1) Protocol Title

Use of embrace device after cutaneous wound closure: a randomized evaluator blinded split wound comparative effectiveness trial

2) Author of Protocol

X UC Davis Researcher
☐ Researcher from other institution
☐ Private Sponsor
☐ Cooperative Group
☐ Other: _____

3) IRB Review History

N/A

4) Objectives

The purpose of this study is to determine whether the use of the embrace device after repair of linear cutaneous surgery wounds improves scar cosmesis. We will use a split wound model, half of the wound is treated with the embrace device and the other half is not treated. Three-months post-surgery, the scar will be measured via the physician observer scar assessment scale, a validated scar instrument. The scar width and adverse events will also be recorded.

5) Background

Following the surgical repair of cutaneous wounds, scar formation is inevitable and results in varying degrees of aesthetic and/or functional impairment. Numerous treatment modalities have been employed to treat scars. Carbon dioxide and pulse dye lasers, as well as dermabrasion can reduce erythema and irregular topology of the scar surface[1,2]. Silicone-based products have also been used to treat post-surgical scars, including gels, sheets, and tape[3–5]. Intralesional steroids are often injected into to induce flattening of a scar[6]. More recent research has highlighted the impact of mechanical forces and tension on scar formation. In one report, incisions in both pigs and humans were treated with a tension-shielding device and showed a reduction in scarring[7]. More recently two clinical trials have been published in the plastic surgery literature showing that the use of the embrace device, a silicone-based dressing designed to minimize wound tension, is effective in improving the aesthetic outcome following scar revision surgery[8,9]. While these initial studies of the embrace device have promising findings, there are significant drawbacks to both studies including small study population, inclusion of patients seeking scar revision (a select group likely predisposed to poor scar cosmesis and not representative of first-time surgical patients), investigator conflict of

interest, and the use of a digital software-based scar assessment tool using patients photos that were not standardized with respect to lighting or distance. Therefore, larger studies in first-time surgical patients with standardized photos for scar assessment are required to validate this potentially promising device for improved scar cosmesis.

6) Inclusion and Exclusion Criteria

All patients scheduled for cutaneous surgical procedures with one of the study investigators at the UC Davis Department of Dermatology will be screened for eligibility.

Inclusion Criteria:

- 18 years of age or older
- Wound defect diameter of at least 1cm on the face and 1.5cm on the body
- Able to give informed consent themselves
- Patient scheduled for cutaneous surgical procedure along a non-concave surface suitable to application of the embrace with predicted primary closure over a high tension area
- Able to apply dressings themselves or have someone else apply it for them
- Willing to return for follow up visits.

Exclusion Criteria:

- Cognitively Impaired
- Incarceration
- Under 18 years of age
- Wounds with predicted closure length less than 3 cm
- Wounds that are less than 1cm in diameter on the face and 1.5cm on the body
- Patients with known adverse reactions to adhesives
- Patients with history of collagen vascular disease

None of these special populations will be included: adults who are unable to consent, individuals who are not yet adults (under the age of 18), or prisoners.

7) Number of Subjects

a) Study- Wide:

This is a single center study; see below.

b) Local*:* We will enroll 50 patients locally in this single center study.

8) Recruitment Methods

a) Study-Wide:

Patients will be recruited from the investigators surgical practices at the time of the procedure at the University of California, Davis, Dept. of Dermatology.

The surgical schedule will be examined to identify potential study subjects. Faculty will be reminded about the study through a flier posted in the doctors charting lounges (Attached).

The patients name, age, gender, medical record number, operative and follow up images and phone number will be recorded in the Redcap data system to allow study personnel to contact patients to arrange their follow up visits. Information will be deleted from the redcap system after 3 years. HIPPA authorization will be obtained from each patient.

9) Compensation to the Subjects

No compensation provided to study subjects.

10) Study Timelines

The duration of an individual subject's participation in the study is 3-12 months.

The duration anticipated to enroll all study subjects is 12 months and the estimated date for the investigators to complete this study (to complete primary analyses) is 12 months.

11) Study Endpoints

Describe the primary and secondary study endpoints.

The primary endpoint will be the two blinded reviewers sum of the component parts of the patient observer assessment score(POSAS) at a three-month assessment visit.

The secondary endpoint will include the width of the scar at the follow-up, patient POSAS sum score, POSAS overall opinion scores for both the observers and the patient, and any complications from the treatment.

Describe any primary or secondary safety endpoints.

Cutaneous surgery is a very low risk procedure. No deaths have ever been observed in our department, minor infections occur at rates of < 3% and

bleeding and dehiscence at much lower rates still. All adverse events will be recorded, and monitored. Serious adverse events will be reported, though none are expected.

12) Procedures Involved

a) Describe and explain the study design.

This is a single center, randomized, evaluator blind, split scar study.

Provide a description of all research procedures being performed and when they are performed, including procedures being performed to monitor subjects for safety or minimize risks.

After screening and informed consent, demographic data will be collected including date of birth, race, gender and medical record number. This will be collected in the redcap database.

Each half of the wound will be labelled with an A or a B. A horizontal wound will be labelled A on the left half and B on the right half. A vertical wound will be labelled A on the upper half and B on the lower half. The patient's wound will be labeled A if it is on the left or superior side of the investigator and B if it is on the right or inferior side. The wound will be labeled before the wound suturing so the wound healing can be effectively determined. The wound is labelled using a surgical marker. Subcuticular sutures (either vicryl or pds, depending on surgeon's preference) will be placed equally on both halves of the wound and 5-0 fast absorbing gut epidermal sutures will be placed equally on both halves of the wound. After the sutures are placed, a predetermined, concealed randomization number will be obtained from the RedCap randomization module, which will specify how side A is to be treated. This randomization number is computer generated. Side B will be treated the opposite way as A. Post-operative digital images will then be obtained; these may be used in scientific talks and/or for publication purposes. Treatment assignment, wound length, demographic data, and digital images will be recorded within the redcap database.

Patients will be taught how to apply the embrace device at the initial study visit. We will also ask that patients watch a short youtube video found at youtube.com/EmbraceScarTherapy prior to initial self application. Following the subcuticular sutures placement, patients will receive a phone call from study personnel to assess the wound for an infection. 10-14 days after the procedure study personnel will conduct a phone call and conduct a questionnaire to assess the status of your wound. If study subjects indicate they have redness beyond the immediate wound edge, pus, or pain at the wound site and an infection is suspected the study subject will be scheduled for a visit to assess the wound and will be

withdrawn from the study if an infection is present. If the wound is healing properly, then subjects will be told to begin using the Embrace device, and to allow the device to remain in place for 10 days. Patients will replace the device every 10 days for 3 months.

Follow-up assessment will be scheduled for three months following the procedure, with a one-month window before or after that time if the patient cannot return at precisely three months.

At the follow-up visit, two blinded observers will record their scores independently using the physician observer scar assessment score instrument (POSAS). The width of the scar on both sides will also be measured and recorded 1 cm from midline on both sides of the scar. The patient part of the instrument will be independently recorded and a copy of the patient (POSAS patient scale) questionnaire has been uploaded to IRBnet. This data will be recorded in the redcap database. The scoring will be of the participant's wound on the day of the follow-up. Digital images will then be obtained again, which may be used for scientific meeting presentation and/or publication purposes. These images will be stored for a maximum of two years following study completion.

Describe:

- *Procedures performed to lessen the probability or magnitude of risks.*

All adverse events will be monitored and recorded. Safety precautions will be the same as for all patients undergoing cutaneous procedures. Patients will be given instructions to call in the event of any complications such as bleeding, infection, pain or any concerns. An on call resident will be available by phone at all hours, every day of the week. Instructions for contacting the on call resident will be given in written form as well.

- *All drugs and devices used in the research and the purpose of their use, and their regulatory approval status.*

The embrace device (FDA Cleared) will be used to cover half of each surgical wounds.

- *The source records that will be used to collect data about subjects. (Attach all surveys, scripts, and data collection forms.)*

We will collect all data, demographic and scientific, in the redcap data collection system. The patient will be queried for demographic data verbally or the patient chart will be examined within the EMR to obtain the date of birth, race, gender, date of surgery, date of follow-up, name,

medical record number, and surgery location. All other data will be recorded from assessments during study evaluation.

- *What data will be collected including long-term follow-up.*

POSAS scores, width of the scar at follow-up, digital images, occurrence of any complications including: spitting sutures, dehiscence, infection, necrosis, bleeding, and hematoma.

- *Describe how much blood is being drawn and how often*

NA

b) Humanitarian Use Device (HUD)

For HUD uses provide a description of the device, a summary of how you propose to use the device, including a description of any screening procedures, the HUD procedure, and any patient follow-up visits, tests or procedures.

NA

13) Data and Specimen Banking

If data or specimens will be banked for future use, describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens.

NA

List the data to be stored or associated with each specimen.

NA

Describe the procedures to release data or specimens, including: the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.

NA

14) Data Management and Confidentiality

Describe the data analysis plan, including any statistical procedures.

Standard data quality control will be conducted and descriptive statistics will be computed. Paired t-test will be performed for POSAS scores. For analysis of complications McNemar test will be used. Since we have one primary outcome and interim analyses will not be performed, we will not adjust our analysis (e.g., confidence interval and p-value) for multiple comparisons and interim looks.

Provide a power analysis.

Using PS software (http://biostat.mc.vanderbilt.edu/wiki/Main/PowerSampleSize), we calculated we would need to enroll 50 patients using a split scar model to detect a difference in 3 points on the 60 point POSAS scale with the following assumptions: alpha of 0.05, beta of 0.20 (so 80% power), and standard deviation of 7 (based upon split scar study performed using embrace device by Longaker et al, using a conservative estimate; personal communication), dropout rate of 10%, targeting at ≥45 patients in the statistical analysis of the primary outcome.

Describe the steps that will be taken secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission.

Redcap database will be used to record all data. It is maintained by the University of California, Davis and encrypted. Passwords for access will not be shared. For analysis, data will only be downloaded without personal identifiers and transferred to an independent statistician at CTSC.

Describe any procedures that will be used for quality control of collected data.

Questions in the data collection forms will have warning text that will appear if users attempt to close them without recording the required data.

a.) Study-Wide:

Describe how data and specimens will be handled study-wide:

NA. Study is single center only.

- *What information will be included in that data or associated with the specimens?*
- *Where and how data or specimens will be stored?*
- *How long the data or specimens will be stored?*
- *Who will have access to the data or specimens?*
- *Who is responsible for receipt or transmission of the data or specimens?*
- *How data and specimens will be transported?*

b.) Local

Describe the local procedures for maintenance of confidentiality.

- *Where and how data or specimens will be stored locally?*

Consent forms will be stored in a locked cabinet. All other study related information will be recorded in the redcap data system.

- *How long the data or specimens will be stored locally?*

3 years.

- *Who will have access to the data or specimens locally?*

Only those listed in the study protocol. A statistician will view de-identified data after collection for analysis purposes.

- *Who is responsible for receipt or transmission of the data or specimens locally?*

The principal investigator; Daniel Eisen, MD

- *How data and specimens will be transported locally?*

Data will only be downloaded onto encrypted computers directly from the redcap database and only when necessary for study administration or data analysis.

15) Provisions to Monitor the Data to Ensure the Safety of Subjects

This is required when research involves more than Minimal Risk to subjects.

The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor.

Describe:

- *The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.*

Risks from this study are minimal. All adverse events (reportable and unanticipated) will be monitored and recorded. Study personnel will immediately share all adverse events with the principal investigator.

- *What data are reviewed, including safety data, untoward events, and efficacy data.*

Only safety data will be reviewed. Efficacy data will be determined after study follow up is completed since this study concerns non-life threatening outcomes.

- *How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).*

Safety information will be collected within the redcap database.

- *The frequency of data collection, including when safety data collection starts.*

Safety data collection begins immediately following the procedure. Patients will be instructed to call immediately with any complications from their procedures. Patients will also be queried at follow up (3 months) regarding complications in case they fail to call and are treated by an outside physician.

- *Who will review the data.*

The principal investigator and study personnel will review the data.

- *The frequency or periodicity of review of cumulative data.*

The study investigator will review safety data weekly after enrollment. But interim analyses of outcomes data are not performed.

- *The statistical tests for analyzing the safety data to determine whether harm is occurring.*

The intervention in this study is low risk and has been studied in two prior clinical trials without any? adverse events. Serious adverse events are not expected. Typically if one occurs, it affects both sides of the wound in the form of infection, bleeding, or dehiscence. If the adverse event is localizable to a single site, it will be recorded as such and the results (e.g., all safety-related data) analyzed after study completion and reported in publication. No hospital admissions have occurred following studies of similar design by our group at this University.

- *Any conditions that trigger an immediate suspension of the research.*

Any serious complication, such as hospital admission for treatment related to the procedure, will trigger cessation of recruitment, until study personnel meet and determine it is safe to continue enrolling patients.

16) Withdrawal of Subjects

Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent.

None

Describe any procedures for orderly termination.

For subjects that do not want to continue to participate in the study, they may do so by informing us by phone, in person or by email. There is no risk for patients in early study termination.

Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.

If patients change their mind about participation prior to or during their procedure, they will receive instructions to care for the wound that is the current Standard? of care. No data collection will occur in the future.

17) Risks to Subjects

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include as may be useful for the IRB's consideration, describe the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks.

The primary risk of participating is that one side of the wound may look different than the other. The author has thus far conducted 5 split scar studies and none of the participants from these trials has requested revision of the scar based upon differences in appearance of the two halves. Typically, differences are not extreme in individuals. Other risks are the same for every cutaneous surgical procedure regardless of study enrollment: infection, bleeding, dehiscence, 100% chance of scar. Risks of bleeding and infection are less than 3% in our facility and typically minor in nature.

If applicable, indicate which procedures may have risks to the subjects that are currently unforeseeable.

The study intervention is commonly performed. Though unforeseeable risks are always possible, they are not probable here.

If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant.

NA

If applicable, describe risks to others who are not subjects.

NA

18) Potential Benefits to Subjects

Describe the potential benefits that individual subjects may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits.

Indicate if there is no direct benefit. Do not include benefits to society or others.

No direct benefit to individual subjects.

19) Vulnerable Populations

If the research involves individuals who are vulnerable to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

NA

20) Multi-Site Research

NA

21) Community-Based Participatory Research

NA

22) Sharing of Results with Subjects

Results of the study participants own outcome measurements will be shared with patient verbally if they request.

23) Setting

Approximately 30 patients undergo cutaneous surgeries every week in our center. We should easily be able to recruit our required number within 3 months.

The principle investigator and procedural dermatology fellow will recruit and treat patients continuously five days a week.

Outpatient, dermatologic surgery facility with 6 procedure rooms, and more than a dozen nursing staff.

No psychological support is likely necessary for those undergoing the procedure. Medical help is available in the event of a complication from 7:30 AM- 5 PM Monday-Friday. An on call resident is available for all times the clinic is not available and patients may also visit the Emergency Department.

A pre-enrollment meeting will occur where the protocol is carefully explained. We will print algorithms for study personnel. They may additionally refer to redcap database where the questions will guide them through data capture and the procedure. We will also have a lab

practicing the procedure on a simulated patient mannequin designed for teaching cutaneous surgical procedures.

Patients will be recruited from the University of California, Davis Department of Dermatology cutaneous surgery practices: 3301 C St, #1400, Sacramento, CA 95816; 77 Cadillac Dr., Sacramento, CA 95825; 1370 Prairie City Road, Folsom, CA 95825.

Research procedures will be performed at the University of California, Davis Department of Dermatology cutaneous surgery practices. 3301 C St, #1400, Sacramento, CA 95816; 77 Cadillac Dr., Sacramento, CA 95825; 1370 Prairie City Road, Folsom, CA 95825.

24) Resources Available

Principle Investigator- Daniel Eisen Board Certified Dermatologist with fellowship training in cutaneous surgery. Will recruit, enroll, evaluate study subjects and oversee study.

Co-Investigator- Jayne Joo Board Certified Dermatologist: will recruit, enroll, and evaluate study subjects.

Board certified dermatologists with fellowship training in cutaneous surgery: will recruit, enroll, and evaluate study subjects.

Board certified dermatologists: will recruit, enroll, and evaluate study subjects.

Dermatology residents: will recruit, enroll, and evaluate study subjects.

Study coordinator: Iryna Rybak will correspond with IRB, perform audits of consent forms, and handle administrative requirements of study

25) Prior Approvals

NA

26) Provisions to Protect the Privacy Interests of Subjects

Only study personnel and nurses normally present during cutaneous procedures and follow-ups will be present. Personal information will be obtained just once at study recruitment. It will not be required at follow up.

Examination of the wound will not differ significantly in practice from standard medical care, during which a faculty member and resident and nurse typically participate in the patients care. In this situation, the number of interactions will be the same or less, since only two study investigators will be required. Medical students will not participate in study patient follow-up evaluation.

Indicate how the research team is permitted to access any sources of information about the subjects.

Access to study information will be permitted only for data entry and for study monitoring. Study staff will be requested to only access this information for these purposes only.

27) Compensation for Research-Related Injury

If the research involves more than Minimal Risk to subjects, describe the available compensation in the event of research related injury.

No compensation will be provided.

Economic Burden to Subjects

No additional cost to participate in the study will be incurred.

28) Consent Process

We will obtain written informed consent from all subjects. Study personnel will be obtaining consent in person at the Dermatology departments at: 3301 C St, #1400, Sacramento, CA 95816; 77 Cadillac Dr., Sacramento, CA 95825; 1370 Prairie City Road, Folsom, CA 95825 Patients will be given as much time as they like to consider enrolling.

We will review the consent form binder once a month to ascertain signatures on the consent and HIPAA forms. The study coordinator, Lam Nguyen will review the binder independently at routine intervals.

Our experience from past studies indicates it takes less than 5 minutes to explain the study. The subject will be allowed to take as much time as they like to read the forms, ask questions or consider participation.

We will inform the subject that enrollment is optional and that we will treat them without bias and with all the quality that they should normally expect outside of study participation.

Subjects will be asked if they understand the study and if they have any questions.

We will not enroll anyone who does not understand written or verbal English. The vast majority of our cutaneous surgical population is English speaking.

Waiver or Alteration of the Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

NA

Subjects who are not yet adults (infants, children, teenagers)

NA

Cognitively Impaired Adults

NA

Adults Unable to Consent

NA

Adults Unable to Consent

NA

For HUD uses provide a description of how the patient will be informed of the potential risks and benefits of the HUD and any procedures associated with its use.

29) Process to Document Consent in Writing

We will follow *"SOP: Written Documentation of Consent (HRP-091)"*

30) Drugs or Devices

NA

References

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3. Maher SF, Dorko L, Saliga S. Linear scar reduction using silicone gel sheets in individuals with normal healing. J Wound Care [Internet] 2012 [cited 2016 Feb 24];21(12):602, 604–6, 608–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23299270

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9. Longaker MT, Rohrich RJ, Greenberg L, et al. A randomized controlled trial of the embrace advanced scar therapy device to reduce incisional scar formation. Plast Reconstr Surg [Internet] 2014 [cited 2016 Feb 24];134(3):536–46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24804638