

Far-UVC efficiently inactivates an airborne pathogen in a roomsized chamber

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Abstract

Many infectious diseases, including COVID-19, are transmitted by airborne pathogens. There is a need for effective environmental control measures which, ideally, are not reliant on human behaviour. One potential solution is Far-UVC which can efficiently inactivate pathogens, such as coronaviruses and influenza, in air. When appropriately filtered, and because of its limited penetration, there is evidence that Far-UVC does not induce acute reactions in the skin or eyes, nor delayed effects such as skin cancer. While there is laboratory evidence for far-UVC efficacy, there is limited evidence in full-sized rooms. In the first study of its type, we show that Far-UVC deployed in a room-sized chamber effectively inactivates aerosolised *Staphylococcus aureus*. At a room ventilation rate of 3 air changes per hour (ACH), with 5 filtered sources the steady-state pathogen load was reduced by 92.1% providing an additional 35 equivalent air changes (eACH). This reduction was achieved using Far-UVC intensities consistent with current regulatory limits. Far-UVC is likely to be more effective against common airborne viruses, including SARS-CoV-2, and should thus be an effective and "hands-off" technology to reduce airborne disease transmission. The findings provide room-scale data to support the design and development of safe and effective Far-UVC systems.

Introduction

Severe acute respiratory coronavirus 2 (SARS-CoV-2), the virus responsible for the COVID-19 pandemic, can be transmitted by a single individual to one or more people through viral transport in fine airborne particles^{1–4}. The risk of airborne SARS-CoV-2 transmission, from such events, increases in indoor environments where large groups of people congregate, especially when the environment is poorly ventilated^{5,6}.

As has been well documented, the high levels of SARS-CoV-2 transmission have overwhelmed national healthcare systems, resulted in millions of deaths and caused long term health problems. The impact on the global economy has been, and will continue to be, devastating, which in turn has resulted in further welfare and public health issues.

It is therefore clear that reducing or preventing SARS-CoV-2 transmission is a critical and unprecedented global challenge. Transmission control measures have included national lockdowns, restrictions on social and business gatherings, improved indoor ventilation, public health campaigns, protective face coverings and vaccination. These control measures have different success rates and each comes with its own challenges. Vaccination has been one of the most effective measures in reducing death and serious illness, although the evidence is unclear on the efficacy of vaccination in reducing disease transmission^{7,8}. Face coverings can be an effective control measure for reducing the risk of airborne transmission but rely on individual behavioural choices, with high levels of compliance required to achieve population level impacts on transmission^{9,10}. As the COVID-19 pandemic progresses in time, there is lower acceptance and adoption of control measures that impact on daily life, and therefore an increased need for effective measures that do not rely upon human behavioural choices^{11,12}. This is also important beyond COVID-19; airborne transmission has been recognised as an important mechanism for a wide range of other viral infections including influenza, measles, other human coronaviruses (SARS-CoV, Middle East Respiratory Syndrome MERS-CoV) and Respiratory Syncytial Virus (RSV) as well as for bacterial infections including Tuberculosis and some pathogens responsible for hospital acquired infections^{13–15}.

Germicidal ultraviolet (GUV) is a control measure which meets the above requirements, with a scientific track record of success. In 1942, Wells et al. demonstrated less transmission of measles and mumps between children within upper-room GUV irradiated classrooms compared to control groups in rooms without GUV¹⁶. Similarly, Escombe et al. demonstrated a greater than 70% reduction in transmission of tuberculosis from patients to guinea pigs when upper-room GUV was utilised, with 35% tuberculosis infection in control group and 9.5% infection in the group with GUV¹⁵. However a major challenge for conventional 254 nm GUV is accidental exposure of humans, which can result in potentially painful sunburn-type reactions in the skin and cornea¹⁷. This limits traditional GUV to carefully designed upper-room systems, enclosed units or to irradiation of unoccupied rooms. Even when adopted in this manner, accidental exposures can still occur and affect technology adoption^{18,19}.

A potential solution is 'Far-UVC', germicidal ultraviolet-C radiation typically in the wavelength range from 200–230 nm. Currently, the most common source of Far-UVC is Krypton Chloride (KrCl) excimer lamps with a primary emission wavelength of 222 nm, and low residual emission throughout the ultraviolet region of the electromagnetic spectrum²⁰. The germicidal properties of KrCl excimer lamps have been shown in laboratory experiments to inactivate gram-positive and gram-negative bacteria, drug-resistant bacteria, influenza viruses and human coronaviruses including the SARS-CoV-2 virus^{21–27}. Importantly, filtered KrCl Far-UVC excimer lamps are much less

likely than conventional (254 nm) GUV sources to induce acute adverse reactions on skin and eyes, and studies to date in animal and human models have not demonstrated any long-term adverse health effects^{20,28–33}.

Whilst the laboratory results are encouraging, inactivation of a pathogen in a controlled bench-scale laboratory environment does not necessarily translate into reduced disease transmission when the technology is deployed with 'real-world' limitations³⁴. Historical precedent with upper-room GUV provides some confidence in the potential for Far-UVC to reduce disease transmission, however there remains an unmet need for real-world evaluations^{16,35}. Such studies are complex and must be performed over prolonged periods of time (typically at least 12 months). A translational step towards real-world studies are experiments in large, room-sized, aerosol chambers. These room-sized chambers, with controlled air-flow, temperature and humidity are designed to replicate a real-room environment. Such spaces have been used to demonstrate the effectiveness of upper-room GUV systems and to study the survival and dispersion of microorganisms^{36–41}. They can also provide significant insight into the application of technologies in rooms where an infectious person may be present over a prolonged period of time, a situation that is common in schools, workplaces, hospitals and hospitality venues. With the continual controlled release of airborne pathogen, achieving a steady-state environment, the air within the chamber can be regularly sampled both with and without the environmental air disinfection technologies, providing an indication closer to real-world performance. Here we investigate for the first time the efficacy of Far-UVC for inactivating an airborne pathogen under steady-state conditions in a full-scale room-sized bioaerosol chamber.

Results

Five Far-UVC lamps were secured to the ceiling of a room-sized bioaerosol chamber at the University of Leeds, with the lamps arranged in a quincunx pattern (Fig. 1) with their emission directed towards the floor. Studies were undertaken either with all five lamps on or with only the central lamp on. The mechanically ventilated 32 m³ chamber was operated at a ventilation rate of three air-changes-perhour (ACH) and a continuous release of aerosolised *Staphylococcus aureus* was introduced to the room. After a 60 minute stabilisation period, 10 air samples were taken over a 50 minute period. Then either one (the central Far-UVC lamp) or five Far-UVC sources were switched on and the sampling continued for a further 50 minutes.

These measurements were repeated using 3 different lamp exposure rates (Table 1). The exposure rates chosen were motivated by existing optical radiation exposure limits ("Medium" scenario) and proposed threshold limit values ("High" scenario)^{17,42}. An additional scenario at much lower lamp intensity was also included ("Low" scenario). Statistical analysis is detailed in Table S1.

As described in the "Methods" sections, the concentration of viable *S. aureus* pathogens in air at the collection location (Fig. 1), was serially assayed for 4 minutes every 5 minutes, both before and after the lamps were switched on ("lamp on"). The results, quantified as colony forming units per cubic metre (cfu m⁻³), are shown in Fig. 2 and Table 1, both for the 45 minutes prior to "lamp on", and serially for 50 minutes after "lamp on". The values after "lamp on" are expressed as percentages of the average values prior to lamp on. Again it is emphasized that the pathogen was continuously released into the room throughout the experiment.

Average percentage pathogen reduction, irradiance and calculated 8-hour exposure dose for three different exposure conditions at two heights from the ground. The bold, italicised 8-hour exposure values are above the 222-nm exposure limit of 23 mJcm⁻². Statistical significance is represented by: ns = p > 0.05, *=p \leq 0.05, *=p \leq 0.01, ***=p \leq 0.001, and ****=p \leq 0.001.

		Peak Values				Average Values				Average % pathogen reduction
										(St Dev)
		Height = 1.7 m		Height = 1 m		Height = 1.7 m		Height = 1 m		
		Irradiance (µWcm ⁻ ²)	8-hour dose (mJcm ⁻	Irradiance (µWcm ⁻ ²)	8-hour dose (mJcm ⁻ ²)	Irradiance (µWcm ⁻ ²)	8-hour dose (mJcm ⁻ ²)	Irradiance (µWcm ⁻ ²)	8-hour dose (mJcm ⁻ ²)	
High	1 lamp	14.4	415	1.93	56	0.57	16.5	0.45	12.9	93.9**** (0.95)
	5 lamps	14.4	415	3.42	98	2.73	78	2.01	58	99.9**** (0.16)
Medium	1 lamp	0.92	26.5	0.13	3.7	0.03	0.87	0.03	0.82	66.1**** (4.0)
	5 lamps	0.92	26.5	0.22	6.3	0.14	4.1	0.13	3.67	92.1**** (0.93)
Low	1 lamp	0.09	2.65	0.01	0.37	0.003	0.09	0.003	0.08	8.7 ^{ns} (2.15)
	5 lamps	0.09	2.65	0.02	0.63	0.01	0.41	0.01	0.37	31.7**

As expected, the highest reduction in the steady-state airborne viable *S. aureus* load was with the "High" exposure scenario. Using all five lamps this reduced the steady-state viable pathogen load by 98.9% compared to ventilation alone (three air-changes-per-hour). The peak 8-hour exposure dose in this "High" scenario is outside the current exposure limits but within, and indeed motivated by, the proposed increase in the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value (TLV) for the skin (415 mJcm⁻² at 222 nm over 8 hours)⁴². A single lamp in the "High" exposure scenario did not exceed the average 8-hour exposure dose and reduced pathogen load by 93.9%, which produces an estimated equivalent air change rate of 46 eACH. Although the single lamp did not irradiate the full room, good air mixing in the chamber is likely to have resulted in this very substantial effect.

The "Medium" exposure scenario, with a peak 8-hour exposure dose motivated by the current exposure limit at 222 nm of 23 mJcm⁻², produced a 92.1% reduction in the steady state viable pathogen load using all five lamps. This corresponds to 35 eACH, equivalent to over 11 times the baseline ventilation with new steady state reached in under 15 minutes. It is relevant to note that while the 8-hour *peak* exposure dose is slightly higher than the current exposure limits, the *average* 8-hour exposure dose was more than 5 times lower (Table 1).

The "Low" exposure scenario, with very low intensity Far-UVC exposure rates (a factor of 10 lower than the "Medium" exposure rate scenario), produced a 9% (one lamp) and 32% (five lamps) reduction in viable pathogen load.

Discussion

We have demonstrated for the first time in a realistically sized room, with typical ventilation and a continuous source of airborne pathogens, the potential for Far-UVC to rapidly produce significant reductions in airborne pathogens. With the lamp intensities at a level where the exposure limits would not be exceeded, a \sim 92% reduction in viable pathogens was demonstrated, taking less than 15

minutes to reach the new ambient level. At much higher lamp intensities, more than 15 times higher, a ~ 99% reduction was demonstrated, taking less than 5 minutes. A comparison of the two scenarios described is shown in Fig. 3.

Although our study was not performed with SARS-CoV-2 for safety reasons, aerosolised *S. aureus* pathogen was used as a surrogate for more relevant (in the current context) airborne viruses such as human coronaviruses and influenza viruses. The rationale for this is shown in Fig. 4, where inactivation rates by Far-UVC of airborne human coronaviruses (OC43 and 229E), airborne influenza virus (H1N1), and airborne *S. aureus* are compared^{26,27}. All these inactivation rates were measured using the same laboratory setup. No corresponding results have been reported for Far-UVC inactivation of airborne SARS-CoV-2, but corresponding results for Far-UVC inactivation of SARS-CoV-2 on surfaces suggest similar sensitivity to human coronaviruses OC43 and 229E ⁴³. Our results demonstrate that airborne *S. aureus* is less sensitive to inactivation by Far-UVC than airborne influenza and human coronaviruses, from which we conclude that *S. aureus* is a conservative surrogate. It is hypothesised that percentage reductions achievable for airborne coronavirus and airborne influenza virus would likely be larger, and have shorter inactivation times.

For installers of Far-UVC it may be challenging to interpret and apply the optical radiation exposure limits 17,42 . Many will opt for the conservative approach of assuming an 8-hour exposure at the peak irradiance. However exposure limits are intended to be used with a Time Weighted Average (TWA) irradiance (E_{TWA}), which considers the actual exposure an individual has received within a space 44 . This allows for a higher peak irradiance if the E_{TWA} remains within limits. In this study, the peak lamp intensities could have been five times higher than the "Medium" scenario, thereby improving inactivation, and the average 8-hour dose would still be within exposure limits.

This highlights the importance of correct installation of Far-UVC, to ensure the designated space is appropriately and safely irradiated. For example, whilst a single lamp in the "High" scenario produced an overall ~ 94% pathogen reduction, there were areas of the chamber which were not fully irradiated. For real rooms, which may be larger and have potentially less effective air mixing than the chamber used in these experiments, the actual pathogen reduction may be significantly lower. As a result of previous modelling studies, we introduced a diffusing material to all of the Far-UVC sources within the chamber to broaden their irradiation pattern and increase Far-UVC coverage⁴⁵.

Our results also provide some initial data that enable comparison to other technologies particularly portable air cleaners. These typically have a clean air delivery rate (CADR) between 200 m³h⁻¹ and 500 m³h⁻¹ depending on the size of units. For the experimental chamber this would result in between 6.2 and 15.5 eACH assuming that the portable air cleaner could mix the air sufficiently in the room to achieve the theoretical maximum performance. Therefore the "Medium" Far-UVC scenario with 5 lamps performs substantially better than even a higher flow HEPA based air cleaner. Although the design and installation of a Far-UVC system has a higher degree of complexity than a "plug and play" portable air cleaner, the approach has the potential to offer far greater eACH and is also silent.

All methodologies designed to reduce airborne transmission of diseases such as COVID-19 would ideally be used within a layered approach involving, as appropriate, vaccination, social distancing, masks and ventilation. Further work is required to explore the influence of parameters such as temperature, humidity, ventilation rates and proximity to infectious source but the results reported here should provide confidence that Far-UVC, when deployed appropriately, and conforming to current (or future) safety regulatory limits, is likely to be an effective, human behaviour independent, control measure to inactivate key airborne pathogens such as human coronavirus and influenza - and thus reduce the airborne, and potentially surface, transmission of these diseases.

Methods

Bioaerosol chamber

Experiments were conducted in a controlled bioaerosol chamber with dimensions 4.26 m in length, 3.35 m width and a height of 2.26 m. The chamber is mechanically ventilated and operated under negative pressure with a full fresh air system that is HEPA filtered on the supply and extract to provide both experimental control and safety in operation. Ventilation air was supplied through a high level wall mounted inlet grille located in one corner of the room. The wall mounted air outlet is located diagonally opposite at low level. The chamber was operated at an air flow rate of 0.027 m³s⁻¹ equivalent to three air-changes-per-hour (ACH). The release location of the aerosolized *Staphylococcus aureus* was at a height of 168 cm from the ground, 50 cm from the air inlet and 64 cm from the adjacent wall (Fig. 1). The sample collection point was at a height of 50 cm, positioned 20 cm from the air outlet and 64 cm from the adjacent wall. Prior studies have indicated that this location is representative of the average concentration within the chamber. Care was taken

to ensure the bacteria release point and sample point were not located directly under a Far-UVC source (Fig. 1). The chamber was operated at a temperature of $28 \, ^{\circ}\text{C} \pm 1 \, ^{\circ}\text{C}$ and relative humidity $50 \, \% \pm 2 \, \%$. As a biocontainment facility, experiments were conducted with the chamber sealed and nebulisation, aerosol sampling and operation of the Far-UVC devices were carried out remotely.

Choice of Aerosolized Pathogen

In practice, the bioaerosol chamber could not be used with aerosolized level-3 pathogens such as SARS-CoV-2. In order to choose a usable aerosolized pathogen which would be a reasonable but conservative model for airborne human coronavirus, we undertook some preliminary studies using the Columbia University laboratory-based aerosolized pathogen UV irradiation system, as described by Welch et al.²⁷. This system consists of a source of aerosolized pathogens which is flowed past a UV irradiation chamber consisting of a far-UVC source and a far-UVC-transparent window; different far-UVC doses are obtained by varying the intensity of the far-UVC exposure and the velocity of the pathogen. The airborne pathogens were collected after irradiation in a Biosampler and assayed for inactivation; specifically, viral infectivity of influenza A H1N1 (A/PR/8/34) and human coronaviruses were quantified with the fluorescent focus unit assay (FFU) and the standard TCID50, respectively^{26,27}. The surviving fraction of *S. aureus* (ATCC 6538) was assessed with the plaque forming unit (PFU) assay on TSA plates^{46,47}.

Figure 4 shows the in-chamber results for aerosolized *S. aureus* compared with earlier published results for aerosolized human coronaviruses 229E and OC43 and H1N1 influenza virus^{26,27}. We concluded from these preliminary studies that use of aerosolized *Staphylococcus aureus* in the current room-chamber studies represents a reasonable but conservative model for Far-UVC inactivation of human coronavirus.

Far-UVC Lamps

Five commercially available filtered Far-UVC lamps were positioned in a quincunx pattern (the pattern of the five spots on a six-sided dice) within the chamber at a height of 2.12 m, with emission directed towards the ground. The lamps operated continuously and were modified to include a diffusing material which broadened the Far-UVC distribution, maximising the irradiated volume. To adjust the intensity of the lamp emission, metal-mesh attenuation filters were custom made by the Medical Physics and Clinical Engineering department at Ninewells Hospital, Dundee. These filters provided nominal emissions of 10% and 1% of the full Far-UVC intensity. The attenuation filters were placed between the lamp and the diffusing material. The irradiation field in the chamber was measured in the horizontal plane with a calibrated UVC radiometer (UV-3727-5 detector with X1-5 optometer, Gigahertz-Optik, Germany). Measurements were made at two heights from the ground, 1.7 m and 1 m, in 0.5 m intervals throughout the chamber. We have made a deliberate decision not to name the Far-UVC device used in this research as these experiments are an investigation of the principle of Far-UVC and not an endorsement of a particular device.

Experiment Procedures

Preparation of suspension fluid and bioaerosol generation.

The generation of aerosols was performed under a controlled environment in which both temperature ($28^{\circ}\text{C} \pm 1^{\circ}\text{C}$) and relative humidity ($50\% \pm 2\%$) are taken into account. The generation of aerosols was performed using a Collison 6-jet nebuliser (BGI, USA) that operates at a flow rate of 12 L/min and is located externally to the chamber; the aerosol enters the chamber through a tube. The suspension fluids (100ml) inside the nebuliser vessel were roughly 1.35×10^6 cfu ml⁻¹ concentration of *Staphylococcus aureus* (ATCC 6538) that was dispensed in sterilised distilled water. Preliminary investigation of pathogen suspension in other materials (i.e. 1% Foetal Bovine Serum) demonstrated no significant effect on results.

Bioaerosol sampling

The sampling process was performed using an Anderson 6-stage impactor (Anderson INC.) at a flow rate of 28L min⁻¹. Samples were taken externally to the chamber, with the sample taken through a tube. The tryptone soy agar (TSA) plates inside the stages 5 and 6 of the Anderson impactor were prepared using 40g of TSA (Oxoid, UK) for each 1L of distilled water. After sampling, the agar plates were incubated at a temperature of 37°C for 24 hours. The Gallenkamp colony counter was then used to count the number of colonies on each plate. Finally, the positive-hole correction tables were used to correct the results and the sampler flow rate was used to determine the concentration in air in terms of colony forming units per m³ ⁴⁸.

The experiment

The airborne *Staphylococcus aureus* was allowed to establish a steady state within the chamber over a period of 60 minutes. This steady state is similar to having an infected individual in the corner of the room breathing aerosolised pathogen into the room. Then, ten air samples of four-minute duration were taken every five minutes at the collection point (Fig. 2), with the other minute being used to prepare the next sample. The Far-UVC lamps were then switched on and the sampling was repeated in the same manner. An average of the first ten air samples was used to determine the concentration of *Staphylococcus aureus* (cfu m⁻³) present in the chamber prior to switching on of the Far-UVC lamps. The concentration (cfu m⁻³) of each subsequent air sample was then plotted as a percentage of the average initial steady state concentration.

Analysis

Concentrations of *Staphylococcus aureus* were normalised by comparing to the mean concentration of all samples prior to switching on the Far-UVC devices to enable comparison within and between experiments. Steady state concentrations with the lamps switched on were determined from the six measurements taken between 20 and 50 minutes when the decay period after switch on had ended. The equivalent air change rate due to the Far-UVC was calculated from the steady state concentrations before (C) and after (C_{UV}) the lamps were switched on based on

$$rac{C}{C_{uv}} = rac{N + N_{uv}}{N}$$

Here N is the ventilation rate of the room (ACH) and N_{uv} is the equivalent air change rate (eACH) due to the Far-UVC.

Statistical Analysis

Unpaired t-tests were used to compare viable pathogen before and 20 minutes after Far-UVC lamps were switched on. Statistical analyses were carried out using GraphPad Prism (Prism 9, GraphPad Software, USA). In all cases, statistical significance is represented by: ns = p > 0.05, $*=p \le 0.05$, $*=p \le 0.01$, $*=p \le 0.001$, and $*=p \le 0.001$.

Data Availability

All data generated or analysed during this study are included in this published article (and its Supplementary Information files).

Declarations

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Author contributions

EE wrote the main manuscript, undertook dosimetry of the Far-UVC sources and was involved in the conceptualization and design of the experiments.

WH undertook the bioaerosol experiments, analysed the resulting data and prepared Figure 2.

LF provided oversight for the bioaerosol experiments, installed the Far-UVC sources and was involved in the conceptualization and design of the experiments.

ET undertook preparatory work in the chamber for the bioaerosol experiments and was responsible for health and safety during the experiments.

PO'M undertook dosimetry of the Far-UVC sources and statistical analysis of results.

MB undertook experiments to determine the inactivation of S. aureus.

DW undertook experiments to determine the inactivation of *S. aureus*.

CA was involved in the conceptualization and design of the experiments.

DB was involved in the conceptualization and design of the experiments and prepared Figures 3 & 4.

CN provided oversight for the bioaerosol experiments, prepared Figure 1a and was involved in the conceptualization and design of the

experiments.

KW undertook dosimetry of the Far-UVC sources and was involved in the conceptualization and design of the experiments.

All authors contributed to and have reviewed the manuscript.

Additional Information

EE, WH, LF, ET, PO'M, CA and KW declare no competing interests.

DJB and other coinventors have a granted US patent entitled 'Apparatus, method and system for selectively affecting and/or killing a virus' (US10780189B2). Columbia University (the parent institution of DJB, DW and MB) has licensed aspects of filtered UV light technology to USHIO Inc, and has received a research gift from LumenLabs, a company producing Far-UVC sources.

CN has received funding from EPSRC, HM government and the Department for Health and Social Care for projects on COVID-19 transmission and mitigation, and she is a member of the UK government Scientific Advisory Group for Emergencies (SAGE) and multiple working groups through which she has advised across UK government departments during the COVID-19 pandemic

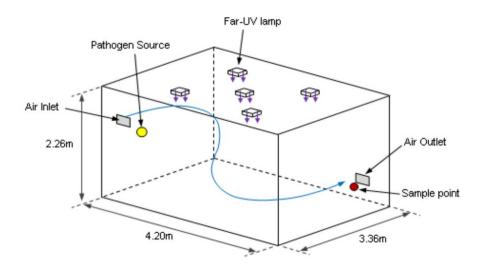
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Figures



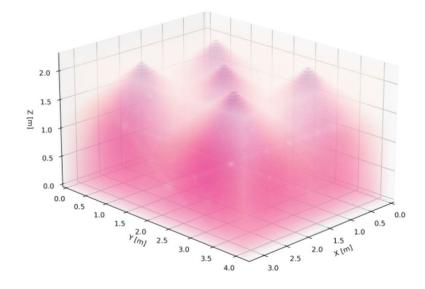


Figure 1

3D schematics of the bioaerosol chamber configuration showing room dimensions, the position of the lamps, pathogen source and collection point (top) with an illustrative example of the Far-UVC lamp emissions (bottom).

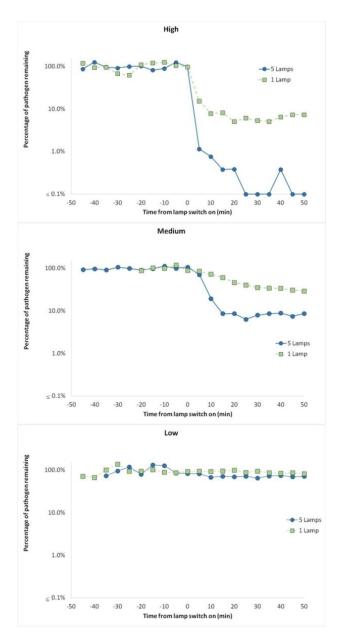


Figure 2

Percentage of viable airborne S. aureus remaining plotted on a logarithmic y-axis against time after switch-on of the Far-UVC sources for three different exposure scenarios – high (top left), medium (top right) and low (bottom left). Note that the pathogen was continuously released into the room throughout the experiment: The studies were undertaken using either a single central lamp (blue, circular data points, solid lines) or all five Far-UVC lamps (green, square data points, dashed lines). An illustration of the room when irradiated by 5 lamps is displayed in the top right of the Figure for reference.

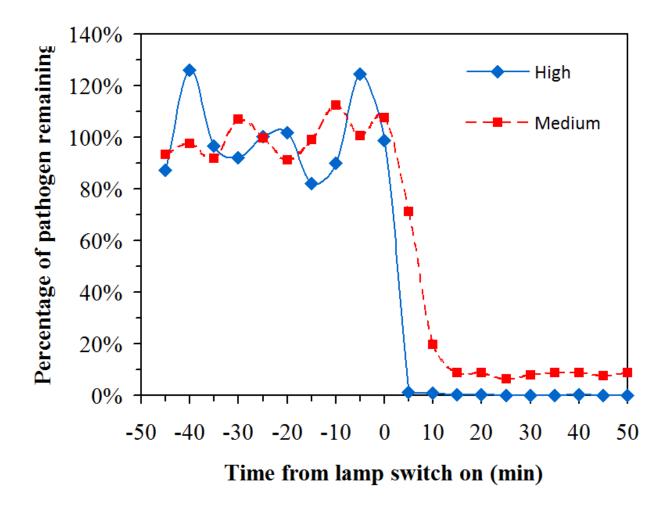


Figure 3

Percentage of viable airborne S. aureus remaining plotted on a linear y-axis for two of the exposure scenarios motivated by current exposure limits (5 lamps "Medium") and proposed increased ACGIH Threshold Limit Values (5 lamps "High"). Note that the pathogen was continuously released into the room throughout the experiment with a mechanical ventilation rate of 3 air changes per hour.

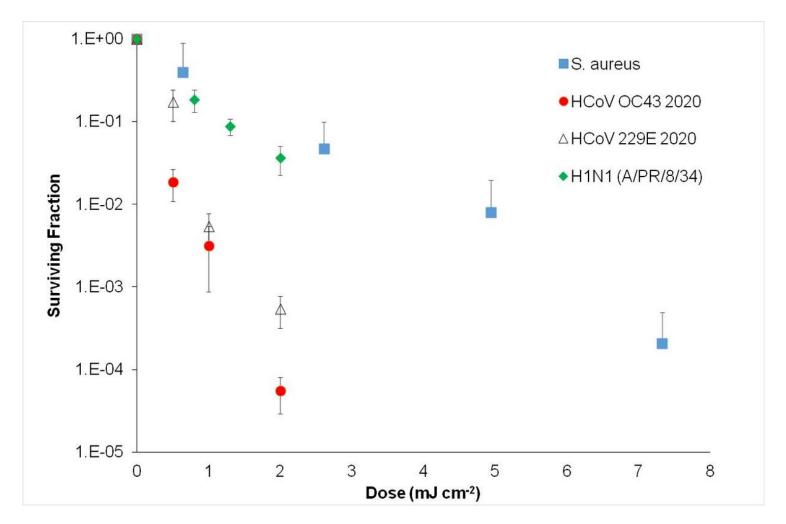


Figure 4

Inactivation of aerosolized human coronaviruses HCoV OC43 and HCoV 229E and H1N1 influenza virus at relevant low far-UVC doses, compared with aerosolized S. aureus. Measurement taken at the Columbia University laboratory-based aerosolized pathogen irradiation system. HCoV OC43, HCoV 229E and H1N1 influenza published previously.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Data.xlsx
- TableS1.docx