Study Title: Efficacy of 1540nm Erbium glass laser to improve benign dermatofibromas

Principal Investigator: Karen Stolman, MD

Sponsor: University of Utah Dermatology Department

Blinded Photography Assessors: Michael Milliken, MD and David Smart, MD

NCT #: 03392935

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BACKGROUND:
Dermatofibromas are benign histiocytic fibrous nodules that arise in the skin, and are reported more often seen on the legs and in women. These nodules can be itchy, painful and unattractive with discoloration or textural irregularities.

Prior to use of lasers to treat dermatofibromas, dermatologists have tried to treat these nodules with liquid nitrogen and intralesional Kenalog injections but both these options are considered less than ideal and pose significant risks for worsening the lesions. In addition, dermatofibromas can be excised, but excision guarantees a scar, and surgical leg wounds and scars in adult women are often compromised in their healing by circulation issues.

There are case reports of improvement of dermatofibromas with other lasers such as the pulsed-dye laser and the CO2 laser (see attachments), but no clinical studies using laser treatment. In addition, the non-ablative Erbium glass laser is a generally safer laser being non-ablative and is being more widely used in medical and cosmetic dermatology practices as it can be operated in most states (in the U.S.) by supervised P.A. or Aestheticians. It would be helpful to have a treatment option that can be so widely used.

PURPOSE & OBJECTIVES

The main objective of this study is to find a more effective treatment for itchy, painful or unsightly dermatofibromas, that will improve symptoms of itch and/or pain and/or improve the appearance of dermatofibromas. A secondary objective of this study is to better understand the 1540nm Erbium glass laser and its impact on the skin.

STATISTICAL CONSIDERATIONS
Data Analysis: Two dermatologists will review all de-identified photos, and will rate them on a color, texture improvement scale as shown in the attached questionnaires. We expect to recruit about 40 patients during the study period. Some of patients will have more than one dermatofibroma treated. Descriptive analyses will be performed to summarize the distribution of dermatofibroma symptoms and appearance at baseline. The primary analysis in this study is to test whether the laser treatment is significantly associated with color and texture improvement. We will use a one-sided, one-sample Wilcoxon signed rank test to determine whether the color and texture improvement is significant at two visits (i.e. visits #4 and #5) after 2 treatments. Furthermore, we will employ two-sided one-sample Wilcoxon signed rank test to examine the change in items in dermatofibroma symptom questionnaire after laser treatment. As an alternative approach, we will also employ the generalized linear mixed effect regression to evaluate the association between laser treatment and dermatofibroma symptom and appearance. All these statistical analyses will be conducted using statistical software R at the significant level of 0.05. We do not anticipate substantial missing data for the outcomes assessed since our physician will be very less likely to miss items in the survey. Even though we don't anticipate that there is a substantial amount of missing data in our study, we will still compare the characteristics of subjects with complete versus incomplete data to assess the possibility of bias due to missing. If subjects with incomplete is systematically different from those with complete data, our complete-case analysis may be biased. We will use inverse probability weighting (IPW) approach, where complete cases are weighted by the inverse of their probability of being a complete case, to correct the bias induced by missing.

Added via Addendum (17MAY2018): We increased laser settings after the 13th patient, and therefore, we are now are going to increase enrollment to 40 total subjects to demonstrate effectiveness of the laser at the higher setting. We also had more loss to follow-up patients than originally anticipated due to patients not wanting to return for follow-up visits since they were not receiving payment or treatment. Since we need more subjects to complete the trial with the higher laser settings we are increasing enrollment to 40 subjects, and we are adding the options to have the follow-up visits done remotely in hopes of increasing the number of subjects that will complete all visits.

STUDY DESIGN:
This is a Prospective, interventional, Single-Blinded, open label trial. Blinded photography outcomes assessors.

Added via Addendum (17MAY2018): Enrollment Goal: 40 patients

PARTICIPANT ELIGIBILITY
Inclusion criteria:

1. Male or Female ages 18-65
2. Must have at least one dermatofibroma of the skin, on the trunk or extremities, diagnosed by dermatologist
3. Dermatofibroma must be either itchy, painful, or unattractive to the patient.

Exclusion criteria:

1. Previous treatment to the dermatofibroma(s)
2. Pregnant or nursing women
3. A diagnosis of diabetes, psoriasis, lupus or other autoimmune diseases.
4. A current tobacco smoker
5. A history of keloids or poor wound healing.
6. Dermatofibroma lesions on the face and genitals.

Recruitment:
Participants will be recruited or identified for inclusion in the study using in-person contact, referrals, and written or electronic record review. Patients who appear to be eligible for the study will be approached during regular clinic visits by study personnel. Electronic record review may be used to find possible subjects from existing patients.

STUDY PROCEDURES:
1. Screening Visit (Visit #1): Perform Informed Consent process. Review inclusion/exclusion criteria with written questionnaire, and review post-laser treatment instruction sheet.
2. Baseline Visit/1st of 2 Laser Treatments (Visit #2): Sign SJHC laser treatment consent form, fill out dermatofibroma symptom questionnaire, take pre-treatment photos of dermatofibroma(s), perform first laser treatment.
3. Visit #3, Second Laser treatment, four weeks after first treatment. Patient will fill out dermatofibroma symptom questionnaire again. Pre-treatment photos taken of dermatofibroma(s) again. Patient will sign SJHC laser treatment consent form, perform second laser treatment.
4. Visit #4, Four weeks follow up after second laser treatment. Patient to fill out dermatofibroma symptom questionnaire, photos taken again. This visit may be completed remotely by completing the questionnaire through MyChart and uploading photos of the dermatofibroma(s) through MyChart. If

subjects are experiencing any side effects or changes to their health, they should be seen in person by the study physician.
5. Visit #5, 12 weeks follow up, 16 weeks after second laser treatment. Patient to fill out dermatofibroma symptom questionnaire, final photos taken. This visit may be completed remotely by completing the questionnaire through MyChart and uploading photos of the dermatofibroma(s) through MyChart. If subjects are experiencing any side effects or changes to their health, they should be seen in person by the study physician.

Study Procedures	Screening Visit (Visit 1)	Baseline Visit (Visit 2 – first treatment)	Visit 3 (2nd Treatment)	Visit 4 (Follow-up #1)	Visit 5 (Follow-up #2)
Week #		Week 0	Week 4	Week 8	Week 12
Informed Consent	X				
Inclusion/Exclusion Criteria Review	X				
Medical History Review	X				
Adverse Event Review		X	X	X	X
Dermatofibroma Assessment	X	X	X	X	X
Questionnaires	X	X	X	X	X
Photographs		X	X	X	X
Laser Treatment		X	X		

Data Monitoring Plan:

- Research intervention is conducted in a prive place
- Study will be discussed with patients individually
- The collection of information about participants is limited to the amount necessary to achieve the aims of the research so that no unneeded information is being collected.
- Research data will be stored on password protected computers
- Photos of participants will be stored in the patient's secure electronic medical record.
- Periodic review and confirmation of participant elegibility, informed consent documentation and conformation that appropriate information has been reported to IRB will occur annually.
- Independent Safety Monitor will review consent documentation, and adverse events after every 10 patients or every 6 months (whichever comes first).

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