Official title of study: Visualizing dermal micropores with OCT

NCT number: NCT0487733

Date of document: Jan 12, 2023

Visualizing micropore closure with OCT

PI: Nicole Brogden
IRB ID #: 202010229

Project Details

I. Project Introduction

I.1 ***Project to be reviewed by:***
IRB-01

I.2 ***Project Title:***
Evaluating racial and ethnic differences in micropore closure using optical coherence tomography

I.3 ***Short Title (optional):***
Visualizing micropore closure with OCT

I.4 ***Provide a short summary of the purpose and procedures of the study proposed in this IRB application.***

- ***DO NOT include information on studies not proposed in this application.***
- ***Use LAY terminology only. This must be easily understandable by IRB community members and nonscientists.***
- ***DO NOT cut and paste technical abstracts from funding applications that may not be understood by a general audience.***

The purpose of this study is to use an innovative, noninvasive imaging technique called optical coherence tomography (OCT) to visualize micropore closure in racial/ethnic skin following micropatch application. Healthy and consenting adult volunteers (18-45 years old) will be enrolled. Subjects will be asked to self-identify their race and ethnicity according to the following groups: Black, Asian, Latinx, White, Indigenous, or Bi-/multi-racial/other. All subjects, regardless of self-identified race/ethnicity, will receive the same micropatch treatment and measurements. The micropatches are patches containing a small array of microneedles on an adhesive patch backing; the whole micropatch fits on the tip of a thumb. The micropatches will be applied to the upper arm, forearm, and the palm. At each of these locations, 3 sites will be identified. One site will receive micropatch application followed by occlusion with a small patch (note: this is just a band-aid like patch, not a micropatch). The other 2 sites will be controls: one site will be treated with a micropatch but will not be covered afterwards, and the other site will be an occlusion control site (covered with an occlusive patch but no micropatch application). Noninvasive measurements will be made at baseline to determine

differences in hydration, skin water loss, electrical resistance (impedance), and color between subject groups. OCT scans will be made on the skin to noninvasively visualize the skin structure, allowing calculations of epidermal thickness and microvasculature density. After the micropatch is applied to one site at each of the 3 body locations, the water loss, impedance, and OCT measurements will be repeated. The micropatches are only applied on the first study day. Impedance and OCT measurements will be repeated at 24 hrs and 48 hrs. The impedance measurements will allow us to mathematically calculate the time it takes for the skin barrier to restore after the micropatch application, and the OCT images will give us an innovative and complementary method for visually confirming the impedance calculations.

I.5 ***Specify your research question(s), study aims or hypotheses (do not indicate "see protocol")***

This study aims to visualize micropores and measure micropore closure rates following micropatch application at 3 anatomical sites in subjects from different racial/ethnic groups. Another study aim is to quantify differences in skin structure and blood flow using OCT imaging. We hypothesize that OCT images of micropores in the skin will provide a complementary approach to calculating micropore lifetime, when combined with impedance calculations.

I.6 ***Background and significance and/or Preliminary studies related to this project. (do not indicate "see protocol")***

TThe skin serves an integral role in protecting the body from harmful environmental stressors. Much of the skin's barrier capabilities can be attributed to the stratum corneum, the outermost layer of the epidermis. Although the stratum corneum is beneficial in protecting against absorption of foreign compounds and excessive loss of water, it is an obstacle for most transdermal drug delivery methods. Transdermal delivery allows a drug to reach the systemic blood supply while avoiding common obstacles such as first pass hepatic metabolism and inconsistent plasma concentrations [1]. Other benefits of transdermal delivery include improved patient compliance, and pain-free delivery [2]. However, few drugs can be transdermally delivered because of strict physicochemical properties required for skin permeation, including molecular weight in Daltons or octanol-water partition coefficient [3]. One way to aid transdermal delivery is through microneedles, which bypass the stratum corneum and increase the list of therapeutics that can be successfully delivered through the skin.

Microneedles are micron-scale projections that form transient micropores in the epidermis. When using solid microneedles, the micropores are created from the initial insertion of the microneedles, but then the microneedles are discarded and do not remain in the skin for any period of time. For this type of microneedle technique, the ability of the micropores to remain open is crucial for effective drug delivery (in a drug delivery study, a medication patch would be applied over the newly-created micropores). There have been some studies quantifying micropore lifetime in human subjects, though the populations studied have been very homogenous and do not represent the full range of skin types that might benefit from microneedle-assisted drug delivery. There has been a lack of studies studying micropore closure kinetics among different racial/ethnic skin types. There is also contradicting evidence that other variables, such as transepidermal water loss (TEWL), skin elasticity, and epidermal and dermal thickness, vary among different skin types as well [4-5]. More research is necessary to better understand this area, and this can be achieved using new imaging methods such as dynamic optical coherence tomography (OCT).

OCT is a noninvasive and nondestructive technique that is already recognized as a powerful medical imaging technique

in the field of ophthalmology, in which it is used for imaging the retina. It is a real time, in-vivo technique that has also been used for skin imaging. The instrument uses an echo technique for image collection that is similar in concept to ultrasound, with the exceptions that OCT uses light waves (instead of sound waves) and provides better resolution. OCT allows for noninvasive observation of the skin in a vertical plane up to a depth of ~1 mm, capturing two and three-dimensional images [6]. This allows for visualization of multiple skin structures such as the epidermis, dermis, epidermal junction, and hair follicles. Dynamic OCT allows for the visualization of the microvasculature, along with the skin structures. Previous studies have successfully utilized OCT to image polymeric microneedles in the skin [7-8]. However, OCT has not been used to visualize the micropores formed from metal microneedles, which is the primary focus of the work in our lab group. To date, there are also no studies using OCT to study the microvasculature differences among different racial/ethnic skin types.

In our research program we recently demonstrated that epidermal barrier restoration is slower after microneedle application in darker skin types [9]. We also demonstrated that the use of tristimulus colorimetry as a quantitative measurement of skin color is a better indicator of skin variability than race self-reported by subjects. Using OCT to visualize the skin structures will provide a visual, complementary confirmation of these findings that will augment the impedance calculations that we use as a surrogate measure to determine how long the micropores remain open.

In the current study we will use dynamic OCT and other noninvasive measurements of epidermal properties to comprehensively examine differences in skin properties and micropore closure timeframes after microneedle application in a population of healthy human subjects with racial/ethnic skin.

I.7 ***Literature cited / references (if attaching a grant or protocol enter N/A).***

1. Thomas, B. J., & Finnin, B. C. (2004). The transdermal revolution. Drug Discovery Today, 9(16), 697 - 703.
2. Miller MA, Pisani E. (1999) The Cost of Unsafe Injections. Bull World Health Organ.77(10):808-11.
3. Prausnitz MR, Mitragotri S, Langer R. (2004) Current status and future potential of transdermal drug delivery. Nat Rev Drug Discov. 3:115–124.
4. Wilson D, Berardesca E, Maibach HI. (1988) In vitro transepidermal water loss: differences between Black and white human skin. Br J Dermatol. 199: 647–52
5. Muizzuddin, N. et al. (2010) Structural and functional differences in barrier properties of African American, Caucasian and East Asian skin. Journal of Dermatological Science 59, 123-128. (2010).
6. Welzel J, Schuh S. (2017) Noninvasive diagnosis in dermatology. JDDG.15(10): 999-1016.
7. Donnelly RF, Majithiya R, Singh TR, et al. (2011) Design, optimization and characterisation of polymeric microneedle arrays prepared by a novel laser-based micromoulding technique. Pharm Res. 28(1):41-57.
8. Donnelly RF, Garland MJ, Morrow DI, et al. (2010) Optical coherence tomography is a valuable tool in the study of the effects of microneedle geometry on skin penetration characteristics and in-skin dissolution. J Control Release. 147(3):333-341.
9. Ogunjimi AT, Carr J, Lawson C, Ferguson N, Brogden NK. (2020) Micropore closure time is longer following microneedle application to skin of color. Sci Rep. Nov 3;10(1):18963.

II. Research Team

II.1 *Principal Investigator*

Name	E-mail	College
Nicole Brogden	nicole-brogden@uiowa.edu	College of Pharmacy

II.2 *Team Members*

UI Team Members

Name	E-mail	College	Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Deactivated
Nicole Brogden, PharmD, PHD	nicole-brogden@uiowa.edu	College of Pharmacy	Yes	Yes	No		Yes	No
Valeria Cota, BS	valeria-cota@uiowa.edu	College of Pharmacy	Yes	No	No		Yes	No
Jakeline Murillo, High School	jakeline-murillo@uiowa.edu	College of Liberal Arts and Sciences	No	No	No		Yes	No

Non-UI Team Members

Name	Institution	Location	FWA	Role	DHHS Contact	Key Prsn	UI COI	VAMC COI	Consent Process Involvement	Email

Nothing found to display.

II.3 *The Principal Investigator of this study is:*

Faculty

II.6 ***Identify the key personnel. The system will automatically designate the PI and all faculty members on the project as "key personnel." For information about other team members who should be designated as "key personnel" please click on the help information.***

Name	Is Key Personnel
Nicole Brogden, PharmD, PHD	Yes
Valeria Cota, BS	No
Jakeline Murillo, High School	No

II.5 ***Select research team member who is the primary contact for study participants.***

Valeria Cota

III. Funding/Other Support

III.1 ***Funding Sources***

Source Entered as Text	DSP Link	Type	Source Grant Title	Name of PI on Grant
Source is entered as text	no	Departmental / PI Discretionary		

* new source name

III.3 ***Does any member of the research team have a financial conflict of interest related to this project according to the Conflict of Interest in Research policy? If yes, please indicate which members below.***

Name	Has Conflict of Interest
Nicole Brogden, PharmD, PHD	No
Valeria Cota, BS	No
Jakeline Murillo, High School	No

IV. Project Type

IV.1 ***Do you want the IRB to give this project***
Regular (expedited or full board) review

IV.2 ***Enter the date you will be ready to begin screening subjects/collecting data for this project. (If you do not have a specified date, add "upon IRB approval")***
Upon IRB approval

IV.3 ***Are you requesting a waiver of informed consent/authorization (subjects will not be given any oral or written information about the study)?***
No

V. Other Committee Review

V.1 ***Does this project involve any substance ingested, injected, or applied to the body?***

- ***Do not answer yes, if the involvement includes a device, wire, or instrument***

No

V.2 ***Are any contrast agents used for any purpose in this study?***
No

V.9 ***Will any subject be asked to undergo a diagnostic radiation procedure (including radiographic, nuclear medicine, DEXA)?***
No

V.14 ***Will any subject be asked to undergo a radiation therapy procedure (including external beam therapy, brachytherapy, or nuclear medicine therapy)?***
No

V.20 ***Does this project involve the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participant?***
No

V.21 ***Will any portion of this project be conducted in the CRU, or does it use any CRU resources?***
No

V.22 ***Will this project use:***

- ***any resource/patients of the Holden Comprehensive Cancer Center***
- ***involve treatment, detection, supportive care, or prevention of cancer***

No

V.25.a ***Will the study involve <u>any</u> of the following activity at UI Health Care, even if subjects or their insurance will not be billed for the item or service, and regardless of the study funding source (including studies with departmental or no funding)?***

- ***Procedures, tests, examinations, hospitalizations, use of Pathology services, use of clinic facilities or clinical equipment, or any patient care services, including services conducted in the Clinical Research Unit; or***
- ***Physician services or services provided by non-physicians who are credentialed to bill (ARNPs, Physician Assistants, etc.)***

No

V.26 ***The study involves Department of Nursing Services and Patient Care nursing, nursing resources or evaluates nursing practices at UI Health Care.***
No

VI. Subjects

VI.1 ***How many adult subjects do you expect to consent or enroll for this project?***
100

VI.2 ***What is the age of the youngest adult subject?***
18.0

VI.3 ***What is the age of the oldest adult subject?***
45.0

VI.4 ***What is the percentage of adult male subjects?***
50

VI.5 ***What is the percentage of adult female subjects?***
50

VI.6 ***How many minor subjects do you expect to consent or enroll for this project?***
0

VI.13 ***Describe EACH of your subject populations***

- ***Include description of any control group(s)***
- ***Specify the Inclusion/Exclusion criteria for EACH group***

There will be no control group for this study.

Inclusion Criteria: Subjects will be healthy men and women between 18 and 45 years of age.

Exclusion Criteria:
1) Unable to give consent
2) Severe general allergies requiring chronic treatment with steroid or antihistamines
3) Previous adverse reaction to microneedle insertion
4) History of keloids
5) Known allergy or adverse reaction to medical tape/adhesive, or aloe vera
6) Any inflammatory diseases of the skin (including but not limited to: psoriasis, atopic dermatitis, and blistering skin disorders)

7) Any disease associated with altered immune function (including but not limited to: rheumatoid arthritis, diabetes, lupus, HIV/AIDS)
8) Any subject taking medication that impairs the immune system (including but not limited to corticosteroids, TNF inhibitors, monoclonal antibodies, chemotherapy agents)
9) Any current malignancy or history of malignancy present at the treatment sites
10) Eczema or scaling present at any treatment site; any current inflammation or irritation present at the treatment sites (including but not limited to: rash, inflammation, erythema, edema, blisters)
11) Uncontrolled mental illness that would, in the opinion of the investigator, affect the subject's ability to understand or reliably participate in the study
12) Subjects taking medications in the following therapeutic classes will be excluded: HMGCoA reductase inhibitors ("statins"), oral or topical steroids (at the local treatment site), oral antibiotics, topical antibiotics at the local treatment site, topical antihistamines at the local treatment site, beta-blockers, and systemic or topical NSAIDS/analgesics. A subject who has recently used oral or topical steroids, antibiotics, antihistamines, or analgesics may be enrolled if more than 5 elimination half-lives of the drug have passed since the last dose (this is a typical parameter in pharmacokinetics, when it is assumed that ~97% of drug in the systemic circulation is eliminated after 5 half-lives). The estimated elimination half-life for any specific drug will be obtained from standard pharmacy references such as Micromedex or other comparable drug information references.
13) Any subjects that are pregnant/nursing will be excluded from participation.
14) Subjects will also be excluded for any condition that would, in the opinion of the PI or physician, place the subject at an unacceptable risk of injury or render the subject unable to meet the requirements of the protocol.

VI.14 ***Provide an estimate of the total number of subjects that would be eligible for inclusion in each of your study populations (include your control population if applicable)***

It is somewhat difficult to know the total number of subjects that would be eligible for the study because we are recruiting generally healthy individuals (of which there will be a large number in the local community). However, it is reasonable to estimate that perhaps several hundred to a few thousand subjects in this local area may be eligible.

VI.15 ***Describe how you will have access to each of your study populations in sufficient number to meet your recruitment goals.***

This is a relatively small study with low numbers of subjects per group, so we do not anticipate significant challenges with recruitment. We have had excellent enrollment in our previous studies, including one with very similar inclusion and exclusion criteria. For these studies, we have used the following methods of advertisement: mass emails, Noon News, advertisement at UIHC outpatient dermatology clinic, and advertisement on the University Cambus system, and will utilize the mass email and noon news for this study.

VI.16 ***Do you <u>plan</u> to recruit/enroll non-English speaking people?***

No

VI.18 ***Do you propose to enroll any of the following in this study as subjects?***

- ***Employee of the PI or employee of a research team member***
- ***Individual supervised by PI or supervised by member of research team***

- ***Individual subordinate to the PI or subordinate to any member of the research team***
- ***Student or trainee under the direction of the PI or under the direction of a member of the research team***

No

VI.20 ***Will subjects provide any information about their relatives?***
No

VI.23 ***Will anyone (other than the subject) provide you with information about the subject (e.g. proxy interviews)?***
No

VI.26 ***Is this project about pregnant women?***
No

VI.27 ***Will this project involve fetuses?***
No

VI.28 ***Does this project involve adult subjects who may be incompetent or have limited decision-making capacity on initial enrollment into the study?***
No

VI.32 ***Does this project involve subjects whose capacity to consent may change over the course of the study?***
No

VI.37 ***Does this project involve prisoners as subjects?***
No

VII.A. Project Description (A)

VII.A.1 ***Where will project procedures take place (check all that apply)?***
- Other UI campus site - College of Pharmacy Building, Room 554

VII.A.2 ***Is this project also being conducted by other researchers at their own sites (e.g. a multi-site collaborative project)?***
No

VII.B. Project Description (B)

VII.B.1. ***Does this project involve any of the following (Check all that apply):***

- ☑ **Interventional** – Includes **Clinical (or Treatment) trial**, **Physiology intervention/study**, **Behavioral intervention/study**, **Diagnostic Trial**.
  - ☐ **Clinical (or Treatment) trial** – A prospective biomedical or behavioral research study of new treatments, new drug or combinations of drugs, new devices, or new approaches to surgery or radiation therapy. (NIH and ClinicalTrials.gov & FDA)
  - ☑ **Physiology intervention/study** – A pharmacologic or measurement study aimed at understanding basic mechanisms of disease and/or of normal human physiology, often without any therapeutic intent (though a clinical trial could include such components, often labeled as "translational" or "basic science" aims.) Measurements in such studies could include, but are not limited to, a blood draw, EKG, EEG, MRI, auditory or sensory testing, checking vital signs, DEXA scans, eye tracking, specimen collection, exercise, fasting, special diets, etc.
  - ☐ **Behavioral intervention/study** – May be used to refer to studies of individual or group behavior. This option does not include drugs, biologics, or devices but could include psychotherapy, lifestyle counseling, behavior modification, etc.
  - ☐ **Diagnostic trial** – Protocol designed to evaluate one or more interventions aimed at identifying a disease or health condition (ClinicalTrials.gov & FDA)
- ☐ **Observational**
- ☐ **Expanded Access** – A process regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with serious diseases or conditions who cannot participate in a clinical trial. Examples of expanded access include non-protocol access to experimental treatments, including protocol exception, single-patient IND, treatment IND, compassionate use, emergency use, continued access to investigational drug, and parallel track (ClinicalTrials.gov & FDA).
- ☐ **Registry** – The collection and maintenance of data (not including biologic samples) in which: (1) the individuals in the registry have a common or related condition(s), and/or (2) the individuals in the registry are interested in being contacted for future studies by investigators other than those listed in Section II of this project.(UI Guide)
- ☑ **Repository** – The collection, storage, and distribution of human biologic samples and/or data materials for research purposes. Repository activities involve three components: (i) the collection of data and/or specimens such as blood, tissue, saliva, etc.; (ii) the storage of data or specimens, and data management function; and (iii) the sharing of data/specimens with recipient investigators other than the original investigators. (paraphrased from OHRP)

- ☐ **Other**

VII.B.2 ***Does this project involve a drug washout (asking subject to stop taking any drugs s/he is currently taking)?***
No

VII.B.11 ***Is there a separate, written protocol that will be submitted in addition to this IRB New Project form? (Note: a grant application is not considered to be a protocol)***
No

VII.B.18 ***Does this project involve the evaluation, or testing, of the safety and/or efficacy of a medical device?***
No

VII.C. Project Description (C)

VII.C.1 ***Does this project involve any research on genes or genetic testing/research?***
No

VII.D. Project Description (D)

VII.D.1 ***Check all materials/methods that will be used in recruiting subjects (you will need to attach copies of all materials at the end of the application):***
- Advertisements -
- E-mail -

VII.D.8 ***Will a member of the research team discuss the study with the subject in person prior to the subject agreeing to participate?***
Yes

VII.D.9 ***Describe the physical location where the consent process will take place:***
In-person consent will be obtained in a private office in the College of Pharmacy Building. Electronic consent will be collected by the subject on their own device.

VII.D.10 ***Will a member of the research team discuss the study with the subject by phone prior to the subject agreeing to participate?***
Yes

VII.D.11 ***Describe:***

Subjects may contact the study site by phone prior to signing the informed consent document if they have any questions about the study or are looking for more information. If individuals contact the study team looking for more information about the study the attached script will be used to provide this information:
202010229_TelephoneInformationScript_v1.doc
Researchers at the study site may contact individuals by phone prior to their consenting if the responses they have supplied on the pre-screening survey require clarification and they have chosen their phone number as their preferred method of communication. Prior to consenting phone calls will be limited to clarifications of answers provided and the information available in the attached document: 202010229_TelephoneInformationScript_v1.doc

VII.D.12 ***Who will be involved in the consent process (including review of consent document, answering subjects' questions)?***

Name	Consent Process Involvement
Nicole Brogden, PharmD, PHD	Yes
Valeria Cota, BS	Yes
Jakeline Murillo, High School	Yes

VII.D.15 ***Check all materials that will be used to obtain/document informed consent:***

- Other - Electronic Consent via REDcap
- Consent Document

VII.D.16 ***Are you requesting a waiver of documentation of consent (either no subject signature or no written document)?***

No

VII.D.19 ***Before the subject gives consent to participate are there any screening questions that you need to directly ask the potential subject to determine eligibility for the study?***

Yes

VII.D.20 ***List any screening questions you will directly ask the potential subject to determine eligibility.***

First name, Last name, Preferred name, preferred pronouns
Are you between 18 and 45 years of age?
What race or ethnicity do you identify with (subject will be provided with the following options: Black, Asian, Latinx, White, Indigenous, bi-/multiracial or More Options)
Do you take any prescription medications (excluding birth control)?
Do you have any chronic or ongoing medical conditions (including skin disorders or pregnancy)?
Do you have any general allergies that require daily treatment with steroids and antihistamines?
Do you have a known allergy or adverse reaction to medical tape, band-aids, adhesive or aloe vera?
Contact information: number, email address
What type of contact do you prefer: phone/email

Prior to consent individuals will complete the pre-screening questionnaire either in paper form (attached doc: 202010229_PreScreeningQuestionnaire_v1) or electronically (attached document: 202010229_RedCap_PreScreeningSurvey_v2).

VII.D.21 ***Will you keep a screening log or other record that would include information on people who do not enroll in the study?***
Yes

VII.D.22 ***Describe the information being collected and the purpose for keeping this information.***
A screening log will be maintained that will document the first and last name of the prospective participant that was screened, date of screening, phone number (if provided), email address (if provided), and whether it was a screen failure or if the subject will continue on to the consent process. This information will be kept until all study activities have been completed for all participating subjects. We will keep the screening information because it is not uncommon for individuals to respond to the same advertisements more than once (for example, Noon News) and we want to know if a subject has previously contacted us about the study. The log will be destroyed after completion of the study for enrollment in future studies.

VII.D.23 ***Will this information be shared with anyone outside the UI research team members?***
No

VII.D.25 ***<u>After</u> the subject agrees to participate (signs consent), are there any screening procedures, tests, or studies that need to be done to determine if the subject is eligible to continue participating?***
Yes

VII.D.26 ***List and describe screening***
After a subject consents to be in the study, baseline demographic data will be collected from the subject including age, sex assigned at birth, race/ethnicity; information regarding current medical conditions/allergies and medications will also be collected. Specifically, the subject's approximate duration of each condition/allergy, what treatments the subject has received, and approximate severity of the conditions, and a current medication list will be collected. All this information will be collected directly from the subject. The subject's medical record will not be reviewed/abstracted for research data.

After consenting subjects will complete a screening questionnaire either in paper form (attached doc: 202010229_ScreeningQuestionnaire_v1) or electronically (attached doc: 202010229_RedCap_ConsentScreening_v1). https://redcap.icts.uiowa.edu/redcap/surveys/?s=v5UPrZbuFR

VII.D.27 ***Discuss how much time a potential subject will have to agree to consider participation and whether or not they will be able to discuss the study with family/friends before deciding on participation.***
There is no limit on the time a potential subject may take to consider participation. The only restriction on time is that the subject will only be allowed to participate if the study is still enrolling subjects when they provide consent. Individuals will

have as much time as needed to discuss with family and friends their participation in the research study.

VII.D.28 ***How long after the subject agrees to participate do study procedures begin?***
Study procedures can begin immediately after consent is obtained.

VII.D.29 ***Provide a description of the enrollment and consent process for adult subjects***

- ***Describe each study population separately including control population***
- ***Include when recruitment and consent materials are used***
- ***Use 3rd person active voice "The Principal Investigator will identify subjects. For example, the principal investigator will identify potential subjects, the study coordinator will discuss the study with subjects over the telephone and schedule the first study visit, etc..."***
- ***Describe the steps that will be taken by the research team to minimize the possibility of coercion or undue influence during the consent process***

Participants in this study will be normal healthy individuals aged 18-45. All participants will act as their own controls.

This study will be advertised through the University of Iowa campus-wide email system and through the University of Iowa Health Care "Noon News," a daily announcement flier for community and faculty members within the UIHC. Advertisements for this study have been created so that specific subject populations may be better reached via targeted advertisements, in order to meet our enrollment goals. (attached docs: 202010229_MassEmail_v1; 202010229_NoonNews_v1)

Prospective participants may be pre-screened through a telephone survey or a survey link created by researchers using a data collection tool called RedCap. Individuals who view our advertisements and contact the site by telephone will be read the information about the study found in (attached document) 202010229_telephoneinformationscript_v1 and will be asked if they would like to answer some pre-screening questions to help determine their eligibility (attached document 202010229_PreScreeningQuestionnaire). Individuals who view the advertisements and complete the pre-screening questionnaire via RedCap (link https://redcap.icts.uiowa.edu/redcap/surveys/?s=9PW7TDTDXF) will have their answers reviewed by the study team. All individuals will be provided with a copy of the consent summary document 202010229_GeneralConsentSumary_v1. If clarification is needed for answers provided, subjects will be contacted via their preferred method of contact (phone or email) by members of the research team. Once it is determined that a subject is potentially eligible to participate in the study they will receive an email from the study team with a link to electronic consent (attached document: 202010229_EmailforSurvey_eligible_v1). If individuals who completed the electronic pre-screening survey have been found to be ineligible to sign the consent document they will receive an email thanking them for their time (attached document: 202010229_EmailforSurvey_Ineligible_v1). This pre-screening process has been created because the number of potentially eligible participants is quite high, since we are seeking normal, healthy individuals aged 18-45. This process helps us to avoid having many people sign the consent form and then become a screen failure. Questions are brief and are all yes/no answers. No identifying information is obtained during the pre-screening process besides for name and contact information.

If a subject is interested in study participation and passes the pre-screening survey, they will be invited to sign an informed

consent document (where they will again be provided an overview of the study rationale, procedures, risks, and benefits). Consent will be obtained either electronically or in person depending on the preference of the individual. An informed consent document will be provided to the subject for review prior to any meeting. This ensures that the individual has the chance to review the material in the informed consent on their own time.

Pre-screening for this study will be streamlined with the use of a survey created by the research team (link provided above). The link to this survey will be sent to potential subjects via the Noon News and Mass Email. Participants who complete the survey will provide their email address or phone number, and the study team will contact them in response to their answers. The information provided by the individual will be used to determine eligibility. All personal information collected for purposes of this study will be collected directly from the individual.

It is recognized that the consent process must be carried out in an environment where no coercion is applied and where subjects can be adequately informed of the purpose, nature, procedures, risks and hazards of the study. One of the important features of our screening process is the ability for the prospective participant to review the informed consent on his/her own time, outside of the study site. This additionally demonstrates the reliability of the subject if they schedule a follow-up meeting to sign the informed consent.

Subjects participating in this study have the option to fill out an electronic consent via REDcap (attached doc: 202010229_RedCap_eConsent_v1)(link: https://redcap.icts.uiowa.edu/redcap/surveys/?s=4296PfQrjT). Subject's electing this option will be first complete a pre-screening survey. Upon completion and review subject's will be sent a copy of the informed consent document via email for their review as well as a link to complete the electronic consent document (contained in attached document: 202010229_emailforsuvey_eligible_v1). To ensure that the subject understands the consent document a series of questions will be asked prior to them being allowed to sign the consent document. These questions are:
True or false: This study visits will be performed at the University of Iowa College of Pharmacy Building (correct answer: True)
True or false: Return visits are scheduled 48 hours apart. (Correct answer: False, visits are scheduled 24 hours apart)
True or false: This study involves the topical administration of drug to the skin after micropatch application. (Correct answer: False, this study contains no drug administration of any kind).
If subject's correctly answer these questions they will be permitted to fill out the electronic consent and will then be directed to complete the screening questionnaire survey on REDcap as well (see attached doc 202010229_RedCap_ConsentScreening_v1) (screening survey link: https://redcap.icts.uiowa.edu/redcap/surveys/?s=v5UPrZbuFR).

To clarify: individuals will be given the option to meet with study personnel in person to complete the pre-screening questionnaire, consent procedures, and the screening questionnaire. This would be completed on the day of the visit 0 procedures prior to any study prior to any study procedures beginning. If individuals do not wish to meet in person with study personnel the option will be made available to complete all the pre-screening questionnaire, consent, and screening questionnaire electronically.

To clarify: The attached document 202010229_EmailinformationScript_v1 will be used if individuals contact the study site prior to completing the electronic pre-screening survey from one of our advertisements. This document contains a link to the pre-screening survey as well as information about the study procedures.

VII.D.37 ***Does the study include any form of deception (e.g., providing participants with false information, misleading information, or withholding information about certain study procedures)?***

Examples:

- ***Procedure includes a cover story that provides a plausible but inaccurate account of the purposes of the research.***
- ***Participants will be provided with false information regarding the particular behaviors of interest in the research.***
- ***Procedures include a confederate pretending to be another participant in the study.***
- ***Participants will be told that the research includes completion of a particular task, when in fact, that task will not be administered.***
- ***Study is designed to introduce a new procedure (or task) that participants are not initially told about.***
- ***If yes, a waiver of informed consent must be requested under question IV.3.***

No

VII.E. Project Description (E)

VII.E.1 ***Will subjects be randomized?***
No

VII.E.3 ***Will any questionnaires, surveys, or written assessments be used to obtain data directly from subjects in this study?***
Yes

VII.E.4 ***List all questionnaires, surveys, written assessments and ATTACH each one to the application. (NOTE: You are NOT prohibited from attaching copyrighted materials to this application)***
202010229_ScreeningQuestionnaire_v1
202010229_PreScreeningQuestionnaire_v1
202010229_DataCollectionSheets_v1.docx
202010229_Emailfollowupscript_v1.docx

VII.E.5 ***Does this project involve creating any audiotapes, videotapes, or photographs?***
No

VII.E.6 ***Provide a detailed description in sequential order of the study procedures following the consent process - DO NOT cut and paste from the Consent Document.***

Describe study populations separately if they will be participating in different procedures - include CONTROL population if

applicable.

DESCRIBE:

- ***What subjects will be asked to do/what happens in the study (in sequential order)***
- ***The time period over which procedures will occur***
- ***The time commitment for the subject for individual visits/procedures***
- ***Long-term followup and how it occurs***

Following consent, the subject will fill out a questionnaire collecting information about demographic information age, race/ethnicity, sex assigned at birth, current medications and ongoing medical conditions. The subject will be asked to elaborate on the duration and severity of medical conditions and any treatments received. No medical records will be consulted to obtain or confirm this information. A member of the research team will use this information to screen out subjects meeting any of the exclusion criteria defined in VI.13. Subjects who pass the screening may proceed to the next step described below. Subjects should allow for both in person and electronic consent and screening procedures to take approximately 1 hour; whenever possible, if in person, this will be done on the same day as when the subject starts the study procedures.

On Day 0 (may be the same day as consent is obtained), the subject will sit in the study room at the College of Pharmacy for 30 minutes prior to any procedures. This allows the subject's skin to acclimate to the ambient environment in the study room (temperature, humidity). During this 30 minute period, the study team member will verify screening information collected through the online survey with the participant, as well as measure height, weight, calculate BMI. If screening information is verified correct from participant research procedures will continue as planned. (This procedure will be followed as do to scheduling constraints it is possible that some time has passed from when the subject consented to when they are scheduled to complete their study procedures. Verifying this information will help us determine if their original answers remain accurate and their eligibility remains.) If participants answers indicate that they are actually ineligible to continue their participation no further procedure will take place and the subject will be removed from the study. Following this acclimation, the researcher will identify and mark with a pen 3 sites each on the upper arm, forearm, and the palm. Hair may be clipped (but not shaved) at any sites if necessary. Noninvasive baseline measurements will be taken at each of the 9 sites as follows:
• Transepidermal water loss (TEWL) will be measured by resting a probe gently against the skin. This measurement will take 1-3 minutes at each site. (TEWL will only be measured on Day 0)
• Electrical resistance (impedance) will be measured with an impedance meter by applying gel electrodes to each site and a reference electrode at a nearby site. The measurement will be repeated 3 times at each site, and will take less than 2 minutes total at each site.
• Skin color and redness will be measured by placing a colorimetry probe gently against each site. This measurement will take less than 30 seconds at each site.
• Dynamic-OCT will be used to obtain an image of the skin by holding a probe lightly on the skin. This measurement will take about 30 seconds at each site. Microvasculature density, epidermis thickness, and epidermal junction depth can be measured using a single scan.

Following baseline measurements on Day 0, micropatches (an adhesive microneedle patch) will be applied to two of the three identified sites at each anatomical location. The sites will first be cleansed with an alcohol swab. A sterilized micropatch

containing 50 tiny projections, each 800 um in length, will be placed perpendicular to the skin, and the researcher will apply gentle pressure to the back of the patch for 15 seconds. A new micropatch will be used for each site, and the micropatches will be discarded immediately after use. Micropatch application will only occur on Day 0. Immediately after treating a site with a micropatch, TEWL, OCT and impedance measurements will be repeated. One of the micropatch sites at each location will be covered with a sterile occlusive covering following micropatch application; this will be secured to the skin using medical tape such as Tegaderm or Bioclusive tape. The second micropatch application site at each location will not be covered. The third site at each location will not receive micropatch application, but will simply be covered with an occlusive covering. This serves as a control for the effect of occlusion alone on normal skin. Day 0 procedures will require 3 - 3.5 hours in total.

Subjects will be asked to return to the College of Pharmacy every 24 hours for the next 2 days. On each day the occlusive coverings will be removed and the OCT and impedance measurements will be repeated at all sites. Fresh occlusive coverings will be applied after measurements have been completed. Procedures on days 1 and 2 will require approximately 2 – 2.5 hrs.

On Day 2 (the final day), the occlusive coverings will be removed and not replaced. Within 3-6 days after the Day 2 visit (or the last completed visit if a participant decides to drop out early) a study team member will contact the subject via phone or email to determine if the subject is experiencing any redness or irritation at any of the measurement sites. No long-term follow-up will be necessary. The overall time commitment for this study is 7 - 10 hours in one week, across 3 – 4 study days if consent is obtained on a different day than the study start day.

To summarize, the 9 sites will receive the following measurements and treatments:
Palm: sites 1 – 3
Site 1: Micropatch application + occlusive covering
Site 2: Micropatch application, no occlusive covering
Site 3: Occlusive covering, no micropatch application

Forearm: sites 4 – 6
Site 4: Micropatch application + occlusive covering
Site 5: Micropatch application, no occlusive covering
Site 6: Occlusive covering, no micropatch application

Upper arm: sites 7 – 9
Site 7: Micropatch application + occlusive covering
Site 8: Micropatch application, no occlusive covering
Site 9: Occlusive covering, no micropatch application

Measurements of TEWL, Dynamic-OCT, colorimetry, and impedance will be made at baseline (Day 0) for all sites. TEWL, Dynamic-OCT, and impedance measurements will be repeated immediately after micropatch application. Dynamic-OCT and impedance measurements will be measured at all sites on days 1 and 2.

VII.E.7 ***Will you attempt to recontact subjects who are lost to follow-up?***
No - those lost to followup will not be recontacted

VII.E.9 ***Will subjects be provided any compensation for participating in this study?***
Yes

VII.E.10 ***Cash***
No

VII.E.11 ***Gift Card***
No

VII.E.12 ***Check***
No

VII.E.16 ***Other***
Yes

VII.E.17 ***Describe:***
Parking passes will be supplied for the subjects to park in the University ramps near the College of Pharmacy building.

The evoucher system will be used to compensate the subjects for their research study visit completion.

VII.E.18 ***If you plan to compensate subjects using cash, checks or cash equivalent does your unit have a Cash Handling Procedure in place that has been approved by Accounting Services?***
Yes

VII.E.19 ***Describe the compensation plan including***

- ***Compensation amount and type per visit***
- ***Total compensation***
- ***Pro-rating for early withdrawal from study***

Subjects will be compensated $175 according to the following schedule:
Day 0 $75
Day 1 $50
Day 2 $50
Total $175
Compensation will be prorated for any subject who does not complete all days of the study. Subjects will only be paid for

the study days whey complete. Subjects will be paid in one check. Subject's who park in the University of Iowa ramps will be supplied with parking vouchers.

VIII. Risks

VIII.1 ***What are the risks to subjects including***
- emotional or psychological
- financial
- legal or social
- physical?
In general, micropatch treatments are well tolerated. However, the skin could become irritated or inflamed from the microneedle insertion or from the adhesives (either on the micropatches, the impedance electrodes used to make measurements, or the medical tape used to hold the occlusive patches in place). There may be mild discomfort, itching, redness, bruising, inflammation, or hyper-/hypopigmentation, and infection at the treatment sites or where adhesives were in contact with the skin. Loss of confidentiality is also a risk.

VIII.2 ***What have you done to minimize the risks?***

- ***If applicable to this study ALSO include:***
  - ***How you (members of your research team at Iowa) will monitor the safety of individual subjects.***
  - ***Include a description of the availability of medical or psychological resources that subjects might require as a consequence of participating in this research and how referral will occur if necessary (e.g. availability of emergency medical care, psychological counseling, etc.)***

During the consent process the subjects will be counseled about the micropatch. The skin will be cleansed thoroughly with alcohol wipes prior to applying the micropatch treatments (cleaning technique similar to that used for insertion of a typical hypodermic needle). They will also be counseled about the possibility of local skin irritation and redness from the adhesive tape. Subjects will be closely observed during the measurements and during treatment with the micropatches. Subjects will be instructed to contact a member of the study team if problems arise at any time during their participation in the study (all pertinent contact information will be provided to the subjects). Within 3 -4 days following study completion, a member of the research team will call or email the subject to follow-up and be sure that no irritation or infection has occurred. The risk of loss of confidentiality will be minimized by keeping all documents in a locked cabinet that is only accessible to members of the research team. All electronic forms of data will be kept on a secure-server supported by the University of Iowa that allows only members of the research team access.

VIII.3 ***Does this study have a plan to have an individual or committee review combined data from all subjects on a periodic basis (such as summary or aggregate safety and/or efficacy data)?***
No

IX. Benefits

IX.1 ***What are the direct benefits to the subject (do not include compensation or hypothesized results)?***
There are no direct benefits to the subjects.

IX.2 ***What are the potential benefits to society in terms of knowledge to be gained as a result of this project?***
Microneedle assisted transdermal delivery shows promise as an alternative to hypodermic needles. While there are increasing numbers of studies involving microneedles, differences in micropore closure kinetics among racial/ethnic groups are lacking. In addition, the use of OCT as a noninvasive skin imaging technique to view the micropores in the skin shows promise but has not been studied in different racial/ethnic groups.

X. Privacy & Confidentiality

X.1 ***What are you doing to protect the privacy interests of the subjects?***
No direct patient identifiers will be recorded on data collection material. Instead, subjects will be assigned a subject number on study materials. Only the data necessary to answer the research questions will be collected, and all in person consent processes and study procedures will take place in a private location in the College of Pharmacy building.

X.2 ***Are you collecting the Social Security Number of any subjects for any purpose?***
Yes

X.3 ***Provide the intended usage of SSN:***

- To provide compensation to subjects

X.4 ***How will information/data be collected and stored for this study (check all that apply):***

- Paper/hard copy records (hard copy surveys, questionnaires, case report forms, pictures, etc.) - Paper/hard copy documents will only be transported, transferred, and stored by study team members. These document will be stored in a secure filing cabinet in a locked office in the College of Pharmacy office 558. This office is shared with people outside of the research study team, but the lock on the cabinet is only available to those on the study team.
- Electronic records (computer files, electronic databases, etc.) - Electronic Records are stored on a secure Shared rdss drive within the university of iowa drives. This drive is access is managed by the Principle Investigator and permission is only permitted to those on the study team.
    - Name - Greg Schwartz
    - Title - IT Director
    - University Job Classification - Faculty/Staff

X.5 ***Do the confidentiality protections indicated above allow only members of the research team to access the data/specimens?***
Yes

X.7 ***Does your study meet the NIH criteria for a Certificate of Confidentiality or will you be applying for Certificate of Confidentiality?***
No

XI. Data Analysis

XI.1 ***Describe the analysis methods you will use, including, if applicable, the variables you will analyze***
Paired t-tests will be performed to compare impedance and TEWL measurements pre- and post-micropatch treatment at each site. Influence of skin color and self-reported ethnicity/race on measured parameters will be compared using one-way ANOVA. Micropore closure kinetics will be calculated by modeling the data and calculating a micropore closure half-life. Epidermal thickness, skin roughness, and microvasculature density will be calculated by the OCT software and compared between groups using one-way ANOVA. For all analyses, $p < 0.05$ will be considered statistically significant. GraphPad Prism Software (GraphPad Software, San Diego, CA) or Microsoft Excel will be used for statistical analyses.

XI.2 ***Provide the rationale or power analysis to support the number of subjects proposed to complete this study.***
This is a pilot study that does not require a power analysis because data regarding the variability in parameters measured via OCT in racial/ethnic groups is not available. We are targeting 20 subjects per group because this is a reasonable number of subjects for a pilot.

XII. Future Research

XII.1 ***Do you wish to keep any information about subjects involved with this research project so that members of the current research team may contact them in the future for your own research projects?***
Yes

XII.2 ***Do you wish to keep any information about subjects involved with this research project so that other researchers may contact them for future research?***
No

XII.3 ***List the data or information you will keep:***
Information from the screening log will be kept only for those individuals who have consented to participate in the study.

XII.4 ***Does this project involve storing any data, tissues or specimens for future research?***

Yes – contribution for future use is mandatory for participation in the study