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RESEARCH ARTICLE

222 nm far-UVC light and skin health: Assessment of DNA damage across different skin types

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Abstract

Due to a limited penetration into skin and eyes combined with a broad germicidal effectiveness, far-UVC light (200–235 nm) has been proposed as an effective intervention for airborne pandemic control. Specifically, 222 nm light is not predicted to damage skin because it is primarily absorbed by the proteins in the superficial stratum corneum of the epidermis. Thus, it is hypothesized that the thickness of the stratum corneum is one of the most significant contributing factors to the risk of skin damage from exposure to far-UVC. From measurements of the stratum corneum thickness in live human skin biopsies, it was found that none of the donor demographics studied had an impact on the thickness of the stratum corneum. While multiple studies suggest that exposure to 222 nm is minimally damaging to skin, a few studies to date have investigated effects as a function of skin characteristics (e.g., individual's age and sex). In selected tissues, the induction of DNA damage following an acute exposure to 100 or 500 mJ/cm^2 from 222 nm light was analyzed as a function of donor demographics. The results agree with previous studies using other models of human skin and show that in human skin biopsies, 222 nm induces minor DNA damage only at high doses, especially in skin with low melanin content (phototype).

KEYWORDS

222 nm safety on human skin biopsies, 222 nm skin safety, far-UVC and human skin safety

INTRODUCTION

Far-UVC light, typically defined as wavelengths in the range of 200–235 nm, has been identified as a practical engineering control to limit the spread of airborne-mediated infectious diseases in occupied indoor locations. Specifically, 222 nm light from filtered KrCl excimer lamps exhibited broad antimicrobial properties[1–11] while posing little or negligible damage to exposed human skin and eyes.[12–34] In skin, far-UVC light is absorbed primarily by the peptide bonds of proteins that compose the superficial epidermal stratum corneum,[19,35–40] which consists of a tightly overlapped layer of flat corneocytes embedded in a continuous, protein- and lipid-rich intercellular matrix.[41] Consequently, far-UVC wavelengths are unable to penetrate deeper into the epidermis and damage the proliferating cells of the basal layer[16,36,42] whose damage is associated with detrimental biological effects including cancer.[43–45] Thus, an important skin feature that could influence the risk of damage from exposure to far-UVC is the stratum corneum thickness, which is estimated to measure between 10 and 30 μm, depending on the skin site location.[41,46,47]

The thickness of the stratum corneum depends on several characteristics of the individual including age,

sex,[46–49], and how the skin responds to UV exposure (i.e., skin phototype).[50] The thickness of the stratum corneum, its barrier functions, and protein composition have been shown in some instances to be age-dependent.[51–55] Differences in healthy skin physiology and immunology between sexes have been observed across all age ranges.[56,57] It was estimated that the stratum corneum in 3–24 month babies can be up to 30% thinner than that of adults.[49,58] Studies have shown that transepidermal water loss (TEWL), which is a measure of differential water holding of the stratum corneum, and skin conductance that indicates transport properties of the stratum corneum were relatively higher in babies up to 49 months but then decreased with age,[59] suggesting that the stratum corneum barrier functions improve up to 70 years of age.[51] Similar TEWL results were obtained across ethnic groups and geographical locations.[51,60–62] Moreover, increasing age affects the ability of the skin to mount a protective immune response against newly encountered antigens.[53]

From the perspective of the incident light, skin color is another feature that could influence the risk of damage from exposure to far-UVC. Skin color is mainly determined by the individual's combination of carotenoids, oxy/deoxy-hemoglobin, different types of melanin, and by the way melanin is packaged and distributed in melanosomes.[63] Besides functioning as a broadband UV absorbent, melanin has antioxidant and radical scavenging properties. Epidemiological data strongly support a photoprotective role of pigments, as skin pigmentation is inversely correlated with the incidence of skin cancers induced by solar exposure.[64] Thus, in the epidermis with a relatively thin stratum corneum, a high cell pigmentation is expected to further absorb the incident far-UVC and mitigate the potential ensuing damage.[63,65]

Bioengineered 3D models and animal models of human skin have greatly advanced our knowledge of the effects of exposure to far-UVC radiation, and studies on how such effects depend on skin characteristics are beginning to emerge.[65–67] Here, we measured the stratum corneum thickness in live human skin biopsies from male and female donors of different ages, ethnicities, and skin phototypes (Fitzpatrick scale/melanin content).[68] We then measured the induction of DNA damage after a single acute exposure to 100 or 500 mJ/cm^2 from 222 nm emitted by a filtered KrCl excimer lamp or by a low-pressure mercury lamp (hereafter referred to as 254 nm source), which was used as a positive control.

The widespread adoption of far-UVC as a tool to reduce transmission of diseases in occupied indoor venues will require accurate exposure limits to avoid adverse health effects to any occupants.[69,70] This demographic study on the far-UVC exposure of skin is a necessary component to determine accurate skin safety limits for a heterogenous population. Additionally, this study addresses the need for an assorted representation in photobiology and dermatology research.

MATERIALS AND METHODS

Human skin biopsies

Skin biopsies were purchased from Genoskin (4 Technology Way Salem, MA 01970, USA). The NativeSkin® samples are surgical discards obtained with donors informed consent in full compliance with the Declaration of Helsinki. The live skin biopsies maintain skin barrier functions, a mature stratum corneum, a functional basal layer, and all cell types and skin appendages of in vivo human skin for up to 7 days after excision.[71] The samples are characterized by age, self-identified sex, ethnicity, and phototype, which is assigned at the time of surgery by a dermatologist based on the Fitzpatrick scale.[50,72] Upon arrival in our laboratory, the samples were incubated at 37°C in 5% CO_2 for 24 h before the experiment, as per manufacturer instructions.

UVC sources

The far-UVC source used in this work was a krypton-chloride (KrCl) excimer lamp (High Current Electronics Institute, Tomsk, Russia) which emits principally at 222 nm. The KrCl lamp was used with the addition of a custom optical filter (Ushio America, Cypress, CA) to reduce the emissions outside the 222 nm peak.[22] Also used in testing was a low-pressure mercury lamp (UVLMS-38, Analytik Jena US LLC, Upland, CA) which principally emits at 254 nm. Irradiance was measured with a calibrated Hamamatsu UV Power Meter (C9536/H9535-222, Hamamatsu Photonics K.K., Japan). An irradiance of 0.5 mW/cm^2 was obtained by positioning the samples 15 or 10 cm from the 222 nm or the 254 nm lamp, respectively.

Measurement of the stratum corneum thickness

Bright field images of hematoxylin and eosin (H&E)-stained skin tissues (5-μm tissue sections) were taken at an Olympus IX70 Inverted Phase Contrast DIC Fluorescence Microscope equipped with a Photometrics CoolSNAP HQ2 camera (Teledyne Technologies, Thousand Oaks, CA) and the Image Pro software. For each sample, 10 different fields of view (40× calibrated using a micrometer

TABLE 1 Demographics of the samples used for measurement of the stratum corneum thickness.

	n female	*n* male	Total
Age			
18–44 years old (adults)[a]	9	2	11
45-64 years old (middle aged)[a]	6	2	8
65–79 years old (aged)[a]	4	2	6
	19	**6**	**25**
Fitzpatrick scale[b]			
2	9	4	13
3	5	0	5
4	3	1	4
5 and 6	3	0	3
	20	**5**	**25**
Ethnicity[b]			
African American and/or Black	3	0	**3**
Caucasian	13	7	**20**
Hispanic	2	0	**2**
	18	**7**	**25**

[a]Age range defined by the Medical Subject Headings (MeSH) thesaurus.[76]
[b]The Fitzpatrick scale and denomination of ethnicity were provided by Genoskin.

in Image Pro Plus 6.0 software Media Cybernetics, Inc., Rockville, Maryland) were analyzed and, for each image, $n = 35$ measurements of the thickness of the stratum corneum were taken using the distance function of the Image Pro software. The distribution of donor self-reported age, sex, ethnicity, and phototype is summarized in Table 1. It is important to note that the samples were not evenly distributed across those categories.

Melanin stain

While the Fitzpatrick scale is commonly used by providers as means of classifying constitutive skin color and ethnicity,[50,72] melanin content is more relevant for this study as it is one of the UV most absorbing proteins that could mitigate potential damage induced by exposure to far-UVC. We used Fontana-Masson stain to measure the content of epidermal melanin and correlated it with measurements of the stratum corneum thickness and DNA damage. Melanin reduces the ammoniacal silver nitrate of the Fontana-Masson stain to metallic silver, resulting in black deposits that can be easily observed under a light microscope.[73] Paraffin-embedded tissue sections were warmed on a slide warmer for 10 min. The sections underwent the following series of washes: two xylene washes for 6 min each, two 100% ethanol washes for 4 min each, two 95% ethanol washes for 3 min, and then rehydrated in distilled water for at least 5 min. The tissue sections were then stained with the Fontana-Masson stain kit (ab150669, Abcam, Inc., Cambridge, United Kingdom) following the manufacturer's protocol. For each sample, several images of melanin-stained tissues were captured with the 20× magnification of a Leica DMi8 microscope in color through LAS EZ software (Leica Microsystems, Wetzlar, Germany) with default settings. Three images of the length of the tissue section were taken and then imported into GNU Image Manipulation Program [(GIMP) Spencer Kimball, Peter Mattis] with image dimensions set to 2048 × 1536 pixels. The stratum corneum was isolated by erasing surrounding tissue areas. Utilizing the "select by color" tool, we isolated the darkly stained melanin cells by setting a 15.0 threshold maximum color difference. This selection was transferred on to a blank, white file within GIMP, maintaining the same pixel dimensions as the original image, thereby enhancing the melanin content. The resulting image file was imported into ImageJ (National Institute of Health) and transformed into a binary image (process → binary → make binary). Using the histogram tool → list, the program counted black and white pixels where 0 is assigned to white is 0 and 255 to black. The black pixel count, indicative of melanin content, was averaged between three images taken per tissue section for each sample.

Measurement of UVC-induced DNA damage

The analysis of DNA dimers was done on the 17 samples from female donors using a standard immunohistochemical method previously described.[20,22] The distribution of donor self-reported age, sex, ethnicity, and phototype is summarized in Table 2. The samples were approximately balanced across age groups and the four phototypes, though not evenly distributed across ethnicities.

The tissues were exposed to a radiant exposure of 100 or 500 mJ/cm^2 from the KrCl (222 nm) or from a low-pressure mercury lamp (254 nm); controls were handled in parallel but were unexposed. Both the sham (controls) and exposed tissues were fixed 30 min after exposure to assess the percentage of epidermal keratinocytes positive for the most abundant premutagenic DNA photolesions, cyclobutene pyrimidine dimers (CPD).[74,75] A separate set of $n = 10$ tissues was fixed 24 h after exposure to 500 mJ/cm^2 from either 222 or 254 nm to measure the percentage

TABLE 2 Demographics of the female samples used for measurements of the induced DNA photodamage.

	n female
Age	
18–44 years old (adults)[a]	9
45–66 years old (middle aged + aged)[a]	8
Fitzpatrick scale[b]	
2	5
3	5
4	3
5 or 6	4
Ethnicity[b]	
African American and/or Black	4
Caucasian	10
Hispanic	3

[a]Age range defined by the Medical Subject Headings (MeSH) thesaurus.[76]
[b]The Fitzpatrick scale and denomination of ethnicity were provided by Genoskin.

of epidermal keratinocytes positive for γH2AX. For each sample, an average of 600 or 1000 cells was counted for CPD or γH2AX assessment, respectively.

Statistical approaches

We used the distance tool Image Pro® Plus 6.0 software to measure the stratum corneum thickness on 20× images of H&E-stained tissue samples. Each value represents the average ± standard error of the mean (SEM) of at least 10 different fields of view with $n = 35$ measurements of the thickness of the stratum corneum for each sample.

DNA photodamage (either CPD or γH2AX) yields represent the average ± SEM of keratinocytes exhibiting the damage measured in at least three randomly selected fields of view for each sample. The total number of cells was determined by counting the number of nuclei positive for 4′,6-diamidino-2-phenylindole (DAPI) using the coverslip mounting medium with DAPI (Vectashield, Burlingame, CA). Comparisons of mean values between treatment groups and controls were performed using Student's *t* test, and comparisons of proportions were assessed with the χ^2 test.

RESULTS

Stratum corneum thickness as a function of donor demographics

We used commercially available live human skin biopsies, which were characterized by body location, donor self-reported age, sex, and ethnicity, and phototype that was assigned by a dermatologist at the time of surgery based on the Fitzpatrick scale.[50,72] The majority of live skin biopsies we obtained were from the abdomen of female donors; thus, to compare the stratum corneum thickness as a function of donor sex, we purchased additional hematoxylin and eosin (H&E)-stained abdominal skin tissues from male donors from Genoskin and from the National Cancer Institute (NCI) Cooperative Human Tissue Network (CHTN). The total number of samples used to measure the thickness of the stratum corneum was $n = 25$ (19 females and 6 males; Table 1).

Because the stratum corneum thickness varies with skin site,[41,46,47] we used only abdominal skin. Of the donors included in this study, we do not have information on the cumulative sun exposure, cosmetic habits, or other extrinsic factors that might influence the interaction of UV light with skin.

The tenet of far-UVC light skin safety assumes that these wavelengths are mainly absorbed by the proteins in the superficial stratum corneum of the skin and do not reach the basal (stem) cells of the epidermis.[19,35,36] Therefore, the thickness of the stratum corneum can be considered one of the key determinants of susceptibility to damage of human skin from exposure to far-UVC light. Our measurements showed that the stratum corneum thickness of male (12.02 ± 1.03 μm) and female (10.83 ± 0.26 μm) donors was comparable ($p > 0.05$; Figure 1A).

We then analyzed the stratum corneum thickness as a function of donor age (Figure 1B). The samples ($n = 25$) were divided into three age groups (Table 1) as defined by the Medical Subject Headings (MeSH) thesaurus[76] produced by the National Library of Medicine: adults (18–44 years old), middle aged (45–64 years old), and aged (65–79 years old). We found that the stratum corneum thickness was 10.68 ± 0.35 μm for adults, 11.10 ± 0.29 μm for middle aged, and 11.94 ± 1.11 μm for the aged group. These results were not statistically significantly different between age ranges ($p > 0.05$). In agreement with previous studies,[77,78] the average thickness of the stratum corneum of the abdominal skin including all donors was 11.12 ± 0.32 μm. It is important to note that in children aged 25–48 months, the thickness of the stratum corneum is 20–30% thinner than that of adults.[49,55,58,79] We were able to obtain only one skin sample from the abdomen of a 6-month-old infant whose stratum corneum thickness was 8.87 ± 1.00 μm.

We subsequently analyzed the stratum corneum thickness as a function of skin pigmentation. Skin phototype was assigned by a dermatologist at the time of surgery according to the Fitzpatrick scale[50,72] (Table 1). The Fitzpatrick scale is commonly used by providers to

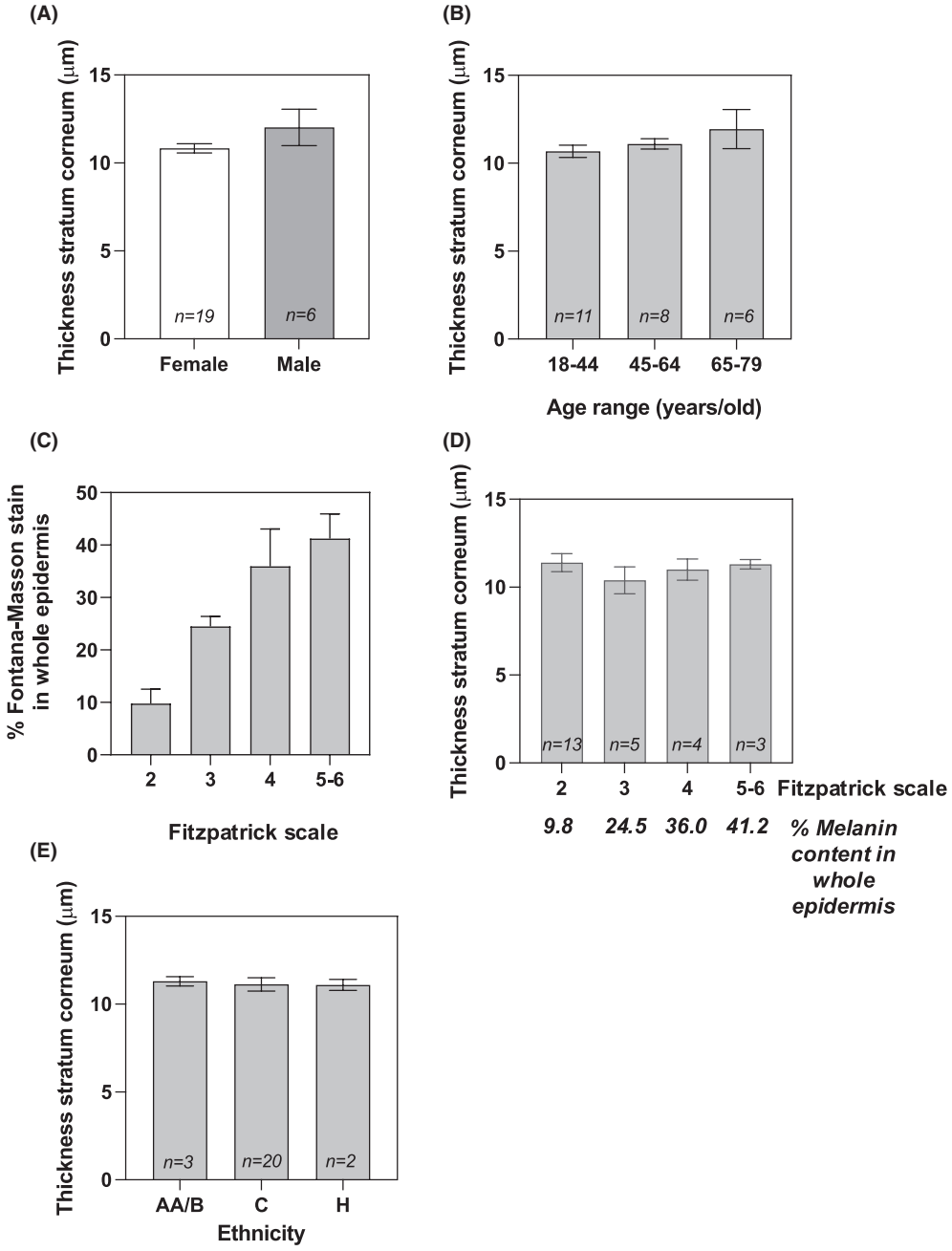

FIGURE 1 Stratum corneum thickness as a function of (A) sex and (B) age; (C) percentage of melanin (i.e., Fontana-Masson stain) in whole epidermis. (D) Stratum corneum thickness as a function of donor phototype based on the Fitzpatrick scale and melanin content; and (E) ethnicity (AA/B = African American and/or Black, C = Caucasian, H = Hispanic). Values represent the average ± SEM; the number within each bar represents the number of biological replicates.

describe constitutive skin color and ethnicity; however, this method is subjective and operator-dependent.[80,81] To validate the Fitzpatrick skin type that was assigned by Genoskin, in each sample, we measured the content of melanin, which is one of the most UV-absorbing proteins that could influence the extent of damage induced by far-UVC exposure. We measured melanin content as the amount of Fontana-Masson stain in skin tissue sections,[73] and showed that the percentage of melanin was directly proportional to the assigned Fitzpatrick scale (Figure 1C) and that the thickness of the stratum corneum did not change with melanin content (Figure 1D). In Figure 1E, the stratum corneum thickness data are reported as a function of the only three ethnicities we had at our disposal (self-reported to Genoskin as African American and/or Black, Caucasian, Hispanic). Similar to the other demographic factors, ethnicity had no impact on the thickness of the stratum corneum.

DNA damage as a function of donor demographics

The results in Figure 1A indicated that donor sex does not influence the thickness of the stratum corneum of abdominal skin. We therefore analyzed the induction of DNA cyclobutene pyrimidine dimers (CPD) in the 17 skin samples from female donors, whose demographics are reported in Table 2. The skin biopsies were exposed to an acute radiant exposure of 100 or 500 mJ/cm^2 from 222 nm light generated by a filtered KrCl lamp or from 254 nm light generated by a low-pressure mercury lamp. Induction of CPD was measured 30 min after exposure.

Compared to sham-irradiated controls, either 100 or 500 mJ/cm^2 from 254 nm induced a higher percentage of keratinocytes with CPD, which was independent from donor age (Figure 2A). It might appear that after exposure to either 100 or 500 mJ/cm^2 from 222 nm or to 100 mJ/cm^2 from the 254 nm light, skin from older donors (45–66 years old) showed less induction of DNA dimers compared with exposed skin of relatively younger donors (18–44 years old; Figure 2A). This finding seems to contradict the concept that older skin typically has reduced DNA repair capacity, so more DNA damage would be expected.[82] However, the differences we measured were not statistically significant ($p > 0.05$). Unsurprisingly, after exposure to 254 nm, the percentage of cells positive for CPD was inversely related to melanin content (or skin phototype; Figure 2B). In the case of exposure to 222 nm, CPDs were generally not observed with a dose of 100 mJ/cm^2 but were observed with a dose of 500 mJ/cm^2.[22] The percentage of CPDs did appear to correlate with the melanin content (Figure 2B), and a statistical significance ($p < 0.01$) was obtained when comparing the percentage of CPD-positive cells in skin phototype 2 compared with positive cells in the combined group of phototypes 5 and 6. When the percentage of CPD-positive cells was analyzed as a function of ethnicity (Figure 2C), we found that after exposure to 100 or 500 mJ/cm^2 from either 222 or 254 nm, skin from Caucasian donors had a higher percentage of CPD-positive cells compared to those of African American and/or Black donors or Hispanic donors ($p < 0.05$ or $p < 0.01$, respectively).

In tissues exposed to 500 mJ/cm^2 from either 222 or 254 nm ($n = 5$ for each wavelength), we measured the formation of phospho-histone H2A.X (Ser 139) foci also known as γH2AX foci,[83] which are typically associated with DNA double strand breaks induced by ionizing radiation. Because DNA double strand breaks are typically more difficult to repair than dimers,[84] the samples were assessed for foci formation 24 h after exposure with the goal of detecting residual DNA damage and inferring the DNA repair capacity of the exposed tissues. We found that while 500 mJ/cm^2 from 222 nm induced residual 1.62 ± 0.98% of foci-positive cells, the percentage

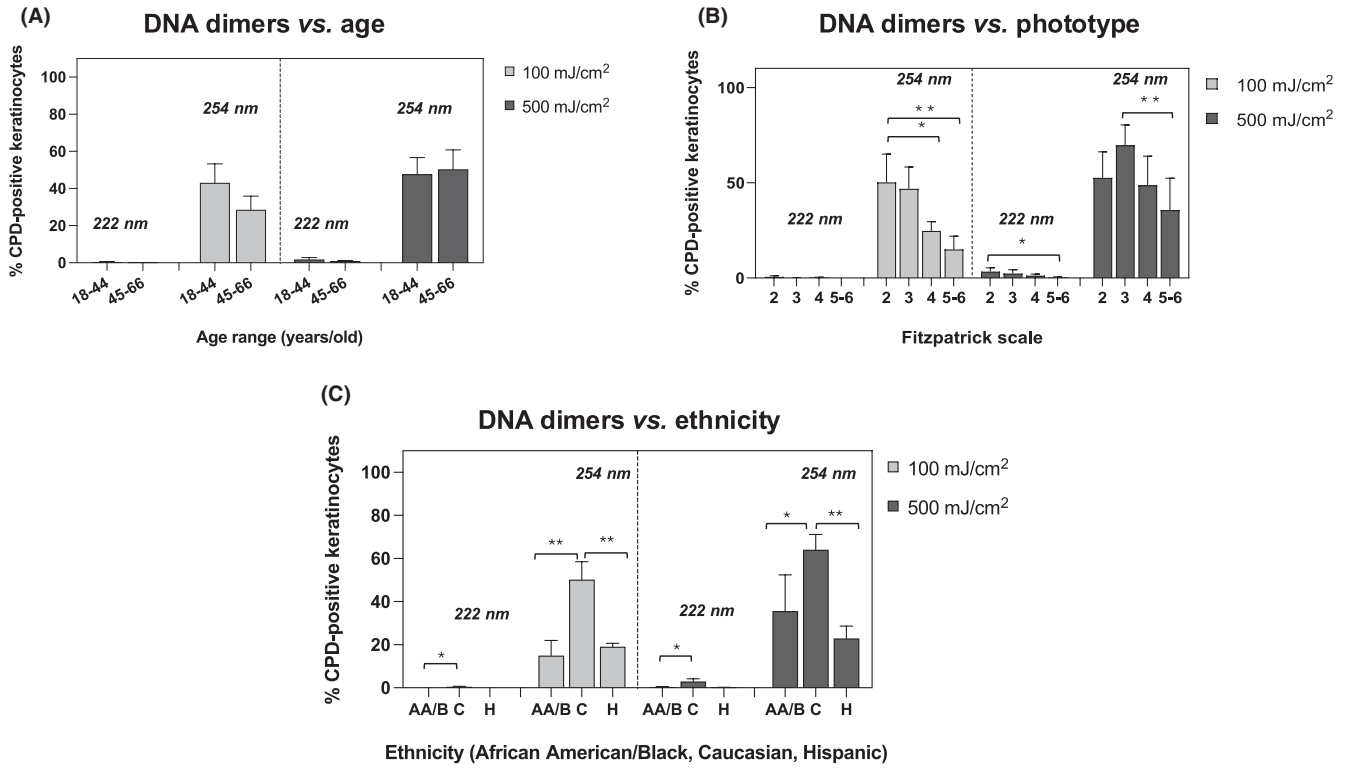

FIGURE 2 Percentage of CPD-positive keratinocytes (average ± SEM) in the whole epidermis of skin 30 min after exposure to 100 or 500 mJ/cm^2 from 222 or 254 nm light as a function of (A) age, (B) phototype, or (C) participant ethnicity. *$p < 0.05$, **$p < 0.01$.

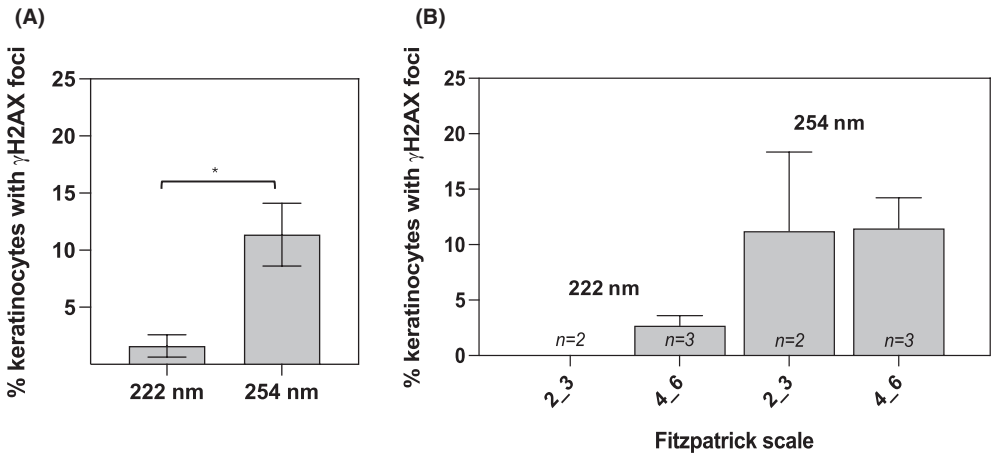

FIGURE 3 (A) Percentage of γH2AX-positive keratinocytes in the whole epidermis 24 h after exposure to 500 mJ/cm^2 from 222 or 254 nm light ($n = 10$), and (B) as a function of skin donor phototype. Values represent the average ± SEM; *$p < 0.05$; the number within each bar represents the number of biological replicates.

increased by 7-fold (to 11.37 ± 2.75) in the case of exposure to 500 mJ/cm^2 from 254 nm ($p < 0.01$; Figure 3A). Because of the limited number of samples for each phototype, the data in Figure 3B compare the percentage of γH2AX in keratinocytes of the whole epidermis as a function of phototype 2 and 3 combined vs. 4 and 6 combined.

DISCUSSION

Published data to date suggest that far-UVC has minimal or negligible adverse effects on human skin.[12–34] This is because far-UVC is not able to pass through the outermost layer of the epidermis, the stratum corneum, which is composed of flat corneocytes embedded in a tight mesh of lipids and proteins. Peptide bonds within the proteins in the stratum corneum absorb shorter wavelengths, such as the far-UVC range, more efficiently than longer wavelengths.[19,35–40] Based on this biophysical rationale, our hypothesis is that the stratum corneum thickness is a contributing factor in the risk of damage from exposure to far-UVC. It is important to note that while the stratum corneum contributes significantly to the attenuation of the incident light, the epidermis and dermis have even higher absorption and scattering coefficients in the far-UVC range, further limiting the penetration depth of these wavelengths into the tissue.[67,85]

Previous analysis of the stratum corneum estimated a thickness between 10 and 30 μm depending on the skin location.[41,46,47] Intrinsic factors such as the individual's sex and age[48,49] as well as extrinsic factors (e.g., exposure to solar radiation, cosmetic habits, etc.)[50] may contribute to its thickness. However, little is known about the impact of these variables on the effectiveness of far-UVC light to induce damage. Objective of this study was to evaluate the thickness of the stratum corneum of abdominal skin as a function of donor age, sex, skin phototype, and ethnicity, and whether these variables affect the induction of damage in skin samples exposed to 222 nm light. We found that the thickness of the stratum corneum of abdominal skin did not vary with sex, age (studied here 18–79 years old), melanin content, or ethnicity (studied here African American and/or Black, Caucasian, and Hispanic; Figure 1). Our results agree with previous studies showing that the stratum corneum thickness of the abdomen does not vary by sex.[77,86] Using two-photon microscopy, Czekalla et al.[77] found that the stratum corneum thickness decreased significantly with age from 18–30 years old to 50–66 years old donors. Other studies, however, using a light microscope like in this study or confocal Raman spectroscopy did not find differences in the thickness of the stratum corneum as a function of age.[47,86–88]

We then analyzed the induction of DNA damage after exposure to 222 or 254 nm light as a function of donor demographics and found expected results: 30 min after exposure, induction of CPD was in part dependent on skin phototype/melanin content and ethnicity (Figure 2). In the case of exposure to 222 nm, and in agreement with previous results,[22] cells with CPD appeared after exposure to 500 mJ/cm^2 and their percentage depended on melanin content, with phototype 2 skin showing a statistically significant higher percentage of damaged keratinocytes than that induced in skin phototype 5 and 6 combined ($p < 0.05$). Similar conclusions could be drawn if ethnicity is considered, with the caveat that we had a relatively low number of samples to analyze for African American/Black ($n = 3$) and Hispanic ($n = 2$) compared to the $n = 20$ samples identified as Caucasian. These

results disagree with recent studies that investigated the dependence of DNA damage on melanin content using reconstructed human epidermis (RHE) models exposed to 233 nm far-UVC.[65] In those studies, RHE with higher melanin content showed higher levels of DNA damage than the same model with lower melanin content. Such disagreement could be attributed to the penetration depth through tissues of the incident light itself (i.e., 222 nm vs. 233 nm) or, more likely, to how melanin is distributed in RHE compared with skin biopsies. Melanin can have toxic properties after exposure to UVC by releasing free radicals in the tissue microenvironment[63,65,89]; however, it is established that especially eumelanin behaves as a physical shield that scatters the incident UV radiation. Melanosomes in dark skin are hardly degraded by lysosomal enzymes, and melanin in vivo typically forms protective perinuclear caps in keratinocytes and melanocytes.[90] By contrast, in lightly pigmented skin, melanosomes are degraded and only persist as "melanin dust" in the suprabasal layers of the epidermis.[63] In RHE models, instead, melanin appeared unevenly distributed and was often extracellular, reducing its shielding properties against damage induced by far-UVC.[65] In addition, the composition of melanin in vivo is a complex combination of lighter red/yellow, alkali soluble sulfur-containing pheomelanin, and darker brown/black insoluble eumelanin,[91,92] which could offer further shielding from the incident UV light.[93,94]

Additionally, we measured the persistence of induced γH2AX foci as a proxy of DNA double strand breaks 24 h after exposure (Figure 3). Because double strand breaks are generally more challenging to repair than dimers,[84] the persistence of foci may indicate a less efficient DNA repair machinery in tissues where they remain. However, this interpretation is based on a phenomenological observation and should be validated through molecular-level investigations.

Our study investigated the effect on skin of an acute exposure to far-UVC light as a function of some skin characteristics of an individual. One limitation of the study is the uneven distribution of samples across the different categories: age, sex, ethnicity, and phototype. As a result, we cannot fully control for all confounding variables given the sample size and exclude the influence of these variables on our findings. Future studies with larger, matched cohorts will be necessary to isolate the effects of individual demographic factors on far-UVC skin responses. Another limitation of the study is the lack of information regarding the cumulative sun exposure, cosmetic habits, or other extrinsic factors that might influence the interaction of UV light with skin.

Future studies could expand the investigation to other skin locations, including those that are void of stratum corneum such as eyelids. Comprehensive epidemiological studies are needed to validate our results and estimate the biological short- and long-term effects of exposure to far-UVC light as a function of intrinsic (age, sex, body location, etc.) as well as extrinsic factors such as smoking habits, medication, or exposure to solar radiation. Inclusion of individuals with sensitive skin is also warranted; notably, though, preliminary studies involving a small cohort of patients with photosensitivity[95] have shown no visual changes after exposure of the skin to up to 23 mJ/cm^2 222 nm.[70]

Far-UVC wavelengths are proposed as a tool to reduce transmission of surface- and aerosol-mediated diseases in indoor locations where people are present. Overall, our results show that acute exposure to 222 nm light causes no significant DNA damage at 100 mJ/cm^2 and only minimal damage at 500 mJ/cm^2; namely, skin with lower melanin content (phototype) exhibited a slightly increased sensitivity at the highest exposure dose. Results from this study can contribute to defining more accurate guidelines for skin safety[69,70] based on a heterogeneous population.

AUTHOR CONTRIBUTIONS

M.B. and D.J.B. conceptualized the experiments; MB collected and analyzed the DNA damage data and wrote the first draft of the manuscript. C.P. performed the stratum corneum measurements and melanin stain analysis. D.W. and R.H. performed dosimetry of the UV sources. All authors contributed to and have reviewed the manuscript.

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CONFLICT OF INTEREST STATEMENT

D.J.B. and other coinventors have a granted US patent entitled "*Apparatus, method and system for selectively affecting and/or killing a virus*" (US10780189B2). Columbia University has licensed aspects of filtered UV light technology to Ushio Inc. and has received research support from Ushio Inc. and LumenLabs Inc., companies producing far-UVC sources.

DATA AVAILABILITY STATEMENT

Raw data can be accessed from the Open Science Framework repository, https://osf.io/973gf/?view_only=5125582d977045e5a074706839b30d1d.

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