STUDY PROTOCOL

Pilot Study for Imaging Human Skin with High-Speed Spectrally Encoded Confocal Microscopy

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1. BACKGROUND AND SIGNIFICANCE:

Reflectance Confocal microscopy (RCM) is a mode of non-invasive imaging which is able to demonstrate nuclear and cellular level morphology of human skin in vivo. It is able to image to a resolution of 0.5-1.0µm, the epidermis and the underlying papillary dermis in small fields of view (1). RCM has been demonstrated to be capable of diagnosing major skin diseases such as melanomas and basal cell carcinomas with a high degree of sensitivity and specificity (2). With the acceptance by US Center for Medicare and Medicaid Services, for reimbursement (3), RCM has gained wide usage in dermatology ranging from biopsies to surgical treatment.

One of the major drawbacks of RCM imaging is the slow speed of imaging, with currently commercially available RCM devices imaging at a speed of 6 frames/sec (1) , which leads to a long duration of examination time, as compared to conventional methods of imaging such as a dermatoscope . If the RCM imaging speed can be increased by an order of magnitude, a single lesion can be examined within seconds and multiple lesions can be examined during a single visit. The increased imaging speed can also facilitate observation of dynamic events such as blood flow and cell migration.

Spectrally encoded confocal microscopy (SECM) is a high speed reflectance confocal microscopy technology (SECM) [redacted]

SECM provides an order of magnitude faster imaging speed than conventional confocal microscopy devices. [redacted] When used for skin imaging, SECM can provide real-time three-dimensional confocal imaging and significantly reduce the imaging time. While SECM has been successfully used for imaging human esophagus in vivo, its utility in skin imaging needs to be tested in a new pilot study.

In this study, we aim to test skin imaging performance of our newly-developed spectrally encoded confocal microscope (SECM) skin imaging device.

2. SPECIFIC AIMS:

To evaluate the imaging performance of Spectrally Encoded Confocal Microscopy for imaging human skin.

3. SUBJECT SELECTION:

A total of 20 subjects, healthy adults 18 years and older, working at the Wellman Center for Photomedicine will be enrolled in this study.

INCLUSION CRITERIA:

- Healthy adults
- 18 years of age or older
- Capable of giving informed consent
- Pigmented skin lesions (such as moles, beauty marks, or sunspots) present on the upper arm, elbow, forearm or hand

EXCLUSION CRITERIA:

- Unable to provide consent
- Open cuts/sores on the skin, skin infection, or any contagious skin condition
- Pregnant women (according to subject)
- Employees under the direct supervision of the investigator

RECRUITMENT METHODS:

An advertisement will be posted on the internal website of the Wellman Center for Photomedicine and an email will be sent to all the employees of the Wellman Centre for photomedicine informing them of this study. An information packet, containing a copy of a recruitment letter and the research center contact information will be sent to individuals who express interest. No subjects under the direct supervision of the investigators will be recruited to this study. The research nurse/coordinator will follow up with a phone call to assess interest in participating in the study, review eligibility, explain the study further and answer any questions. The contact details of the study staff will be provided to all potential subjects to be able to contact the research team with any questions or concerns regarding the research study prior to the exam.

If a potential subject is interested in participating in this study, he/she will be scheduled to be imaged. To be certain that all subjects understand the study procedure and have an opportunity to change their mind about participation, the potential subjects will be able to discuss the study again with the clinical staff such as a study nurse, clinical research fellow or physician. Informed consent will be obtained prior to the procedure by a clinical research nurse or a clinical research fellow.

4. STUDY PROCEDURES:

- **DEVICE DESCRIPTION:**

[redacted]

- **PROCEDURE**

Study procedures will take place in the Bartlett building at the Wellman Center for Photomedicine. The subject will be asked to sit on a chair and relax the area being imaged (upper arm, elbow, forearm, or hand). There will be no sedation or medication involved.

The SECM skin imaging procedure will be very similar to that by the FDA approved RCM devices. First, the pigmented skin lesion (such as a mole) will be identified on either the upper arm, elbow, forearm, or hand of the subject by a clinician or trained study staff. The lesion will be imaged first with a dermatoscope, and then with the SECM probe. A dermatoscope is a hand-held device used for the visual observation of the epidermis. It is a superior surface contact microscope used to examine skin lesions (7). [redacted]

After the lesion is scanned with the dermatoscope, we will image the lesion with the SECM skin imaging probe. We may use either the fluorinated ethylene propylene (FEP) imaging window cover, or separate components (double sided tape, cover glass, and metal ring) as attachments to the probe to assist with probe imaging. The FEP sheet and film used for the imaging window are FDA compliant. [redacted] If the FEP imaging window cover is used during the procedure, then no other components (double sided tape, cover glass, and metal ring) are necessary.

If the FEP window is not used for imaging, other components will be used during imaging with SECM imaging probe. A small amount of double-sided tape in the shape of a ring will be placed around the identified skin lesion. Water or ultrasound gel will be placed on the skin lesion and a No 2 cover glass will be placed on the double-sided tape. A thin metal ring will be placed on the double-sided tape. Ultrasound gel will be placed on the cover glass (Figure 1). [redacted] A clinician or trained study staff will connect the skin SECM imaging probe (Figure 3) to the electronic box and the SECM console. Once the connections are secured both the console and electronics box will be turned on. The SECM laser will be turned on and SECM skin imaging will be conducted on the skin lesion. We will image both the skin lesion and the section of nearby normal skin area.

For any given skin lesion, we will collect up to 3 confocal image stacks ( ) from both non-pigmented and pigmented areas, for each subject. Once the SECM imaging is completed, the SECM skin imaging setup will be removed from the area being imaged (upper arm, elbow, forearm or hand) of the subject, as well as the metal ring and the double-sided tape. Subjects will be asked to wash the area of skin that is in contact with the FEP window or separate components, following the procedure.

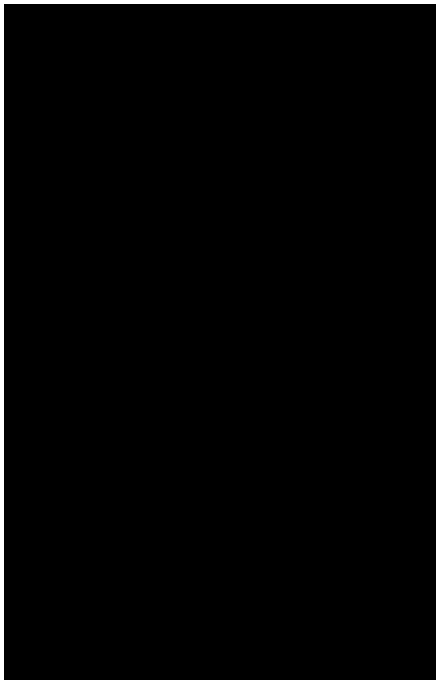

Figure 1: .

Figure 2:

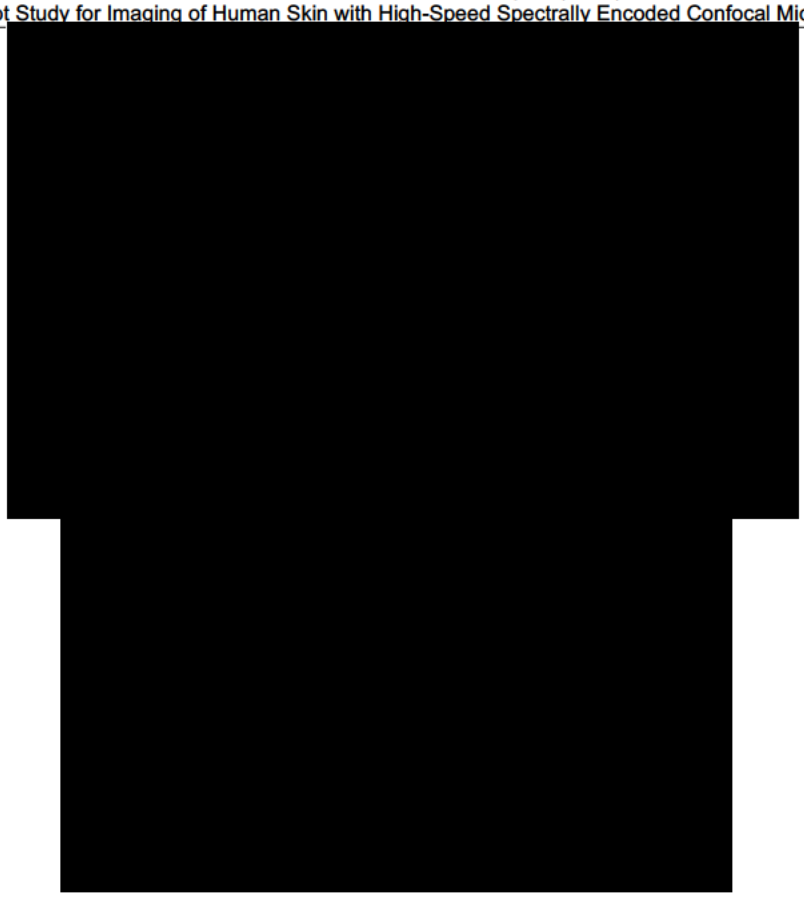

Figure 3: [redacted]

The entire procedure, including informed consent, set up and imaging with both the dermatoscope and SECM microscope, will not exceed 30 minutes.

The DermLite DL1 dermatoscope, attached to an encrypted smartphone to be used exclusively for this study, will be used to take a photo of the subject's skin. The smartphone has no sim card and will not connect to wifi. The skin photo will be transferred from the smartphone to a lab computer using the USB connection. It will be securely stored on the lab servers, accessible only by the study staff. Once the photo is saved on the lab server it will be deleted from the smartphone.

Participation is voluntary. If at any time a subject feels uncomfortable and wants to stop the procedure for any reason, imaging will be suspended immediately and the device will be removed from the subject. If, at any time during the study, the clinical study staff feels that it is ill-advised to continue imaging, imaging will be suspended, and the device will be removed from the subject.

Device Re-Use and Disinfection

[redacted]

[redacted]

[redacted]

5. COSTS

The experimental procedure will be done at no cost to the subject or his/her insurance company and the subjects will not be responsible for any costs incurred for participation in this study.

The subjects will receive a $50 gift card for their time.

6. BIOSTATISTICAL ANALYSIS:

This will be a prospective, nonrandomized pilot study. This study is designed as a feasibility study, which may serve as the basis for future larger-scale studies.

7. RISKS AND DISCOMFORT:

SECM imaging is low risk, non-invasive imaging technique. We have previously demonstrated the safety of the SECM device in the form of a capsule endoscope. SECM imaging technology has been used to image the esophagus' of over 60 human subjects, without any serious adverse events or complications.

The SECM laser can produce 5.5 mW of optical power at a wavelength of 1300 nm on the tissue, which is a class 3R device and safe for both eyes and skin. Therefore, the subject's skin tissue has very low chance to be damaged under our laser illumination. For the eye safety, the laser will be turned on only while the device has been introduced to the subject skin and the system is acquiring the images. Since the objective lens with high numerical aperture of 0.95 and short working distance of 180 μm, it is impossible to see the beam spot for the patient or the operator during the imaging. Even if they could see the spot, the beam is highly diverging and its wavelength (1300 nm) is in the high attenuation range of the water, it is unlikely to damage the retina.

The dermatoscope that will be used in this study is a commercially available, smart phone dermatoscope, designed to be attached to a cell phone or a tablet. It consists of LED lighting, a full-size 15 mm optical lens, a polarizer, and a mounting case. It has been approved by the FDA for use to image human skin.

The fluorinated ethylene propylene (FEP) sheet and film used in the imaging window are FDA compliant, and are considered low-risk by the FDA for biocompatibility when in contact with intact human skin. FEP is an excellent electrical insulator, and is resistant to high temperatures, UV and chemicals (10,11). FEP is not likely to be hazardous when in contact with intact skin, and no irritant effects are anticipated. However, to mitigate any possible discomforts, subjects will be asked to wash the area of skin that is in contact with the FEP imaging window and other components following the imaging procedure.

In order to minimize a potential risk of breach of confidentiality, any imaging data, and any other subject information will be assigned a unique subject ID number. All other personal information will be removed. A master log will be maintained with full names and medical record numbers, which will be secured in the locked office. This will be accessible only when deemed necessary and only to members of the study team.

We will collaborate with Prof. Dongkyun Kang, Assistant Professor of Biomedical Engineering at the University of Arizona and will be sharing coded subject data with him.

We will also be collaborating with Dr. Jihuen Ryu who is a former post-doctoral fellow who worked on technological development of the devices, we will be sharing deidentified subject data with Dr. Jihuen Ryu.

8. POTENTIAL BENEFITS

There are no direct benefits for the individual subjects participating in the study. The individuals with skin disorders may benefit in the future from what we learn in this study.

9. MONITORING AND QUALITY ASSURANCE

Dr. Tearney is the Principal Investigator of this study and is directly responsible for the conduct of the study. Dr. Tearney will be responsible for ensuring that the study is conducted according to the IRB-approved protocol and regulations, and for protecting the rights, safety and welfare of the subjects. Dr. Tearney is also responsible for reporting any unexpected and adverse events to the IRB. According to the Partners Human Research Committee (PHRC) guidelines, unexpected adverse events will be reported to the PHRC within the required time frame as determined by the PHRC requirements.

All imaging data obtained as a part of this research study will be reviewed by Dr. Guillermo Tearney, an expert in this type of imaging. Although rare, there is a possibility that while reviewing the research imaging we may see something that we did not expect to see. We call this a “finding.” If we think the finding could be important to the research participant’s health, we will contact them to find out if they would like to learn more. If it is unclear how to best communicate the information to the participant, the IRB will be contacted for guidance. Whenever a finding is communicated to a research participant, an “Other Event” (OE) will be submitted to the IRB and internal documentation will be filed appropriately.

10. REFERENCES

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