Gamma Knife radiosurgery for bilateral trigeminal neuralgia

Corbin A. Helis, MD,¹ Emory McTyre, MD,¹ Michael T. Munley, PhD,¹ J. Daniel Bourland, PhD,¹ John T. Lucas Jr., MS, MD,³ Christina K. Cramer, MD,¹ Stephen B. Tatter, MD, PhD,² Adrian W. Laxton, MD,² and Michael D. Chan, MD¹

Departments of ¹Radiation Oncology and ²Neurosurgery, Wake Forest Baptist Medical Center, Winston-Salem, North Carolina; and ³Department of Radiation Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee

OBJECTIVE A small subset of patients with trigeminal neuralgia (TN) will experience bilateral symptoms. Treatment in these patients is controversial because the population is heterogeneous and patients may have nonvascular etiologies of their pain. This study reports treatment outcomes in the largest cohort of patients with bilateral TN who have undergone Gamma Knife radiosurgery (GKRS) to date.

METHODS A retrospective chart review identified 51 individual nerves in 34 patients with bilateral TN who were treated with GKRS at the authors' institution between 2001 and 2015, with 12 nerves in 11 patients undergoing repeat GKRS for recurrent or persistent symptoms. Long-term follow-up was obtained by telephone interview. Pain outcomes were measured using the Barrow Neurological Institute (BNI) pain scale, with BNI IIIb or better considered a successful treatment.

RESULTS There was sufficient follow-up to determine treatment outcomes for 48 individual nerves in 33 patients. Of these nerves, 42 (88%) achieved at least BNI IIIb pain relief. The median duration of pain relief was 1.9 years, and 1-, 3-, and 5-year pain relief rates were 64%, 44%, and 44%, respectively. No patients experienced bothersome facial numbness, and 1 case of anesthesia dolorosa and 2 cases of corneal dryness were reported. Patients with a history of definite or possible multiple sclerosis were significantly more likely to experience BNI IV–V relapse. There was no statistically significant difference in treatment outcomes between patients in this series versus a large cohort of patients with unilateral TN treated at the authors' institution. There was sufficient follow-up to determine treatment outcomes for 11 individual nerves in 10 patients treated with repeat GKRS. Ten nerves (91%) improved to at least BNI IIIb after treatment. The median duration of pain relief was 2.8 years, with 1-, 3-, and 5-year rates of pain relief of 79%, 53%, and 53%, respectively. There was no statistically significant difference in outcomes between initial and repeat GKRS. One case of bothersome facial numbness and 1 case of corneal dryness were reported, with no patients developing anesthesia dolorosa with retreatment.

CONCLUSIONS GKRS is a safe, well-tolerated treatment for patients with medically refractory bilateral TN. Efficacy of treatment appears similar to that in patients with unilateral TN. GKRS can be safely repeated in this population if necessary.

<https://thejns.org/doi/abs/10.3171/2018.6.JNS172646>

KEYWORDS bilateral; trigeminal neuralgia; Gamma Knife; stereotactic radiosurgery; pain

TRIGEMINAL neuralgia (TN) is a rare facial pain syndrome generally characterized by episodic, severe, lancinating facial pain.²¹ Although typically unilateral, approximately 1%–12% of patients experience bilateral symptoms.^{4,5,20,22} Multiple sclerosis (MS), a fam-

ily history of TN, hypertension, and dysfunction of other cranial nerves are all associated with an increased risk of bilateral symptoms in patients with TN. However, many patients with bilateral TN have no apparent risk factors.^{5,20} This suggests that bilateral TN occurs in a heterogeneous

ABBREVIATIONS BNI = Barrow Neurological Institute; CMT = Charcot-Marie-Tooth; DM = diabetes mellitus; EMR = electronic medical records; GKRS = Gamma Knife radiosurgery; HR = hazard ratio; IQR = interquartile range; MS = multiple sclerosis; MVD = microvascular decompression; PN = peripheral neuropathy; PTR = percutaneous trigeminal rhizotomy; REZ = root entry zone; TN = trigeminal neuralgia.

SUBMITTED December 19, 2017. **ACCEPTED** June 11, 2018.

INCLUDE WHEN CITING Published online November 30, 2018; DOI: 10.3171/2018.6.JNS172646.

patient population with multiple possible causes of symptoms.^{5,10,20} Furthermore, because of the subset of patients with bilateral TN who have potential nonvascular etiology of their pain (such as MS and Charcot-Marie-Tooth [CMT] disease, which has been associated with bilateral TN),²⁷ it has been unclear whether the standard treatment options remain effective for this population.

Gamma Knife radiosurgery (GKRS) is a widely accepted, noninvasive treatment option for medically refractory unilateral TN. Multiple large series have reported pain relief rates ranging from 80% to 90%; however, the pain can recur over time.^{7,13,16,17,26} In these cases, repeat GKRS is an established treatment option.^{8,12,19} Multiple predictive factors for treatment success or failure after GKRS have been identified, including decreased efficacy in those with a history of diabetes mellitus (DM) or a history of MS, and increased efficacy in smokers with MS-associated TN.^{17,29}

GKRS in the setting of bilateral symptoms has not been well studied. Only a single dedicated series with 8 patients has been reported in the literature thus far, and 2 of the patients received repeat GKRS for treatment failure.²² Additionally, a small subgroup of patients in a series reporting GKRS outcomes for MS-associated TN had bilateral symptoms.²⁸ Small numbers of patients with bilateral symptoms have been included in large series of GKRS for TN; however, detailed results regarding bilateral treatment have not been published.^{7,15,17,23} In this article we report the outcomes of patients with bilateral TN who underwent GKRS at our institution.

Methods

Patient Population

A retrospective review of our institution's electronic medical records (EMR) and GKRS treatment database was performed to identify patients with medically refractory bilateral TN. Fifty-one individual nerves in 34 patients with bilateral symptoms of TN were treated with GKRS between 2001 and 2015. Twelve individual nerves in 11 patients were treated with repeat GKRS after initial failure. Demographic data, past history, treatment outcomes, and other relevant data were collected from the EMR and GKRS treatment database. Available demographic data were included for all patients, even those with limited follow-up data, in order to provide more accurate estimates of the incidence of various risk factors in this population. Long-term follow-up data, including maximal pain relief, time to BNI IIIb and BNI I pain relief (if applicable), duration of pain relief, and treatment toxicities such as facial numbness, anesthesia dolorosa, and corneal numbness, as well as any relevant background data not available in the EMR were collected by telephone interview when possible. Telephone interviews were conducted between March and June 2015 by a single author. Patients were classified as having classic facial pain if their symptoms were consistent with Burchiel type 1 pain.⁶ All others were classified as having nonclassic pain. As with prior reports on bilateral TN, patients with a history of MS were included in this series.^{4,5,22} Institutional review board approval was obtained for this study, and a waiver of informed consent was obtained from the institutional review board.

Radiosurgery Technique

GKRS was performed using the Gamma Knife model B (2001–2004), 4C (2004–2009), or Perfexion (2009–2015; Elekta). On the day of the procedure, the patient underwent placement of a Leksell model G stereotactic headframe. A high-resolution MRI study of the brain was then performed without contrast. Procedures in 2 patients were planned using CT scans because these patients were unable to undergo MRI. A treatment plan was generated using the Leksell GammaPlan treatment planning software (Elekta). Details of treatment planning, including targeting of the nerve, have been previously reported for both MRI- and CT-based planning.^{2,8} The median dose for the initial treatment was 85 Gy. Prior to 2012, the standard institutional dose for initial GKRS was 90 Gy. As data regarding dose response and treatment toxicity became available, the standard initial dose was decreased to 85 Gy, which is our current institutional standard.¹⁷ The median dose for repeat treatment was 82.5 Gy. In general, the dose for a second GKRS treatment to the same nerve was decreased. All doses were prescribed to the 100% isodose line. The collimator output factor for models B and 4C was 0.87, and it was 0.81 for the Perfexion model.

Radiosurgery Dosimetry

Dosimetric information was obtained from the treatment planning system regarding prescription dose, and dose to the surface of the pons, root entry zone (REZ), and petrous dura. The definitions of these landmarks have been previously reported.¹⁷ If a treatment plan was not able to be retrieved from older archived media, data were obtained from the EMR and prior databases if possible. Nine initial and 4 repeat treatment plans were unavailable for review.

Follow-Up Protocol

Patients were instructed to taper off of their medications once their pain had resolved and were scheduled for a follow-up appointment approximately 3–6 months after the procedure. If at that time they had achieved an acceptable level of pain control, they were instructed to follow up as needed. Posttreatment neuroimaging was not routinely obtained. Long-term follow-up was obtained by telephone interview. The median follow-up periods from the date of initial and repeat GKRS treatments were 2.89 years and 3.76 years, respectively.

Treatment Outcomes

Pain outcomes were measured using the BNI pain scale for each individual nerve treated.^{24,25} Patients who achieved a score of BNI IIIb or better were defined as having had a successful procedure. Partial failure was defined as occurring in patients who had initially reached a BNI I but now regressed to BNI II–IIIb. Complete failure was defined as reaching BNI IV or V. Patients who never reached BNI IIIb or better were recorded as having a duration of relief of 0.

Statistical Analysis

Patient and treatment characteristics were summarized with descriptive statistics using the median and interquar-

TABLE 1. Characteristics in 34 patients with bilateral TN

Variable	Value	Median (IQR) or %
Age at GKRS (yrs)	51	71.2 (55.8–76.0)
Sex		
Male	17	33.3
Female	34	66.7
Side of initial presentation		
Rt	32	62.7
Lt	16	31.4
Bilat	3	5.9
Side of GKRS		
Rt	29	56.9
Lt	22	43.1
Type of pain		
Classic	45	88.2
Nonclassic	6	11.8
Smoking status		
Never smoker	20	39.2
Former smoker	25	49.0
Current smoker	6	11.8
History of		
MS		
Definite	7	13.7
Possible	2	3.9
Hypertension	29	56.9
CMT disease/PN	5	9.8
DM	4	7.8
Other cranial nerve dysfunction	6	11.8
Family history of TN	7	13.7
Procedures prior to initial GKRS		
MVD	5	9.8
PTR	7	13.7
MVD & PTR	3	5.9

tile range (IQR) for continuous variables and using frequency and relative frequency for categorical variables. Logistic regression models were created for all variables of interest for the binary outcome of at least BNI IIIb pain relief following initial GKRS. Time-to-event outcomes were defined beginning at the time of GKRS for each nerve and ending at the time of both partial (BNI I) and complete (BNI IIIb) treatment failure or time of last follow-up. Time-to-event outcomes were summarized using the Kaplan-Meier estimator, and stratified outcomes were compared using the log-rank test. Univariate Cox proportional hazards models were created for all variables of interest for each time-to-event outcome. A multivariate Cox proportional hazards model was created using statistically significant factors on univariate Cox proportional hazards models as well as previously described predictors of treatment failure. Probability values of ≤ 0.05 were considered statistically significant. Statistical analysis was performed using R version 3.3.2 software (R Foundation for Statistical Computing).

TABLE 2. Initial GKRS outcomes and toxicity

Variable	Value	Median (IQR) or %
BNI score prior to initial GKRS		
IV	18	35.3
V	33	64.7
BNI score after initial GKRS		
I	25	52.1
II	1	2.1
IIIa	8	16.7
IIIb	8	16.7
IV	2	4.2
V	4	8.3
Time to BNI IIIb response (wks)	30	4.0 (0–9.1)
Time to BNI I response (wks)	19	10 (4.00–16.00)
Numbness after initial GKRS		
Mild	5	10.4
Bothersome	0	0
Unable to determine severity	12	25.0
Anesthesia dolorosa	1	2.0
Corneal dryness	2	4.1
Masseter weakness	1	2.0
Burning mouth syndrome	1	2.0
Hearing loss	1	2.0
Change in taste	0	0
Trismus/lockjaw	0	0

Results

Initial GKRS

Demographic information and past history are summarized in Table 1. The prevalence of bilateral TN at our institution was 3.1% (34/1083 patients). All 3 patients with bilateral symptoms at presentation had a history of definite or possible MS. Treatment outcomes and toxicities of initial GKRS are summarized in Table 2. Of the individual 51 nerves in 34 patients treated with GKRS, 48 had sufficient follow-up to determine BNI pain outcomes. The median follow-up was 2.99 years. Of the 48 nerves in 33 patients with follow-up, 42 (88%) achieved at least BNI IIIb pain relief after initial GKRS, with 25 (52%) achieving BNI I pain relief. The median duration of BNI IIIb pain relief after initial GKRS was 1.9 years. Figure 1 shows the Kaplan-Meier curve for BNI IIIb pain relief after initial GKRS. The 1-, 3-, and 5-year rates of BNI IIIb or better pain relief were 64%, 44%, and 44%, respectively.

Durability of BNI IIIb or better pain relief for bilateral TN was compared with pain control rates of a prior series of patients with unilateral TN from our institution.¹⁶ There was no statistically significant difference between the current series of bilateral TN and the pain control rates in a large cohort of patients with unilateral TN treated with GKRS at our institution, as shown in Fig. 2. The median duration of pain relief was 1.9 years for bilateral TN and 4.2 years for unilateral TN ($p = 0.25$).

FIG. 1. Kaplan-Meier curve showing time to BNI IV–V relapse after initial GKRS. The actuarial probability of maintaining pain relief at 1, 3, and 5 years was 64%, 44%, and 44%, respectively.

The most common toxicity after initial GKRS was facial numbness, which was reported in 17 nerves (35.4%). None of the numbness events were reported as definitely bothersome. One case of anesthesia dolorosa (2%) and 2 cases of corneal dryness (4.1%) were reported. The one case of anesthesia dolorosa was treated early in the series to a dose of 90 Gy.

Repeat GKRS

Treatment outcomes and toxicities of repeat GKRS are summarized in Table 3. Twelve individual nerves in 11 patients were treated with repeat GKRS. Of the 12 nerves treated, 11 (in 10 patients) had sufficient follow-up to determine BNI pain outcomes. Ten of 11 (91%) of the nerves treated achieved at least BNI IIIb pain relief after repeat GKRS, with 5 (45.5%) reaching BNI I pain relief. The median duration of BNI IIIb or better pain relief after repeat GKRS was 2.8 years. There was not a statistically significant difference in median duration of pain relief for initial versus repeat GKRS ($p = 0.36$). Figure 3 shows the Kaplan-Meier curve for BNI IIIb pain relief after repeat GKRS. The 1-, 3-, and 5-year rates of BNI IIIb or better pain relief after repeat GKRS were 79%, 53%, and 53%, respectively.

The most common toxicity after repeat GKRS was numbness, which was seen in 4 of the 11 nerves treated (36.4%). One patient reported that the numbness was significantly bothersome. There were no cases of anesthesia dolorosa and 1 case of corneal dryness after repeat GKRS.

Dosimetric Data

The median dose for initial GKRS was 85 Gy. The me-

dian dose for repeat GKRS was 82.5 Gy. Data from 42 initial treatment plans and 9 repeat treatment plans were able to be retrieved from storage media or prior databases. These data, including dose to multiple anatomical landmarks, are summarized in Table 4.

Predictors of Pain Relief

Cox proportional hazards and logistic regression models were created to evaluate for variables associated with pain relief. Cox proportional hazards analysis showed that patients with a history of MS had a higher likelihood of BNI IIIb failure (hazard ratio [HR] 3.24, $p = 0.01$). Notably, a family history of TN, nonclassic TN, a history of prior procedures, a history of DM, smoking, or CMT disease/peripheral neuropathy (PN) did not predict for treatment failure. Table 5 describes the outcomes for several subgroups of the population. A history of definite or possible MS remained statistically significant on multivariate Cox proportional hazards analysis (HR 3.57, $p = 0.01$). No statistically significant factors predictive of BNI IIIb or better pain relief were identified by the logistic regression model.

Discussion

GKRS for Bilateral TN

GKRS is an effective, noninvasive, well-tolerated treatment option for unilateral TN. Multiple large series have reported initial pain relief rates ranging from 86% to 92% and 5-year pain relief rates from 46% to 65%. Facial numbness rates ranged from 11% to 42%.^{13,16,23} However, data on the more rare and generally difficult to treat scenario of

FIG. 2. Kaplan-Meier curve showing time to BNI IV–V relapse after initial GKRS in bilateral TN (*dashed line*) compared with a large cohort of patients with unilateral TN (*solid line*). There was no statistically significant difference in durability of pain relief between the 2 groups ($p = 0.25$).

bilateral TN are limited, with only 1 dedicated series on GKRS for bilateral TN reported to date.²² Here we report the largest series to date on GKRS for bilateral TN. Our results show that GKRS in the setting of bilateral TN is effective, with 88% of patients achieving at least BNI IIIB pain relief and 52% achieving a BNI I response. Forty-two percent of patients maintained BNI IIIB pain relief in the treated nerve at 5 years. This is consistent with the results of GKRS for unilateral TN, and there was no statistically significant difference in durability of pain relief between patients with bilateral TN and a large cohort of patients with unilateral symptoms treated at our institution.

Initial GKRS was a very well-tolerated treatment, with minimal toxicity. Thirty-five percent of patients reported posttreatment facial numbness, which is similar to prior large series of patients with unilateral TN.^{13,14,17,23} The rate of facial numbness is probably increased due to the fact that patients earlier in the study were typically treated to a dose of 90 Gy, which has since been shown to have a higher risk of toxicity.⁷ Despite this, severe toxicity was rare, with no patients reporting bothersome numbness, and only 1 case of anesthesia dolorosa, which was seen in a patient treated to an initial dose of 90 Gy.

We noted that a history of definite or possible MS was associated with an increased risk of BNI IV–V relapse. This association has been previously reported in patients with mostly unilateral MS-associated TN, so this finding is not entirely unexpected in patients with bilateral MS-associated TN.²⁸ Patients with familial TN responded similarly to the remainder of the population. No genetic traits have yet been identified as a potential cause of familial TN. Despite prior reports suggesting that diabetic patients

TABLE 3. Repeat GKRS outcomes and toxicity

Variable	Value	Median (IQR) or %
BNI score prior to repeat GKRS		
IV	4	33.3
V	8	66.7
BNI score after repeat GKRS		
I	5	45.5
II	1	9.1
IIIA	1	9.1
IIIB	3	27.3
IV	1	9.1
V	1	9.1
Time to BNI IIIB response (wks)	9	8 (6–12)
Time to BNI I response (wks)	4	11 (6.8–16)
Numbness after repeat GKRS		
Total	4	36.4
Bothersome	1	9.1
Unable to determine severity	3	27.3
Anesthesia dolorosa	0	0
Corneal dryness	1	9.1
Masseter weakness	0	0
Burning mouth syndrome	0	0
Hearing loss	0	0
Change in taste	1	9.1
Trismus/lockjaw	1	9.1

FIG. 3. Kaplan-Meier curve showing time to BNI IV–V relapse after repeat GKRS. The actuarial probability of maintaining pain relief at 1, 3, and 5 years was 79%, 53%, and 53%, respectively.

and those with smoking histories have different risks of failure than the general TN population, no difference was seen in this series.^{17,29} However, the power to detect a difference is limited by the small numbers of the various subgroups. We were unable to demonstrate any statistically significant predictors of durability of pain relief. However,

previously reported series have noted that in patients with unilateral TN, patients with atypical facial pain and a history of prior surgical procedures have a shorter duration of pain relief than those with classic TN.^{7,16} Given the similarity in treatment outcomes when compared to patients with unilateral disease, it seems reasonable to extrapolate these data to patients with bilateral TN.

The use of repeat GKRS after initial treatment failure has been reported in multiple series for patients with unilateral TN. Overall, pain relief outcomes are similar to those of the initial treatment, with a slightly increased risk of toxicity.^{8,19} In this series, durability of pain relief was not statistically significantly different between initial and repeat GKRS. Repeat GKRS was well tolerated, with toxicity rates similar to those of previously published series for unilateral TN.^{8,19} The safety and efficacy of repeat GKRS observed in this study is reassuring, because significant bilateral toxicity could lead to substantial morbidity. Because avoiding severe toxicity is of paramount importance in these patients, a personalized treatment dose based on integral dose and trigeminal nerve volume as described by Mousavi and colleagues could be considered.¹⁸

Other Procedures for Bilateral TN

Treatment of bilateral TN with microvascular decompression (MVD) and percutaneous trigeminal rhizotomy (PTR) has also been reported. Pollack and colleagues reported a series of 35 patients with bilateral TN who underwent MVD on at least one side, with 89% of patients achieving good initial pain relief, and with a relatively durable response: 82%, 66%, and 60% had pain relief at 1, 5, and 10 years after treatment, respectively.²⁰ As with

TABLE 4. Dosimetric data

Variable	Value	Median (IQR)
First GKRS dose (Gy)	51	85 (85–90)
To REZ	39	28.3 (13.8–57.6)
To pons	39	45.5 (29.5–53.2)
To petrous dura	39	37.2 (17–71.9)
Second GKRS dose (Gy)	12	82.5 (80–86.3)
To REZ	10	25.4 (10.1–48.9)
To pons	10	36.8 (19.2–54.8)
To petrous dura	9	30.7 (10.2–66.9)
Distance to landmarks from isocenter for 1st GKRS (mm)		
To REZ	40	4.1 (2.3–5.4)
To pons	39	2.9 (2.7–3.7)
To petrous dura	40	3.1 (1.7–4.5)
Distance to landmarks from isocenter for 2nd GKRS (mm)		
To REZ	9	4.6 (3.3–6.5)
To pons	10	3.1 (2.3–4.3)
To petrous dura	9	3.4 (1.6–5.7)

TABLE 5. Initial GKRS outcomes of subgroups with bilateral TN

Subgroup	% (no.) w/ BNI IIIb or Better Outcome	% (no.) w/ BNI IV–V Relapse	Median BNI IIIb Relief Duration (yrs)	HR (BNI IV–V relapse)	p Value
MS-associated TN	78% (7/9)	89% (8/9)	0.45	3.24	0.01
Nonclassic TN	100% (6/6)	67% (4/6)	1.8	1.18	0.76
Prior procedures for TN	80% (12/15)	53% (8/15)	1.6	1.24	0.63
Familial TN	86% (6/7)	29% (2/7)	5.5	0.67	0.58
Ever smoker	77% (24/31)	71% (17/24)	1.4	2.13	0.10
History of CMT disease or PN	100% (5/5)	20% (1/5)	8.65	0.20	0.12
History of DM	100% (4/4)	25% (1/4)	2.6	0.30	0.24

GKRS, initial pain relief rates and durability of pain relief appear to be similar to those of patients with unilateral TN, with 70% of patients having BNI I at 10 years after MVD.³

Multiple series have evaluated the use of PTR in patients with bilateral TN. Brisman reported a series of 32 patients with bilateral symptoms who underwent 54 radiofrequency electrocoagulation procedures on at least one side.⁵ Ten of the 54 procedures were also accompanied by a glycerol injection. There was no difference in relapse rates between patients with bilateral symptoms and those without. Bozkurt et al. reported a series of 89 patients with bilateral TN who underwent radiofrequency rhizotomy on at least one side with good results but higher toxicity rates.⁴ Overall, PTR has been reported to have pain relief rates similar to GKRS, with possibly increased rates of facial numbness and other toxicities.^{1,9,11}

Treatment Paradigm for Medically Refractory Bilateral TN

Our institutional practice for patients with bilateral TN has been similar to that for patients with unilateral disease. For the majority of patients younger than 70 years and with no history of MS, we prefer MVD as the first-line intervention for medically refractory TN. For elderly patients, or for those with MS or medical comorbidities that place them at high risk for poor postoperative outcomes, we typically perform GKRS as the first procedural treatment. These patients are also offered a PTR as the initial procedure.

One of the challenges of bilateral TN is the diagnostic uncertainty it presents. In cases in which there is a question of whether the symptoms are truly due to TN (particularly those with atypical bilateral pain and no known risk factors for bilateral symptoms), we will consider GKRS a first-line treatment due to its excellent response rates for TN and its excellent side effect profile. If the patient has an outcome from GKRS consistent with classic TN, we would then consider MVD if the pain recurs in the future.

A particular difficulty in treating bilateral TN is the importance of avoiding severe side effects due to the risk of severe morbidity if the side effects occur bilaterally. Therefore, we prefer to intervene only on one side at a time if at all possible, with a sufficient interval to allow treatment-related toxicity (such as anesthesia dolorosa or corneal anesthesia) to manifest prior to treating the contralateral nerve.

Limitations of the Study

Although this is the largest series reported to date on the subject, it is still limited by the overall small number of patients, its single-institution, retrospective nature, and the inherent selection bias that is seen in any retrospective series. Recall bias by the patient, particularly those with long intervals between treatment and last follow-up, is also a limitation of this series. The use of telephone interviews for long-term follow-up introduces the possibility of interviewer bias. In an attempt to limit this confounder, all telephone interviews were conducted by a single author not involved in treatment planning. Furthermore, the population in this study is heterogeneous, including patients with idiopathic TN, familial TN, and MS-associated TN, among other groups, limiting the generalizability of the findings of this study. Many of these limitations could be addressed in a prospective clinical trial, although the rarity of bilateral TN would make conducting such a trial quite difficult.

Conclusions

Bilateral TN is a rare condition that can be challenging to treat. Whereas GKRS is well described for unilateral TN, data for its use in patients with bilateral symptoms have not been well reported. To our knowledge, this is the largest series on the subject reported to date. Initial and long-term outcomes are not significantly different from those of GKRS for unilateral TN for either initial or repeat GKRS. Patients with bilateral MS-associated TN have a higher risk of BNI IV–V relapse. GKRS was well tolerated, with toxicity rates similar to those in patients with unilateral symptoms in both the initial and repeat settings. These findings suggest that GKRS is a safe, effective treatment option for patients with medically refractory bilateral TN, and that the procedure can be safely and effectively repeated when necessary.

References

- Alvarez-Pinzon AM, Wolf AL, Swedberg HN, Barkley KA, Cuccalon J, Curia L, et al: Comparison of percutaneous retrogasserian balloon compression and Gamma Knife radiosurgery for the treatment of trigeminal neuralgia in multiple sclerosis. *World Neurosurg* 97:590–594, 2017
- Attia A, Tatter SB, Weller M, Marshall K, Lovato JF, Bourland JD, et al: CT-only planning for Gamma Knife radiosurgery in the treatment of trigeminal neuralgia: methodology

- and outcomes from a single institution. **J Med Imaging Radiat Oncol** 56:490–494, 2012
3. Barker FG II, Jannetta PJ, Bissonette DJ, Larkins MV, Jho HD: The long-term outcome of microvascular decompression for trigeminal neuralgia. **N Engl J Med** 334:1077–1083, 1996
 4. Bozkurt M, Al-Beyati ESM, Ozdemir M, Kahilogullari G, Elhan AH, Savas A, et al: Management of bilateral trigeminal neuralgia with trigeminal radiofrequency rhizotomy: a treatment strategy for the life-long disease. **Acta Neurochir (Wien)** 154:785–792, 2012
 5. Brisman R: Bilateral trigeminal neuralgia. **J Neurosurg** 67:44–48, 1987
 6. Burchiel KJ: A new classification for facial pain. **Neurosurgery** 53:1164–1167, 2003
 7. Dhople AA, Adams JR, Maggio WW, Naqvi SA, Regine WF, Kwok Y: Long-term outcomes of Gamma Knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Clinical article. **J Neurosurg** 111:351–358, 2009
 8. Helis CA, Lucas JT Jr, Bourland JD, Chan MD, Tatter SB, Laxton AW: Repeat radiosurgery for trigeminal neuralgia. **Neurosurgery** 77:755–761, 2015
 9. Henson CF, Goldman HW, Rosenwasser RH, Downes MB, Bednarz G, Pequignot EC, et al: Glycerol rhizotomy versus gamma knife radiosurgery for the treatment of trigeminal neuralgia: an analysis of patients treated at one institution. **Int J Radiat Oncol Biol Phys** 63:82–90, 2005
 10. Jensen TS, Rasmussen P, Reske-Nielsen E: Association of trigeminal neuralgia with multiple sclerosis: clinical and pathological features. **Acta Neurol Scand** 65:182–189, 1982
 11. Kanpolat Y, Savas A, Bekar A, Berk C: Percutaneous controlled radiofrequency trigeminal rhizotomy for the treatment of idiopathic trigeminal neuralgia: 25-year experience with 1,600 patients. **Neurosurgery** 48:524–534, 2001
 12. Kimball BY, Sorenson JM, Cunningham D: Repeat Gamma Knife surgery for trigeminal neuralgia: long-term results. **J Neurosurg** 113 Suppl:178–183, 2010
 13. Kondziolka D, Zorro O, Lobato-Polo J, Kano H, Flannery TJ, Flickinger JC, et al: Gamma Knife stereotactic radiosurgery for idiopathic trigeminal neuralgia. **J Neurosurg** 112:758–765, 2010
 14. Kotecha R, Kotecha R, Modugula S, Murphy ES, Jones M, Kotecha R, et al: Trigeminal neuralgia treated with stereotactic radiosurgery: the effect of dose escalation on pain control and treatment outcomes. **Int J Radiat Oncol Biol Phys** 96:142–148, 2016
 15. Loescher AR, Radatz M, Kemeny A, Rowe J: Stereotactic radiosurgery for trigeminal neuralgia: outcomes and complications. **Br J Neurosurg** 26:45–52, 2012
 16. Lucas JT Jr, Nida AM, Isom S, Marshall K, Bourland JD, Laxton AW, et al: Predictive nomogram for the durability of pain relief from gamma knife radiation surgery in the treatment of trigeminal neuralgia. **Int J Radiat Oncol Biol Phys** 89:120–126, 2014
 17. Marshall K, Chan MD, McCoy TP, Aubuchon AC, Bourland JD, McMullen KP, et al: Predictive variables for the successful treatment of trigeminal neuralgia with gamma knife radiosurgery. **Neurosurgery** 70:566–573, 2012
 18. Mousavi SH, Niranjana A, Akpinar B, Monaco EA III, Cohen J, Bhatnagar J, et al: A proposed plan for personalized radiosurgery in patients with trigeminal neuralgia. **J Neurosurg** 128:452–459, 2018
 19. Park KJ, Kondziolka D, Berkowitz O, Kano H, Novotny J Jr, Niranjana A, et al: Repeat gamma knife radiosurgery for trigeminal neuralgia. **Neurosurgery** 70:295–305, 2012
 20. Pollack IF, Jannetta PJ, Bissonette DJ: Bilateral trigeminal neuralgia: a 14-year experience with microvascular decompression. **J Neurosurg** 68:559–565, 1988
 21. Pollock BE: Surgical management of medically refractory trigeminal neuralgia. **Curr Neurol Neurosci Rep** 12:125–131, 2012
 22. Raval AB, Salluzzo J, Dvorak T, Price LL, Mignano JE, Wu JK: Salvage Gamma Knife radiosurgery after failed management of bilateral trigeminal neuralgia. **Surg Neurol Int** 5:160, 2014
 23. Régis J, Tuleasca C, Resseguier N, Carron R, Donnet A, Gaudart J, et al: Long-term safety and efficacy of Gamma Knife surgery in classical trigeminal neuralgia: a 497-patient historical cohort study. **J Neurosurg** 124:1079–1087, 2016
 24. Rogers CL, Shetter AG, Fiedler JA, Smith KA, Han PP, Speiser BL: Gamma knife radiosurgery for trigeminal neuralgia: the initial experience of The Barrow Neurological Institute. **Int J Radiat Oncol Biol Phys** 47:1013–1019, 2000
 25. Rogers CL, Shetter AG, Ponce FA, Fiedler JA, Smith KA, Speiser BL: Gamma knife radiosurgery for trigeminal neuralgia associated with multiple sclerosis. **J Neurosurg** 97 (5 Suppl):529–532, 2002
 26. Sheehan J, Pan HC, Stroila M, Steiner L: Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. **J Neurosurg** 102:434–441, 2005
 27. Tacconi L, Miles JB: Bilateral trigeminal neuralgia: a therapeutic dilemma. **Br J Neurosurg** 14:33–39, 2000
 28. Tuleasca C, Carron R, Resseguier N, Donnet A, Roussel P, Gaudart J, et al: Multiple sclerosis-related trigeminal neuralgia: a prospective series of 43 patients treated with gamma knife surgery with more than one year of follow-up. **Stereotact Funct Neurosurg** 92:203–210, 2014
 29. Weller M, Marshall K, Lovato JF, Bourland JD, deGuzman AF, Munley MT, et al: Single-institution retrospective series of gamma knife radiosurgery in the treatment of multiple sclerosis-related trigeminal neuralgia: factors that predict efficacy. **Stereotact Funct Neurosurg** 92:53–58, 2014

Disclaimer

The views expressed in this article/book/speech are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US government.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Helis, Tatter, Laxton, Chan. Acquisition of data: Helis, Lucas. Analysis and interpretation of data: Helis, McTyre, Munley, Lucas, Cramer, Tatter, Laxton, Chan. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Helis. Statistical analysis: McTyre.

Correspondence

Corbin A. Helis: Wake Forest Baptist Medical Center, Winston-Salem, NC. chelis@wakehealth.edu.