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Trigeminal neuralgia pain relief after gamma knife stereotactic radiosurgery

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ABSTRACT

Objectives: To report outcomes of patients with medical and/or surgical refractory trigeminal neuralgia (TN) treated with gamma knife stereotactic radiosurgery (GK SRS).
Methods: One hundred and forty-nine patients with 152 cases of TN treated with GK SRS were analyzed. All patients, except one, received a dose of 40 Gy to the 50% isodose volume. The Barrow Neurological Institute (BNI) pain intensity score was used to grade pain. Actuarial rates of pain relief were calculated. Multiple factors were analyzed for association with pain relief.
Results: The median follow up was 27 months (4–71 months). Overall 92% of cases achieved a BNI score I–III after GK SRS. Of those who had pain relief after GK SRS, 32% developed pain recurrence defined as a BNI score of IV or V. The actuarial rate of freedom from pain recurrence (BNI scores I–III) of all treated cases at 1, 2 and 3-years was 76%, 69% and 60%, respectively. On univariate analysis age ≥70 was predictive of better pain relief ($p = 0.046$). Type of pain, prior surgery, multiple sclerosis, number of isocenters, treated nerve length, volume and thickness and distance from the root entry zone to the isocenter were not significant for maintaining a BNI score of I–III. Those who achieved a BNI score of I or II were more likely to maintain pain relief compared to those who only achieved a BNI score of III (93% vs 38% at three years, $p < 0.01$). The rate of pain relief of twenty-seven patients who underwent repeat GK SRS was 70% and 62% at 1 and 2 years, respectively. Toxicity after first GK SRS was minimal with 25% of cases experiencing only new or worsening post-treatment numbness.
Conclusion: GK SRS provides acceptable pain relief with limited morbidity in patients with medical and/or surgical refractory TN.

1. Introduction

Trigeminal neuralgia (TN) is a debilitating nerve disorder that affects approximately 4.5 per 100,000 people each year [1]. TN is generally thought to be caused by vascular compression resulting in demyelination of the trigeminal nerve. In addition, compression of the trigeminal nerve roots by tumors and demyelinating plaques from multiple sclerosis can cause TN [2]. Medical management is the first line of treatment; however, when symptoms are refractory to medical management, surgical intervention or stereotactic radiosurgery can be used [3]. Stereotactic radiosurgery (SRS) is a form of single fraction radiation therapy in which a stereotactic coordinate system is used for precise targeting. Gamma knife (GK) is a common and accurate method of delivering SRS. The goal of GK SRS is to disrupt the pain fibers of the trigeminal nerve by delivering a single fraction of 70–90 Gy to the root entry zone of cranial nerve V as it enters the pons [4,5]. GK SRS is minimally invasive and is given in the outpatient setting in a single day. The overall success rate (freedom from pain recurrence) has been reported to be approximately 70% [6–8].

We report our experience and outcomes of using GK for the treatment of 149 patients with 152 cases of TN refractory to medical and/or surgical management. We also examined predictors of pain relief and analyzed the rate of pain relief in a subset of patients who were retreated with GK.

2. Methods and materials

From January 2007 to July 2012 one-hundred and eighty-four patients with TN were treated with GK SRS at Beaumont Health System with follow up data entered prospectively into a research

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Table 1
Barrow Neurological Institute (BNI) pain intensity score.

I	No trigeminal pain, no medication
II	Occasional pain, not requiring medication
III	Some pain, adequately controlled with medication
IV	Some pain, not adequately controlled with medication
V	Severe pain/no pain relief

database. Patients considered eligible for GK SRS treatment had TN refractory to medical and/or surgical management, medically not suitable for surgical intervention or chose GK SRS over other methods of surgical management when refractory to medical management. Fifteen patients who had previous SRS at an outside institution and twenty patients without any follow up information were excluded. One hundred and forty-nine patients were therefore available for this analysis. The study was reviewed and granted approval by the William Beaumont Hospital Human Investigation Committee (HIC# 2013-044).

2.1. Radiosurgical technique

All patients were treated with the Leksell Gamma Knife Model 4C (Elekta). The Leksell stereotactic head frame was affixed to the patient's skull with 4 pins. All patients then underwent a non-contrast enhanced CT scan and a contrast-enhanced MRI. An axial MP-RAGE (or equivalent) post-contrast sequence with 1 mm thick slices and a T2-weighted high-resolution 3-D gradient echo constructive interference in steady state (CISS) sequence were both obtained. Patients with contraindication to MRI had a CT cisternogram to define the trigeminal nerve. The Leksell GammaPlan, the 3D-based treatment planning system with multiview was utilized by the treating radiation oncologist, neurosurgeon and medical physicist to design an optimal treatment plan. All patients except one received a dose of 40 Gy prescribed to the 50% isodose line, with 84% of the treatments using a single 4 mm isocenter along the long axis of the nerve. The choice of single or multiple isocenters as well as the location of the isocenter placement was based on treating physician preference. For retreatment cases the isocenter was placed at a different location than the original isocenter of the initial treatment.

2.2. Follow up protocol

Patients were seen ≤2 weeks post-GK, then every 3–6 months. Pain response was evaluated by the Barrow Neurological Institute (BNI) Score [9] (Table 1) which was obtained at each follow up visit and prospectively entered into the research database. In addition, periodic mail surveys and telephone interviews were used to obtain follow up information. Facial and trigeminal nerve dysfunction were also assessed at each follow up visit and entered prospectively into our database. Trigeminal nerve dysfunction was assessed according to whether the patient had normal facial sensation, decreased sensation, no sensation or any weakness of the muscles of mastication.

2.3. Statistical analysis

Time intervals were calculated from the date of GK. Actuarial rate of pain relief was analyzed by the Kaplan–Meier method. Obtaining a BNI score of I, II or III was considered a treatment success and a BNI score of IV or V after GK was considered a treatment failure. Freedom from pain recurrence was defined as having a BNI score I–III at last follow up. Treatment response after GK was defined as achieving a BNI score of I–III. Univariate analysis was performed using the log-rank test and a Cox regression model. A p-value of ≤0.05 was considered significant. Statistical analyses were performed utilizing the Statistical Package for the Social Sciences v.20 (SPSS; IBM, Somers, NY).

Table 2
Patient characteristics.

Patients	149
Treatments	151
Median age in years (range)	70 (29–94)
Gender	
Male	49 (33%)
Female	100 (67%)
Type of TN	
Typical	125 (83%)
Atypical	24 (16%)
Postherpetic neuralgia	2 (1%)
Pre-GK BNI score	
IV	100 (66%)
V	51 (34%)
Patients with multiple sclerosis	15 (10%)
Prior surgical procedure	51 (34%)
Type of prior surgical procedure	
Microvascular decompression	24 (47%)
Radiofrequency rhizotomy	17 (33%)
Glycerol rhizotomy	6 (12%)
Balloon compression	1 (2%)
Other	3 (6%)

3. Results

3.1. Initial pain relief

Patient characteristics are given in Table 2 and treatment characteristic in Table 3. Thirty-four percent had a previous surgical

Table 3
Treatment characteristics.

Prescribed dose	
40 Gy to 50% IDL	150 (99%)
35 Gy to 50% IDL	1 (1%)
Number of isocenters	
One	127 (84%)
Two	24 (16%)
Isocenter location in relation to CN V	
Anterior 1/3	50 (36%)
Middle 1/3	86 (54%)
Posterior 1/3	15 (10%)
Collimator size	
4 mm	127 (84%)
4 and 4 mm	13 (9%)
4 and 8 mm	11 (7%)
Treated trigeminal nerve thickness (cm)	
Mean	0.31
Median (range)	0.29 (0.14–0.52)
Treated trigeminal nerve length (cm)	
Mean	0.57
Median (range)	0.57 (0.36–0.98)
Total trigeminal nerve length (cm)	
Mean	1.15
Median (range)	1.15 (0.36–2.29)
Ratio of treated length to total length	
Mean	0.52
Median (range)	0.50 (0.25–1.00)
Treated trigeminal nerve volume (cc)	
Mean	0.030
Median (range)	0.030 (0.010–0.11)
Total trigeminal nerve volume (cc)	
Mean	0.068
Median (range)	0.06 (0.014–0.51)
Ratio of treated volume to total volume	
Mean	0.48
Median (range)	0.48 (0.17–1.00)
Distance from the root entry zone (cm)	
Mean	0.64
Median (range)	0.62 (0.21–0.12)