Received: 22 February 2024 | Revised: 12 April 2024 | Accepted: 8 May 2024
DOI: 10.1002/lio2.1286

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Long-term outcomes following impedance-controlled radiofrequency ablation for the treatment of chronic rhinitis

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Funding information
Neurent Medical, Ltd.

Abstract

Objective: To assess long-term safety and effectiveness of a multipoint, impedance-controlled, RF ablation device for treatment of chronic rhinitis through 12-month follow-up.

Methods: A prospective, multicenter study. Bilateral posterior nasal nerve (PNN) ablation was performed on all participants. Assessments at 6-, 9-, and 12-month visits included Visual Analog Scale Nasal Symptom Score (VAS NSS), reflective Total Nasal Symptom Score (rTNSS), mini-Rhinoconjunctivitis Quality of Life Questionnaire (mini RQLQ), and adverse events.

Results: Thirty-six participants were enrolled and 35 completed the 12-month follow-up. All 5 VAS NSS items demonstrated statistically significant improvement ($p < .0001$) over baseline at all 3 time points. The total rTNSS improved from 7.9 ± 1.8 at baseline to 4.3 ± 2.1 at 6-months, 3.8 ± 2.4 at 9-months, and 4.0 ± 2.1 at 12-months (all $p < .0001$). At 12-months, 91% (31/35) of participants had achieved the minimum clinically important difference (MCID) of a reduction from baseline of ≥1 point and 80% (28/35) of the participants met the responder criteria of ≥30% reduction from baseline. The total mean mini RQLQ was reduced from 3.0 ± 1.0 at baseline to 1.4 ± 0.8 at 6-months, 1.4 ± 1.0 at 9-months, and 1.3 ± 0.8 at 12-months (all $p < .0001$). At 12-months, 86% (30/35) of participants achieved the MCID of a reduction from baseline of ≥0.4 points for the mini RQLQ. No related serious adverse events occurred during the study.

Conclusions: Impedance-controlled RF ablation of the PNN is safe and resulted in durable, significant improvement in rhinitis symptoms and quality of life through 12-month follow-up.

Trial Registration: The study is registered at www.clinicaltrials.gov with the unique identifier of NCT05324397.

Level of Evidence: 4.

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

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1 | INTRODUCTION

Chronic rhinitis is a common chronic condition with predominant symptoms of rhinorrhea and nasal congestion. Chronic rhinitis significantly impacts a patient's quality of life, including work productivity, daily activities, and sleep.[1–3] The NEUROMARK® system (Neurent Medical Ltd., Oranmore, Galway, Ireland) is a multipoint, impedance-controlled RF device that provides PNN ablation. The single-use device uses low-power, bipolar radiofrequency through proximal and distal flexible leaflets that conform to patient anatomy. The design maximizes coverage of tissue on the lateral wall of the nasal cavity, with posterior placement. Individual impedance thresholds and automatic cutoffs for each leaflet create microlesions at the target site. The device provides feedback to the physician confirming appropriate positioning and delivery of complete treatment.

The primary objective of this study was to evaluate long-term safety and effectiveness of the device in patients with chronic rhinitis. In an earlier report of this study, the device was shown to be safe and effective at 3 months.[4] This article is the first to describe outcomes at the 6-, 9-, and 12-month follow-ups with this technology.

2 | MATERIALS AND METHODS

2.1 | Study design and population

This is a prospective, single-arm, multicenter study to evaluate the safety and efficacy of a multipoint, impedance-controlled, RF ablation device for the treatment of chronic rhinitis. Ethics approval was obtained through Allendale IRB (Old Lyme, CT). Written informed consent was obtained from all participants before participating in the study. The study was registered at www.clinicaltrials.gov (NCT05324397).

Participants were adults (≥18 years old) who had chronic rhinitis symptoms for 6 months or longer. Participants were required to have moderate to severe rhinorrhea with minimum rhinorrhea scores of 5.0 on the individual visual analog score nasal symptom score (VAS NSS) and 2.0 on the individual reflective Total Nasal Symptom Score (rTNSS). Participants were also required to have mild to severe nasal congestion with minimum nasal congestion scores of 2.5 on the individual VAS NSS and 1.0 on the individual rTNSS. The minimum combined VAS NSS for rhinorrhea and nasal congestion was 10.0. Participants were required to have nasal anatomy appropriate to receive the NEUROMARK System. Exclusion criteria included clinically significant anatomic obstruction limiting access to the posterior nasal cavity, atrophic rhinitis, seasonal allergies only, previous rhinitis procedure/surgery, epistaxis within the past 12 months, anticoagulation medication use, and septal perforation or nasal mucosal erosion. Medication regimens prior to enrollment were not standardized, although current medications were collected at baseline. Participants were excluded from the study if they started a new sinonasal medication regimen within 4 weeks before treatment that had not yet stabilized. Allergy medication regimen was to remain unchanged throughout the study unless instructed by the investigator.

Bilateral posterior nasal nerve ablation was performed on all participants in an office setting under local anesthesia according to the investigator's usual practice. No lateralization of the turbinate was performed to gain access to the nasal cavity.

2.2 | Assessments

This report documents 6-, 9-, and 12-month follow-up visits for study participants. VAS NSS,[5] rTNSS,[6] mini Rhinoconjunctivitis Quality of Life Questionnaire (mini RQLQ) scores,[7] and adverse events are reported. The VAS NSS included symptoms of nasal congestion, rhinorrhea, nasal itching, sneezing, and postnasal drip. Adverse events were proactively collected at the procedure, 24–48 h post procedure, and at 1-, 3-, 6-, 9-, and 12-month follow-ups.

2.3 | Statistical analyses

Categorical variables are summarized using frequency distributions for categorical variables and means and standard deviations for continuous variables, unless otherwise noted. The minimal clinically important difference (MCID) for the total rTNSS was defined as a reduction from baseline of ≥1 point.[6] For the mini RQLQ, the MCID was defined as a reduction from baseline of ≥0.4 point.[8] A reduction from baseline of 30% or more was used to define the rTNSS responder rate.[9]

A sample size of 21 participants was determined for assessment of the primary endpoint of the VAS NSS for rhinorrhea and nasal congestion at 3-months, which was previously reported.[10] Student's paired *t*-test (parametric outcomes) or Wilcoxon's signed-rank test (nonparametric outcomes) were used to evaluate mean changes from baseline in VAS NSS, rTNSS, and mini RQLQ outcomes, with a 2-sided alpha level of 0.05 indicating significance. The Symmetry Test was used to assess changes from baseline in distribution of severity levels in rTNSS subscores.

Stata version 17 or higher was used for the statistical analysis.

3 | RESULTS

A total of 36 participants were enrolled and treated at 4 US otolaryngology centers from March 2022 through September 2022. One participant was lost to follow-up after the 3-month visit; all remaining 35 participants completed the 12-month follow-up. Demographics and medical history for the 35 participants are shown in Table 1.

The primary efficacy and safety endpoints, through the 3-month follow-up, were met and have previously been reported.[4]

The VAS NSS for baseline and the 6-, 9-, and 12-month follow-ups are shown in Figure 1. All 5 symptoms (rhinorrhea, nasal congestion, nasal itching, sneezing, and postnasal drip) demonstrated

statistically significant improvement ($p < .0001$) over baseline at all 3 time points.

The total rTNSS improved from 7.9 ± 1.8 at baseline to 4.3 ± 2.1 at 6-months, 3.8 ± 2.4 at 9-months, and 4.0 ± 2.1 at 12-months (all $p < .0001$). The rTNSS subscores at baseline and follow-up through 12 months are shown in Figure 2. Each of the 4 symptoms demonstrated significant improvement over baseline at all 3 time periods ($p < .0001$ for rhinorrhea, nasal congestion, nasal itching, and $p < .001$ for sneezing).

A MCID reduction from baseline of 1 point at 12-months was achieved by 91% (31/35) of participants. A total of 80% (28/35) of the participants met the responder criteria of ≥30% reduction from baseline.

Figure 3 presents the percentage of participants reporting each rTNSS subscore severity level (severe, moderate, mild, or none) at baseline and through 12-months follow-up. The distributions of all subscores were significantly improved over baseline at all time points ($p \leq .0001$ for rhinitis, nasal congestion, and nasal itching; $p \leq .001$ for sneezing). The greatest changes were seen in rhinorrhea and nasal congestion.

The total mean mini RQLQ was reduced from 3.0 ± 1.0 at baseline to 1.4 ± 0.8 at 6-months, 1.4 ± 1.0 at 9-months, and 1.3 ± 0.8 at 12-months (all $p < .0001$). All subscores were significantly reduced at all follow-up time points ($p < .0001$ for activities, sleep, practical problems, nose symptoms, and other symptoms; $p < .001$ for eye symptoms) (Figure 4). A MCID reduction from baseline of 0.4 points or more for the mini RQLQ was achieved by 86% (30/35) of participants at 12 months. Individual question responses to the mini RQLQ were also examined. All 14 questions were significantly reduced ($p < .01$) at all follow-up time points (Figure 5). The 6 most burdensome items at baseline were runny nose (Q8), need to blow nose (Q5), stuffy blocked nose (Q7), regular activities at home and at work (Q1), recreational activities (Q2), and sleep (Q3). Improvements in all 6 of these items reached a significance level of $p < .0001$ at 12-months follow-up.

A subgroup analysis was performed by participants with (n = 15) and without (n = 20) a history of seasonal/perennial allergies for changes from baseline in the 5 VAS NSS symptoms at 12 months. Both subgroups showed statistically significant improvements from

TABLE 1 Demographics and medical history.

Characteristic	All Participants $N = 35$
Age (years)	63.2 ± 14.0
Sex (male)	45.7% (16/35)
Race	
Asian	2.9% (1/35)
Black or African American	8.6% (3/35)
White or Caucasian	88.6% (31/35)
History of seasonal/perennial allergies	42.9% (15/35)
Severity of chronic rhinitis[a]	
Mild	0% (0/35)
Moderate	25.7% (9/35)
Severe	74.3% (26/35)
Previous sinus or nasal surgery[b]	40.0% (14/35)
Medications	
Total on baseline medications	37% (13/35)[c]
Antihistamine	17% (6/35)
Corticosteroid	11% (4/35)
Anticholinergic	11% (4/35)
Leukotriene receptor antagonist	3% (1/35)

Note: Results are presented as mean ± SD or % (*n*/*N*).
[a]Severity of chronic rhinitis, as determined by the physician.
[b]Previous sinonasal surgeries include: septoplasty (4), deviated septum repair (3), sinus surgery (3), turbinate reduction (2), and balloon dilation (2).
[c]Medication totals will not sum to the total on baseline medications because some participants were on multiple medications.

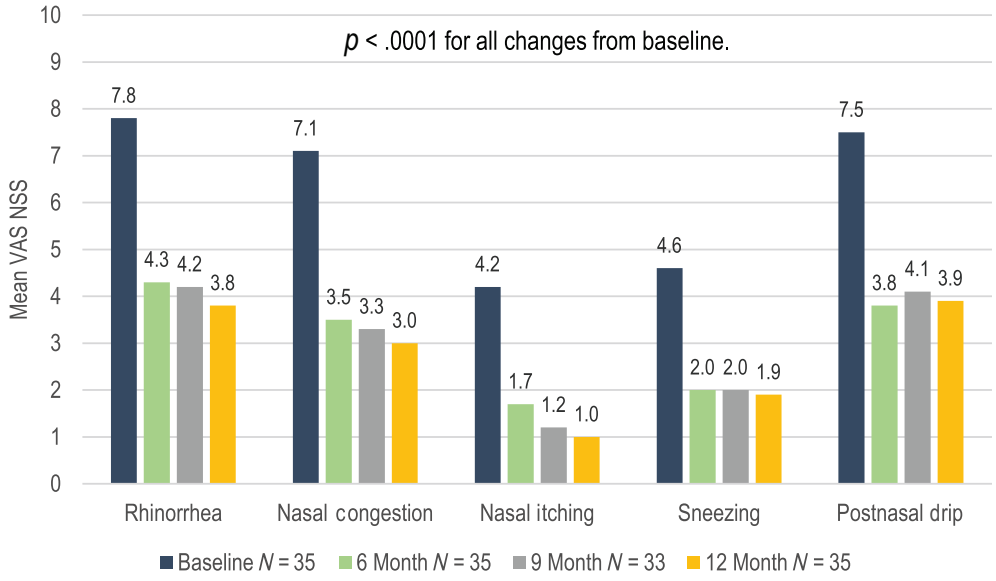

FIGURE 1 Visual analog score nasal symptoms scores (VAS NSS). Two participants inadvertently did not have assessments collected at the 9-month visit ($N = 33$).

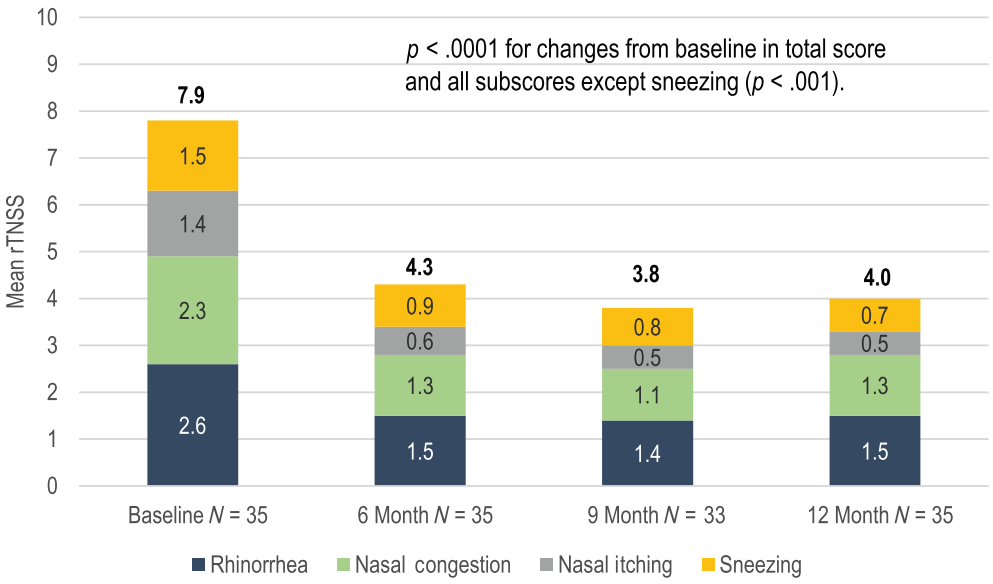

FIGURE 2 Reflective total nasal symptom score (rTNSS) total and subscores. Total rTNSS (bold score on top of columns) is the total of the subscores. Two participants inadvertently did not have assessments collected at the 9-month visit ($N = 33$).

baseline in all 5 symptoms (rhinorrhea, nasal congestion, nasal itching, sneezing, and postnasal drip) ($p \leq .01$ for all). There were no significant differences in any of the 5 VAS NSS symptoms between the subgroups.

Participants were asked to refrain from starting any new allergy medications or changing any existing allergy medications throughout the study, unless instructed by the investigator. A total of 30 of the 35 participants (85.7%) completing the study complied with this requirement. Two participants started new allergy medications: 1 participant started an antihistamine and an anticholinergic and 1 participant started a nasal steroid. One participant changed their medications (stopped an anticholinergic and started an antihistamine). Two participants stopped their medications: 1 participant stopped an anticholinergic and a nasal steroid and 1 participant stopped a leukotriene receptor antagonist.

No related serious adverse events were reported for the duration of the study. One nonserious adverse event of sinusitis occurred 170 days after treatment that was considered possibly related to the procedure. The participant was prescribed antibiotics and the event resolved 6 days later.

4 | DISCUSSION

This study reports longer-term follow-up (through 12 months) for the first published clinical study of a multipoint, impedance-controlled, RF ablation device for treatment of chronic rhinitis. The primary efficacy and safety endpoints at 1 and 3 months have previously been reported.[4]

All 5 VAS nasal symptoms were significantly improved over baseline at the 6-month visit, with stable or slight continued improvements at the 9- and 12-month follow-ups. Nasal congestion, rhinorrhea, and postnasal drip demonstrated the greatest improvement. These longer-term results are consistent with our earlier published results in this same population at 1 and 3 months.[4] Our observation of an improvement in postnasal drip after radiofrequency ablation is in agreement with other studies.[11–15]

The total rTNSS improved from baseline to all time points and the responder rate was 80% at 12 months. These findings are consistent with findings of our device and other devices for rhinitis.[4,15,16] Confirming chronic rhinitis specific quality of life improvement, the total mini RQLQ score and all 5 domains significantly improved over baseline and the 12-month MCID rate was 86%. These findings are consistent with our device and other ablation devices that found responder rates >80%.[4,12,17]

The duration and severity of rhinitis symptoms impact work productivity, daily activities, and sleep quality.[1,3] A total of 80% of patients with moderate-to-severe rhinitis reported impairment in daily activities.[2] This is similar to our study in which 86% (30/35) of participants reported moderate to extreme troubles with daily activities at baseline. The mini RQLQ[7] has patients indicate changes in their regular activities done at work or around the home and/or garden, recreational activities (including sports, social activities, and hobbies), and sleep (difficulties getting a good night's sleep and or getting to sleep at night). The mean percent changes from baseline in daily activities, recreational activities, and sleep scores at 12 months were 56%, 63%, and 57%, respectively. Our results demonstrate significant improvements in nasal symptoms and in regular activities, recreational activities, and sleep, which lead to an improvement in overall quality of life.

The mini RQLQ showed significant improvement in all 3 eye symptom scores (itchy eyes, sore eyes, and watery eyes). Although, we did not determine the number of participants with conjunctivitis at baseline, a number of participants had allergies to dogs/cats, pollen, and mold, with symptoms of itching and runny eyes, suggesting possible allergic conjunctivitis. Like allergic rhinitis, allergic conjunctivitis is an inflammatory condition that results from hyperactivity of the parasympathetic nervous system. Both the nasal and ocular parasympathetic nerves are fed through the sphenopalatine ganglion.[18] Since the current device targets the postganglionic branches, it is reasonable

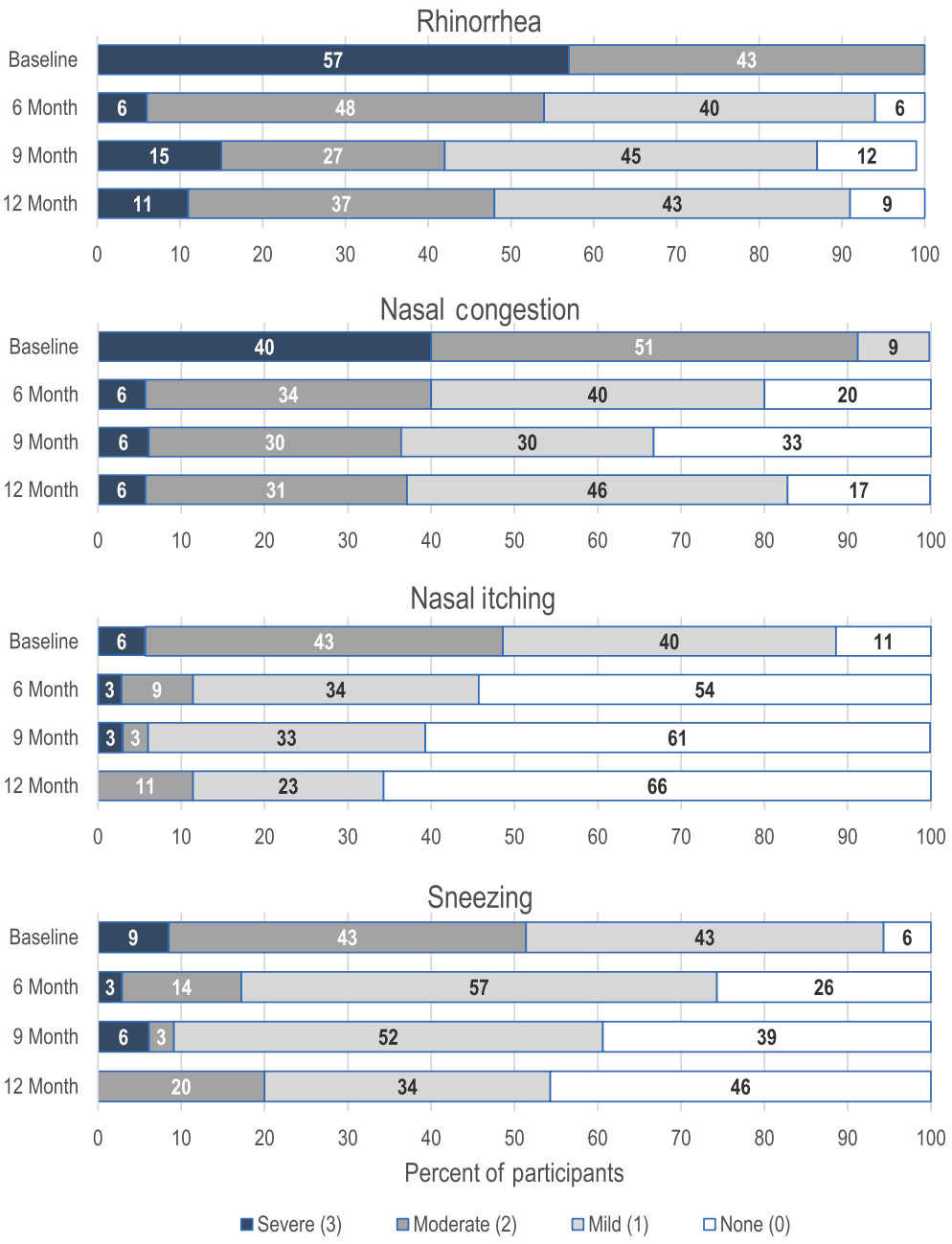

FIGURE 3 Percentage of participants with each reflective total nasal symptom score (rTNSS) nasal congestion subscore value at baseline and all follow-ups. The distributions of all subscores were significantly improved over baseline at all time points ($p \leq .0001$ for rhinitis, nasal congestion, and nasal itching; $p \leq .001$ for sneezing).

to hypothesize that the improvement in eye symptoms we observed is a result of the PNN ablation treatment.

There are potential applications for PNN ablation in any disease state where the nerve hyperactivity results in predominant symptoms such as congestion, rhinorrhea, and itchy eyes. Future studies could examine the potential added benefit of PNN ablation for patients with other inflammatory conditions (e.g., allergy conjunctivitis, sinusitis, asthma).

The low adverse event rate observed in this study confirms the safety of RF ablation for the treatment of rhinitis. Notably, RF ablation avoids the postprocedural "ice cream headache" experienced by some patients undergoing cryoablation for rhinitis.[17,19]

Strengths of the study include the excellent follow-up compliance with 35 of the 36 (97.2%) participants completing the 12-month follow-up. We controlled for any allergy medication use by requiring that participants not start, stop, or change any allergy medications during the study, unless instructed by the investigator. A total of 87% of the participants complied with this requirement.

This multicenter, prospective study used validated assessments in a pre-to-post comparison with each participant as their own control through 12-month follow-up. Although we did not include a concurrent control, previous randomized trials have demonstrated the superiority of RF ablation and cryoablation over sham treatment for chronic rhinitis.[10,19] The study outcomes were subjective measures, which are susceptible to bias, but we used validated patient-reported measures that had overlapping questions that demonstrated consistent improvements over time. Finally, the sample size was deemed adequate for the primary endpoint[4] but was not powered for subgroup analyses. However, a post hoc subgroup analysis found no differences in the changes from baseline for the 5 VAS scores between

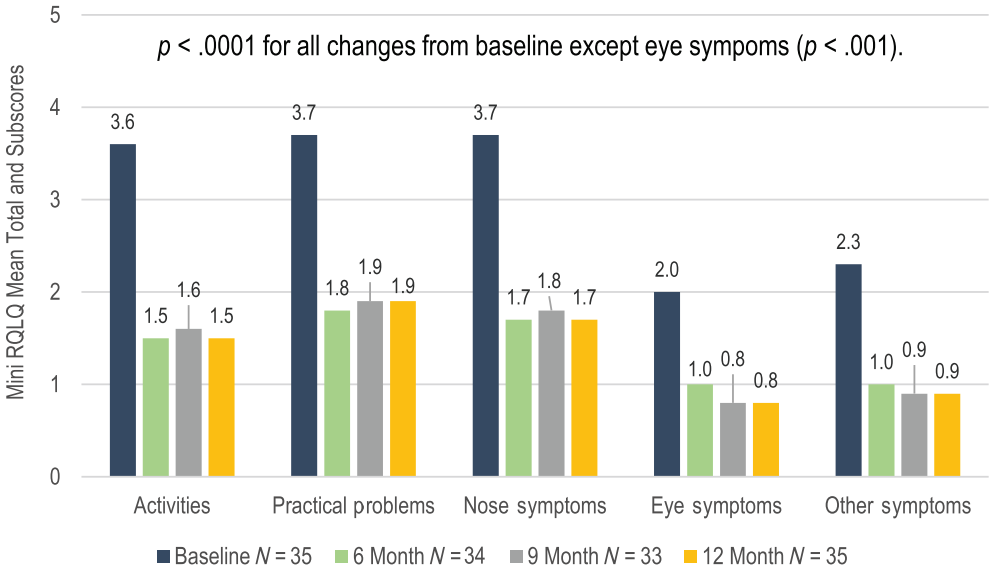

FIGURE 4 Mini rhinoconjunctivitis quality of life questionnaire (RQLQ) subscores. One participant did not have the assessment collected at the 6-month visit ($N = 34$) and two participants did not have assessment collected at the 9-month visit ($N = 33$).

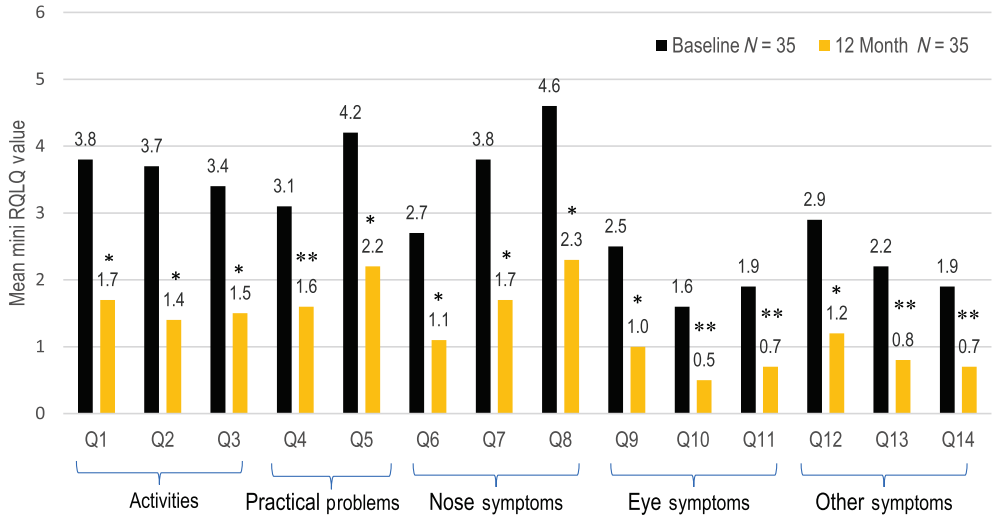

FIGURE 5 Changes from baseline to 12 months for individual mini RQLQ items. Q1: Regular activities at home and work. Q2: Recreational activities. Q3: Sleep. Q4: Need to rub nose/eyes. Q5: Need to blow nose. Q6: Sneezing. Q7: Stuffy blocked nose. Q8: Runny nose. Q9: Itchy eyes. Q10: Sore eyes. Q11: Watery eyes. Q12: Tiredness and/or fatigue. Q13: Thirst. Q14: Feeling irritable. * $p < .0001$, ** $p < .001$ for change from baseline.

participants with or without a history of seasonal/perennial allergies. This is consistent with other studies of PNN treatment.[11,20,21]

5 | CONCLUSION

The long-term results of this study demonstrate that impedance-controlled RF ablation of the PNN is safe and effective. Participants experienced durable, significant improvement in symptoms and quality of life through 12-month follow-up.

ACKNOWLEDGMENTS

The authors thank Manya Harsch, MS, from Technomics Research, LLC for the statistical analysis. The authors also thank the following participating study coordinators: Brittany Spates and Rachel Norris, Alabama Nasal and Sinus Center; Shayne Litz and Holly Stadden, Centers for Advanced ENT Care; Rachel Kelly and Jonathan Crandall, ENT and Allergy Associates; David Campbell, Specialty Physician Associates.

FUNDING NFORMATION

Neurent Medical, Ltd. has sponsored the study.

CONFLICT OF INTEREST STATEMENT

DDR, GD, MGD, DMY, and MS are medical advisor consultants and EMO is a medical writer consultant to Neurent Medical. KL has no conflicts to report.

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How to cite this article: Reh DD, Lay K, Davis G, et al. Long-term outcomes following impedance-controlled radiofrequency ablation for the treatment of chronic rhinitis. *Laryngoscope Investigative Otolaryngology*. 2024;9(3):e1286. doi:10.1002/lio2.1286