Porcine skin damage threshold from mid-infrared optical parametric oscillator radiation at 3.743 µm

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Abstract: There is increasing use of mid-infrared optical parametric oscillator radiation operating in the wavelength range of 3–5 µm. To expand existing damage data for skin exposure to lasers in this wavelength region, the in-vivo damage threshold at the wavelength of 3.743 µm was determined in a Guizhou miniature pig model for an exposure duration of 1.0 s. The irradiance of the laser spot was nearly Gaussian-distributed and the 1/e² beam diameter on the animal skin surface was fixed at 0.94 and 0.88 cm along horizontal and vertical directions. Damage lesion determinations were performed at 1- and 24-hour post-exposure. The probit analysis was employed to establish the ED₅₀ values. The ED₅₀ expressed in peak radiant exposure for the Gaussian spot was 4.04 J/cm² at the 24-hour post-exposure. Sufficient margin existed between the damage threshold and MPE from the current laser safety standard. The obtained data may contribute to the knowledge base for refinement of laser safety standard in the wavelength range of 2.6–1000 µm.

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1. Introduction

Laser systems operating in the wavelength range of 3–5 µm are in widespread use in military and scientific applications [1–3]. Comparing to chemical deuterium fluoride lasers developed in 1970s, optical parametric oscillator (OPO) technology is receiving much attention in recent years due to diverse advantages including better control, no risk of explosion and avoiding use of toxic gases [4–9]. With the advances on nonlinear crystals and fiber lasers, technology in fiber laser pumped OPO advanced rapidly and the output power increased continually [10–14]. In international public reports, the maximum power of continual-wave infrared OPO laser has been increased above 30 W, with wavelength tuning range of 3.2–3.9 µm [15]. Considering the increasing applications of continuous wave systems around 3.8 µm, it may be necessary to evaluate the need to refine existing laser safety exposure limits (ELs) or maximum permissible exposures (MPEs) for these systems.

EL or MPE is the level of laser radiation to which persons may be exposed without suffering adverse effects [16]. The ELs for various wavelengths and pulse widths are defined by the International Commission on Non-Ionizing Radiation Protection [16], and then MPEs are specified in laser safety standards including IEC 60825-1 and ANSI Z136.1 [17,18]. The determination of ELs and MPEs is done based on the evaluation of minimum visible lesion threshold data, modeling, and understanding of the mechanisms for damage [16]. For skin, ELs or MPEs are specified in all three documents and currently are largely same with some difference in certain wavelength bands [16–18]. For the refinement of MPE values, several in vivo studies over the past two decades have been conducted to determine porcine skin damage thresholds in the wavelength range of 1.0–2.0 µm [19–28]. At the wavelength of 2.0 µm, Chen et al. performed experimental and simulation studies to investigate skin damage effects for...
various exposure durations (0.25–2.5 s) and incident beam diameters (5–15 mm) [19–21]. At the wavelength of 1.94 µm, skin damage thresholds were determined by Oliver et al. for exposure durations from 10 ms to 10 s and beam diameters of 4.8 to 18 mm [22]. At the wavelength of 1.54 µm, damage threshold measurements were performed by Cain et al. for two exposure durations (600 µs and 31 ns) and three spot sizes (0.7, 1.0 and 5.0 mm) [23]. At the wavelength of about 1.32 µm, damage thresholds for two exposure durations (0.35 ms and 50 ns) and three spot sizes (0.7, 1.3 and 5.0 mm) were determined by Cain et al. [24]. Oliver et al. and Jiao et al. determined damage thresholds for various exposure durations (0.25–10 s) and beam diameters (0.4–3.0 cm) and revealed damage characteristics through histology studies [25,26]. At the wavelength of 1070 nm, damage threshold measurements were performed by Vincelette et al. for a range of beam diameters (0.6–9.5 cm) and exposure durations (0.01–10 s) [27], and DeLisi et al. determined damage thresholds for multiple-pulsed laser exposures at a constant beam diameter of 1 cm [28].

Existing reports give considerable attention to skin damages in the wavelength range of 1.0–2.0 µm. However, fewer studies for wavelengths above 2.6 µm could be found. Table 1 shows skin MPE in the wavelength range of 2.6–1000 µm for the exposure durations of 10⁻⁷ to 10 s [18]. Considering that ELs or MPEs in the three laser safety documents are same for this wavelength range [16–18], only the MPE from IEC 60825-1 standard was cited in the following. It is pointed out that MPEs for wavelengths beyond 2.6 µm are based on very little experimental data [16], totally from the damage effects induced by CO₂ lasers at 10.6 µm. It is worth noting that the specified MPEs show no spectral dependence in this wavelength range. One important fact should be noted that MPEs are always specified according to the damage threshold dependences on wavelength and pulse duration but significant simplifications were made for ease of use. Therefore, MPEs for wavelengths above 2.6 µm may don’t reflect the damage threshold dependence on wavelength, although the absorption coefficient of water (main content of skin) changes from the minimum value 112.44 cm⁻¹ at 3.802 µm to the maximum value 12026 cm⁻¹ at 2.951 µm [29].

Considering the lack of damage data in this wavelength range and the increasing use of lasers at wavelengths around 3.8 µm, we employed a fiber laser pumped OPO source at the wavelength of 3.743 µm to determine porcine skin damage threshold. The obtained data may contribute to the knowledge base for the refinement of laser safety standard in this wavelength range.

Table 1. Maximum permissible exposure (MPE) for skin exposure to laser radiation in the wavelength range of 2.600 to 1000 µm for the exposure duration of 10⁻⁷ to 10 s [18].

| Wavelength (µm) | Exposure Duration (s) | MPE (J/cm²) | Limiting Aperture Diameter (mm) |
|----------------|-----------------------|-------------|--------------------------------|
| 2.600 to 1000  | 10⁻⁷ to 10             | 0.560²⁵     | 3.5 mm for 2.600 to 100 µm     |
|                |                       |             | 11 mm for 100 to 1000 µm       |

2. Methods

2.1. Experimental set-up for porcine skin exposures by mid-infrared OPO radiation

Figure 1 shows the experimental set-up for porcine skin exposures. The source was a fiber laser pumped MgO:PPLN OPO continuous wave laser (National University of Defense Technology, Changsha, China), having three kinds of laser radiation with wavelengths of 1.070 µm (pump laser), 1.498 µm (signal laser) and 3.743 µm (idler laser). After two mirrors M1 and M2, the idler laser radiation was separated with the pump and signal laser radiations. The two mirrors had a high reflectivity (R > 99%) in the wavelength bands of 1.0–1.1 µm and 1.4–1.7 µm, and a high transmittance (T > 95%) in the wavelength range of 2.5–4.1 µm with the incidence angle of 45°. The maximum power of the idler laser was about 8.3 W, with the relative power peak fluctuation within ± 5.0% for two hours operating time. A GaF₂ beam splitter and a laser power meter PM1 (3A, Ophir, Jerusalem, Israel) were utilized to monitor the stability of the laser power.
during laser exposures. Three beam dumps BD1, BD2 and BD3 were used to collect un-needed laser radiation. Exposure duration was controlled by an electronically-controlled mechanical shutter ES. The laser power incident on the skin surface was adjusted by changing the driving current of the OPO system and adding GaF$_2$ plate attenuators. A laser power meter PM2 (30A, Ophir, Jerusalem, Israel) was positioned to measure the laser power incident on the skin surface. Two low-power 655-nm laser pointers, crossing at the center of the laser spot, facilitated the targeting of the un-visible infrared laser radiation. We adjusted the beam diameter to be about 1 cm by changing the distance between the OPO source and the animals. At the skin surface, the irradiance of the laser spot was nearly Gaussian-distributed. Using the knife-edge method [30], the $1/e^2$ beam diameters in the horizontal and vertical directions were determined as about 0.94 cm and 0.88 cm respectively. The $1/e^2$ diameter refers to the diameter of the smallest circle which contains 86.5% of the total laser power.

![Schematic drawing of the exposure setup.](image)

**Fig. 1.** Schematic drawing of the exposure setup for the porcine skin damage effects induced by an infrared optical parametric oscillator (OPO, Fiber laser pumped MgO: PPLN optical parametric oscillator. M1, Mirror having a high reflectivity (R > 99%) in the wavelength ranges of 1.0–1.1 µm and 1.4–1.7 µm, and simultaneously having a high transmittance (T > 95%) in the wavelength range of 2.5–4.1 µm. M2, Mirror having same coating with the mirror M1. BD1: Beam dump for collecting the pump and signal lasers. BD2: Beam dump for collecting the residual pump and signal lasers. W: GaF$_2$ beam splitter with the wedge angle of 8°. BD3: Beam dump for collecting the idler laser radiation reflected from the first surface of the wedge beam splitter. PM1: Laser power meter 1#. ES: Electronically-controlled mechanical shutter. AS: Attenuators including GaF$_2$ plates. LP1 and LP2: Low-power 655 nm laser pointers. PM2: Laser power meter 2#).

2.2. Animal subjects

Guizhou miniature pigs of either sex, weighing 15–20 kg and having white hair and skin, were selected. The animal study was approved by the ethics review board of Academy of Military Medical Science, Beijing, China. All animals were procured and maintained in the Center for Laboratory Animal Medicine and Care, Academy of Military Medical Science, Beijing and used in accordance with the institutional guidelines of the Animal Care and Use Committee. All pigs were anesthetized with an intramuscular injection of Sumianxin II (0.15 ml/kg) pre-exposures. After animal reached a surgical plane of anesthesia, electric clippers were used to remove hair from the flank. The flank was cleaned with soap and warm water, rinsed, and dried with a lint-free disposable cloth. A grid pattern was drawn on the flank of the pigs using a black permanent marker with grid spacing of about 4.0 cm. Figure 2 shows the grid patterns on the skin surface of Guizhou miniature pig.
2.3. Experimental procedures and data analysis

The anesthetized animals were placed in a customized holder where they were positioned with the aid of the two low-power 655 nm laser pointers. The holder was mounted on rails and motorized for rapid and repeatable horizontal position adjustments. The vertical position could be adjusted by a hand-controlled elevation system. In this way, each grid that had been drawn on the flanks of the pigs was sequentially irradiated. The selected exposure duration was 1.0 s. When exposing the pigs to laser radiation, we adjusted the animal position so that the beam cross-point of the two 655 nm laser pointers was at the skin surface. The distance between the irradiated skin surface and the laser exit was kept constant as 325.6 cm. The location error for the skin surface was no more than ± 3 mm along the incident 3.743 µm laser direction. We could estimate the maximum variance for the spot size along the 6 mm range. As a rough estimate, the beam divergence was 2.9 mrad (0.94/325.6 rad), so the maximum variance along a 6 mm range would be less than 0.002 cm. Therefore, the beam diameter on the skin surface would have a negligible variance due to location errors. A pilot study was firstly conducted to generate damages in different exposure levels, from no skin damage to obvious skin burns. From the post-exposure readings, the approximate range of the damage threshold was estimated. Based on the estimation, five different power levels were chosen in the subsequent experiment to determine the damage threshold. Following each exposure session, lesion/no lesion determinations were made for each exposure site by three investigators, with at least two of three in agreement to confirm a positive reading. Any change in the appearance of the skin surface was recorded as a lesion, including erythema, blistering, or change in pigmentation viewed by the eye. Examinations were performed at 1- and 24-h post-exposure. The lesion/no lesion data were collected and analyzed using the SAS statistical package (version 6.12, SAS Institute, Inc., Cary, NC). Specifically, using the collected damage probabilities at different laser power levels, the dose response curve could be obtained, and then the widely accepted Bliss probit analysis was performed to determine the \( ED_{50} \) value, fiducial limits at the 95% confidence level and probit slopes \( S(ED_{84}/ED_{50}) \). The \( ED_{50} \) refers to the effective dose corresponding to 50% damage probability [31]. For the expressions of the \( ED_{50} \) and fiducial limits at the 95% confidence, the central peak radiant exposure for the Gaussian spot is usually used in the laser safety community.

3. Results

Table 2 shows the detailed experimental conditions, including laser spot diameter, exposure duration, selected five laser power levels, corresponding central peak radiant exposures for Gaussian spot and involved animal number. The number of damage lesions at 1- and 24-h post-exposure for the five power levels were also included.

Figure 3 shows the probit analysis of skin damages. The red square points were damage probabilities at 24 hours post-exposure for the selected five power levels. By probit analysis, the
Table 2. Experimental conditions and corresponding damage lesion numbers at 1- and 24-h post-exposure.

| Laser Spot Diameter and Exposure Duration | Power Level (W) | Peak Radiant Exposure for Gaussian Spot (J/cm²) | Involved Animal Number | Number of Damaged Lesions/Number of Exposures at 1-h Post-Exposure | Number of Damaged Lesions/Number of Exposures at 24-h Post-Exposure |
|------------------------------------------|----------------|-----------------------------------------------|------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| 1/e² diameter (cm) 0.94 (Horizontal) 0.88 (Vertical) Exposure Duration (s) 1.0 | 1.11 | 3.68 | 18/44 | 17/44 |
| | 1.33 | 4.41 | 30/44 | 28/44 |
| | 1.53 | 5.07 | 39/44 | 37/44 |
| | 1.74 | 5.76 | 44/44 | 42/44 |
| | 2.08 | 6.89 | 44/44 | 44/44 |

$ED_{50}$, the fiducial limits at the 95% confidence level and the probit slope ($ED_{84}/ED_{50}$) could be determined.

Table 3 shows the determined $ED_{50}$ values, the fiducial limits at the 95% confidence level and the probit slope. The skin MPE from IEC 60825-1 standard and the safety factor ($ED_{50}$/MPE) were also included.

Table 3. Damage threshold and IEC 60825-1 MPE value [18] for exposure duration of 1.0 s.

| Exposure Duration (s) | Damage threshold expressed in peak radiant exposure $H_{th\text{--peak}}$ at 1-h post-exposure (Fiducial limits at the 95% confidence) (J/cm²) | Damage threshold expressed in peak radiant exposure $H_{th\text{--peak}}$ at 24-h post-exposure (Fiducial limits at the 95% confidence) (J/cm²) | Probit Slope ($ED_{84}/ED_{50}$) | MPE (J/cm²) | Safety Factor ($ED_{50}$/MPE) |
|-----------------------|----------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------|-------------|---------------------------|
| 1.0                   | 4.02 (3.82, 4.20)                                                                                                                | 4.04 (3.73, 4.26)                                                                                                                | 1.26                          | 0.56        | 7.2                      |

Images from (A) to (C) in Fig. 4 show the skin lesions respectively at 5 minutes, 1-h and 24-h post-exposure, with the peak radiant exposure of 1.1 times of the $ED_{50}$ value shown in Table 3. Pictures from (D) to (F) show the damage lesions respectively at 5 minutes, 1-h and 24-h post-exposure, with the peak radiant exposure of 1.7 times of the $ED_{50}$ value. Lesions near the...
damage threshold appeared as red, flat spots at the site of irradiation at 5 minutes post-exposure. Some of them disappeared at the 1-hour post-exposure and the area of the persisted red lesions obviously reduced compared to the 5-minutes appearance. At 24-h post-exposure, most of the lesions persisted. When incident power was 1.7 times of the threshold, obvious skin coagulation occurred. The lesion sizes at 24-h post-exposure for (C) and (F) were about 3.1 and 3.6 mm.

Fig. 4. Skin damage images induced by laser at the wavelength of 3.743 µm. The black circles indicated the lesions. Laser power for (a), (b) and (c) was 1.33 W, and the peak radiant exposure was about 1.1 times of the ED50 value. Laser power for (d), (e) and (f) was 2.08 W, and the peak radiant exposure was about 1.7 times of the ED50 value. (a) 5 minutes post exposure, (b) 1 hour post exposure, (c) 24 hours post exposure, (d) 5 minutes post exposure, (e) 1 hour post exposure, And (f) 24 hours post exposure.

4. Discussion

We summarized laser-induced skin damage thresholds for the exposure duration of 1.0 s at diverse wavelengths including 1.06, 1.319, 2.0, 3.743 and 10.6 µm, as shown in Table 4 [19,25,26,32–35]. Some conclusions could be drawn. Firstly, no obvious difference could be found for the damage data between porcine skin and human skin, indicating that white pig is the ideal animal model for the determination of skin damage thresholds. Miniature pigs are always used in the determinations of laser-induced skin damage thresholds because their skin has an anatomical similarity to human skin and there are no obvious difference for the optical properties between the porcine skin and human skin. According to Eggleston et al. [36], the mean thickness of porcine flank epidermis (68 ± 34 µm) is comparable to the thickness of human epidermis from the face (68 ± 26 µm), neck (68 ± 24 µm) and arms (68 ± 21 µm). Thus almost all existing reports selected the flank area of miniature pig to determine the skin damage thresholds. According to Shimojo et al. and Du et al. [37,38], in the wavelength range of 400–1400 nm, the absorption coefficient of Asian epidermis differ prominently from those of Caucasian and African epidermises, while the reduced scattering coefficients of each skin layer in Asian skin tissue are similar to those of the other ethnic skin tissues. Comparisons between human and porcine skin tissue shows that no obvious difference could be found for the optical properties in the near-infrared region. For wavelengths above than about 2.6 µm, water is the dominant light absorber thus optical properties of the porcine and human skin should also nearly same. Thus porcine damage threshold determined in this report
is applicable to humans. Secondly, at the wavelength of 1.06 µm, slight decrease of damage thresholds could be noticed when skin color becomes darker. While at the wavelength of 10.6 µm, there is no obvious difference for people with different skin colors. This phenomenon is relevant with the absorption characteristic of chromophore in skin. At the wavelength of 1.06 µm, melanin and water contribute to the light absorption of skin and melanin content varies with skin colors, thus the damage data shows slightly dependence on skin colors [39]. At the wavelength of 10.6 µm, water is the main chromophore for light absorption and there is no difference for the water content of skin having different colors, so the damage data is nearly identical for people with different colors. Thirdly, the damage thresholds decrease as the incident spot expands in diameter. This phenomenon is determined by the heat accumulation and thermal diffusion in skin. As the incident spot size is small, the temperature rise of the central area by laser radiation is strongly influenced by the heat diffusion to the surrounding region. With the increase of spot size, influence by heat diffusion decreases and absorbed energy is more easily to accumulate in the exposed central area, so the damage threshold decreases. Previous reports indicate that beam diameter of about 1 cm is large enough to obtain lower damage values. So we selected the beam diameter of about 1 cm in this work. Finally, by comparing the damage data for different wavelengths at a nearly constant beam size (around 1.0 cm), it can be seen that the damage thresholds have a significant decrease as the wavelength increases from 1.06 µm to 2.0 µm. This phenomenon is due to different penetration depths for the three wavelengths. Radiation will penetrate deepest into skin at the wavelength of 1.06 µm among the three wavelengths; that is, most energy is needed for 1.06 µm to increase skin temperature to the critical level that generates thermal damage. However, as the wavelengths increase from 2.0 to 10.6 µm, skin damage thresholds decrease slightly, although the absorption coefficients for the three wavelengths of 2.0, 3.742 and 10.6 µm are 69.2, 115.0 and 847.1 cm⁻¹ respectively and have significant differences [25]. Especially when comparing the damage data for 3.743 µm and 10.6 µm, we found the light absorption depth varies by about 7.4 times but the damage

| Laser Wavelength (µm) | Exposure Duration (s) | Beam Diameter (cm) | Damage Threshold (J/cm²) | Subject | Reference |
|-----------------------|-----------------------|--------------------|--------------------------|---------|-----------|
| 1.06                  | 1.0                   | 0.5                | 59.4                     | White pig | [32]      |
|                       |                       | 0.5                | 65.5                     | Human-light complexion Chinese | [32] |
|                       |                       | 0.5                | 61.0                     | Human-Yellow complexion Chinese | [32] |
|                       |                       | 0.5                | 52.3                     | Human-Dark complexion Chinese | [32] |
|                       |                       | 1.05               | 55                       | Human-Black | [33]     |
| 1.319                 | 1.0                   | 1.05               | 70                       | Human-Caucasian | [33] |
|                       |                       | 0.61               | 42.4                     | Yucatan miniature pig | [25] |
|                       |                       | 0.97               | 37.4                     | Yucatan miniature pig | [25] |
|                       |                       | 0.98               | 40.8                     | Guizhou miniature pig | [26] |
| 2.0                   | 1.0                   | 0.48               | 10.2                     | Yucatan miniature pig | [19] |
|                       |                       | 0.97               | 7.9                      | Yucatan miniature pig | [19] |
|                       |                       | 1.47               | 6.0                      | Yucatan miniature pig | [19] |
| 3.743                 | 1.0                   | 0.94               | 4.04                     | Guizhou miniature pig | This work |
| 10.6                  | 1.0                   | 1.05               | 3.0                      | White pig | [34] |
|                       |                       | 0.5                | 3.1                      | Human-Chinese | [35] |
|                       |                       | 1.05               | 2.8                      | Human-Black | [33] |
|                       |                       | 1.05               | 2.8                      | Human-Caucasian | [33] |
data only varies by about 1.4 times. Schulmeister et al. have established computer models to calculate the laser induced injury thresholds of cornea and skin [40,41]. For the skin damage in the wavelength range of above about 3 µm, the computer data show that there is little wavelength dependence for 1.0 s exposure duration and the wavelength dependence become even lower for longer exposure durations, but with the decrease of the exposure duration from about 1.0 s, the wavelength dependence become more pronounced. Our experimental data and published damage data for 1.0 s exposure duration are consistent with the theoretical predictions. The decreasing of the wavelength dependence for longer exposure durations is due to heat transfer during the exposure. For short exposure durations, heat diffusion during exposure is not significant thus the difference in optical penetration depth is reflected in the wavelength dependence of damage thresholds. With the increase of exposure durations, heat diffusion become significant and heat flow along laser axial direction evens out differences from the optical penetration depth, thus the wavelength dependence become less pronounced. One important fact is that significant simplifications are always made for the establishment of MPE. In current laser safety standard, MPE in the wavelength range of 2.6–1000 µm doesn’t reflect the wavelength dependence of damage threshold.

5. Conclusion

The porcine skin damage threshold for OPO radiation at the wavelength of 3.743 µm was determined. For 1/e² beam spot diameter of about 1 cm and exposure duration of 1.0 s, the ED₅₀ at 24-h post-exposure was 4.04 J/cm². Our result would contribute to the knowledge base for the refinement of laser safety standard and also have high reference value for laser parameter selections of some biomedical applications in which safe exposure doses should be demarcated to avoid skin damages.

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The authors declare that there are no conflicts of interest related to this article.

References

1. U. Willer, M. Saraji, A. Khorsandi, P. Geiser, and W. Schade, “Near- and mid-infrared laser monitoring of industrial processes, environment and security applications,” Opt. Lasers Eng. 44(7), 699–710 (2006).
2. M. Vainio, M. Siltanen, J. Peltola, and L. Halonen, “Grating-cavity continuous-wave optical parametric oscillators for high-resolution mid-infrared spectroscopy,” Appl. Opt. 50(4), A1–A10 (2011).
3. R. Tuttle, “Large aircraft infrared countermeasures system,” Aerospace Daily Defense Report 210, 6–7 (2004).
4. L. Xu, H.-Y. Chan, S.-U. Alam, D. J. Richardson, and D. P. Shepherd, “Fiber-laser-pumped, high-energy, mid-IR, picosecond optical parametric oscillator with a high-harmonic cavity,” Opt. Lett. 40(14), 3288–3291 (2015).
5. J. B. Barria, S. Roux, J. B. Dherbecourt, M. Raybaut, J. M. Melkonian, A. Godard, and M. Lefebvre, “Microsecond fiber laser pumped, single-frequency optical parametric oscillator for trace gas detection,” Opt. Lett. 38(13), 2165–2167 (2013).
6. E. Lippert, H. Fonnum, G. Arisholm, and K. Stenersen, “A 22-watt mid-infrared optical parametric oscillator with V-shaped 3-mirror ring resonator,” Opt. Express 18(25), 26475–26483 (2010).
7. A. Hemming, J. Richards, and S. Bennetts, “A high power hybrid mid-IR laser source,” Opt. Commun. 283(20), 4041–4045 (2010).
8. A. Hemming, J. Richards, A. Davidson, N. Carmody, S. Bennetts, N. Simakov, and J. Haub, “99 W mid-IR operation of a ZGP OPO at 25% duty cycle,” Opt. Express 21(8), 10062–10069 (2013).
9. B. Q. Yao, Y. J. Shen, X. M. Duan, T. Y. Dai, Y. L. Ju, and Y. Z. Wang, “A 41-W ZnGeP₂ optical parametric oscillator pumped by a Q-switched Ho:YAG laser,” Opt. Lett. 39(23), 6589–6592 (2014).
10. P. Gross, M. E. Klein, T. Walde, K. J. Boller, M. Auerbach, P. Wessels, and C. Fallnich, “Fiber-laser-pumped continuous-wave singly resonant optical parametric oscillator,” Opt. Lett. 27(6), 418–420 (2002).
11. A. Henderson and R. Stafford, “Low threshold, singly-resonant CW OPO pumped by an all-fiber pump source,” *Opt. Express* 14(2), 767–772 (2006).

12. M. Vainio, J. Peltola, S. Persijn, F. J. Harren, and L. Halonen, “Singly resonant cw OPO with simple wavelength tuning,” *Opt. Express* 16(15), 11141–11146 (2008).

13. V. Ramaihabadara, S. C. Kumar, and M. Ebrahimm-Zadeh, “Fiber-laser-pumped, dual-wavelength, picosecond optical parametric oscillator,” *Opt. Lett.* 39(9), 2739–2742 (2014).

14. K. S. Chaitanya, J. Wei, J. Debray, V. Kemlin, B. Boulanger, H. Ishizuki, T. Taira, and M. Ebrahim-Zadeh, “High-power, widely tunable, room-temperature picosecond optical parametric oscillator based on cylindrical 5% Mg O:PPNL,” *Opt. Lett.* 40(16), 3897–3900 (2015).

15. X. Li, X. J. Xu, Y. P. Shang, H. Y. Wang, and L. Liu, “Study on high-power continuous-wave mid-infrared optical parametric oscillator,” *Proc. SPIE* 9251, 925101 (2014).

16. International Commission on Non-Ionizing Radiation Protection, “Guidelines on limits of exposure to laser radiation of wavelength between 180 nm and 1,000 microns,” *Health Phys.* 105(3), 271–295 (2013).

17. ANSI, *American National Standard for Safety Use of Lasers, Z136.1* (Laser Institute of America, 2014).

18. International Electrotechnical Commission, IEC 60825-1, *Safety of Laser Products-Part 1: Equipment Classification and Requirements*, 3rd edn (2014).

B. Chen, D. C. O’Dell, S. L. Thomsen, B. A. Rockwell, and A. J. Welch, “Porcine skin ED_{50} damage thresholds for 2,000 nm laser irradiation,” *Lasers Surg. Med.* 37(5), 373–381 (2005).

B. Chen, S. L. Thomsen, R. J. Thomas, and A. J. Welch, “Modeling thermal damage in skin from 2000-nm laser irradiation,” *J. Biomed. Opt.* 11(6), 064028 (2006).

B. Chen, S. L. Thomsen, R. J. Thomas, J. Oliver, and A. J. Welch, “Histological and modeling study of skin thermal injury to 2.0 µm laser irradiation,” *Lasers Surg. Med.* 40(5), 358–370 (2008).

J. W. Oliver, D. J. Stolarski, G. D. Noojin, H. M. Hodnett, C. A. Harbert, K. J. Schuster, M. F. Foltz, S. S. Kumru, C. P. Cain, C. J. Finkeldei, G. D. Buffington, I. D. Noojin, and R. J. Thomas, “Infrared skin damage thresholds from 1940-nm continuous-wave laser exposures,” *J. Biomed. Opt.* 15(6), 065008 (2010).

C. P. Cain, K. J. Schuster, J. J. Zohner, K. L. Stockton, D. J. Stolarski, R. J. Thomas, B. A. Rockwell, and W. P. Roach, “Visible lesion thresholds with pulse duration, spot size dependency, and model predictions for 1.54-µm, near-infrared laser pulses penetrating porcine skin,” *J. Biomed. Opt.* 11(2), 024001 (2006).

C. P. Cain, G. D. Polhamus, W. P. Roach, D. J. Stolarski, K. J. Schuster, K. L. Stockton, B. A. Rockwell, B. Chen, and A. J. Welch, “Porcine skin visible lesion thresholds for near-infrared lasers including modeling at two pulse durations and spot sizes,” *J. Biomed. Opt.* 11(4), 041109 (2006).

J. W. Oliver, R. Vincelette, G. D. Noojin, C. D. Clark, C. A. Harbert, K. J. Schuster, A. D. Shingledecker, S. S. Kumru, J. Maughan, N. Kitzis, G. D. Buffington, D. J. Stolarski, and R. J. Thomas, “Infrared skin damage thresholds from 1319-nm continuous-wave laser exposures,” *J. Biomed. Opt.* 18(12), 125002 (2013).

L. G. Jiao, J. R. Wang, Y. Fan, and Z. F. Yang, “Porcine skin damage thresholds and histological damage characteristics from 1319-nm laser radiation,” *J. Biomed. Opt.* 24(9), 1 (2019).

R. Vincelette, G. D. Noojin, C. A. Harbert, K. J. Schuster, A. D. Shingledecker, D. J. Stolarski, S. S. Kumru, and J. W. Oliver, “Porcine skin damage thresholds for 0.6 to 9.5 cm beam diameters from 1070-nm continuous-wave infrared laser radiation,” *J. Biomed. Opt.* 19(03), 1 (2014).

M. P. DeLisi, M. S. Schmidt, A. F. Hoffman, A. M. Peterson, G. D. Noojin, A. D. Shingledecker, A. R. Boretsky, D. J. Stolarski, S. S. Kumru, and R. J. Thomas, “Thermal damage thresholds for multiple-pulse porcine skin laser exposures at 1070 nm,” *J. Biomed. Opt.* 25(03), 1 (2020).

D. J. Segelstein, *The complex refractive index of water*, Dissertation, University of Missouri-Kansas City (1981).

L. Jiao, J. Wang, X. Jing, H. Chen, and Z. Yang, “Ocular damage effects from 1338-nm pulsed laser radiation in a rabbit eye model,” *Biomed. Opt. Express* 8(5), 2745–2755 (2017).

D. H. Sliney, J. Mellerio, V. P. Gabel, and K. Schulmeister, “What is the meaning of threshold in laser injury experiments? implications for human exposure limits,” *Health Phys.* 82(5), 335–347 (2002).

B. Z. Ma, W. Y. Xia, R. P. Zhuo, L. Y. Jiang, Q. S. Hu, Z. Z. Li, and J. N. Wu, “Study of injury threshold of CW Nd:YAG laser light for human skin,” *J. Biomed. Opt.* 25(03), 1 (1985).

R. J. Rockwell and L. Goldman, *Research on Human Skin Laser Damage Thresholds*, USAF School of Aerospace Medicine (1974).

D. H. Sliney and M. L. Wolbarsht, *Safety with Lasers and Other optical Sources* (Plenum, 1980).

H. M. Shi, J. S. Li, Y. K. Tan, P. X. Luo, Z. B. Chen, X. B. Xie, and Y. H. Yuan, “Acute injury threshold level of CO2 laser light for skin of yellow race,” *Chin. J. Lasers* 12, 589–591 (1985).

T. A. Eggleston, W. P. Roach, M. A. Mitchell, K. Smith, D. Oler, and T. E. Johnson, “Comparison of two porcine (Sus scrofa domestica) skin models for in vivo near-infrared laser exposure,” *Comp. Med.* 50(4), 391–397 (2000).

Y. Shimojo, T. Nishimura, H. Hazama, T. Ozawa, and K. Awa, “Measurement of absorption and reduced scattering coefficients in Asian human epidermis, dermis, and subcutaneous fat tissues in the 400- to 1100-nm wavelength range for optical penetration depth and energy deposition analysis,” *J. Biomed. Opt.* 25(04), 1 (2020).

Y. Du, X. H. Hu, M. Cariveau, X. Ma, G. W. Kalinus, and J. Q. Lu, “Optical properties of porcine skin dermis between 900 nm and 1500 nm,” *Phys. Med. Biol.* 46(1), 167–181 (2001).

E. Salomatina, B. Jiang, J. Novak, and A. N. Yaroslavsky, “Optical properties of normal and cancerous human skin in the visible and near-infrared spectral range,” *J. Biomed. Opt.* 11(6), 064026 (2006).
40. K. Schulmeister and M. Jean, “Modelling of laser induced injury of the cornea,” in *Proceeding of the International Laser Safety Conference* (2011), pp. 214–217.

41. M. Jean, K. Schulmeister, and B. E. Stuck, “Computer modeling of laser induced injury of the skin,” in *Proceeding of the International Laser Safety Conference* (2013), pp. 366–370.