

# Cryosurgical posterior nasal tissue ablation for the treatment of rhinitis

Peter H. Hwang, MD<sup>1</sup>, Bryant Lin, MD<sup>2</sup>, Raymond Weiss, MD<sup>3</sup>, James Atkins, MD<sup>4</sup> and Jacob Johnson, MD<sup>5</sup>

**Background:** Endoscopic posterior nasal nerve (PNN) resection has been described as an efficacious surgical treatment of allergic and nonallergic rhinitis, but the requirement for surgery under general anesthesia has limited its acceptance. We report the first series of patients treated for chronic rhinitis using a novel device designed for office-based cryosurgical ablation of the PNN.

**Methods:** Twenty-seven patients with chronic rhinorrhea and/or nasal congestion for >3 months were recruited (allergic or nonallergic rhinitis), with minimum rhinorrhea and/or congestion subscores of 2 as part of the Total Nasal Symptom Score [TNSS]). Under local anesthesia, the cryotherapy device was applied endoscopically to the posterior middle meatus and was used to freeze the PNN region bilaterally. Patients were followed up after 7, 30, 90, 180, and 365 days to assess TNSS.

**Results:** The procedure was successfully completed in 100% of patients, with no complications; 74% reported no or mild discomfort by the first postprocedure day. TNSS was reduced significantly at 30 days (mean  $\pm$  standard deviation:  $6.2 \pm 0.5$  at baseline,  $2.6 \pm 0.3$  at 30 days,  $n = 27$ ,  $p < 0.001$ ), with continued reduction at 90 ( $2.7 \pm 0.4$ ,  $n = 24$ ,  $p < 0.001$ ), 180 ( $2.3 \pm 0.5$ ,  $n = 21$ ,  $p < 0.001$ ), and 365 days ( $1.9 \pm 0.3$ ,  $n = 15$ ,  $p < 0.001$ ). Both rhinorrhea and

congestion subscores decreased significantly at 30, 90, 180, and 365 days compared to baseline ( $p < 0.001$ ). Allergic and nonallergic subcohorts both appeared to benefit from treatment.

**Conclusion:** Office-based cryotherapy of the PNN region is safe and well tolerated. Symptom scores were significantly decreased by 7 days postprocedure and remained lower at 30, 90, 180, and 365 days. © 2017 The Authors International Forum of Allergy & Rhinology, published by ARSAAOA, LLC. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

#### Key Words:

allergic rhinitis; nonallergic rhinitis; rhinorrhea; posterior nasal nerve; vidian neurectomy; cryosurgery; cryoablation; congestion; parasympathetic; endoscopic

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Allergic and nonallergic rhinitis are estimated to impact over 58 million people in the United States alone.<sup>1</sup> While rhinitis has conventionally been perceived to be an illness primarily treated with medication, surgical

treatments have been considered as early as 1961. Vidian neurectomy has been the predominantly favored surgical procedure to date, with demonstrated long-term efficacy for both vasomotor and allergic rhinitis.<sup>2-5</sup> The vidian nerve supplies most of the parasympathetic innervation to the secretory nasal mucosa via the preganglionic parasympathetic fibers of the greater petrosal nerve, which synapses at the pterygopalatine ganglion, giving rise to postganglionic innervation to the nasal mucosa via the posterior nasal nerves (PNN).<sup>6,7</sup> Whereas electrical stimulation of the vidian nerve has been shown to cause profuse secretion, mucosal swelling, and sneezing,<sup>8</sup> transection of the vidian nerve has been thought to correct the imbalance of autonomic input to the nasal mucosa,<sup>9</sup> reducing nasal antigen responses and vascular hyperreactivity.<sup>6,7</sup>

Though efficacious for rhinitis, vidian neurectomy may be complicated by persistent dry eye symptoms due to collateral disruption of the parasympathetic innervation of

<sup>1</sup>Department of Otolaryngology-Head and Neck Surgery, Stanford University School of Medicine, Stanford, CA; <sup>2</sup>Department of Medicine, Stanford University School of Medicine, Stanford, CA; <sup>3</sup>Sinus Center of the South, Ocean Springs, MS; <sup>4</sup>Texas Sinus Center, San Antonio, TX; <sup>5</sup>San Francisco Otolaryngology, San Francisco, CA

Correspondence to: Peter H. Hwang, MD, 801 Welch Road, Stanford, CA 94305; e-mail: hwangph@stanford.edu

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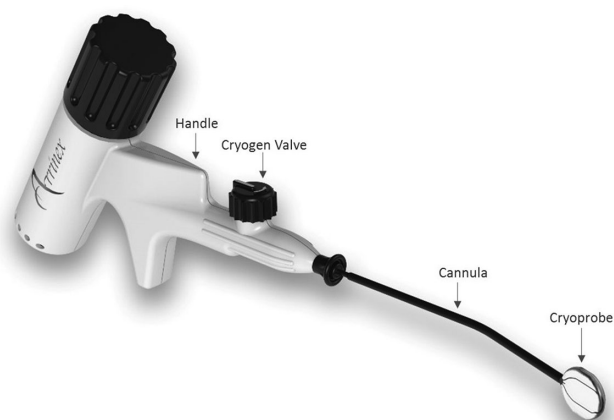
the lacrimal gland arising partially from the vidian nerve.<sup>4</sup> The PNN, whose postganglionic parasympathetic fibers are anatomically distal to the lacrimal innervation branch point, has been proposed as an alternative surgical target in order to avoid dry eye complications. First described in the 1980s, posterior nasal neurectomy has been reported to successfully treat both allergic and nonallergic rhinitis while sparing lacrimal innervation.<sup>6,10–15</sup> The technical nuances of the procedure and the need for general anesthesia have limited the broad acceptance of both vidian neurectomy and PNN resection.

A novel cryotherapy device (ClariFix™; Arrinex, Inc., Redwood City, CA) has been developed for office-based cryosurgical ablation of the PNN region, which requires minimal training and can be performed under local anesthesia. We report the first series of patients treated in a pilot study with this device for reduction of rhinitis symptoms. The study objectives were to describe the tolerability, safety, and feasibility of this novel device-based procedure to improve symptoms in patients that suffer from chronic rhinitis.

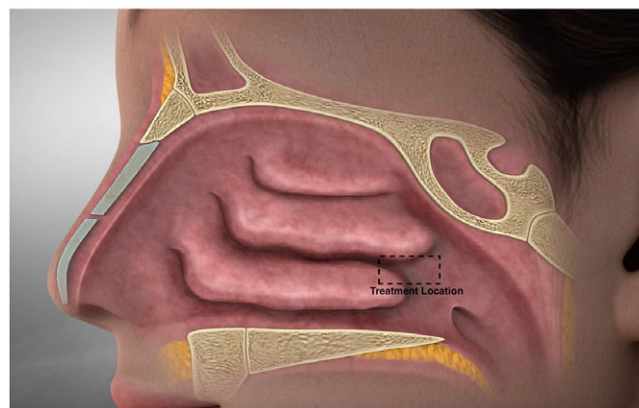
## Patients and methods

This protocol was approved by Quorum Independent Review Board. Candidates for the study were adult patients with rhinorrhea with or without nasal congestion symptoms despite medical therapy >3 months. The study was performed across 3 sites: Sinus Center of the South Bay Area ENT; Texas Sinus Center; and San Francisco Otolaryngology. Patients who had persistent symptoms were screened with the reflective Total Nasal Symptom Score (TNSS). TNSS is a validated symptom severity scoring system that consists of the sum of 4 individual subject-assessed symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing, each evaluated using a scale of 0 = none, 1 = mild, 2 = moderate, or 3 = severe. The reflective TNSS is a maximum 12-point scale based on the subject's evaluation of symptom severity over the preceding 12 hours. Patients who had a minimum rhinorrhea and/or congestion subscore of 2 were eligible for the study. Patients were also screened with a diagnostic nasal endoscopy. Exclusion criteria included patient-reported history of chronic rhinosinusitis, severe septal deviation precluding visualization of the middle meatus, endoscopic findings of polyps or purulence in the middle meatus, septal perforation, or prior sinus or nasal surgery that significantly altered the anatomy of the posterior nasal cavity. Upon entry to the study, patients completed the TNSS to assess symptoms of rhinorrhea, nasal congestion, nasal itching, and sneezing. Patient demographics and medical history were also recorded, including atopic status based on blood or skin test. Patients were asked to report their baseline medication use for treatment of rhinitis.

The intervention was performed in the office using a novel cryotherapy device called the ClariFix device. The device is a hand-held, endoscopically placed cryoprobe through



**FIGURE 1.** A drawing of the ClariFix cryotherapy device (image source: Arrinex, Inc.).



**FIGURE 2.** Anatomic drawing of the targeted area of treatment of the PNN (image source: Arrinex, Inc.).

which nitrous oxide cryogen is delivered at the tip in a closed system (Fig. 1).

The cryogen cartridge is inserted into the handle immediately prior to the procedure. The cryogen is released into the probe tip by the surgeon via a control dial. The device is designed for single-patient use and is disposable.

The procedures were performed under local anesthesia in the office setting using topical anesthetic (4% tetracaine or 3% bupivacaine) or injected 1% lidocaine with 1:100,000 epinephrine, per surgeon's preference. After application of anesthesia, the tip of the cryodevice was applied endoscopically to the posterior middle meatus, and the surgeon then activated the cryogen to perform cryoablation of the mucosa in the region of the PNN (Fig. 2). The cryogen cartridge was then changed and the contralateral side was treated in an identical fashion.

Patients then returned for follow-up nasal endoscopy at 7, 30, and 90 days postprocedure. Additionally, patients were interviewed to assess nasal symptoms and side effects at 1, 7, 30, 90, 180, and 365 days.

A research assistant unaffiliated with the sponsor collected data at each site. Descriptive statistics were used to

evaluate and summarize the data. Changes from baseline were evaluated using a paired *t* test examining the distribution of within-patient changes from baseline for each of the follow-up intervals. Statistical analysis was performed by an independent biostatistician funded by Arrinex.

## Results

Twenty-seven patients were enrolled in the study from 3 centers. The mean  $\pm$  standard deviation age was  $53.3 \pm 3.3$  years with 37% male and 63% female patients. Forty-eight percent of patients were atopic (allergic). All procedures were completed successfully with most procedures completed in less than 20 minutes, and treatment was well tolerated under both topical and injected local anesthesia ( $n = 15$  topical anesthetic,  $n = 12$  injected anesthetic). Patients reported a mean pain rating of  $1.19 \pm 0.18$ , using a 0 to 5 Wong-Baker FACES pain rating scale. Immediate posttreatment endoscopy typically showed minor bleeding and transient blanching at the treatment sites, with no other significant findings reported. Typical endoscopic findings for 1 patient are shown in Figure 3. Physicians rated treatment delivery as “easy” to “moderately easy” in 89% of the procedures (24/27), and “moderately difficult” in 11% of the procedures (3/27).

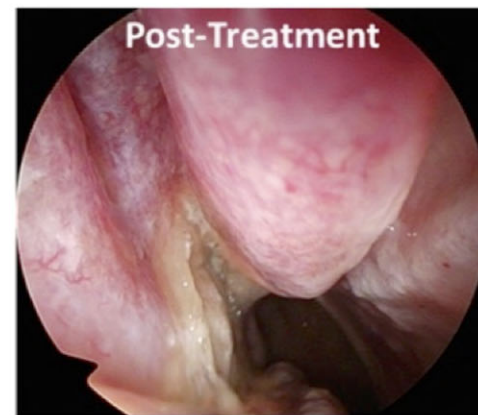
At 7 days postprocedure, TNSS decreased significantly from a mean score of  $6.2 \pm 0.5$  out of 12 at baseline to a mean of  $4.3 \pm 0.4$  ( $p < 0.005$ ) with continued significant reduction at 30 days ( $2.6 \pm 0.3$ ,  $n = 27$ ,  $p < 0.001$ ), 90 days ( $2.7 \pm 0.4$ ,  $n = 27$ ,  $p < 0.001$ ), 180 days ( $2.3 \pm 0.5$ ,  $n = 21$ ,  $p < 0.001$ ), and 365 days ( $1.9 \pm 0.3$ ,  $n = 15$ ,  $p < 0.001$ ) (Fig. 4). Six patients were lost to follow-up at 180 days, and 12 patients could not be reached at 365 days.

The largest reductions in symptoms were seen in rhinorrhea and congestion. The average baseline rhinorrhea score of  $2.4 \pm 0.8$  (out of 3) was significantly reduced at 30 days ( $1.1 \pm 0.2$ ,  $n = 27$ ,  $p < 0.001$ ), 90 days ( $1.1 \pm 0.2$ ,  $n = 27$ ,  $p < 0.001$ ), 180 days ( $1.1 \pm 0.2$ ,  $n = 21$ ,  $p < 0.001$ ), and 365 days ( $1.2 \pm 0.2$ ,  $n = 15$ ,  $p < 0.001$ ). The average baseline congestion score of  $1.9$  (out of 3)  $\pm 0.2$  was significantly reduced at 30 days ( $0.8 \pm 0.2$ ,  $n = 27$ ,  $p < 0.001$ ), 90 days ( $0.7 \pm 0.1$ ,  $n = 27$ ,  $p < 0.001$ ), 180 days ( $0.5 \pm 0.2$ ,  $n = 21$ ,  $p < 0.001$ ), and 365 days ( $0.5 \pm 0.2$ ,  $n = 15$ ,  $p < 0.001$ ).

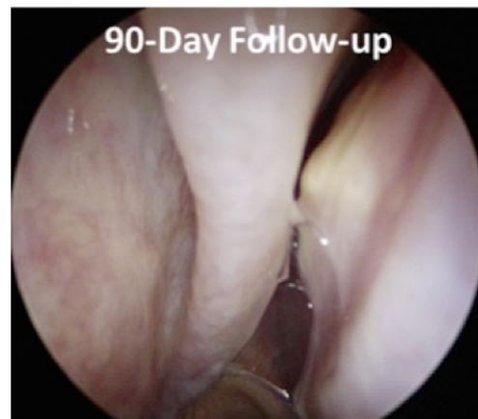
The symptom data were also analyzed with respect to the success of cryoablation according to atopic status. In the study, there were 13 nonallergic patients and 13 allergic patients confirmed atopic by either prior skin test or blood test. One subject who had not been tested for allergy was thus excluded from this analysis. In nonallergic patients, TNSS decreased significantly from a mean of  $6.5 \pm 0.7$  at baseline to  $2.6 \pm 0.3$  ( $n = 13$ ,  $p < 0.001$ ) at 30 days and  $2.4 \pm 0.4$  ( $n = 13$ ,  $p < 0.001$ ) at 90 days. TNSS was still reduced at 180 days ( $1.7 \pm 0.4$ ,  $n = 10$ ,  $p < 0.001$ ) and 365 days ( $1.6 \pm 0.4$ ,  $n = 9$ ,  $p < 0.001$ ). In allergic patients, TNSS decreased significantly at 30 days ( $2.5 \pm 0.6$ ,  $n = 13$ ,  $p < 0.01$ ) and 90 days ( $3.1 \pm 0.6$ ,  $n = 13$ ,  $p < 0.01$ ).



3.A



3.B

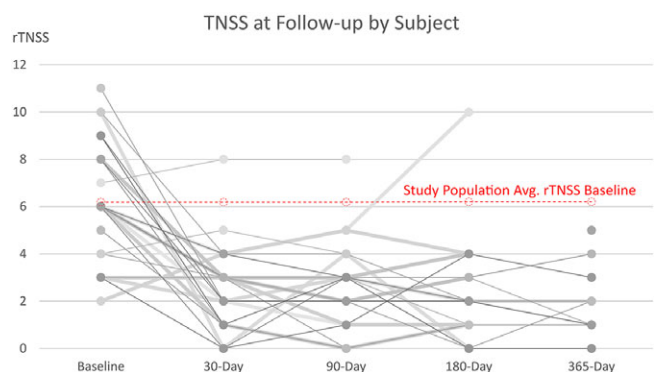


3.C

**FIGURE 3.** Endoscopic images from a subject at (A) treatment, (B) immediately posttreatment, and (C) 90-day follow-up (image source: Arrinex, Inc.).

At 180 days, TNSS trended lower ( $2.7 \pm 0.9$ ,  $n = 10$ ,  $p = 0.05$ ) but did not reach statistical significance. At 365 days, the TNSS was significantly lower for those patients not lost to follow-up ( $2.5 \pm 0.6$ ,  $n = 6$ ,  $p < 0.05$ ). Comparison of allergic and nonallergic subjects is summarized in Figure 5.

With regard to side effects of treatment, on the first post-procedure day, 74% ( $n = 20$ ) of patients reported no or



## Discussion

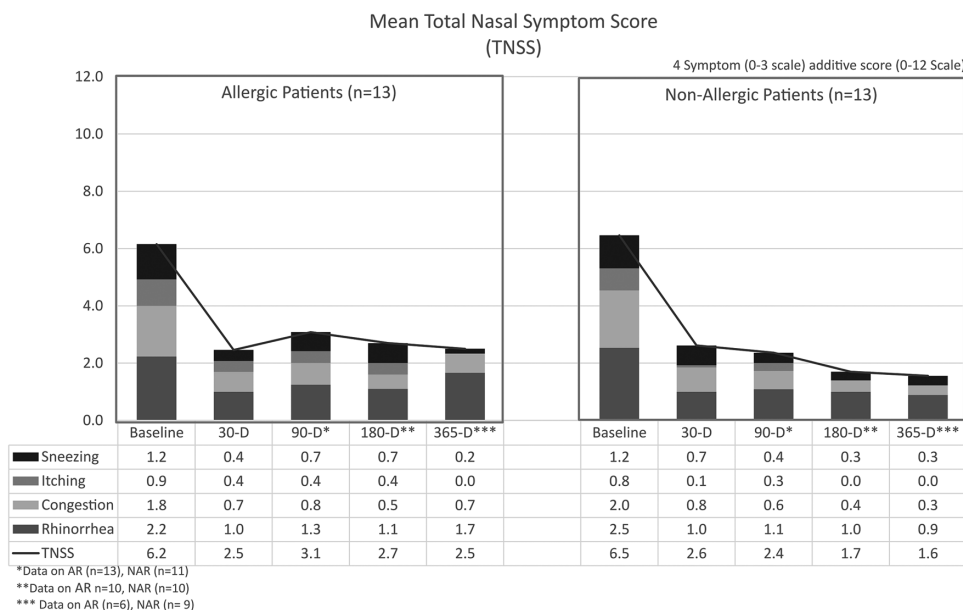
Cryoablative techniques have been used in the head and neck region for a number of different applications.<sup>15-20</sup> Cryotherapy offers the advantage of ablating soft tissue and nerve with predictable depth of penetration, while preserving arterial vascular supply to the region, hence minimizing the risk of necrosis. Cryoablative neurolysis for the treatment of rhinitis has been described in papers dating back as early as the 1970s with some promising results, but the replicability of these outcomes was challenged by non-ergonomic probe design, lack of endoscopic visualization, and the need for external cryogen reservoirs.<sup>15-18</sup> In contrast, the cryoablative procedure presented here uses endoscopic visualization for anatomic precision and specificity. Furthermore, the procedure utilizes a novel cryoprobe that is light, hand-held, and easily manipulated, with an internally contained and controlled cryogen reservoir that delivers cryogen at a standardized, predictable rate.

**FIGURE 4.** Graph of the rTNSS for each patient at baseline, 30, 90, 180, and 365 days. rTNSS = reflective Total Nasal Symptom Score.

mild pain/discomfort, 100% (n = 27) reported no or mild bleeding, 44% of patients (n = 12) experienced severe ear blockage, and 4% (n = 1) reported severe nasal dryness at 1 day postprocedure. By 7 days, 7% (n = 2) reported severe nasal dryness and only 4% (n = 1) reported severe ear blockage; in all cases these side effects improved or fully resolved by the 30-day follow-up interval. There were no reported instances of dry eye or palatal numbness in either the immediate or extended postoperative period. One adverse event was reported in the study period; this consisted of a moderate nosebleed that occurred 27 days after the index procedure. The event, managed operatively by electrocautery of the bleeding site, was reported by the surgeon as “possibly related to the study device/procedure.” Healing was otherwise uneventful in all patients, with no infectious complications or reports of scarring, mucosal atrophy, or bone exposure at the treatment sites assessed by endoscopic examination.

Cryoablation with the ClariFix device was safe and well tolerated by all patients in the study. All patients were able to complete the procedure in an office setting, and minimal pain and discomfort were reported by the first postprocedure day. The possibility of a blocked ear sensation was a concern given the anatomic proximity of the treatment area to the Eustachian tube and was experienced by 12 patients on postprocedure day 1. Reassuringly, by 7 days, only 1 patient reported a sensation of severe blockage, which subsided completely by the 30-day follow-up. There were no device-related or procedure-related serious adverse events. Last, consistent with prior studies on endoscopic PNN section, no patients reported dry eye in our series.

The feasibility of this procedure as an efficacious treatment for improving rhinitis symptoms was supported by



**FIGURE 5.** Bar graph comparing TNSS and symptom subscores of allergic (left) and nonallergic patients (right) at baseline, 30, 90, 180, and 365 days. TNSS = Total Nasal Symptom Score.




favorable reductions in all nasal symptom scores by TNSS, seen as early as 7 days postprocedure. The greater than 50% reduction in TNSS seen as early as 30 days compares favorably to those reductions seen in nasal steroid spray pharmacologic trials.<sup>21</sup> Cryoablation appears to be beneficial for both rhinorrhea and congestive components of rhinitis, reflective of the beneficial impact of reducing parasympathetic tone on both secretory and vasoactive components of nasal physiology. Although this study involved a small cohort, there is suggestion that cryoablation may benefit patients with both nonallergic rhinitis and allergic rhinitis. This is consistent with prior studies of PNN surgery, which have shown benefit in both allergic and nonallergic populations.<sup>10–15</sup> Larger series of stratified patient cohorts would be necessary to confirm these preliminary findings.

While we observed symptom improvements in 74% of the original cohort of patients by 6 months postprocedure, our data regarding the longevity of the therapeutic effect of cryotherapy are suggestive but not definitive, primarily due to subject attrition at follow-up. The observed reduction in subjects' symptoms at 365 days, in particular rhinorrhea and congestion, suggest potential benefit up to 1 year after treatment. However, as 12 subjects were lost to follow-up at the 1-year mark, we feel that a larger long-term cohort would be needed to definitively characterize long-term benefits of cryotherapy. We do believe that the duration of treatment benefit of this procedure may exceed

that described in historical trials of cryoneurolysis, owing to more precise anatomic localization of treatment by endoscopy, and standardization of the duration and amount of cryotherapy application.<sup>19,20,22</sup>

The limitations of the study include the small sample size and loss to follow-up during the extended period. Medication use was not systematically tracked in this study but will be tracked in future studies. In addition to following the current cohort for an extended period of time, larger cohort studies for both allergic rhinitis and nonallergic rhinitis will be conducted, to fully assess this device and procedure for these patient subsets.

## Conclusion

Office-based cryotherapy of the PNN using the ClariFix device is safe, well tolerated, and results in decreased symptom scores for at least 6 months and the effect may persist up to 1 year. Longer-term and larger studies are necessary to further characterize duration of treatment effect. 

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