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ORIGINAL ARTICLE

Temperature-controlled radiofrequency neurolysis for treatment of chronic rhinitis: 12-month outcomes after treatment in a randomized controlled trial

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Abstract

Background: Temperature-controlled radiofrequency (TCRF) neurolysis of the posterior nasal nerve (PNN) area for the treatment of chronic rhinitis was previously reported as superior to a sham-control procedure at 3 months post-procedure in a randomized controlled trial (RCT). The primary endpoint was a responder rate of ≥30% improvement (decrease) for 24-hour reflective total nasal symptom score (rTNSS) compared with baseline. Herein, 12-month outcomes after active treatment are reported.

Methods: In this prospective, multicenter, patient-blinded RCT, patients in the index active treatment arm were unblinded at 3 months and followed through 12 months. At 3 months, eligible patients from the sham-control arm of the study were invited to crossover to active treatment. Eligibility criteria included rTNSS ≥6, with moderate-severe rhinorrhea and mild-severe congestion. The TCRF stylus was applied bilaterally to nonoverlapping areas in the region of the PNN.

Results: Patients in the index active treatment arm (n = 77) had a mean baseline rTNSS of 8.3 (95% confidence interval [CI], 7.9-8.7). At 12 months, the responder rate was 80.6% (n = 67) (95% CI, 69.1%-89.2%). At 12 months, the mean change in rTNSS was −4.8 (95% CI, −5.5 to −4.1; $p < 0.001$), a 57.8% improvement. The available initial rTNSS-based outcomes in the crossover active treatment arm ($n = 27$)

were following the same course as the index treatment arm. No serious adverse events and 8 adverse events related to the device/procedure were reported in the trial to date.

Conclusion: TCRF neurolysis of the PNN area is safe and the symptom burden improvement that was superior to a sham procedure at 3 months was sustained through 12 months.

KEYWORDS
congestion, neurolysis, posterior nasal nerve, radiofrequency ablation, rhinitis, rhinorrhea

1 | INTRODUCTION

Temperature-controlled radiofrequency (TCRF) neurolysis of the posterior nasal nerve (PNN) is a minimally invasive treatment option for chronic rhinitis patients. The PNN is composed of both sensory and autonomic nerves and provides parasympathetic innervation of the nasal mucosa. Neurolysis of the PNN in the nasal cavity, distal to the pterygopalatine ganglion, helps to minimize the dry eye side effects seen in surgical procedures such as vidian neurectomy. The RhinAer™ system (Aerin Medical, Inc., Sunnyvale, CA) is a device designed for TCRF neurolysis of the PNN. The target tissue is the posterior middle meatus and superior portion of the posterior inferior turbinate, in the region of the PNN. TCRF technology monitors tissue temperature and automatically adjusts the radiofrequency (RF) current to maintain a therapeutic treatment temperature of ~60°C, minimizing adjacent tissue injury.

In an earlier report of this randomized controlled trial (RCT) at 3 months, TCRF neurolysis of the PNN was shown to be superior to a sham-control procedure for the treatment of patients with chronic rhinitis.[1] The technology has also demonstrated efficacy over the long term in a single-arm study at 12 months.[2] Herein we report on the 12-month safety and efficacy results for the index active treatment arm of this RCT and the progress of those index sham-control arm patients who elected to cross over to active treatment at 3 months.

2 | PATIENTS AND METHODS

2.1 | Design

This was a prospective, multicenter, single-blinded (patient) RCT with a sham procedure control arm. The trial was a superiority design with 1-way crossover available to the patients randomized to the sham control arm after their 3-month follow-up visit, if still eligible. Patients were enrolled at 16 centers in the United States. The investigation was approved by either the Western Institutional Review Board (IRB) or center-specific IRBs (Rush University Medical Center, Vanderbilt University, Houston Methodist). The trial was registered at clinicaltrials.gov (NCT04533438). All enrolling center principal investigators were board-certified otolaryngologists. All patients gave written informed consent before undergoing any trial-specific procedures.

2.2 | Trial arm and baseline definitions

In this report, the study arms are referred to as: (i) index active treatment, (ii) index sham control, and (iii) crossover active treatment. The term "baseline" refers to the outcome measure value before a procedure: In the case of the index active treatment and index sham-control arms, baseline is before active treatment procedure and sham procedure, respectively. In the case of the crossover active treatment arm, baseline refers to the outcome measure value reported at the time of requalification for crossover.

2.3 | Randomization, unblinding, and crossover to active treatment

A 2:1 center-stratified block randomization scheme was used. Patients were blinded to their assignment and blindfolded during the index procedure (active treatment or sham control). Patients were unblinded after the 3-month visit (primary endpoint) and index sham-control arm patients were transitioned to crossover active treatment if they still met eligibility criteria and agreed to continue participation in the trial. Index sham-control patients who were not eligible for crossover or did not wish to further participate in the trial were exited from the trial. Patients who underwent additional nasal procedures at any time during follow-up were also exited from further trial participation.

2.4 | Eligibility criteria

A complete list of eligibility criteria is available in the Supporting Information. Key inclusion criteria for patients were: age 18 to 85 years; seeking treatment for chronic rhinitis symptoms of ≥6-month duration; and total 24-hour reflective total nasal symptom score (rTNSS) of ≥6, with moderate to severe symptoms of rhinorrhea (rhinorrhea subscore of 2-3) and mild to severe symptoms of nasal congestion (congestion subscore of 1-3). Key exclusion criteria for patients were: anatomic obstructions limiting access to the posterior nasal passage; altered anatomy of the posterior nose as a result of previous sinus or nasal surgery or injury; active nasal or sinus infection; history of significant dry eye, chronic epistaxis, rhinitis medicamentosa, or head or neck irradiation; seasonal allergic rhinitis; a predisposition to excessive bleeding; anticoagulation therapy that could not be discontinued before the trial procedure; previous procedure or surgery for chronic rhinitis; and a predisposition to poor wound healing (in the opinion of the investigator).

2.5 | Active treatment with TCRF device

Crossover active treatment patients underwent the same procedure and follow-up regimen as index active treatment patients. The RhinAer System consists of the Aerin Console and the RhinAer Stylus, and the single-use disposable stylus delivers bipolar RF energy to tissue. The protocol allowed treatment at 1 to 5 nonoverlapping positions along the distribution of the PNN, based on target anatomy size. The treatment area was the posterior middle meatus and superior portion of the posterior inferior turbinate, in the region of the PNN. Patients were treated in-office and received topical anesthesia. Lidocaine (with or without epinephrine, per investigator preference) was administered by submucosal infiltration in the target area. Treatment settings per lesion were as follows: temperature, 60°C; power, 4 Watts; and a treatment time of 12 seconds. No repeat (touch-up) procedures were permitted in the follow-up period. Patients marked a 10-cm visual analog scale (VAS) to capture their pain level immediately postprocedure.

2.6 | Outcome measures

The primary endpoint and secondary endpoint measures of this RCT at 3 months have been defined and reported elsewhere.[1] A new baseline rTNSS was collected for patients crossing over to active treatment and was recorded for all patients over time. Responder rate, wherein a responder was defined as ≥30% improvement (decrease) in rTNSS from baseline,[3,4] was determined for all patients over time. Postnasal drip and cough scores were collected using a 4-point scale (0-3) for baseline at index and crossover baselines and throughout follow-up. The frequencies of device- and procedure-related adverse events were recorded throughout the trial in all patients. A pain VAS score was collected at 1 and 3 months for the crossover active treatment arm. Patients will be followed through at least 2 years in this trial, and the results presented herein represent those observed up to the time of submission for publication.

2.7 | Statistical analysis

The sample size justification for this RCT has been described previously.[1] Demographic and baseline characteristics of the index active treatment and crossover active treatment arms were compared using *t* tests for continuous data and Fisher exact tests for categorical measures. Adjusted mean rTNSS and rTNSS subscores and postnasal drip and cough scores and 95% confidence intervals (CIs) were determined at baseline and all follow-up timepoints. A negative change indicates a decrease (improvement) in rTNSS total score, rTNSS subscore, postnasal drip score, and cough score. The within-arm changes in rTNSS total scores were compared using a restricted maximum-likelihood–based, mixed-model, repeated-measures analysis to account for multiple follow-up timepoints. Unadjusted means and CIs are presented for the crossover active treatment arm data due to only 6-month reporting at this time. Postnasal drip and cough scores are reported as median and interquartile range (IQR) for comparison with previous between-arm reports in this trial and as adjusted mean and CIs for comparison with other studies.[2] Due to data not meeting the normality assumption necessary for *t* tests, between-arm changes in postnasal drip and cough scores at 3 months were compared using Wilcoxon-Mann-Whitney tests. Generalized estimating equations were used to assess repeated multinomial ordered categorical distributions. For the pain VAS, change from immediately postprocedure through follow-up pain VAS data were analyzed using a restricted maximum-likelihood–based, mixed-model, repeated-measures analysis to account for both 1- and 3-month timepoints. Statistical analysis was performed using SAS version 9.4 and SAS/STAT version 15.2 (SAS Institute, Cary, NC).

3 | RESULTS

A total of 117 patients were enrolled, randomized 2:1, and treated in this RCT, with 78 assigned to the index active treatment arm and 39 assigned to the index

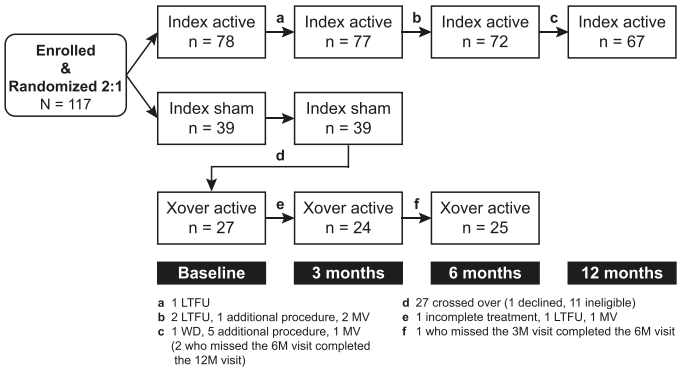

FIGURE 1 Patient disposition, including crossover of the index sham-control arm to active treatment at 3 months, if eligible. Patients who underwent additional nasal procedures were excluded from the trial. Abbreviations: LTFU = lost to follow-up; MV = missed visit; WD = withdrawal from the trial.

TABLE 1 Patients' demographics and index baseline characteristics by arm[a]

	Index active (n = 77)	Index sham (n = 39)	Crossover active (n = 27)	*p* value[b]
Female sex	49 (63.6%)	26 (66.7%)	16 (59.3%)	0.818
Age (years)	57.3 ± 14.8	57.8 ± 14.4	57.4 ± 14.6	0.974
BMI (kg/m^2)	27.8 ± 5.6	28.3 ± 6.3	28.6 ± 6.8	0.528
Race				
Asian	1 (1.3%)	0 (0.0%)	0 (0.0%)	—
Asian, white	0 (0.0%)	1 (2.6%)	1 (3.7%)	—
Black or African American	5 (6.5%)	1 (2.6%)	0 (0.0%)	—
Black or African American, white	0 (0.0%)	1 (2.6%)	0 (0.0%)	—
White	69 (89.6%)	36 (92.3%)	26 (96.3%)	—
Declined choices	2 (2.6%)	0 (0.0%)	0 (0.0%)	—
Nasal exam				
Turbinate enlargement	16 (20.8%)	8 (20.5%)	4 (14.8%)	0.582
Nasal polyps	3 (3.9%)	0 (0.0%)	0 (0.0%)	0.566
Previous nasal surgery	27 (35.1%)	13 (33.3%)	11 (40.7%)	0.646
Medication use[c]				
Antihistamines	46 (59.7%)	26 (66.7%)	16 (59.3%)	>0.999
Decongestants	12 (15.6%)	6 (15.4%)	4 (14.8%)	>0.999
Oral leukotriene inhibitors	5 (6.5%)	4 (10.3%)	3 (11.1%)	0.425
Intranasal steroid sprays	31 (40.3%)	23 (59.0%)	15 (55.6%)	0.184
Intranasal anticholinergic sprays	20 (26.0%)	7 (17.9%)	5 (18.5%)	0.602

Abbreviations: BMI = body mass index; rTNSS = 24-hour reflective total nasal symptom score.

[a]Continuous variables presented as mean ± standard deviation. Categorial measures presented as number (% of total). Characteristics of the index active treatment and index sham-control arms have been reported previously, except as noted for the medications below.

[b]Characteristics of the index active and crossover active arms were compared using *t* tests for continuous data and Fisher exact tests for categorical measures. Comparison of the characteristics of the index active treatment and index sham-control arms have been reported previously, except as noted for the medications below.

[c]Ongoing trial monitoring of medication data resulted in updates to medication statuses, and therefore the results for the index active treatment arm and index sham-control arm are updates of previously reported values.

sham-control arm (Fig. 1). Patients underwent index procedures between July 2020 and December 2020. Primary endpoint analysis was previously reported on 77 and 39 patients from the index active treatment and sham-control arms, respectively.[1] After unblinding at 3 months after the index procedure, 27 index sham-control arm patients crossed over to active treatment (Fig. 1). As of this writing, the crossover active treatment arm has reached 6-month follow-up. Figure 1 summarizes the patient disposition in each arm throughout follow-up. Demographics and index baseline characteristics of the patients in each arm are shown in Table 1.

TABLE 2 Percentage of patients in index active treatment arm classified as responders[a] with no data imputation and with data imputation for increased medication use

	3 months, n = 77	6 months, n = 72	12 months, n = 67
No imputation	67.5% (55.9%-77.8%)	75.0% (63.4%-84.5%)	80.6% (69.1%-89.2%)
Medication increase imputation[b]	62.3% (50.6%-73.1%)	59.7% (47.5%-71.1%)	61.2% (48.5%-72.9%)
Number of datapoints imputed[c]	4	11	13

[a]Responders defined as patients with ≥30% improvement in 24-hour reflective total nasal symptom score from baseline and as percentage of total (95% confidence interval).

[b]Responder rate after imputing data from patients with an increase in at least 1 medication class (antihistamines, decongestants, oral leukotriene inhibitors, intranasal steroid sprays, intranasal anticholinergic sprays) to nonresponder status if not already a nonresponder.

[c]Number of datapoints imputed at each timepoint. Data were imputed at all timepoints after an increase in at least 1 medication class. The numbers are cumulative over time.

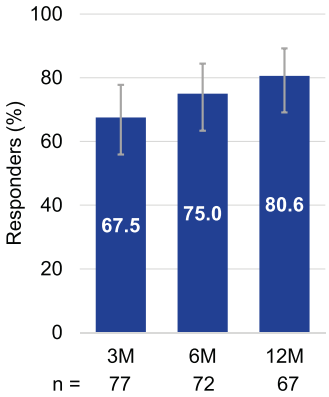

FIGURE 2 Responder rate of the index active treatment arm through 12 months, defined as ≥30% improvement in 24-hour reflective total nasal symptom score (rTNSS) from baseline. The responder rate of the index active treatment arm, which was previously reported as superior to the index sham-control arm at 3 months, was sustained through 12 months. Bars represent 95% confidence intervals.

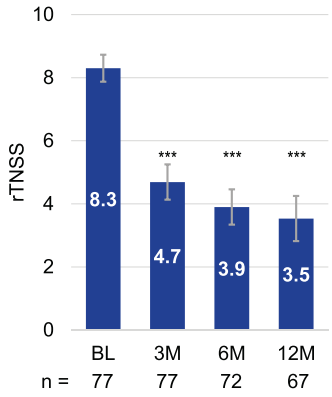

FIGURE 3 Adjusted mean reflective total nasal symptom score (rTNSS) of the index active treatment arm at baseline and follow-up. The improvement in rTNSS of the index active treatment arm, which was previously reported as significantly greater than that in the index sham-control arm at 3 months, was sustained through 12 months; $p < 0.001$, when comparing each follow-up timepoint vs baseline. Bars represent 95% confidence interval.

3.1 | Index active treatment arm through 12 months

The responder rate of the index active treatment arm, superior to the index sham-control arm at 3 months,[1] was sustained through 12 months (Fig. 2, and included in Table 2). The responder rate was 67.5% (95% CI, 55.9%-77.8%), 75.0% (95% CI, 63.4%-84.5%), and 80.6% (95% CI, 69.1%-89.2%) at 3, 6, and 12 months, respectively.

The improvement in rTNSS of the index active treatment arm, significantly greater than of the index sham-control arm at 3 months,[1] was also sustained through 12 months (Fig. 3). The mean baseline rTNSS for the index active treatment arm was 8.3 (95% CI, 7.9-8.7). The adjusted mean change in rTNSS was −3.6 (95% CI, −4.2 to −3.0), −4.4 (95% CI, −5.0 to −3.8), and −4.8 (95% CI, −5.5 to −4.1) at 3, 6, and 12 months; $p < 0.001$, when comparing each follow-up timepoint vs baseline. This represents improvement of 43.3%, 53.0%, and 57.8% over baseline at 3, 6, and 12 months, respectively.

As previously reported, exploratory analysis of the distribution of rTNSS subscores at 3 months between the index active treatment and index sham-control arms showed significantly greater improvements over baseline in rhinorrhea and nasal congestion subscores in the index active treatment arm.[1] When following the index active treatment arm over time, the distribution of each rTNSS subscore (rhinorrhea, nasal congestion, nasal itching, and sneezing) improved significantly over baseline at 3 months, and was sustained through 12 months (Fig. 4); $p < 0.001$, when comparing each follow-up timepoint vs baseline for each subscore. Adjusted mean rTNSS subscores were also significantly improved over baseline over time (Supporting Information).

Postnasal drip and cough symptom scores were also recorded throughout the trial. Similar to the rTNSS subscores, the distribution of postnasal drip and cough scores within the index active treatment arm were improved over baseline at all timepoints (Fig. 5); $p < 0.001$, when comparing each follow-up timepoint vs baseline for each subscore.

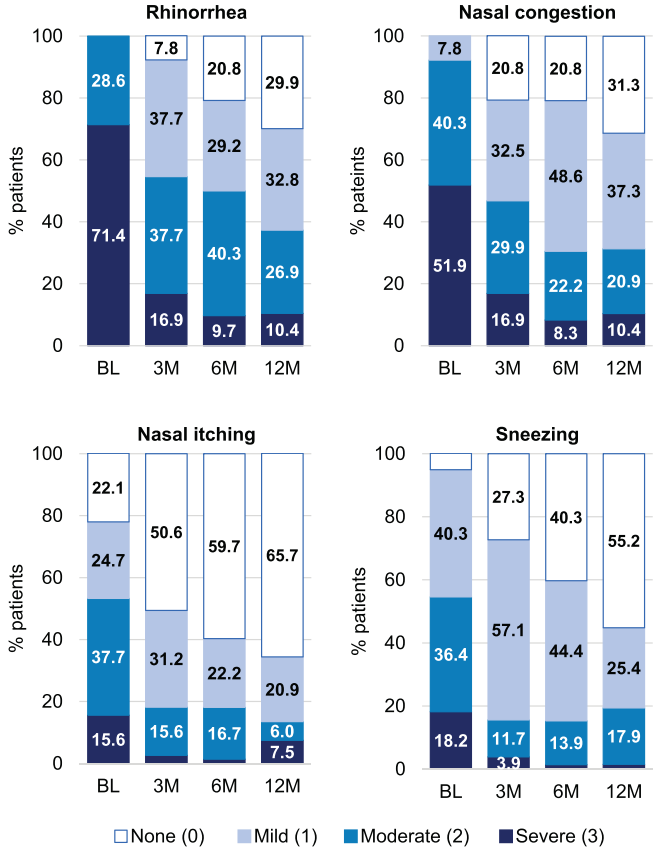

FIGURE 4 The percentage of patients in the index active treatment arm reporting each reflective total nasal symptom score (rTNSS) subscore at baseline and follow-up. The distributions of rTNSS subscores were significantly improved over baseline at all timepoints; $p < 0.001$, when comparing each follow-up timepoint vs baseline for all subscores. Nasal itching was severe in 2.6% and 1.4% of patients at 3 and 6 months, respectively; no sneezing was reported by 5.2% at baseline, and severe sneezing was reported by 1.4% and 1.5% at 6 and 12 months, respectively. Baseline and 3 months, n = 77; 6 months, n = 72; 12 months, n = 67.

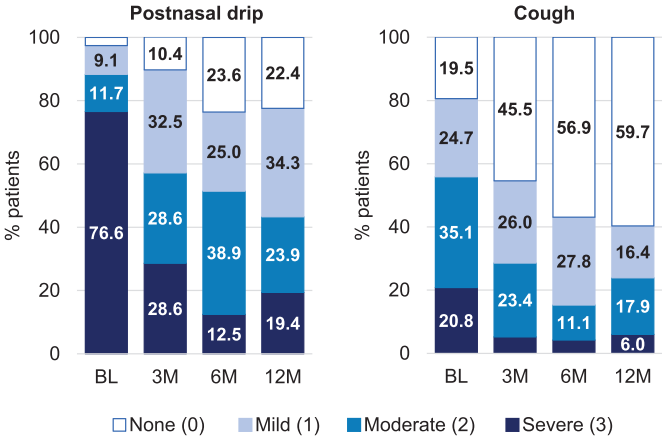

FIGURE 5 The percentage of patients in the index active treatment arm reporting each postnasal drip and cough score at baseline and follow-up. The distributions of both scores were significantly improved over baseline at all timepoints; $p < 0.001$, when comparing each follow-up timepoint vs baseline for both scores. No postnasal drip at baseline was reported by 2.6% of patients; severe cough at 3 months was reported by 5.2%, and severe cough at 6 months was 4.2%. Baseline and 3 months, n = 77; 6 months, n = 72; 12 months, n = 67.

Adjusted mean drip and cough subscores were also significantly improved over baseline over time (Supporting Information).

For comparison with the exploratory analysis of the distribution of rTNSS subscores between the index active treatment and index sham-control arms before unblinding,[1] an exploratory analysis of the distribution of postnasal drip and cough scores between the index active treatment and index sham-control arms at 3 months was performed. There were no significant differences in the distribution of postnasal drip and cough scores between the index active treatment and index sham-control arms at 3 months postprocedure (Supporting Information).

The protocol of this pragmatic trial did not limit or otherwise prescribe medication use. However, medication use based on a number of classes (antihistamines, decongestants, oral leukotriene inhibitors, intranasal steroid sprays, intranasal anticholinergic sprays) was tracked over time. Baseline medication use is presented in Table 1. To determine the potential effect of an increase in medication use on trial results, the 16 patients with an increase in medication use in the index active treatment arm were assigned to nonresponder status if not already nonresponders from the point of medication increase onward (Table 2). The imputed responder rates were not substantially different over time (Table 2). The majority of increases were seen for antihistamines and/or steroid sprays (further details in the Supporting Information). Of the 16 patients with increases, 3 had increased use in anticholinergic sprays (1 previously reported at 3 months[1] and 2 patients increased use at 6 months).

Ongoing trial monitoring of medication data resulted in updates to medication statuses, and therefore the sensitivity analysis on the primary endpoint was repeated since the previous report.[1] The updated imputed responder rate in the index active treatment arm remained superior to that of the index sham-control arm after patients when an increase in medication use in both arms were assigned to nonresponder status if not already nonresponders: 62.3% (95% CI, 50.6%-73.1%) vs 33.3% (95% CI, 19.1%-50.2%); $p = 0.006$, where 4 patients were changed to nonresponder status in the index active treatment arm and 3 patients were changed to nonresponder status in the index sham-control arm.

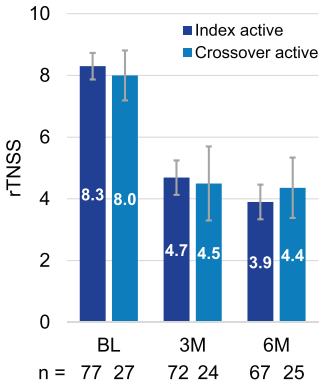

FIGURE 6 Unadjusted mean reflective 24-hour reflective total nasal symptom score (rTNSS) of the index active treatment arm and the crossover active treatment arm at their respective baseline and through 6 months. The mean rTNSS of the crossover active treatment arm has continued to follow the same course as that of the index active treatment. Bars represent 95% confidence intervals.

3.2 | Index sham-control crossover to active treatment and follow-up through 6 months

The baseline characteristics (at the time of study enrollment) of the crossover active treatment arm were not significantly different from those of the index active treatment arm (Table 1). After unblinding, the new baseline rTNSS of those patients in the index sham-control arm who were eligible to cross over to active treatment was not significantly different from the baseline score of the index active treatment arm. The mean baseline rTNSS of the index active treatment arm was 8.3 (95% CI, 7.9-8.7) and the mean baseline rTNSS for the crossover active treatment arm was 8.0 (95% CI, 7.2-8.8); $p = 0.488$, based on t test.

To date, the mean rTNSS of the crossover active treatment arm is has followed the same course as that of the index active treatment (Fig. 6). The responder rates in the crossover active treatment arm were 75.0% (95% CI, 53.3%-90.2%) at 3 months and 64.0% (95% CI, 42.5%-82.0%) at 6 months. No significant difference was observed when comparing the responder rates in the index active and crossover active treatment arms according to Fisher exact test: $p = 0.615$ at 3 months and $p = 0.309$ at 6 months.

Periprocedural pain after the crossover active treatment was recorded immediately postprocedure and at 1 and 3 months postprocedure. Immediately postprocedure, the mean pain VAS score on a 10-cm scale was 2.4 (95% CI, 1.4-3.3), which decreased to 0.2 (95% CI, 0.0-0.3) at 1 month and 0.3 (95% CI, −0.1 to 0.6) at 3 months. The pain VAS score immediately postprocedure for the crossover active treatment arm (2.4; 95% CI, 1.41-3.34) was on par with previously reported results from the index active treatment arm (2.1; 95% CI, 1.6-2.6).[1] The change in pain VAS score at 1 month in the crossover active treatment arm was significantly less than the change seen in the index active treatment arm ($p = 0.049$). The change in pain VAS score at 3 months in the crossover active treatment arm was not significantly lower than the change in score in the index active treatment arm ($p = 0.292$).

3.3 | Adverse events

A total of 117 patients underwent a procedure (sham control, active treatment, or crossover active treatment) in this trial. No serious adverse events with a relationship to the device and/or procedure have been observed so far. To date, 8 adverse events with at least a possible relationship to either the study device and/or procedure have been reported in 5 patients, including mild purulent nasal drainage, moderate dry eye, mild headache, ear discomfort, and 2 instances each of mild nasal soreness and nasal bleeding (1 mild and 1 moderate). Both bleeding events occurred the evening after the study procedure. The mild bleeding event resolved within 24 hours with no intervention. The patient with the moderate bleeding event had a history of taking an anticoagulant (rivaroxaban) that had been stopped before the procedure and the bleeding event resolved with placement of nasal packing for 48 hours. Only the event of dry eye was ongoing at the time of this report (further details in the Supporting Information).

4 | DISCUSSION

The primary endpoint of this RCT previously showed that TCRF neurolysis of the PNN is superior to a sham-control procedure in reducing the overall symptom burden experienced by patients with chronic rhinitis. The results presented herein demonstrate the treatment effect is sustained through 12 months postprocedure. The criterion used to define a responder in the primary endpoint (≥30% improvement [decrease] in rTNSS from baseline) is accepted as a minimal clinically important difference and is used to evaluate TCRF and other minimally invasive technologies targeting the PNN for the treatment of chronic rhinitis.[5,6] With any trial over time, it is important to consider whether the patients lost to follow-up or withdrew/were terminated from the trial are biasing the results over time. Of the 10 patients who exited the trial between 3 and 12 months (including the patient who missed the 12-month visit) in the index active treatment arm, 8 had an improvement in rTNSS at trial exit and 6 were responders (≥30% improvement in rTNSS from baseline) at trial exit. Because the larger proportion of patients exiting the trial had a reduction in symptom burden,

the trial results over time may be considered reasonably conservative.

The sustained reduction in symptom burden in the index active treatment arm through 12 months, as measured by the rTNSS, is a significant observation when considering that peripheral nerve regeneration may occur at a rate of 1 to 5 mm/day.[7,8]

As reported previously, the improvements in rhinorrhea and congestion rTNSS subscores were significantly greater in the index active treatment arm than in the index sham arm.[1] These observations are consistent with the belief that TCRF neurolysis of the PNN interrupts parasympathetic stimulation of the nasal mucosa, similar to vidian neurectomy and surgical PNN neurectomy. The observations are also consistent with cryoablation technology targeting the PNN for the treatment of chronic rhinitis.[6] Submucosal gland secretion, blood flow in the submucosa, and stromal edema can be reduced by blocking parasympathetic innervation.[9] Botulinum toxin A is also thought to suppress parasympathetic nerves in the nasal mucosa, and its application has shown efficacy in rhinitis symptom reduction.[10,11] Although nasal itching and sneezing did not exhibit a difference between the index active treatment and index sham-control arms at 3 months,[1] there was a sustained reduction in the severity of these symptoms over baseline through 12 months. Postnasal drip and cough, which are common and troublesome symptoms of chronic rhinitis, showed a similar improvement compared with baseline over time, although there was no significant difference between the index active treatment and index sham-control arms at 3 months.

The trial's pragmatic design did not dictate medication use at any time during the trial. Changing the status of patients with an increase in medication classes to nonresponders (if not already nonresponders) did not affect the primary outcome of the trial,[1] and the effect on the responder rate was similar over time. These results support the hypothesis that medication effects do not significantly confound the treatment effect delivered by the device.

Although no allergy testing was performed specifically for this trial, patients with both allergic and nonallergic rhinitis were included (based on patient self-report and medical record review). It is possible that TCRF neurolysis of the PNN can reduce neurogenic inflammation in patients with allergic rhinitis.[12–14]

The frequency of device- or procedure-related adverse events experienced while using this technology is low. The low reported levels of periprocedural pain in the crossover active treatment arm were on par with those observed in the index active treatment arm immediately postprocedure. The lower scores at 1 month after crossover treatment (compared with the index active treatment arm) may be a consequence of the fact that the crossover active treatment represented the second time the patients had undergone a procedure, including injection of anesthesia, and therefore knew what to expect.

The crossover design of this trial incorporated repeated confirmation of eligibility before treatment. To date, the crossover active treatment arm has followed the same trajectory as the index active treatment arm in terms of baseline rTNSS and change in rTNSS over time. Therefore, it is reasonable to assume the crossover active treatment arm is not introducing any bias into the combined active treatment group, and longer term analyses of this RCT will be performed on the combined active treatment group.

There are some limitations to our study. The investigators were not blinded in the initial stages of the trial. However, the rTNSS used in endpoint evaluation is a patient-reported outcome, mitigating the risk of bias. Medication use was not controlled and could potentially have had some confounding effect on symptom relief, as measured by the rTNSS. However, analysis of the results when assigning all patients in the index active treatment arm who reported an increase in medication use to nonresponders did not substantially affect the responder rate over time.

In conclusion, the results of this RCT after the primary endpoint and patient unblinding demonstrate that the treatment effect of TCRF neurolysis of the PNN area is safe and effective in reducing the symptom burden of chronic rhinitis patients through 12 months postprocedure. To date, eligible patients in the index sham-control arm who elected to cross over to active treatment have continued to exhibit the same course of symptom improvement as the index active treatment arm. The combined active treatment group will be followed through 2 years in this trial to demonstrate the durability of this effect.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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