HRP-503B – BIOMEDICAL RESEARCH PROTOCOL
(2017-1)

Protocol Title: Follicular revival in fibrosing alopecia: evaluating use of micro-needling

Principal Investigator: Brett King, MD, PhD

Version Date: 18 December 2020

(*If applicable*) Clinicaltrials.gov Registration #: NCT04342091

INSTRUCTIONS
This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:** 1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library. 2. If a section or question does not apply to your research study, type "Not Applicable" underneath. 3. Once completed, upload your protocol in the "Basic Information" screen in IRES IRB system.

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SECTION I: RESEARCH PLAN

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.
   To evaluate the efficacy microneedling via a professional tattoo machine in revitalizing hair follicles in patients with fibrosing alopecia.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.
   Subject participation will be 8 months, the protocol will be kept open for 24 months for patient enrollment, and the entire project length including data analysis and publication will be 32 months

3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.

   Fibrosing alopecias are autoimmune hair loss conditions, with two subtypes that primarily affect women, central centrifugal cicatricial alopecia (CCCA) and frontal fibrosing alopecia (FFA). They often result in significant and irreversible hair loss associated with scarring of the hair follicle[1]. Little is known about the pathogenesis of these conditions, and there is not a single treatment for reversing them.[1,2] Usually, therapy is directed at preventing progression of disease, and even this is often futile.

   CCCA predominantly affects African American women. Historically, physicians attributed hair loss in these women to use of hair combs and chemical relaxers.[3] This remained the viewpoint of medicine for nearly 30 years until it was questioned after a retrospective study.[4] Contemporary work has debunked this prejudice by describing the presence of this disorder in countries that do not use these grooming practices,[5–7] and, more recently, a genetic predisposition underlying CCCA has been described.[8] The implicit bias regarding pathogenesis of CCCA has hindered its treatment, with many patients being told to discontinue hair grooming practices or that nothing could be done. Currently, there are no therapies that achieve clinically meaningful results (i.e. hair regrowth) for patients with CCCA. It has been shown that there is upregulation of multiple matrix metallopeptidases (MMPs 2, 7 and 9) in CCCA.[9] Tissue inhibitors of metalloproteinase (TIMPs) inhibit MMPs.[10] TIMPs expression is upregulated after microneedling procedures.[11]

   FFA is a fibrosing alopecia that primarily affects women. It involves hair loss with a receding frontal hair line. FFA can be disfiguring, leading to loss of several inches of hairline or even the entire top and sides of the scalp. Treatment of FFA, like for CCCA, is difficult, and no therapy can reverse the hair loss.[12] There is even less known about FFA pathogenesis than for CCCA.

   Microneedling has been associated hair regrowth in patients with other forms of hair loss, i.e. alopecia areata[13,14] and androgenic alopecia.[15] In mouse models, microneedling is associated with upregulation of molecules involved in hair growth and regeneration such as Wnt3a, β-catenin, VEGF, and Wnt10b.[16]

   We propose evaluating the use of microneedling via the SOL Nova Device to stimulate and revitalize hair follicles and growth in women with CCCA and FFA. This device has previously been used by dermatologists in Brazil that perform this procedure and was recommended for use by a colleague who has previously had success performing this procedure with the SOL Nova device.

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4. Research Plan: Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths. Describe the setting in which the research will take place.

   We propose an open label trial of tattoo machine microneedling in ten patients with fibrosing alopecia (five patients with CCCA and five with FFA). Ten healthy female patients older than 18 years will undergo 6 microneedling sessions. Over the course of six months, subjects will undergo up to six treatment sessions (one session every 30 day). Photographs will be taken at each session. Patients will be evaluated at 8 visits over 8 months with the first visit for screening purposes. Each visit will last about an hour. Approximately 30 minutes will be spent on consenting and time for patient to ask questions during the first visit. The remaining 30 minutes will be allotted for the investigator to determine if the patient meets criteria for trial enrollment. During the remaining visits, 20 minutes will be allotted for photography, 15-20 minutes for the procedure and 10-15 minutes for post-procedure patient assessment. Remaining 10 minutes on visits 2 and 8 will be used for biopsy.

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
Screening Visit Consent Signed	First Treatment Photographs taken Biopsy (optional)	Second Treatment Photographs taken	Third Treatment Photographs taken	Fourth Treatment Photographs taken	Fifth treatment Photographs taken	Final Treatment Photographs taken	Follow up visit Photographs taken Biopsy (optional)

Procedure:
The procedure will occur in an outpatient dermatology office either at YCCI or Yale Dermatology in Middlebury (YDM). The patient will be positioned in a conformable seated position. The entire scalp will be cleansed using an alcohol swab. A nerve block will be offered, using up to 3 ml of 2% lidocaine with 1:100,000 epinephrine. The IRB understands that a block will be used to numb the entire scalp at each visit, prior to microneedling. The surgeon will use a professional tattoo machine, SOL Nova (Cheyenne, MT.DERM, Berlin, Germany), attached to Cheyenne needle cartridge 27 magnum-bugpin-Soft Edges (MT.DERM, Berlin, Germany) to perform microneedling to the scalp, setting the needle exposure to approximately 1mm and the repetition rate in the tattoo machine power source to 120-150 Hz. Sterile water or sterile saline will be used to lubricate the skin during the procedure.

Post procedure aftercare:
Patients will be provided with verbal and written aftercare recommendations. Patients will be advised to wear a hat, avoid sun protection and continue their normal hair care routine. Additionally, expected side effects (skin

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flaking a few days post procedure (will be discussed. Concerning side effects will be listed with a number to call if patient is concerned.

Biopsy

One biopsy will be taken on visits two and eight (two biopsies total). The biopsy on visit eight will be taken prior to the tattooing procedure. The area for biopsy will be cleaned with an alcohol swab. The area will be anesthetized using up to 0.5 ml of lidocaine HCL 1% and epinephrine 1:100,000 injection. A 4 mm punch biopsy will be obtained. The biopsy site will be closed using a 4-0 monocryl absorbable suture. Biopsy specimens will be fixed in formalin for routine histology (H&E) and immunohistochemistry. Both biopsies will be optional

Primary and Secondary Outcome Measures:

The primary outcome will be change in total area hair count over 6 months. Hair growth will be accessed by a board-certified dermatologist. We will also measure change in hair shaft diameters, number of follicular units with one or more hair follicles, number of yellow dots, white dots, presence of perifollicular halo, hair density, percentage of anagen hairs, catagen hairs, ratio of vellus hairs and terminal hairs over an area of 1 cm^2.

Photographs will be taken prior to each session. Subjects will be consented at the time of screening and informed of the risks and benefits of the participation. Subjects will be informed that participation is voluntary, and withdrawal can occur at any time.

Early Termination:

The IRB understands that early stopping rules (e.g., 3 months with no response) may not be applicable as subjects may be delayed in showing a response of hair growth, which can take up to 6 months.

5. Genetic Testing N/A ☒

A. Describe

i. the types of future research to be conducted using the materials, specifying if immortalization of cell lines, whole exome or genome sequencing, genome wide association studies, or animal studies are planned *Write here*

ii. the plan for the collection of material or the conditions under which material will be received *Write here*

iii. the types of information about the donor/individual contributors that will be entered into a database *Write here*

iv. the methods to uphold confidentiality *Write here*

B. What are the conditions or procedures for sharing of materials and/or distributing for future research projects? *Write here*

C. Is widespread sharing of materials planned? *Write here*

D. When and under what conditions will materials be stripped of all identifiers? *Write here*

E. Can donor-subjects withdraw their materials at any time, and/or withdraw the identifiers that connect them to their materials? *Write here*

i. How will requests to withdraw materials be handled (e.g., material no longer identified: that is, anonymized) or material destroyed)? *Write here*

F. Describe the provisions for protection of participant privacy *Write here*

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G. Describe the methods for the security of storage and sharing of materials *Write here*

6. Subject Population: Provide a detailed description of the types of human subjects who will be recruited into this study.
   A total of 10 patients, over the age of 18 and female. All patients will have a diagnosis of fibrosing alopecia, five with CCCA and five with FFA.

7. **Subject classification:** Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement.

☐Children	☒ Healthy	☐Fetal material, placenta, or dead fetus
☐Non-English Speaking	☐ Prisoners	☐Economically disadvantaged persons
☐Decisionally Impaired	☐ Employees	☐Pregnant women and/or fetuses
☐Yale Students	☐ Females of childbearing potential	

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes ☐ No ☒

8. **Inclusion/Exclusion Criteria**: What are the criteria used to determine subject inclusion or exclusion?
   Inclusion criteria:
   - Female
   - Healthy
   - 18 years of age or older
   - Fibrosing alopecia

   Exclusion criteria-
   - Any female with hair loss for other reasons
   - Males
   - Patients with cardiac conditions or renal insufficiency
   - Pregnant patients
   - Patients containing the following who would make poor candidates for microneedling:
     - Skin conditions
     - Diabetes
     - History of keloid formation
     - Anything additional existing comorbidities that in the opinion of the investigator may cause unnecessary risk for the patient to participate

9. How will eligibility be determined, and by whom?
   Eligibility will be determined by Dr. Brett King the PI.

10. Risks: Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

Risk associated with tattooing procedure:
Discomfort during tattooing process
Scalp irritation

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Redness immediately afterwards (usually decreases within an hour)
Sensitivity to sunlight
Skin infection
Scarring
Hyperpigmentation of skin
Skin flaking a day after the procedure
Minimal (pinpoint) bleeding
Given the limited depth of the needles, large bleeding or hematoma formation is unlikely

Risks associated with privacy
Breach of confidentiality

11. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

Patients will be instructed on the risks associated with treatment (as listed above) and instructed to notify the PI immediately if experiencing any side effects. Blood pressure will be measured fifteen minutes post procedure. Subjects who experience severe side effects such as hypotension will be instructed on how to obtain appropriate medical care (i.e. outpatient follow up or emergency care) and will be discontinued from the study.

Risks of confidentiality breach will be minimized by using a password protected excel spread sheet on a password protected encrypted Yale laptop to which only the principal investigator and subinvestigators will have access to. Patient information will be deidentified during and after the trial to protect patient information. Deidentified data will remain stored on the password protected encrypted Yale laptop and then destroyed after the study has been concluded and the results have been published.

12. Data and Safety Monitoring Plan: Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)
    a. What is the investigator's assessment of the overall risk level for subjects participating in this study?
        Greater than minimal risk
    b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? N/A
    c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates for
        i. Minimal risk
        ii. Greater than minimal

Greater Than Minimal Risk DSMP

1. Personnel responsible for the safety review and its frequency:

The principal investigator will be responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency, which must be conducted at a minimum of

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every 6 months (including when reapproval of the protocol is sought). During the review process, the principal investigator (monitor) will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment. Either the principal investigator, the IRB or the Yale Cancer Center Data and Safety Monitoring Committee (DSMC) have the authority to stop or suspend the study or require modifications.

2. The risks associated with the current study are deemed greater than minimal for the following reasons:

We do not view the risks associated with scalp microneedling via tattoo device as minimal risks. Although we have assessed the proposed study as one of greater than minimal risk, the potential exists for anticipated and/or unanticipated adverse events, serious or otherwise, to occur since it is not possible to predict with certainty the absolute risk in any given individual or in advance of first-hand experience with the proposed study methods. Therefore, we provide a plan for monitoring the data and safety of the proposed study as follows:

3. Attribution of Adverse Events:
Adverse events will be monitored for each subject participating in the study and attributed to the study procedures / design by the principal investigator, Brett King, according to the following categories:

a.) Definite: Adverse event is clearly related to investigational procedure/agent.
b.) Probable: Adverse event is likely related to investigational procedures/agent.
c.) Possible: Adverse event may be related to investigational procedures/agent.
d.) Unlikely: Adverse event is likely not to be related to the investigational procedures/agent.
e.) Unrelated: Adverse event is clearly not related to investigational procedures/agent.

4. Plan for Grading Adverse Events:

The following scale will be used in grading the severity of adverse events noted during the study:

1. Mild adverse event
2. Moderate adverse event
3. Severe

5. Plan for Determining Seriousness of Adverse Events:

Serious Adverse Events:
In addition to grading the adverse event, the PI will determine whether the adverse event meets the criteria for a Serious Adverse Event (SAE). An adverse event is considered serious if it results in any of the following outcomes:

1. Death;
2. A life-threatening experience in-patient hospitalization or prolongation of existing hospitalization;
3. A persistent or significant disability or incapacity;
4. A congenital anomaly or birth defect; OR

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5. Any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

An adverse event may be graded as severe but still not meet the criteria for a Serious Adverse Event. Similarly, an adverse event may be graded as moderate but still meet the criteria for an SAE. It is important for the PI to consider the grade of the event as well as its "seriousness" when determining whether reporting to the IRB is necessary.

6. Plan for reporting UPIRSOs (including Adverse Events) to the IRB

The principal investigator will report the following types of events to the IRB:

Any incident, experience or outcome that meets ALL 3 of the following criteria:

1. Is unexpected (in terms of nature, specificity, severity, or frequency) given (a) the research procedures described in the protocol-related documents, such as the IRB-approved protocol and informed consent document and (b) the characteristics of the subject population being studied; AND
2. Is related or possibly related to participation in the research (*possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); AND
3. Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, legal, or social harm) than was previously known or recognized.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) may be medical or non-medical in nature, and include – but are not limited to – *serious, unexpected, and related adverse events* and *unanticipated adverse device effects*. ***Please note*** that adverse events are reportable to the IRB as UPIRSOs **only** if they meet all 3 criteria listed above.

These UPIRSOs/SAEs will be reported to the IRB in accordance with IRB Policy 710, using the appropriate forms found on the website. All related events involving risk but not meeting the *prompt* reporting requirements described in IRB Policy 710 should be reported to the IRB in summary form at the time of continuing review. If appropriate, such summary may be a simple brief statement that events have occurred at the expected frequency and level of severity as previously documented**.** In lieu of a summary of external events, a current DSMB report can be submitted for research studies that are subject to oversight by a DSMB (or other monitoring entity that is monitoring the study on behalf of an industry sponsor).

7. Plan for reporting adverse events to co-investigators on the study, as appropriate the protocol's research monitor(s), e.g., industrial sponsor, Yale Cancer Center Data and Safety Monitoring Committee (DSMC), Protocol Review Committee (PRC), DSMBs, study sponsors, funding and regulatory agencies, and regulatory and decision-making bodies.

For the current study, the following individuals, funding, and/or regulatory agencies will be notified (choose those that apply):

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X All Co-Investigators listed on the protocol.

☐ Yale Cancer Center Data and Safety Monitoring Committee (DSMC)

☐ National Institutes of Health

☐ Food and Drug Administration (Physician-Sponsored IND #_____)

☐ Medical Research Foundation (Grant_____)

☐ Study Sponsor

☐ Other Data Safety Monitoring Board (DSMB) or Committee (DSMC)

The principal investigator, Brett King, will conduct a review of all adverse events upon completion of every study subject. The principal investigator will evaluate the frequency and severity of the adverse events and determine if modifications to the protocol or consent form are required.

Please note: For any study that may be considered high risk, the IRB will be more focused on the safety requirements for the study and a DSMB will likely be required.

For more guidance on Adverse Event reporting and DSMPs, see **IRB Policy 710 Reporting Unanticipated Problems Involving Risks to Subjects or Others, including Adverse Events**

d. For multi-site studies for which the Yale PI serves as the lead investigator:
   i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? N/A
   ii. What provisions are in place for management of interim results? N/A
   iii. What will the multi-site process be for protocol modifications? N/A

13. Statistical Considerations: Describe the statistical analyses that support the study design. Statistics will be descriptive only.

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SECTION II: RESEARCH INVOLVING DRUGS, BIOLOGICS, RADIOTRACERS, PLACEBOS AND DEVICES

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS ☒N/A

1. Name of the radiotracer: King

2. Is the radiotracer FDA approved? ☐YES ☐NO

If NO, an FDA issued IND is required for the investigational use unless RDRC assumes oversight.

3. Check one: ☐IND# *Write here* or ☐RDRC oversight (RDRC approval will be required prior to use)

4. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this radiotracer is being administered to humans, include relevant data on animal models.
Write here

4. **Source:** Identify the source of the radiotracer to be used. *Write here*

5. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, method of sterilization and method of testing sterility and pyrogenicity.
Write here

B. DRUGS/BIOLOGICS ☒N/A

1. If an **exemption from IND filing requirements is** sought for a clinical investigation of a drug product that is lawfully marketed in the United States, review the following categories and complete the category that applies (*and delete the inapplicable categories)*:

Exempt Category 1: The clinical investigation of a drug product that is lawfully marketed in the United States can be exempt from IND regulations if all of the following are yes:	
1. The intention of the investigation is NOT to report to the FDA as a well-controlled study in support of a new indication for use or to be used to support any other significant change in the labeling for the drug.	☐
2. The drug that is undergoing investigation is lawfully marketed as a prescription drug product, and the intention of the investigation is NOT to support a significant change in the advertising for the product.	☐
3. The investigation does NOT involve a route of administration or dosage level or use in populations or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product	☐
4. The investigation will be conducted in compliance with the requirements for institutional (HIC)	☐

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review and with the requirements for informed consent of the FDA regulations (21 CFR Part 50 and 21 CFR Part 56).	
5. The investigation will be conducted in compliance with the requirements regarding promotion and charging for investigational drugs.	☐

Exempt Category 2 (all items i, ii, and iii must be checked to grant a category 2 exemption)

☐i. The clinical investigation is for an *in vitro* diagnostic biological product that involves one or more of the following (check all that apply):

☐ Blood grouping serum
☐ Reagent red blood cells
☐ Anti-human globulin

☐ii. The diagnostic test is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and

☐iii. The diagnostic test is shipped in compliance with 21 CFR §312.160.

Exempt Category 3

☐ The drug is intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.60

Exempt Category 4

☐ A clinical investigation involving use of a placebo if the investigation does not otherwise require submission of an IND.

2. **Background Information:** Provide a description of previous human use, known risks, and data addressing dosage(s), interval(s), route(s) of administration, and any other factors that might influence risks. If this is the first time this drug is being administered to humans, include relevant data on animal models.

2. **Source:** Identify the source of the drug or biologic to be used.

a) Is the drug provided free of charge to subjects? ☐YES ☐NO
If yes, by whom?

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4. **Storage, Preparation and Use:** Describe the method of storage, preparation, stability information, and for parenteral products, method of sterilization and method of testing sterility and pyrogenicity.

Check applicable Investigational Drug Service utilized:

☐ YNHH IDS ☐ CMHC Pharmacy ☐ West Haven VA
☐ PET Center ☐ None
☐ Other:

Note: If the YNHH IDS (or comparable service at CMHC or WHVA) will not be utilized, explain in detail how the PI will oversee these aspects of drug accountability, storage, and preparation.

5. Use of Placebo: ☒Not applicable to this research project

If use of a placebo is planned, provide a justification which addresses the following:

a) Describe the safety and efficacy of other available therapies. If there are no other available therapies, state this.
b) State the maximum total length of time a participant may receive placebo while on the study.
c) Address the greatest potential harm that may come to a participant as a result of receiving placebo.
d) Describe the procedures that are in place to safeguard participants receiving placebo.

6. Continuation of Drug Therapy After Study Closure ☐Not applicable to this project

Are subjects provided the opportunity to continue to receive the study drug(s) after the study has ended?

☐ Yes If yes, describe the conditions under which continued access to study drug(s) may apply as well as conditions for termination of such access.

☐ NO If no, explain why this is acceptable.

B. DEVICES ☐N/A

1. Are there any investigational devices used or investigational procedures performed at Yale-New Haven Hospital (YNHH) (e.g., in the YNHH Operating Room or YNHH Heart and Vascular Center)? ☒Yes ☐No

***If Yes, please be aware of the following requirements*:**

A YNHH New Product/Trial Request Form must be completed via EPIC: **Pull down the Tools tab in the EPIC Banner, Click on Lawson, Click on "Add new" under the New Technology Request Summary and fill out the forms requested including the "Initial Request Form," "Clinical Evidence Summary", and attach any other pertinent documents. Then select "save and submit" to submit your request**; AND

Your request must be reviewed and approved **in writing** by the appropriate YNHH committee before patients/subjects may be scheduled to receive the investigational device or investigational procedure.

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2. Background Information: Provide a description of previous human use, known risks, and any other factors that might influence risks. If this is the first time this device is being used in humans, include relevant data on animal models.

   The SOL Nova tattoo machine will be used for drug delivery microneedling using needle cartridge 27-magnum-bugpin-soft edges (27-MG-BP-SE). The cartridge 27-magnum-bugpin-soft edges (27-MG-BP-SE) are single use disposable needles which include a guard that prevents going to deep in the skin, which minimizes the risk of bleeding or infection. This equipment is commonly used commercially for human tattoos worldwide. Needle cartridges will be run at 120-150 Hz. This device has previously been used by dermatologists in Brazil that perform this procedure and was recommended for use by a colleague who has previously had success performing this procedure with the SOL Nova device.

3. Source:
   a) Identify the source of the device to be used. Cheyenne professional tattoo equipment, Berlin Germany
   b) Is the device provided free of charge to subjects? ☒Yes ☐No The procedure, not the device, is offered free to the subjects.

4. Investigational device accountability: State how the PI, or named designee, ensures that an investigational device is used only in accordance with the research protocol approved by the HIC, and maintains control of the investigational device as follows:

   a) Maintains appropriate records, including receipt of shipment, inventory at the site, dispensation or use by each participant, and final disposition and/or the return of the investigational device (or other disposal if applicable): Shipments of needle cartridges (27-magnum-bugpin-Soft Edges) will be documented by the principal investigator and/or sub-investigators. Inventory of needles will be kept at YCCI. A single needle cartridge will be used for each patient at each treatment session. Serial numbers and expiration dates will be documented with the patient's unique identifier. Disposal of cartridges will be in sharps containers.

   b) Documents pertinent information assigned to the investigational device (e.g., date, quantity, batch or serial number, expiration date if applicable, and unique code number): New needle cartridges (27-magnum-bugpin-Soft Edges) will be used for each patient. Needles are sterile and single use. Surgeons will document serial number and expiration date for each needle cartridge on procedure note in the case of malfunction or error. Needles past expiration date will not be used for the procedure and will be discarded.

   c) Stores the investigational device according to the manufacturer's recommendations with respect to temperature, humidity, lighting, and other environmental considerations: The Sol Nova tattoo machine will be stored at the YCCI clinic in the manufacturer provided case at room temperature in a key locked cabinet. There are no manufacture specific requirements for lighting or humidity control with regards to this device.

   d) Ensures that the device is stored in a secure area with limited access in accordance with applicable regulatory requirements: The Sol Nova tattoo machine will be stored in a locked cabinet at YCCI. Only the surgeon and principle investigator will have access to the machine.

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e) Distributes the investigational device to subjects enrolled in the IRB-approved protocol: Only Dr. King and Dr. Peterson will access to the Sol Nova tattoo machine for subjects enrolled in the trial during their designated treatment visits per protocol.

SECTION III: RECRUITMENT/CONSENT AND ASSENT PROCEDURES

1. Targeted Enrollment: Give the number of subjects:
   a. Targeted for enrollment at Yale for this protocol: 10
   b. If this is a multi-site study, give the total number of subjects targeted across all sites: N/A

2. Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.

☐ Flyers	☐ Internet/web postings	☐ Radio
☐ Posters	☐ Mass email solicitation	☒ Telephone
☐ Letter	☐ Departmental/Center website	☐ Television
☐ Medical record review*	☒ Departmental/Center research boards	☐ Newspaper
☐ Departmental/Center newsletters	☐ Web-based clinical trial registries	☐ Clinicaltrails.gov
☐ YCCI Recruitment database	☐ Social Media (Twitter/Facebook):	
☒ Other: Dr. King's Clinic		

* Requests for medical records should be made through JDAT as described at
http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx

3. Recruitment Procedures:

a. Describe how potential subjects will be identified.
Dr. King sees numerous patients with hair loss and so patients will be recruited directly from his clinic.

b. Describe how potential subjects are contacted.
Patients will be informed about the trial in clinic during their appointment.

c. Describe how potential subjects are contacted.
Patients will be informed of trial enrollment in clinic during their appointment and by phone by their physician.

d. Who is recruiting potential subjects? Dr. King

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:
Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

☒Yes, all subjects

☐Yes, some of the subjects

☐No

If yes, describe the nature of this relationship. Dr. King is the dermatologist for all potential study subjects.

5. **Request for waiver of HIPAA authorization:** (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)
Choose one:

☐ For entire study

☐ For recruitment/screening purposes only

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☐ For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: *Write here*

ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: *Write here*

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Assent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

   Patients will be recruited by Dr. Brett King in his outpatient clinical setting. He will explain to patients the treatment procedure, benefits, risks, and the study details as documented in the consent form.

7. Evaluation of Subject(s) Capacity to Provide Informed Consent/Assent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.

   Individuals will be assessed for comprehension and capacity with the following questions:
   (1) Explain to me in your own words what will happen once you start the study
   (2) Is there an option to stop the study if you decide to?
   (3) How would withdraw from the study if you didn't want to keep going?

8. Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.

   None will be included in this study

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES ☐ NO ☐

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

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Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. ***Please review the guidance and presentation on use of the short form available on the HRPP website.***

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.

☒Not Requesting any consent waivers

☐Requesting a waiver of signed consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study (Note that an information sheet may be required.)

For a waiver of signed consent, address the following:

- Would the signed consent form be the only record linking the subject and the research? YES ☐ NO ☐
- Does a breach of confidentiality constitute the principal risk to subjects? YES ☐ NO ☐

OR

- Does the research pose greater than minimal risk? YES ☐ NO☐
- Does the research include any activities that would require signed consent in a non-research context? YES ☐ NO ☐

☐ Requesting a waiver of consent:

☐ Recruitment/Screening only *(if for recruitment, the questions in the box below will apply to recruitment activities only)*

☐ Entire Study

For a full waiver of consent, please address all of the following:

- Does the research pose greater than minimal risk to subjects?
  - ☐ Yes *If you answered yes, stop. A waiver cannot be granted.*
  - ☐ No
- Will the waiver adversely affect subjects' rights and welfare? YES ☐ NO☐
- Why would the research be impracticable to conduct without the waiver? *Write here*
- Where appropriate, how will pertinent information be returned to, or shared with subjects at a later date? *Write here*

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SECTION IV: PROTECTION OF RESEARCH SUBJECTS

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? Name, age, diagnosis of fibrosing alopecia (CCCA or FFA), duration of disease, other comorbidities, course of disease, social history, family history, other failed therapies, current medications, baseline SALT score, change in score, reported patient side effects, photographs. Key to this identifier with patient name and identifier will be maintained in a separate password protected file that will be destroyed immediately after the conclusion of the trial according to ITS guidelines.

2. How will the research data be collected, recorded and stored? Data will be stored in a password protected excel spreadsheet on an encrypted Yale Laptop.

3. How will the digital data be stored? ☐CD ☐DVD ☐Flash Drive ☐Portable Hard Drive ☐Secured Server ☒Laptop Computer ☐Desktop Computer ☐Other

4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study? All study information will be contained on Yale encrypted laptop. Information will be deindentified during and after the conclusion of the trial. Only principal investigator and sub investigators will have access to the data.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url http://its.yale.edu/egrc or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.
   Within 6 months of the trial conclusion, all patient identifiers will be destroyed by the principal investigator Dr. Brett King according to ITS guidelines. Any remaining data will be completely deidentified. After the publication of the results (anticipated within 24 months of the trial) all data will be destroyed according to ITS guidelines.

6. If appropriate, has a Certificate of Confidentiality been obtained? *N/A*

SECTION V: POTENTIAL BENEFITS

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)
Patients who are otherwise poorly responsive to therapies for hair growth may grow hair.

SECTION VI: RESEARCH ALTERNATIVES AND ECONOMIC CONSIDERATIONS

1. Alternatives: What other alternatives are available to the study subjects outside of the research?

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Alternatives to trial therapy:

- Topical steroids
- Topical tacrolimus
- Topical Minoxidil
- Oral doxycycline
- Oral plaquenil
- Oral cyclosporine
- Oral Finasteride
- No therapy

2. Payments for Participation (Economic Considerations): Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.
   There is no monetary compensation for participation in this trial.

3. Costs for Participation (Economic Considerations): Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.
   The tattooing procedure and evaluation of hair growth by clinicians will be provided to the patient free of charge.

4. In Case of Injury: This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

    a. Will medical treatment be available if research-related injury occurs? *Yes*
    b. Where and from whom may treatment be obtained? *Staff at YNHH*
    c. Are there any limits to the treatment being provided? *No*
    d. Who will pay for this treatment? *Patient's insurance company or the patient*
    e. How will the medical treatment be accessed by subjects? *Patients will be referred to outpatient clinics or urgent care unless the issue is serious and urgent, then they will be referred to the emergency room.*

IMPORTANT REMINDERS

Will this study have a billable service? Yes ☐ No☒

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT

scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities?
Yes ☒ No ☐

If Yes, please answer questions a through c and note instructions below.

a. Does your YNHH privilege delineation currently include the specific procedure that you will perform? Yes ☒ No ☐

b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? Yes ☐ No ☒

c. Will a novel approach using existing equipment be applied? Yes ☐ No ☒

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.

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