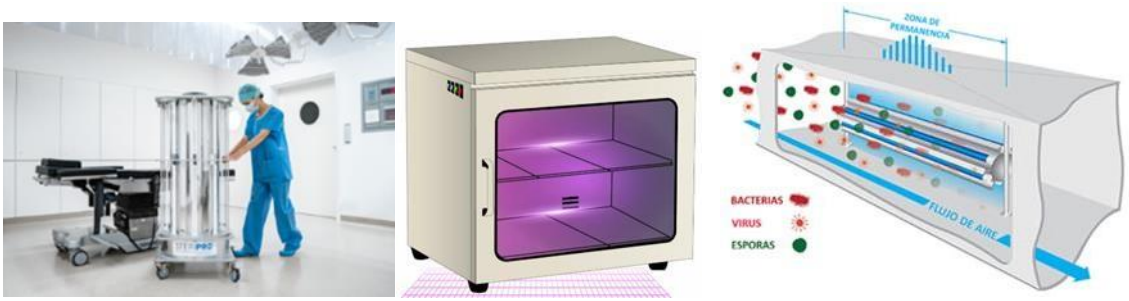
DIVISIÓN DE BIOSEGURIDAD



Aplicaciones de ultravioleta para mejorar la calidad de la vida humana y proteger el medio ambiente

INDUSTRIAL & BIOSAFETY DIVISION

Caso de Estudio UV-C Ver. 1.2
Mayo 2020

IUVA Fact Sheet on UV Disinfection for COVID-19

http://www.iuva.org/IUVA-Fact-Sheet-on-UV-Disinfection-for-COVID-19

The International Ultraviolet Association (IUVA) believes that UV disinfection technologies can play a role in a multiple barrier approach to reducing the transmission of the virus causing COVID-19, SARS-CoV-2, based on current disinfection data and empirical evidence. UV is a known disinfectant for air, water and surfaces that can help to mitigate the risk of acquiring an infection in contact with the COVID-19 virus when applied correctly. "The IUVA has assembled leading experts from around the world to develop guidance on the effective use of UV technology, as a disinfection measure, to help reduce the transmission of COVID-19 virus. Established in 1999, the IUVA is a nonprofit dedicated to the advancement of ultraviolet technologies to help address public health and environmental concerns," says Dr. Ron Hofmann, Professor at the University of Toronto, and President of the IUVA.

It must be noted that “UVC”, “UV disinfection” and “UV” as used here and in the scientific, medical and technical literature, specifically and importantly refers to UVC light energy (200-280nm light) in the germicidal range which is not the same as the UVA and UVB used in tanning beds or sunlight exposure.

Facts on UV and COVID-19

Can UVC help prevent COVID-19 transmission by reducing contamination?

Based on existing evidence, we believe so. Here’s why:

UVC light has been used extensively for more than 40 years in disinfecting drinking water, waste water, air, pharmaceutical products, and surfaces against a whole suite of human pathogens

https://www.iuvanews.com/stories/pdf/archives/180301_UVSensitivityReview_full.pdf

All bacteria and viruses tested to date (many hundreds over the years, including other coronaviruses) respond to UV disinfection. Some organisms are more susceptible to UVC disinfection than others, but all tested so far do respond at the appropriate doses.

- UVC disinfection is often used with other technologies in a multibarrier approach to ensure that whatever pathogen is not “killed” by one

method (say filtering or cleaning) is inactivated by another (UVC). In this way UVC could be installed now in clinical or other settings to augment existing processes or to shore up existing protocols where these are exhausted by excessive demands due to the pandemic.

- COVID-19 infections can be caused by contact with contaminated surfaces and then touching facial areas (less common than person-to-person, but still an issue) [vi]. Minimizing this risk is key because COVID-19 virus can live on plastic and steel surfaces for up to 3 days[vii]. Normal cleaning and disinfection may leave behind some residual contamination, which UVC can treat suggesting that a multiple disinfectant approach is prudent. UVC has been shown to achieve a high level of inactivation of a near-relative of COVID-19's virus (i.e., SARS-CoV-1, tested with adequate dose of 254nm UV while suspended in liquid) [viii]. IUVA believes similar results can be expected when treating COVID-19's virus, SARS-CoV-2. However, the key is applying UVC in such a way that it can effectively reach any remaining viruses on those surfaces.

- IUVA also concurs with CDC guidance to hospitals that the germicidal effectiveness of UVC is influenced by the UVC absorbing properties of the suspension, the surface or aerosol that the organism is in; by the type or action spectra of the microorganism; and by a variety of design and operating factors that impact the delivered UV dose to the microorganism https://www.cdc.gov/infectioncontrol/guidelines/disinfection/

- IUVA recognizes that in the cases where the UVC light cannot reach a particular pathogen, that pathogen will not be disinfected. However in general, reducing the total number of pathogens reduces the risk of transmission. The total pathogenic load can be reduced substantially by applying UV to the many surfaces that are readily exposed, as a secondary barrier to cleaning, especially in hurried conditions. This would be a relatively straight-forward matter of illuminating the relevant surfaces with UVC light, for example the air and surfaces around/in rooms and personal protective equipment.

- UV light, specifically between 200-280nm[i] (UVC or the germicidal range), inactivates (aka, 'kills') at least two other coronaviruses that are near-relatives of the COVID-19 virus: 1) SARS-CoV-1[ii] and 2) MERS-CoV[iii] [iv] [v]. An important caveat is this inactivation has been demonstrated under controlled conditions in the laboratory. The effectiveness of UV light in practice depends on factors such the exposure time and the ability of the UV light to reach the viruses in water, air, and in the folds and crevices of materials and surfaces.

Are UVC disinfection devices safe?

Like any disinfection system, UVC devices must be used properly to be safe.) They all produce varying amounts of UVC light in wavelengths of 200nm-280nm. This UVC light is much "stronger" than normal sunlight, and can cause a severe sunburn-like reaction to your skin, and similarly, could damage the retina of your eye, if exposed. Some devices also produce ozone as part of their cycle, others produce light and heat like an arc welder, others move during their cycles. Hence, general machine-human safety needs to be considered with all disinfection devices, and these considerations should be addressed in the operations manual, in the user training, and appropriate safety compliance.

Are there performance standards and UVC validation protocols for UV disinfection devices?

Given the wide array of UVC devices marketed for disinfection of air, water and solid surfaces, the lack of uniform performance standards and the highly variable degree of research, development and validation testing that is performed on different devices, the IUVA urges consumers to exercise caution when selecting equipment and look for evidence of third party testing as well as certification of device materials and electrical components by well-known organizations such as NSF, UL, CSA, DVGW-OVGW or other international requirements as applicable.

For UVC devices designed to inactivate air and solid surfaces in the healthcare industry, members of IUVA are working diligently with other national standards organizations in the lighting and healthcare industry to develop disinfection testing standards[x]. The goal is to develop guidance that will help healthcare providers world-wide choose the best possible technologies for their institutions to use in the fight against multiple drug resistant organisms and other pathogens[xi], like the COVID-19 virus.

IUVA will soon post a website dedicated to UV and COVID-19, please email us at info@iuva.org if you would like for us to send you alerts on website postings and other IUVA activities.

Resources

-Please find presentations, posters, and other information from the NIST/IUVA

https://www.nist.gov/news-events/events/2020/01/workshop-ultraviolet-disinfection-technologies-healthcare-associated

-Supporting Global Action to Reduce the Transmission Of COVID-19, CIE Releases Two Publications on Ultraviolet Radiation Disinfection - FOR FREE

http://cie.co.at/news/cie-releases-two-key-publications-uv-disinfection

-Advice (i.e., tips) for the selection and operation of equipment for the UV disinfection of air and surfaces

http://www.iuva.org/Advice-selection/operation-of-equipment-for-the-UV-disinfection-of-air-and

-Standards for European medical devices and personal protective equipment available free of charge from The German Institute for Standardization (DIN)

https://www.din.de/en/din-and-our-partners/press/press-releases/covid-19-din-makes-standards-for-medical-equipment-available-708628

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[v] Ibid.

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UVSolutions
Innovations for Industry, Public Health & the Environment

Evaluating the Efficacy of a 'No-Touch' UV-C Radiation Device as a High-Touch Disinfectant

03/05/2020 https://uvsolutionsmag.com/articles/2020/evaluating-the-efficacy-of-a-no-touch-uv-c-radiation-device-as-a-high-touch-disinfectant/

Steve Reinecke

Nosocomial pathogens, commonly referred to as healthcare-associated infections (HAIs), cause life-threatening complications for patients and costly consequences for healthcare facilities. One in 31 patients hospitalized in the United States in 2017 had at least one HAI on any given day [1]. In a public health report, an estimated 1.7 million people a year acquire an HAI during a hospital stay, costing the healthcare industry $35.7 billion to $45 billion annually [2,3].

High-touch surfaces are a source of HAIs that cause secondary transmissions of bacteria, directly through patient contact or indirectly through the hands of healthcare workers who touched a contaminated Surface [4]. Infectious pathogens, including Clostridium difficile (C. diff), vancomycin-resistant Enterococci (VRE), methicillin-resistant Staphylococcus aureus (MRSA), Acinetobacter baumannii, Pseudomonas aeruginosa and norovirus can contaminate high-touch surfaces, survive disinfection attempts, transfer to the hands of healthcare workers and infect patients upon contact [5].

Multiple studies have demonstrated how frequently touched surfaces can contain pathogens. A study in a medical ICU found colonization rates were higher for keyboards in rooms with patients positive for MRSA, and another study found keyboards tested positive for the growth of two or more microorganisms, including coagulase-negative Staphylococci (100% of keyboards), diphtheroids (80%), Micrococcus species (72%), Bacillus species (64%) and oxacillin-resistant Staphylococcus aureus (4%) [6,7].

In addition to keyboards in patient rooms, portable medical equipment (PME) and computers on carts – also known as workstations on wheels (WOWs) – can be used hundreds of times a day, acting as a mobile reservoir for multidrug-resistant microorganisms. The top three most common interactions involving PME and patients were WOW to patient (22.6% of total sequences), patient to WOW (20.4%) and patient to IV pump (16.1%), demonstrating that frequently touched PME and WOWs are potential sources of contamination from patients or the environment [8]. Pathogens can spread from WOW to patient and patient

to WOW, as established in a study that revealed daily cleaning of WOWs was nonexistent over a baseline evaluation period [9].

If a health system's cleaning and disinfection protocols are insufficient, harmful microorganisms can be transmitted, underscoring the need for an extensive review aimed at improving cleaning and disinfection techniques [10].

UV-C

A way to expand cleaning protocols is with the advent of ultraviolet (UV) disinfection devices. Used as early as 1878 by Arthur Downes and Thomas P. Blunt, the short wavelength light was investigated to sterilize bacteria [11]. Since then, UV light has been used in air and water treatment and as a surface disinfectant of fruit and vegetables [12]. The short wavelength of UV, UV-C (between 250 and 280 nm), is considered germicidal and can inactivate bacteria, viruses and other microorganisms by damaging their deoxyribonucleic acid (DNA) to prevent the spread of HAIs [13,14].

New no-touch decontamination technologies can offer benefits for disinfecting high-touch surfaces in a healthcare environment, such as in-room computer workstations, WOWs and PME. A recent article reported that ultraviolet light disinfection is "successful in reducing the bio burden of a room and [has] been shown to stop outbreaks associated with environmental contamination" [15]. Multiple studies also have demonstrated the effectiveness of UV light to reduce HAIs. Specifically no-touch methods, including UV devices, have confirmed their ability to reduce HAIs on high-touch surfaces [16].

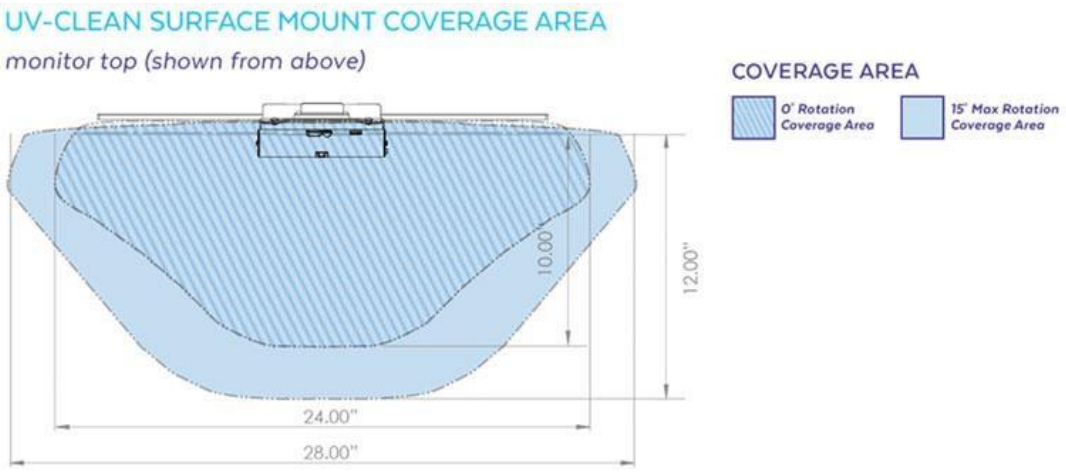

Figure 1. UV-CLEAN Surface Mount configuration attaches to the top of any monitor bezel.

Point-of-care UV units, such as UV-CLEAN (Proximity Systems, Tomball, Texas), are attached to or positioned above high-touch surfaces (Figure 1). The unit provides automated cleaning cycles of UV-C light to inactivate microorganisms at the genetic level by damaging their DNA. A built-in motion sensor enables the unit to safely emit UV-C light to disinfect when in-room workstations, stationary equipment, WOWs or PME are not in use and no motion is detected. The following clinical study evaluated the effectiveness of UV-CLEAN in a hospital setting.

Materials and methods

Location

In an effort to reduce cross-contamination of HAIs in its facility, HCA Houston Healthcare Southeast partnered with Proximity Systems to complete a study of the use an automated UV-C disinfection unit in the neurology unit and Intermediate Medical Care Unit (IMCU) at HCA Houston Healthcare Southeast, a fully accredited, 345-bed medical facility located in Pasadena, Texas, from March 2019 to April 2019.

The study involved 52 computer workstations. Of these workstations, 16 were Ergotron StyleView mobile computing carts (two different models) that were primarily used and stored in the hallways. There were also 36 wall-mounted Proximity Systems workstations (two different models) in 36 individual patient rooms. Of the 36 rooms, 32 were occupied, and the other four rooms had been occupied within the past 24 hours of initial swabbing.

Collection of baseline data

Baseline keyboard cultures were taken before UV exposure of all 52 workstations using the COPAN ESwab 480c Collection Kit. Using sterile saline, sterile gauze was moistened, and the swab was wetted using an aseptic technique to prevent cross-contamination. Keys A-Z were swabbed by rolling the swab over the surface of each key. The entire surface of the spacebar and enter key were also sampled. A single swab was used for each workstation.

Negative controls were processed at the beginning, during and end of the sampling process using a wet sterile gauze with the saline solution to ensure aseptic conditions were maintained throughout the sampling process. Samples were sent to Lodestar Diagnostic Laboratory in Houston, Texas. Samples were plated on Blood Agar and Rose A66 aerobically and Chocolate Agar anaerobically. Catalase and Staphtex testing were performed on all suspected Staphylococcus aureus and all positives were tested for Cefoxitin sensitivity. VRA screening was using PYR and vancomycin sensitivity.

Installation of UV disinfection units

After samples were obtained, the UV-CLEAN disinfection unit was installed. Both cart models had sliding keyboard trays that stored under the work surface when not in use and pulled out to the front of the work surface when in use. Because of the difference in cart models, two different locations were chosen to mount the unit. Additionally, 10 carts were older models that offered minimal space between the keyboard and bottom of its work surface, resulting in the development of a custom bracket designed to mount the unit to the back of the keyboard storage area. Six of the second cart type had sufficient space to use the standard keyboard mount stand supplied with the unit, allowing the unit to be positioned three inches above the back of the keyboard, directly over the function keys.

There were two different models of wall-mounted workstations, consisting of a flip-down work surface, which holds a keyboard and mouse. When the work surface is down, a monitor is revealed, and the keyboard and mouse are 20 inches from the UV-C light disinfection unit. When the work surface is closed, the keyboard and mouse are still exposed to UV-C light. Fourteen of the workstations allowed for the use of the standard retrofit configuration that features a bracket to mount the UV-CLEAN unit to a shelf directly above the monitor. Twenty-two units used the standard surface-mount configuration that attached the unit to the top of a monitor. Both solutions were approximately 20 inches from the work surface where the keyboard was placed, allowing for a large area of exposure to UV-C light.

Device settings

At the time of the testing, the units were set up in the following preset time configuration:

- Clean time (the period the device is producing UV-C light): 300 seconds (five minutes).
- No motion time (the length of time the device will allow to pass before producing UV-C after the motion sensor has communicated an absence of movement): 60 seconds (one minute).
- Wait time (downtime scheduled between cleaning cycles that are unrelated to motion sensor activity): 60 minutes (one hour).

Collection of post-disinfection data

After two weeks of usage, identical samples were taken from carts and wall-mounted units using the identical sampling procedure (one wall-mounted unit was removed from the study as no access was allowed by the collectors due to an airborne isolation protocol patient being in the room). As with the pre-

disinfection samples, post-disinfection samples were sent to Lodestar Diagnostic Laboratory in Houston, Texas.

Results

Comparison of computer workstation bioburden at baseline vs. post-UV light disinfection

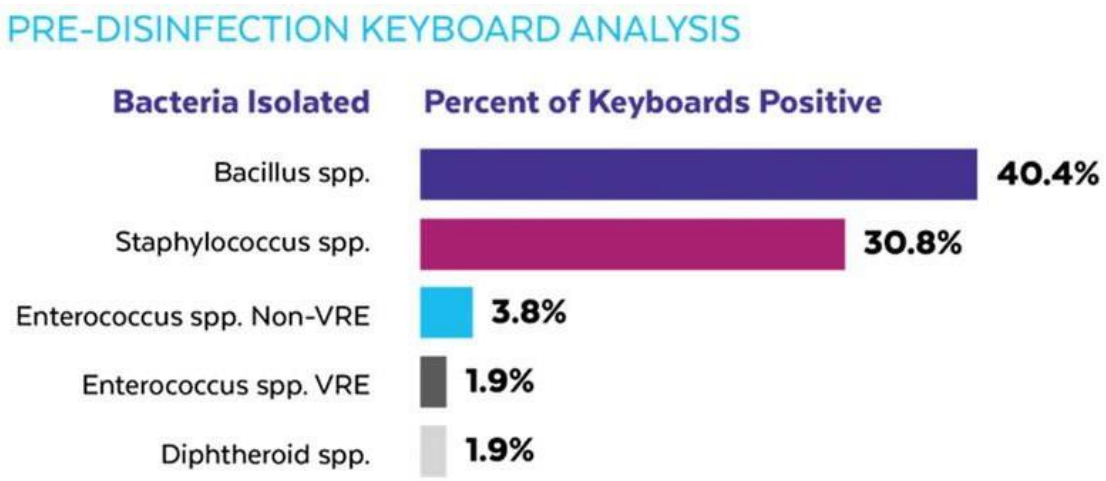

Figure 2. Percent of keyboards after intial culturing positive for various bacteria isolates

Initial culturing of the computer workstation keyboards prior to the installation of UV-CLEAN units identified bacteria in 75% of the units. Of the 16 mobile computing carts, seven (44%) were found to have bacteria on the surface of the keyboard. Of the 35 wall-mounted units, 31 (89%) were found to have bacteria on the surface of the keyboard. Wall-mounted units in three patient rooms had multiple bacteria isolated. A variety of bacteria was isolated on the mobile computing carts and wall-mounted computer workstations as shown in Figure 2.

The post-UV light disinfection cultures were sent for evaluation of the effectiveness of the units. All samples came back negative for growth on all surfaces swabbed, indicating a 100% reduction in keyboard bioburden, as shown in Figure 3. All negative controls taken during the study were negative for bacterial growth.

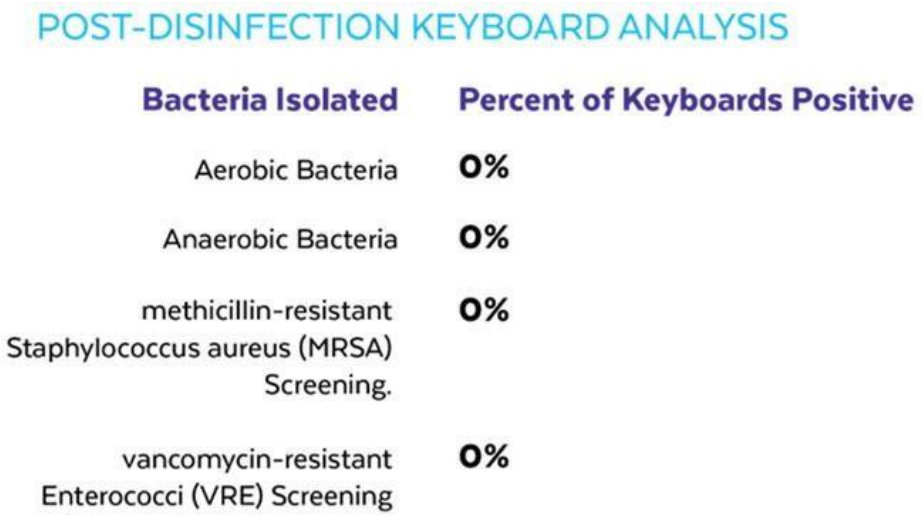

Figure 3. Percent of keyboards after post-disinfection culturing positive for various bacteria isolates

Internal audit data

BREAKDOWN OF RECORDED CLEANING CYCLES DURING CLINICAL STUDY

Disinfection Time *(UV light production)*	**Number of Recorded Cycles**
5 minutes *(complete cycle)*	15,672
4 minutes	1,328
3 minutes	1,960
2 minutes	3,058
1 minutes	5,605
< 1 minute	14,411

Table 1. Breakdown of recorded cleaning cycles during clinical study

The UV-CLEAN unit has an internal audit feature that records when the unit disinfected and when the unit registered motion. During the 14-day study, the 51 computer workstations recorded 42,034 cycles with 15,672 being complete, uninterrupted 300-second cleaning cycles, as shown in Table 1.

During the study, the mobile computing carts saw significantly more activity than did the in-room computer workstations (Fig 4A, 4B). It was observed during the study that the motion sensor on the carts was being triggered by activity other than the use of the keyboard.

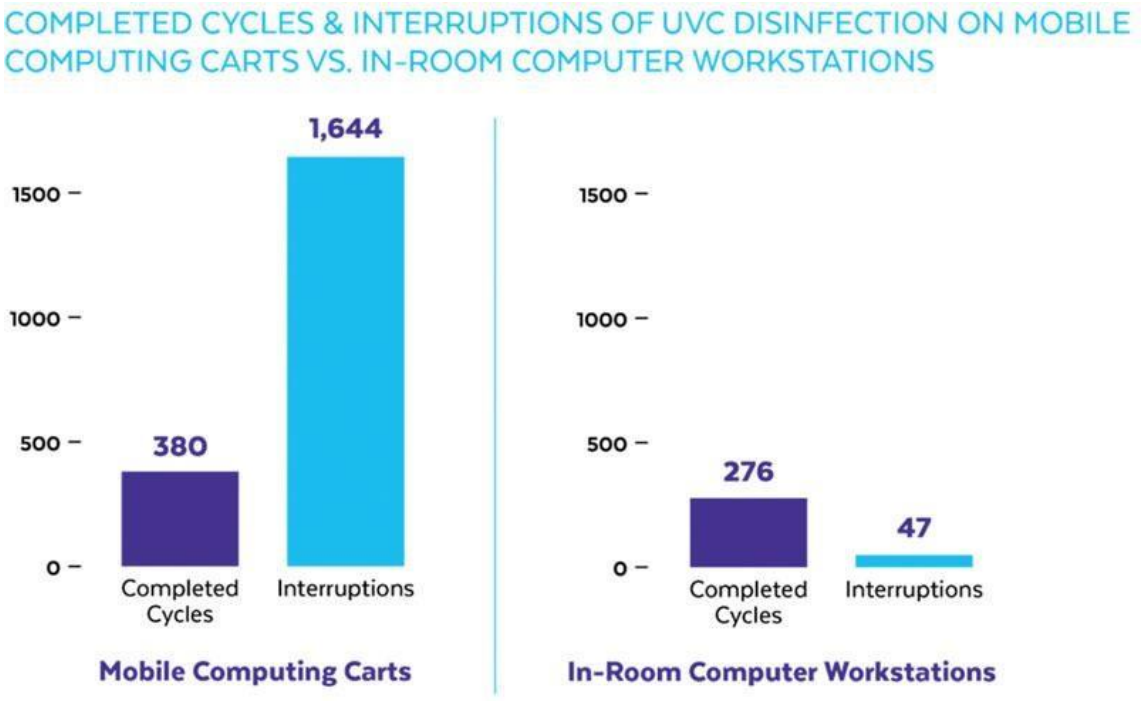

Figure 4. (A) Average number of completed disinfection cycles vs. average number of interruped disinfection cycles for unit placement on mobile computing cards. (B) Average number of completed disinfection cycles vs. average number of interrupted disinfection cycles for unit placement on in-room computer workstations.

UV-C exposure

Using high-speed photography, it was determined that the maximum UV-C exposure obtained prior to the motion sensor triggering the bulb to turn off was 30 μW/cm². Total exposure time never exceeded one second. The National Institute for Occupational Safety and Health (NIOSH) recommends that the time of exposure to an intensity of 100 microwatts per sq. cm. at wavelength 254 nm not exceed one minute; and based on the NIOSH recommendation, the maximum time to be exposed of 30 μW/cm² should not exceed 200 seconds during an eight-hour period [17].

As noted previously, the settings for the unit during this study was five minutes of cleaning time per hour or after a one-minute period of inactivity after motion is detected. The data from the more than 42,034 records was analyzed, and 63% of cleanings were interrupted. This resulted in 13.3 interruptions on average per eight-hour shift. Based on the exposure testing done, this would give 13.3 seconds of 30 μW/cm2, resulting in just under 7% of the maximum dosage recommendation set by the NIOSH for an eight-hour shift (Table 2).

UVC EXPOSURE CALCULATION	
Total Number of Complete Cycles	42,034
Total Number of Interrupted Cycles	15,672
Total Number of Completed Cycles	26,362
Average Daily Number of Cycles Initiated	63.4
Average Daily Interruptions	39.8
Rate of Interruptions	63%
Average Interruptions per 8-Hour Period	13.3
Average Completed Cycles per 8-Hour Period	23.6
Average UVC Exposure per 8-Hour Period	13.3 seconds
Percent of NIOSH Limit	6.7%

Table 2. UV-C exposure calculation

Discussion

The need for hand washing protocols and chemical disinfection on high-touch surfaces in healthcare environments has been long recognized; however, studies have shown cleaning regimens are not always followed. Healthcare workers touch many surfaces daily, resulting in the need for consistent hand hygiene, including use of hand sanitizer before and after interaction with patients, workstations or PME. Although considered a standard practice, hand hygiene compliance throughout the US is only 40%, which is why daily disinfection of frequently touched surfaces is also a standard procedure critical for reducing HAIs [18,19].

When hand hygiene is followed consistently, as was the case in this study with healthcare workers using mobile computing carts, high-touch surfaces like keyboards have less chance of contamination. During the initial culturing, there was a lesser percentage of mobile computing carts that tested positive for bacteria than the wall-mounted workstations in patient rooms. Hospital protocol was to sanitize hands prior to entering and after leaving a patient's room. Since mobile computing carts were seldom brought into a patient room, and nurses sanitized their hands after leaving a patient's room and prior to touching the keyboard, the keyboard had less chance of contamination than the wall-mounted workstations in a patient's room.

Also vital to reduce microbial contamination is environmental cleaning, as described as the physical act of cleaning a surface followed by an application of a disinfectant. Yet data from a recent study proves not all disinfecting agents are implemented correctly in relation to dwell time and type of surface – both impacting their effectiveness [20].

Infectious pathogens can spread if disinfection measures are inconsistent, which is why an automated cleaning modality is an effective complement to existing cleaning protocols. When used as a supplemental strategy, UV light can enhance disinfection and decrease bioburden to decrease HAI rates [21]. This study found that UV-CLEAN, an automated, low-intensity UV-C radiation point-of-care unit, was effective at eliminating harmful pathogens on keyboards attached to WOWs and wall-mounted workstations.

When used in conjunction with existing cleaning protocols, the unit's timed disinfection cycles also mitigated human error, a contributing factor to the spread of infection within a hospital. Because the unit is small (6″ x 1″ diameter) and available in multiple configurations, it also can be installed on other PME, including pumps and imaging machines, that may or may not be cleaned prior to or after patient use.

This study also found that the UV-C light motion sensor was being triggered by activity other than use of the keyboard. To mitigate this, the no-motion time default setting on the UV-CLEAN unit was changed from one minute to four minutes post-study. The data suggests this change would significantly decrease the amount of cycling and extend the bulb life but not impact the effectiveness of the UV disinfection. Based on that change and using the UV-C exposure data collected, the exposure limit would decrease to 3% of the maximum dosage recommendation set by the NIOSH for an eight-hour shift.

Conclusions

While increased access to information at the bedside has proved to deliver better patient outcomes, it has also introduced greater risk for patients to acquire an HAI. This study demonstrates the efficacy of UV-CLEAN as an automated UV disinfection unit, reducing bacterial burden on high-touch surfaces in and out of a patient's room.

When used as a complement to existing cleaning protocols, UV-CLEAN can safely target high-touch surfaces with no disruption to patient care or staff workflow and provide an audit to ensure disinfection is taking place.

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UV-C LED Irradiation for the Inactivation of Biofilm-bound Pseudomonas Aeruginosa Bacteria

09/20/2019 https://uvsolutionsmag.com/articles/2019/uv-c-led-irradiation-for-the-inactivation-of-biofilm-bound-pseudomonas-aeruginosa-bacteria/

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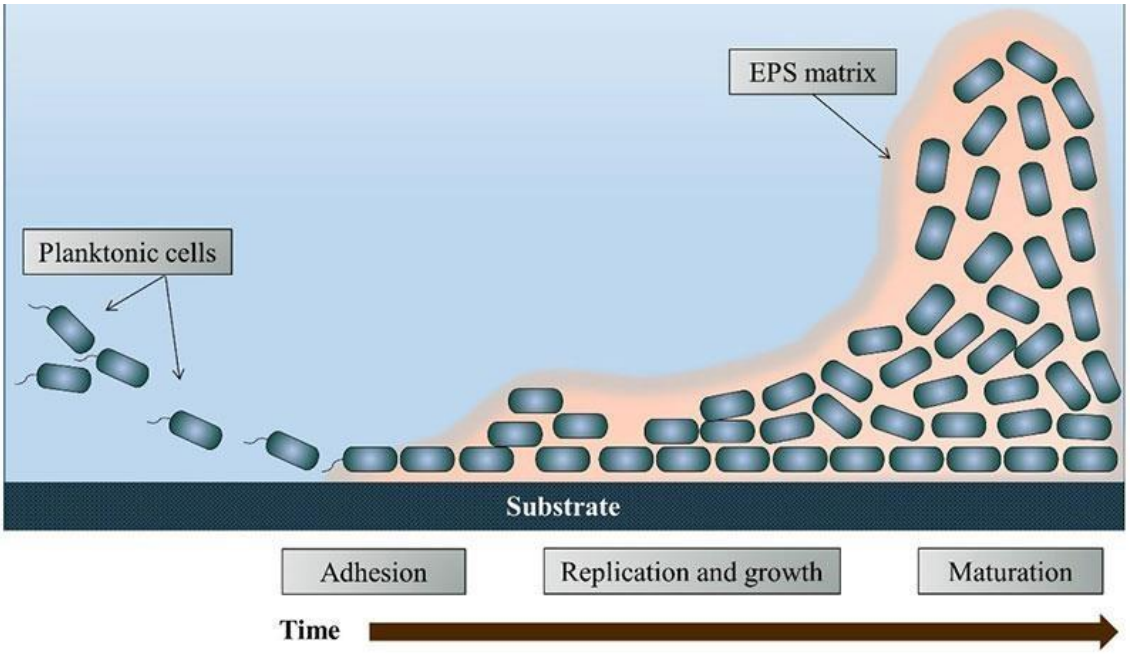
Biofilms are ubiquitous in nature and have the potential to harbor dangerous, opportunistic pathogens. Biofilms form when planktonic bacteria come into contact with a wetted surface and begin to release extracellular polymeric substances (EPS), allowing them to adhere to the solid substrate (Figure 1). Once the bacteria have adhered, they begin to replicate and increase EPS production, thickening the layer of the biofilm and securing the structure to the substrate.



The EPS matrix provides protection against common disinfection methods and makes disinfection of microorganisms encased in the biofilm increasingly difficult. This increased challenge to disinfection becomes even more problematic when opportunistic pathogens (e.g. Pseudomonas aeruginosa and

Legionella pneumophila) find refuge in the biofilms. Infections acquired from biofilm-bound bacteria can cause severe illness and even death in individuals with compromised immune systems.[1] Biofilm-bound bacteria have been associated with 80% of bacterial infections in the US[2] and are a common concern for food and healthcare industries.

In a clinical setting, biofilms can contaminate a wide range of infrastructure, tools and devices including, but not limited to, showerheads, hot water storage, dental water lines, endoscopes, catheters, pacemakers and prosthetic heart valves etc.[3] P. aeruginosa infections acquired in the clinical setting have been shown to increase the rate of illness and death rates of patients.[4,5]

In the food industry, meat, dairy, fish, poultry and produce are all at risk of biofilm contamination that can arise at any point from farming to consumption. Major risks of contamination stem from the product coming into contact with tainted process water, work surfaces and equipment.2 Contamination of food products can ultimately cause serious health consequences if the food is consumed and also can cause financial losses for a company through increased spoilage and loss of product.[3]

Biofilms are also a common concern in the water industry, as they can form on water treatment process equipment (e.g. membrane filters), distribution system infrastructure, premise plumbing, water storage tanks and secondary storage containers. The results of previous studies suggest that opportunistic pathogens, including Legionella, can grow inside of biofilm-dwelling hosts (e.g. protozoa) in drinking water infrastructure.[6] These risks often are exacerbated in remote and/or decentralized applications where water treatment technology is limited and the maintenance of onsite drinking water systems is the responsibility of residents or building owners with minimal training (e.g. Farenhorst et al.[7]).

In the food, healthcare and water sectors, many biofilm control strategies have been implemented, including chemical control with such agents as sodium hypochlorite, hydrogen peroxide, peracetic acid and ozone [2]; however, introduction to chemical agents eventually may lead to the development of resistant microbial populations.[8,9] Other types of control methods – such as ultrasonication, phages, enzymatic solutions, UV/H2O2 and UV/Cl2 – also have been employed to mitigate biofilms.[2]

UV irradiation alone also has been studied by many researchers with varying results.[10,11] The different methods employed by the researchers applying UV irradiation in different niche applications may have given rise to the inconsistent results. However, common across these studies is the finding that much higher UV fluences are required to achieve similar levels of inactivation of biofilm-bound microorganisms compared to planktonic (free floating) microorganisms.[10,12,13]

One study has shown that this is likely due to the high cellular density within the EPS matrix, which leads to increased attenuation of the UV light through the depth of the biofilm.[10] Furthermore, the complex EPS matrix also may provide shielding effects.[14]

A previous study suggests that a control strategy that first disrupts or dissolves the EPS matrix using surfactant should be adopted, as it will increase the penetration of chemical disinfectants.[15] A similar method potentially could be employed to allow for better penetration of UV-C irradiation into biofilms.

The objectives of this work were to develop a standard protocol for inactivating P. aeruginosa in biofilms with a UV-C LED collimated beam apparatus, compare inactivation from UV-C irradiation to commercial disinfecting wipes and investigate the impacts that the application of commercial disinfecting wipes before UV-C irradiation have on inactivation.

UV-C LED method development

The methodologies employed in previous studies focused on the application of UV for biofilm mitigation reflecting the industry-specific questions being addressed by the researchers who developed the experiments and apparatus. As a result, it is difficult to compare and generalize the results of these studies. A robust and repeatable method was developed for growing, treating and recovering biofilms for UV-C LED inactivation experiments. A full description of this standardized method can be found in Gora, et al.[16]

A CDC biofilm reactor and the method developed by the US EPA[17] were employed to grow stable P. aeruginosa (PA01) biofilms on polycarbonate coupons. The growth process included two stages designed to encourage biofilm adhesion and maturation. In the first stage, 500 mL of nutrient-rich media was inoculated with 1 mL of a highly concentrated P. aeruginosa stock and maintained at room temperature for 24 hours. This stage ensured the bacteria adhered to the surface of the coupon and initialized biofilm formation.

In the second stage, the nutrient-rich media was fed slowly into the reactor at approximately 10 mL/min at room temperature for an additional 24 hours. This stage allowed the attached biofilm to develop and mature.

Next, treatment was optimized with the UV-C LED collimated beam apparatus (Aquisense Technologies, Kentucky, US) based on three factors: the number of coupons being treated, rotation vs. no rotation and UV intensity (Figure 2). The study found that increased inactivation was achieved when samples were rotated at 5 RPM and that the number of coupons and intensity of the UV-C LEDs had no impact on inactivation. Thus, it was decided to treat three coupons

at a time with a rotation of 5 RPM at the highest possible intensity for the remainder of the study.

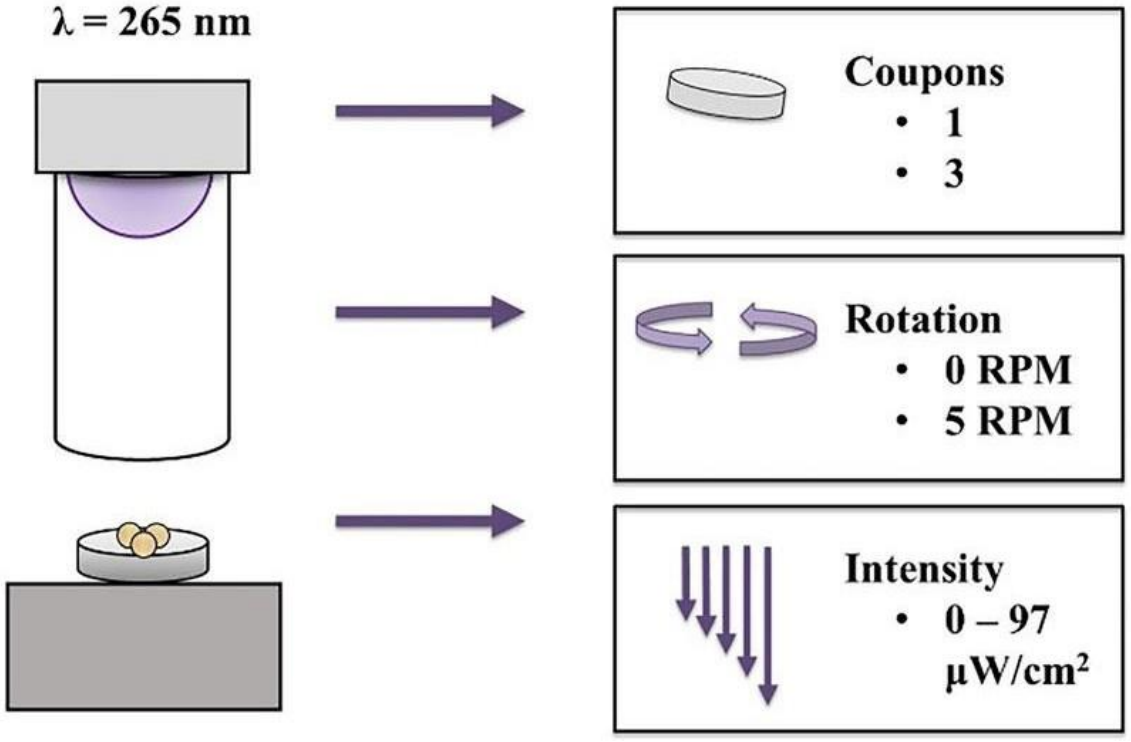


Figure 2. Factors examined for optimization of UV-C LED treatment of CDC biofilm reactor coupons coated in P. aeruginosa biofilms

Scraping and swabbing were compared as biofilm recovery methods and hand mixing, vortexing, sonicating and stomaching as biofilm resuspension methods. The materials and settings used for the different recovery methods were adapted from a previous study examining efficient biofilm removal from annular reactor coupons.[18]

The resuspended samples were enumerated on tryptic soy agar (TSA) plates at 37°C for 18 to 24 hours. We determined the combination of recovery and resuspension methods that gave the highest yield of P. aeruginosa cells and used it in the remainder of the study. A summary of the recommended standard method for UV-C LED treatment of P. aeruginosa biofilms is outlined in Figure 3.

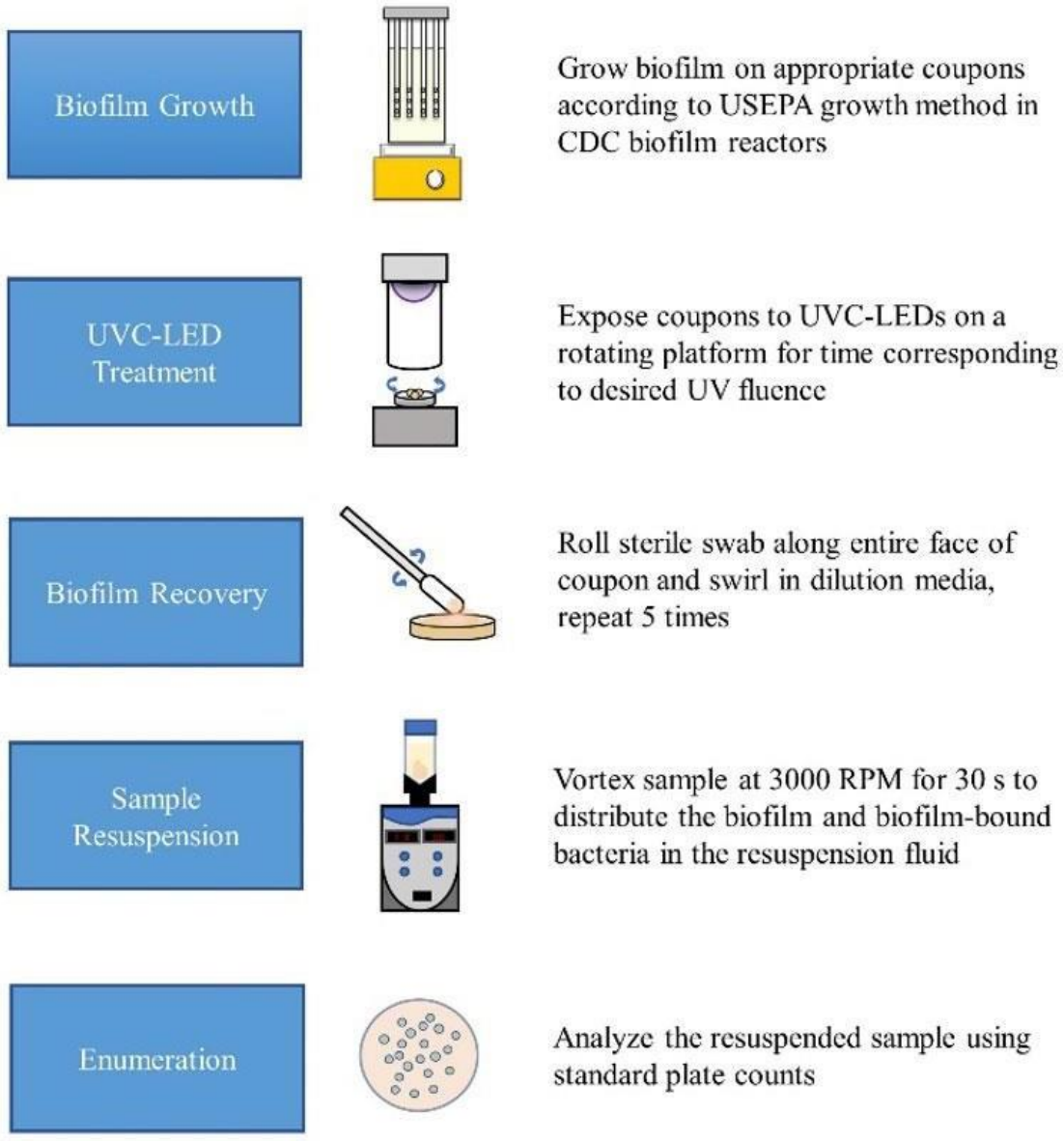


Figure 3. Standardized protocol for growth, treatment, recovery and analysis of Pseudomonas aeruginosa biofilms during UV-C LED inactivation experiments

Experimental

The 265 nm UV-C LED used in this study was characterized and found to have a peak wavelength of 268 nm and an FWHM of 11.5 nm. The intensity of the UV-C light delivered to the samples was determined by measuring the average intensity over the treatment field of the three coupons with a USB4000 spectrometer equipped with a DET4-200-850 detector (Ocean Optics Inc., Florida, US).

Intensity measurements were collected with a 0.5 cm spatial resolution at the surface of the coupons. The total intensity under the spectrum of the UV-C LED was collected by integrating the peak from 220 nm to 300 nm for each point in the treatment field. Once the average intensity was measured, the exposure times required to achieve UV fluences ranging from 0 to 12 mJ/cm2 were calculated by dividing the required fluence by the average intensity.

P. aeruginosa biofilms were grown on polycarbonate coupons in a CDC biofilm reactor using the above method. Following growth, treatment with UV-C LED irradiation, common disinfectant wipes or a combination of wiping followed by UV-C LED irradiation was applied to the contaminated coupons. UV fluences between 0 and 60 mJ/cm2 were applied using a UV-C LED collimated beam apparatus (Aquisense Technologies).

For the wiping treatments, a conventional disinfecting wipe (Cavi-Wipes, Metrex; Orange, California, US) were used in either a single pass or contacted with the surface for 15 seconds. Isopropyl alcohol (17.2%) and ammonium chloride (0.28%) are the active ingredients in Cavi-Wipes.

Results and discussion

Inactivation from UV treatment alone was shown to plateau at approximately 1.3-log reduction after a UV fluence of 8 mJ/cm² (data not shown, see publication for kinetics[16]). This was not entirely unexpected, as the inactivation of biofilm-bound microorganisms has been shown to require significantly higher fluences compared to free floating planktonic cells.

For example, research has shown that a fluence of approximately 4 mJ/cm² can achieve a similar log inactivation of 2 log in a pure suspension of planktonic P. aeruginosa.[19]

When examining indigenous bacterial communities in catheters, it was shown that the UV fluence required to achieve 4 log inactivation in the biofilm community was 10 times greater than that of the resuspended biofilm.[10] In another study, authors examined UV-C LED inactivation of P. aeruginosa in biofilms formed on catheters and found that a 4-log inactivation could be achieved with a fluence of 7.9 mJ/cm2.[20]

Treatment with commercial disinfecting wipes alone resulted in minimal differences between the single pass and the 15-second contact time and saw a slightly increased disinfection potential when compared to UV-C LED treatment alone.

However, when used in combination with UV-C LED irradiation, synergistic effects were observed. For example, a 2.3-log reduction was achieved with a

single pass of the commercial disinfecting wipe, and when a 12 mJ/cm² fluence was applied to the biofilm a 1.3-log reduction was achieved.

When the two methods were used in combination, the resulting plates contained too few colonies to count, indicating that more than 7.8-log inactivation was achieved. This suggests that up to 4.2-log inactivation was potentially related to synergistic effects between the wiping and UV-C LED treatments.

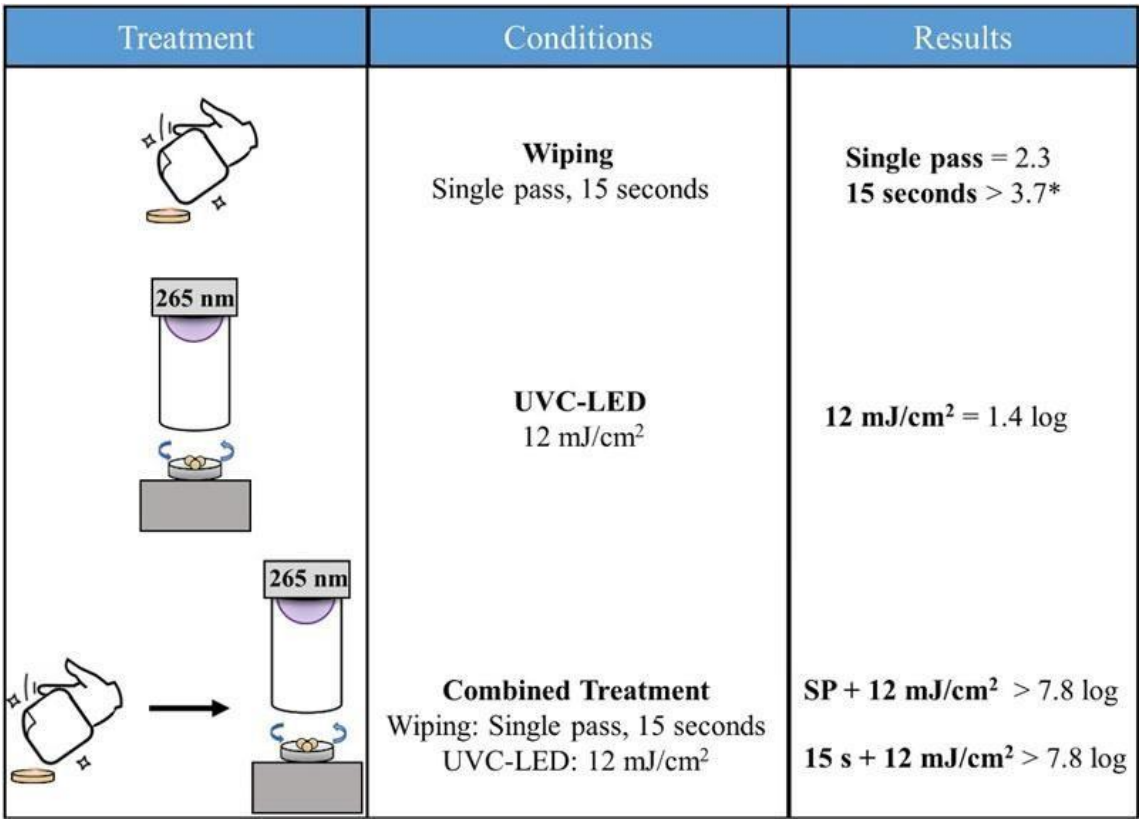


*Figure 4. Combined treatment with commercial disinfectant wipes and UV-C LEDs had potential synergistic impacts on P. aeruginosa (*one replicate had >7.8 log reduction)*

It was hypothesized that these effects may have occurred because the wiping treatment disrupted the biofilm and decreased any shielding effect the EPS matrix may have been providing to the cells (see Figure 4).

Interactions between the residual chemicals from the wipes and UV-C irradiation also may have contributed to the improvement in inactivation. The mechanism(s) underlying the synergistic effects reported here is the focus of current research into biofilm prevention and mitigation on surfaces.

This study demonstrated that the effectiveness of treating polycarbonate surfaces contaminated with P. aeruginosa biofilms was greatly improved by wiping with commercial disinfecting wipes followed by UV-C LED irradiation.

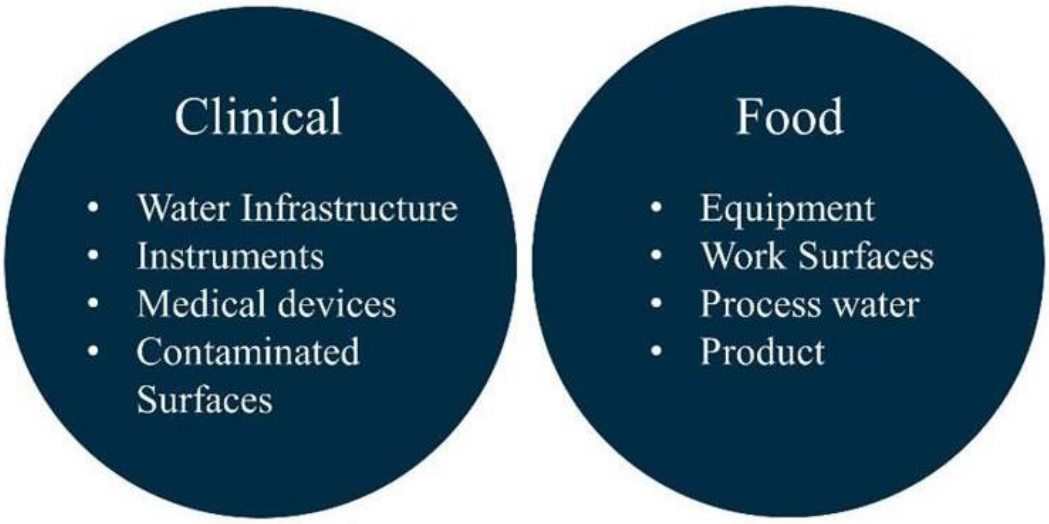


Figure 5. Potential applications for UV-C LED-based biofilm prevention and biofilm mitigation control strategies in clinical and food settings

While these findings may not be appropriate for all the areas where biofilm control strategies may be required (Figure 5), it is believed that the protocol presented will allow researchers to examine how factors such as active ingredients in disinfecting wipes, substrate materials, bacterial species and UV wavelengths impact the inactivation of biofilm-bound microorganisms.

Conclusion

This study examined the best method to systemically treat P. aeruginosa biofilms grown on polycarbonate coupons with a UV-C LED collimated beam apparatus. The method developed from this work provides a robust, bench-scale protocol to investigate inactivation responses of biofilm-bound bacteria that could be adapted for other industry-specific needs. This study also investigated the effectiveness of commonly used isopropanol disinfectant wipes on biofilm mitigation and the impacts of combing the wipes with UV-C LED irradiation.

When the two methods were combined, a 7.9-log reduction in P. aeruginosa was achieved, well above the reductions observed for either treatment alone. The mechanisms behind these synergistic effects were not explored in this study, but it is hypothesized that the increased reduction in cells was likely due to mechanical and/or chemical disruption of the EPS matrix prior to the application of UV-C irradiation. This hypothesis is currently being tested in the laboratory. The findings from this study suggest a two-stage treatment approach combining disinfectant wipes and UV-C LED irradiation could prove to be highly effective for biofilm control on surfaces.

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REPORTE BREVE Nº 15

USO DE LA LUZ ULTRAVIOLETA COMO SUSTITUTO A LA PRESIÓN NEGATIVA EN UNIDADES DE CUIDADOS INTENSIVOS EN EL CONTEXTO DE SARS-CoV-2

Elaboración: 30 de marzo de 2020

EsSalud

IETSI EsSalud INSTITUTO DE EVALUACIÓN DE TECNOLOGÍAS EN SALUD E INVESTIGACIÓN

USO DE LA LUZ ULTRAVIOLETA COMO SUSTITUTO A LA PRESIÓN NEGATIVA EN UNIDADES DE CUIDADOS INTENSIVOS EN EL CONTEXTO DE SARS-CoV-2

A medida que se incrementan las infecciones con el virus SARS-CoV-2, existe una sobredemanda de pacientes con COVID-19 en los servicios de salud de los países afectados por la pandemia, que ha sobrepasado la capacidad de respuesta en algunos países (Dalglish 2020). Ante ello, los servicios de salud requieren adoptar una serie de medidas para garantizar que durante la atención de pacientes con COVID-19 no se generen un riesgo de contagio de paciente a pacientes y de paciente a profesionales de la salud.

Los pacientes con COVID-19 requieren una serie de cuidados médicos. Un 5% de los pacientes hospitalizados requieren ser manejados en una Unidad de Cuidados Intensivos (UCI) (Guan et al. 2020). La atención en estas unidades requiere un alto nivel de asepsia para interrumpir la transmisión de microorganismos y reducir la incidencia de infecciones intrahospitalarias (Sallés and Ricart 2001). Para lograrlo existe una serie de medidas como la presión negativa en UCI cuyo objetivo principal es evitar la propagación de microorganismos a otras salas o espacios abiertos y que la Organización Mundial de la Salud recomienda en la medida de lo posible su uso cuando se realizan procedimientos que generan aerosoles (ej. broncoscopías) con un mínimo de 12 recambios de aire por hora o al menos 160 litros/según/paciente en instalaciones con ventilación natural (Alhazzani et al. 2020, World Health Organization 2020). Es así que, la urgencia de contar con mayor infraestructura hospitalaria y que todo ambiente o superficie de ambientes hospitalarios que atienden pacientes con COVID-19 sean desinfectados, hace que se proponga la utilización de otras medidas de desinfección. Una de ellas, es la luz ultravioleta que a diferencia de otras, requiere que las salas estén libres de pacientes durante su funcionamiento, debido a que la sobreexposición puede ocasionar lesiones en piel y ojos (fotoqueratitis) (Reed 2010).

Ante la pandemia por SARS-CoV-2 es necesario el cumplimiento de las mejores prácticas de limpieza y desinfección; no obstante, por su reciente aparición es esperable que la evidencia acerca de la eficacia de las medidas de control sea escasa.

MÉTODOS

Se llevó a cabo una búsqueda sistemática de la literatura el día 28 de marzo de 2020 con respecto al uso de la luz ultravioleta como sustituto a la presión negativa en UCI. Para ello se realizó una búsqueda sistemática (ver Anexos) en las bases de datos bibliográficas: PubMed, Cochrane Library, Medline vía OVID, Embase y EBSCO. Asimismo, se realizó una búsqueda manual avanzada en Google, y en páginas web de las principales sociedades o instituciones especializadas, tales como la *World Health Organization* (WHO) y *Centers for Disease Control and Prevention* (CDC). Se consideró la revisión de las listas de referencias de los estudios seleccionados para la identificación de otros estudios de relevancia. Finalmente, con la estrategia de búsqueda diseñada para PubMed y Embase, se generaron alertas diarias vía correo electrónico con el objetivo de actualizar el presente reporte según evolucione el conocimiento acerca del SARS-CoV-2.

La selección de documentos se realizó en el siguiente orden: guías de práctica clínica, evaluaciones de tecnologías sanitarias, revisiones sistemáticas y estudios primarios.

RESUMEN DE LA EVIDENCIA

No se encontraron guías de práctica clínica, evaluaciones de tecnologías sanitarias, revisiones sistemáticas o estudios primarios en las bases de datos bibliográficas que evalúen el uso de uso de la luz ultravioleta como sustituto a la presión negativa en UCI en el contexto de SARS-CoV-2.

La búsqueda de manual en Google se encontró el Manual de Prevención y Tratamiento de COVID-19 (Facultad de Medicina de la Universidad de Zhejiang 2020) y una revisión narrativa acerca de las lecciones aprendidas sobre COVID-19 (Yi et al. 2020). Asimismo, debido a que la secuenciación del genoma completo y el análisis filogénico indican que SARS-CoV-2 es un betacoronavirus del mismo subgénero que el virus del síndrome respiratorio agudo severo (SARS) y del virus del síndrome respiratorio del Medio Oriente (MERS) (Zhou et al. 2020, Zhu et al. 2020), se buscaron estudios que evaluaron la sensibilidad de SARS o MERS a la luz ultravioleta y que se describen a continuación (ver Anexos).

Manual de Prevención y Tratamiento de COVID-19 (Facultad de Medicina de la Universidad de Zhejiang 2020).

Se trata de un documento elaborado por el Primer Hospital Afiliado de la Facultad de Medicina de la Universidad de Zhejiang (FAHZU) conforme a la experiencia clínica que ofrece consejos y referencias al personal médico sobre de cómo tratar el coronavirus.

La guía considera que para el manejo de paciente con COVID-19 es necesaria la implementación de áreas de aislamiento que incluye un área de observación, salas de aislamiento y un área de UCI en aislamiento. Los proveedores de servicios médicos que cuenten con habitaciones de presión negativa deberán aplicar una gestión normalizada de acuerdo con los requisitos aplicables. En cuanto a los procedimientos de desinfección del Área de la Sala de Aislamiento del COVID-19, para la Desinfección del Aire, el manual considera que, si no se dispone de esterilizadores de aire de plasma, utilice lámparas ultravioletas durante una hora cada vez, realizando esta operación tres veces al día.

Los autores de la revisión no proporcionan detalles sobre el tipo de luz UV empleada y las especificaciones del procedimiento como tipo de fuentes recomendadas y área de cobertura de cada una de las fuentes.

COVID-19: what has been learned and to be learned about the novel coronavirus disease (Yi et al. 2020).

En una revisión narrativa publicada por Yi et al., publicado en el presente año, con el objetivo de revisar los conceptos básicos de epidemiologia, etiología, virología, diagnóstico, tratamiento, pronóstico y prevención de la enfermedad (Yi et al. 2020). Según señala esta revisión, en lo que se refiere a las propiedades fisicoquímicas del SARS-CoV-2 aún no se conocen en gran medida y que se ha informado que el SARS-CoV-2 es sensible a la luz ultravioleta y al calor da 56 °C basado en un reporte del Nuevo plan de diagnóstico y tratamiento de la neumonía por coronavirus (quinta edición) de la Comisión Nacional de Salud de la República Popular de China del 5 de febrero de 2020 (National Health Commission 2020).

Efficacy of an automated multi-emitter whole room UV-C disinfection system against Coronaviruses MHV and MERS-CoV (Bedell, Buchaklian, and Perlman 2016).

Se trata de un estudio publicado en 2016 que evaluó la eficacia de un sistema de luz ultravioleta (UV) tipo C (UV-C) automatizado como sistema de desinfección contra el MHV-A59 y MERS-CoV.

La prueba de sensibilidad del MERS-CoV a la luz UV-C se realizó mediante la colocación de los virus en cubreobjetos de vidrio y se expuso a la fuente de luz UV-C a una distancia de cuatro pies. Los autores reportan que un tiempo de exposición a UV-C de solo cinco minutos resultó en niveles indetectables del virus, que se mantuvieron hasta 30 minutos de exposición. Concluyendo los autores que la exposición de más de cinco minutos a la luz UV-C de gotas con virus MERS-CoV obtuvo una reducción porcentual del 99.999%.

Effect of ultraviolet germicidal irradiation on viral aerosols (Walker and Ko 2007).

Se trata de un estudio publicado en 2007 que evaluó la susceptibilidad a la luz UV de tres aerosoles virales, entre ellos un coronavirus (virus de la hepatitis murina (VHM)). El coronavirus VHM se analizó mediante un ensayo en placa utilizando la línea celular DBT y mediante una cámara experimental de diseño u sistema para medir la susceptibilidad a la luz UV de los aerosoles virales (generados por un nebulizador Collison a 20 psi) expuestas a varias dosis de luz UV. Se encontró que el coronavirus fue muy sensible a 254 nm de UV-C donde solo el 12% de los virus en aerosol permanecieron activos a una exposición a 599 µW s/cm^2 de UV-C. Los autores del estudio concluyen que la desinfección del aire usando 254 nm UV-C puede ser una herramienta efectiva para inactivar aerosoles virales, pero que se requieren más estudios de laboratorio y epidemiológicos para determinar la efectividad de la desinfección con aire UV en la reducción de enfermedades virales respiratorias.

Inactivation of SARS Coronavirus by Means of Povidone-Iodine, Physical Conditions and Chemical Reagents (Kariwa, Fujii, and Takashima 2006).

El estudio tuvo como objetivo evaluar la eficacia antiviral en condiciones de inactivación física entre las que se incluye la exposición a luz UV. Para evaluar la eficacia de la irradiación ultravioleta (UV), se colocaron alícuotas de 2 ml de virus de stock en placas de Petri de plástico de 3 cm abiertas, colocadas bajo la fuente de luz UV en un gabinete de bioseguridad e irradiadas con 134 µW / cm^2.

Se evaluó la resistencia del SARS-CoV-2 a la luz UV. Luego de la irradiación en una cabina de bioseguridad, la cantidad de virus se redujo de 3.8 x 107 a 180 TCID 50/ml en 15 minutos, pero el virus aún fue detectado con cifras de 18.8 TCID 50/ml, hasta después de 60 minutos de irradiación. Con lo cual los autores concluyen que el SARS-CoV-2 es relativamente resistente a luz UV.

Inactivation of the coronavirus that induces severe acute respiratory syndrome, SARS-CoV (Darnell et al. 2004).

Se trata de un estudio que evaluó la eficacia de varios métodos de inactivación viral, incluidos los métodos que pueden inhibir la replicación o entrada viral.

Para la evaluación in vitro los investigadores emplearon células de riñón de mono verde africano (Vero E6) con SARS-CoV que se mantuvieron en un medio de cultivo DMEM. El tratamiento con luz ultravioleta (UV) se colocó sobre la placa, a una distancia de 3 cm del fondo de los contenedores con las muestras de virus. A la distancia establecida, la fuente de luz UVC (254 nm) emitió 4016 μW/cm^2 (donde μW = 10^{-6} J/s) y la fuente de luz UVA (365 nm) emitió 2133 μW/cm^2. La exposición del virus a la luz UVC durante un minuto resultó en una inactivación parcial con una eficiencia creciente de hasta seis minutos, lo que resultó en una disminución de 400 veces en el virus infeccioso. No se observó inactivación adicional entre los seis a diez minutos. Después de 15 minutos, el virus se inactivó y no se detectó hasta el límite de detección de la prueba (≤1.0 TCID 50 (log_{10}) por ml). En contraste, la exposición a la luz UVA no demostró efectos significativos sobre la inactivación del virus durante un período de 15 minutos. Concluyendo que la luz UVC inactivó el virus del SARS a una distancia de 3 cm durante 15 minutos.

Stability of SARS coronavirus in human specimens and environment and its sensitivity to heating and UV irradiation (Duan et al. 2003).

Se estudió el efecto de la inactivación de la luz ultravioleta en cultivos celulares (Vero-E6) de SARS. Se colocaron un total de 10^6 $TCID_{50}$ virus en un medio de cultivo para ser irradiados con luz UV a >90 μw/cm^2 a una distancia de 80 cm. Irradiación de UV durante 15 resultó en una inactivación del SARS y a los 60 minutos se hicieron indetectables. Concluyendo los autores que el SARS es sensible a la irradiación con luz UV y llegan a ser indetectables luego de 60 minutos de irradiación.

CONCLUSIÓN.

No se han encontrado estudios que proporcionen evidencia científica a la fecha sobre el uso de luz ultravioleta como sustituto a la presión negativa en UCI. La propuesta del uso de luz ultravioleta ante la falta de esterilizadores de aire en salas de aislamiento de pacientes con COVID-19 se basa en manual recomendaciones que no proporciona detalles sobre el tipo de luz UV empleada y las especificaciones del procedimiento como tipo de fuentes recomendadas y área de cobertura de cada una de las fuentes. Cabe precisar que el uso de luz ultravioleta para la desinfección de ambientes o superficies hospitalarias requiere que las salas estén libres de pacientes por las lesiones en piel y ojos que puede ocasionar por la sobreexposición. No obstante, existen estudios in vitro sobre la inactivación por luz ultravioleta de los coronavirus MERS y SARS, cuyo componente genético es similar al SARS-CoV-2, que muestran que la luz ultravioleta tiene la capacidad de inhibir el crecimiento de ambos virus.

Por lo tanto, con la evidencia disponible a la fecha (29 de marzo de 2020), no es posible establecer si la luz ultravioleta inactiva al SARS-CoV-2; sin embargo, estudios en otros tipos coronavirus han mostrado resultados positivos, especialmente con la luz UVC, por lo que sería razonable su uso en ausencia o escacez de otras medidas para desinfección de ambientes o superficies hospitalarias. No obstante, es menester continuar con la investigación de su uso específicamente para SARS-Cov-2 dados estos resultados promisorios previos en otros coronavirus.

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ANEXOS

Estrategia de búsqueda en PubMed

("spike glycoprotein, COVID-19 virus"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "COVID-19"[Supplementary Concept] OR “COVID-19”[tiab] OR COVID19[tiab] OR “2019-nCoV”[tiab] OR “SARS-CoV-2”[tiab] OR “SARS-CoV2”[tiab] OR “2019 novel coronavirus infection”[tiab] OR “coronavirus disease 2019”[tiab] OR “coronavirus disease-19”[tiab] OR “2019 novel coronavirus disease”[tiab] OR (pneumonia[tiab] AND Wuhan[tiab] AND 2019[tiab]) OR (coronavirus[tiab] AND 2019[tiab])) AND (Ultraviolet* OR “Ultra Violet” OR “Ultra-Violet” OR UV[tiab] OR Actinic Ray*[tiab])

Estrategia de búsqueda en Medline vía OVID, Embase y EBSCO

('severe acute respiratory syndrome coronavirus 2' OR 'COVID-19' OR 'COVID-19' OR 'COVID19' OR '2019-nCoV' OR 'SARS-CoV-2' OR 'SARS-CoV2' OR '2019 novel coronavirus infection' OR 'coronavirus disease 2019' OR 'coronavirus disease-19' OR '2019 novel coronavirus disease' OR ('pneumonia' AND 'Wuhan' AND '2019')) AND ('Ultraviolet' OR 'Ultra Violet' OR 'Ultra-Violet' OR 'UV' OR 'Actinic Ray')

Estrategia de búsqueda en PubMed para otros tipos de coronavirus

(“SARS-CoV” OR “MERS-CoV” OR coronavirus*[tiab]) AND (Ultraviolet* OR “Ultra Violet” OR “Ultra-Violet” OR UV[tiab] OR Actinic Ray*[tiab])