Study Title: The Effect of Violet Device Dosed UV-C Exposure on Healthy Hand Skin

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The Effect of the Violet Device Dosed UV-C Exposure on Healthy Hand Skin

Study Protocol

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Synopsis

The purpose of this investigation is to test the Violet UV-C device and quantify any changes in cellular and molecular properties of normal healthy (non-diseased) pale human skin after exposure to UV-C light (222nm). This protocol is designed to provide small skin biopsies from adults of ages 18-55 years with pale skin, either type 1 or type 2. Up to 10 subjects per week may be enrolled to reach a total of 30 individuals. Two visits will be required. During the first visit, subject consent, evaluation of general health and skin health, Violet use, punch biopsy, and photos of skin site(s) that are collected may be performed. During the second visit any sutures placed will be removed and optional follow-up photos of skin site(s) may be collected. Subjects may not participate in this study more than once. Specimens will be subjected to histology and/or a number of biochemical assays, which may include measurements of DNA damage, enzyme assays, and protein analysis. Tissue will be used for analysis within three years of its acquisition, as analysis of the tissue will cause its destruction, no other provisions to destroy tissue will be made. Any remaining tissue will be discarded in accordance with GLP after analysis.

1. Background

As we expand new methods to sanitize surfaces, germicidal UV-C research requires an in depth understanding of the cellular and molecular effects of UV-C light on normal human skin. UV-C light has a 100-year history as a sterilization method and is poised to be an efficient, new first line of defense against ESKAPE and other pathogens such as SARS-CoV-2 (1-9). UV-C light is absorbed by the DNA and proteins of pathogens, causing damage that renders the pathogens unable to infect or reproduce (10, 11). UV-C light is rapidly absorbed and scattered the further it travels through tissue due to its short wavelength, making UV-C unable to pass through the dead stratum corneum layer to cause any effect on the living tissue for thicker regions of skin such as hands (12-14). This means UV-C effects are limited to the pathogens on the surface of hands. UV-C has already been demonstrated safe and effective at up to 500mJ/cm^2 in relatively thin-skinned mouse models (15, 16) and higher doses up to 6,100mJ/cm^2 without erythema or significant CPD-based DNA damage in recent introductory human studies (17-19). We intend to use the same filtered UV-C wavelengths of 200-230nm as tested in these references for our device. Since there are many examples of results from animal skin research results that have not held true for human skin, there remains a strong need for well controlled data directly from "living" human skin. Furthermore, skin thickness plays a profound role in the relationship between UV light dose and any cellular or sub-cellular changes. The few human studies have focused on regions such as the inner forearm and back that have thin stratum corneum and is generally protected from UV exposure (18, 19). Thus, the aim of this protocol is to procure both the stratum corneum and the living skin tissue below in samples taken from the comparatively thick skin of the hand to look for any damage caused by a targeted UV-C light

sanitization approach. We will also capture any change in coloration or erythema that would further indicate damage. The biochemical changes of UV-C treated skin would have an instantaneous effect to reduce bioburden after Violet UV-C device use.

Violet is a UV-C based device under development by Archimedes Innovation, PBC (doing business as JustLight pbc). Violet is tabletop device that emits filtered Far UV-C (200nm-230nm; peak at 222nm) within the bounds of the device. The current device is roughly 12in x 15in x 10in with a form similar to that of a 2-handed manicuring light. To use the device, a user places their hands beneath the light sources, triggering the lights to turn on from an IR sensor mounted on the exterior of the device. Following prompts, users will have a set dose of UV-C light applied to backsides of hands, then hands pulled out and re-inserted, and a second dose applied to the backsides of hands before the cleaning cycle is complete. Violet is in the process of application for clearance by the FDA for use on human hands to reduce bioburden. The purpose of this study is to test Violet on human hands and capture any effects on the superficial and living skin cells.

An Ultralight UVB lamp will be used to treat the subject's skin with a specific wavelength from the light spectrum: broad band UVB 290-320nm. We will compare the human skin response to different segments of UV spectrum. This device will be used as a control.

2. Objectives

The objective of this protocol is to obtain small samples of human hand skin in order to quantify cellular and molecular properties of normal healthy human skin before and after exposure to the Violet UV-C device or UV-B as a control.

3. Study Design

This study involves research treatment and tissue procurement.

4. Subjects

a. Source

Study subjects will be recruited from the University of Michigan clinics, and/or local announcement, including advertisements in various media including newspapers, UMHealthResearch.org, Archimedes' Newsletter, and bulletin boards (see attached flyer).

b. Characteristics of Study Group

Per week, up to 10 male or female subjects, 18 years of age to 55 years, of skin type 1 or 2 (lightly colored skin), and in good general health. A total of 30 individuals will be sampled, subdivided into 5 cohorts of 6 people each. Experimental groups (4) will receive either 1 use, 10 uses, 15 uses, or 25 uses of Violet. A control group (1) will receive a UV-B exposure as a positive control. The sample size is based on a power analysis to detect a 25% difference between groups.

c. Inclusion Criteria

Subjects must meet all of the following criteria for inclusion in the study:

i. Male or female
ii. 18 years of age to 55 years
iii. Good general health
iv. Type 1 or type 2 skin (lightly colored skin)
v. No history of skin disorders, disease states or physical conditions which would impair evaluation of the test sites

vi. Willingness and ability to follow the protocol
vii. No use of lotion or hand sanitizer 3 hours before the experiment
viii. Signed, written and witnessed, Informed Consent Form

d. Exclusion Criteria

Subjects who meet any of the following criteria will be excluded from the study:

i. Has received an experimental drug or used an experimental device in the 30 days prior to admission to the study
ii. Undergoing treatment or taking medication that increases sun sensitivity
iii. History of keloids
iv. History of sensitivity to lidocaine or epinephrine
v. Pregnant or nursing women, pregnancy status will be self-reported, women unsure of their pregnancy status will be excluded.

5. Study Procedures

a. Screening/ Experiment (45-60 Minutes)

i. Obtain written, witnessed informed consent.
ii. Review inclusion/exclusion criteria.
iii. Obtain complete medical history and skin examination.
iv. Clinically evaluate areas to be sampled.
v. Discuss the 5 available groups and assign subject a group per randomization chart, see below. The groups are: UVB device as control (50mJ/cm2); UV-C (1 use); UV-C (10 uses); UV-C (15 uses); or UV-C (25 uses).
vi. Wash hands with soap and water to minimize presence of oils or debris that could alter evenness of light application.
vii. Color photographs of areas under study may be taken.
viii. Before and after measurements of skin color will be taken using a colorimeter (Minolta Colorimeter).
ix. Procure skin specimens of areas under study with punch biopsy instruments. Closures will be made with 4-0 or 5-0 prolene sutures. The area sampled will be the dorsal region of the hand, in the space between (but not including) the knuckles and the pisiform bone. Subjects will have 2 skin samples collected, one from each hand. Before harvesting from the treated site, the hand will be exposed to between 1-25 cycles (25-625mJ/cm^2) of UV-C from the Violet UV-C device or 50mJ/cm^2 of UV-B (290-320nm) light as a positive control. One cycle of 222nm UV-C Violet delivers 25mJ/cm^2. Subjects will not be allowed to re-enroll in this study.

b. Follow Up (10-14 days after baseline)

i. Review any adverse events.
ii. Remove biopsy sutures (for punch biopsies).

c. Premature Withdrawal from Study

Any subject who experiences adverse effects associated with study participation may be withdrawn from the study. Participation in the study may be discontinued for any of the following reasons: 1) adverse events; 2) concurrent illness; 3) administrative reasons; 4) subject's decision to withdraw participation; or 5) protocol violation. Complete information on all adverse events will be recorded on the Adverse Event Report.

6. Laboratory Methods

Laboratory studies will be used to determine cellular and molecular properties of normal human skin. Macroscopic changes to skin, in the form of properties Minimal Erythemal Dose (MED) and skin cell shape changes will be characterized using photographic images and stained skin cross sections visualized using microscopy. Skin specimens will be fixed in formalin and stained with hematoxylin/eosin for routine histologic evaluation. Additionally, molecular markers of DNA damage will be quantified. Laboratory studies will determine the presence of DNA damage in the form of DNA base pair dimers using ELISA or immunohistochemistry microscopy with statistical analysis.

7. References

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UVC Randomization Chart

Subject #	Group Assigned	Group Description
1	A	UVB
2	D	UVC - 15 uses
3	C	UVC - 10 uses
4	A	UVB
5	D	UVC - 15 uses
6	C	UVC - 10 uses
7	E	UVC - 25 uses
8	B	UVC - 1 use
9	C	UVC - 10 uses
10	B	UVC - 1 use
11	B	UVC - 1 use
12	A	UVB
13	D	UVC - 15 uses
14	B	UVC - 1 use
15	D	UVC - 15 uses
16	B	UVC - 1 use
17	E	UVC - 25 uses
18	D	UVC - 15 uses
19	C	UVC - 10 uses
20	D	UVC - 15 uses
21	A	UVB
22	E	UVC - 25 uses
23	B	UVC - 1 use
24	E	UVC - 25 uses
25	A	UVB
26	C	UVC - 10 uses
27	E	UVC - 25 uses
28	E	UVC - 25 uses
29	A	UVB
30	C	UVC - 10 uses

Group Assignments

A= UVB
B= UVC - 1 use
C= UVC - 10 uses
D= UVC - 15 uses
E= UVC - 25 uses

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