

ORIGINAL ARTICLE

Outcome of radiosurgery treatment with a linear accelerator in patients with trigeminal neuralgia[☆]



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KEYWORDS

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Radiosurgery;
Linear accelerator;
Typical pain;
Neurosurgery;
Facial numbness

Abstract

Introduction: An overview of the effectiveness of radiosurgery in patients diagnosed with trigeminal neuralgia with an analysis of potential predictors of good outcome.

Methods: All patients treated with linear accelerator radiosurgery between 2004 and 2011 were analysed. A dose of 60 Gy dose was administered 1 to 2 mm from the root entry zone with a maximum isodose of 20% delivered to the brainstem. Clinical results for pain control and any side effects were analysed at 12 and 36 months (BNI score).

Results: The study included 71 patients (mean follow-up 50.5 months). Pain improvement at 12 months was observed in 68.11% of the total (28.98% with BNI score I–II; 39.12% with BNI score III) and at 36 months in 58.21% (23.88% BNI score I–II; 34.32% BNI score III). Average recovery time was 3.69 months and the relapse rate was 44.68%. Patients with typical pain displayed statistically significant differences in improvement rates at 12 and at 36 months ($P < .047$ and $P < .002$). Onset of improvement was analysed using Kaplan–Meyer plots. Statistically significant differences were observed between patients with typical and atypical pain at 36 months ($P < .012$) in Kaplan–Meyer plots. Side effects were recorded in 15 patients (20.89%), including 9 cases of facial numbness (13.43%); only 2 cases were clinically relevant (2.98%).

Conclusion: According to our results, radiosurgery is an effective treatment for trigeminal neuralgia, with few side effects. Typical pain seems to be a good predictor of pain relief.

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PALABRAS CLAVE

Neuralgia del trigémino;
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Dolor típico;
Neurocirugía;
Adormecimiento facial

Resultados de la aplicación de radiocirugía con acelerador lineal en pacientes con neuralgia del trigémino**Resumen**

Introducción: Comprobación de la efectividad de la radiocirugía en pacientes diagnosticados de neuralgia del V par y análisis de posibles factores predictores.

Métodos: Se analizaron todos los pacientes entre 2004 y 2011 tratados mediante radiocirugía con acelerador lineal. Se administraron dosis de 60 Gy a 1-2 mm de la entrada del nervio con isodosis de 20% máxima sobre el tronco. Se analizaron los resultados clínicos de control del dolor y efectos secundarios a los 12 y 36 meses (escala BNI).

Resultados: Se incluyó a 71 pacientes en el estudio (seguimiento medio 50,50 m). La mejoría del dolor a los 12 meses fue del 68,11% (28,98% BNI score I-II; 39,12% BNI score III) y a los 36 meses del 58,21% (23,88% BNI score I-II; 34,32% BNI score III). El tiempo medio de mejoría fue de 3,69 meses y la tasa de reincidencia tras mejoría del 44,68%. Se aprecian diferencias estadísticas en la mejoría para pacientes con dolores típicos a los 12 y 36 meses ($p < 0,047$ y $p < 0,002$). Se analiza el inicio de la mejoría mediante gráficas de Kaplan-Meier. En el análisis en función de variables se obtuvo diferencia estadísticamente significativa entre dolores típicos y atípicos a los 36 meses ($p < 0,012$). En 15 pacientes se registraron efectos secundarios (20,89%), 9 de ellos por adormecimiento facial (13,43%) y solo 2 con relevancia clínica (2,98%).

Conclusiones: De acuerdo con nuestra experiencia, la radiocirugía es un tratamiento eficaz de la neuralgia del trigémino, con escasos efectos secundarios. El dolor típico parece un factor de buen pronóstico para la mejoría del dolor.

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Introduction

Trigeminal neuralgia was described as a clinical entity as early as in ancient Greece. It is characterised by chronic unilateral paroxysmal pain extending to one or more branches of the trigeminal nerve. However, a few clinical variants of this condition are currently classified as classical trigeminal neuralgia with concomitant persistent facial pain.¹ Different aetiologies have been described, including compression: in the classic study by Hardy et al., compression was responsible for trigeminal neuralgia in 50% of the studied nerves.² In trigeminal neuralgia, compression is mainly vascular (especially involving the superior cerebellar artery, although it can also be caused by a persistent primitive trigeminal artery or basilar dolichoectasia). Trigeminal neuralgia has also been associated with multiple sclerosis (MS) and presence of demyelinating plaques in the nerve root entry zone (REZ).³ However, in most cases the cause is undetermined; trigeminal neuralgia is therefore considered to be mainly idiopathic.

Many treatment approaches have been developed throughout history. Pharmacological treatment is the main approach, and it achieves good outcomes in most patients. However, approximately 25% of the patients do not respond to treatment or show poor tolerance. There are several treatment options for these patients, including microvascular decompression (MVD), thermocoagulation (THC), chemical ablation with glycerol rhizotomy (GR), balloon compression, and radiosurgery; success rates differ among treatments.⁴ Radiosurgery, introduced by Leksell in 1951, is a procedure with minimal complications and very little mortality which has emerged as one of the best treatment options for elderly patients and those who are not eligible

for surgery. In addition, it has proved exceptionally effective for trigeminal neuralgia.

This study presents a series of patients with trigeminal neuralgia who underwent radiosurgery with a linear accelerator (LINAC) in our centre. We performed a statistical analysis of treatment outcomes according to different variables (typical pain patterns, previous treatment, etc.). Our results are presented as survival curves.

Patients and methods**Patient characteristics**

Between 2004 and 2011, 71 patients with trigeminal neuralgia were treated in the radiosurgery unit at Hospital Virgen de las Nieves in Granada. All patients included in our study underwent a single session of radiosurgery. Based on our hospital's treatment protocol for trigeminal neuralgia, all patients were assessed by the neurology department (11 patients came from other centres since our hospital is a reference centre for radiosurgery). Patients were diagnosed with trigeminal neuralgia according to the criteria of the International Classification of Headache Disorders.⁵ They initiated progressive pharmacological treatment (each patient received a mean of 3.8 drugs) and underwent complementary tests. The patients with relevant MRI findings and those cases refractory to pharmacological treatment were referred to our department to evaluate potential treatment options (Fig. 1). Patients who were eligible for radiosurgery were informed about the procedure and signed informed consent forms before being added to the waiting list.

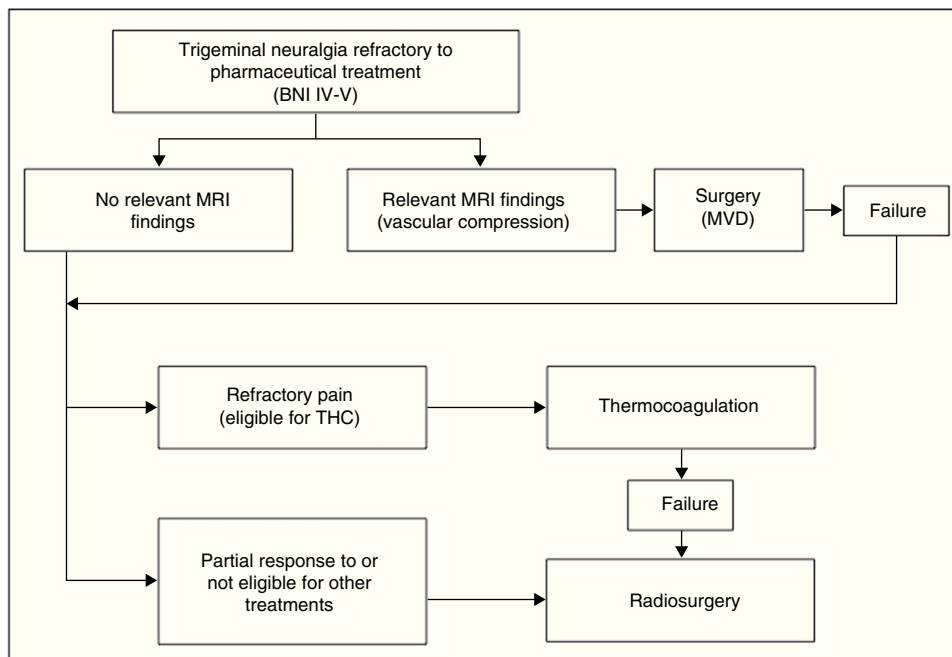


Figure 1 Protocol applied in the neurosurgery department at Hospital Virgen de las Nieves for treating trigeminal neuralgia.

We recorded different clinical and demographic variables for our patient sample. Patients were classified in 3 age groups: younger than 55, 55 to 70, and older than 70. Four patients had a previous diagnosis of MS. We classified patients by pain characteristics. Patients with recurrent paroxysmal attacks of unilateral facial pain, trigger points, no motor or sensory alterations, and a response to pharmacological treatment at some point were considered to have 'typical pain characteristics'. We subsequently classified these patients in 2 groups: patients who had undergone surgery previously and patients who had only received pharmacological treatment. We performed brain FIESTA MRI scans on all patients to rule out structural lesions. One patient had a meningioma in a region not related to pain (this patient was also treated with radiosurgery); another patient had an arachnoid cyst with no pathological relevance. One of the patients had bilateral pain; each side was treated in different sessions.

Characteristics of radiosurgery

Surgeries were planned by a multidisciplinary team including oncologists, radiotherapists, physicists, radiologists, and neurosurgeons. Radiosurgery was performed with a 6 MeV linear accelerator using Brainlab software. MR images were acquired and fused to CT slices, which were acquired using a stereotactic frame. We used 3-mm or 5-mm circular collimators, depending on the case. Our protocol established a maximum dose of 60 Gy centred at 1 or 2 mm from the REZ and using 3 to 6 arcs (Fig. 2).

Follow-up

After radiosurgery, patients underwent a series of follow-up MRI scans at 3, 6, and 12 months. Follow-up visits after

the 12-month mark were scheduled on a yearly basis. The Barrow Neurological Institute (BNI) pain intensity scale was administered at 1 and 3 years (Fig. 3).⁶ Scores I and II on the BNI scale were grouped together since patients may have difficulties differentiating them. Scores I–II and III were considered to indicate treatment success whereas categories IV and V indicated treatment failure. Recourse to additional treatment for pain during the follow-up period was regarded as radiosurgery failure. During follow-up visits, we recorded onset of symptom improvement and worsening after the initial improvement, when applicable. We also gathered data about complications and secondary effects at all follow-up visits.

Statistical analysis

We performed frequency analyses for all variables. We subsequently compared means applying ANOVA for the variables sex, age group, history of MS, typical pain, previous treatments, and secondary effects broken down by treatment success at 12 and 36 months. The McNemar-Bowker test was used to compare changes in results. Data on improvement over time were plotted as Kaplan–Meier curves. We conducted a statistical analysis of improvements at both follow-up times by sex, age group, previous treatments, and typical pain using the Mantel–Cox test. *P*-values < .05 were considered to be statistically significant. Statistical analysis was conducted using SPSS statistical software version 20.0.

Results

During the study period we identified 71 patients. Four patients (5.63%) were lost to follow-up (2 patients before 12

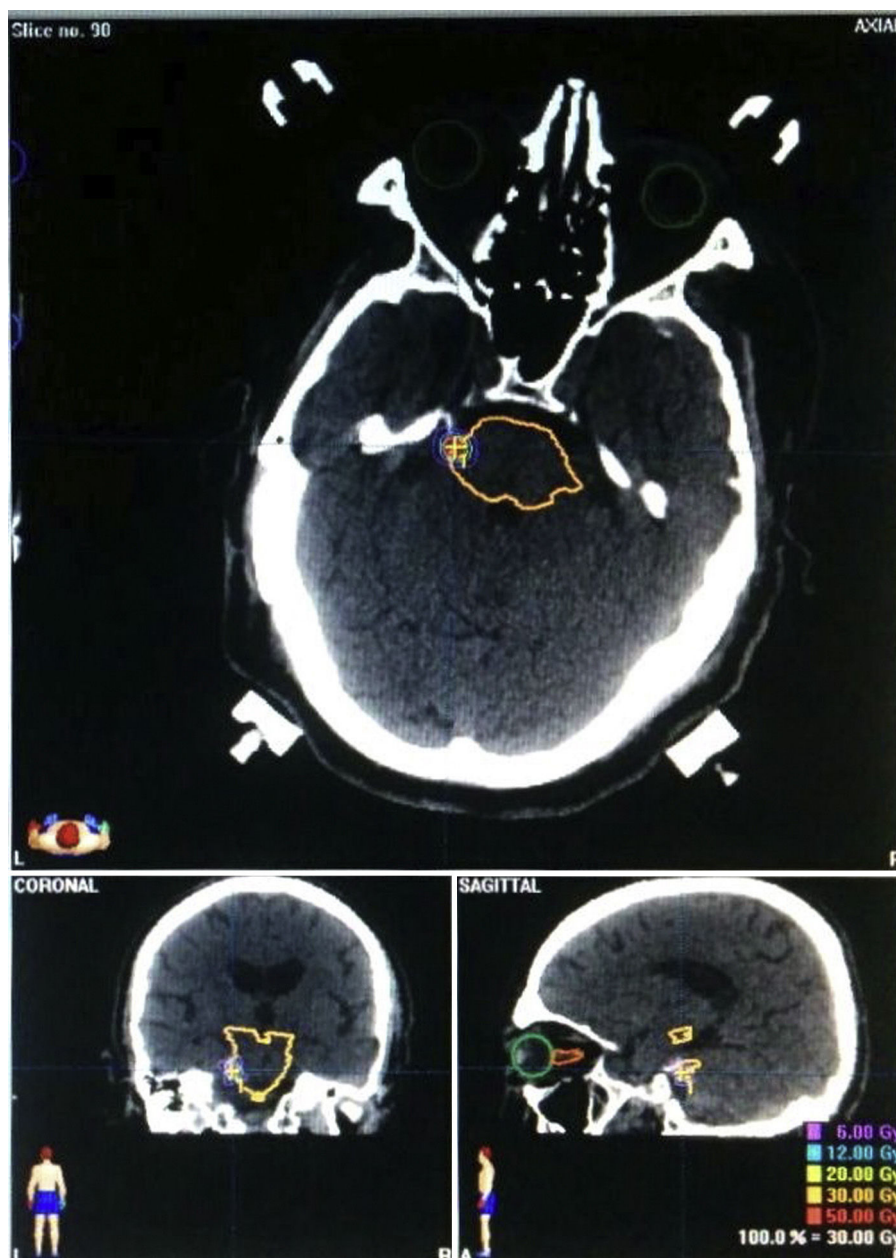


Figure 2 Example of radiosurgery planning with Brainlab® software, using CT images and stereotactic localisation. The target was located 1 to 2 mm from the trigeminal RExZ.

months and 2 before 36 months), including 2 deaths unrelated to treatment. Fourteen patients (20.3%) were younger than 55, 28 (40.6%) were between 55 and 70, and 27 (39.1%) were older than 70. We conducted a descriptive study of frequencies by the variables pain type and previous treatments and recorded demographic data and treatment outcomes at 12 and 36 months using the BNI scale (Table 1). Mean follow-up time was 50.5 months (range, 8–84 months, median = 49). Mean time to onset of symptom improvement was 3.69 months (range, 0.25–32 months, median = 1.5 months). Twenty-one (44.68%) of the patients showing improvements experienced subsequent exacerbations. Mean time to

symptom exacerbation was 14.07 months (range, 0.5–52 months, median = 8).

At 12 months, treatment was successful in 47 patients (68.11%) and had failed in 22 (31.88%). Treatment success was achieved by 37 of the 48 patients (77.08%) with typical pain and 10 of the 21 patients (47.61%) with atypical pain. At 36 months, 39 patients achieved treatment success (58.21%) whereas treatment failed in 28 patients (41.78%). Treatment succeeded in 25 of the 47 patients (53.19%) with typical pain and 6 of the 20 patients (30%) with atypical pain.

We then used ANOVA to analyse the differences between means for the variables sex, age group, history of MS, and

Table 1 Distribution of demographic and outcome data by pain type and type of previous treatment (BNI pain intensity scale).

	Typical pain: 48 (67.6%)		Atypical pain: 23 (32.4%)	
	Previous drug treatment	Previous surgical treatment	Previous drug treatment	Previous surgical treatment
	35 (49.29)	13 (18.3)	12 (16.9)	11 (15.49)
Sex (M, F), n (%)	19 (26.76)	3 (4.22)	3 (4.22)	3 (4.22)
	16 (22.53)	10 (14.08)	9 (12.67)	8 (11.26)
Age (y), mean (range)	64.32 (35–81)	68.3 (55–81)	51 (22–73)	63.45 (15–87)
Disease progression (m)	85.2 (6–240)	103 (12–240)	63.77 (8–192)	78.3 (12–156)
P50	60	120	36	72
Previous treatment, n (%)				
THC		4 (5.63)		4 (5.63)
Infiltrations		6 (8.45)		3 (4.22)
MVD		2 (3.81)		4 (5.63)
GR		1 (1.4)		0 (0)
Branch, n (%)				
V1	4 (5.63)	0 (0)	0 (0)	0 (0)
V2	8 (11.26)	2 (3.81)	1 (1.4)	5 (7.04)
V3	10 (14.08)	7 (9.85)	5 (7.04)	2 (3.81)
2 branches	12 (16.9)	4 (5.63)	3 (4.22)	1 (1.4)
All branches	1 (1.4)	0 (0)	1 (1.4)	2 (3.81)
Follow-up (m), mean (range)	53 (35–82)	51.23 (34–70)	46.5 (17–84)	46.27 (8–69)
Outcome at 12 m				
I–II	12 (17.3)	4 (5.79)	2 (2.89)	2 (2.89)
III	13 (18.8)	8 (11.59)	4 (5.79)	2 (2.89)
IV	8 (11.59)	1 (1.44)	4 (5.79)	5 (7.24)
IV	2 (2.89)	0 (0)	1 (1.44)	1 (1.44)
Outcome at 36 m				
I–II	12 (17.91)	4 (5.97)	0 (0)	0 (0)
III	13 (19.4)	4 (5.97)	3 (4.47)	3 (4.47)
IV	2 (2.98)	1 (1.49)	5 (7.46)	2 (2.98)
V	8 (11.94)	3 (4.47)	2 (2.98)	5 (7.46)

M: male; F: female; y: years; m: months; n: number; THC: thermocoagulation; MVD: microvascular decompression; GR: glycerol rhizotomy.

BNI pain intensity scale	
Score	Pain description
I	No pain, no medications
II	Occasional pain, no medications required
III	Some pain, adequately controlled with medications
IIIa	No pain, continued medication
IIIb	Persistent pain, controlled with medication
IV	Some pain, not adequately controlled with medications
V	Severe pain or no pain relief

Figure 3 Barrow Neurological Institute (BNI) pain intensity scale to assess the level of pain in patients with trigeminal neuralgia. BNI values I–III were considered to indicate good outcomes whereas BNI values IV and V indicate poor response to treatment.

previous treatments as a function of treatment success at 12 and 36 months. No statistically significant differences were found except for the variable typical pain, both at 12 months ($P < .047$) and at 36 months ($P < .002$). We also conducted a statistical analysis of changes in the variables treatment

outcome at 12 and 36 months using the McNemar-Bowker test; differences were statistically significant ($P < .016$).

Lastly, we represented the time when symptoms began to improve in each patient, both at 12 and at 36 months, as Kaplan–Meier curves (Fig. 4). We then compared Kaplan–Meier curves at 12 and 36 months adjusted by sex, age group, previous treatments, secondary effects, and typical pain using the Mantel–Cox test. Differences were statistically significant only for the variable typical pain at 36 months ($P < .012$).

Complications were registered during subsequent follow-up visits. One patient exhibited radiation necrosis, which was managed successfully with conservative treatment; response to treatment in this patient was categorised as III on the BNI pain intensity scale. One patient experienced anaesthesia dolorosa after treatment and another displayed abolished corneal reflexes. Two patients developed dysaesthesia, one had dry eye syndrome, and another exhibited dry eye syndrome plus facial numbness. Nine patients, including the latter, experienced facial hypoaesthesia (13.43%), although their symptoms did not have a substantial impact on daily life. A total of 15 patients (20.89%) experienced complications. We used ANOVA to analyse differences in treatment outcomes at 12 and 36 months between patients who experienced secondary effects and those who did

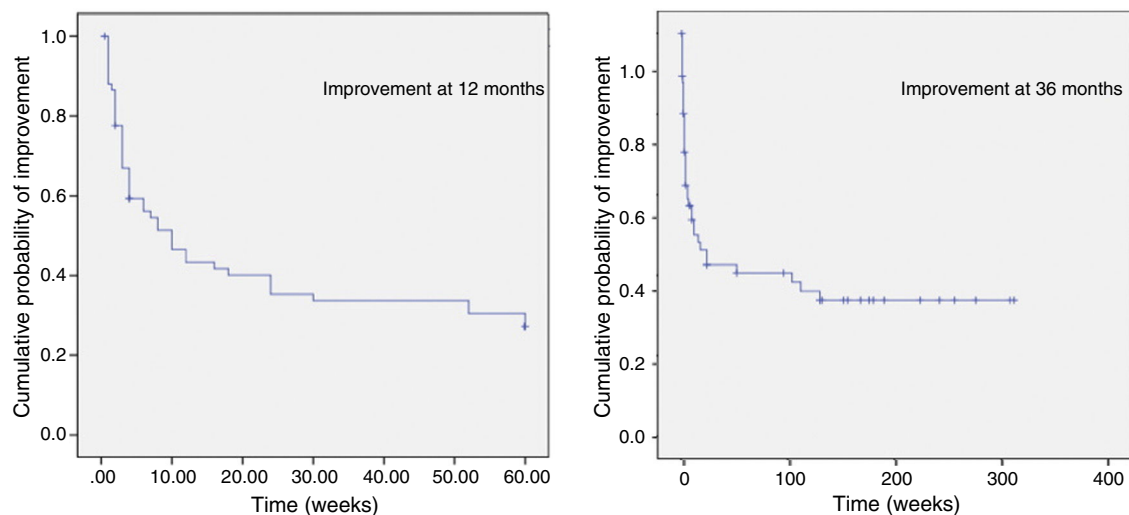


Figure 4 Kaplan–Meier curves showing onset of pain relief at 12 (left) and 36 months (right).

not; differences were not significant ($P < .505$ and $P < .519$, respectively).

Discussion

Radiosurgery for patients with trigeminal neuralgia is now a safe alternative to conventional surgical treatments. Currently available treatment options show little differences between success rates. MVD remains the gold standard treatment, especially for young patients, and it has a low rate of complications.⁴ The main advantages of surgery over radiosurgery are the immediacy of results, lower recurrence rates, and less probability of experiencing facial numbness.^{7–9} Such other invasive techniques as radiofrequency THC, balloon compression, and GR are associated with low rates of perioperative complications. However, radiosurgery has an even lower complication rate since it is performed in a single day. In addition, this treatment option is suitable for virtually all patients since it does not require sedation or general anaesthesia.^{9,10} In any case, radiosurgery is still considered a second-line treatment, for use in patients who are not eligible for surgery. In our centre, which implemented the protocol described above several years ago, surgery is the first treatment choice for patients displaying relevant MRI findings. However, trends are changing since patients are showing increasing interest in less invasive techniques. This tendency has also been observed by other authors^{7,8} and it affects the results reported in the literature: the effectiveness of radiosurgery has risen to become very similar to that of surgery. This phenomenon may be explained by the fact that patients initially selected for radiosurgery were considered to be more treatment-resistant: they were normally elderly, had received one or more treatments before radiosurgery, and displayed more severe MRI features.¹¹ It is a well-known fact that patients who have received no previous treatments, especially MVD, are now more likely to achieve better pain relief after radiosurgery.^{12–15}

Another interesting debate revolves around the ideal target area and dose of radiation used in radiosurgery. The preliminary studies by Pollock et al.¹⁶ established a direct relation between improvements in pain management and contrast uptake in the REZ, which led many researchers to use the REZ as their target. However, other researchers continue to target the retrogasserian cisternal portion of the trigeminal nerve.¹⁷ No definitive conclusion has been reached about which target is better for radiosurgery.¹⁸ Differences in the effectiveness of Gamma Knife, Cyberknife, and LINAC are not significant. However, some studies claim that the Gamma Knife is more effective for small targets¹⁹ but LINAC is more cost-effective in terms of initial investment and maintenance costs²⁰ since it can be used for other treatments, as in our case. Determining the dose of radiation is equally important. The mechanism by which radiation acts on the nerve is still a source of debate. Some authors, including Régis et al.,¹⁴ state that radiosurgery has the ability to select the nerve fibres that cause pain while sparing the fibres responsible for facial sensitivity. In contrast, Kondziolka et al.²¹ conducted a histological study of primate brains to determine the effect of radiation on nerves, and found axonal degeneration and oedema at the target after applying doses between 80 and 100 Gy on the trigeminal nerve. According to other authors, such as Massager et al.,²² the most important factor is the dose of radiation delivered to the nerve root rather than the maximum dose. As a general rule, 100 Gy is considered the maximum dose due to the associated risk of necrosis; most studies apply doses between 70 and 90 Gy. There is a widespread belief that doses between 85 and 90 Gy are optimal^{23,24}; however, numerous studies have failed to find a significant difference between doses of 90 Gy and 70 Gy.^{14,15} Other review articles suggest that the best target is located 2 to 4 mm from the REZ.²⁵ In our series, we used a target located 1 to 2 mm from the REZ and applied a dose of 60 Gy, which is significantly lower than those applied in published series. However, our results are similar to those reported by other researchers in terms of overall pain relief and pain relief without medication. In our sample, pain relief was achieved

Table 2 Summary of the main studies of radiotherapy conducted recently.

Author	Dose (Gy)	<i>n</i>	Initial imp. (%)	Imp. during follow-up (%)	SE	Comments
Han et al. ²⁸ (2009)	75–80	62	90	45.8	—	Relapses: 52%
Kondziolka et al. ¹² (2010)	80	503	85	56 29 ^a	10.5	Relapses: 43%
Park et al. ¹⁸ (2010)	50–90	119	87	57	21	Retreatment
Smith et al. ²³ (2011)	70–90	169	79	60.3	49.7 ^b	
Hayashi et al. ⁷ (2011)	90	130	80	66 ^a	24 ^b 12 ^c	Relapses: 18%
Fraioli et al. ¹⁷ (2012)	40	45	97.78	20	8.7 ^b	Used RT/HSRT
Li et al. ²⁷ (2012)	80–90	114	95.6	87.7	42.98 ^b	
Young et al. ²⁴ (2013)	90	315	89.5	43.7 ^a	34.8 ^b 17.3 ^c	
Aykol et al. ³² (2015)	70–90	93	78.8	58	68.8 ^b	
Cordero et al. (2015)	60	71	68.11 28.98 ^a	58.11 23.88 ^a	20.89 ^b 2.98 ^c	

^a Pain-free without medication.

^b Non-disturbing side effects.

^c Uncomfortable side effects.

SE: side effects; imp.: improvements; *n*: number of patients; RS: radiosurgery; HSRT: hypofractionated stereotactic radiotherapy.

in 68.11% (BNI I–II: 28.98%; III: 39.12%) of the patients at 12 months and 58.21% (BNI I–II: 23.88%; III: 34.32%) at 36 months. In a recent study including 503 patients, Kondziolka et al.¹² applied a dose of 80 Gy, with a maximum dose of 16 Gy on the pons, and achieved pain relief in 85% of the patients (BNI I–II) just after the procedure and in 56% in the long term (mean follow-up time of 6 years); 29% of the patients required no medication. Park et al.²⁶ administered doses between 50 and 90 Gy to a series of patients and monitored them for more than 15 years on average, achieving pain relief in 57% of the sample (BNI I–III). Young et al.²⁴ treated a series of 315 patients with a maximum dose of 90 Gy and 18 Gy on the pontine surface (20% isodose line), and achieved pain relief in 89.5% of the patients; 43.7% of the patients were pain-free without medication. It should be noted, however, that 21% of the patients in this study were lost to follow up. Li et al.²⁷ conducted a study in a sample of 114 patients. Using 2 isocentres and doses between 80 and 90 Gy, the authors achieved initial pain relief in 95% of the sample (BNI I–III). However, the follow-up period in this study was shorter. Smith et al.²³ used a LINAC to treat 169 patients with doses between 70 and 90 Gy; pain relief was achieved in 79% of the sample after completing the procedure, and in 60.3% after follow-up. In summary, the results of these studies do not differ substantially from ours considering that our sample size was smaller but follow-up was very thorough (Table 2). Pain recurrence after initial relief has also been reported in other studies. In the study by Han et al.,²⁸ although 90% of the patients achieved initial pain relief, 52% of them experienced pain recurrence (appearing at 2–56 months). For this reason, many patients opt for additional radiosurgery sessions, with success rates above 50%.²⁹ A similar phenomenon was observed in our series: pain reappeared in 44.68% of the patients. This is probably due to the partial effects of radiation on the nerve, or to reinnervation processes.

The topic of maximum dose inevitably leads us to reflect on the complications of radiosurgery. The most frequent

complications are facial hyperaesthesia and hypoaesthesia, affecting between 7% and 49% of the patients in the published series.^{8–10,12,13,15,17,18,27,30–32} The percentage increases considerably when the procedure is repeated.^{29,33–35} It seems logical to think that the frequency of facial numbness would be dose-dependent and although several studies supporting this idea have been published,^{16,22,30} other studies have also refuted it.^{10,12,33} There is controversy regarding whether facial numbness should be considered a true complication or rather an effect of the treatment since it rarely affects the patient's activities of daily living. However, other complications involving facial discomfort (dysaesthesia, hyperaesthesia, burning, etc.) may have a negative impact on daily living, especially when they affect the oral mucosa. In a series of 130 patients treated with 90 Gy, Hayashi et al.⁷ reported pain relief in 80% of the sample, with 60% of patients remaining pain-free without medication. However, complications appeared in 24% of the patients, and discomfort in 12%. Young et al.²⁴ also applied doses between 70 and 90 Gy, achieving pain relief in 89.5% of the patients (43.7% patients were pain-free without medication); however, 17.3% of the patients experienced severe or extreme discomfort. In the study by Aykol et al.,³² 78.8% of the patients achieved pain relief after the procedure and 58% maintained pain relief during follow-up. There was also a statistically significant correlation between dysaesthesia and good outcome. These data suggest that greater doses result in better outcomes, although these are accompanied by increasing complications, especially those causing discomfort. However, according to Fraioli et al.¹⁷ these results can be achieved with a much lower dose (40 Gy) if radiation is delivered to the retrogasserian cisternal portion of the trigeminal nerve. In light of the above, doses applied in our hospital are lower than normal, which results in very low rates of severe complications: only 2 patients in our sample (2.98%) developed dysaesthesia affecting daily living (Table 2). In addition, and considering all the complications in general, no significant correlations were found between

complications and pain relief either after the procedure or during follow-up.

A number of factors may be linked to better responses to radiosurgery treatment. These include younger age,^{12,14,28} pain in a single branch of the trigeminal nerve,⁷ pain on the right side,¹⁰ and smaller size of the trigeminal cistern.¹⁴ No history of surgery is considered an indicator of good prognosis^{12–15,24}; for some authors, having undergone surgery on fewer occasions before radiosurgery is also an indicator of good outcome.^{10,12} We observed this tendency in our sample, although it was not statistically significant. Other factors, such as MS,¹⁵ have been associated with poor outcome. Although our sample included some patients with MS, numbers were not high enough to draw conclusions. Another factor potentially affecting outcomes is whether or not trigeminal pain has typical features. Some studies have reported good response to radiosurgery in patients with paroxysmal remitting unilateral pain with typical characteristics and trigger points.¹⁵ In the study by Kondziolka et al.,¹² patients with atypical pain were found to respond to radiosurgery but they were significantly more likely to experience relapses. Smith et al.²³ observed that improvement rates were lower in patients with atypical pain (27.3%). However, other authors have found no significant associations between pain features and response to treatment.^{11,36} In our series, we found a statistically significant correlation between pain relief and typical pain, both after the procedure and at 36 months. In our view, this finding reflects patients' characteristics and previous treatments: patients with atypical pain have usually received several treatments before radiosurgery since atypical pain tends to be more treatment-resistant. As other authors have proposed, studies featuring longer follow-up periods are needed to validate treatment.^{4,21,22}

Conclusions

Radiosurgery is seeing increasing use in trigeminal neuralgia. It is currently considered a good option as a second-line treatment due to its high success rates and low rate of associated complications. Radiosurgery achieves good rates of pain relief, especially just after the procedure; a high percentage of patients undergoing this treatment will remain pain-free without medication. Several factors, such as whether or not pain is typical, seem to be associated with better outcomes. Studies with longer follow-up periods should be conducted to determine the predictors of good outcome in radiosurgery.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33:629–808.
2. Hardy DG, Rhoton AL. Microsurgical relationships of the superior cerebellar artery and the trigeminal nerve. *J Neurosurg*. 1978;49:669–78.
3. Woolfall P, Coulthard A. Trigeminal nerve: anatomy and pathology. *Br J Radiol*. 2001;74:458–67.
4. Varela-Lema L, López-García M, Maceira-Rozas M, Muñoz-Garzón V. Linear accelerator stereotactic radiosurgery for trigeminal neuralgia. *Pain Physician*. 2015;18:15–27.
5. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia*. 2004;24 Suppl 1:9–160.
6. Rogers C, Shetter AG, Fiedler JA, Smith KA, Han PP, Speiser BL. Gamma Knife radiosurgery for trigeminal neuralgia: the initial experience of de Barrow Neurological Institute. *Int J Radiat Oncol*. 2000;47:1013–9.
7. Hayashi M, Chernov M, Tamura N, Taira T, Izawa M, Yomo S, et al. Stereotactic radiosurgery of essential trigeminal neuralgia using Leksell Gamma Knife model C with automatic positioning system: technical nuances and evaluation of outcome in 130 patients with at least 2 years follow-up after treatment. *Neurosurg Rev*. 2011;34:497–508.
8. Pollock BE, Schoeberl KA. Prospective comparison of posterior fossa exploration and stereotactic radiosurgery dorsal root entry zone target as primary surgery for patients with idiopathic trigeminal neuralgia. *Neurosurgery*. 2010;67:633–9.
9. Tatli M, Satici O, Kanpolat Y, Sindou M. Various surgical modalities for trigeminal neuralgia: literature study of respective long-term outcomes. *Acta Neurochir*. 2008;50:243–55.
10. Kano H, Kondziolka D, Yang HC, Zorro O, Lobato-Polo J, Flannery TJ, et al. Outcome predictors after gamma knife radiosurgery for recurrent trigeminal neuralgia. *Neurosurgery*. 2010;67:1637–45.
11. Dos Santos MA, Pérez de Salcedo JB, Gutiérrez Díaz JA, Nagore G, Calvo FA, Samblás J, et al. Outcome for patients with essential trigeminal neuralgia treated with linear accelerator stereotactic radiosurgery. *Stereot Funct Neuros*. 2011;89:220–5.
12. 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*. 2010;112:758–65.
13. Pan HC, Sheehan J, Huang CF, Sheu L, Yang DY, Chiu WT. Quality-of-life outcomes after gamma knife surgery for trigeminal neuralgia. *J Neurosurg*. 2010;113:191–8.
14. Régis 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;104:913–24.
15. Verheul JB, Hanssens PEJ, Lie ST, Leenstra S, Piersma H, Beute GN. Gamma knife surgery for trigeminal neuralgia: a review of 450 consecutive cases. *J Neurosurg*. 2010;113:160–7.
16. Pollock BE, Phuong LK, Gorman DA, Foote R, Stafford S. Stereotactic radiosurgery for idiopathic trigeminal neuralgia. *J Neurosurg*. 2002;97:347–53.
17. Fraioli MF, Strigari L, Fraioli C, Lecce M, Lisciani D. Preliminary results of 45 patients with trigeminal neuralgia treated with radiosurgery compared to hypofractionated stereotactic radiotherapy, using a dedicated linear accelerator. *J Clin Neurosci*. 2012;19:1401–3.
18. Park SH, Hwang SK, Kang DH, Park J, Hwang JH, Sung JK. The retrogasserian zone versus dorsal root entry zone: comparison of two targeting techniques of gamma knife radiosurgery for trigeminal neuralgia. *Acta Neurochir*. 2010;152:1165–70.
19. Mindermann T. Erratum to: Gamma Knife, CyberKnife or multileaf collimator LINAC for intracranial radiosurgery? *Acta Neurochir*. 2015;157:567.
20. Gamma Knife surgery compared with Linac based radiosurgery systems in the treatment of intracranial lesions or tumours and functional neurosurgery: a review of the precision, accuracy, clinical effectiveness, cost-effectiveness, and guidelines

- Internet. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2014 [actualizado 11 Mar 2014], [accessed 1 Abr 2015]. Available from: www.cadth.ca.
21. Kondziolka D, Lacomis D, Niranjan A, Mori Y, Maesawa S, Fellows W, et al. Histological effects of trigeminal nerve radiosurgery in a primate model: implications for trigeminal neuralgia radiosurgery. *Neurosurgery*. 2000;46:971–7.
 22. Massager N, Nissim O, Murata N, Devriendt D, Desmedt F, Vandertinden B, et al. Effect of beam channel plugging on the outcome of gamma knife radiosurgery for trigeminal neuralgia. *Int J Radiat Oncol*. 2006;65:1200–5.
 23. Smith ZA, Gorgulho AA, Bezrukiy N, McArthur D, Agazaryan N, Selch MT, et al. Dedicated linear accelerator radiosurgery for trigeminal neuralgia: a single-center experience in 179 patients with varied dose prescriptions and treatment plans. *Int J Radiat Oncol*. 2011;81:225–31.
 24. Young B, Shivazad A, Kryscio RJ, St Clair W, Bush HM. Long-term outcome of high-dose Gamma Knife surgery in treatment of trigeminal neuralgia. *J Neurosurg*. 2013;119:1166–75.
 25. Amutio-Gutiérrez S, Soto-González M. Efectividad del tratamiento con bisturí de rayos gamma en pacientes afectados por la neuralgia del trigémino idiopática recurrente. *Neurología*. 2014;29:327–33.
 26. Park KJ, Kondziolka D, Berkowitz O, Kano H, Novotny J, Niranjan A, et al. Repeat gamma knife radiosurgery for trigeminal neuralgia. *Neurosurgery*. 2012;70:295–305.
 27. Li P, Wang W, Liu Y, Zhong Q, Mao B. Clinical outcomes of 114 patients who underwent gamma-knife radiosurgery for medically refractory idiopathic trigeminal neuralgia. *J Clin Neurosci*. 2012;19:71–4.
 28. Han JH, Kim DG, Chung HT, Paek SH, Kim YH, Kim CY, et al. Long-term outcome of gamma knife radiosurgery for treatment of typical trigeminal neuralgia. *Int J Radiat Oncol*. 2009;75:822–7.
 29. Tempel ZJ, Chivukula S, Monaco EA 3rd, Bowden G, Kano H, Niranjan A, et al. The results of a third Gamma Knife procedure for recurrent trigeminal neuralgia. *J Neurosurg*. 2015;122:169–79.
 30. Matsuda S, Nagano O, Serizawa T, Higuchi Y, Ono J. Trigeminal nerve dysfunction after gamma knife surgery for trigeminal neuralgia: a detailed analysis. *J Neurosurg*. 2010;113 Suppl:184–90.
 31. Riesenburger RI, Hwang SW, Schirmer CM, Zerris V, Wu JK, Mahn K, 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.
 32. Aykol S, Börcek AO, Emmez H, Öcal Ö, Paşaoğlu A. Results of radiosurgery for trigeminal neuralgia: Ankara experience. *Brit J Neurosurg*. 2015;29:54–8.
 33. Huang CF, Shiou SY, Wu MF, Tu HT, Liu WS. Gamma knife surgery for recurrent or residual trigeminal neuralgia after a failed initial procedure. *J Neurosurg*. 2010;113 Suppl:172–7.
 34. Kimball BY, Sorenson JM, Cunningham D. Repeat gamma knife surgery for trigeminal neuralgia: long-term results. *J Neurosurg*. 2010;113 Suppl:178–83.
 35. Tuleasca C, Carron R, Resseguier N, Donnet A, Roussel P, Gaudart J, et al. Repeat Gamma Knife surgery for recurrent trigeminal neuralgia: long-term outcomes and systematic review. *J Neurosurg*. 2014;121:210–21.
 36. Chen JC, Rahimian J, Rahimian R, Arellano A, Miller MJ, Girvigian MR. Frameless image-guided radiosurgery for initial treatment of typical trigeminal neuralgia. *World Neurosurg*. 2010;74:538–43.