Clinical Trial Protocol

Title of study: Skin Tag Removal Device; A Clinical Study to Determine Outcomes of Treating Adults with Acrochordons (Skin Tags)

NCT06463613

Date: 06/05/2025

Clinical Investigation Protocol

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Protocol: UKI-001

Sponsor: UK Innovations GP LTD

Version: 2

Date: TBD

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organization, and members of the Research Ethics Committee and Regulatory Authorities unless authorized to do so.

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Protocol signature page

The undersigned has read and understood the trial protocol detailed above and agrees to conduct the trial in compliance with the protocol.

Principal Investigator Name (Please print)	Principal Investigator Signature	Date

Protocol Section	Protocol Version 1	Protocol Version 2	Rationale
Section 3.1-3.2, 4, 6.2.1-6.2.3	Use of micro STR on 2-4 mm skin tags	Use of micro STR on approximately 4-6mm skin tags	The micro STR band has not reached the desired level of efficacy on 2-4mm skin tags per use under protocol version 1. The Sponsor recommends the use of a micro STR band to be placed on larger skin tags, 4-6mm, where they may be more effective at restricting blood flow to the skin tag and removing the tag. .
Section 6.2.4, 6.2.6	Daily eDiaries Day 1-10	Daily eDiaries at screening visit, Day 1-20	An eDiary has been added to the screening visit to capture a photo of the skin tag at the time of banding. The number of daily diaries have been extended to 20 days to allow tracking for skin tags which may fall off after day 10.
Section 6.2.4	Virtual Visit 2 window Day 5-8	Virtual Visit 2 window Day 5-9	Visit window was extended to allow for more time to conduct the visit with no impact to patient safety
Section 6.2.4	Virtual Visit 3 window Day 11-14	Virtual Visit 3 window Day 21-24	The visit was moved to one day after the last daily diary completed by participants, which is now day 20 under protocol version 2.
Section 6.2.1	6.2.1 Stratification schematic to reflect 1:1 ratio of micro:standard STR device type	6.2.1 Stratification schematic to reflect 3:1 ratio of micro:standard STR device type	Due to micro and standard devices not reaching desired level of success in removing skin tags for 2-4 and 4-6 mm, respectively, the new recruitment efforts will focus on large skin tags and use of the micro device only
Section 4	Indications for use statement per device type	General indications for use statement to be determined upon completion of the study	Indications for use have been updated to be determined upon competition of the study
Section 6.2.1	80% compliance for eDiary completion to	participant payment of $10 per eDiary completed	Participant compensation has been changed from overall compliance calculation to daily diary completion

	receive $100 payment		to increase retention & eDiary completion through Day 20
Sections 6.2.3; 6.2.6	Rebanding not permitted; participants were withdrawn if device detached prematurely.	Participants may receive up to two rebanding visits per skin tag at the site in the event of premature device detachment. Rebanding details (e.g., timing, outcome) will be captured in the eDiary.	To allow controlled reapplication of the device and preserve participant data in cases of device failure, while maintaining consistency in study execution and analysis.
Section 6.2.3	No bandage was used after device placement.	A small adhesive bandage is applied at the screening visit to cover the banded skin tag. Participants receive approximately 20 bandages and instructions for replacement as needed.	To reduce risk of premature band detachment due to friction from clothing and improve retention of the device throughout the study period.
Section 6.2.1	No guidance on re-enrollment of prior participants	Participants previously enrolled may be re-enrolled if a different, previously unbanded skin tag is selected	To allow enrollment of individuals who meet inclusion criteria and had a device failure in a prior protocol version, without compromising data integrity
Sections 6.1, 14	The observed percentage of successful removal is 80%	The observed percentage of successful removal is 60%	Updated to reflect realistic expectations of effectiveness in a real-world setting.
Section 11.2	Not included	New section on withdrawal for non-compliance (e.g. missed rebanding)	Ensures clear criteria for withdrawal tied to study adherence.

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1. SPONSOR CONTACT INFORMATION

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2. SUMMARY AND BACKGROUND INFORMATION

2.1. Skin tag background

The occurrence of potentially life-threatening malignant neoplasia in the skin has focused the public to address skin abnormalities, especially when they deviate from the skin's normal appearance. This produces an opportunity for early detection, by the patient and their physician, of potentially dangerous neoplasms such as malignant melanoma, squamous cell cancer and a long list of other rare neoplasms. However, the vast majority of skin lesions are benign, prompting many individuals to pursue options for the removal of lesions for cosmetic reasons.

Common benign skin lesions include verruca, seborrhea , keratoses, fibromas, histiocytomas (dermatofibromas), nevi and skin tags (acrochordons). A skin tag is a small outgrowth of epidermal and dermal tissue. Their size can range from one to several mm; usually flesh-colored and pedunculated (see Image 1)[1]. Skin tags are exceedingly common benign skin lesions with a reported prevalence of around 45-50% in the general population. Typically, they are small, soft, noncancerous fibromas or fibroepithelial polyps, bumps of tissue connected to the skin's surface by a narrow stalk. The color, texture, size, and width of the base can vary[2].

While the exact cause of skin tags is not known, they can be found around folds of the skin or where areas of friction from clothes occur. Elevated blood sugar and insulin are linked to higher prevalence, but the mechanism, in this case, is still unknown. Some skin tags can become irritated, the most common motivation for removing skin tags is cosmetic.

Tags can be removed by a dermatologist using excision, cauterization, or cryosurgical means, but

[1] Image from product's UK labeling
[2] My Face Aesthetics Clinic: Skin Tags

there is a growing interest in home-based methods. Some devices, such as cryo-based cauterization, have been cleared for marketing by FDA for "over-the-counter" (OTC) use and claimed acceptable removal levels.

Patients are motivated to remove skin tags, but the health care infrastructure is often less interested because skin tags are benign, and the cost of a clinical intervention can be hard to justify, regardless of the psychological impact on the patient. Skin anomalies such as skin tags may strongly affect the patient's quality of life. Even slight changes in the skin may result in adjustments to social life, relationships, and even the ability to carry out daily tasks.

Histologically, a skin tag shows localized hyperplasia of the dermis with loosely arranged collagen fibers and dilated capillaries and lymphatic vessels[3], indicating that a skin tag is softer, more elastic, and about as vascularized as the surrounding skin. The epidermis can be slightly hyperplastic.

The cellular characteristics of the skin tag are important from the point of view of removal by pressure at the base. Externally exerted pressure would result in little resistance from the tissue, and the vasculature would easily collapse. These lesions tend to be smaller. However, the presence of nevus cells and a firm connective tissue network may protect the vasculature at the base from pressure. These lesions are often larger, broader in base, and "dome-shaped" and exert more resistance to compression of the base.

The current device and study are based upon the mechanism of action that includes an occlusion of the vasculature at the base. This action results in a necrosis of the skin tag. When occlusion of the base is complete, the necrosis leads to the tag simply falling off.

2.2. Purpose of Investigative Study

The aim of this study is to investigate the safety and effectiveness of a mechanical device to remove skin tags in adults. The device utilizes the ligation method by applying a silicone band around the base of a skin tag, therefore restricting the blood supply, which is vital to its growth and survival. Because this method does not include freezing or burning of tissue in or around the skin tag, it could be considered less invasive and less risky than other options.

A clinical validation study to demonstrate the safe and effective removal of skin tags will be completed under the direction of an investigator (dermatologist or other health care professional) led protocol. This study will assess the proportion of skin tags successfully removed within a 20-day period, and to evaluate associated safety outcomes. Adult (22 years and above) subjects fitting the inclusion/exclusion criteria will be recruited, given they have one or more skin tags consistent with device labeling. All subjects entering the clinical study will have the device applied by the healthcare professional and proceed through the study, recording their experience using an electronic clinical diary to collect data.

Since this device is to be sold over-the-counter, evaluation of the subject's self-selection and label comprehension abilities will be completed under a separate Human Factors and Usability study and is therefore not required in the scope of this clinical trial.

[3] UC Davis Dermatology Online Journal

3. STUDY DEVICE NAME AND DESCRIPTION

3.1. Study Device Name: Skin Tag Remover (STR)

For this Protocol, the study device will be referred to as "Skin Tag Removal" study device or "STR" study device. There are two versions of the STR study device, automatic and manual. Each version is also manufactured in two sizes which correspond to the size of the skin tag to be removed.

Under protocol version 1, t he smaller size (to be referred to as "micro" for the remainder of this document) is designed to be used with skin tags having a base measuring between 2–4mm. The larger size (to be referred to as "standard" for the remainder of the document) is to be used with tags having a base measuring between 4–6 mm.

Under protocol version 2, the micro size band will be used on all skin tags measuring between 4-6mm. The standard size will no longer be used and skin tags measuring between 2-4mm will not be enrolled.

Product labeling has a helpful guide for determining size of band to use. All four versions function in the same manner by placing a band at the base of the skin tag, therefore, this document will collectively refer to all four iterations of the study device as "STR."

3.2. General Description of Study Device

The STR study devices are designed for the removal of skin tags from the body by ligation of the blood supply to the skin tag through the application of a small elastic band. Bands are placed around the base of the skin tag by using an applicator, which pushes the band from a cylindrical extension on the device over the skin tag and to the base of the tag.

The study device(s) are available in two different sizes to ensure the bands being used are tight enough to restrict the blood supply for skin tags that vary in size[4].

- Under protocol version 1: The micro version of the STR study device has been designed to remove skin tags that measure 2-4mm at the base, and the standard version is designed to remove skin tags that measure 4-6mm at their base. When determining band size, it is suggested to use the smaller (micro) device for tags that are in-between micro and standard for best results.

- Under protocol version 2: Tthe micro size will be used on skin tags that measure 4-6mm at their base. The standard size will not be used. Additional Skin tags measuring 2-4mm will not be enrolled.

[4] Image from product's UK labeling

For general information about this device, currently sold in the UK, please reference https://tagband.co.uk.

3.2.1. Device Kit Description

The STR study device(s) for this study are provided in kits containing:

- STR study device
- Band loader
- Ten (10) bands
- Isopropyl alcohol (70%) cleansing swabs (4) – used to cleanse the skin tag and surrounding area before applying the band

In addition to the study device kits, the site will receive packages of ~30 bandages for each skin tag expected to be included in this study. These bandages will be provided to the participant at their in-clinic Baseline Visit.

4. INDICATIONS FOR USE STATEMENT

Micro Versions - Manual and Automatic*:* The STR device is indicated for the OTC treatment/ removal of skin tags with a diameter of 2-6 mm at the base. Use of the device will be restricted from skin tags in sensitive areas of the body such as on eyelids, near the eye, or in the groin area. The STR device is for use by adults 22 years of age or older. Micro Versions will now be used on all skin tags with a diameter of 4-6mm at the base under protocol version 2. Skin tags measuring 2-4mm will no longer be enrolled.

Standard Versions - Manual and Automatic*:* The STR device is indicated for the OTC treatment/ removal of skin tags with a diameter of 4-6mm at the base. Use of the device will be restricted from skin tags in sensitive areas of the body such as on eyelids, near the eye or the groin area. It is for use by adults 22 years of age or older. Standard versions will not be used under protocol version 2.

The statements above were only the intended Indications For Use of the STR Device.

Instructions For Use documents are provided to the Investigator for each study device and size.

5. REPORT OF PRIOR TESTING

The STR study device has been designed and manufactured following ISO13485 Quality Management. Sponsor management has implemented a Quality Management System during the design of the device and followed it through manufacturing. Failure modes for design/production (DFMEA and

PFMEA) processes have been completed and evaluated and are a part of the Design History File (DHF).

In preparation for clinical testing, the STR study devices have completed testing regimens to document conformity to normalized standards, including ISO-10993 Biocompatibility. Biological testing for this device was completed in 2022 and a Biological Evaluation Report is available for review by contacting the Sponsor.

6. INVESTIGATIONAL PLAN

The Sponsor has developed the following investigational plan to clinically evaluate the safety and efficacy of the STR study device to remove skin tags from adult participants.

6.1. Purpose and Study Arms

This pivotal investigational study is designed to evaluate the safety and efficacy of a skin tag removal (STR) study device. This is a non-significant risk interventional clinical study that will be conducted by a Clinical Research Organization (CRO) with a licensed dermatologist(s) to serve as Principal Investigator. There are two arms of the study that are only differentiated by the type of STR study device used; arm 1 will be conducted using the manual version, and arm 2 will use the automatic version.

After consultation with the FDA, the Sponsor has modified the original protocol to include the following changes:

- Exclusion of all skin tags located around the eye, on the eyelid, or the groin area (6.2.1)
- Clarification of covered medical expenses while enrolled in the study (6.2.4)
- Protocol includes updated exclusion conditions (excluding those with known hypertrophic scarring or keloid scarring)
- Protocol includes the addition of an electronic daily diary for all participants
- A study was conducted to power the investigation for biostatistical relevance properly (please see the report in the Reference section). The conditions for power analysis were:
    - The primary endpoint is the removal of the skin tag (effectiveness)
    - The observed percentage of successful removal is 60%; i.e. 60% of the skin tags treated are expected to be successfully removed with use of the device
    - A 95% Confidence Interval (CI) was used to determine the number of subjects necessary for participation

Determination: if a successful clinical trial is established at 60% of treated skin tags removed, a study powered with 200 treated tags will have a 95% confidence interval of 5.5%

The power analysis determined that the sponsor should enroll enough subjects to treat a total of 200 skin tags. Typically, patients seeking skin tag removal have from 1 to 5 tags that could be treated for removal, however, for this study, only a maximum of 2 tags per person will be treated. Therefore, the number of tags for intention to treat (ITT) in each arm is 100 for a study total of 200 tags. This approach will ensure that the study has been powered to a 95% confidence interval of 5.5%.

Approximately two thirds of the subjects in each arm are to receive micro bands (2-6 mm skin tags treated), while the other one third is to receive standard size bands (4-6mm size skin tags treated). The PI will manage the number of treated skin tags such that a variety of locations on the body (face, neck, arms, and torso) are represented in the study.

Under Protocol Version 1:

Arms	Assigned Interventions
Arm 1 – Manual Version Goal: successful removal of 60% of the skin tags treated with the STR device. Subjects will have up to two (2) tags treated, therefore, 50-100 subjects are anticipated for this arm. A total of 100 skin tags is the ITT (intention to treat).	*Subject treatment data collected on:* ● Band size; 2-4mm (micro), or 4-6mm (standard) ● Subject pool divided ~equally by band size ● All skin tags will be banded by a healthcare professional
Arm 2 – Auto Version Goal: successful removal of 60% of the skin tags treated with the STR device. Subjects will have up to two (2) tags treated, therefore, 50-100 subjects are anticipated for this arm. A total of 100 skin tags is the ITT (intention to treat).	*Subject treatment data collected on:* ● Band size; 2-4mm (micro), or 4-6mm (standard) ● Subject pool divided ~equally by band size ● All skin tags will be banded by a healthcare professional

Under Protocol Version 2:

Arms	Assigned Interventions
Arm 1 – Manual Version Goal: successful removal of 60% of the skin tags treated with the STR device. Subjects will have up to two (2) tags treated, therefore, 50-100 subjects are anticipated for this arm. A total of 100 skin tags is the ITT (intention to treat).	Subject treatment data collected on: ● Tag size; 4-6 mm (micro band) ● All skin tags will be banded by a healthcare professional

Arm 2 – Auto Version Goal: successful removal of 60% of the skin tags treated with the STR device. Subjects will have up to two (2) tags treated, therefore, 50-100 subjects are anticipated for this arm. A total of 100 skin tags is the ITT (intention to treat).	Subject treatment data collected on: ● Tag size; 4-6 mm (micro band ● All skin tags will be banded by a healthcare professional licensed dermatologist

For subjects meeting the inclusion/exclusion criteria and entering the study and having two skin tags being treated as a part of this study, please see the study design details on how both skin tags are to be treated in Section 6.2 below.

6.2. Study Design

This protocol was developed after consultation with the FDA under a Q-submission, Q222756, where it was determined to be a non-significant risk trial.

6.2.1. Recruitment Population

For both arms of the study, subjects located in the U.S. will be recruited from the general population and/or through an invitation presented by the Principal Investigator or CRO. Potential participants may self-complete an IRB-approved online pre-screening survey. Every effort will be made to recruit well-represented subjects from the following groups:

- Age (22-50 and 51+)
- Sex assigned at birth (M/F)
- Race/Ethnicity
- Fitzpatrick Skin Type

The study cohort target is between 30 and 70 subjects per arm (depending on how many skin tags each subject presents for treatment), as determined by the power analysis.

Under Protocol Version 1, the study included two arms (manual and automatic STR application), and participants were treated with either the micro (2–4mm) or standard (4–6mm) sized band depending on the measured base width of the skin tag. Each arm included a roughly equal number of tags treated with each device size.

It is anticipated that some subjects will likely have several skin tags that could be treated with the STR study device. A maximum of two skin tags per subject may be chosen for treatment. For purposes of pooling the data more effectively, if a subject opts to have two skin tags treated in the study, the

following must apply;

- both skin tags must be of the same size; either micro (2-4mm); or standard (4-6mm). U nder protocol version 2, only skin tags measuring between 4-6mm will be banded with the micro size.
- both skin tags must be treated in the same arm (e.g. using the same STR study device, manual or automatic)
- skin tags must be in two different, distinguishable locations on the body (i.e. right side of neck and left armpit)

As of Protocol Version 2, only skin tags measuring 4–6mm at the base will be eligible for enrollment, and only the micro version of the STR device will be used. The standard-sized band will no longer be used in this version of the study. Participants may still have up to two eligible skin tags treated, provided both are within the 4–6mm size range, in different anatomical locations, and treated using the same device arm (manual or automatic).

Participants previously enrolled under an earlier version of the protocol may be eligible to reenroll, provided a different, previously unbanded skin tag(s) is selected for treatment. Skin tags previously banded are not eligible for rebanding under this protocol version.

Therefore, the total intention to treat (ITT) is 200 skin tags for arms 1 and 2 combined. If the study is completed with subjects only having one skin tag treated, then the study would need to recruit 200 subjects. If each subject had two skin tags treated, only 100 subjects would need to be recruited. It is anticipated that between 100 and 200 subjects will be required to treat a total of 200 skin tags.

The figures below depict how the total subject pool would be divided into the two arms under both versions of the protocol, where "N" is the number of subjects:

Under Protocol Version 1: Figure 1

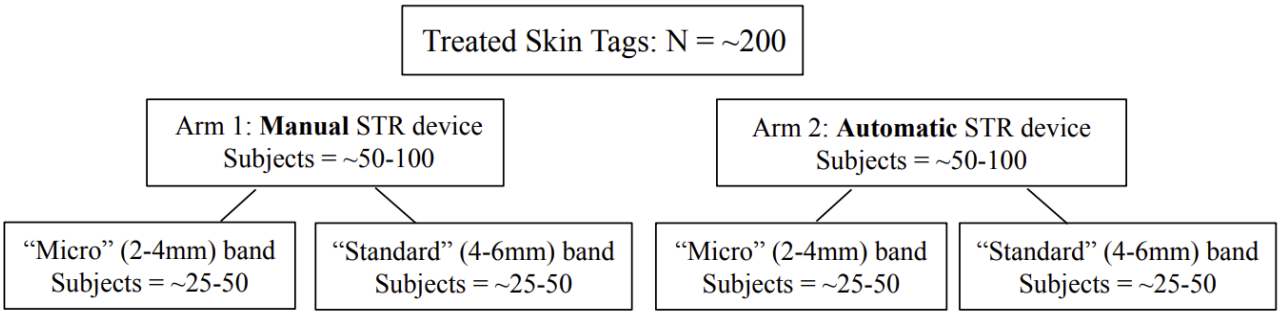

Figure 1: Breakdown of subjects into each arm and size of band used to be stratified as equally as possible in the targeting of ~200 treated skin tags.

Under Protocol Version 2: Figure 2

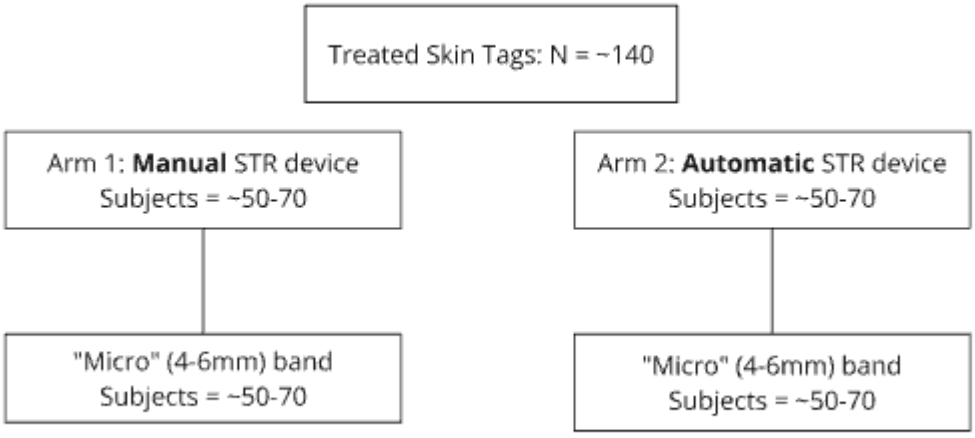

Figure 2: Breakdown of subjects into each arm to be stratified as equally as possible in the targeting of ~200 treated skin tags.

Once enrolled in the study, the Investigator will assign an STR version for use (manual/ automatic . Only the micro-sized band will be used in this version of the protocol, and only skin tags measuring 4–6mm at the base will be eligible for treatment. The Investigator will also review the subject's skin tags and agree with the subject on the body location and skin tag(s) that will be treated (see exclusion criteria) . The Investigator will also verify that the skin tag does not present a morphology representing implications of cancerous tissue. After signing informed consent and reviewing device lab,eling as well as determining eligibility , the subject will then have the band(s) placed on the skin tag(s) by the healthcare professional.

Once the band has been placed, the Investigator will examine the skin tag, complete study documentation, and answer any questions or concerns the subject has regarding the device or procedure. A small adhesive bandage will be placed over each treated skin tag immediately following banding. The subject will then review trial diary instructions, including but not limited to the documentation of all observable characteristics regarding the banded skin tag(s). The subject will complete their first eDiary at the visit including photo upload(s) of the banded skin tags. They will continue eDiary completion every evening starting at Day 1 through Day 20. This diary is electronic (eDiary) and accessed through the CRO's secure website. All subjects must be able to access the eDiary via smartphone to participate in the study, as defined in the informed consent. per day for eDiary completion, up to a maximum of $200.

6.2.2. Inclusion/Exclusion Criteria

Enrollment in the study will be limited to participants who meet all of the following inclusion criteria and none of the exclusion criteria:

Inclusion Criteria

1. Adults at least 22 years of age.
2. Must be able to understand, speak, and read English sufficiently for completion of the trial.
3. Subject has at least one skin tag meeting ALL of the following requirements:
    a. no previous attempts to remove the skin tag(s) of investigation, including skin tags that were treated in a previous version of this protocol
    b. measuring between 4 mm and ~6mm at the base. S kin tags measuring larger than 6mm can be rounded down based on investigator's discretion.
    c. not located around the eye, on the eyelid, or in the groin area
    d. if treating two tags, only one may be located in axilla
    e. free of any active skin infection & area to treat tag has no severe eczema
    f. located in an area where participant can take a self-taken photo
    g. does not, in the opinion of the Investigator, require an evaluation by pathology at the time of screening
4. Subject has access to the internet via smartphone to complete the eDiary.

Exclusion Criteria

1. Significant medical condition or other circumstance which, in the opinion of the Investigator, would preclude compliance with the protocol, adequate cooperation in the trial or providing informed consent, or may prevent the subject from safely participating in the trial
2. Any prior history of skin-related cancer
3. Subject states that they are currently pregnant or intending to become pregnant during the course of the study
4. Has an allergy to latex
5. Current diagnosis of a bleeding disorder included but not limited to Hemophilia or Von Willebrand disease
6. Currently being treated with blood thinners (use of 81 mg of Aspirin is not exclusionary)
7. Currently being treated with topical steroids at site of skin tag of interest or oral steroids
8. Currently immunocompromised by conditions such as diabetes (either Types 1 or 2, regardless of level of control) or receiving immunosuppressant therapy
9. Current MRSA infection
10. Diagnosis or any history of keloid or hypertrophic scarring

11. Current or recent participation within the last 30 days in another interventional clinical trial

6.2.3. Study Procedures

Demographics
Participants will provide demographic information at the baseline visit. They will provide a full date of birth (for the calculation of age), gender, and race/ethnicity.

Medical History
A verbal medical history that provides specific information regarding inclusion and exclusion (eligibility) criteria will be taken at screening including diagnoses and surgical procedures within the last 6 months.

Concomitant and Prohibited Medications
Investigator to review & document all current concomitant medications at day of screening and confirm eligibility per inclusion/exclusion criteria.

While enrolled in the study, participants should refrain from starting any anticoagulants, immunosuppressive therapies, oral steroids, or topical steroids applied near the area of the banded skin tag.

The use of a daily 81mg Aspirin is allowed, but note that this is a concomitant medication of interest and may increase bleeding and/or delay healing.

Modified Fitzpatrick Skin Type
Study team will administer to each participant who self-reports where their skin falls on the Fitzpatrick scale of burn versus tan with the ranking of I through VI.

SKIN TYPE	SKIN COLOR	REACTION TO SUN	
		SUNBURN	TANNING
I	Light, pale white	Always burns	Never Tans
II	White, fair	Usually burns	Tans with difficulty
III	Medium, white to olive	Sometimes mild burns	Gradually tans to olive
IV	Beige olive, moderate brown	Rarely burns	Easy tan to moderate brown
V	Brown, dark brown	Very rarely burns	Tans very easily
VI	Very dark brown to black	Never burns	Always tans

Image 5: Fitzpatrick Skin Type Chart

Limited Dermatological Exam

Investigator to examine potential skin tags to determine eligibility per inclusion criteria. Skin tag(s) will be measured and recorded. . No further dermatological exam to be performed.

Device Use and Band Application

The Investigator will complete training on device use for both automatic and manual options. Once a participant has met all inclusion and no exclusion criteria, the Investigator will apply the band(s) to the selected skin tag(s) and record location. Under protocol version 2, skin tags measuring between 4-6mm will all be banded using the micro size. The Investigator will place an adhesive bandage over each skin tag, following band application to prevent premature device detachment due to friction with clothing. Participants will receive a supply of bandages with their study kit, along with instructions for daily bandage removal and replacement for photo documentation. For those with two skin tags using the STR device, it is important to note which tag will be designated as #1 and which will be designated as #2 for eDiary reporting.

In the event of premature device detachment, the participant will note a detachment event in their daily eDiary. They will be instructed to contact the site to schedule a reapplication by the Investigator. The same device kit and application method (Auto or Manual) will be used for each rebanding. No more than two rebandings per skin tag will be permitted. The timing of rebanding, including the interval between band loss and reapplication, will be captured in the eDiary system. If a participant is unable to schedule a rebanding visit within 3 business days, they may be withdrawn from the study.

6.2.4. Schedule of Events

Potential participants may self-complete an IRB-approved online pre-screening survey. Those eligible based on survey responses will meet with the study team & Principal Investigator for the screening and baseline visit. If the subject agrees to take part in the study, they must read and sign a consent form, which will include the Inclusion/Exclusion criteria, information on completing the study

diary electronically as well as the covered medical expenses by the clinical study (see 6.2.5).

Schedule of Events

	Pre-Screening Phase	Treatment Phase			Post-Treatment	Unscheduled
		Visit 1	Visit 2	Visit 3	Visit 4	Unscheduled
Visit Type	Pre-Screening	Screening/ Baseline	Follow-Up	Follow-Up	End of Study	Unscheduled
Visit Location	(virtual)	(in clinic)	(virtual)	(virtual)	(virtual)	(in clinic)
Window	(-42 to Day 1)	Day 1	Days 5-9	Days 21-24	Days 30-37	N/A
Procedure						
Pre-Screening Survey	X					
Informed Consent		X				
Demographics		X				
Medical History		X				
Concomitant Medications		X	X	X	X	
Modified Fitzpatrick Skin Type		X				
Limited Dermatological Exam		X				X
Eligibility Determination		X				
Device Use/ Band Application4		X				
Band Re-application(s)		X[5]				
eDiary Training		X				
eDiary/Photo Review		x	X	X[1]	X[2]	
Adverse Events		X	X	X	X	X
Surgical Excision						X[3]

1 if treated skin tag(s) has/have not fallen off by Visit 3, participant has option to have skin tag(s) removed at an Unscheduled Visit by calling the Investigator's office and making an appointment

2 no eDiary entries for this visit; only photo(s) to be submitted by participant and reviewed by Investigator to confirm coordinator may exit participant from study. If Investigator has concerns about participant's D30 photo, participant will have an Unscheduled Visit for examination

3 optional: presented to subject in the event the skin tag was not removed by STR study device by D10

4 Participants will complete the initial eDiary and photo(s) upload at the Day 1, in-clinic visit.

5 Band -Repplication to be performed by PI or Sub-I as needed at the site in the event of the band falling off. Participants will be allowed 2 re-applications per skin tag throughout the course of the study.

6.2.5. Medical Expenses and Clinic Visits

Certain medical expenses will be covered during the study by the Sponsor. These include the following:

- investigational device costs
- clinical care costs for the placement and follow-up of the investigational device
- clinical care costs to remove skin tag in the event of failed treatment by device
  - removal of skin tag via surgical excision if STR device unsuccessful
- up to 2 on site rebanding visits in instances of premature band detachment
- clinical care costs relating to the following adverse event when using the device:
  - infection of the skin tag site

The following medical expenses will NOT be covered;

- cosmetic treatment related to pigment change or minor scarring at the skin tag site
- treatment related to hypertrophic scarring and/or keloids (subjects with these prior to consenting are excluded from study participation)

The study subjects will have access to a healthcare professional at the Investigator's clinic, including a 24-hour number to contact the investigator. If at any time the subject is concerned about treatment complications, they shall contact the PI immediately. An unscheduled visit may be performed.

6.2.6. Clinical Endpoints

Primary clinical endpoints and data collected are defined as follows:

Primary Outcome	Time Frame	Description and Data Collected
Successful removal of acrochordons using the STR device	Visit 1: subject screening and band placement (in-clinic)	• Obtain subject's informed consent • Study team member to verify inclusion/exclusion criteria • Identification of skin tag(s) to be used in study, including size (micro or standard) and location • Documentation of body location and number of tags • Investigator to stratify subject into either manual or automatic device arm • Placement of band(s) by Investigator • Placement of bandage(s) by investigator • Subject to read after-care instructions & review any questions with study team • Subject will receive clinical eDiary instructions comprising of device use, comprehension, and adverse events and later complete Day 1 entry • Subject will upload a photo of the banded skin tag(s) in clinic

		during Visit 1, which will be reviewed by the site staff ● Study team member to remind subject that an in-clinic visit is always available upon request and to call with any questions or concerns ● Study team member to remind subject to schedule an in-clinic rebanding visit at their earliest convenience in the event of premature band detachment
	Visit 2 (virtual)	At Visit 2, the subject is to complete a remote visit where the following activities are performed: ● Subject and study team member will review the photos and verify eDiary compliance for all days up to Visit 2 and also identify any signs of infection, irritation, or other adverse events ● Study team member to record general observations of tag(s) treated, flagging any concerns to Investigator ● Study team to review any instances of premature band detachment, and to remind participant to schedule a rebanding visit if not already completed ● Subject to continue filling out eDiary through Day 2 O regardless if skin tag(s) remain(s) ● Study team member to review after care instructions that are to be followed through Visit 4 ● Study team member to remind subject that an in-person visit is always available upon request and to call with any questions or concerns
	Visit 3 (virtual)	At Visit 3, the subject is to complete a remote visit where the following activities are performed: ● The subject and study team member will review the eDiary and photos to verify completion through day 2 O ● Subject to report any signs of infection, irritation, and adverse events to study team member. Subject should also provide information in eDiary identifying these issues ● Ensure recording of successful removal of the skin tag via STR study device (if applicable) ● Study team member and subject to review after care instructions to be followed through Visit 4 ● If skin tag has not fallen off, study team member to discuss the following options with subject: ○ If subject wants skin tag to be removed, study team member instructs them to call Investigator's office for an Unscheduled Visit to have skin tag removed by Investigator

		○ If subject is not interested in skin tag removal by Investigator, study team member instructs them to follow directions provided on After Care Instructions on proper self-removal of the band around treated skin tag ● Study team member to remind subject that an in-clinic visit is always available upon request up to Visit 4 and to call with any questions or concerns

Secondary clinical endpoints and data collected are defined as follows:

Secondary Outcomes	Time Frame	Description and Data Collected
Discomfort, issues, or adverse events occurring during the study	Visit 2 (virtual)	The subject is to complete a virtual visit where the following activities are performed: ● General observations, as described by the subject, of the skin tag site ● Review photos uploaded to eDiary and discuss any issues with irritation, infection, or other adverse events ● Study team to review any instances of premature band detachment, and to remind participant to schedule a rebanding visit if not already completed ● Study team member to record and report any safety-related issues regarding irritation or infection to Investigator ● Remind subject to continue daily recordings in eDiaryto remain in study ● Study team member to review AEs and Concomitant Medications at virtual visit ● Study team member to remind subject that an in-clinic visit is always available upon request and to call with any questions or concerns
	Visit 3 (virtual)	The subject is to complete a virtual visit where the following activities are performed: ● General observations, as described by the subject, of the skin tag site. ● Review photos uploaded to eDiary and discuss any issues with irritation, infection, or other adverse events ● If skin tag(s) has/have not been removed by STR study device, study team member to review options with subject for tag removal. ○ If subject wants skin tag to be removed, study team member instructs them to call Investigator's office for an Unscheduled Visit to have skin tag removed by Investigator ○ If subject is not interested in skin tag removal by Investigator, study team member instructs them to follow directions provided on After Care Instructions on proper self-removal of the band around treated skin tag ● Study team member to review AEs and Concomitant Medications at virtual visit ● Study team member and subject to review After Care Instructions that are to be followed until Visit 4 (and beyond if

		necessary). Study team member to remind subject that an in-clinic visit is always available upon request, up to Visit 4, and to call with any questions or concerns
	Visit 4 (virtual)	The subject is to complete a remote visit where the following activities are performed: ● Photo submission(s) of skin tag site(s) approximately 30 days (but not earlier than Day 30) after band(s) was/were placed ● Investigator will review photo(s) and verify the subject is either cleared to exit study or needs to return to clinic for an Unscheduled Visit ● Study team member to review AEs and Concomitant Medications at virtual visit once subject is cleared to exit study by Investigator

6.2.6.1. Reported Post Study Data

Case Report Forms will be used by the CRO to collect and organize data. All data collected during the investigational study will be compiled by the CRO and securely stored by the Sponsor. Data collected will be captured and archived using a per-protocol approach.

The following table provides a list of the reported primary outcomes, as evidenced by the study. Data subgroup analysis following the completion of the study and performance data analysis reported by:

- Age (22-50 vs. 51+)
- Sex assigned at birth (M/F)
- Band size (micro vs. standard)
- Band detachment events, including duration of detachment
- Body location of band placement
- Mechanism of device used (automatic vs. manual)

Data Collected	Description
Proper band placement	Source: Visit 1, Investigator Records STR study device bands will be placed on up to two (2) skin tag(s) by t he Investigator. Source: eDiary Participant will upload a photo(s) of the banded skin tag(s) in the eDiary at the Visit 1 in-clinic visit.

Efficacy of skin tag removal	Source: Days 2-2 0, Case Report Forms and Subject eDiary The total number of skin tags treated and those successfully removed by use of the STR study device will be compiled and reported. In all cases, the removal rate will be categorized by skin tag size (micro or standard) and body location as well as subject demographics
Safety and Potential Health Impacts	Source: Case Report Forms and Subject eDiary There are not any serious adverse effects anticipated with this study; potential non-serious side effects during the use of the STR study device are as follows and will be collected: • Irritation • Tenderness • Pigment change • Scarring Less common but potential side effects that need to be collected and addressed are: • Infection • Redness or swelling at the base of tag • Bleeding • Pain • Delayed healing (greater than 14 days after tag falling off/removal) • Hypertrophic or Keloid scarring • Other (as defined/described in the eDiary manual) General use comments by the subjects, including photos depicting the progression of the skin tag(s) treatment and after the tag has fallen off. Only adverse events associated with the device will be recorded and documented as Adverse Device Effects (ADEs).

7. INVESTIGATIONAL SITE MONITORING

7.1. Direct Access to Source Data/Documents

Sponsor or agents of sponsor, the reviewing IRB/EC, and health authorities from the US or other countries will have access to source documents at the investigational site for monitoring, auditing or inspection purposes.

7.2. Monitoring

Details of planned monitoring for the trial may be found in a Site Monitoring Plan developed prior to the start of the trial.

8. DEVICE ACCOUNTABILITY

The investigational devices shall be securely maintained, controlled, and used only in this clinical trial. The sponsor shall keep records to document the physical location of all investigational devices from shipment of investigational devices from designated facility/equipment to the investigation site until return or disposal.

Records shall be kept by the investigation site to document the physical location and conditions of storage of all investigational devices.

The Principal Investigator or an authorized designee shall keep records documenting the receipt, use, and disposal of the investigational devices, which shall include the following:

- Date of receipt
- Identification of each investigational device (unique code)
- Expiry date, as applicable
- Date on which the investigational device was dispensed and to which participant
- Date of disposal for all used devices
- Date of disposal for unused, expired, or malfunctioning investigational devices, if applicable

Standard size kits used under protocol version 1 I will not be used under protocol version 2.

9. ADVERSE EVENTS, ADVERSE DEVICE EFFECTS, AND DEVICE MALFUNCTIONS

9.1. Adverse Event (AE)

An Adverse Event is defined as untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users, or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

For the purpose of this study, the only AEs to be collected are Adverse Device Effects (ADE) as mentioned in section 9.2 and Serious Adverse Events mentioned in Section 9.3.

9.2. Adverse Device Effect (ADE)

An Adverse Device Effect is an AE related to the use of an investigational medical device. For this study, the following ADEs will be collected if they occur at the location of the skin tag removal band placement including, but not limited to:

- Irritation
- Pain
- Bleeding
- Infection
- Hypertrophic or keloid scarring

- Prolonged healing, defined as the healing process taking longer than 14 days after the tag has fallen off or been removed by the Investigator
- Any other symptom or abnormality that led to permanent discontinuation of the trial device.

These events will be rated a mild, moderate or severe intensity using the following definitions:

Mild: Mild events are usually transient and do not interfere with the Participant's daily activities

Moderate: Moderate events introduce a low level of inconvenience or concern to the Participant and may interfere with daily activities. A medication may be necessary.

Severe: Severe events interrupt the Participant's usual daily activity

9.3. Serious Adverse Event (SAE)

A serious adverse event is any adverse event that leads to:

a) death

b) serious deterioration in the health of the subject , users, or other persons as defined by one or more of the following:

   a. a life-threatening illness or injury, or

   b. a permanent impairment of a body structure or a body function including chronic diseases, or

   c. in-patient or prolonged hospitalization, or

   d. medical or surgical intervention to prevent life-threatening illness or injury, or permanent impairment to a body structure or a body function;

   e. fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment.

Serious adverse events must be reported to the sponsor within 24 hours of coming to the investigator's attention. Any serious adverse event that occurs any time after the participant has signed the informed consent form for the trial, up to the Participant's final trial visit, inclusive, is to be reported through the EDC within 24 hours following when the event was first recognized, discovered, or reported, regardless of severity or relationship to the trial device.

The investigator is to also notify the IRB/EC of the serious adverse event promptly, and according to IRB/EC requirements. Documentation of the serious adverse event reports (using Form FDA 3500A or equivalent) should be submitted to Lindus Health at skintag@lindushealth.com. Documentation is to be kept in the investigational site's trial files and is to be checked routinely by the clinical research associate (CRA).

After receipt of a serious adverse event report, the sponsor will notify all appropriate regulatory authorities as necessary, within the required time frames. Written safety reports submitted to

regulatory authorities will be completed by the sponsor with the assistance of the investigator and other site personnel as needed.

Serious adverse events must be followed up by the investigator until resolution or stabilization.

9.4. Causality or Association of the Device with an AE or SAE

When the device caused or was associated with an AE or SAE, the event is an Adverse Device Event (ADE), or Serious Adverse Device Event (SADE), respectively.

9.5. Serious Adverse Device Event Expectedness

A SADE may be anticipated, an anticipated serious adverse device event (ASADE), or unanticipated, an unanticipated serious adverse device event (USADE).

Unanticipated serious adverse device events (USADEs) require expedited reporting to health authorities.

9.6. Device Deficiency

A device deficiency is a failure of the device to meet requirements for identity, quality, durability, reliability, usability, safety, or performance.

Device deficiencies should be documented by the investigator using Form FDA 3500A or equivalent. Form should be submitted to skintag@lindushealth.com. Documentation is to be kept in the investigational site's trial files and is to be checked routinely by the clinical research associate (CRA).

10. PROTOCOL DEVIATIONS

A trial related deviation is a departure from the ethically approved trial protocol or other trial document or process (e.g. consent process or IMP administration) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the trial master file.

A Lindus Health SOP is in place describing the procedure for identifying non-compliances, escalation to the central team and assessment of whether a non-compliance /deviation may be a potential Serious Breach.

11. SUSPENSION OR PREMATURE CLINICAL INVESTIGATIONAL TERMINATION

A Investigator, IRB/EC, or regulatory authority may suspend or prematurely terminate participation in a clinical investigation at the investigation sites for which they are responsible.

Should the investigation suspend the trial or the reviewing IRB/EC withdraw the approval for a trial, the Investigator shall report the suspension or withdrawal to the sponsor within 24 hours.

The sponsor may suspend the whole trial at any time for other reasons, but will document why. In the unlikely event this should occur, efforts will be made to allow already enrolled affected participants to complete their participation in the trial as planned.

11.1. Suspension or Termination for Participant Safety Reasons

In case of a USADE, the sponsor will suspend the trial immediately while analyzing available information for a decision about further action. Should less serious new information become available that change the benefit/risk balance in an unfavorable direction, the sponsor may suspend the trial immediately while analyzing available information for a decision about further action.

11.2. Withdrawal Due to Participant Non-Compliance

A participant may be withdrawn from the study at the discretion of the Investigator and/ or Study Team in the event of non-compliance with the study protocol. In particular, if the study device detaches prematurely and the participant fails to contact the site or schedule a rebanding appointment, the participant may be withdrawn from the study. Failure to comply with rebanding procedures may render the participant ineligible to continue in the study.

All withdrawals and the reasons for withdrawal will be documented in the participant's source documentation and eCRF, as applicable.

11.3. Communication to Participants

In case of suspension or termination the Investigator or other investigative staff communicates this to participants and makes arrangements for the completion and follow up.

12. INVESTIGATOR INFORMATION

12.1. Investigator Information

A licensed dermatologist shall serve as Principal Investigator for this trial while supported by other qualified healthcare providers. All facilities participating in this trial, along with the names of every Investigator that will participate in and/or review the trial information, will be required to sign an Investigator Agreement in accordance with 21 CFR 812.43. The sponsor will collect this information as a condition of the facilities' involvement and shall maintain copies with the rest of the study materials.

12.2. Initial Clinical Trial

The sponsor has received feedback from the FDA that this investigational study is a non-significant risk (NSR) device study, and therefore, a formal Investigational Device Exemption (IDE) application and approval are not required. However, the study is still subject to the FDA's abbreviated requirements for device clinical studies. A Central IRB's review of the protocol will be completed under the CRO's contract.

13. BIBLIOGRAPHY/FOOTNOTES

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14. BIOSTATISTICIAN POWER ANALYSIS

Confidence intervals were calculated based on the following specifications:

1. Endpoint: Skin Tag Removal
2. Observed percentage = 60%, 65%, or 70%
3. Sample Size: 25, 50, 75, 100, 125, 150, 175, or 200
4. Normal approximation 95% CIs

The confidence intervals are presented in Table 1.

Table 1: Confidence Intervals for Skin Tag Removal

Sample size	95% Confidence intervals for selected observed success rates*		
	60%	65%	70%
25	.42 to .78	.47 to .83	.50 to .90
50	.45 to .75	.51 to .79	.57 to .83
75	.48 to .72	.54 to .76	.59 to .81
100	.50 to .70	.55 to .75	.60 to .80
125	.51 to .69	.56 to .74	.61 to .79
150	.52 to .68	.57 to .73	.62 to .78
175	.53 to .67	.58 to .72	.63 to .77
200	.54 to .66	.59 to .71	.64 to .76

*Using Binomial exact method