm). The relevant laser wavelength, exposure duration, beam diameter, radiant exposure threshold, species, literature sources and notes on exposure details are listed in each table.

Table A.1. Corneal damage thresholds between 100 nm and 290 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference	Notes
193	50 ns	0.1	0.0063	--	--	Dutch-belted rabbits	[71] Taboada(1981)	
193	50 ns	0.1	0.0012	--	--	Dutch-belted rabbits	[71] Taboada(1981)	
193	25 ns	0.25 x 0.70	0.0154	0.0111	0.0261	Dutch-belted rabbits	[72] Zulich(1985)	
193	20 - 48 μ s*	14 x 1	0.025	$\pm$ 0.005	--	Bovine enucleated	[39] Krueger(1985) 1 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
193	2 - 4.8 μ s*	14 x 1	0.022	$\pm$ 0.006	--	Bovine enucleated	[39] Krueger(1985) 10 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
193	0.8 - 1.9 μ s*	14 x 1	0.020	$\pm$ 0.005	--	Bovine enucleated	[39] Krueger(1985) 25 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
207	231 – 16,116 s	16 x 18	12.500	--	--	Sprague-Dawley rats	[55] Kaidzu(2021)	Broadband. Varied exposure duration to vary dose.
210	--	18 x 18	0.700	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
210	--	18 x 18	0.3270	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
210	--	--	0.700	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
220	--	18 x 18	0.046	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.

220	--	18 x 18	0.0210	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
220	120 - 256 s	4	0.0100	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
220	--	--	0.046	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
222	6 - 1190 s	30 x 32	4.250	± 5.000		Sprague-Dawley rats	[55] Kaidzu(2021)	Broadband. Varied exposure duration to vary dose.
230	--	18 x 18	0.030	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
230	--	18 x 18	0.0220	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
230	32 - 45.5 s	4	0.0130	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
230	--	--	0.030	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
235	90 -2700 s	2 x 2.25	0.200	± 0.300	--	Sprague-Dawley rats	[55] Kaidzu(2021)	Broadband. Varied exposure duration to vary dose.
240	--	18 x 18	0.033	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
240	--	18 x 18	0.0120	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
240	14 - 17.0 s	4	0.0076	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
240	--	--	0.033	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
248	50 ns	6 x 1.9	0.003	--	--	Dutch-belted rabbits	[76] Taboada(1981B)	

248	50 ns	6 x 1.9	0.059	--	--	Dutch-belted rabbits	[76] Taboada(1981B)	
248	50 ns	6 x 1.9	0.071	--	--	Dutch-belted rabbits	[76] Taboada(1981B)	
249	20 - 48 μ s*	~14 x 1	<0.010	--	--	Bovine enucleated	[39] Krueger(1985) 1 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
249	2 - 4.8 μ s*	~14 x 1	<0.010	--	--	Bovine enucleated	[39] Krueger(1985) 10 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
249	0.8 - 1.9 μ s*	~14 x 1	<0.010	--	--	Bovine enucleated	[39] Krueger(1985) 25 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
250	--	18 x 18	0.041	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
250	--	18 x 18	0.0200	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
250	12.2 - 22 s	4	0.0080	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
250	--	--	0.041	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
254	18 - 273 s	47 x 73	<0.020	--	--	Sprague-Dawley rats	[55] Kaidzu(2021)	Broadband. Varied exposure duration to vary dose.
254	--	--	0.05	--	--	Albino rabbits	[56] Bachem(1956)	Broadband.
254	--	--	0.20	--	--	Guinea pig	[56] Bachem(1956)	Broadband.
260	--	18 x 18	0.018	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
260	--	18 x 18	0.0110	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
260	4.9 - 6.7 s	4	0.0075	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.

260	--	--	0.018	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
265	450 ps	2.9, 1..6, 1.1, 0.76	0.0082	.0063	.0107	Rhesus monkeys	[77] Bruckner(1980)	Varied beam diameter to change radiant exposure.
270	--	18 x 18	0.005	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
270	--	18 x 18	0.0040	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
270	2.9 - 9.9 s	4	0.0040	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
270	--	--	0.005	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
280	--	18 x 18	0.011	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
280	--	18 x 18	0.0060	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
280	--	18 x 18	0.0052	--	--	Live human	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
280	2.3 - 7.5 s	4	0.0059	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
280	--		0.011	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
290	--	18 x 18	0.012	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
290	--	18 x 18	0.0070	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
290	4.8 - 8.3 s	4	0.0070	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.

290	8486 – 24,348 s	--	0.012	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
290	--	--	0.012	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.

Table A.2. Corneal damage thresholds between 290 nm and 320 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference	Notes
295	130 s	1.6 x 1.8	0.020	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
295	5.18 - 8064 s	--	0.020	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
295	--	--	0.020	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
297	--	--	0.04	--	--	Albino rabbits	[56] Bachem(1956)	Broadband.
297	--	--	0.15	--	--	Guinea pig	[56] Bachem(1956)	Broadband.
300	--	18 x 18	0.022	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
300	--	18 x 18	0.0110	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
300	5.6 - 7.4 s	4	0.0070	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
300	137 s	1.6 x 1.8	0.050	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.

300	14.0 - 1866 s	--	0.050	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
300	15.9 - 478.8 s	--	0.010	--	--	Primate (Galago senegalensis)	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
300	--	--	0.052	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
302	--	--	2.50	--	--	Albino rabbits	[56] Bachem(1956)	Broadband.
302	--	--	20.00	--	--	Guinea pig	[56] Bachem(1956)	Broadband.
305	182 s	1.6 x 1.8	0.070	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
305	124 - 4583 s	--	0.070	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
305	--	--	0.070	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
308	20 - 48 μ s*	~14 x 1	0.030	$\pm$ 0.015	--	Bovine enucleated	[39] Krueger(1985) 1 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
308	2 - 4.8 μ s*	~14 x 1	0.025	$\pm$ 0.015	--	Bovine enucleated	[39] Krueger(1985) 10 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
308	0.8 - 1.9 μ s*	~14 x 1	0.025	$\pm$ 0.015	--	Bovine enucleated	[39] Krueger(1985) 25 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
308	25 ns	0.045	0.0210	0.017	0.026	Fascicularis monkeys	[80] Zuclich(1984)	
310	--	18 x 18	0.047	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
310	--	18 x 18	0.0200	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
310	8.5 - 10.0 s	4	0.0140	--	--	Live human	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.

310	201 s	1.6 x 1.8	0.055	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
310	201 - 3247 s	--	0.055	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
310	--	--	0.055	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
311	13 - 300 s	39 x 55	0.375	± 0.600	--	Sprague-Dawley rats	[55] Kaidzu(2021)	Broadband. Varied exposure duration to vary dose.
313	--	--	--	--	--	Albino rabbits	[56] Bachem(1956)	Broadband.
315	3882 s	1.6 x 1.8	2.250	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
315	90 – 10,924 s		2.250	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
320	--	18 x 18	0.600	--	--	Checker and Polish rabbits	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
320	--	18 x 18	0.3500	--	--	Rhesus monkeys	[73] Pitts(1970)	Broadband. Varied exposure duration to vary dose.
320	23,217 s	1.6 x 1.8	7.500	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
320	1164 – 11,439 s	--	7.250	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
320	--	--	7.250	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
320	--	1.36 x 1.48	9.57	8.5	10.7	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.

Table A.3. Corneal damage thresholds between 320 nm and 400 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference	Notes
325	10,251 – 36,000 s	--	18.000	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
325	--	--	18.000	--	--	Pigmented rabbits	[74] Pitts(1978)	Broadband. Varied exposure duration to vary dose.
325	--	1.78	32	30.6	35.6	Rhesus monkeys	[82] Ebbers(1975)	CW laser. Varied exposure duration to vary dose.
325	--	1.6	13.7	± 0.1	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
330	--	16 x 18	5.000	--	--	Pigmented rabbits	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
330	--	1.36 x 1.48	41.1	35.3	47.7	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.
334	--	--	1000	--	--	Albino rabbits	[56] Bachem(1956)	Broadband.
334	--	--	10000	--	--	Guinea pig	[56] Bachem(1956)	Broadband.
335	18,581 s	1.6 x 1.8	10.990	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
335	6400 – 26,339 s	--	30.000	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
337.1	800 ms [‡]	--	8.4	± 3.3	--	Rhesus monkeys	[83] Zuclich(1979)	[‡] Exposed to a train of 10 ns pulses.
337.1	30 s [‡]	--	8.4	± 3.3	--	Rhesus monkeys	[84] Zuclich(1976)	[‡] Exposed to a train of 10 ns pulses.
340	--	1.36 x 1.48	58.3	51.6	65.8	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.

345	5187 s	--	50.000	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
350	--	16 x 18	5.000	--	--	Pigmented rabbits	[75] Pitts(1973)	Broadband. Varied exposure duration to vary dose.
350	--	1.36 x 1.48	61.5	55.05	68.5	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.
351	20 - 48 μ s*	~14 x 1	0.360	$\pm$ 0.040	--	Bovine enucleated	[39] Krueger(1985) 1 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
351	2 - 4.8 μ s*	~14 x 1	0.150	$\pm$ 0.03	--	Bovine enucleated	[39] Krueger(1985) 10 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
351	0.8 - 1.9 μ s*	~14 x 1	0.100	$\pm$ 0.03	--	Bovine enucleated	[39] Krueger(1985) 25 Hz	*Exposed to a train of 10 ns – 16 ns pulses.
351	40 s	1.75	55.3	46.9	64.5	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	10,000 s	1.75	26	$\pm$ 1	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	1000 s	1.75	21	$\pm$ 4	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	120 s	1.75	53	$\pm$ 8	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	45 s	1.75	62	$\pm$ 6	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	30 s	1.75	66	$\pm$ 8	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	30 s	1.75	67	--	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	18 s	1.75	66	$\pm$ 8	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.

351	4 s	1.75	79	--	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
351	30 s [†]	1.75	66	± 9	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 1 s pulses.
351	30 s [†]	1.75	67	± 6	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 20 ms pulses.
351	30 s [†]	1.75	63	± 10	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 5 ms pulses.
351	30 s [†]	1.75	71	± 15	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 2 ms pulses.
351	30 s [†]	1.75	67	± 12	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 1 ms pulses.
351	30 s [†]	1.75	71	± 10	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 0.5 ms pulses.
351	30 s [†]	1.75	64	± 12	--	Rhesus monkeys	[83] Zuclich(1979)	[†] Varied number of 0.25 ms pulses.
351	18 s, 30 s, 45 s, 120 s	--	67.000	--	--	Rhesus monkeys	[84] Zuclich(1976)	Varied exposure duration to vary dose.
351	30 s	--	66	± 8	--	Rhesus monkeys	[84] Zuclich(1976)	Exposed to a train of pulses with varying pulse duration.
355	17,578 – 27,368 s	--	50.000	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
355	17 s ^{**}	0.87	87	77	96	New-Zealand white rabbit enucleated	[46] Wang(2015)	^{**} Exposed to a train of 550 ps pulses.
355	46 s ^{**}	1.4	231	212	248	New-Zealand white rabbit. Live	[46] Wang(2015)	^{**} Exposed to a train of 550 ps pulses.
355	22 s ^{**}		110	86	162	Human enucleated	[46] Wang(2015)	^{**} Exposed to a train of 550 ps pulses.
355	10 s ^{††}	1.1	52	47	57	Porcine enucleated	[46] Wang(2015)	^{††} Exposed to a train of 800 ps pulses.
355	800 ps	0.06	--	--	--	Porcine enucleated	[46] Wang(2015)	
360	--	1.36 x 1.48	88.4	--	--	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.

364	30 s	1.75	82	± 23	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
364	4 s	1.75	96	± 14	--	Rhesus monkeys	[83] Zuclich(1979)	CW laser. Varied exposure duration to vary dose.
364	30 s	--	82	± 23	--	Rhesus monkeys	[84] Zuclich(1976)	CW laser. Varied exposure duration to vary dose.
364	4 s	--	96	± 14	--	Rhesus monkeys	[84] Zuclich(1976)	CW laser. Varied exposure duration to vary dose.
364	30 s	--	82	58	104	Rhesus monkeys	[49] Zuclich(1977)	CW laser. Varied exposure duration to vary dose.
365	16647 s	1.6 x 1.8	42.500	--	--	Pigmented rabbits	[79] Pitts(1977B)	Broadband. Varied exposure duration to vary dose.
365	8993 – 62,239 s	--	65.000	--	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
370	--	1.36 x 1.48	130	116	147	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.
375	28,800 s	--	58.800	>58.80	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
380	--	1.36 x 1.48	179	157	205	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.
385	28,800 s	--	28.200	>28.20	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.
390	--	1.36 x 1.48	258	230	288	Rhesus monkeys	[81] Kurtin(1978)	Broadband. Varied exposure duration to vary dose.
395	28,800 s	--	23.500	>23.5	--	Pigmented rabbits	[78] Pitts(1977)	Broadband. Varied exposure duration to vary dose.

APPENDIX B – IR Cornea Laser Damage Threshold Tables

The following three tables contain the corneal damage thresholds from the reviewed literature in the three spectral bands: NIR (780 – 1400 nm), the mid-IR (1400 – 3000 nm), and the FIR (3000 – 10000 nm). The relevant laser wavelength, exposure duration, beam diameter, radiant exposure threshold, species, and literature source are listed in each table.

Table B.1. Corneal damage thresholds between 1000 nm and 1400 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference
1060	100 ms	1	191	--	--	Gray chinchilla rabbits	[85] Campbell(1968)
1064	25 – 35 ps		13	3	--	Rhesus monkey	[86] Ham(1988)
1064	5 s	1.84	825	--	--	Rhesus monkey	[34] Stuck(1980)
1315	350 μs	< 1	42	39	46	Dutch belted rabbits and rhesus macaques	[87,88] Zuclich(2001)
1318	--	1	71.3	68	81	Rhesus monkey	[89] Zuclich(1995)
1318	--	1	174	154	199	Rabbit	[89] Zuclich(1995)
1318	10 s	0.8	1890	910	2060	Dutch belted rabbits and rhesus macaques	[87,88] Zuclich(2001)
1318	500 μs	0.07	383	352	428	Dutch belted rabbits	[90] Roach(2002)
1319	75 ms	2	51.5	47.8	55.0	New Zealand rabbits	[91] Wang(2016)
1319	350 ms	2	87.2	84.4	95.1	New Zealand rabbits	[91] Wang(2016)
1319	2 s	2	156	141.4	172.1	New Zealand rabbits	[91] Wang(2016)
1319	10 s	2	311	243.0	335.9	New Zealand rabbits	[91] Wang(2016)
1319	0.4 s	2	86.1	83.4	88.8	New Zealand rabbits	[92] Chen(2011)
1319	50 ns	0.15	540	390	740	Dutch belted rabbits	[93] Zuclich(2004)
1330 ^a	250 μs	0.4	45	39	48	Rhesus monkey	[34] Stuck(1980)
1330	5 s	1.4	212	212	220	Rhesus monkey	[34] Stuck(1980)
1338	5 ms	2	27	25.8	28.1	New Zealand rabbits	[91] Wang(2016)
1356	--	0.7	87	67	102	Rhesus monkey	[89] Zuclich(1995)

1356	--	0.7	58	48	72	Rabbit	[89] Zuclich(1995)
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^aPulsed neodymium laser with output at 1138 and 1338 nm.

Table B.2. Corneal damage thresholds between 1400 nm and 3000 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference
1410	250 ns	1.093	2.1	--	--		[94] Archibald(1981)
1540	930 μ s	1	9.6	--	--	Rhesus monkey	[95] Stuck(1981)
1540	40 ns	1.06	4.7	2.4	--	Gray chinchilla rabbits	[96] Avdeev(1978)
1540	1 ms	1.06	7.2	1.2	--	Gray chinchilla rabbits	[96] Avdeev(1978)
1540	800 μ s	0.05	56	54.7	57.6	Dutch belted rabbits	[97] Clarke(2002)
1540	800 μ s	0.29	33	--	--	Dutch belted rabbits	[98] Johnson(2000)
1540	50 ns	0.28	21	< 17 no damage	> 30 always damage	Owl monkeys	[99] Lund(1970)
1540	1.04 s	0.53	70.1	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	1.04 s	1	32.3	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	1.04 s	2.19	14.7	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	1.04 s	4.99	12.8	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	2.05 s	0.53	116	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	2.05 s	1	59.4	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	2.05 s	2.19	28.9	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	2.05 s	6.98	18.9	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	11 s	0.53	367	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	11 s	1	158	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	11 s	2.19	79.3	--	--	New Zealand white rabbits	[100] McCally(2004)

1540	11 s	6.98	40.3	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	100 s	2.19	370	--	--	New Zealand white rabbits	[100] McCally(2004)
1540	100 s	6.98	137	--	--	New Zealand white rabbits	[100] McCally(2004)
1550	100 s	1.85	15.6	--	--		[101] Ham(1991)
1732	225 μ s	0.515	29	27	31	Rhesus monkey	[102] Stuck(1982)
1732	225 μ s	0.74	26	23	29	Rhesus monkey	[102] Stuck(1982)
1732	225 μ s	0.92	22	20	23	Rhesus monkey	[102] Stuck(1982)
2000	100 ms	0.83	4.39	.05	--	Dutch belted rabbits	[103] Chen(2007)
2000	250 ms	0.83	7.17	.17	--	Dutch belted rabbits	[103] Chen(2007)
2000	500 ms	0.83	10.8	0.10	--	Dutch belted rabbits	[103] Chen(2007)
2000	1 s	0.83	21.4	0.95	--	Dutch belted rabbits	[103] Chen(2007)
2000	2 s	0.83	32.6	0.71	--	Dutch belted rabbits	[103] Chen(2007)
2000	4 s	0.83	54.5	0.60	--	Dutch belted rabbits	[103] Chen(2007)
2000	100 ms	2.84	3.58	0.07	--	Dutch belted rabbits	[103] Chen(2007)
2000	250 ms	2.84	4.76	0.09	--	Dutch belted rabbits	[103] Chen(2007)
2000	500 ms	2.84	6.21	0.04	--	Dutch belted rabbits	[103] Chen(2007)
2000	1 s	2.84	8.48	0.96	--	Dutch belted rabbits	[103] Chen(2007)
2000	2 s	2.84	12.7	1.53	--	Dutch belted rabbits	[103] Chen(2007)
2000	4 s	2.84	19.1	0.22	--	Dutch belted rabbits	[103] Chen(2007)
2020	(0.08 – 4.3) s	0.94		--	--	New Zealand white rabbits	[58] McCally(1992)
2020	82 ms	0.94	5.26	--	--	New Zealand white rabbits	[58] McCally(1992)
2020	235 ms	0.94	8.46	--	--	New Zealand white rabbits	[58] McCally(1992)

2020	4.28 s	0.94	49.2	--	--	New Zeland white rabbits	[58] McCally(1992)
2020	404 ms	0.94	13.3724	--	--	Rabbit En.	[58] McCally(1992)
2020	300 ms	0.938	9.75	--	--	New Zeland white rabbits	[104] McCally(2003)
2060	100 μ s	1.8	2.9	--	--	Rhesus monkey	[95] Stuck(1981)
2060	42 ns	0.32	5.2	--	--	Rhesus monkey	[95] Stuck(1981)
2060	100 μ s	1.8	2.9	--	--	Rhesus monkey	[95] Stuck(1981)
2060	100 μ s	1.1	4.1	--	--	Rhesus monkey	[95] Stuck(1981)
2060	42 ns	0.32	5.2	--	--	Rhesus monkey	[95] Stuck(1981)
2060	50 ns	0.7	3.25	--	--	Monkey	[105] Viveash(1980)
2500	8 ns	0.538 x 0.195	3.67	--	--	Rabbit En. Fresh	[106] Guo(2011)
2500	--	--	3.62	--	--	Rabbit En. Frozen	[106] Guo(2011)
2500	--	--	3.68	--	--	Pig En. Frozen	[106] Guo(2011)
2700	8 ns	0.667 x 0.233	0.81	--	--	Rabbit En. Fresh	[106] Guo(2011)
2700	--	--	0.83	--	--	Rabbit En. Frozen	[106] Guo(2011)
2700	--	--	0.88	--	--	Pig En. Frozen	[106] Guo(2011)
2500 – 3000 ^b	4 ns	10.8	5.5×10^{-3}	1.3×10^{-3}	6.8×10^{-3}	Rhesus monkey	[86] Ham(1988)
2500 - 3000 ^b	100 ns	10.8	5.5×10^{-3}	1.3×10^{-3}	6.8×10^{-3}	Rhesus monkey	[86] Ham(1988)
2500 - 3000 ^b	(4 + 100) ns	10.8	5.5×10^{-3}	1.3×10^{-3}	6.8×10^{-3}	Rhesus monkey	[86] Ham(1988)

^b HF pulsed laser with broad emission in this range. Data is plotted at 2750 nm.

Table B.3. Corneal damage thresholds between 3000 nm and 10600 nm

Wavelength (nm)	Exposure Duration	Beam Diameter (mm)	Damage Threshold (J/cm ²)	Uncertainty or Lower Fiducial (J/cm ²)	Upper Fiducial (J/cm ²)	Sample	Reference
2706.2 ^c	45 ns	0.82	0.156	.153	.160	Rhesus macaques	[107] Dunskey(1973)
2727	25 ms	--	1.548	1.525	1.571	Rhesus macaques	[107] Dunskey(1973)
2727	100 ms	--	2.805	2.742	5.870	Rhesus macaques	[107] Dunskey(1973)
2727	500 ms	1.06	6.985	6.555	7.440	Rhesus macaques	[107] Dunskey(1973)
2795	10 ms	0.90	0.8571	0.8514	.8628	Rhesus macaques	[107] Dunskey(1973)
2795	100 ms	--	2.057	1.956	2.163	Rhesus macaques	[107] Dunskey(1973)
2795	500 ms	--	4.76	4.62	4.9	Rhesus macaques	[107] Dunskey(1973)
2900	100 ns	--	0.0055	4.3×10^{-3}	6.83×10^{-3}	Rhesus monkey	[86] Ham(1988)

2900	100 ns	10	0.008	.006	.010	Rabbit	[63] Mueller(1975)
2900	100 ns	0.3	0.3	--	--	Chinchilla rabbits	[63,108] Ham(1986)
2940	150 ns	85 μ m strip	3	--	--	Rabbits	[109] Cubeddu(1996)
3721.1 ^d	0.125 s	--	4.61	4.32	4.92	Rhesus macaques	[107] Dunskey(1973)
3721.1 ^d	0.5 s	--	7.685	7.300	8.090	Rhesus macaques	[107] Dunskey(1973)
3743	100 ms	1.55	3.73	--	--	New Zealand white rabbits	[110] Jiao(2021)
3743	1 s	1.55	7.91	--	--	New Zealand white rabbits	[110] Jiao(2021)
3743	10 s	1.55	31.1	--	--	New Zealand white rabbits	[110] Jiao(2021)
3767.5 ^e	100 ns	0.96	0.377	0.368	0.385	Rhesus macaques	[107] Dunskey(1973)
10600	1.4 ns	0.95	0.005	--	--	Rhesus monkey	[86] Ham(1988)
10600	1.4 ns	10	0.005	--	--	Rabbit	[63] Mueller(1975)
10600	553 ms	5.84	5.53	--	--	Rabbit En.	[58] McCally(1992)
10600	1.4 ns	4.75	0.2	--	--	Chinchilla rabbits	[88] Ham(1986)
10600	1 ms	--	0.8	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	2 ms	--	0.8	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	6 ms	--	0.9	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	10 ms	--	0.73	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	100 ms	--	2.3	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	1 s	--	7.7	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)

10600	5 s	--	--	--	--	Rabbits, Macaca Mulatta, Aotus Trivirgatus	[111] Brownell(1972)
10600	960 μ s	1.02	0.599	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	3.9 ms	1.8	0.69	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	9.2 ms	2.52	0.79	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	15 ms	1.78	0.964	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	18.5 ms	1.8	0.945	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	19.1 ms	2.54	1.09	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	30.9 ms	2.6	1.2	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	101 ms	1.58	2.07	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	498 ms	1.82	4.48	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	500 ms	2.24	4.69	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	977 ms	2.44	6.31	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	9.73 ms	2.48	28.1	--	--	New Zealand white rabbits	[69] Farrell(1985)
10600	900 s	5.2	220	--	--	Albino rabbits	[64] Fine(1968)
10600	1800 s	5.2	360	--	--	Albino rabbits	[64] Fine(1968)
10600	1.7 ns	2.19	0.66	0.64	0.68	Dutch belted rabbits	[80] Zuclich(1984)
10600	25 ns	2.19	1.08	0.92	1.18	Dutch belted rabbits	[80] Zuclich(1984)
10600	250 ns	2.19	0.36	0.34	0.4	Dutch belted rabbits	[80] Zuclich(1984)
10600	80 ns	3.72	0.31	--	--	New Zealand white rabbits	[67] McCally(1997)
10600	3.5 ms	3	0.57	--	--	Rabbit	[68] Vassiliadis(1967)
10600	10 ms	3	0.77	--	--	Rabbit	[68] Vassiliadis(1967)

10600	55 ms	3	1.2	--	--	Rabbit	
10600	70 ms	2.5	0.48	--	--	Monkey (Maccaca mulatta)	[65] Borland(1971)
10600	70 ms	2.5	0.41	--	--	Rabbit (Cuniculus oryctolagus)	[65] Borland(1971)
10600	120 ms	6.4	1.31	--	--	Dutch belted rabbit	[112] Leibowitz(1969)
10600	3.5 ms	0.02	0.55	--	--	Rabbit	[113] Peppers(1969)
10600	10 ms	0.02	0.77	--	--	Rabbit	[113] Peppers(1969)
10600	55 ms	0.02	1.2	--	--	Rabbit	[113] Peppers(1969)
10600	100 ms	0.03	0.95	--	--	Rabbit	[114] Gullberg(1967)
10600	1 s	0.03	3	--	--	Rabbit	[114] Gullberg(1967)

^cHF pulsed pin discharge.

^dCW deuterium fluoride with emission at 3698 and 3731 nm. Data is plotted at 3721.1 nm.

^eDF pulsed pin discharge.