Title: Treatment of lateral nasal wall collapse -- a comparison of bone anchored suture suspension versus radiofrequency thermotherapy.

Protocol Director

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<th>Name</th>
<th>Degree (program/year if student)</th>
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<tr>
<td>Sam Peyvand Most</td>
<td>Assoc Prof-Med Ctr Line</td>
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<td>Otolaryngology/Head &amp; Neck Surgery (ENT)</td>
<td>5739</td>
<td>(650) 736-3223</td>
<td></td>
<td><a href="mailto:smost@ohns.stanford.edu">smost@ohns.stanford.edu</a></td>
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CITI Training current: Y

Admin Contact

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<th>Name</th>
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<tr>
<td>Joshua D Weissman</td>
<td>Resident</td>
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<td>Otolaryngology/Head &amp; Neck Surgery (ENT)</td>
<td>650.723.6661</td>
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<td><a href="mailto:jweissman@stanford.edu">jweissman@stanford.edu</a></td>
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CITI Training current: Y

Co-Protocol Director

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CITI Training current

Other Personnel

Participant Population(s) Checklist

- Children (under 18) N
- Pregnant Women and Fetuses N
Title: Treatment of lateral nasal wall collapse -- a comparison of bone anchored suture suspension versus radiofrequency thermotherapy.

Approval Period: Draft

- Neonates (0 - 28 days) N
- Abortuses N
- Impaired Decision Making Capacity N
- Cancer Subjects N
- Laboratory Personnel N
- Healthy Volunteers Y
- Students N
- Employees N
- Prisoners N
- Other (i.e., any population that is not specified above) N

Study Location(s) Checklist Yes/No

- Stanford University Y
- Clinical & Translational Research Unit (CTRU)
- Stanford Hospital and Clinics
- Lucile Packard Children’s Hospital (LPCH)
- VAPAHCS (Specify PI at VA)
- Other (Click ADD to specify details)

General Checklist

Multi-site Yes/No

- Is this a multi-site study? A multi-site study is generally a study that involves one or more medical or research institutions in which one site takes a lead role. (e.g., multi-site clinical trial) N

Collaborating Institution(s) Yes/No

- Are there any collaborating institution(s)? A collaborating institution is generally an institution that collaborates equally on a research endeavor with one or more institutions. N

Cancer Institute Yes/No

- Cancer-Related Studies (studies with cancer endpoints), Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Specimens (e.g., blood, tissue, cells, body fluids with a scientific hypothesis stated in the protocol) N
Drug /Device

- Investigational drugs, biologics, reagents, or chemicals? N
- Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)? N
- Investigational Device / Commercial Device used off-label? Y
- IDE Exempt Device (Commercial Device used according to label) Y
- Protocol involves studying potentially addicting drugs? N

Clinical Trials

- Click "yes" to confirm that you have accessed the website and read the clinicaltrials.gov reporting requirements provided.
- This study will be registered on clinicaltrials.gov?

Tissues and Specimens

- Human blood, cells, tissues, or body fluids (tissues)? N
- Tissues to be stored for future research projects? N
- Tissues to be sent out of this institution as part of a research agreement? For guidelines, please see http://stanford.edu/group/ICO/researcher/reMTA.html
  http://stanford.edu/group/ICO/researcher/reMTA.html

Biosafety (APB)

- Are you submitting a Human Gene Transfer investigation using biological agent or recombinant DNA vector? If yes, please complete and attach the Gene Transfer Protocol Application Supplemental Questions to section 16 of the eProtocol application. N
- Are you submitting a Human study using samples from subjects that contain biohazardous/infectious agents? If yes, refer to the https://ehsappprd1.stanford.edu/eprobio/ Administrative Panel on BioSafety website prior to performing studies. N

Human Embryos or Stem Cells

- Human Embryos or gametes? N
Title: Treatment of lateral nasal wall collapse -- a comparison of bone anchored suture suspension versus radiofrequency thermotherapy.

Approval Period: Draft

- Human Stem Cells (including hESC, iPSC, cancer stem cells, progenitor cells). N

Veterans Affairs (VA)

- The research recruits participants at the Veterans Affairs Palo Alto Health Care System (VAPAHCS).
  N
- The research involves the use of VAPAHCS non-public information to identify or contact human research participants or prospective subjects or to use such data for research purposes.
  N
- The research is sponsored (i.e., funded) by VAPAHCS.
  N
- The research is conducted by or under the direction of any employee or agent of VAPAHCS (full-time, part-time, intermittent, consultant, without compensation (WOC), on-station fee-basis, on-station contract, or on-station sharing agreement basis) in connection with her/his VAPAHCS responsibilities.
  N
- The research is conducted using any property or facility of VAPAHCS. N

Equipment

- Use of Patient related equipment? If Yes, equipment must meet the standards established by Hospital Instrumentation and Electrical Safety Committee (650-725-5000)
  Y
- Medical equipment used for human patients/subjects also used on animals?
  N
- Radioisotopes/radiation-producing machines, even if standard of care?
  N

Payment

- Subjects will be paid for participation? See payment considerations.
  N

Funding

- Training Grant?
  N
- Program Project Grant?
  N
- Federally Sponsored Project?
  N
- Industry Sponsored Clinical Trial?
  N

Funding - Grants/Contracts
a) Qualified staff.

Please state and justify the number and qualifications of your study staff.

The study staff will consist of otolaryngology faculty member, fellowship-trained in facial plastic and reconstructive surgery (Dr. Most) and an otolaryngology resident (Dr. Weissman).

b) Training.

Describe the training you will provide to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.

All study staff will read the study protocol. The staff will be trained on appropriate recruitment and evaluation of patients.

c) Facilities.

Please describe and justify.

The study will use the clinic space at 801 Welch Road. This is the home of the Otolaryngology - Head and Neck Surgery Department and the Stanford Division of Facial Plastic and Reconstructive Surgery, and it will be used to recruit patients and evaluate them post-operatively as would have been normally in non-study patients.

d) Sufficient time.

Explain whether you will have sufficient time to conduct and complete the research. Include how much time is required.

This study will last for as long as it takes to enroll 45 patients. Each patient will be enrolled in the study for one year to allow for twelve months of follow-up. As there is no deadline for completion of this study, there will be sufficient time to complete it.

e) Access to target population.

Explain and justify whether you will have access to a population that will allow recruitment of the
required number of participants.
The study will recruit patients from the Stanford Center for Facial Plastic and Reconstructive Surgery. The faculty member and otolaryngology resident see dozens of patients weekly in clinic and perform 4-6 operations weekly. This population will allow ample opportunities to recruit patients into the study.

f) Access to resources if needed as a consequence of the research.
State whether you have medical or psychological resources available that participants might require as a consequence of the research when applicable. Please describe these resources.
It is not intended that any such additional resources will be necessary. They will have an appropriate medical evaluation as is standard in the Facial Plastic and Reconstructive Surgery clinic. Psychological resources are not believed to be necessary, although the main hospital and the Dept of Psychology would be available should there be a need.

g) Lead Investigator or Coordinating Institution in Multi-site Study.
Please explain (i) your role in coordinating the studies, (ii) procedures for routine communication with other sites, (iii) documentation of routine communications with other sites, (iv) planned management of communication of adverse outcomes, unexpected problems involving risk to participants or others, protocol modifications or interim findings.

1. Purpose

a) In layperson’s language state the purpose of the study in 3-5 sentences.
Lateral nasal wall collapse is a source of nasal congestion which plagues many people as the sidewall of the nose collapses due to negative pressure and structural weaknesses of the nose. Bone anchored suture suspension is used by many surgeons to treat it, and involves anchoring the nasal sidewall to the bony rim below the eye. A recently described technique involves treating the sidewall soft tissue with radiofrequency heat to cause scar contraction of the tissue to minimize laxity. This study aims to compare the two treatments to each other, and to non-operative treatment of otherwise surgically-eligible candidates.

b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.
We hope to determine the relative efficacy of the new technique in the management of lateral nasal wall collapse as compared to one of the standard surgical treatments as well as non-surgical treatments. This knowledge could change surgical management as radiofrequency thermotherapy is less invasive, could be performed with only local anesthesia, and does not involve implants -- in contrast to the more established bone anchored suture suspension.

c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)
The purpose of the study is to assess the efficacy of different treatment options of human lateral nasal wall collapse.
2. Study Procedures

a) Describe all the research procedures, from screening through closeout, which the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care.

Patients with lateral nasal wall collapse who are eligible for surgical repair will be presented with the opportunity to participate. Once consented, standard pre-operative evaluation will be performed including evaluation of degree of lateral nasal wall collapse with an endoscopic video recording of their anteriormost nasal wall. They will also be screened with validated quality of life screening tools for nasal congestion, which include the NOSE scale and a visual analog scale. They will then be randomized to treatment either with radiofrequency thermotherapy or bone anchored suture suspension, in combination with likely other areas of functional rhinoplasty such as septoplasty and turbinate reduction. Those subjects who are eligible for surgery but choose not to have surgery at the time will be offered a spot as a non-operative control for treatment with Breathe Right strips.

b) Explain how the above research procedures are the least risky that can be performed consistent with sound research design.

While radiofrequency thermotherapy of the lateral nasal wall is a new technique, radiofrequency treatment itself is well established in the field of otolaryngology, being used to induce scar contraction of various magnitudes in the base of tongue (for sleep apnea) and inferior turbinates (in the nose, for nasal obstruction due to turbinate hypertrophy). All other treatment aspects of this study are within standards of care, including the bone anchored suture suspension which is routinely employed by Dr. Most, and Breathe Right strips, which are sold over the counter as a way to stent open the nasal valve.

c) State if deception will be used. If so, provide the rationale and describe debriefing procedures. Since you will not be fully informing the participant in your consent process and form, complete an alteration of consent (in section 13). Submit a debriefing script (in section 16).

As a randomized study, the patients will be assigned to one of the two treatment groups randomly. They will however be made aware of which of the two treatments they will receive for lateral nasal wall collapse, so deception will not be used. The surgeon of course will also be aware of the treatment option.

d) State if audio or video recording will occur. Describe what will become of the recording after use, e.g., shown at scientific meetings, erased. Describe the final disposition of the recordings.

Video recording of the nasal examinations will occur and will be recorded to DVD. The DVDs will be labelled with each subjects random-generated study number (described later) and will be stored in a locked cabinet. Specific consent for video recording will be obtained in the consent form.

e) Describe alternative procedures or courses of treatment, if any, that might be advantageous to the participant. Describe potential risks and benefits associated with these. Any standard treatment that is being withheld must be disclosed in the consent process and form. (i.e. standard-of-care drug, different interventional procedure, no procedure or treatment, palliative care, other research studies).

Alternate courses of treatment would be to not undergo surgery. Non-operative management will be offered to all patients with the possibility for conservative management -- such patients will be offered a spot as a control subject. Treatment of controls with Breathe Right strips, however, is often not an efficacious means of treatment and many of these patients will eventually elect for surgery.

f) Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

As the surgical arms will undergo a one-time surgical treatment for lateral nasal wall collapse, followup treatment will not be necessary although we certainly aim to follow them in clinic for at least one year.
g) Study Endpoint. What are the guidelines or end points by which you can evaluate the different treatments (i.e. study drug, device, procedure) during the study? If one proves to be clearly more effective than another (or others) during the course of a study, will the study be terminated before the projected total participant population has been enrolled? When will the study end if no important differences are detected?

The study endpoints will be evaluations performed by endoscopic nasal examination of the lateral nasal wall collapse, as well as by the NOSE and Visual Analog Scale symptom scales. These assessments will be made at followup appointments up to one year post-operatively. If one treatment proves to be significantly more effective prior to the completion of enrolling subjects, the study will be terminated early.

3. Background

a) Describe past experimental and/or clinical findings leading to the formulation of the study.

Bone anchored suture suspension was introduced to the field of rhinoplastic surgery in the mid 1990s and has been validated by studies utilizing the NOSE scale as an effective means of treating lateral nasal wall collapse. It is used frequently at Stanford by our facial plastic surgeons in clinical practice. Radiofrequency thermotherapy is a well-established practice in otolaryngology known to induce thermal contraction in areas such as sleep surgery (base of tongue RF treatment) and rhinology (RF reduction of inferior turbinates). Recently, a study was published describing treatment of the lateral nasal wall with RF thermotherapy, which led to significant improvement in lateral nasal wall collapse as well as being tolerated well with few transient side effects and no visible external skin changes.

b) Describe any animal experimentation and findings leading to the formulation of the study.

There are no notable animal studies to discuss.

4. Radioisotopes or Radiation Machines

a) List all standard of care procedures using ionizing radiation (radiation dose received by a subject that is considered part of their normal medical care). List all research procedures using ionizing radiation (procedures performed due to participation in this study that is not considered part of their normal medical care). List each potential procedure in the sequence that it would normally occur during the entire study. http://www.stanford.edu/dept/EHS/prod/researchlab/radlaser/Human_use_guide.pdf

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<th>Identify Week/Month of study</th>
<th>Name of Exam</th>
<th>Identify if SOC or Research</th>
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b) For research radioisotope projects, provide the following radiation-related information:

Identify the radionuclide(s) and chemical form(s).

Provide the number of times the radioisotope and activity that will be administered (mCi) and the route of administration.

If not FDA approved provide dosimetry information and reference the source documents (package insert, MIRD calculation, peer reviewed literature).

c) For research radiation machine projects, provide the following diagnostic procedures:
For well-established radiographic procedures describe the exam.

Identify the number of times each will be performed on a single research subject.

For each radiographic procedure, provide the setup and technique sufficient to permit research subject dose modeling. The chief technologist can usually provide this information.

For radiographic procedures not well-established, provide FDA status of the machine, and information sufficient to permit research subject dose modeling.

d) For research radiation machine projects, provide the following therapeutic procedures:

For a well-established therapeutic procedure, identify the area treated, dose per fraction and number of fractions. State whether the therapeutic procedure is being performed as a normal part of clinical management for the research participant's medical condition or whether it is being performed because the research participant is participating in this project.

For a therapeutic procedure that is not well-established, provide FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions.

5. Devices

a) Please list in the table below all Investigational Devices (and Commercial Devices used off-label) to be used on participants.

5.1 **Device Name:** TCRF Turbinate Handpiece

Describe the device to be used.

Standard radiofrequency probe used for RF treatment of the inferior turbinates. Is a handpiece with a pointed probe tip which is standardly used at our institution to deliver RF energy to the inferior turbinates. The proximal length of the probe is insulated. catalog # 1120-4110-05

Manufacturer: Olympus/Gyrus

Risk: Non-significant

Y I confirm the above are true.

**Rationale for the device being non-significant risk:**

The device is already in common use the field of otolaryngology - head & neck surgery for delivery of RF energy to the inferior turbinates and the base of the tongue. Moreover, the handpiece device incorporates temperature-controlled radiofrequency (TCRF) thermal energy with thermocouples at the needle tip to monitor the temperature -- this allows us to set the maximum temperature of the probe to avoid damage to surface mucosa and overlying skin.

**Sponsor of Project**

Indicate who is responsible for submitting safety reports to the FDA:

Y The sponsor is the STANFORD (SU, SHC, LPCH, VA) investigator.

Please read the following:
Sponsor-Investigator Research Requirements

If you would like further information on this process and/or assistance prior to submitting your protocol contact: The Stanford Center for Clinical and Translational Education and Research (Spectrum) at clinicaltrials@med.stanford.edu or for cancer research contact: cc-to-regulatory@stanford.edu

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate, handled according to VAPAHCS memo 151-05-10. If no, please provide an explanation:

Y Confirm?

b) Please list in the table below all Commercial devices to be used on participants

5.1 Device Name: Mitek Soft Tissue Anchor Suspension System

Describe the device to be used.

System consisting of drill bit, bone anchor, and an attached suture. Allows for drilling an anchor device near the infraorbital rim (below the eye) medially, to which an anchoring suture is attached to the cartilaginous lateral nasal wall for support. This is currently the most common method of treatment for lateral nasal wall collapse at Stanford Hospital by the Otolaryngology service.

Manufacturer: DePuy Mitek
IDE Exemption
Y This is a legally marketed device being used in accordance with its labeling.

5.2 Device Name: Breathe Right Strips

Describe the device to be used.

Breathe Right Strips are semi-firm, semi-flexible strips with adhesive meant to be placed over the nasal tip and ala (nostrils) for gentle up and outwards retraction to stent the nasal airway open.

Manufacturer: GlaxoSmithKline
IDE Exemption
Y This is a legally marketed device being used in accordance with its labeling.

6. Drugs, Reagents, or Chemicals

a) Please list in the table below all investigational drugs, reagents or chemicals to be administered to participants.

b) Please list in the table below all commercial drugs, reagents or chemicals to be administered to participants.

7. Medical Equipment for Human Subjects and Laboratory Animals
If medical equipment used for human patients/participants is also used on animals, describe such equipment and disinfection procedures.

n/a

8. Participant Population

a) State the following: (i) the number of participants expected to be enrolled at Stanford-affiliated site(s); (ii) the total number of participants expected to enroll at all sites; (iii) the type of participants (i.e. students, patients with certain cancer, patients with certain cardiac condition) and the reasons for using such participants.

We expect to enroll 45 total subjects through the Division of Facial Plastic and Reconstructive Surgery at Stanford. They will all be patients of the the Division eligible for functional rhinoplasty to improve breathing through the nose which will include at minimum treatment for lateral nasal wall collapse.

b) State the age range, gender, and ethnic background of the participant population being recruited.

We will plan to enroll healthy adults over age 18, of any gender, of any ethnic background.

c) State the number and rationale for involvement of potentially vulnerable subjects in the study (including children, pregnant women, economically and educationally disadvantaged, decisionally impaired, homeless people, employees and students). Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects and the additional safeguards that have been included in the protocol to protect their rights and welfare.

We will not include children, pregnant women, decisionally impaired, homeless people, employees, or students. All participants will possess the right to cancel their involvement in the study at any time. If economically or educationally disadvantaged patients are able to give their own consent and are eligible for the study they will be included in the study. If patients cannot read or sign the consent form, they will not be enrolled.

d) If women, minorities, or children are not included, a clear compelling rationale must be provided (e.g., disease does not occur in children, drug or device would interfere with normal growth and development, etc.).

Children will not be included in this study. We would like to study treatment of lateral nasal wall collapse. Childrens' noses are still developing and as such would not be candidates to undergo surgery as it may adversely affect normal growth.

e) State the number, if any, of participants who are laboratory personnel, employees, and/or students. They should render the same written informed consent. If payment is allowed, they should also receive it. Please see Stanford University policy.

We do not anticipate participation of any laboratory personnel, employees, or students, unless they are also patients of the Stanford Otolaryngology and undergoing functional rhinoplasty with treatment of lateral nasal wall collapse. If they do participate, they will render the same written informed consent.

f) State the number, if any, of participants who are healthy volunteers. Provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which participants may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to the volunteers and the additional safeguards that have been included in the protocol to protect their rights and welfare.

We will only be studying the management options for lateral nasal wall collapse in 45 healthy adults who are candidates for functional rhinoplasty.
g) Describe how potential participants will be identified for recruitment (e.g., chart review, referral from individual's treating physician, responses to an ad). Describe how participants will be recruited and how they will initially learn about the research (e.g., clinics, advertising). If this is a clinical trial, indicate the recruitment option selected in registering the trial on the Stanford Clinical Trials website—whether recruitment is limited to "invitation only" (e.g. your own patients), or whether recruitment will be open to the general public. Attach recruitment materials in Section #16 (Attachments). You may not contact potential participants prior to IRB approval. See guidance Advertisements: Appropriate Language for Recruitment Material.

Potential participants will be identified by those about to undergo functional rhinoplasty through the Stanford Division of Facial Plastic and Reconstructive Surgery. They will be informed of the study, and, if they wish to enroll, consent will be obtained. They will subsequently be screened for eligibility at the time of their pre-operative appointment. Control subjects will meet the same inclusion criteria and undergo the same assessments, only instead of surgery, they will be treated conservatively with Breathe Right nasal strips. All subjects seen and considered for study involvement will be seen and first contacted about it by their treating physician during their routine clinic visit -- be it with the attending (Dr. Most) or resident (Dr. Weissman), both of whom will have treating relationships with the patients.

h) Inclusion and Exclusion Criteria.

Identify inclusion criteria.

Eligible subjects with be healthy, adults with lateral nasal wall collapse who have had symptomatic nasal congestion for at least one year, with or without septal deviation, turbinate hypertrophy, or narrowed internal nasal valve. They must have failed prior medical management with topical nasal steroid or topical or oral antihistamines. They must be able to read, sign, and demonstrate understanding of the research protocol, including agreement to randomization for treatment of their lateral nasal wall collapse.

Identify exclusion criteria.

All subjects shall be excluded with evidence or history of prior rhinoplasty or nasal surgery, trauma to the nose within the past year, immunocompromise, smokers, chronic sinusitis, history of radiation to the head and neck, septal perforation, granulomatous disease, or pregnancy.

i) Describe your screening procedures, including how qualifying laboratory values will be obtained. If you are collecting personal health information prior to enrollment (e.g., telephone screening), please request a limited waiver of authorization (in section 15).

We will review the charts of patients eligible for functional rhinoplasty through the Stanford Division of Facial Plastic and Reconstructive Surgery for inclusion and exclusion criteria. The charge for the radiofrequency thermotherapy will be the same as the bone anchored suture suspension procedure.

j) Describe how you will be cognizant of other protocols in which participants might be enrolled. Please explain if participants will be enrolled in more than one study.

We will ask the patients at the initial time of screening if they are involved in any other study protocols. We will not enroll patients that are enrolled in other studies at the time of screening.

k) Payment. Explain the amount and schedule of payment, if any, that will be paid for participation in the study. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of participants and that they do not constitute undue pressure on participants to volunteer for the research study. Include provisions for prorating payment. See payment considerations

Study subjects will not receive any payment for their involvement in the study.

l) Costs. Please explain any costs that will be charged to the participant.

There will be no additional costs charged to the patient for their participation in the study. We will ask the
subjects to follow-up in clinic over the year, but this is standard for all patients who have undergone functional rhinoplasty. Control patients will only have required followup of one month. The charge for the radiofrequency thermotherapy will be the same of the bone anchored suture suspension procedure.

m) Estimate the probable duration of the entire study. Also estimate the total time per participant for: (i) screening of participant; (ii) active participation in study; (iii) analysis of participant data.

We anticipate the duration of the study to be as long as it takes to enroll 45 patients, plus their time in the study. We anticipate being able to recruit at least 3 patient per 2 weeks. With one year of total participation per patient, we anticipate the study duration to be approximately just under two years to complete follow-up.

Time for screening patients: 15 minutes (explaining study, signing consent, performing initial examination).
Total time for active participation in study: 1 year
Time per post-operative interaction: 5 minutes (examination)
Analysis of participant data: 5 minutes per patient for data entry, 5 minutes per patient for data analysis.

9. Risks

a) For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data on risk, a statement to this effect should be included. (In describing these risks in the consent form to the participant it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.)

Investigational devices.
Radiofrequency thermotherapy of the lateral nasal wall is itself a newer treatment method for lateral wall collapse but has its basis in decades of radiofrequency therapy of other sites in the head and neck, including the nasal turbinates and base of tongue. The treatment of lateral nasal wall collapse is an off-label use of the technology. There has been one published study using RF for lateral wall collapse utilizing 28 subject, and the only reported adverse reactions were pain in three (which responded to plain tylenol) and one case of edema (which resolved with oral steroids). There were no reports of atrophic changes to the skin or nasal mucosa -- such risks are minimized by using the newere temperature controlled RF devices (TCRF) which allow us to set the maximum temperature at the tip of the probe, thus greatly minimizing the risk of transmural damage to skin or nasal mucosa.

Investigational drugs. Information about risks can often be found in the Investigator’s brochure.
N/A

Commercially available drugs, reagents or chemicals. Information about risks can often be found in the package insert.
N/A

Procedures to be performed. Include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).
Bone Anchored Suture Suspension -- There are a few potential side effects or adverse consequences of the bone anchored suture suspension, which include some risks which are inherently associated with functional rhinoplasty. These include pain, bleeding, numbness, infection, lack of efficacy, slight widening of the sidewall of the nose, and numbness.
Radiofrequency therapy of the lateral nasal wall is a newer technique which has therefore not been studied as much, although it is rooted in over a decade of research in the field of otolaryngology. In the one reported study specifically on treatment of the nasal sidewall, side effects were minimal and included pain and swelling. Other potential risks include atrophic changes to the skin or nasal mucosa, lack of efficacy, bleeding, and infection.

**Radios isotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and associated risks.**

| N/A |

**Physical well-being.**

We do not anticipate that participation in this study will place the subjects' physical well-being at risk. They will be monitored post-operatively for one year to ensure there is no harm to their well-being.

**Psychological well-being.**

We do not anticipate that participation in this study will place the subjects' psychological well-being at risk.

**Economic well-being.**

We do not anticipate that participation in this study will place the subjects' economic well-being at risk as no additional costs will be incurred for their participation, aside from possibly travel which is more or less standard for non-study patients.

**Social well-being.**

We do not anticipate that participation in this study will place the subjects' social well-being at risk.

**Overall evaluation of Risk.**

Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

b) **In case of overseas research, describe qualifications/preparations that enable you to both estimate and minimize risks to participants.**

| N/A |

c) **Describe the planned procedures for protecting against and minimizing all potential risks. Include the means for monitoring to detect hazards to the participant (and/or to a potential fetus if applicable). Include steps to minimize risks to the confidentiality of identifiable information.**

We will advise the study subjects to contact the study authors at any time if they have any nasal or systemic symptoms that they are concerned about. The study subjects will have the right to request removal from the study or to cease their participation in the study at any time.

We will minimize the risks to the confidentiality of identifiable information in the following ways: 1) we will store the nasal symptom sheets, DVDs, and scoring sheets in a locked cabinet and a password-protected computerized database; 2) the nasal symptom and scoring sheets will be coded with a number to represent to full identity of the study subject with the code and the identity linked sheet being kept separate from the rest of the data; 3) data will not be shared with anyone other than those physicians directly involved in implementing and carrying out the study.

d) **Explain the point at which the experiment will terminate. If appropriate, include the standards for the termination of the participation of the individual participant Also discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the participants.**

We will terminate the experiment when we have enrolled 45 patients and followed the 30 surgical patients for 1 year each, having completed the surgery and ideally at least four follow-up appointments/evaluations on each patient.
e) Data Safety and Monitoring Plan (DSMP). See guidance on Data Safety and Monitoring.

A Data and Safety Monitoring Plan (DSMP) is required for studies that present Medium or High risk to participants. (See Overall Evaluation of Risk above). If Low Risk, a DSMP may not be necessary. Multi-site Phase III clinical trials funded by NIH require the DSM Plan to have a Data Safety Monitoring Board or Committee (DSMC or DSMB). The FDA recommends that all multi-site clinical trials that involve interventions that have potential for greater than minimal risk to study participants also have a DSMB or DSMC.

The role of the DSMC or DSMB is to ensure the safety of participants by analyzing pooled data from all sites, and to oversee the validity and integrity of the data. Depending on the degree of risk and the complexity of the protocol, monitoring may be performed by an independent committee, a board (DSMC/DSMB), a sponsor's Data Safety Committee (DSC), a Medical Monitor, a sponsor's safety officer, or by the Protocol Director (PD).

Describe the following:

What type of data and/or events will be reviewed under the monitoring plan, e.g. adverse events, protocol deviations, aggregate data?

We will collect nasal congestion symptom scores via the NOSE scale and Visual Analog Scales (both validated outcomes scales), along with a DVD recordings of their anterior lateral nasal wall (which involves inserting a pencil-like camera a few millimeters into the nose) and the physician grading of lateral nasal wall collapse.

Identify who will be responsible for Data and Safety Monitoring for this study, e.g. Stanford Cancer Institute DSMC, an independent monitoring committee, the sponsor, Stanford investigators independent of the study, the PD, or other person(s).

The protocol director will be responsible for the function of Monitoring Entity.

Provide the scope and composition of the monitoring board, committee, or safety monitor, e.g., information about each member's relevant experience or area of expertise. If the Monitor is the Stanford Cancer Center DSMC or the PD, enter N/A.

The Monitoring Entity's information is listed above.

Confirm that you will report Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), or Unanticipated Problems (UPs) to the person or committee monitoring the study in accordance with Sponsor requirements and FDA regulations.

All adverse events and unanticipated problems will be reported immediately to the ME.

If applicable, how frequently will the Monitoring Committee meet? Will the Monitoring Committee provide written recommendations about continuing the study to the Sponsor and IRB?

We will meet with the study subjects at a minimum of 4 times points after the surgical treatment over a one year period. These time points will also serve as assessments for any possible adverse events. They will also be encouraged to contact us any time between appointments to speak to one of the study coordinators or to request a more urgent evaluation.

Specify triggers or stopping rules that will dictate when the study will end, or when some action is required. If you specified this in Section 2g [Study Endpoints], earlier in this application enter 'See 2g'.

Patient symptoms or signs seen during examination that appear dangerous or severe will indicate whether stopping the study is warranted.
Indicate to whom the data and safety monitoring person, board, or committee will disseminate the outcome of the review(s), e.g., to the IRB, the study sponsor, the investigator, or other officials, as appropriate.

Immediate email notification of adverse events will occur.

Select One:

Y The Protocol Director will be the only monitoring entity for this study.

This protocol will utilize a board, committee, or safety monitor as identified in question #2 above.

10. Benefits

a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc.

Study subjects may benefit from the conclusions obtained from this study in developing future therapies and possibly procedures to be performed without general anesthesia to treat lateral nasal wall collapse.

11. Privacy and Confidentiality

Privacy Protections

a) Describe how the conditions under which interactions will occur are adequate to protect the privacy interests of participants (e.g., privacy of physical setting for interviews or data collection, protections for follow-up interactions such as telephone, email and mail communications).

Consent and data collection are conducted in the settings where the privacy of physical setting is preserved; patients are seen, interviewed, and consented in the private room preoperatively. No telephone, email or mail data collection will be done.

Confidentiality Protections

b) Specify the PHI (protected health information) or other individually identifiable data or specimens you will obtain, use or disclose to others. PHI is health information linked to one or more of the HIPAA identifiers listed above. List BOTH health information AND identifiers.

Before de-identification, PHI (Name, MRN, Date of birth, Gender, Date of sinus surgery) will be obtained and the patients are de-identified by assigning a study number, under which all the corresponding study data are collected and stored.

c) You are required to comply with University Policy that states that ALL electronic devices: computers (laptops and desktops; OFFICE or HOME); smart phones; tablets; external hard disks, USB drives, etc. that may hold identifiable participant data will be password protected, backed up, and encrypted. See http://med.stanford.edu/datasecurity/ for more information on the Data Security Policy and links to encrypt your devices.

Provide any additional information on ALL data security measures you are taking. You must use secure databases such as RedCap https://clinicalinformatics.stanford.edu/services/redcap.html. If you are unsure of the security of the system, check with your Department IT representative. Please see http://med.stanford.edu/irt/security/ for more information on IRT Information Security Services and
http://www.stanford.edu/group/security/securecomputing/mobile_devices.html for more information for securing mobile computing devices. Additionally, any PHI data on paper must be secured in a locked environment.

By checking this box, You affirm the aforementioned.

The data are maintained as the data files in the password protected computers, as well as the paper files in the locked office and file cabinets.

d) Describe how data or specimens will be labeled (e.g. name, medical record number, study number, linked coding system) or de-identified. If you are de-identifying data or specimens, who will be responsible for the de-identification? If x-rays or other digital images are used, explain how and by whom the images will be de-identified.

At the completion of the study, the patient's data will be entered under the corresponding patient's study number.

e) Indicate who will have access to the data or specimens (e.g., research team, sponsors, consultants) and describe levels of access control (e.g., restricted access for certain persons or groups, access to linked data or specimens).

Dr. Most and Dr. Weissman will have the access to the data during the collection.

f) If data or specimens will be coded, describe the method in which they will be coded so that study participants' identities cannot be readily ascertained from the code.

A random number generator will be used to formulate a three digit number which will be linked to the subject's identity.

g) If data or specimens will be coded, indicate who will maintain the key to the code and describe how it will be protected against unauthorized access.

The data are maintained as the data files in the password protected computers, as well as the paper files in the locked office and file cabinets.

Dr. Most and Dr. Weissman will have the access to the code during the collection.

h) If you will be sharing data with others, describe how data will be transferred (e.g., courier, mail) or transmitted (e.g., file transfer software, file sharing, email). If transmitted via electronic networks, describe how you will secure the data while in transit. See http://www.stanford.edu/group/security/securecomputing/ Additionally, if you will be using or sharing PHI see http://hipaa.stanford.edu/policy_security.html. Data will not be transferred and will be kept in a security cabinet.

i) How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected (e.g. conscious of oral and written communications, conducting insurance billing, and maintaining paper and electronic data)?

All research staff involved in data collection has completed the Stanford required IRB courses for protecting the patient's privacy. The necessary steps for protecting the confidentiality and patient's privacy are constantly emphasized and monitored by the PI and co-PI of the study.

12. Potential Conflict of Interest

a) Does anyone who:
- recruits, selects, consents, or treats participants
- plans to analyze data
- plans to serve as an author on any papers originating from this research
- is an immediate family member (spouse, dependent child as defined by IRS, domestic partner of any of the above)

N i) have consulting arrangements, responsibilities or equity holdings in the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N ii) have a financial relationship with the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s) including the receipt of honoraria, income, or stock/stock options as payment?
N iii) serve as a member of an advisory board with the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N iv) receive any gift funds from the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N v) have an ownership or royalty interest in any intellectual property utilized in this protocol?

b) N To your knowledge, does any one in a supervisory role to you have a conflict of interest related to this study?

c) N To your knowledge, has Stanford University licensed to a company any intellectual property utilized in this protocol?

If one or more of the above relationships exist, please include a statement in the consent form to disclose this relationship, i.e., a paid consultant, a paid member of the Scientific Advisory Board, has stock or stock options, or receives payment for lectures given on behalf of the sponsor (see sample consent form). The consent form should disclose what institution(s) or companies are involved in the study through funding, cooperative research, or by providing study drugs or equipment (see sample consent form).

If you answer yes to any of the questions above, you must file a Conflict of Interest (CoI) disclosure. See http://doresearch.stanford.edu/policies/research-policy-handbook/conflicts-commitment-and-interest/faculty-policy-conflict for more information. Contact Barbara Flynn at (650) 723-7226, or bflynn@stanford.edu.

13. Consent Background

13.1 Consent

Consent for all patients

a) Describe the informed consent process. Include the following.
   i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)
   ii) When and where will consent be obtained?
   iii) How much time will be devoted to consent discussion?
   iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?
   v) What steps are you taking to minimize the possibility of coercion and undue influence?
   vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.
Drs. Most and Weissman will obtain consent in clinic during the study subject's first recruitment visit. Ten minutes will be dedicated to the consent discussion. This period of time should provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent. If not, the study subject may take more time and get back in touch with us if they decide to participate later. There is no payment to influence people to participate. We will not coerce anyone into participation. People are free to decline involvement at anytime. No children will be recruited.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See /hrpp/Chapter12.html for guidance.

We will read the consent form to the patients and answer any questions that they have. We will only be using English speaking patients and patients who are able to hear.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent, (iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

We will only use patients who are able to communicate well enough with us to be able to sign the consent forms fully and appropriately. If they are unable to sign the consent forms, they will not be enrolled in the study.

14. Assent Background (less than 18 years of age)

15. HIPAA Background

16. Attachments

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Obligations

The Protocol Director agrees to:
- Adhere to principles of http://humansubjects.stanford.edu/research/documents/eval_study_designGUI03017.pdf sound scientific
research designed to yield valid results

- Conduct the study according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and be trained in Human Research protection, ethical principles, regulations, policies and procedures
- Ensure all research personnel are adequately trained and supervised
- Ensure that the rights and welfare of participants are protected including privacy and confidentiality of data
- Ensure that, when de-identified materials are obtained for research purposes, no attempt will be made to re-identify them.
- Disclose to the appropriate entities any potential conflict of interest
- Report promptly any new information, modification, or http://humansubjects.stanford.edu/research/documents/Events-Info-Report-to-IRB_GUI03P13.pdf unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

VA Protocol Directors also certify that:
- All unanticipated internal or local SAEs, whether related or unrelated to the research, will be/have been reported to the IRB
- All subjects entered onto the master list of subjects for the study will sign/have signed an informed consent form prior to undergoing any study interactions or interventions, unless granted a waiver by the IRB.

Any change in the research protocol must be submitted to the IRB for review prior to the implementation of such change. Any complications in participants or evidence of increase in the original estimate of risk should be reported at once to the IRB before continuing with the project. Inasmuch as the Institutional Review Board (IRB) includes faculty, staff, legal counsel, public members, and students, protocols should be written in language that can be understood by all Panel members. The investigators must inform the participants of any significant new knowledge obtained during the course of the research.

IRB approval of any project is for a maximum period of one year. For continuing projects and activities, it is the responsibility of the investigator(s) to resubmit the project to the IRB for review and re-approval prior to the end of the approval period. A Notice to Renew Protocol is sent to the Protocol Director 7 weeks prior to the expiration date of the protocol.

Department Chair must approve faculty and staff research that is not part of a sponsored project. VA applicants must have Division Chief or Ward Supervisor approval. E-mail the Department Chair approval to IRBCoordinator@lists.stanford.edu.

All data including signed consent form documents must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, or other entities. (Policy on Retention of and Access to Research Data, Research Policy Handbook, http://www.stanford.edu/dept/DoR/rph/2-10.html)

PLEASE NOTE: List all items (verbatim) that you want to be reflected in your approval letter (e.g., Amendment, Investigator's Brochure, consent form(s), advertisement, etc.) in the box below. Include number and date when appropriate.

Y The Protocol Director has read and agrees to abide by the above obligations.