

ORIGINAL RESEARCH

Cyberknife radiosurgery in treating trigeminal neuralgia

Bryan M Lazzara,¹ Orlando Ortiz,¹ Ritu Bordia,¹ Matthew R Witten,² Jonathan A Haas,² Alan J Katz,² Jeffrey A Brown³¹Department of Radiology, Winthrop-University Hospital, Mineola, New York, USA²Department of Radiation Oncology, Winthrop-University Hospital, Mineola, New York, USA³Department of Neurosurgery, Winthrop-University Hospital, Mineola, New York, USA**Correspondence to**Orlando Ortiz, Chairman, Department of Radiology, Winthrop-University Hospital, 259 First Street, Mineola, NY 11501, USA; OOrtiz@winthrop.orgReceived 16 August 2011
Revised 15 November 2011
Accepted 21 November 2011
Published Online First
26 January 2012**ABSTRACT****Purpose** To assess the short term efficacy of Cyberknife stereotactic radiosurgical treatment of trigeminal neuralgia (TN).**Methods** 17 consecutive patients with medically or surgically refractory unilateral TN were treated with Cyberknife radiosurgery. Using superimposed CT cisternogram and MR images, the target segment of the trigeminal nerve was consistently defined as a 6 mm length of nerve approximately 2–3 mm distal to the dorsal root entry zone of the brainstem. A radiosurgical rhizotomy was performed with the Cyberknife utilizing a single collimator to deliver an average maximum dose of 73.06 Gy (range 72.91–73.73) to the target.**Results** Follow-up data were available for 16 of the 17 patients post-treatment (range 1–27 months, average 11.8 months). Overall, 14 of 16 (88%) patients responded favorably with either partial or complete relief of symptomatology. 11 of these patients were successfully free of all pain at some point in their post-treatment course, with seven patients pain free to the last follow-up visit (average 5.0 months, range 1–13 months). Symptoms recurred in four patients, taking place at 3, 7.75, 9 and 18 months after Cyberknife therapy. Only two patients reported side effects. One patient developed a bothersome feathery dysesthesia while the second patient reported a non-bothersome mild jaw hypoesthesia. There were no substantial complications related to stereotactic radiosurgery.**Conclusion** Cyberknife radiosurgery is a viable treatment alternative in patients with TN with competitive efficacy demonstrated in our group of patients while minimizing adverse effects.**INTRODUCTION**

Trigeminal neuralgia (TN), also known as tic dolooureux, is an idiopathic disorder that is characterized by paroxysmal attacks of sharp, lancinating or electric shock-like pain that occur within the trigeminal nerve distribution, most often unilateral in the maxillary or mandibular nerve divisions. These painful episodes are often brief, lasting only minutes, but occur in bouts over the course of weeks or months with periods of remission that can last years. These symptoms affect 4–5 people in 100 000. An atypical version of TN involves a constant, or nearly constant, burning and aching pain. Most cases affect patients in their sixties but the disorder can occur in any age.

Firstline therapies include anticonvulsant and antidepressant medications. However, medical

therapies fail to maintain relief for many patients and are associated with various side effects, leading patients to seek other treatments options. Surgical alternatives have included percutaneous procedures consisting of balloon compression, glycerol rhizotomy or thermal radiofrequency rhizotomy targeting the nerve at the level of the foramen ovale, while open microvascular decompression has traditionally been the gold standard. Unfortunately, the duration of patients' responses to percutaneous rhizotomies has been variable, and some patients are simply poor surgical candidates.

Since the mid-1990s, stereotactic isocentric gamma knife and linear accelerator radiosurgery has been implemented to perform a rhizotomy targeting various portions of the proximal trigeminal nerve. This modality demonstrated improving success rates although with notable side effects, including numbness and dysesthesias of varying degrees, trismus, anesthesia dolorosa, masticator weakness, diplopia and others. The Cyberknife system, on the other hand, delivers a non-isocentric beam of radiation better suited for targeting the trigeminal nerve with greater target fidelity and enhanced patient comfort. These attributes hold promise for improved patient outcomes with fewer side effects. The optimal treatment parameters regarding length and target segment of nerve irradiated, treatment dose and various other factors continue to be refined.

We present our experience of patients treated with a Cyberknife radiosurgical rhizotomy targeting a consistent nerve length and narrow dose range. We treated 17 consecutive patients with refractory TN by consistently irradiating a 6 mm length of nerve 2–3 mm from the dorsal root entry zone with a narrow dose range centered at 73.06 Gy.

PATIENTS AND METHODS

Seventeen consecutive patients with TN underwent Cyberknife stereotactic radiosurgery between May 2007 and July 2009 at our institution. Patients were referred for treatment with a previous diagnosis of TN, reporting paroxysmal episodes of sharp, stabbing or lancinating pain in a trigeminal nerve distribution. All patients were evaluated by an experienced neurosurgeon, interventional neuroradiologist and radiation oncologist prior to radiosurgery. This evaluation consisted of a clinical assessment for pain, a neurological examination and imaging (table 1).

Table 1 Patient demographics

Characteristic	No (%)
No of patients	17
Women	11 (65)
Men	6 (35)
Age (years) (mean (range))	69.4 (36–90)
Mean duration of symptoms (months)	83
Patients with prior surgeries*	4 (24)
Laterality	
Left	8
Right	9
Distribution	
V1	1 (5.9)
V2	2 (11.8)
V3	6 (35.3)
V1 + V2	2 (11.8)
V2 + V3	5 (29.4)
V1 + V2 + V3	1 (5.9)

*Microvascular decompression, glycerol injection, balloon compression, radiofrequency ablation, radiosurgery or cranioplasty.

Eleven women and six men were included in the study, with a mean age of 69.4 years (range 36–90). Patients reported TN symptom duration ranging from 1 to 11 years (mean 83 months) and a failed response to medical management, ablative procedure or a combination thereof. All but one of the 17 patients documented an initial trial of medical therapy, each with inadequate symptom relief. Four patients had unsuccessfully responded to surgical interventions. This included one patient who failed to permanently respond to two microvascular decompressions and a gamma knife rhizotomy 8 years before the referral. A second patient's history included microvascular decompression with skull reconstruction and a cranioplasty revision. A third patient reported a history of balloon compression.

The most common distribution of symptoms resided in the mandibular V3 (n=6) and a combination of maxillary and mandibular V2+V3 (n=5) divisions of the trigeminal nerve. No patients reported hypoesthesia or other parasthesia prior to Cyberknife lesioning.

All patients underwent CT cisternography for treatment planning. An experienced interventional neuroradiologist performed a single atraumatic lumbar puncture on each patient and CSF was sent for analysis. Low osmolar iodine contrast

media 4–10 ml (300 mg/ml) was injected into the lumbar subarachnoid space. Contrast was subsequently repositioned to the basal cisterns using a gravity technique with a table tilt maneuver and positioning the patient's head toward the side of TN symptomatology. The patient was transferred to a stretcher with the head down in a prone position and immediately transported to the CT scan suite. High resolution CT images (1.5 mm) of the head were obtained with a stereotactic thermoplastic mask secured into place. All patients underwent high resolution stereotactic MR with FSE T1 weighted axial images.

The target segment of the CN V and target volume were defined during treatment planning on a work station. The retrogasserian cisternal segment of the involved trigeminal nerve was identified on the superimposed CT cisternogram and MR images. The target segment was consistently defined as a 6 mm length of nerve approximately 2–3 mm distal to the dorsal root entry zone of the brainstem (figure 1). Dose to the brainstem and the gasserian ganglion within Meckel's cave was minimized to decrease the likelihood of post-treatment related hypoesthesia. The Cyberknife (Accuray Inc, Sunnyvale, California, USA) was then used to perform a radiosurgical rhizotomy utilizing a single collimator (5 or 7.5 mm) to deliver an average maximum dose of 73.06 Gy (range 72.91–73.73) to the target and a mean marginal prescription dose of 57.17 Gy (range 54.75–58.50). The mean target volume was 73.01 mm³ (range 39.74–145.74). A typical radiation plan is shown in figure 2.

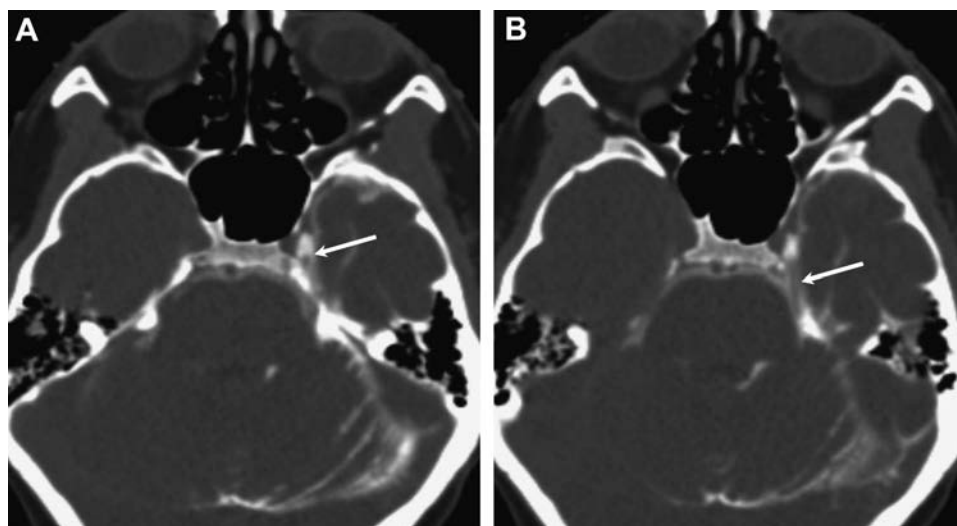
Initial follow-up visits were scheduled for 3 weeks post-radiosurgery treatment and then subsequent visits in the following months on an outpatient basis with both a neurosurgeon and radiation oncologist. Patients were physically examined and asked to provide a self-assessed degree of improvement regarding pain severity and frequency. A retrospective review of the results evaluated time to pain relief, degree of pain improvement, intensity and time of symptom recurrence, and assessment for side effects related to the procedure, including hyper- or hypoesthesia and anesthesia dolorosa.

RESULTS

CT cisternography

The most optimal CT cisternographic technique employed 10 ml of iohexal contrast agent (300 mg/ml) for superior and consistent trigeminal nerve visualization. All CSF analyses were negative. Only one transient complication related to the CT

Figure 1 (A) CT cisternogram image shows the trigeminal nerve entering Meckel's cave (arrow). (B) CT cisternogram image shows the cisternal segment of the trigeminal nerve.



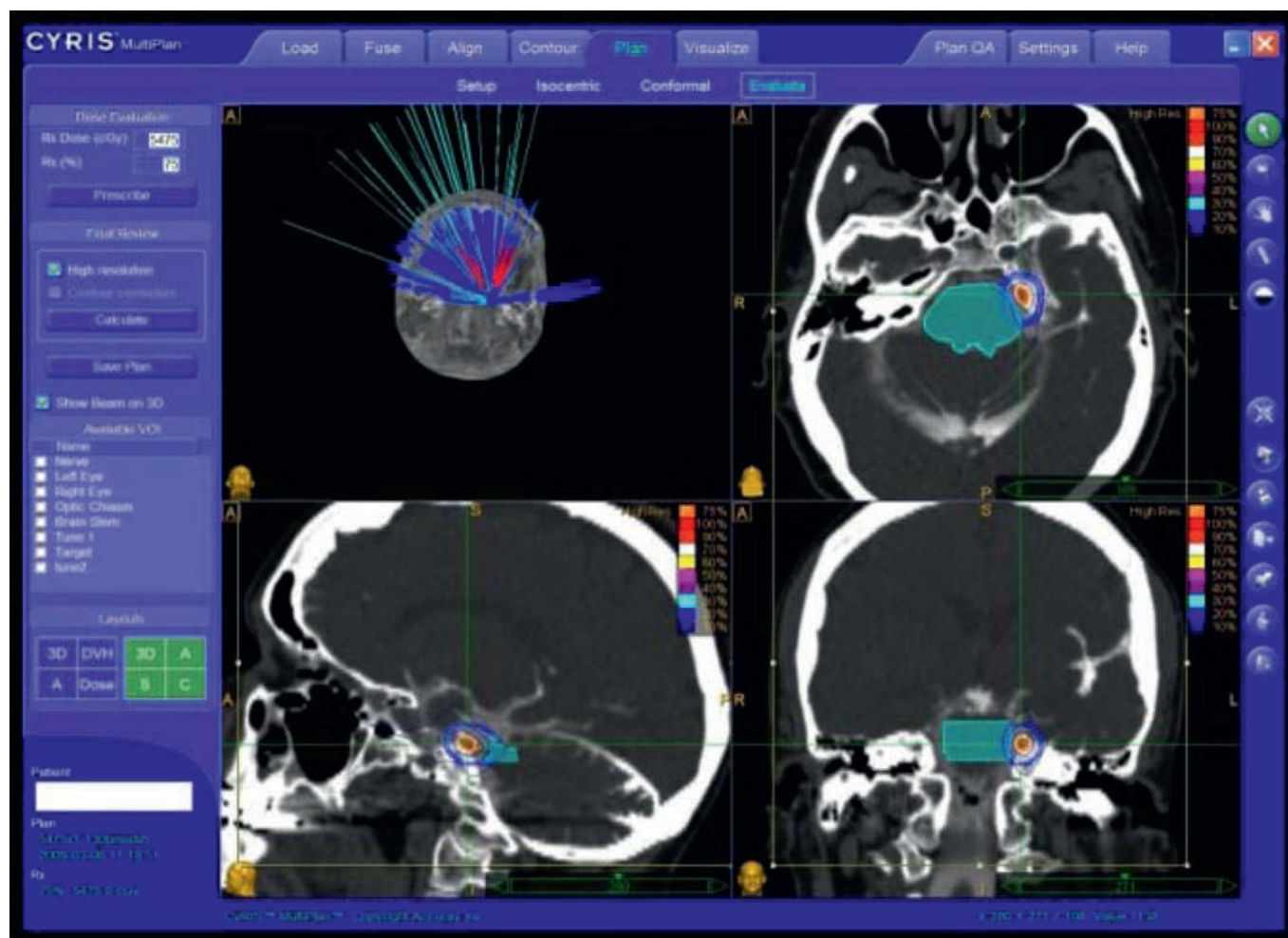


Figure 2 Example of treatment plan with isodose distribution. Light blue, brainstem; red, target, anterior portion of the trigeminal nerve in the prepontine cistern; orange, prescription isodose line.

cisternogram was encountered. One patient experienced transient aggravation of her symptoms during the table tilt and also developed post-procedure spinal tap headache for 2 days, successfully managed with conservative treatment.

Clinical follow-up

Follow-up data were available for 16 of the 17 patients post-treatment (ranging from 1 to 27 months, average 11.8). One patient was lost to follow-up. Overall, 14 of 16 (88%) patients responded favorably to Cyberknife radiosurgery with either partial or complete relief of symptomatology. Eleven of these patients were successfully pain free at some point in their post-treatment course, whether continuing or having withdrawn their medication use, with seven patients benefitting from this positive response through to the last follow-up visit (average 5.0 months, range 1–13). The average time to achieve maximum response was 1.9 months, with a range commencing with the first follow-up visit at 3 weeks to as late as 6 months after radiosurgery.

Four patients in total experienced a relapse in their symptoms, occurring at 3, 7.75, 9 and 18 months after Cyberknife therapy. The first patient, whose history did not include any prior procedures, gained only a moderate degree of relief before submitting to a balloon compression procedure 3 months after Cyberknife radiosurgery. Two other patients underwent balloon compressions after pain free intervals of 6 and 7 months

post-treatment (7.75 and 9 months after Cyberknife treatment). The fourth patient with the more durable pain free period reported only mild occasional symptoms that were successfully relieved with medical management.

In the more refractory cases of TN—that is, those four patients with prior ablative procedures—one demonstrated near complete pain relief by 2 months and a second patient mild–moderate improvement by 5 months of follow-up. Insufficient follow-up (3 weeks) for the other two patients (the non-responders in this series) did not allow for proper assessment. To emphasize the refractory nature of these two patients who did not attain pain relief, one had previously undergone two microvascular decompressions and a gamma knife radiosurgery while the other failed treatments ranging from ethanol/radio-frequency ablation to orbital neurectomy.

Side effects

Only two patients reported side effects related to the Cyberknife radiosurgery. One patient remained pain free after treatment of her mandibular TN but developed a bothersome feathery dysesthesia in the V2 and V3 distribution after 13 months. A second patient reported a non-bothersome mild jaw hypoesthesia at 2 months. This second patient also only achieved moderate pain relief while still continuing her medication with 5 months of follow-up available. There were no substantial complications related to stereotactic radiosurgery, including anesthesia dolorosa, trismus, masticator weakness or diplopia.

DISCUSSION

TN is a debilitating disease that is often refractory to the firstline treatment of pharmacotherapy. Alternative treatment options have included percutaneous procedures targeting the nerve at the level of the foramen ovale and craniectomy with microvascular decompression. These invasive procedures have proven successful with a low rate of side effects and recurrences. However, not all patients are candidates for anesthesia and others are simply unwilling to elect for an invasive treatment modality.

Stereotactic radiosurgery targeting the trigeminal nerve has demonstrated improved efficacy in the treatment of TN over the past few decades. Time to pain relief, durability of response and the incidence of side effects were early criticisms of this treatment method. Initial pain relief has been reported in 50–90% of patients treated with radiosurgical rhizotomy performed with (isocentric) a gamma knife and the linear accelerator,^{1–8} with long term (>1 year) pain relief observed in 58.5–83% of patients treated with radiosurgery.^{6 9–12} These improved successes have come as the treatment parameters have been better refined, specifically the length of nerve targeted, radiation dose and distance from the brainstem. However, facial numbness continues to be an issue, with higher rates of sensory loss apparently correlating with better pain relief. Facial hypoesthesia and parasthesias have been demonstrated in up to 54% of treated patients.^{6 9 12–19}

With the objective of improving stereotactic radiosurgery pain relief and reducing the incidence of side effects, the relatively recent Cyberknife system has been implemented with the inherent improvement in patient comfort and targeting. The stereotactic Cyberknife does not require the fixation of a frame onto the patient's skull but rather instead uses a non-invasive thermoplastic mask, an advanced image tracking system and a linear accelerator on a robotic arm. Periodic real time images are acquired during the course of treatment and compared with digitally reconstructed x-rays from the computerized treatment plan, with tracking of head movement and re-registration of the radiation beam to the initially designated target. Fused images from a CT cisternogram and MRI were accurately used in this study to define the TN target. Of note and for the future, Adler *et al* comments in his group's most recent publication that the cisternal segment of the TN could be reliably defined on T2 weighted MR images alone, eliminating the need for an invasive procedure for the Cyberknife treatment.²⁰

The ability of the Cyberknife to deliver a non-isocentric beam has advantages for treating elongated structures such as the TN nerve. The isocentric gamma knife system may require more than one overlapping spherical isocenter to treat longer nerve lengths, thereby delivering a non-conformal radiation dose with a theoretically greater incidence of side effects by irradiating adjacent structures, such as the brainstem. The non-isocentric Cyberknife, on the other hand, can radiate non-spherical structures with greater dose homogeneity and fidelity to the target. Adjacent structures are thereby less affected, potentially reducing the likelihood of adverse events.

The initial rate of pain relief achieved in this cohort of patients is competitive with the published clinical series using Cyberknife non-isocentric rhizotomy, especially in those patients with more refractory neuralgia. Fourteen of 16 patients (88%) demonstrated meaningful relief after treatment, with 11 patients (69%) reporting complete pain relief at some point in their follow-up course. Published preliminary (short term)

meaningful response rates (moderate to excellent) have ranged from 70% to 96% with more recent outcomes tilted toward the higher end as treatment parameters have been better optimized.^{20–24} Within these groups, however, patient inclusion criteria, prescribed dose, length of nerve treated and number of treatments have varied in addition to a lack of a standard definition of treatment response, making comparisons somewhat difficult. The target length of nerve has ranged from 3 mm to 12 mm,^{20–24} with optimization nearing 5–6 mm.^{20 21 24} Adler *et al*'s most recent series of 46 patients demonstrated 96% good to excellent pain relief by consistently targeting a 6 mm length of nerve with a mean maximal dose of 73.5 Gy.²⁰ The value with our series of patients resides in the narrow treatment parameters; a consistent target length of nerve (6 mm) was lesioned with a relatively narrow range of maximum radiation dose (mean 73.06 Gy, range 72.91–73.73). The outcomes were simply favorable with few reported side effects.

Hypoesthesia is the most commonly encountered complication following radiosurgery, with factors related to the length of nerve treated, distance from the brainstem and dose. Our rate of numbness is more than competitive with most previously published groups using the Cyberknife, which have ranged from 0% to 51%, likely from a shorter length of nerve treated (6 mm) and lower doses.^{20–24} The measurement and evaluation of numbness, dysesthesia and patient inclusion varied among groups, making reliable comparison difficult. One patient in our series reported a non-bothersome jaw hypoesthesia approximately 2 months after treatment, and a second patient was affected by a bothersome dysesthesia after 13 months. As facial numbness has typically developed as a delayed side effect of treatment, longer follow-up in this series is necessary for a true assessment. One of the shortcomings in the clinical evaluation was that no formalized scale, such as the Barrow Neurologic Institute Facial Numbness scale, was instituted in this assessment. As patients were requested to revisit if any new adverse effect occurred later in their follow-up course, not all mild hypoesthesias were likely accounted due to non-compliance. No major adverse effects related to the Cyberknife radiosurgery were noted.

The approximate time to achieve the maximum response was on average 1.9 months (range by the first follow-up visit at 3 weeks to 6 months). Four patients (25%) experienced a relapse in their TN symptoms 3, 7.75, 9 and 18 months after Cyberknife radiosurgery, which is similar to the rate in other Cyberknife treatment groups (2–33%).^{20–22 24} The relatively short period of follow-up for several patients in this group may predate complete assessment for recurrence.

Microvascular decompression, along with other invasive procedures, has historically been the means of treating patients with TN failing medical therapy. However, the minimally invasive nature of radiosurgery is an attractive alternative with improving efficacy, particularly in those patients without vascular compression and as the first lesioning procedure. Further investigation and future comparative studies between Cyberknife, gamma knife and surgical treatment potentially will show Cyberknife's viable role in treating TN.

CONCLUSION

Our cohort of patients treated with Cyberknife radiosurgery for TN targeting a consistent nerve length and dose demonstrated effective and safe outcomes in terms of initial pain relief and incidence of sensory loss. Non-isocentric radiosurgery can be

used as an alternative to more invasive treatments and warrants further follow-up and investigation.

Competing interests None.

Ethics approval This was a retrospective review of short term treatment outcomes with patient data recorded in a non-identifiable manner. A standard Health Insurance Portability and Accountability Act compliant protocol was followed.

Contributors All listed authors met the criteria for authorship according to *BMJ* guidelines.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Data are available on request.

REFERENCES

1. **Kondziolka D**, Perez B, Flickinger JC, *et al*. Gamma knife radiosurgery for trigeminal neuralgia: results and expectations. *Arch Neurol* 1998;**55**:1524–9.
2. **Kanner AA**, Neyman G, Suh JH, *et al*. Gamma knife radiosurgery for trigeminal neuralgia: comparing the use of a 4-mm versus concentric 4- and 8-mm collimators. *Stereotact Funct Neurosurg* 2004;**82**:49–57.
3. **Knafo H**, Kenny B, Mathieu D. Trigeminal neuralgia: outcomes after gamma knife radiosurgery. *Can J Neurol Sci* 2009;**36**:78–82.
4. **Smith ZA**, De Salles AA, Frighetto L, *et al*. Dedicated linear accelerator radiosurgery for the treatment of trigeminal neuralgia. *J Neurosurg* 2003;**99**:511–16.
5. **Zheng LG**, Xu DS, Kang CS, *et al*. Stereotactic radiosurgery for primary trigeminal neuralgia using the Leksell Gamma unit. *Stereotact Funct Neurosurg* 2001;**76**:29–35.
6. **Kondziolka D**, Zorro O, Lobato-Polo J, *et al*. Gamma knife stereotactic radiosurgery for idiopathic trigeminal neuralgia. *J Neurosurg* 2010;**112**:758–65.
7. **Han PP**, Shetter AG, Smith KA, *et al*. Gamma knife radiosurgery for trigeminal neuralgia: experience at the Barrow Neurological Institute. *Stereotact Funct Neurosurg* 1999;**73**:131–3.
8. **Kondziolka D**, Lunsford LD, Flickinger JC. Gamma knife radiosurgery as the first surgery for trigeminal neuralgia. *Stereotact Funct Neurosurg* 1998;**70**(Suppl 1):187–91.
9. **Regis J**, Metellus P, Hayashi M, *et al*. Prospective controlled trial of gamma knife surgery for essential trigeminal neuralgia. *J Neurosurg* 2006;**104**:913–24.
10. **Dhople AA**, Adams JR, Maggio WW, *et al*. Long-term outcomes of gamma knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Clinical article. *J Neurosurg* 2009;**111**:351–8.
11. **Riesenburg RI**, Hwang SW, Schirmer CM, *et al*. Outcomes following single-treatment gamma knife surgery for trigeminal neuralgia with a minimum 3-year follow-up. *J Neurosurg* 2010;**112**:766–71.
12. **Maesawa S**, Salame C, Flickinger JC, *et al*. Clinical outcomes after stereotactic radiosurgery for idiopathic trigeminal neuralgia. *J Neurosurg* 2001;**94**:14–20.
13. **Sheehan J**, Pan HC, Stroila M, *et al*. Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. *J Neurosurg* 2005;**102**:434–41.
14. **Tawk RG**, Duffy-Fronckowiak M, Scott BE, *et al*. Stereotactic gamma knife surgery for trigeminal neuralgia: detailed analysis of treatment response. *J Neurosurg* 2005;**102**:442–9.
15. **Fountas KN**, Lee GP, Smith JR. Outcome of patients undergoing gamma knife stereotactic radiosurgery for medically refractory idiopathic trigeminal neuralgia: Medical College of Georgia's experience. *Stereotact Funct Neurosurg* 2006;**84**:88–96.
16. **Kondziolka D**, Flickinger JC, Lunsford LD, *et al*. Trigeminal neuralgia radiosurgery: the University of Pittsburgh experience. *Stereotact Funct Neurosurg* 1996;**66**(Suppl 1):343–8.
17. **Longhi M**, Rizzo P, Nicolato A, *et al*. Gamma knife radiosurgery for trigeminal neuralgia: results and potentially predictive parameters—part I: idiopathic trigeminal neuralgia. *Neurosurgery* 2007;**61**:1254–60.
18. **Massager N**, Murata N, Tamura M, *et al*. Influence of nerve radiation dose in the incidence of trigeminal dysfunction after trigeminal neuralgia radiosurgery. *Neurosurgery* 2007;**60**:681–7.
19. **Pollock BE**, Phuong LK, Foote RL, *et al*. High-dose trigeminal neuralgia radiosurgery associated with increased risk of trigeminal nerve dysfunction. *Neurosurgery* 2001;**49**:58–62.
20. **Adler JR Jr**, Bower R, Gupta G, *et al*. Nonisocentric radiosurgical rhizotomy for trigeminal neuralgia. *Neurosurgery* 2009;**64**(2 Suppl):A84–90.
21. **Villavicencio AT**, Lim M, Burneikiene S, *et al*. Cyberknife radiosurgery for trigeminal neuralgia treatment: a preliminary multicenter experience. *Neurosurgery* 2008;**62**:647–55.
22. **Lim M**, Villavicencio AT, Burneikiene S, *et al*. CyberKnife radiosurgery for idiopathic trigeminal neuralgia. *Neurosurg Focus* 2005;**18**:E9.
23. **Romanelli P**, Heit G, Chang SD, *et al*. Cyberknife radiosurgery for trigeminal neuralgia. *Stereotact Funct Neurosurg* 2003;**81**:105–9.
24. **Fariselli L**, Marras C, De Santis M, *et al*. CyberKnife radiosurgery as a first treatment for idiopathic trigeminal neuralgia. *Neurosurgery* 2009;**64**:A96–101.



Cyberknife radiosurgery in treating trigeminal neuralgia

Bryan M Lazzara, Orlando Ortiz, Ritu Bordia, et al.

J NeuroIntervent Surg 2013 5: 81-85 originally published online January 25, 2012

doi: 10.1136/neurintsurg-2011-010125

Updated information and services can be found at:

<http://jnis.bmj.com/content/5/1/81.full.html>

These include:

References

This article cites 24 articles

<http://jnis.bmj.com/content/5/1/81.full.html#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections

Articles on similar topics can be found in the following collections

[Head and neck](#) (30 articles)

[Press releases](#) (9 articles)

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>