Received: 22 December 2022 | Revised: 15 February 2023 | Accepted: 27 February 2023
DOI: 10.1002/lio2.1040

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Clinical evaluation of a novel multipoint radiofrequency ablation device to treat chronic rhinitis

Douglas D. Reh MD[1] | **Kristopher Lay MD**[2] | **Greg Davis MD**[3] | **Marc G. Dubin MD**[1] | **David M. Yen MD**[4] | **Ellen M. O'Malley MS**[5] | **Michael Sillers MD**[2]

[1]Centers for Advanced ENT Care, Baltimore, Maryland, USA

[2]Alabama Nasal and Sinus Center, Birmingham, Alabama, USA

[3]ENT and Allergy Associates, Seattle and Puyallup, Washington, USA

[4]Specialty Physician Associates, Bethlehem, Pennsylvania, USA

[5]O'Malley Medical Communications, LLC, Victoria, Minnesota, USA

Correspondence
Douglas D. Reh, Centers for Advanced ENT Care, 6565 N. Charles Street, Suite 601, Baltimore, MD 21204, USA.
Email: doug.reh1@gmail.com

Funding information
Neurent Medical Ltd

Abstract

Objective: Safety and efficacy of the NEUROMARK® system for treating chronic rhinitis.

Methods: A prospective, single-arm, multicenter study was performed on adults with chronic rhinitis who underwent radiofrequency ablation to the posterior nasal nerves. Primary endpoints were device-related serious adverse events (SAEs) at 1 month and change from baseline in visual analog scale nasal symptom scale (VAS NSS) for rhinorrhea and nasal congestion at 3 months. Total nasal symptom score (rTNSS) and mini Rhinoconjunctivitis Quality of Life Questionnaire (mini RQLQ) score were also evaluated.

Results: Thirty-six participants were enrolled and completed follow-up at 1 and 3 months. Mean VAS NSS scores for rhinorrhea and nasal congestion demonstrated significant improvement at 3 months (both $p < .0001$). The mean percent changes from baseline in VAS rhinorrhea and nasal congestion were 53% and 55%, respectively. Total scores and all individual rTNSS items significantly improved (all $p < .001$) over the measured interval. Percent responder rate (≥30% reduction from baseline in total rTNSS) at 3 months was 78%. The total mean mini RQLQ scores, as well as all subdomains, improved significantly (all $p < .0001$). At 3 months, 89% of participants reported a minimal clinically important difference of ≥0.4 point improvement in the mini RQLQ score. No SAEs occurred during the study.

Conclusions: The NEUROMARK System is a novel radiofrequency ablation device that provides safe and effective treatment to the posterior nasal nerves for patients with chronic rhinitis. Study participants experienced statistically significant and clinically meaningful improvement in symptoms and quality of life assessments at 3 months post-procedure.

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

1 | INTRODUCTION

Surgical treatment of rhinitis is considered when medical therapy fails to adequately improve symptoms or when patients prefer to avoid long-term topical therapy. Historically, disruption of the nasal nerves by vidian neurectomy was done to improve rhinitis symptoms. This treatment has some morbidity, requires general anesthesia, and has documented side effects including dry eye.[1] More recently, less invasive, in-office, endoscopic procedures using cryotherapy[2–6] and radiofrequency (RF) ablation[7–9] have been shown to be effective techniques to interrupt the posterior nasal nerves. However, not all patients have adequate resolution of their symptoms with currently available techniques. One hypothesis for this lack of improvement is inadequate treatment of nerves due to natural anatomic variations that are not addressed by the current devices/technology.[10,11]

The NEUROMARK® System, a novel multipoint impedance-controlled RF ablation device, has been designed to address these limitations. The device comprises a two-stage design, where proximal and distal flexible leaflets conform to patient anatomy, maximizing access to nerve-rich areas on the lateral wall of the nasal cavity, and allowing more posterior placement than the other available devices. This is the first published study to evaluate the safety and efficacy of the NEUROMARK System in patients with chronic rhinitis.

2 | MATERIALS AND METHODS

2.1 | Study design and population

The CLARITY study is a prospective, single-arm, multicenter study to evaluate the safety and efficacy of the NEUROMARK System (Neurent Medical Ltd.) in adults with chronic rhinitis. The study received ethics approval through the Allendale IRB (Old Lyme, CT). Written informed consent was provided by all participants before entering the study. The study was registered at www.clinicaltrials.gov (NCT05324397).

Participants were adults (≥18 years old) with symptoms of chronic rhinitis for 6 months or longer. Rhinorrhea was required to be moderate to severe, as defined by a minimum score 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) for runny nose. Nasal congestion was required to be mild to severe, as defined by a minimum score of 2.5 on the individual VAS NSS and 1.0 on the individual rTNSS for congestion. A total minimum VAS NSS (rhinorrhea and nasal congestion) of 10.0 was required. Exclusion criteria were any previous surgery or anatomic obstruction that limits access to the posterior nasal cavity, atrophic rhinitis, chronic sinusitis within the past year (Lund-Mackay score >3), history of previous procedure/surgery to disrupt the posterior nasal nerve, history of epistaxis within past 12 months, use of anticoagulation medication, and septal perforation or nasal mucosal erosion. Participants were requested to not start or change their allergy medication regimen during the study unless instructed by the investigator.

2.2 | Study device and procedure

All enrolled participants underwent bilateral posterior nasal nerve disruption with the NEUROMARK System (Figure 1) under local anesthesia in an office setting. The type of local anesthesia was individualized based on the performing surgeon's preference. The device uses a proprietary algorithm to deliver controlled RF energy to create microlesions at the target site while minimizing collateral injury. An array of distal and proximal electrode leaflets simultaneously creates up to 20 ablation sites at the posterior lateral nasal nerves and accessory parasympathetic nerves from the pterygopalatine ganglion (Figure 2). Impedance thresholds are monitored individually for each leaflet, ensuring treatment is delivered adequately to the intended tissue and also discontinued at the optimal time.

2.3 | Assessments

VAS NSS,[12] VAS postnasal drip, rTNSS,[13] and mini RQLQ[14] were assessed at baseline and 1, 3, 6, and 12-months post-procedure for all participants. Adverse events were recorded at all time periods. Endoscopic nasal exams were performed at baseline, procedure, and at the 1- and 3-month follow-up visits. Procedure tolerability (0–10 scale) was assessed on day 0 and at 24–28 hours post procedure. Initial data analysis was performed for all participants through the 3-month visit. Longer-term follow-up is ongoing.

2.4 | Statistical analysis

Summary statistics were calculated for endpoints and additional patient-reported outcomes (PROs). Categorical variables are summarized using frequency distributions and continuous variables are summarized with means and standard deviations (normal distributions) or medians and ranges (non-normal distributions). Minimal clinically important differences (MCID) were defined as a reduction of ≥1 point for the total rTNSS[13] and ≥0.4 point for the mini RQLQ.[15] The responder rate for the total rTNSS was defined as a reduction of 30% or more from baseline.[16]

Safety outcomes were evaluated for all participants and efficacy outcomes were assessed for participants with at least one follow-up

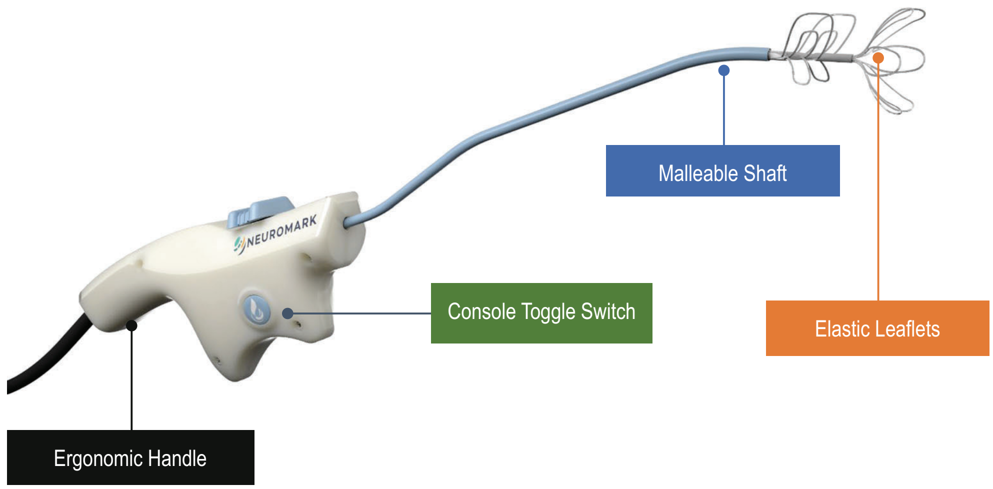

FIGURE 1 The NEUROMARK device.

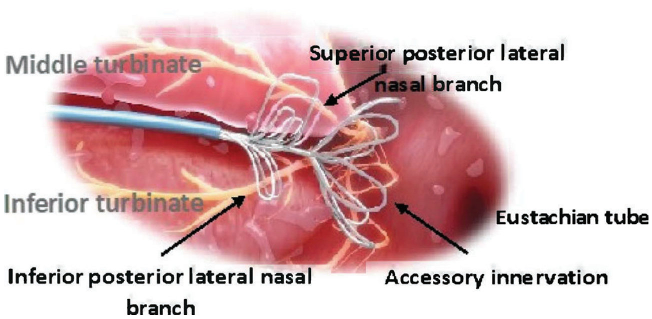

FIGURE 2 The NEUROMARK positioning.

visit. Each participant served as their own comparison for outcome scores. A reduction from baseline to 3 months in the VAS NSS for rhinorrhea and nasal congestion score was the primary efficacy outcome. Using 90% power, a two-sided alpha of 0.05, and a 10% attrition rate, a sample size of 21 enrolled participants using one-sample Student's *t* test is adequately powered to assess the primary efficacy endpoint. All evaluations were tested using the paired *t* test (parametric outcomes) or Wilcoxon Signed Rank test (nonparametric outcomes) with a two-sided alpha level of 0.05 indicating significance.

Statistical software was Stata version 17 or higher.

3 | RESULTS

Thirty-six participants were enrolled at four investigational centers in the United States. Demographic and medical history data are presented in Table 1. All 36 participants were evaluated at 1 and 3 months with no participant drop out.

The primary efficacy endpoints of change from baseline to 3 months in the VAS NSS for rhinorrhea and nasal congestion are shown in Figure 3. Mean VAS score for rhinorrhea significantly improved from baseline (7.78 ± 1.59) to 3 months (3.68 ± 2.66) ($p < .0001$), and mean VAS score for nasal congestion significantly improved from baseline (7.08 ± 2.06) to 3 months (3.21 ± 2.04) ($p < .0001$). The mean percent changes from baseline in VAS rhinorrhea and congestion were 53% and 55%, respectively.

TABLE 1 Demographics and medical history.

Characteristic	All participants $N = 36$
Age (years)	62.8 ± 14.0
Sex (male)	47.2% (17/36)
Race	
Asian	2.8% (1/36)
Black or African American	8.3% (3/36)
White or Caucasian	88.9% (32/36)
Allergies	63.9% (23/36)
Severity of chronic rhinitis	
Mild	0% (0/36)
Moderate	25.0% (9/36)
Severe	75.0% (27/36)
Previous sinus or nasal surgery	41.7% (15/36)

Note: Results are presented as mean ± SD or % (n/N).

Rhinorrhea, nasal congestion, nasal itching, sneezing, and postnasal drip domains of the VAS NSS all demonstrated significant improvement at 1 and 3 months compared with baseline (all $p < .001$) (Table 2). While all symptoms improved, the greatest changes were seen in rhinorrhea, nasal congestion, and postnasal drip ($p < .0001$).

There were significant improvements in the total and all individual items of the rTNSS at 1 month and 3 months post-procedure (all $p < .001$) (Table 3). The mean change from baseline in total rTNSS at 3 months is -3.72 ± 2.92 ($p < .0001$). Seventy-eight percent (78%, 28/36) of participants met the responder rate of ≥30% change from baseline. Eighty-nine percent (89%, 32/36) of participants met the MCID for the rTNSS of ≥1 point reduction from baseline.

The total mean score in the mini RQLQ demonstrated significant improvement from baseline (3.00 ± 1.02) to 3 months post-procedure (1.34 ± 0.93) ($p < .0001$) (Table 4). The mean percent improvement from baseline at 3 months is 55%, and 89% (32/36) of participants met the MCID criterion of a reduction ≥0.4. Analysis of mini RQLQ

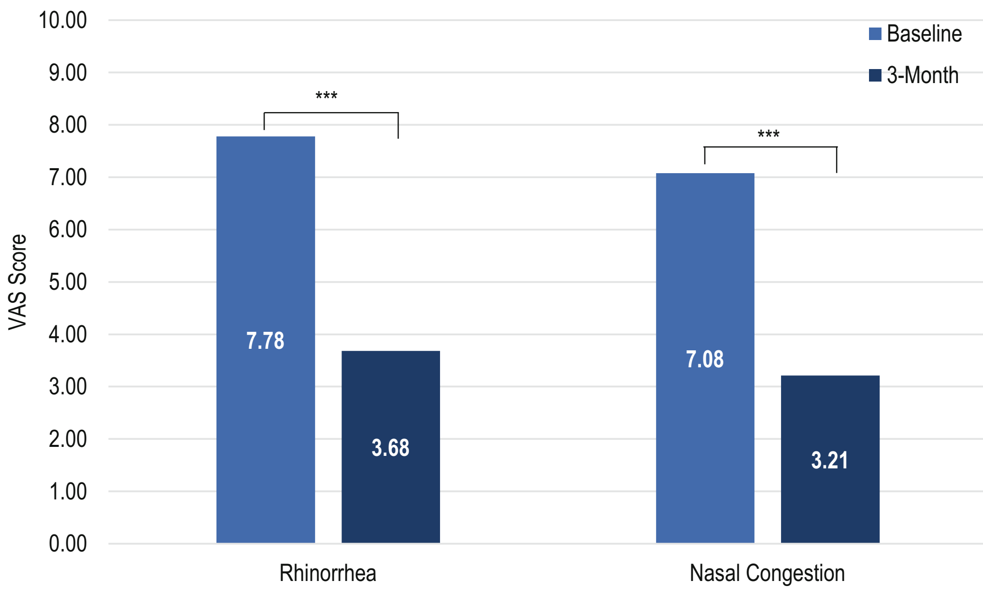

FIGURE 3 Primary efficacy endpoint—Change from baseline to 3-month follow-up in VAS NSS for Nasal Rhinorrhea and Congestion. *** indicates $p < .0001$ compared with baseline.

TABLE 2 Change from baseline in VAS NSS.

		1-month follow-up ($N = 36$)			3-month follow-up ($N = 36$)		
VAS NSS Item	Baseline $N = 36$	Follow-up	Change	*p*-value	Follow-up	Change	*p*-value
Rhinorrhea	7.78 ± 1.59	4.42 ± 2.77	−3.36 ± 2.77	<.0001	3.68 ± 2.66	−4.09 ± 3.50	<.0001
Nasal congestion	7.08 ± 2.06	3.32 ± 2.29	−3.76 ± 2.46	<.0001	3.21 ± 2.04	−3.86 ± 2.18	<.0001
Nasal itching	4.09 ± 2.98	1.99 ± 2.25	−2.09 ± 2.96	<.001	1.70 ± 2.23	−2.39 ± 3.38	<.001
Sneezing	4.51 ± 2.44	2.26 ± 2.30	−2.25 ± 2.86	<.0001	2.11 ± 2.18	−2.40 ± 2.82	<.0001
Postnasal drip	7.40 ± 2.59	4.11 ± 2.81	−3.29 ± 3.14	<.0001	4.02 ± 3.00	−3.37 ± 3.04	<.0001

Note: Results are presented as mean ± SD. Each VAS NSS item is scored from 0 to 10 with higher scores indicating worse symptoms.

TABLE 3 Change from baseline in rTNSS scores.

		1-month follow-up ($N = 36$)			3-month follow-up ($N = 36$)		
rTNSS Item	Baseline $N = 36$	Follow-up	Change	*p*-value	Follow-up	Change	*p*-value
Rhinorrhea	2.56 ± 0.50	1.36 ± 0.87	−1.19 ± 0.89	<.0001	1.39 ± 0.87	−1.17 ± 1.00	<.0001
Nasal congestion	2.31 ± 0.62	1.28 ± 0.81	−1.03 ± 0.84	<.0001	1.19 ± 0.79	−1.11 ± 0.85	<.0001
Nasal itching	1.39 ± 0.80	0.67 ± 0.79	−0.72 ± 0.97	<.0001	0.61 ± 0.77	−0.78 ± 1.10	<.001
Sneezing	1.53 ± 0.74	0.89 ± 0.78	−0.64 ± 1.02	<.001	0.86 ± 0.80	−0.67 ± 1.01	<.001
Total	7.78 ± 1.82	4.19 ± 2.00	−3.58 ± 2.73	<.0001	4.06 ± 2.24	−3.72 ± 2.92	<.0001

Note: Results are presented as mean ± SD. Each rTNSS item is scored from 0 to 3 with higher scores indicating worse symptoms. The total score is the sum of the individual scores.

subdomains—activities (regular, recreational, sleep), practical problems, nose symptoms, eye symptoms, and other symptoms (e.g., tiredness/fatigue, feeling irritable)—demonstrated significant improvement in all subdomains at both follow-ups (all $p < .0001$).

Mean discomfort during the procedure was 4.4 and at 24 to 48 h post-procedure, the mean score for discomfort was 1.2, with 72% of participants rating their discomfort as 0.

No SAEs were reported during the clinical study. There were no reports of epistaxis. There was only one nonserious AE reported that was considered possibly related to the device and/or procedure (pain/discomfort).

4 | DISCUSSION

Ogi et al. confirmed the existence of extensive networks of posterior nasal nerves along the lateral wall of the choana, posterior to the sphenopalatine.[11] NEUROMARK is uniquely designed to provide

TABLE 4 Change from baseline in the mini RQLQ scores.

Mini RQLQ domain	Baseline ($N = 36$)	1-month follow-up ($N = 36$) Follow-up	Change	p-value	3-month follow-up ($N = 36$) Follow-up	Change	p-value
Activities	3.58 ± 1.05	1.46 ± 0.89	−2.12 ± 1.28	<.0001	1.51 ± 1.22	−2.07 ± 1.53	<.0001
Practical problems	3.68 ± 1.21	1.79 ± 0.94	−1.85 ± 1.01	<.0001	1.79 ± 1.52	−1.89 ± 1.90	<.0001
Nose symptoms	3.68 ± 1.01	1.78 ± 0.93	−1.86 ± 1.09	<.0001	1.73 ± 1.10	−1.94 ± 1.44	<.0001
Eye symptoms	1.94 ± 1.60	0.79 ± 0.99	−1.15 ± 1.21	<.0001	0.93 ± 0.99	−1.02 ± 1.36	<.0001
Other symptoms	2.34 ± 1.46	0.85 ± 0.77	−1.53 ± 1.44	<.0001	0.88 ± 0.98	−1.46 ± 1.43	<.0001
Total	3.00 ± 1.02	1.30 ± 0.68	−1.69 ± 0.92	<.0001	1.34 ± 0.93	−1.66 ± 1.26	<.0001

Note: Results are presented as mean ± SD. The mini RQLQ consists of 14 items grouped into 5 domains. Each item is scored from 0 (not troubled) to 6 (extremely troubled). Each domain score is the mean of the items in that domain.

access and treatment coverage to these extensive networks in the posterior regions of the lateral nasal wall. The novel flexible electrode design (Figure 1) allows for accurate targeting of the posterior lateral nasal nerves and the accessory parasympathetic nerves of the pterygopalatine ganglion that innervate the posterior nasal cavity. Full device deployment results in distal and proximal stage placement in the choana, posterior to the middle turbinate attachment. After initial deployment in the choana, the proximal stage is rotated into the middle meatus.

NEUROMARK use resulted in statistically significant and clinically meaningful symptom and quality of life measure improvements at 3 months post-procedure. Our primary efficacy endpoints, mean rhinorrhea and nasal congestion VAS NSS scores, significantly improved from baseline to 3 months post-procedure ($p < .0001$). VAS rhinorrhea and congestion mean percent changes from baseline were 53% and 55%, respectively. These efficacy results are consistent with previously published data on cryoablation and legacy RF ablation devices, including two randomized sham-controlled trials.[2–9] Consistent with NEUROMARK results, in these studies, mean scores for the total rTNSS demonstrated statistically significant improvement at 3 months (all $p < .001$). Additionally, our percent responder rate (≥30% reduction from baseline in total rTNSS) of 78% is in line with previously published percent responder rates at 3 months of 73%,[2] 74%,[5] 76%,[7] 88%,[8] and 67.5%.[9] Furthermore, in Lee et al,[7] 80% of their participants met the MCID of 0.4 for the mini RQLQ, which compares well with our rate of 89%. Participant follow-up is ongoing with long-term data pending analysis.

The safety profile of the NEUROMARK device and procedure is excellent. No SAEs were reported during the study and only one participant reported minor pain/discomfort "possibly related to the device/procedure." These safety results are more favorable than those for cryoablation, where Chang et al. reported 38.9% (28/72) of their participants experienced "ice cream headache" post cryotherapy.[5] Our safety results are also more favorable than other previously published data for other devices.[2,5,6,8]

Although this multicenter study used validated rhinitis and quality of life tools, it is limited by the lack of a concurrent control. We attempted to mitigate this by using each participant as their own control, as we compared pre to post-procedure measures. However, previous randomized sham-controlled trials have demonstrated that cryoablation and RF ablation procedures perform significantly better than sham-controls, thereby validating posterior nasal nerve procedures for rhinitis symptoms. Additionally, while we currently present only short-term results, longer-term follow-up will be reported for this study cohort. Subgroup comparison is limited by our sample size. Additional studies of real-world evidence in a large group of participants would add to the evidence for this novel device.

5 | CONCLUSION

The NEUROMARK System is a novel RF ablation device that provides safe and effective treatment to the posterior nasal nerves for patients with chronic rhinitis. Study participants experienced statistically significant and clinically meaningful improvements in symptoms and quality of life assessments at 3 months post-procedure.

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 INFORMATION

Neurent Medical, Ltd sponsored the study.

CONFLICT OF INTEREST STATEMENT

Douglas D. Reh, Greg Davis, Marc G. Dubin, David M. Yen, and Michael Sillers are medical advisor consultants and Ellen M. O'Malley is a medical writer consultant to Neurent Medical. Kristopher Lay has no conflicts to report.

ORCID

Ellen M. O'Malley https://orcid.org/0000-0002-3751-764X

REFERENCES

1. Yan CH, Hwang PH. Surgical management of nonallergic rhinitis. *Otolaryngol Clin N Am*. 2018;51(5):945-955.
2. Del Signore AG, Greene JB, Russell JL, Yen DM, O'Malley EM, Schlosser RJ. Cryotherapy for treatment of chronic rhinitis: 3-month outcomes of a randomized, sham-controlled trial. *Int Forum Allergy Rhinol*. 2022;12(1):51-61.
3. Ow RA, O'Malley EM, Han JK, Lam KK, Yen DM. Cryosurgical ablation for treatment of rhinitis: two-year results of a prospective multicenter study. *Laryngoscope*. 2021;131(9):1952-1957.
4. Yen DM, Conley DB, O'Malley EM, Byerly TA II, Johnson J. Multiple site cryoablation treatment of the posterior nasal nerve for treatment of chronic rhinitis: an observational feasibility study. *Allergy Rhinol (Providence)*. 2020;7(11):2152656720946996.
5. Chang MT, Song S, Hwang PH. Cryosurgical ablation for treatment of rhinitis: a prospective multicenter study. *Laryngoscope*. 2020;130(8): 1877-1884.
6. Hwang PH, Lin B, Weiss R, Atkins J, Johnson J. Cryosurgical posterior nasal tissue ablation for the treatment of rhinitis. *Int Forum Allergy Rhinol*. 2017;7(10):952-956.
7. Lee JY, Abbas GM, Charous DD, et al. Clinical and quality of life outcomes following temperature-controlled radiofrequency neurolysis of the posterior nasal nerve (RhinAer) for treatment of chronic rhinitis. *Am J Rhinol Allergy*. 2022;36:747-754.
8. Ehmer D, McDuffie CM, Scurry WC, et al. Temperature-controlled radiofrequency neurolysis for the treatment of rhinitis. *Am J Rhinol Allergy*. 2021;36(1):149-156.
9. Stolovitzsky JP, Ow RA, Silvers SL, Bikhazi NB, Johnson CD, Takashima M. Effect of radiofrequency neurolysis on the symptoms of chronic rhinitis: a randomized controlled trial. *OTO Open*. 2021; 5(3):2473974X211041124.
10. Fan T, Chandna M, Gorelik D, et al. Correlation between middle turbinate insertion in relation to sphenopalatine foramen and failure rates of cryotherapy and radiofrequency treatment for chronic rhinitis. *Int Forum Allergy Rhinol*. 2022;13:88-91. doi:10.1002/alr.23058
11. Ogi K, Valentine R, Suzuki M, Fujieda S, Psaltis AJ, Wormald PJ. The anatomy of the foramina and efferent nerve fibers from the pterygopalatine ganglion in posterolateral nasal wall. *Laryngoscope Investig Otolaryngol*. 2022;7(3):679-683.
12. Klimek L, Bergmann KC, Biedermann T, et al. Visual analogue scales (VAS): measuring instruments for the documentation of symptoms and therapy monitoring cases of allergic rhinitis in everyday health care. *Allergo J Int*. 2017;26(1):16-24.
13. Downie SR, Andersson M, Rimmer J, et al. Symptoms of persistent allergic rhinitis during a full calendar year in house dust mite-sensitive subjects. *Allergy*. 2004;59(4):406-414.
14. Juniper EF, Thompson AK, Ferrie PJ, Roberts JN. Development and validation of the mini rhinoconjunctivitis quality of life questionnaire. *Clin Exp Allergy*. 2000;30(1):132-140.
15. Barnes ML, Vaidyanathan S, Williamson PA, Lipworth BJ. The minimal clinically important difference in allergic rhinitis. *Clin Exp Allergy*. 2010;40(2):242-250.
16. Meltzer EO, Wallace D, Dykewicz M, Shneyer L. Minimal clinically important difference (MCID) in allergic rhinitis: agency for healthcare research and quality or anchor-based thresholds? *J Allergy Clin Immunol Pract*. 2016;4:682-688.

How to cite this article: Reh DD, Lay K, Davis G, et al. Clinical evaluation of a novel multipoint radiofrequency ablation device to treat chronic rhinitis. *Laryngoscope Investigative Otolaryngology*. 2023;8(2):367-372. doi:10.1002/lio2.1040