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Research Article

One-year Ocular Safety Observation of Workers and Estimations of Microorganism Inactivation Efficacy in the Room Irradiated with 222-nm Far Ultraviolet-C Lamps

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ABSTRACT

Two krypton-chloride germicidal excimer lamp units (Care222 TRT-104C11-UI-U3, USHIO Inc.) were installed in the examination room of an ophthalmology department. The irradiation dose was set not to exceed the former (*i.e.*, before 2022) threshold limit value (TLV) (22 mJ cm^{-2}/8 h) recommended by the ACGIH. Section 1: The eyes and lids of the six ophthalmologists (5 wore glasses for myopic correction) who worked in the room for a mean stay of 6.7 h week^{-1} were prospectively observed for 12 months. Slitlamp examinations revealed neither acute adverse events such as corneal erosion, conjunctival hyperemia, and lid skin erythema nor chronic adverse events such as pterygium, cataract, or lid tumor. The visual acuity, refractive error, and corneal endothelial cell density remained unchanged during the study. Section 2: The irradiation of samples placed on the table or floor using the same fixtures in the room (5–7.5 mJ cm^{-2}) was associated with >99% inhibition of φX174 phage and >90% inhibition of *Staphylococcus aureus*. In conclusion, no acute or chronic health effects in human participants was observed in a clinical setting of full-room ultraviolet germicidal irradiation by 222-nm lamp units, and high efficacy in deactivation of microorganisms was determined in the same setting.

INTRODUCTION

Ultraviolet (UV) radiation covers the wavelength region between 100 and 400 nm and can be sub-categorized based on the photobiological wavelength ranges of UV-C (100–280 nm), UV-B (280–315 nm), and UV-A (315–400 nm). The germicidal effect of UV-C is particularly potent against viruses and bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (1–3). However, when UV-C is intended for use in human-occupied settings, conventional germicidal 254-nm UV-C fixtures can only be employed to expose unoccupied spaces, such as the upper room air, because of the potential hazards associated with direct exposure of the skin (erythema) or eyes (photokeratitis) at this wavelength (2,3). With the recent development of shorter-wavelength ("far UV-C") ultraviolet germicidal irradiation (UVGI) sources, such as the krypton-bromide (KrBr) and krypton-chloride (KrCl) excimer lamps emitting at 207 and 222 nm respectively, full-room irradiation with levels safe to humans, but still effective in inactivating microbes, has been getting much attention (4,5). An ideal application of whole-room UVGI is in clinical settings where a physician is facing the patient directly, as during an ophthalmic examination.

Previous experimental and epidemiological studies have shown that exposures of longer UV wavelength bands such as UV-B and UV-A to the eye were associated with photokeratitis and corneal opacity as acute effects (6), and pterygium, droplet keratopathies, and cortical cataract as chronic effects (7–9). In the UV-C wavelength band, there is the strong evidence between its chronic exposure and formation of eyelid malignancies including basal cell carcinoma and squamous cell carcinoma (10). Others have reported the acute effects of UV-C to the eye by using a light source with relatively wide bandwidth (11–13) in animal and human experimental settings or by using a narrow-bandwidth 222-nm lamp in animal experimental settings (14,15). So far, the literature for both the long-term and the real-world assessments of human eye safety for far UV-C UVGI are lacking.

The germicidal/inactivation effects of far UV-C have been reported against Gram-positive [*Staphylococcus (S.) aureus* and *Listeria monocytogenes*] and Gram-negative [*Salmonella typhimurium* and *Escherichia (E.) coli* O157:H7] pathogenic bacteria, fungus, and virus in suspension (16,17); *E. coli* and P1 phages on cultured agar plates (18); tissue culture-infected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19) (19,20); airborne H1N1 influenza virus (21) and human coronaviruses alpha HCoV-229E and beta HCoV-OC43 (22) in experimental chambers, and aerosolized *S. aureus* in a room-sized chamber (23). In an animal study, 222-nm lamp exposure efficiently inhibited MRSA that infected mouse skin (24,25). In humans, bacterial

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detection or colony formation counts from skin surface obtained by skin swab cultures were significantly reduced following 222-nm lamp irradiation with sub-erythema doses in healthy volunteers (26) or in patients with pressure ulcers (27). Accordingly, further evaluation of the efficacy of 222-nm UV-C irradiation in reducing the contamination of real-world surfaces was needed (19).

In July 2020, we installed 222-nm lamp units in the examination room of the outpatient clinic in our ophthalmology department. We conducted a prospective observational eye-safety study of workers in that room at the time of the installation of the lamps (Section 1). The UVGI efficacy also were assessed in the same room (Section 2).

MATERIALS AND METHODS

Study designs. This manuscript contains two studies; one is a human prospective observational study (Section 1) and the other one is a non-clinical study of microorganism inactivation (Section 2). Both studies were conducted in the same outpatient examination room of the Department of Ophthalmology, Shimane University Hospital. The human study adhered to the tenets of the Declaration of Helsinki and Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. The protocol was reviewed and approved by the Institutional Review Board of Shimane University Hospital (IRB No. 20200517–2, approval date July 20, 2020); all the participants provided written informed consent for participation to the study. The human study included six male ophthalmologists who were expected to work in the room for >4 h per week (mean ± SD age of 39.3 ± 7.9 years). Five of the six wore glasses for myopic correction; no one was a contact lenses user.

Installation of UV-C lamps in the room. For the purpose of viral and bacterial inactivation, two units of a mercury-free, KrCl excimer lamp (Care222 TRT-104C11-UI-U3, USHIO Inc., Tokyo, Japan) were installed in the examination room of the outpatient clinic (Fig. 1a,b). The spectral distribution measured by a spectrometer (QE-PRO Ocean Optics) is shown in Fig. 2a,b. Each unit emitted a peak wavelength of 222 nm and had a cut-off filter that cut wavelengths longer than 230 nm and totally cut wavelength longer than 240 nm. The device was installed at a height of 240 cm (Fig. 1a, lamp 1) or 230 cm (Fig. 1a, lamp 2) above the floor and directed to the irradiation target (Fig. 1a, red star). To assure that the threshold limit value (TLV) for 222 nm of 22 mJ cm^{-2} recommended by American Conference of Governmental Industrial Hygienists (ACGIH) (2) was not exceeded even if the top of the head of a worker with a height of 170 cm were to be irradiated for 8 h while standing in the room directly under the lamps (*i.e.*, distance between lamps and top of the head was 60–70 cm) (Fig. 1a, black squares). The lamps were cycled; the cycle was set for 200 s on and for 1600 s off. One of the two units was installed at 250 cm and the second unit at 350 cm from the desk. The vertical irradiances measured at the desk position (Fig. 1a, red star) with an ultraviolet irradiance meter (VUV-S172/UIT-250 USHIO Inc.) by directing the detector to the lamps were 0.003 mW cm^{-2} for the first unit and 0.002 mW cm^{-2} from the second unit. The maximum irradiance at the participant's eye position was 0.002 mW cm^{-2}. This was measured by assuming the participant (*i.e.*, ophthalmologist) was sitting in front of the slit lamp and facing the patient (Fig. 1a, black triangle). The detector was placed perpendicular to the floor plane and directed to the patient's face (direct to left in the Fig. 1a). The irradiation dose after 8 h of duty cycle irradiation was calculated to be 6.4 mJ cm^{-2}. The transmittance of 222 nm wavelength by the glasses was less than 0.002%. However, both computer-aided design simulation (Fig. 3a) and demonstration experiment with a mannequin head (Fig. 3b–e) suggested that the UV irradiation to most part of the cornea was equivalent between with and without glass wearing, while wearing glasses might block UV irradiation to lower eyelid.

Scheduled examinations (section 1). For acquisitions of ocular safety profiles, the participants were examined before the start of working in the room (for baselines), and at the end of the first day (within 24 h after the expsoure), and at 1, 3, 6, and 12 months after the start of working in the room. In each examination, the duration of stay in the room, bilateral best-corrected visual acuity (BCVA), spherical equivalent refractive error (SERE), slitlamp examination findings, corneal endothelial density (CECD), subjective symptoms, and any other potentially adverse events were recorded. Measurements of SERE and CECD were omitted in the first-day examination. The subjects were asked their duration of stays in the room (per day at the first day examination and hours-per-week for the other follow-up periods). Visual acuity was measured using a decimal visual acuity chart and converted into the logarithm of the minimum angle of resolution (LogMAR) for statistical analysis. SERE was measured by using an autorefract-keratometer (TonoRef III, Nidek, Gamagori, Japan). A slitlamp examination using a slitlamp microscope 4ZL (Takagi, Nagano, Japan) was used to obtain a corneal erosion score, conjunctival hyperemia score, and presence or absence of pterygium or cataract. The slitlamp microscope was also used to record any potential lid skin changes (erythema and increase or decrease of pigmentation). Lid skin change was assessed with 6.3× magnification (Fig. 4a–f), and the other signs were assessed with 10× magnification (Fig. 4g–r). For assessment of corneal erosion, the ocular surface was stained with a sodium-fluorescein solution for observation under a blue light (Fig. 4m–r). For assessment of cataract, both thin slit-beam and diffuse lights were used for observation (Fig. 4g–l), while the other examinations were observed with diffuse light (Fig. 4a–f, m–r). Corneal erosion was scored in each area (0–3) and the presence (density, 0–3) of superficial punctate keratopathy (SPK) (28). Scoring of conjunctival hyperemia was determined based upon the Japanese Guidelines for Allergic Conjunctival Disease 2020; where a score 0 = no manifestation, a score 1 = dilatation of several vessels, a score 2 = dilation of many vessels, and a score 3 = impossible to distinguish individual blood vessels (29). CECD was measured using a specular microscope (EM-3000; Tomey Corporation, Nagoya, Japan). All the examinations/measurements were performed by experienced ophthalmologists and orthoptists.

Microorganism inactivation experiment (section 2). The strains used were *S. aureus* (NBRC 12732), φX174 phage (NBRC 103405), and *E. coli* for φX174 phage host (NBRC 13898). A 2-ml aliquot of the samples containing 10^4 colony-forming units (CFU) of *S. aureus* or 10^5 plaque-forming units (PFU) of φX174 suspended in physiological saline were placed in 35-mm diameter plastic dishes for the inactivation experiment. Three plastic dishes were placed on a paper tray (Fig. 1c), and the paper tray was placed in the examination room for irradiation by the UV-C. In each experimental session, the paper trays were placed in four different places (Fig. 1a, blue circles): on the desk, on the slit lamp table, on the floor near the slitlamp footswitch, and on the desk outside of the irradiated area; the last one was covered by a white paper and was considered unirradiated control (Fig. 1d). Each exposure session followed a cycle of 200 s on and 1600 s off for a total 12.5-h session (*i.e.*, "on" cycle for 1.4 h). By placing the detector facing up on each place, the measured irradiances (and radiant exposures) for each session were 0.001 mW cm^{-2} (5.0 mJ cm^{-2}) on the desk and 0.0015 mW cm^{-2} (7.5 mJ cm^{-2}) on the slit lamp table and on the floor. After irradiation, the test samples were collected. For *S. aureus*, the samples were diluted 1000× with a NBRC 702 medium and were cultured on a standard agar plate (9-cm-diameter dish) at 37 ± 1°C for 24 h. For the φX174 phage, the samples were diluted 1000× with NBRC 702 medium and were cultured using a multi-layer method (30) on the plate at 37 ± 1°C for 24 h. The number of colonies or plaques was then counted under a stereomicroscope. The session was repeated twice for each *S. aureus* and φX174 phage to yield $N = 6$ experiments.

Statistical analysis. The parameters obtained during the observational periods were analyzed by using a mixed-effects regression model in which each patient's study number was regarded as a random effect and the time period as a fixed effect. $P < 0.05$ was considered significant. The number of microorganisms counted on a culture plate was compared among groups by one-way analysis of variance (ANOVA). All statistical analyses were performed using the JMP Pro version 15.2.1 statistical software (SAS Institute, Inc., Cary, NC).

RESULTS

Section 1: Five of the six participants in the human study completed the 12-month follow-up examinations, while one (eyeglasses wearer) only completed the examinations up to 6 months. The data obtained are summarized in Table 1. During the observational period, the participants stayed in the room for

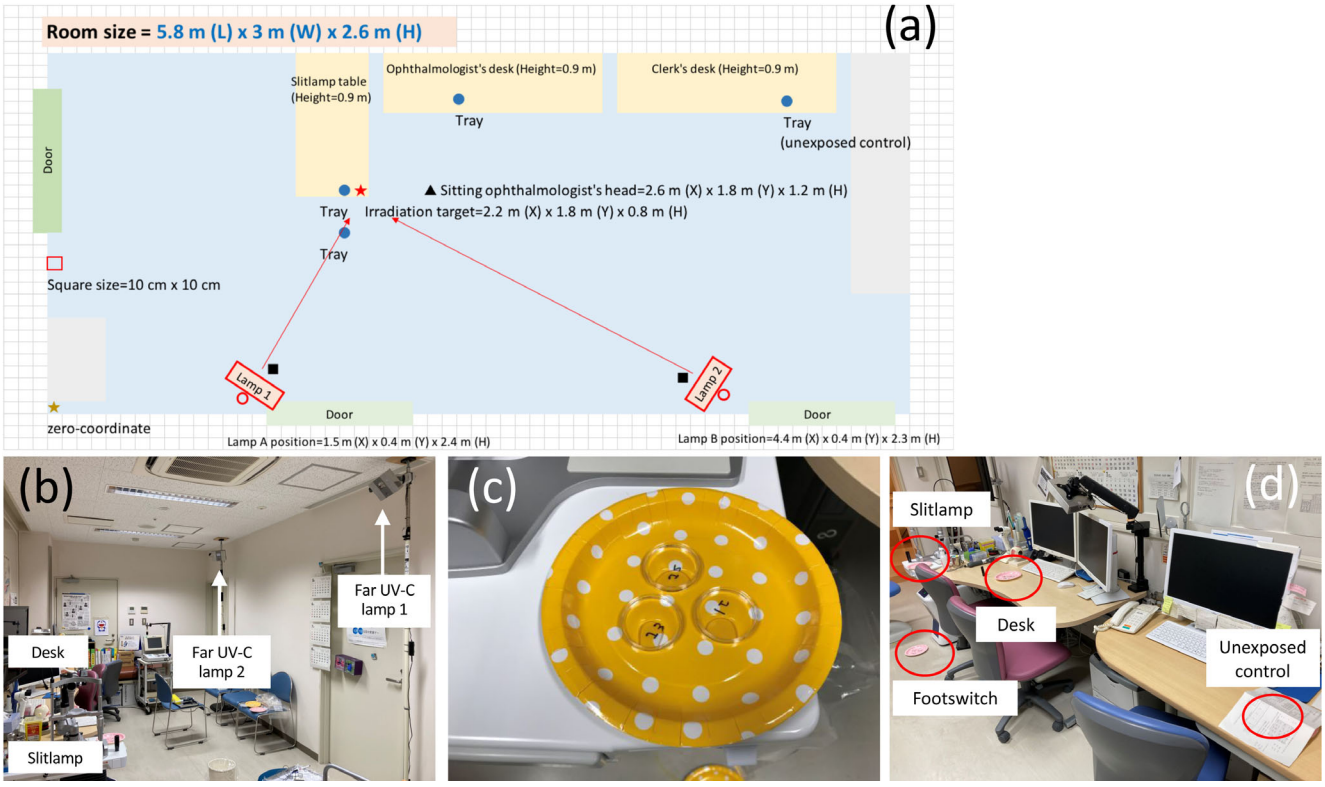

Figure 1. Installation of 222-nm UV-C lamps in the Ophthalmology Department's examination room (a) Schematic drawing of the examination room. (b) Two units of the 222-nm UV-C lamp are set up in the room facing the physicians' desk and slit-lamp. (c) In each microorganism study session, three plastic dishes containing *Staphylococcus aureus* or φX174 phage are placed on paper trays. (d) In each microorganism study session, paper trays are placed on the desk, the slit lamp table, on the floor near the slitlamp footswitch, and on the desk outside of the irradiated area. The last one was covered by a white paper and considered the unirradiated control.

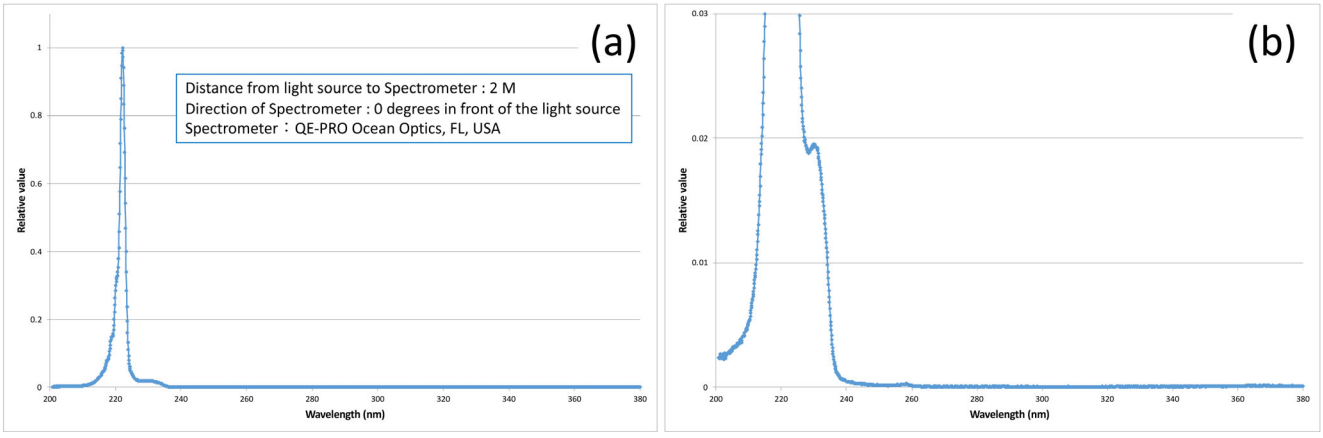

Figure 2. Spectral distribution of the 222-nm far UV-C lamps used in this study. (a) Plot with a maximum *y*-axis value of 1.0. (b) Plot with a maximum y-axis value of 0.03.

6.7 h weekly on average; the staying time was unchanged during the study period ($P = 0.11$, mixed-effects regression model). BCVAs were −0.08 LogMAR (equivalent to 1.2 in decimal visual acuity) in both eyes of the six participants during the study. The average SERE was −4.67 D in the right eye and −4.33 D in the left eye; SERE remained unchanged during the study period in both eyes ($P = 0.64$ for right eye, and $P = 0.34$ for left eye). Representative slit lamp examination photographs obtained for the right eye of Participant 3, who was not the eyeglass wearer, are shown in Fig. 4. In this case, corneal erosion area and density scores were all 0 during the observation period. In participants, there was no clinically significant corneal erosion observed, with the area and density scores above a score of 1 during the examinations. The scores recorded for conjunctival hyperemia was all 0 during the observational period, and no pterygium, cataract, and lid changes were recorded. BCVAs were

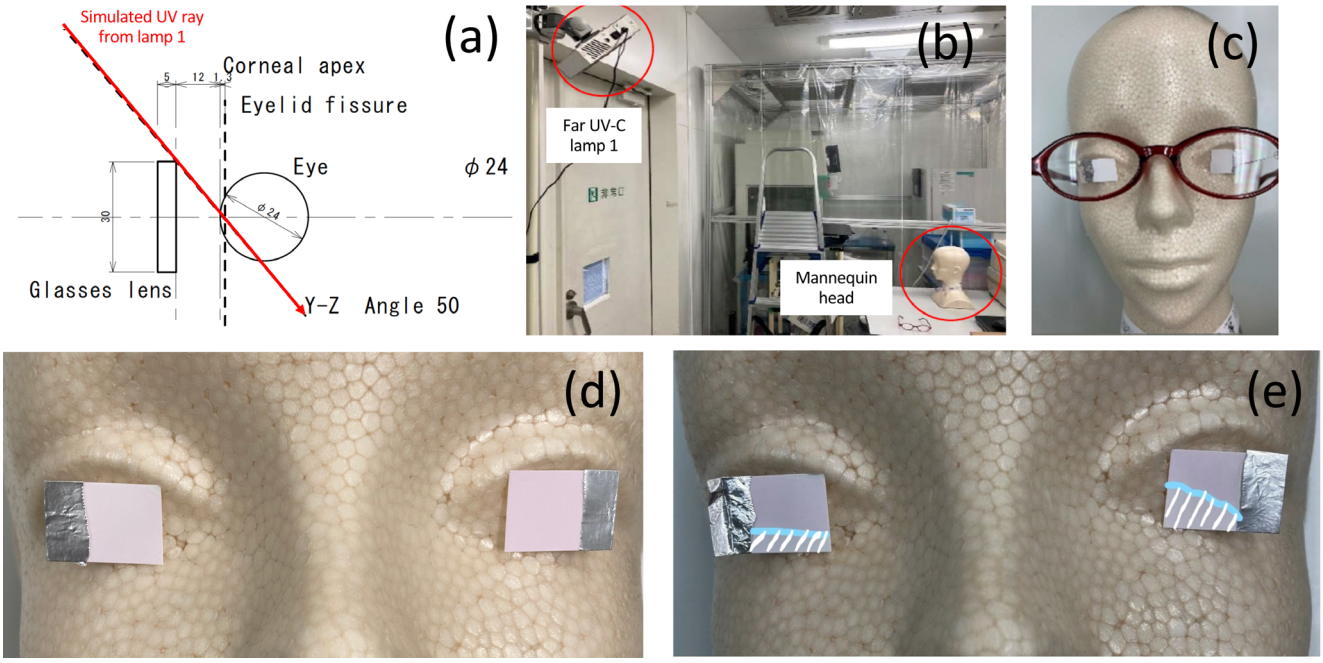

Figure 3. UV blocking effects of wearing glasses. (a) Computer-aided design (CAD) simulates ocular exposure of UV-C radiation from lamp 1 position of Fig. 1a. Wearing glasses can block UV irradiation at the lower eyelid. (b) Setting of the demonstration experiment using a mannequin head. In this experiment, lamp 1 position of Fig. 1a is reproduced. (c) A mannequin head wearing glasses. (d) Pinkish discoloration of photosensitive paper is seen in positions of both eyes after UV-C exposure at 1.6 μW cm^{-2} for 3 min without glasses. (e) After the same UV-C exposure with (d), discoloration is not seen in lower part of the paper (indicated by white diagonal lines) with glasses wearing.

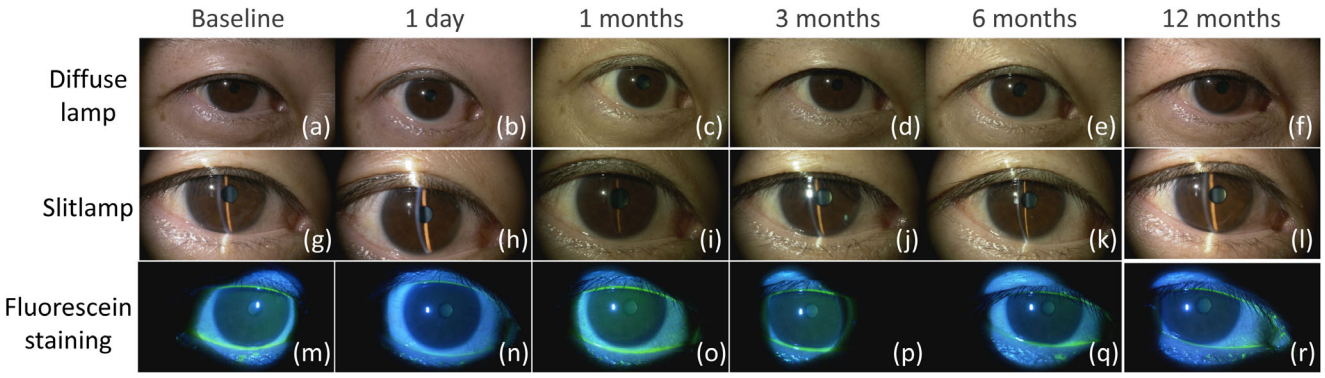

Figure 4. Representative slitlamp photographs (case 3, right eye). Conditions for observation of lid skin change (a–f), conjunctival hyperemia, pterygium, cataract (g–l), and corneal erosion (m–r).

−0.08 LogMAR in both eyes of the six participants during the study. The average CECD was 2742 cells mm^{-2} in the right eye and 2759 cells mm^{-2} in the left eye; and the CECD was unchanged during the study period in both eyes ($P = 0.92$ for right eye, and $P = 0.74$ for left eye). No one reported any subjective symptoms nor any other systemic or ocular adverse events.

Section 2: The non-clinical study results are summarized in Table 2 with representative agar plates from each sample shown in Fig. 5. Compared with the control (42 170 CFU), the colony number of cultured *S. aureus* were significantly lower in the UV-C-exposed samples (2830–7120 CFU; $P < 0.0001$, ANOVA). The inhibition rate by UV-C exposure was calculated to be 83.1–93.3%. Compared with the control (147 000 PFU), the plaque numbers of φX174 cultured plates were significantly lower in the UV-C-exposed samples (40–950 PFU; $P < 0.0001$). The inhibition rate by UV-C exposure was calculated to be 99.4–99.97%.

DISCUSSION

In this clinical study, the ocular safety of physicians working in an ophthalmic examining room with installed 222 nm lamps were carefully assessed for up to 12 months. At the day 1 examination, the findings of the ophthalmic assessments of the study group having a mean stay of 4.8 h day^{-1} were almost totally negative, with at most a corneal area score of 1 and a density score of 1 in one eye of one subject without an accompanying conjunctival hyperemia; this level of corneal staining is frequently seen physiologically; thus, no signs of acute photokeratitis were observed in the participants. In the previous human studies, by 9 h after the

exposures of 205–215 nm UV-C, corneal epithelial debris and an increase of corneal light scattering were induced by 3.6 or 5.5 mJ cm^{-2} exposure, and corneal epithelial debris, haze, and granulation were observed, along with a decrease in visual acuity, increase of corneal light scattering, and symptoms of photokeratitis were induced by 10 mJ cm^{-2} exposure (12,13). Based on these observations, Pitts determined the photokeratitis thresholds for 215–225 as 46 mJ cm^{-2} in rabbit, 21 mJ cm^{-2} in primate, and 10 mJ cm^{-2} in human (12). The working duration of 4.8 h day^{-1} (the longest duration among participants was 6 h day^{-1}) assumed to be 13.2 mJ cm^{-2} (16.5 mJ cm^{-2}) exposure when the person with 170 cm height stayed standing and gazed the lamp directly for the entire duration. In real, the physicians sit in the room for most of the workday, and they merely saw the lamp directly; thus, sub-threshold exposure lower than Pitt's threshold was one possible explanation of the absence of acute keratitis among participants. In the previous experiments by Pitts, a 5000 W xenon-mercury high-pressure lamp was used; because of its small throughput, his experiments were done with very wide (10 nm full width at half maximum) monochromator bands, and therefore introducing large uncertainties could be derived by the stray-light (out-of-pass-band) spectral radiant energy (2). In the rat model using the high-throughput KrBr and KrCl excimer lamps, we have previously reported that the minimal threshold dose of photokeratitis for 207 nm and 222 nm was 15 000 and 5000 mJ cm^{-2}, respectively (15). Thus, we can expect that even the participants received the full dose of irradiation (*i.e.*, standing and direct gazing) for the working time still did not cause any photokeratitis in that room.

Although the safety of long duration irradiation of 222 nm radiant energy was reported in mouse skin and eyes (31,32), this study was aimed to detect potential delayed side effects of UV-C irradiation of the human eye, such as the development of pterygium, droplet keratopathies, cortical cataract, or lid skin

Table 1. Summary of clinical study data.

	Baseline	1 day	1 month	3 months	6 months	12 months	*P*-value†
N	6	6	6	6	6	5	
Stay in the room							
Mean ± SD, hour $week^{-1}$	6.8 ± 1.8	4.8 ± 0.8	6.8 ± 2.1	6.8 ± 2.1	6.8 ± 2.6	5.8 ± 3.2	0.11
95%CI, hour $week^{-1}$	4.9, 8.8	4.0, 5.6	4.6, 9.1	4.6, 6.8	4.1, 9.5	1.8, 9.8	
BCVA, right eye							
Mean ± SD, LogMAR	−0.08	−0.08	−0.08	−0.08	−0.08	−0.08	–
BCVA, left eye							
Mean ± SD, LogMAR	−0.08	−0.08	−0.08	−0.08	−0.08	−0.08	–
SERE, right eye							
Mean ± SD, D	−4.54 ± 3.56	–	−4.69 ± 3.7	−4.50 ± 3.55	−4.52 ± 3.58	−5.18 ± 3.52	0.64
95%CI, D	−8.28, −0.81		−8.62, −0.75	−8.23, −0.77	−8.28, −0.76	−9.55, −0.80	
SERE, left eye							
Mean ± SD, D	−4.27 ± 3.01	–	−4.27 ± 3.10	−4.31 ± 3.15	−4.10 ± 2.98	−4.78 ± 3.03	0.34
95%CI, D	−7.43, −1.11		−7.53, −1.01	−7.62, −1.01	−7.23, −0.98	−8.54, −1.01	
Corneal erosion area score, right eye							
Mean ± SD	0	0	0	0	0	0	–
Corneal erosion density score, right eye							
Mean ± SD	0	0	0	0	0	0	–
Corneal erosion area score, left eye							
Mean ± SD	0	0.17 ± 0.41	0	0	0	0	–
95%CI	–	−0.26, 0.60	–	–	–	–	
Corneal erosion density score, left eye							
Mean ± SD	0	0.17 ± 0.41	0	0	0	0	–
95%CI	–	−0.26, 0.60	–	–	–	–	
Conjunctival hyperemia score, right eye							
Mean ± SD	0	0	0	0	0	0	–
Conjunctival hyperemia score, left eye							
Mean ± SD	0	0	0	0	0	0	–
Pterygium, right eye	None	None	None	None	None	None	
Pterygium, left eye	None	None	None	None	None	None	
Cataract, right eye	None	None	None	None	None	None	
Cataract, left eye	None	None	None	None	None	None	
Lid change, right eye	None	None	None	None	None	None	
Lid change, left eye	None	None	None	None	None	None	
CECD, right eye							
Mean ± SD, cells mm^{-2}	2792 ± 245	–	2742 ± 252	2757 ± 247	2748 ± 221	2658 ± 213	0.92
95%CI, cells mm^{-2}	2535, 3049		2478, 3007	2498, 3016	2516, 2980	2394, 2923	
CECD, left eye							
Mean ± SD, cells mm^{-2}	2785 ± 189	–	2705 ± 321	2793 ± 168	2794 ± 210	2710 ± 166	0.74
95%CI, cells mm^{-2}	2586, 2984		2368, 3042	2617, 2969	2574, 3014	2504, 2917	
Subjective symptoms	None	None	None	None	None	None	
Adverse event	None	None	None	None	None	None	

BCVA = best-corrected visual acuity; CECD = corneal endothelial cell density; CI = confidence interval; LogMAR = logarithm of the minimum angle of resolution; *N* = number; SD = standard deviation; SERE = spherical equivalent refractive error. †*P* values obtained by a mixed-effects regression model. Stay in the room for 1 day data is expressed in hour/day.

Table 2. Inhibiting efficacy of 222 nm UVC room lamps for *Staphylococcus aureus* and φX174.

	Control	Desk	Slitlamp	Footswitch	*P*-value†
Irradiation dose, mJ cm^{-2}	0	5	7.5	7.5	
Staphylococcus aureus					
N	6	6	6	6	
Mean ± SD, CFU	42 170 ± 5980	7120 ± 1580	3630 ± 1690	2830 ± 520	<0.0001
95%CI, CFU	35 890, 48 443	5459, 8778	1858. 5409	2287, 3379	
%Inhibition		83.1%	91.4%	93.3%	
P-value, *vs* Control‡		<0.0001	<0.0001	<0.0001	
φX174					
N	2	6	6	6	
Mean ± SD, PFU	147 000 ± 7071	950 ± 654	40 ± 19	330 ± 62	<0.0001
95%CI, PFU	83 469, 210 531	264, 1636	20, 59	265, 395	
P-value, *vs* Control‡		<0.0001	<0.0001	<0.0001	
%Inhibition		99.4%	99.97%	99.8%	

CI = confidence interval; CFU = colony-forming unit; *N* = number; PFU = plaque-forming unit; SD = standard deviation. †*P* values calculated among groups by one-way analysis of variance (ANOVA). ‡*P* values for pair comparisons by Tukey–Kramer honesty significant difference tests. For *Staphylococcus aureus*, UVC-unexposed dishes left in the room for relevant duration are used as control, while for φX174, the dishes dispensed during seeding are used as control since the dishes of the corresponding UVC-unexposed control are uncountable due to too many colonies.

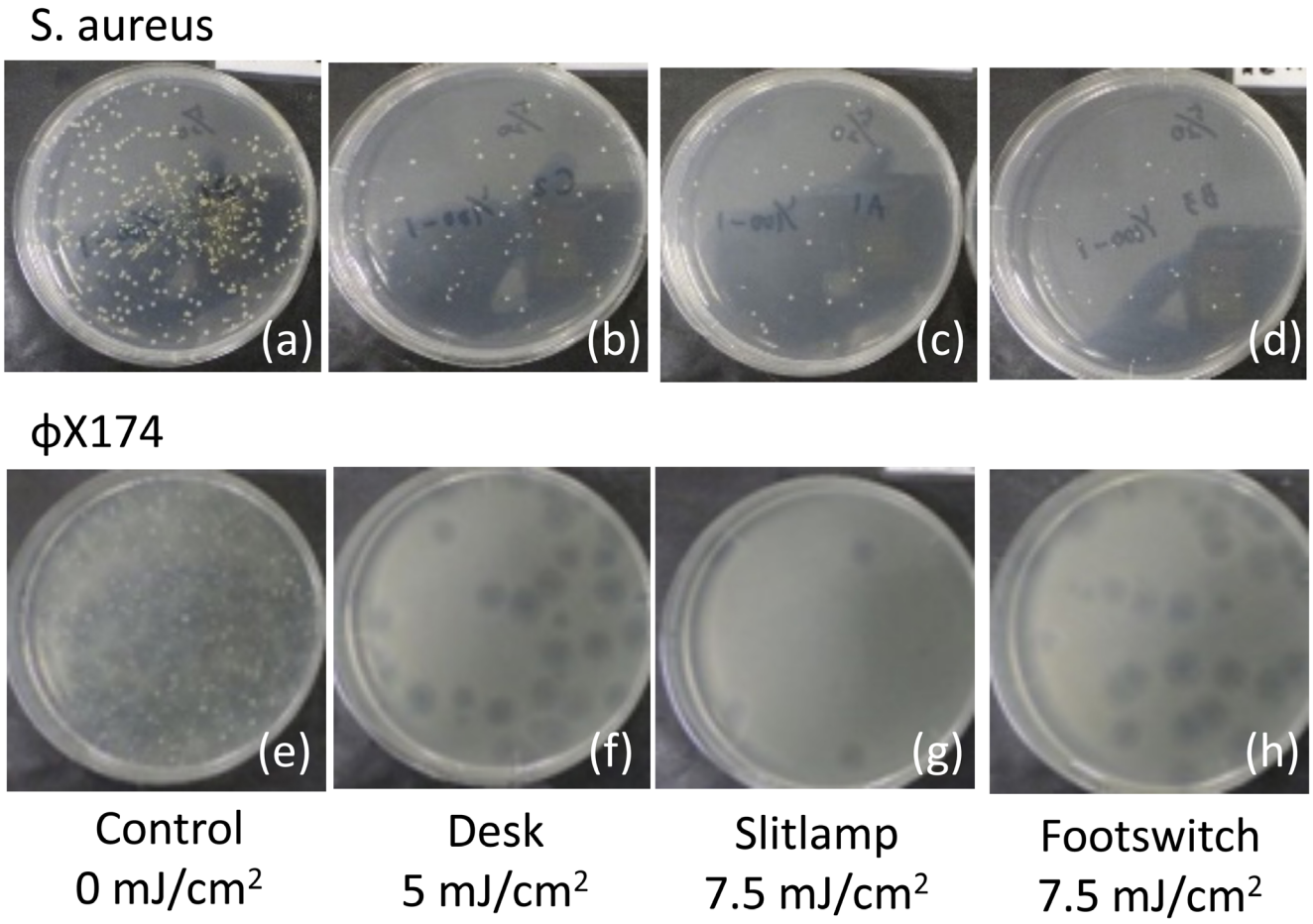

Figure 5. Representative agar plates cultured for *Staphylococcus aureus* (a–d) or φX174 phage (e–h) of UV-C unexposed (a, e) and exposed (b–d, f–h) samples.

malignancies, which were previous concerns for human exposures at longer, more penetrating UV wavelengths (7–10). Among the participants, none of these pathologies were observed, and the quantitative parameters, including BCVA, SERE, and CECD, were unchanged during the study period. After the end of the study period of 12 months, none of the five subjects who continued to work in the room reported any of the potential ocular side effects throughout an additional 1 year (*i.e.*, 2 years after the lamps installation). Throughout the UV-C spectral band, the thresholds of detectable skin damage were

significantly higher than those of detectable corneal surface epithelial damage because of the strong pre-absorption by the stratum corneum (33). In the UV-C band, all energy is absorbed in the corneal epithelium; hence, cataract of the crystalline lens cannot result from chronic UV-C exposure since the energy does not transmit deeply into the cornea (2,34). The surface epithelial cells of the cornea do not have a substantial pre-absorbing shield such as the stratum corneum of the skin; the transmittance of UV at 220 nm was 88% through the human tear film (35). The typical lifetime of corneal surface cells is about 48 h, so they serve as a "sacrificial" surface cells soon to be sloughed off in the normal corneal epithelial life cycle to act as a protective shield for the underlying corneal epithelium (2). The germinative cells in the corneal limbus are shielded by at least three cell layers (36). In the layered cell sheets, the UV transmittance of 222 nm was 10 times less than that of 254 nm (37); thus, the 222 nm UV-C is far less likely to be a causative factor of pterygium than 254 nm. Collectively, we can indicate that the full-room UVGI with the current study's conditions is safe for the eyes and lid skin at least for a year period.

The non-clinical study clearly demonstrated the germicidal efficacy of 222 lamps installed in the examining room; the inhibition rates by the lamps seemed larger for φX174 phage (99.4–99.97%) than that for *S. aureus* (83.1–93.3%). In a previous study, the susceptibility of *E. coli* and P1 phages differed in response to 254 nm and 222 nm; *E. coli* was more sensitive to 254 nm than to 222 nm, whereas P1 phages were more sensitive to 222 nm than to 254 nm (18). In another previous study, the germicidal efficacy of 222 nm was equivalent to, or even better than, 254 nm for some bacteria, yeasts and viruses, while the efficacy was weaker with 222 nm than 254 nm for fungal spores (17). The particle diameters of the *S. aureus* and φX174 phage we used were approximately 1 μm and 26 nm, respectively (38). The irradiance of far UV-C such as 207 nm radiant energy was reduced by half in about 0.3 μm of tissue (4). Accordingly, differences in particle diameters can explain the different efficacies of inhibition between bacteria and phage observed in our study. Disinfection by 222-nm UV-C was effective for MRSA and aerobic bacteria contamination on doctors' hospital-use-only mobile phones (39). Our study suggested the possible inactivation efficacy for microorganisms by 222-nm irradiation on the desk surfaces where the PC keyboards were located, the table where the slitlamp microscope was there, and the floor where the device's footswitch was there in the full-room UVGI settings.

Weekly use of the examining room for 6.7 h by study participants corresponded to roughly 1 h per day irradiation (2.8 mJ cm^{-2} per day); thus, the demonstrated safety by this study applies to an irradiation dose well under the former ACGIH's TLV of 22 mJ cm^{-2} per day (2) and by far under the recently revised TLV for 222 nm (*i.e.*, 160 mJ cm^{-2} per day) (40,41). Wearing glasses for myopic correction might further reduce the actual UV-C irradiation of the eyes and should affect the results. Furthermore, we also did not observe any changes in facial skin. Based on the safety profile obtained from this study, we now can plan to adopt the revised TLV for the UVGI in our examination room. The merit of using UV-C over other disinfection methods such as ethanol is that UV-C can be effective even for airborne microbes as previously reported (22,23). Although we did not show such data in this manuscript, we are now conducting the assessment of air disinfection efficacy under the full-room UVGI condition with 222-nm lamps.

In conclusion, our study of full-room germicidal UV using 222-nm lamp units clearly demonstrated no associated health hazards to the eye and the lid skin of persons who stayed in the room for an average of 6.7 h weekly for up to 12 months when exposed under the former ACGIH-recommended TLV (22 mJ cm^{-2}). The irradiation in their setting using the same fixtures was associated with >99% inhibition of φX174 phage and >90% inhibition of *S. aureus* on the irradiated surfaces of tables or the floor in the same room.

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