

Radiosurgery for trigeminal neuralgia using a linear accelerator with BrainLab[®] system: report on initial experience in Lausanne, Switzerland

Marc Pusztazeri^a, Jean-Guy Villemure^b, Luca Regli^b, Huu-Phuoc Do^c, Alessia Pica^a

^a Department of Radiation Oncology

^b Department of Neurosurgery

^c University Institute of Applied Radiation Physics, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland

Summary

Background/aims: Radiosurgery is an effective treatment for trigeminal neuralgia (TN) with minimal complications. Most experience is based on gamma knife radiosurgery (GKRS) and to a lesser extent on linear accelerators.

Methods: We report our initial experience in 17 patients with TN treated by an adapted linear accelerator using the BrainLab[®] system. The trigeminal root entry zone immediately adjacent to the pons (target volume: 0.01–0.09 cm³, mean: 0.02 cm³) was targeted by use of a multileaf collimator to deliver 40–45 Gy to the 80% isodose (dose max 50–56 Gy). Median follow-up was 12 months (range: 1–60).

Results: All patients reported some initial improvement in level of pain after treatment (mean time: 1 month). Initial pain responses were as follows: 6 patients (35%) had complete pain relief and required no medication, 6 (35%) had occasional pain but were off medication, and 5 (30%)

experienced partial relief of pain but still required medication, usually in lower doses. Five patients (29%) who experienced initial pain relief had recurrences ranging from 4–13 months after procedure. There were no major or minor complications of radiosurgery except one case of mild facial itching.

Conclusion: Stereotactic radiosurgery using a linear accelerator appears to be effective and can be a favourable alternative to other procedures, including GKRS. The procedure is very safe and side effects are rare and minor. However, a randomised trial with a longer follow-up comparing radiosurgery to other surgical procedures is needed to assess the long term effectiveness of this treatment.

Key words: trigeminal neuralgia; radiosurgery; linear accelerator

Introduction

Trigeminal neuralgia (TN) is the best defined and one of the most common causes of facial pain, especially in the elderly. It is described as sudden, usually one-sided, severe, brief, sharp or lancinating, recurrent episodes of spontaneous or stimulation-triggered pain in the territory of one or more branches of the trigeminal nerve [1, 2]. Most cases of TN are caused by compression of the trigeminal nerve root, usually within a few millimeters of entry into the pons, the root entry zone (REZ) [3]. The mechanism by which compression of the nerve causes symptoms appears to be related to demyelination in a circumscribed area around the compression [4, 5]. Precisely how demyelination results in the symptoms of TN is

not entirely clear. Pharmacological therapy is the initial treatment in most patients with TN not caused by a structural lesion (multiple sclerosis or tumour mass). Surgery is confined to patients who are refractory to medical therapy or if the latter causes side effects which prevent its use. A variety of surgical procedures may relieve symptoms in patients with TN refractory to drug therapy. They include microvascular decompression, radiofrequency rhizotomy, glycerol rhizolysis and balloon compression. Microvascular decompression is invasive, although the overall mortality and complication rate are low and the procedure is associated with the best long-term outcome [6]. Rhizotomy is less invasive and associated with a

high initial response rate, but recurrence is common and the incidence of facial numbness is higher than with microvascular decompression.

Stereotactic radiosurgery is a procedure that can be attempted in TN patients if drug therapy and/or surgery fail. In addition, it causes few side effects, the principal being facial numbness. The commonest experience in this field is based on gamma knife radiosurgery (GKRS) [7-16]. Re-

ports on radiosurgery using a linear accelerator (LINAC) in the treatment of TN conclude that treatment with LINAC can be as effective as GKRS [17-23].

To contribute to the data on LINAC treatment for TN we report our initial experience of 17 TN patients treated by dedicated linear accelerator using the BrainLab® system.

Material and methods

Patient profile

From 2000 to 2005, 17 patients with TN were treated in the Radiation Oncology Department of the CHUV, Lausanne, Switzerland. Patient characteristics are shown in table 1. Median age at the time of radiosurgery was 71 years (range: 48-77). In the majority of patients TN had failed to respond to medical therapy, either because the TN was refractory to medication or the patient experienced side effects which precluded the use of the medication. Ten patients (59%) had undergone one or more previous unsuccessful procedures including microvascular decompression, thermal rhizotomy or retrogasserian glycerol rhizolysis. Seven patients underwent radiosurgery as their primary procedure after medical failure.

One patient had documented multiple sclerosis (MS) and one probable MS based on MRI scan. There was one case of atypical TN with neck pain.

Patient preparation and immobilisation

One day before the radiosurgical procedure all patients underwent non-stereotactic 3D inversion-recovery-based T1-weighted (magnetisation-prepared rapid acquisition with gradient-echo [MPRAGE]) magnetic resonance imaging (MRI) with gadolinium contrast enhancement and three-dimensional T2-weighted volume acquisitions divided into 1 mm slices before stereotactic frame placement through the trigeminal nerve root entry zone (REZ). On the day of radiosurgery a BrainLab® stereotactic frame was placed on the patient's head after local infiltration of an anaesthetic agent.

For treatment planning a contrast enhanced treatment planning CT scan was performed with 2.5 mm slice thickness with the stereotactic frame in place.

Treatment planning and delivery

CT and MRI image registration was performed using an image fusion software tool of the stereotactic planning system (BrainSCAN System, BrainLab®). The target volume was the trigeminal root entry zone (REZ), immediately adjacent to the pons, and ranged from 0.01 to 0.09 cm³ (mean: 0.02 cm³). The planning target volume (PTV), mimicking the 6 mm collimator used for the treatment, was placed at the REZ and 50 to 56 Gy were prescribed to isocentre resulting in 40 to 45 Gy to the 80% isodose surface, so that the 30 Gy isodose surface was tangential to the brainstem (fig. 1). One isocentre was used for radiosurgery, which was delivered with an average number of 18 fixed, non-coplanar conformal beams (range: 17-24). Treatments were performed with a 6-MV photon beam provided by a Primus linear accelerator

Table 1

Patients characteristics.

Total Number		17
Age (years)	Median	71
	Range	48-77
Gender	Male	9
	Female	8
Duration of pain (years)	Median	12
	Range	0.5-20
Location of neuralgia	Right	11
	Left	6
	Bilateral	1
Number of dermatomes involved	1 (V1, V2, V3)	7 (1.5.1)
	2 (V1-V2, V2-V3)	6 (3.3)
	3 (V1-V3)	4
Multiple Sclerosis		2*
Prior invasive treatment	Yes	10
	No	7
Type of prior procedure		
Microvascular decompression		6
Thermal rhizotomy		5
Alcoholisation		1
Number of invasive procedure	1	5
	2	3
	3 or more	2
Follow-up (months)	Median	12
	Range	1-60

*: one patient had probable MS based on MRI scan

Figure 1

Axial reconstruction showing target selection at the root entry zone of the fifth cranial nerve.

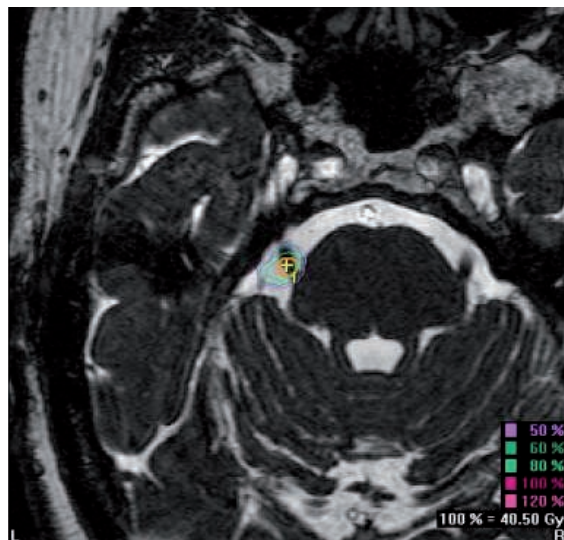


Table 2
Barrow Neurological Institute (BNI) pain intensity score [13].

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

(Siemens), using the BrainLab® system with a micromulti-leaf collimator.

Pain evaluation

Pain before and after radiosurgery was scored according to the Barrow Neurosurgical Institute (BNI) pain intensity scale (table 2) [14]. Before radiosurgery, 6 patients had severe pain or no improvement with medication (BNI score V), 10 patients had some pain not

adequately controlled with medication (BNI score IV), 1 patient had pain adequately controlled with medication (BNI score III) but wished to stop the drugs.

Follow-up

Median follow-up was 12 months (range: 1–60). No patients were lost to follow-up. Patients were usually seen initially 6–12 weeks after treatment by neurosurgeons to evaluate the initial treatment response and complications. If they were pain-free at that time, they were subsequently seen regularly by their general practitioner and/or neurologist. If they were not pain-free and/or still required medication at the first neurosurgical evaluation, they were usually seen again by neurosurgeons to further evaluate the need of medication or of another surgical procedure in the event of treatment failure. MRI was not usually performed for follow-up.

Results

Initial pain relief

All patients reported some initial improvement in the level of pain after treatment. The mean time lapse to pain improvement was one month (range: 2 weeks to 6 months). Initial pain responses were as follows: 6 patients (35%) had complete pain relief and required no medication (BNI score I), 6 (35%) had occasional pain but did not require medication (BNI score II), 5 (30%) had partial relief of pain and still required some medication (BNI score III), usually in lower doses. The degree of initial pain did not influence the pain response rate.

Durability of pain response

The patients' BNI pain scores before and after radiosurgery are summarised in table 3. At last follow-up, 5 patients had BNI score I (median

follow-up 8 months; range 2–60), 2 patients had BNI score II (median follow-up 14 months; range 12–16), 5 patients had BNI score III (median follow-up 21 months; range 1–45). Five patients (29%) with initial pain relief (BNI score I–III) had a recurrence (BNI score IV) 4–13 months after radiosurgery (mean 7 months). Recurrence was defined as an initial improvement followed by deterioration of BNI score. Of the 5 patients with a recurrence, four had undergone one or more previous unsuccessful procedures prior to radiosurgery. They required further treatment, usually consisting of thermal rhizotomy. One of them suffering a recurrence 12 months after radiosurgery underwent thermal rhizotomy 15 months after radiosurgery and was pain-free again 2 months after that procedure.

Table 3
BNI pain score before and after radiosurgery.

Patient no	BNI before treatment	BNI after radiosurgery at 6–12 weeks	BNI after radiosurgery at last follow-up	Follow-up (months)
1	4	3	4	12
2	5	2	2	12
3	4	1	1	11
4	5	3	3	45
5	3	1	3	20
6	5	3	1	17
7	5	2	3	21
8	5	2	1	60
9	4	2	4	12
10	4	1	1	8
11	4	3	3	28
12	4	1	1	6
13	4	1	1	2
14	4	3	3	1
15	4	1	4	5
16	5	2	4	5
17	4	2	2	16

Complications

No immediate side effect occurred in any of the patients. At last follow-up, no complications of radiosurgery were seen except for one case of

mild facial itching. Two patients already had facial numbness prior to radiosurgery which was related to a previous procedure, but none developed facial numbness consecutive to radiosurgery.

Discussion

Radiosurgery is an attractive alternative to open surgery because it is performed on an out-patient basis, the treatment is well tolerated and morbidity is low. This modality is particularly suitable for the treatment of patients who are poor candidates for surgery, in whom other therapies have failed, or who are unwilling to undergo an invasive procedure. Some investigators have explored the use of GKRS as the primary treatment for TN in elderly patients or in those with significant comorbidities [2, 7, 9]. They concluded that patients with TN who are treated with GKRS as primary management experience better pain relief than those treated with GKRS as secondary management. Reports on earlier clinical studies have demonstrated the efficacy of GKRS in targeting the root entry zone of the trigeminal nerve and thus alleviating pain in many patients with TN [7, 9, 10, 14]. Approximately 75% of patients report complete relief initially and for the first three months [24], but this number decreases to 50% after three years. Less than 50% of patients can permanently stop drug therapy after surgery. Sensory disturbances including numbness, paresthesias and dysesthesias are the most frequent complications. Patients who fail to respond to radiosurgery or who experience recurrence of symptoms may respond to repeat treatment [13, 15, 25].

Recently linear accelerator (LINAC) radiosurgery for TN has also been shown to be safe and effective as a primary non-invasive treatment for selected patients with essential TN [19]. In our study the results in terms of pain relief are comparable with the data obtained in the literature with both GKRS and LINAC. Interestingly, the complication rate in our small series (one case of facial itching) was much lower than is usually reported in the literature (3–29% of facial numbness) with GK or LINAC radiosurgery. None of our patients developed facial numbness after radiosurgery. Previous reports have shown a correlation between facial numbness and improvement in pain score [12–14, 26]. In a recent study by McNatt et al. [12], 77% of patients who developed new-onset facial numbness had favourable outcomes, with BNI pain scores of III or better, whereas only 30% of patients who did not develop facial numbness had favourable outcomes. In this study, we were not able to show a correlation between pain improvement and facial numbness after radiosurgery.

In our centre we used a very proximal target located 2–4 mm from the REZ with a central dose of 50–56 Gy. Some centres use a very anterior

target, located immediately posterior to the gasserian ganglion as originally described by Régis et al. [27] with a maximum dose ranging from 70–90 Gy. This difference in dose prescription and in target localisation might in part explain the lower incidence of complications in our series when compared to others' reports. A longer follow-up and a larger population are required to compare results in terms of pain outcome and morbidity with the GK experience.

As in most studies in this field, the median follow-up has been less than 2 years. Because pain improvement usually occurs in the first few months after treatment (mean: 1–2 months [9–11]), the initial pain response can be adequately quantified. Moreover, most recurrences occur in the first year after treatment and thus the majority of cases can usually be reported. However, due to the short follow-up period in this study late treatment failure and long-term outcome cannot be estimated. In our series, with a median follow-up of 12 months, the recurrence rate was 29% and was thus in the middle range of recurrence rates reported in the literature (5–63%; median 15%). However, given the slightly shorter follow-up period in our study compared with the mean follow-up period in other studies, the rate of recurrence may be underestimated. Our results are also in agreement with the data in the literature showing that excellent or good relief (at least 50% reduction in pain and less medication) is more likely to occur in patients treated by radiosurgery as primary management [7]. Indeed, 4 out of 5 patients with a recurrence had undergone one or more previous unsuccessful procedures prior to radiosurgery.

Because TN and pain in general is a subjective symptom which can be influenced by many factors including duration of disease, age, gender, tolerance capacity and psychology, studies evaluating successful interventions for pain depend largely on patients' subjective evaluation. Unfortunately there is no precise pain scale that can be applied and direct comparison between different studies is difficult.

Stereotactic radiosurgery using a linear accelerator seems to be effective and may offer a favourable alternative to other procedures including GKRS. The procedure is also very safe and side effects are rare and minor, even with a high dose. Depending on the target and some other dosimetric parameters, a dose of 70 Gy to the maximum point is currently recommended for the LINAC-based system and the gamma knife

system, with pain control rates of 35% to 74%. However, a randomised trial with a longer follow-up comparing radiosurgery to other surgical procedures is needed to assess the long-term effectiveness of this treatment.

Correspondence:

Dr Marc Pusztazeri

Department of Radiation Oncology, CHUV

1011 Lausanne, Switzerland

E-Mail: Marc.Pusztazeri@chuv.ch

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