Clinical Study

Stereotactic and Functional Neurosurgery

Stereotact Funct Neurosurg 2011;89:220–225
DOI: 10.1159/000325672

Received: September 13, 2010
Accepted after revision: February 12, 2011
Published online: May 25, 2011

Outcome for Patients with Essential Trigeminal Neuralgia Treated with Linear Accelerator Stereotactic Radiosurgery

Marcos Antonio dos Santos[a, d] José Bustos Pérez de Salcedo[a, b]
José Angel Gutiérrez Diaz[a, b] Gorka Nagore[a] Felipe A. Calvo[a, c]
José Samblás[a, b] Hugo Marsiglia[a, d] Kita Sallabanda[a, b]

[a]Radiotherapy Department, Instituto Madrileño de Oncologia/Grupo IMO, [b]Neurosurgery Department, Sanatório San Francisco de Asis and [c]Department of Oncology, Hospital General Universitario Gregório Marañon, Madrid, Spain; [d]Institut de Cancerologie Gustave Roussy, Ville Juif, Paris, France

Key Words
Trigeminal neuralgia · Radiosurgery · Facial pain

Abstract
Background: Stereotactic radiosurgery (SRS) is one option for treatment of trigeminal neuralgia, after unsuccessful conservative approaches. ***Objectives:*** The objective of this study was to retrospectively evaluate our institutional results in the management of patients with idiopathic trigeminal neuralgia treated with linear accelerator SRS. ***Methods:*** Fifty-two patients were treated between January 1998 and December 2009 and were followed for more than 6 months (median: 26.6 months). Forty-seven patients (90%) had undergone previous surgery before SRS. The target dose ranged from 50 to 80 Gy. ***Results:*** After SRS, 9 patients presented complete remission of the pain, and 21 were pain free but still under medication. Eleven patients reported a relief of more than 50% in crisis frequency. In 9 patients, no significant improvements were seen, and 2 presented an exacerbation of the pain. After an average period of 20 months, 15 patients reported pain recurrence. Results were better in patients older than 60 years ($p = 0.019$). Nineteen patients presented facial numbness after SRS, with a trend toward favorable treatment response ($p = 0.06$). ***Conclusion:*** SRS is an effective alternative to the treatment of essential trigeminal neuralgia, with long-lasting pain relief in more than 50% of the patients. Better results were seen with patients aged more than 60 years.

Introduction

Trigeminal neuralgia, also known as tic douloureux, is a pain syndrome that affects the fifth cranial nerve. It is idiopathic in most cases. Multiple sclerosis and tumors are among the most frequent causes of the secondary forms [1]. The incidence of trigeminal neuralgia is approximately 5 new cases per 100,000 people annually [2].

First-line treatment is medical therapy, but many patients do not respond or develop intolerable side effects [3–5]. Surgical options include decompression of the nerve, percutaneous rhizotomies, mechanical compression or chemical injury to interrupt pain transmission [5–18]. Stereotactic radiosurgery (SRS) is a treatment option when conservative or surgical approaches are unsuccessful. This treatment strategy is based on the principle that a large number of cross-fired beams target and injure the planned anatomic area specifically and selectively

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1011–6125/11/0894–0220$38.00/0

Accessible online at:
www.karger.com/sfn

Marcos Antonio dos Santos, MD
Calle Eusebio Sempere 1
5° piso, puerta E
ES–03003 Alicante (Spain)
Tel. +34 66 086 3881, E-Mail marcosrxt@gmail.com

Table 1. Patient characteristics (n)

Sex	
Men	15 (28.8%)
Women	37 (71.2%)
Age	
<60 years	28 (53.8%)
≥60 years	24 (46.2%)
Previous surgery	
Radiofrequency rhizotomies	34
Balloon compression	8
Other	17
No previous procedure	5
Affected branches	
1	15 (28.8%)
2	25 (48.1%)
3	12 (23.1%)
Side	
Right	24 (46.2%)
Left	28 (53.8%)
Etiology	
Typical	39 (75%)
Tumors	8 (15.4%)
Multiple sclerosis	3 (5.8%)
Herpes virus	1 (1.9%)
Trauma	1 (1.9%)
Dose	
50–60 Gy	8 (15.4%)
>60 and ≤70 Gy	16 (30.8%)
>70 Gy	28 (53.8%)
Collimators	
1	37 (71.2%)
2	15 (28.8%)
Target	
Cisternal portion of the nerve	6 (11.5%)
Near the gasserian ganglion	19 (36.5%)
Between the previous targets	27 (51.9%)
Results	
Favorable	42 (80.7%)
Partial improvement	7 (13.5%)
Unfavorable	3 (5.7%)
Recurrence	
Yes	18 (34.6%)
No	34 (65.3%)

[19]. It also has the attractive advantages of being almost noninvasive and having a relatively low incidence of morbidity [3, 4, 20].

The mechanism of pain relief is still unknown. Patients usually describe it as a two-step event: initially, there is a decrease in the level of pain, and even if the attacks still occur, these attacks are less painful and less frequent. Some weeks later, the episodes tend to disappear completely [21]. Kondziolka et al. [22] suggest that early pain relief following SRS is a result of the cessation of ephaptic transmission, and a delayed and persistent benefit may be achieved after demyelination or injury to the nerve microvasculature. The permanence of a certain degree of sensitivity would be related to reminiscent myelinated axons. Adler et al. [23] advocate that the demyelination is related to facial numbness, which has been correlated with a good response to the treatment, and they suggest that it could be avoided by the use of free radical scavengers such as amifostine [23]. Of course, these hypotheses are unproven and require further investigation.

There is some evidence that increasing the dose of radiation (from the 70 Gy that was usually prescribed up to 90 Gy, lately tested) may produce better results in pain relief, although this conclusion is based on remarkably heterogeneous findings previously published. The discrepancies are probably due to different methods of outcome evaluation, and also to the high variability in techniques used in the series [3]. The strategy of dose escalation may lead to an increase in morbidity but may be counterbalanced by the choice of a different target, safely distant from the brainstem [3]. The objective of this study was to evaluate our experience in the management of essential trigeminal neuralgia treated with linear accelerator (Linac) SRS, and to try to assess the prognostic factors of this treatment.

Patients and Methods

Sixty patients were treated for essential trigeminal neuralgia between January 1998 and December 2009. Among them, 52 who were followed for more than 6 months (median: 26.6 months; range: 6.3–99.9 months) were selected and retrospectively reviewed. Patients were referred by different specialists from different regions of the country (Spain), and because of that, according to different initial approaches. Some of the patients returned to their regions of origin to be followed and, eventually, treated in case of recurrence (information was sent to our center by E-mail or fax).

There were 15 men and 37 women, whose median age was 51.7 years. The distribution of pain in the divisions of the trigeminal nerve was: V1 – n = 3 (5.8%); V2 – n = 7 (13.5%); V3 – n = 5 (9.6%); V1 and V2 – n = 8 (15.4%); V2 and V3 – n = 17 (32.7%), and V1, V2 and V3 – n = 12 (23.1%). Ninety percent of the patients had received some kind of surgical treatment before SRS, including 34 radiofrequency rhizotomies, 8 balloon compressions and 17 other procedures. Five cases had not received any other surgical procedure, but all were refractory to pharmacological treatment. The target dose varied progressively from 50 to 80 Gy. Five-millimeter collimators were used, 1 of them in 37 cases, and 2 of them in 15 cases (table 1). The median follow-up time was 26.6 months (range: 6.3–99.9 months). All patients were followed up for at least 6 months.

Table 2. Regis classification of efficacy of treatment

Class I	complete relief of neuralgy
Class II	complete relief of neuralgy with use of medications
Class III	>90% reduction in crisis frequency
Class IV	50–90% reduction in crisis frequency
Class V	no significant reduction in crisis frequency
Class VI	worsening of pain

In all cases, SRS was carried out using a Linac with a high-precision positioning system and mechanical fixation of the tertiary collimator (SRS 200; University of Florida, Gainesville, Fla., USA) with 6-MV photons. To locate the target, MR images were obtained, after which the stereotactic frame was positioned with the patient under local anesthesia during the CT planning phase. An image fusion program was used to delineate the target volume. Three-dimensional treatment planning was performed in all cases, although different planning units were used during the period of the study (Philips SRS 200, Philips, Madison, Wisc., USA; Brain Lab, Brain-Lab, Feldkirchen, Germany; Plato-Nucletron, Nucletron, Veenendaal, The Netherlands; ERGO-3D Line, 3DLine Medical Systems, Milan, Italy). The target was determined by a neurosurgeon prior to treatment. It was located at the cisternal trigeminal nerve in 6 cases, near the gasserian ganglion in 19 cases, and between these two targets in 27 cases. The dose was prescribed to the maximum (100%) isodose line. The maximum dose at adjacent structures, including the brainstem, was calculated.

After SRS, all patients were subjected to prophylactic treatment with dexamethasone and remained in the hospital for 24 h in order to prevent any early complication. Follow-up was carried out after 6 and 12 months, and yearly thereafter. Treatment outcomes were defined in accordance with the Regis classification scale (table 2). Recurrence was defined as progression from class I to a lower score [3]. Treatment results were considered favorable when patients reached class I, II or III, partial improvement when patients reached class IV, and adverse when they were classified as class V or VI.

Statistical Analysis

To compare groups for significant differences, cross-tabulations were performed with the Pearson χ^2 test. To analyze factors correlating with the development of facial numbness, we studied the following: the site of the target (the cisternal portion of the nerve, near the gasserian ganglion or between the previous targets), the dose, the number of collimators used (1 or 2) and the response to treatment (favorable, partial or adverse). The Kaplan-Meier method was used to establish the survival curves [24], which were compared by the log rank test.

To analyze factors correlating with pain-free survival (PFS), the following parameters were assessed: age (<60 years compared with ≥60 years), the dose applied (doses of ≤70 Gy compared with doses of >70 Gy), the site of the target, and the number of collimators used. When we had patients who received a considerably large number of treatments, before and after SRS, we considered, for the results, the pain status of these patients at the last follow-up. SPSS version 12.0 was used to analyze the results.

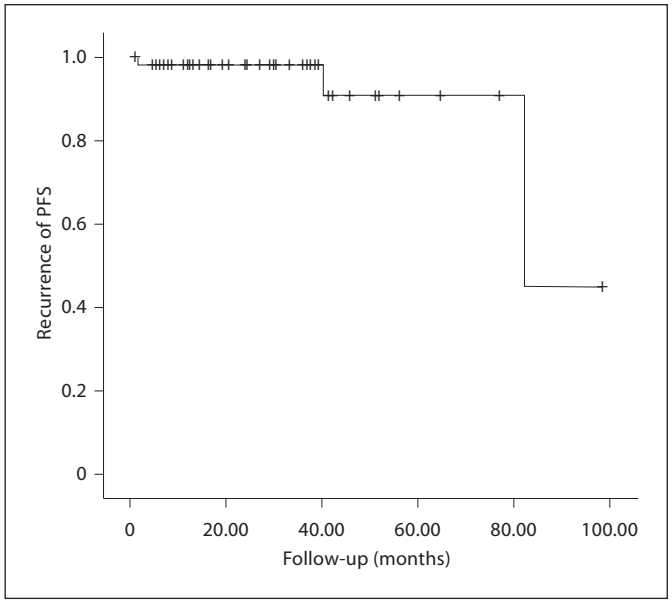

Fig. 1. Recurrence of PFS.

Results

After SRS, 9 patients presented complete remission of the pain and remained free of medications, and 21 patients were pain free but still under medication. Seven patients reported a relief of more than 90% in crisis frequency, while 4 patients showed a reduction between 50 and 90%. In 9 patients, no significant reductions in crisis frequency were seen. Two patients had an adverse outcome, and presented an exacerbation of the trigeminal pain.

Thereafter, 15 patients reported a recurrence of the pain after an average period of 20 months (range: 4–47 months). Salvage treatment included adjustment to the medications used, 7 repeated SRS procedures and 8 instances of surgical intervention. After 5 years of follow-up, 90% of the patients remained pain free (fig. 1). We observed better results in patients older than 60 years ($p = 0.019$) (fig. 2). Concerning the dose, 24 patients received 70 Gy or less (46.2%) and 28 patients received more than 70 Gy (53.8%). No differences were observed when those two groups were compared. No differences related to the site of the target or to the number of collimators used were observed either.

Regarding toxicity, increased or new facial numbness was reported by 19 patients (36%) who received SRS. This factor was not related to the site of the SRS target ($p = 0.96$), to the number of collimators used ($p = 0.23$), or to

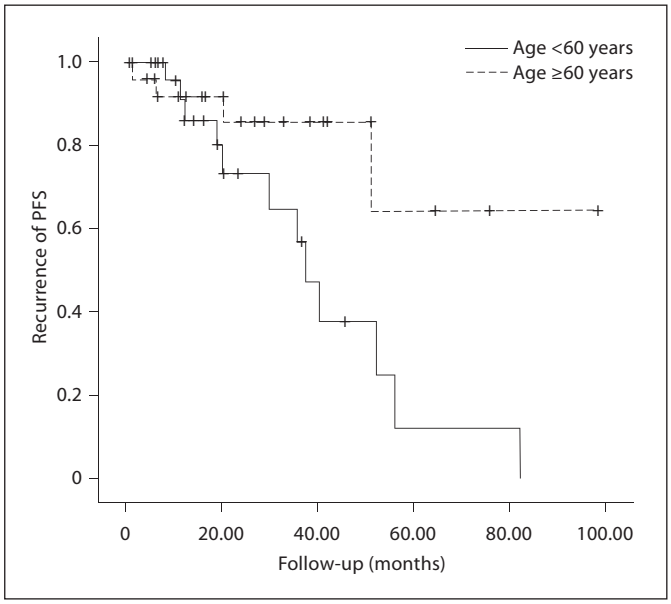

Fig. 2. Recurrence of PFS according to age (p = 0.019).

the application of a dose higher than 70 Gy (p = 0.91). We detected a tendency for correlation, although not statistically significant, between this effect and a favorable response to SRS (p = 0.06). No evidence of motor neuropathy or anesthesia dolorosa was noted.

We also had 3 cases of brainstem edema. This complication was probably related to the use of 2 collimators to perform the SRS. The median dose to 10 mm^3 of the brainstem, with 1 collimator, was 4.5 Gy. When the technique was used with 2 collimators, we saw an increase in median dose to 7.2 Gy. After documentation of those 3 cases, the use of 2 collimators was abandoned.

Discussion

SRS is a less invasive alternative to other surgical procedures in the treatment of refractory trigeminal neuralgia. Its role has continously been defined as recent studies have elucidated long-term outcomes. The dose used most frequently varied from 70 to 90 Gy, which resulted in substantial pain relief. The degree of initial pain cessation ranged from 35 to 100%, and recurrence rates ranged from 0 to 42%, with manageable side effects reported (trigeminal injury: 0–57%) [18, 21, 22, 25–48]. Despite technical factors, this wide spectrum of findings may be the result of different methods of evaluating pain control, and also of the high variability in techniques used in the series [3, 49, 50].

Because patients typically underwent a host of different treatments before and after SRS, and because pain is a subjective symptom that can improve or worsen without any medical intervention, we decided to consider the final outcome only. And, because of that, we make clear that all conclusions refer to the whole treatment. In order to build the survival curve, we analyzed pain status at the last follow-up. Overall, we showed an initial positive response in 80% of patients. These findings support the value of SRS and of the salvage treatments that were applied. Because only 5 patients had not been treated before, it was not possible to analyze the results for treatment with SRS alone.

It has been stated that SRS has better effects on those patients on whom it is used as first-line therapy [36, 41, 47, 49, 51]. Older patients, because of a higher likelihood of comorbidities, tend not to be good candidates for more invasive approaches. The fact that those patients tend to receive SRS sooner than they probably would if they were younger may be a possible explanation for the superior results observed in this group of patients.

There was no correlation between higher doses and improved pain relief at the end of follow-up. On the other hand, Regis et al. [3] reported that they observed good outcomes with high doses and are now prescribing, when possible, 90 Gy to a target that is approximately 7.5–8 mm from the brainstem. This dose increase seems to be in accordance with results previously published. The majority of our patients received 70 or 75 Gy. Only 1 patient actually received 80 Gy. This low number may explain the absence of a dose-response effect in our series.

Facial numbness has been reported to occur in 6–54% of patients treated by gamma knife or Linac [25, 36, 42, 52–55]; thus, our results are similar to those previously published. Flickinger et al. [25] suggested that this effect could be related to the length of the nerve treated. Alpert et al. [56] report that whereas facial numbness is related to the extent of the nerve treated, it is also related to the response to treatment. This correlation corroborates previous results obtained by percutaneous techniques [14]. We were not able to determine any relationship between the development of hypoesthesia and an improved response to treatment, although we did observe a trend toward better results (p = 0.06). A possible explanation for our relatively high level of facial numbness with the low dose levels used is that, in our series, 90% of the patients have been previously treated by other techniques. A correlation between previous surgery and facial numbness has been described by Regis et al. [3].

This study has some limitations. First, we point out its retrospective nature. Because of the rarity of the disease,

prospective studies on this topic are very rare. Also, a considerable proportion of patients had traveled from various parts of the country and, for this reason, were referred after heterogeneous initial approaches. We also point out that this series covers a long period of time and, because of that, included patients treated with very different dose levels. Unfortunately, only a low number of patients were treated with higher doses (above 80 Gy), as recommended by recent studies. Our results reflect the situation in referring centers with a relatively low number of treated patients. With more patients treated at this dose level, we will be able to find out if there actually is a tendency toward better results with higher doses of radiation.

Conclusions

Trigeminal neuralgia radiosurgery continues to evolve. It has been shown to be a safe and efficient part of treatment for drug-resistant trigeminal neuralgia. A relevant part of our patients obtained long-lasting pain relief with acceptable side effects, but we had a relatively short median follow-up to draw more solid conclusions on the long-term development. Dose selection must be balanced with the goals of pain relief and preservation of trigeminal function. Further follow-up is required to confirm the durability of the responses and to evaluate late sequelae.

References

1 Gruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, Nurmikko T, Zakrzewska JM, American Academy of Neurology Society, European Federation of Neurological Society: AAN-EFNS guidelines on trigeminal neuralgia management. Eur J Neurol 2008;15:1013–1028.

2 Laurent B, Keravel Y, Sindou M: Aspects cliniques de la névralgie du trijumeau. Neurochirurgie 2009;55:181–184.

3 Regis J, Arkha Y, Yomo S, Murata N, Roussel P, Donnet A, Peragut JC: La radiochirurgie dans le traitement de la névralgie trigéminale: résultats à long terme et influence des nuances techniques. Neurochirurgie 2009; 55:213–222.

4 Sheehan J, Pan HC, Stroila M, Steiner L: Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. J Neurosurg 2005;102:434–441.

5 Sindou M, Keravel Y: Neurochirurgie fonctionnelle dans les syndromes d'hyperactivité des nerfs crâniens: conclusions. Neurochirurgie 2009;55:291–292.

6 Barker FG 2nd, Jannetta PJ, Bissonette DJ, Larkins MV, Jho HD: The long-term outcome of microvascular decompression for trigeminal neuralgia. N Engl J Med 1996; 334:1077–1083.

7 Broggi G, Flanzini A, Lasio G, Giorgi C, Servello D: Long-term results of percutaneous retrogasserian thermorhizotomy for 'essential' trigeminal neuralgia: considerations in 1,000 consecutive patients. Neurosurgery 1990;26:783–786, discussion 786–787.

8 Flaioli B, Esposito V, Guidetti B, Cruccu G, Manfredi M: Treatment of trigeminal neuralgia by thermocoagulation, glycerolization, and percutaneous compression of the gasserian ganglion and/or retrogasserian rootlets: long-term results and therapeutic protocol. Neurosurgery 1989;24:239–245.

9 Fujimaki T, Fukushima T, Miyazaki S: Percutaneous retrogasserian glycerol injection in the management of trigeminal neuralgia: long-term follow-up results. J Neurosurg 1990;73:212–216.

10 Håkanson S: Trigeminal neuralgia treated by injection of glycerol into trigeminal cistern. Neurosurgery 1981;9:638–646.

11 Jho HD, Lunsford LD: Percutaneous retrogasserian glycerol rhizotomy: current technique and results. Neurosurg Clin North Am 1997;8:63–74.

12 Leston JM: Anatomie functionnelle du nerf trijumeau. Neurochirurgie 2009;55:99–112.

13 Lunsford LD, Apfelbaum RI: Choice of surgical therapeutic modalities for treatment of trigeminal neuralgia: microvascular decompression, percutaneous retrogasserian thermal, or glycerol rhizotomy. Clin Neurosurg 1985;32:319–333.

14 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 2000;47: 1013–1019.

15 Scrivani JS, Keith DA, Mathews ES: Percutaneous stereotactic differential radiofrequency thermal rhizotomy for the treatment of trigeminal neuralgia. J Oral Maxillofac Surg 1999;57:104–111.

16 Slettebø H, Hirschberg H, Lindegaard KF: Long-term results after percutaneous retrogasserian glycerol rhizotomy in patients with trigeminal neuralgia. Acta Neurochir (Wien) 1993;122:231–235.

17 Sweet WH, Wepsic JG: Controlled thermocoagulation of trigeminal ganglion and rootlets for differential destruction of pain fibers. 1. Trigeminal neuralgia. J Neurosurg 1974; 40:143–156.

18 Young RF, Vermulen S, Posewitz A: Gamma knife radiosurgery for the treatment of trigeminal neuralgia. Stereotact Funct Neurosurg 1998;70(suppl 1):192–199.

19 Leksell L: Stereotaxic radiosurgery in trigeminal neuralgia. Acta Chir Scand 1971; 137:311–314.

20 McNatt SA, Yu C, Gianotta SL, Zee CS, Apuzzo MLJ, Petrovich Z: Gamma knife radiosurgery for trigeminal neuralgia. Neurosurgery 2005;56:1295–1301, discussion 1301–1303.

21 Chang JW, Chang JH, Park YG, Chung SS: Gamma knife radiosurgery for idiopathic and secondary trigeminal neuralgia. J Neurosurg 2000;93(suppl 3):147–151.

22 Kondziolka D, Perez B, Flickinger JC, Habeck M, Lunsford LD: Gamma knife radiosurgery for trigeminal neuralgia: results and expectations. Arch Neurol 1998;55:1524–1529.

23 Adler JR Jr, Bower R, Gupta G, Lim M, Efron A, Gibbs IC, Chang SD, Soltys SG: Nonisocentric radiosurgical rhizotomy for trigeminal neuralgia. Neurosurgery 2009;64(suppl): A84–A90.

24 Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–481.

25 Flickinger JC, Pollock BE, Kondziolka D, Phuong LK, Foote RL, Stafford SL, Lunsford LD:. Does increased nerve length within the treatment volume improve trigeminal neuralgia radiosurgery? A prospective double-blind, randomized study. Int J Radiat Oncol Biol Phys 2001;51:449–454.

26 Goss BW, Frighetto L, DeSalles AA, Smith Z, Solberg T, Selch M: Linear accelerator radiosurgery using 90 gray for essential trigeminal neuralgia: results and dose volume histogram analysis. Neurosurgery 2003;53:823–828, discussion 828–830.

27 Han PP, Shetter AG, Smith KA, Fiedler JA, Rogers CL, Speiser B, Feiz-Erfan I: Gamma knife radiosurgery for trigeminal neuralgia: experience at the Barrow Neurological Institute. Stereotact Funct Neurosurg 1999;73: 131–133.
28 Headache Classification Subcommittee of the International Headache Society: The international classification and diagnostic criteria for headache disorders, cranial neuralgia and facial pain, ed 2. Cephalalgia 2004; 24(suppl 1).
29 Kannan V, Deopujari CE, Misra BK, Shetty PG, Shroff MM, Pendse AM: Gamma-knife radiosurgery for trigeminal neuralgia. Australas Radiol 1999;43:339–341.
30 Kondziolka D, Flickinger JC, Lunsford LD, Habeck M: Trigeminal neuralgia radiosurgery: the University of Pittsburgh experience. Stereotact Funct Neurosurg 1996; 66(suppl 1):343–348.
31 Kondziolka D, Lunsford D, Flickinger JC, Young RF, Vermeulen S, Duma CM, Jacques DB, Rand RW, Regis J, Peragut JC, Manera L, Epstein MH, Lindquist C: Stereotactic radiosurgery for trigeminal neuralgia: a multiinstitutional study using the gamma unit. J Neurosurg 1996;84:940–945.
32 Kondziolka D, Lunsford LD, Flickinger JC: Gamma knife radiosurgery as the first surgery for trigeminal neuralgia. Stereotact Funct Neurosurg 1998;70(suppl 1):187–191.
33 Kondziolka D, Lunsford LD, Flickinger JC: Stereotactic radiosurgery for the treatment of trigeminal neuralgia. Clin J Pain 2002;18: 42–47.
34 Kondziolka D, Lunsford LD, Habeck M, Flickinger JC: Gamma knife radiosurgery for trigeminal neuralgia. Neurosurg Clin N Am 1997;8:79–85.
35 Lunsford LD, Young RF: Radiosurgery for trigeminal neuralgia. Surg Neurol 2000;54: 285–287.
36 Maesawa S, Salame C, Flickinger JC, Pirris S, Kondziolka D, Lunsford LD: Clinical outcomes after stereotactic radiosurgery for idiopathic trigeminal neuralgia. J Neurosurg 2001;94:14–20.
37 Massager N, Lorenzoni J, Devriendt D, Desmedt F, Brotchi J, Levivier M: Gamma knife surgery for idiopathic trigeminal neuralgia performed using a far-anterior cisternal target and a high dose of radiation. J Neurosurg 2004;100:597–605.
38 Mehta V, Meier R, Gilrein J, Vermeulen S, Young R: Gamma knife radiosurgery for treatment of trigeminal neuralgia. Int J Radiat Oncol Biol Phys 2003;57(suppl 2):136.
39 Nicol B, Regine WF, Courtney C, Meigooni A, Sanders M, Young B: Gamma knife radiosurgery using 90 Gy for trigeminal neuralgia. J Neurosurg 2000;93(suppl 3):152–154.
40 Petit JH, Herman JM, Nagda S, DiBiase SJ, Chin LS: Radiosurgical treatment of trigeminal neuralgia: evaluating quality of life and treatment outcomes. Int J Radiat Oncol Biol Phys 2003;56:1147–1153.
41 Pollock BE, Phuong LK, Gorman DA, Foote RL, Stafford SL: Stereotactic radiosurgery for idiopathic trigeminal neuralgia. J Neurosurg 2002;97:347–353.
42 Pollock BE, Phuong LK, Foote RL, Stafford SL, Gorman DA: High-dose trigeminal neuralgia radiosurgery associated with increased risk of trigeminal nerve dysfunction. Neurosurgery 2001;49:58–62.
43 Rand RW: Leksell Gamma Knife treatment of tic douloureux. Neurosurg Clin N Am 1997;8:75–78.
44 Romanelli P, Heit G, Chang SD, Martin D, Pham C, Adler J: Cyberknife radiosurgery for trigeminal neuralgia. Stereotact Funct Neurosurg 2003;81:105–109.
45 Smith ZA, de Salles AA, Frighetto L, Goss B, Lee SP, Selch M, Wallace RE, Cabatan-Awang C, Solberg T: Dedicated linear accelerator radiosurgery for the treatment of trigeminal neuralgia. J Neurosurg 2003;99: 511–516.
46 Urgosik D, Liscak R, Novotny J Jr, Vymazal J, Vladyka V: Treatment of essential trigeminal neuralgia with Gamma-knife radiosurgery. J Neurosurg 2005;102(suppl):29–33.
47 Young RF, Vermeulen SS, Grimm P, Blasko J, Posewitz A: Gamma knife radiosurgery for treatment of trigeminal neuralgia: idiopathic and tumor related. Neurology 1996;48: 608–614.
48 Young RF: Functional neurosurgery with the Leksell Gamma knife. Stereotact Funct Neurosurg 1996;66:19–23.
49 Brisman R: Gamma knife surgery with a dose of 75 to 76.8 Gy for trigeminal neuralgia. J Neurosurg 2004;100:848–854.
50 Regis J, Metellus P, Hayashi M, Roussel P, Donnet A, Bille-Turc F: Prospective controlled trial of gamma knife surgery for essential trigeminal neuralgia. J Neurosurg 2006;104:913–924.
51 Little AS, Shetter AG, Shetter ME, Bay C, Rogers CL: Long-term pain response and quality of life in patients with typical neuralgia treated with gamma knife stereotactic radiosurgery. Neurosurgery 2008;63:915–923, discussion 923–924.
52 Fariselli L, Marras C, de Santis M, Marchetti M, Milanesi I, Broggi G: CyberKnife radiosurgery as a first treatment for idiopathic trigeminal neuralgia. Neurosurgery 2009; 64(suppl):A96–A101.
53 Massager N, Murata N, Tamura M, Devriendt D, Levivier M, Regis J: Influence of nerve irradiation dose in the incidence of trigeminal dysfunction after trigeminal neuralgia radiosurgery. Neurosurgery 2007;60: 681–687, discussion 687–688.
54 Shetter AG, Roger CL, Pomce F, Fiedler JA, Smith K, Speiser BL: Gamma knife radiosurgery for recurrent trigeminal neuralgia. J Neurosurg 2002;97:536–538.
55 Urgosik D, Vymazal J, Vladyka V, Liscak R: Gamma knife treatment of trigeminal neuralgia: clinical and electrophysiological study. Stereotact Funct Neurosurg 1998; 70(suppl 1):200–209.
56 Alpert TE, Chung CT, Mitchell LT, Hodge CJ, Montgomery CT, Bogart JA, Kim DY, Bassano DA, Hahn SS: Gamma knife surgery for trigeminal neuralgia: improved initial response with two isocenters and increasing dose. J Neurosurg 2005;102(suppl):185–188.