Efficacy of Laser Debridement on Pain and Bacterial Load in Chronic Wounds (NCT03182582)

Study Protocol

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PROTOCOL SYNOPSIS

Title	The assessment of bio-burden reduction and procedural pain after chronic ulcer debridement.
Sponsor	Sciton, Inc. 925 Commercial Street, Palo Alto, CA 94303 650-493-9155
Clinical site	Stanford Advanced Wound Care Center 450 Broadway Street, Redwood City, CA 94063 650-721-8800
Rationale	Chronic ulcers are a significant source of morbidity and pain. Biofilms are present in all chronic ulcer types. Additional methods for safe, effective, and tolerable chronic ulcer bed debridement are needed.
Study design	Randomized-controlled cross over, open label study
Primary objective	To determine the efficacy of the reduction of bioburden in chronic ulcers after laser and sharp debridement.
Secondary objectives	To determine the tolerability of laser and sharp debridement of chronic ulcers.
Number of subjects	Twenty
Subject selection inclusion criteria	• Aged eighteen years or older • Having a non-healing chronic ulcer of any etiology present for at least four weeks • Willing and able to adhere to protocol requirements • Signed Informed Consent Form prior to any study related procedure
Subject selection exclusion criteria	• Any unstable medical condition • Documented medical history of any significant disease or condition • Documented medical history of immunosuppression • Receiving dialysis • Having osteomyelitis • Pregnancy • Participation in another clinical study involving ulcers within thirty days prior to enrollment
Control treatment	Sharp (scalpel or curette) debridement with standard of care
Test treatment	Laser debridement with standard of care
Duration of subject participation	Subjects will be enrolled in the study for two weeks
Duration of study	The total duration of the study is expected to be six weeks. Recruitment and enrollment: up to four weeks Treatment: two weeks
Prohibited concomitant medications	Current topical or systemic antibiotic therapy
Efficacy evaluations	Significant bioburden reduction as determined by quantitative polymerase chain reaction (PCR) analysis after the debridement procedures.

Primary endpoint	Comparison of the two treatment modalities to reduce bioburden as determined by quantitative polymerase chain reaction (PCR) analysis, DNA sequencing.
Secondary endpoint	Comparison of the procedural pain from the two treatment modalities as determined by subject reported visual analog scale (VAS) pain scores. Comparison of the procedural bleeding from the two treatment modalities as determined by physician assessment. Procedural bleeding
Other evaluations	Overall subject satisfaction from the two treatment modalities.
Safety evaluations	Incidence of adverse events.
Planned interim analysis	Serious adverse events will be audited by the study team on an ongoing basis throughout the study duration.
Primary statistical analysis plan	Treatment effectiveness will be assessed by a two-sample t-test comparing the evaluation criterion at the two study intervals.
Rationale for number of subjects	This is a pilot study to determine treatment feasibility and efficacy.

SUBJECT INCLUSION CRITERIA

A subject will be eligible for inclusion in this study if ALL of the following criteria apply:

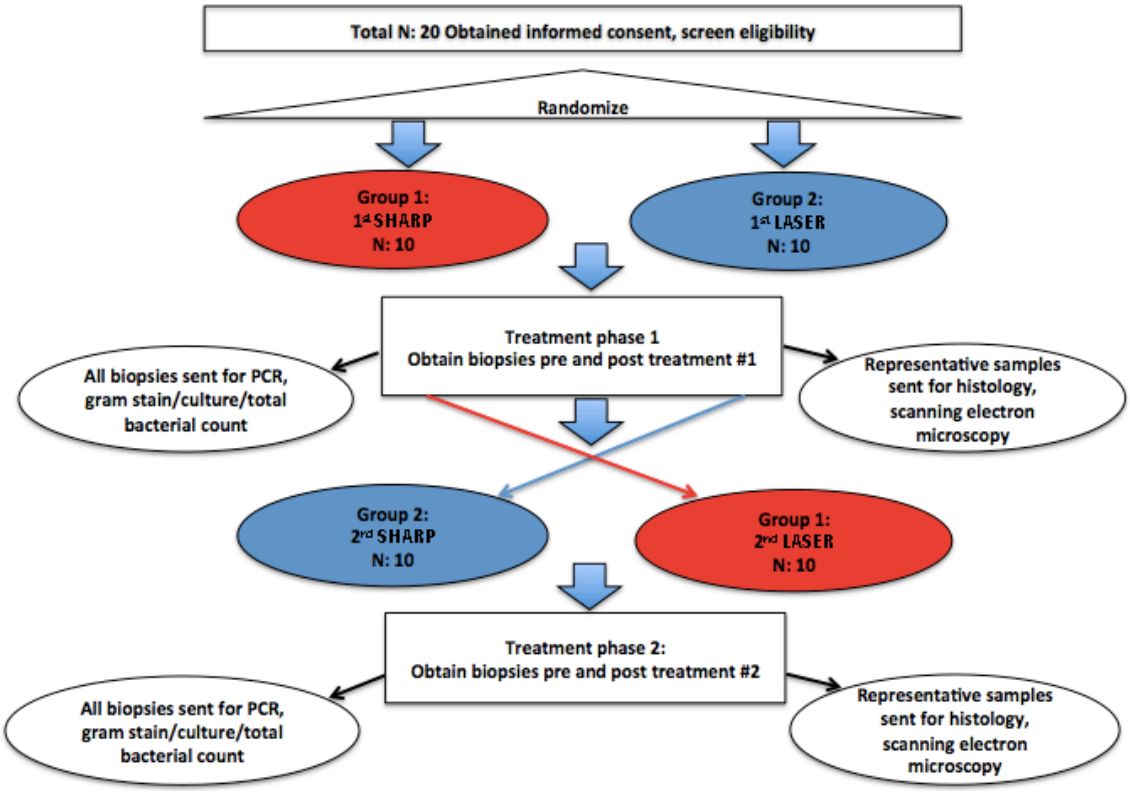
- Aged eighteen years or older
- Having an ulcer of any etiology
- Has signed the informed consent form prior to any study protocol related procedure
- Willing and able to adhere to protocol requirements

SUBJECT EXCLUSION CRITERIA

The subject will not be eligible for study inclusion if ANY of the following criteria apply:

- Any unstable medical condition that would cause the study treatment to be detrimental to the subject, as judged by the Principle Investigator
- Documented medical history of significant cardiac, pulmonary, gastrointestinal, endocrine (*other than Diabetes Mellitus type 1 or 2*), metabolic, neurological, hepatic or nephrologic disease would impede the subject's participation, as judged by the Principle Investigator
- Documented medical history of immunosuppression, immune deficiency disorder, or currently using immunosuppressive medications
- Having clinical presentation of active osteomyelitis
- Pregnancy or lactation
- Participation in another clinical study involving ulcers within thirty days prior to enrollment

STUDY DESIGN



ULCER DEBRIDEMENT

Multiple methods can be used for ulcer debridement, however evidence supporting a superior method is still lacking. Sharp debridement uses scalpel, scissors, curette, or other instruments to remove the necrotic tissue. Sharp debridement is the current standard of care, and produces rapid results. The major drawbacks of sharp debridement include the lack of a uniform technique and the potential for bacterial cross contamination. Sharp debridement may also result in bleeding or damage to underlying tissue structures.

The method of laser debridement is based upon the well-established efficacy of laser skin resurfacing utilized in dermatology and plastic surgery. The laser energy will provide controlled vaporization of the superficial layers of the ulcer bed. The potential advantages of laser debridement include precision and uniformity of tissue ablation, reduced trauma to the ulcer bed, improved patient comfort, enhanced biofilm clearance, and promotion of ulcer healing. Anecdotally, laser debridement has shown a decrease in procedural pain scores, thereby facilitating a more complete debridement.

Ulcers will be treated with a fully ablative erbium-doped yttrium aluminum garnet (erbium) laser treatment. The erbium laser system (Sciton, Inc.) has the FDA clearance for use in surgical applications requiring the excision, incision, ablation, vaporization, and coagulation of soft tissue.

The laser system is comprised of five interconnected components:

1. Laser Console - The laser console is connected to the footswitch, the articulated arm, and the user screen. The laser console houses the laser and the power supply.
2. Footswitch - The footswitch is connected to the laser console. Footswitch depression by the clinician enables laser energy delivery.
3. Articulated Arm - The articulated arm is connected to the laser console and the handpiece. The articulated arm rotates and is used to deliver the laser energy.
4. Handpiece - The handpiece is connected to the articulated arm, and steers the pattern of energy onto the patient.
5. User Screen - The user screen is connected to the console, and serves as an interface to allow the clinician to select different laser applications or laser treatment parameters.

The laser provides precise control over the depth of ablation per pass, ranging from twenty five to two hundred microns. Ablation depth is tunable in twenty five-micron increments. The laser system handpiece allows the laser beam to be scanned to form two-dimensional spots onto the pattern size. The range of the pattern size is 0.64 - 9.00 centimeters squared. The handpiece scanner provides complete and uniform application of the laser energy. This application will cover forty percent of the surface within the scanned pattern. An aiming beam, displayed as a red square on the intended treatment surface, allows the clinician to visualize the treatment area. The laser energy will be delivered inside this red square. The adjoining scans will be delivered without gaps or overlaps to ensure even treatment.

Protective eye shields to safeguard against laser light exposures will be provided to the subjects and personnel in treatment room. The eye shields will remain in place until after the completion of the laser treatment. The thermal destruction of tissue creates a smoke by-product. A smoke evacuator attached to the laser handpiece will immediately remove any smoke generated throughout the laser treatment. This removal will prevent the smoke and debris from irritating the ulcer bed.

Laser ablation will be continued until the slough tissue is completely removed. Patient pain and pinpoint bleeding will represent the clinical endpoint of laser debridement. Pinpoint bleeding signifies the laser energy approaching the healthy underlying tissue. Laser debridement will be administered to only slough tissue and ulcer edges. Healthy granulation tissue in the ulcer bed will not be laser treated. After the completion of the laser debridement procedure, sterile gauze will be used to gently clean the ulcer bed to remove any remaining debris.

STUDY SCHEDULE

<u>Screening and Enrollment (Study Week One):</u>

- Obtain signed Informed Consent Form
- Review medical history to determine eligibility
- Perform medical examinations needed to determine eligibility

- Collect ulcer measurements and photos
- Randomize patients to treatment groups
- Provide subjects instructions needed for study participation
- Immediately proceed to the Treatment

Treatment (Study Week One):

1. Before debridement procedure:
    - Record VAS pain score, Present Pain Intensity, and Brief Pain Inventory
    - Collect ulcer photos and measurements
    - Collect biopsies
2. Apply anesthetic
3. Perform debridement procedure
    - Record technique or laser settings used during treatment
4. After debridement procedure:
    - Collect ulcer photos
    - Record VAS pain score, Present Pain Intensity, and Brief Pain Inventory
    - Record bleeding assessment
    - Collect biopsies
    - Provide Standard of Care

Follow Up Visit (Study Week Two):

- Subjects cross over to other study group
- Remove ulcer dressing

1. Before debridement procedure:
    - Record VAS pain score, Present Pain Intensity, and Brief Pain Inventory
    - Collect ulcer photos and measurements
    - Collect biopsies
2. Apply anesthetic
3. Perform debridement procedure
    - Record technique or laser settings used during treatment
4. After debridement procedure:
    - Collect ulcer photos
    - Record VAS pain score, Present Pain Intensity, and Brief Pain Inventory
    - Record bleeding assessment
    - Collect biopsies
    - Provide Standard of Care