VivAer: A Correlation between Symptom Scores and Objective Findings

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Nasal obstruction that is not responding to appropriate medical therapy may be an indication for surgery. Recently, the minimally invasive VivAer procedure may also be an option.

In a multi-center, prospective study, 89% of patients who underwent the VivAer procedure reported improved sleep quality, and 94% of patients reported improved ability to breathe through their nose during exercise or exertion. Furthermore, there was a 97% overall response rate with a 67% reduction in Nasal Obstruction Symptom Evaluation (NOSE). No serious adverse events were reported with the use of VivAer.[1,2] While impressive, these positive outcomes were measured using patient symptom scores.

In patients with nasal obstruction, we propose to assess the objective improvement in nasal airflow secondary to the VivAer procedure. In an open-label, prospective single center study, patient questionnaires and objective measurements prior to and after the VivAer procedure will be conducted.

BACKGROUND AND SIGNIFICANCE

The VivAer intranasal remodeling treatment is a minimally invasive procedure, which uses a stylus to deliver controlled and targeted low energy radiofrequency heating to the nasal sidewall to gently reshape the tissues. Unlike most established treatments, it is an outpatient intervention administered under local anesthesia. The investigators of this study are each fellowship trained in rhinology and skull base surgery and not only understand which patients would benefit most from this treatment, but also be able to deliver the treatment safely.

Specific Aims:

- Eligible patients will show significant clinical improvement on the following patient questionnaires and on objective measurements.

Specific Aim 2:

- Improvement in Nasal Obstructive Symptom Evaluation (NOSE) score

Specific Aim 3:

- Improvement in SinoNasal Outcome Test (SNOT)-22 score

RESEARCH DESIGN AND METHODS

Study Design:

This is a prospective, non-randomized trial to assess objective improvement in nasal patency after undergoing treatment of the nasal valve with VivAer. Up to twenty-six subjects will be enrolled in this trial. Patients presenting with nasal obstruction and no notable septal deviation will be instructed to complete four weeks of intranasal steroid sprays. After patients complete the intranasal steroid spray, they will return to the clinic to assess nasal patency. If nasal obstruction symptoms persist, their eligibility for the VivAer procedure is assessed. The inclusion and exclusion criteria outlined below will be reviewed. If the patient is eligible and interested in receiving the VivAer procedure, they will be consented and receive a date to undergo the procedure. At the procedure date, they will perform baseline peak nasal inspiratory flow (PNIF) measurements and complete baseline Sino-Nasal Outcome Test (SNOT-22) scores and Nasal Obstructive Symptom Evaluation (NOSE) scores. After the procedure, subjects will be off steroid sprays for 2 weeks and will only use nasal saline irrigations during the procedure-recovery period. Subjects will return to clinic for evaluation at 4 weeks, 12 weeks and 24 weeks post procedure and during each of these visits will complete interval PNIF measurements, SNOT-22 scores, and NOSE scores.

Eligibility:

Inclusion Criteria:

1. Adults 18 years and older seeking treatment for nasal obstruction and willing to undergo an office-based procedure.
2. Nasal obstruction, defined as ≥60 by the NOSE scale.
3. The nasal valve is the primary or significant contributor to the subject's nasal obstruction as determined by the investigator, based on clinical presentation, physical examination, or nasal endoscopy.
4. Subjects has symptomatic improvement with use of external or internal nasal dilators, Q-Tip or curette test (manual intranasal lateralization), or the Cottle Maneuver (manual lateral retraction of the cheek).
5. Subject experienced minimal symptomatic improvement after the four-week fluticasone steroid nasal spray regimen.

Exclusion Criteria:

1. Prior surgery to the nasal valve, rhinoplasty, septoplasty, inferior turbinate reduction or other surgical nasal procedures within the past 12 months.
2. Severe and/or chronic sinusitis, recurrent sinusitis, or allergies leading to nasal obstruction and currently requiring *oral* corticosteroid therapy.
    a. Treated allergic rhinitis is not an exclusion criteria and eligible patients will be permitted to continue use of oral and/or topical medications throughout the trial.
3. Severe case of any of the following; septal deviation, turbinate hypertrophy, polyps, or ptotic nasal tip believed to be the primary contributor to the subject's nasal obstruction symptoms and warranting surgical intervention.

4. Known or suspected allergies or contraindications to the anesthetic agents and/or antibiotic medications to be used during the study procedure session.
5. Known or suspected pregnancy, or lactation.
6. Other medical conditions that the investigator believed would predispose subject to poor wound healing or increased surgical risk.

Study Calendar

	Consent	**Procedure**	**Four Week Follow-up (One Month; +/- one week)**	**Twelve Week Follow-up (Three Months; +/- 2 weeks)**	**Twenty-four Week Follow-up (Six Months; +/- 2 weeks)**
Exam	**X**		**X**	**X**	**X**
Determine Eligibility	**X**				
Procedure		**X**			
PNIF Measurements	**X**		**X**	**X**	**X**
SNOT-22 Questionnaire	**X**		**X**	**X**	**X**
NOSE Questionnaire	**X**		**X**	**X**	**X**
Adverse Event Monitoring		**X**	**X**	**X**	**X**

Description of Procedure

The region of the upper lateral cartilage is anesthetized intranasally using either topical lidocaine 4% or tetracaine 4%. Lidocaine 1% with epinephrine is subsequently injected to achieve complete local anesthesia.

Bilateral radiofrequency treatment is applied in a single visit using Aerin Medical's VivAer Stylus with a Model ORA-50S generator (Fig. **1**) at a setting of 60°C and 4 watts. The stylus is placed intranasally onto the mucosa overlying the lower edge of the upper lateral cartilage and three non-overlapping loci along the nasal valve angle are treated on each side

(Fig. 2). No incisions are made. Tissue temperature feedback is constantly provided by the stylus before, during and after treatment to allow the generator to modulate power for maintaining treatment temperature at 60°C, and procedure safety.

Each treatment cycle consists of an 18-second treatment pulse and 12-second cooling time while applying continuous upward pressure with the stylus in an outward direction perpendicular to the upper lateral cartilage at each position. A standardized approach is used based on animal and human pilot studies where temperature and duration parameters were determined for optimal safety and efficacy

Efficacy endpoint will be determined at 26 weeks using the NOSE and SNOT survey scores. Scores are assessed at baseline, 4, 12, and 26 weeks post procedure and the responder rate, defined as a ≥15-point decrease, was determined. In two studies, the minimally clinically important difference (MCID) in the NOSE score was calculated as approximately 4 to 6.3 points, so a ≥15-point was selected as the minimal clinically relevant change.[3,4]

Additionally, peak nasal inspiratory flow (PNIF) meters will be used at baseline, 4, 12, and 26 weeks.

Statistical Analysis:

Patient characteristics, objective measurements and patient questionnaires will be summarized using descriptive statistics such as mean with standard deviation and mean or frequency with percentage. Comparisons of outcomes measured between baseline and postop will be assessed using the paired t-test or McNemar's test. A total of 26 patients is required to achieve 80% power for a paired t-test with a significance level of $\alpha=0.05$ and a moderate effect size of $d=0.50$. All statistical analysis will be performed using SAS 9.4 (SAS Institute, Cary, NC) with two-sided tests and $p<0.05$ considered statistically significant.

FORESEEABLE RISKS AND DISCOMFORTS

Discomfort that is expected in the treatment area rarely will include inflammation/redness, swelling/edema, blanching, numbness, bruising, soreness/pain, bleeding at local anesthetic injection site, bleeding at the treatment site, nasal obstruction from tissue edema, disruption of mucosal flow/crusting.

Potential risks that have not been reported with VivAer but are theoretical risks after this treatment include the following: infection, bleeding greater than anticipated by the investigator, scar formation with subsequent nasal obstruction, sensory changes at the treatment site.

EXPECTED BENEFITS

It is anticipated that this procedure will improve nasal breathing. VivAer is minimally invasive. The objective data received from this study will help clinicians provide better guidance to patients interested in receiving this treatment.

EQUITABLE SELECTION OF SUBJECTS

Patients will not be categorically excluded from this research. The study population will be limited to those who are eligible based on the inclusion criteria for this study. If an eligible patient speaks another language aside from English, the study team will follow the institutions short form consent process. This will ensure all patients have the equitable right to participate in this research, while maintaining their comprehension of the study.

RECRUITMENT PROCEDURES

Physician's practices will be the basis of recruitment for this clinical trial.

CONSENT PROCEDURES

All subjects will receive the consent form for the study. This document will be read by the patients and reviewed by the patient with a licensed physician investigator and/or research study staff prior to participating in the study. The patient will be given as much time as they need to review the consent. Joseph R. Raviv MD, Auddie M. Sweis MD, or another licensed physician investigator will clarify any questions, concerns, or ambiguities prior to the patient signing consent. Patients will sign informed consent and only then will begin participation in the study. If new information is ascertained during the study, we will modify our consent and re-consent our patients.

DATA AND SAFETY MONITORING

Each site will conduct weekly research meetings with co-investigators and study staff to review study progress, including recruitment strategies, enrollment numbers, protocol issues, and safety issues. The PIs will participate in monthly conference calls regarding study progress.

Documentation of the presence of any side effect or adverse event will be completed at every visit using the adverse event classification available in appendix 1. Patients will be asked to contact an investigator or study staff member at any time concerning adverse events or worsening symptoms. All treatment related Serious Adverse Events (SAE) will be documented and reported immediately to the NorthShore IRB in line with institutional and regulatory requirements. In the event that a patient becomes ill or injured as a direct result of participation in the research study, necessary medical care will be available. All SAEs will be followed to resolution or stabilization.

MONITORING AND QUALITY ASSURANCE

Auddie Sweis, MD and Joseph Raviv, MD will oversee and monitor the study at an ongoing basis to ensure that it is being executed accurately and per protocol. Both will be responsible for monitoring the data collected, and the reporting of study-related adverse events to the IRB in accordance with adverse event reporting policies.

PRIVACY AND CONFIDENTIALITY

Medical information produced by this study will be stored in the investigator's file and identified by code number only. The code key connecting a specific name to specific information will be kept in a separate, secure location. Information contained in the records will not be given to anyone unaffiliated with NorthShore in a form that could identify the subject without the subjects written consent, except as described in the consent form or as required by law. It is possible that medical and research records, including sensitive information and/or identifying information, may be inspected and/or copied by federal or state government agencies, or hospital accrediting agencies, in the course of carrying out their duties. However, they are required to maintain confidentiality in accordance with laws and policies of the Hospital.

REFERENCES:

1. Jacobowitz, O., Driver, M. and Ephrat, M. (2019), In-office treatment of nasal valve obstruction using a novel, bipolar radiofrequency device. Laryngoscope Investigative Otolaryngology, 4: 211-217. https://doi.org/10.1002/lio2.247
2. Ephrat, M, Jacobowitz, O, Driver, M. Quality-of-life impact after in-office treatment of nasal valve obstruction with a radiofrequency device: 2-year results from a multicenter, prospective clinical trial. Int Forum Allergy Rhinol. 2021; 11: 755– 765. https://doi.org/10.1002/alr.22667
3. Stewart M, Smith T, Weaver E, et al. Outcomes after nasal septoplasty: results from the Nasal Obstruction Septoplasty Effectiveness (NOSE) study. Otolaryngol Head Neck Surg 2004;130(3):283–290. [PubMed] [Google Scholar]
4. Lipan M, Most S. Development of a severity classification system for subjective nasal obstruction. JAMA Facial Plast Surg 2013;15(5):358–361. [PubMed] [Google Scholar]

Appendices:

Appendix 1:

Adverse Events Definitions

1. **Adverse Event (AE)**
    a. Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational medical device.
2. **Serious Adverse Event (SAE): any AE that**
    a. Led to death, or
    b. Led to serious deterioration in the health of the subject, that either:
        i. Resulted in a life-threatening illness or injury, or
        ii. Resulted in a permanent impairment of a body structure or a body function, or
        iii. Required in-patient or prolonged hospitalization, or
        iv. Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or
    c. Led to fetal distress, fetal death, or a congenital abnormality or birth defect.
3. **Unanticipated Adverse Device Effect (UADE)**
    a. *Unanticipated adverse device effect* means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

4. **Severity**

    a. The Investigator or designee is required to determine severity of the AEs reported. The following definitions are used for determination:

        Mild – Easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities. These events generally do not require treatment.

        Moderate – Sufficiently discomforting to interfere with normal everyday activities. These events are usually relieved by simple therapeutic measures.

        Severe – Prevents normal, everyday activities. These events may require systemic drug therapy, other medical treatment, or return to the operating room.

5. Relationship to Investigational Device

a. The Investigator or designee is required to determine the relationship of each AE to the investigational device. The following definitions are used for determination:

i. **Definite** – The AE follows a known or expected response pattern to the device and the physician confirms the relationship through further testing or evidence.

ii. **Probable** – The AE follows a known or expected response pattern to the device.

iii. **Possible** – The AE follows a known or expected response pattern to the device but could readily have been produced by a number of other factors.

iv. **None** – An AE for which sufficient information exists to indicate that the etiology is unrelated to the device; the AE is readily explained by the subject's clinical state or other therapies.