Radiosurgery Practice Guideline Initiative

Stereotactic Radiosurgery for Patients with
Intractable Typical Trigeminal Neuralgia Who Have Failed Medical Management
Radiosurgery Practice Guideline Report #1-03
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This practice guideline, together with a report on "Trigeminal Neuralgia: Overview and Surgical Management" is an original guideline approved by the IRSA® (International RadioSurgery Association) Board of Directors and issued in January 2009.

Preface

Summary
The IRSA® (International RadioSurgery Association) Radiosurgery Practice Guideline Initiative aims to improve outcomes for typical trigeminal neuralgia patients by assisting physicians and clinicians in applying research evidence to clinical decisions while promoting the responsible use of health care resources.

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Key Words **o trigeminal neuralgia o tic douloureux o stereotactic radiosurgery o Gamma Knife® o linear accelerator o irradiation o CyberKnife**

Consensus Statement

Objective
To develop a consensus-based radiosurgery practice guideline for trigeminal neuralgia treatment recommendations to be used by medical and public health professionals following the diagnosis of trigeminal neuralgia.

Participants
The working group included physicians and physicists from the staff of major medical centers that provide radiosurgery.

Evidence
The first authors (LDL/AN) conducted a literature search in conjunction with the preparation of this document and development of other clinical guidelines. The literature identified was reviewed and opinions were sought from experts in the diagnosis and management of trigeminal neuralgia, including members of the working group.

Consensus Process
The initial draft of the consensus statement was a synthesis of research information obtained in the evidence gathering process. Members of the working group provided formal written comments that were incorporated into

the preliminary draft of the statement. No significant disagreements existed. The final statement incorporates all relevant evidence obtained by the literature search in conjunction with final consensus recommendations supported by all working group members.

Group Composition
The radiosurgery guidelines group is comprised of neurosurgeons, radiation oncologists and physicists. Community representatives did not participate in the development of this guideline.

Names of Group Members: L. Dade Lunsford, M.D., Neurosurgeon, Chair; Ajay Niranjan, M.B.B.S., M.Ch., Neurosurgeon; Ron Young, M.D., Neurosurgeon; Ronald Brisman, M.D., Neurosurgeon; David Cunningham, M.D., Neurosurgeon; Christer Lindquist, M.D., Neurosurgeon; David Newell, M.D., Neurosurgeon; John C. Flickinger, M.D., Radiation Oncologist; Ann Maitz, M.S., Medical Physicist; Tonya K. Ledbetter, M.S., M.F.S, Editor; Rebecca L. Emerick, M.S., M.B.A., C.P.A., ex officio.

Conclusions
Specific recommendations are made regarding target population, treatment alternatives, interventions and practices and additional research needs. Appropriate use of radiosurgery to those with intractable trigeminal neuralgia following medical management may be beneficial.

This guideline is intended to provide the scientific foundation and initial framework for patients who have been diagnosed with trigeminal neuralgia. The assessment and recommendations provided herein represent the best professional judgment of the working group at this time, based on clinical research data and expertise currently available. The conclusions and recommendations will be regularly reassessed as new information becomes available.

Stereotactic Radiosurgery

Brain Stereotactic Radiosurgery (SRS) involves the use of precisely directed, closed skull, single fraction (one session) of radiation to create a desired radiobiologic response within the brain with minimal effects to surrounding structures or tissues. In the case of trigeminal neuralgia a relatively high dose of focused radiation is delivered precisely to the trigeminal nerve under the direct supervision of a radiosurgery team. In Centers of Excellence, the radiosurgery team is composed of a neurosurgeon, radiation oncologist, physicist and registered nurse.

Trigeminal Neuralgia: Overview and Surgical Management

Background

Trigeminal neuralgia (TN), also known as tic douloureux, is a pain syndrome recognizable by patient history alone. The condition is characterized by intermittent unilateral facial pain. The pain follows the unilateral (>95%) sensory distribution of trigeminal nerve (V), typically radiating to the maxillary (V2) or mandibular (V3) area. Ophthalmic division (V1) pain alone occurs in <5% patients. Physical examination findings are typically normal, although mild light touch or pin perception loss has been described in the central area of the face. Significant sensory loss suggests that the pain syndrome is secondary to another process, and requires high-resolution neuroimaging to exclude other causes of facial pain.

Epidemiologic Features

Sex

Male-to-female ratio is 2:3.

Age

The average age of pain onset in idiopathic TN typically is the sixth decade of life, but it may occur at any age. Symptomatic or secondary TN tends to occur in younger patients. Trigeminal neuralgia caused by arterial

compression is more likely in older patients.

Pathophysiology

The mechanism of pain production remains controversial. One theory suggests that peripheral injury or disease of the trigeminal nerve increases afferent firing in the nerve, perhaps by ephaptic transmission between afferent unmyelinated axons and partially damaged myelinated axons; failure of central inhibitory mechanisms may also be involved. Pain is perceived when nociceptive neurons in a trigeminal nucleus involve thalamic relay neurons. Blood vessel-nerve cross compression, aneurysms, chronic meningeal inflammation, tumors or other lesions may irritate trigeminal nerve roots along the pons. Uncommonly, an area of demyelination, such as may occur with multiple sclerosis, may be the precipitant. In some cases no vascular or other lesion is identified, rendering the etiology uncertain. Development of trigeminal neuralgia in a young person (<45 years) raises the possibility of multiple sclerosis, which should be investigated. Lesions of the entry zone of the trigeminal roots within the pons may cause a similar pain syndrome. Thus, although TN typically is caused by a dysfunction in the peripheral nervous system (the roots or trigeminal nerve itself),[11,14,25,30] a lesion within the central nervous system (1–8%) may also cause similar problems.[9]

Causes

Some patients' conditions are idiopathic, but compression of the trigeminal root entry zone by blood vessels (especially branches of the superior cerebellar arteries or venous channels) or tumors may cause pain.

Clinical Presentation

Nature of Pain

Pain is stabbing or an electric shock-like sensation and is typically quite severe. Pain is brief (few seconds to 1–2 minutes) and paroxysmal, but it may occur in volleys of multiple attacks. Pain may occur several times a day; patients typically experience no pain between episodes.

Distribution of Pain

Pain is unilateral (rarely bilateral).[45] One or more branches of the trigeminal nerve (usually maxillary or mandibular) are involved. It is rare that pain is simultaneously bilateral, but pain on the contralateral side is seen in about 5% of patients with TN and about 20% of patients with trigeminal neuralgia and multiple sclerosis.

Trigger Points

Various triggers may commonly precipitate a pain attack. Light touch or vibration is the most evocative. Activities such as shaving, face washing or chewing often trigger an episode. Over years periods of remission are less and less and severity of pain increases.

Course

The disease course is usually one of clusters of attacks that wax and wane in frequency. Over the years recurrences become sharper and exacerbations longer. Some patients report that their exacerbations commonly occur in the fall and spring.

Imaging Studies

Patients with characteristic history and normal neurologic examination may be treated without further workup. An MRI scan with and without contrast is essential to rule out the presence of a tumor, arteriovenous malformation, or multiple sclerosis, all of which can cause trigeminal neuralgia in a small number of patients. In addition, skull base conditions such as maxillary sinusitis may mimic symptoms of TN.

Management Options

Medical Management

The goal of pharmacologic therapy is to reduce pain. Carbamazepine is regarded as the most effective medical treatment. Oxcarbazepine (Trileptal) is often effective like carbamazepine, but has fewer side effects. Additional agents that may benefit selected patients include baclofen, gabapentin (Neurontin), and Klonazepin. The combination of carbamazepine and baclofen may provide relief from episodic pain. Other anticonvulsants, including phenytoin, reportedly are beneficial in some patients. Topiramate may be beneficial in refractory cases; however, controlled studies have not been performed. Some patients are not helped by these medications, experience breakthrough pain, or suffer with undesirable side effects. In such cases a referral to a neurosurgeon is indicated.[57]

Surgical Management

Prior to considering surgery, all eligible patients should have an MRI, with close attention being paid to the posterior fossa. Imaging is performed to rule out other causes of compression of the trigeminal nerve such as mass lesions, large ectatic vessels, or other vascular malformations. Thin section MRI (with contrast) may be helpful (although not with 100% accuracy) in identifying blood vessel contact and/or compression of the trigeminal nerve. The surgical options for TN include peripheral nerve blocks or ablation, gasserian ganglion and retrogasserian ablative procedures, microvascular decompression (MVD) and stereotactic radiosurgery.[8] Percutaneous transovale techniques include radiofrequency trigeminal electrocoagulation, glycerol rhizotomy and balloon microcompression.[8,36,61,64] Microvascular decompression is often preferred for younger patients with typical trigeminal neuralgia. High initial success rates (>90%) have led to the widespread use of this procedure. Pain control rate after single MVD at 10 years is 64% with good results in an additional 4%.[5] This procedure provides treatment of the cause of TN in many patients. Percutaneous techniques are advocated for elderly patients, patients with multiple sclerosis, patients with recurrent pain after MVD, and patients with impaired contralateral hearing;[4] however, some authors recommend percutaneous techniques as the first surgical treatment for most patients.[60,64] In a comparative study of three techniques, Lee et al. noted initial success rates of 96.5%, 92% and 83% for MVD, radiofrequency trigeminal electrocoagulation and glycerol rhizolysis, respectively.[31] Facial dysesthesias were reported for 6.3%, 5% and 3% of patients, respectively. In a review of different techniques, Lovely and Jannetta reported excellent or good pain control for 78%, 74% and 56% of patients using MVD, radiofrequency trigeminal electrocoagulation, and glycerol rhizolysis, respectively.[37] Microvascular decompression was associated with a 0.5% mortality rate and 3–29% facial numbness rates. In a study of balloon microcompression treatment of trigeminal neuralgia, 62.5% of patients achieved excellent pain control, whereas 32.5% developed recurrences (after a median interval of 51 months). Sensory dysesthesia was noted for 3% and hearing impairment was observed for 11% of patients. It is generally agreed that MVD provides the longest duration of pain relief while preserving facial sensation. In experienced hands, MVD can be performed with low morbidity and mortality. Most authors offer MVD to young patients with TN.[37,63]

Radiosurgery

Several reports have documented the efficacy of Gamma Knife® stereotactic radiosurgery for TN.[1,3,16,18,20,26,27,29,32,35,39-42,46,50-53,58,62,68] Because radiosurgery is the least invasive procedure for TN, it is a good treatment option for patients with co-morbidities, high-risk medical illness, or pain refractory to prior surgical procedures. Radiosurgery is a good alternative for most patients with medically refractory trigeminal neuralgia, especially those who do not want to accept the greater risk of an MVD for a greater chance of pain relief.

To date, the largest reported series are still characterized by a wide spectrum of success rates after radiosurgery with Grade I outcome in 21–76.8% of patients and Grade II outcome in 65–88% of patients.[6,7,21,29,38,48,52,58,67] Regis et al. reported that 87% of patients were initially free of pain in their series of 57 patients treated with a maximum dose of 75–90 Gy.[52,54] In many patients, they used the higher maximum dose of 90 Gy, and their target was placed at a more anterior site (closer to retrogasserian portion). In a series of 441 patients presented at the 2001 meeting of the International Stereotactic Radiosurgery Society, Young et al. noted that 87% of patients were free of pain after radiosurgery, with or without medication (median follow-up period, 4.8 years, including repeat procedures). Brisman et al. noted vascular contact with trigeminal nerve on thin section MRI in 59% of patients with TN. These authors reported a complete (100%) pain relief without medicines in 22% of patients, 90% or greater relief with or without small doses of medicines in 30% of patients, 75–89% relief in 11% of patients, 50–74% relief in 7% of patients, and less than 50% relief in 8% of patients. Recurrent pain requiring a second procedure occurred in 24% of patients.[7]

In a study, Petit et al. assessed the safety, efficacy and quality of life associated with radiosurgical treatment for TN in 112 patients treated with Gamma Knife® radiosurgery using a standard questionnaire. Ninety-six patients completed questionnaires for a median follow-up of 30 months. Seventy-four patients (77%) reported pain relief at a median of three weeks after the procedure.[44] A decrease in medication usage was noted in 66% of patients. Seven (7.3%) patients reported new or increased trigeminal dysfunction; however, only 3.1% reported these symptoms as bothersome. Patients with sustained pain relief reported an average of 100% improvement in their quality of life as a direct result of pain relief after radiosurgery, and 100% believed that the procedure was successful. Furthermore, among those patients with temporary pain relief and subsequent recurrence, 65% felt their treatment was a success with an average of 80% improvement in their quality of life.[44] Smith et al. recently published the results of trigeminal neuralgia radiosurgery using a dedicated linear accelerator.[59] These investigators treated 60 patients with central doses of 70–90 Gy delivered to trigeminal nerve root entry zone using a 5-mm collimator. Pain relief was experienced at a mean of 2.7 months. Significant pain relief was obtained in 87.5% of the patients who had essential TN and in 58.3% of the patients who had secondary facial pain. In a recent article, Longhi et al. reported on the results of Gamma Knife® radiosurgery for treatment of medically and, in some instances, surgically refractory TN.[35] These authors found 57% Grade I and 33% Grade II pain control after Gamma Knife® radiosurgery. These favorable results are similar to those reported by Pollock et al.[49] and Kondziolka et al.[28] Recurrence of pain occurred in 18% of patients at a mean interval of 14.2 months after radiosurgery. The side effects of trigeminal paresthesia or hypoesthesia were observed in 9.5% of patients; no cases of anesthesia dolorosa were observed. A higher radiosurgical dose and no previous neurosurgical intervention for TN were positive predictors of a pain-free outcome. The growing body of recent literature suggests that low rates of complications of Gamma Knife® radiosurgery, coupled with high success rates and patient satisfaction, allow it to be increasingly used as primary intervention for trigeminal neuralgia for appropriate patients.[2,12,13,18,20,22,26,34]

Predictive Factors

Several factors have been associated with the positive results achieved by Gamma Knife® radiosurgery in treating TN: the absence of multiple sclerosis, greater radiation dose, no previous surgery, typical pain features, and proximity of the isocenters to the brainstem edge.[6,9] In a population of 54 patients, Rogers et al.[56] found a higher Grade I outcome in patients with idiopathic typical TN in comparison with those with atypical features: 49% (21 of 43) as opposed to 9% (1 of 11). In their series of 179 patients, Brisman et al.[9] reported that 41% of their patients had a Grade I outcome and 17% had a Grade II outcome. Better results were achieved in patients with no previous surgery (60% [35 of 58]). Similar results were reported by Young et al.[67] and Maesawa et al.,[38] who described the presence of atypical pain as the most important factor yielding a poor response to Gamma Knife® radiosurgery (84.4% versus 43.8%). Several authors have reported similar results using linear accelerator based radiosurgery.[17,19,33,43,55,65]

Recurrence After Radiosurgery

Recurrence is still a major concern in the Gamma Knife® treatment of trigeminal neuralgia. The experience suggests that longer follow-up periods are needed before drawing any conclusion.[62] Thirty–one patients underwent repeat radiosurgery at the University of Pittsburgh due to pain recurrence. The time to recurrence after the first radiosurgical procedure varied from 3 to 64 months. The mean time to recurrence was 18.2 months, and the mean interval between the first and second radiosurgical procedures was 22.3 months (range, 6–73 months).[21] The duration of pain relief after the initial response was analyzed in all patients using the Kaplan-Meier product-limit method. Complete pain relief (excellent or good) was maintained in $63.6 \pm 3.3\%$ of patients at one year and in $56.6 \pm 3.8\%$ at three years. Greater than 50% pain relief was maintained in $75.8 \pm 2.9\%$ of patients at one year and in $67.2 \pm 3.9\%$ at three years. A history of no prior surgery was significantly associated with achieving and maintaining complete pain relief ($p = 0.01$). The absence of preradiosurgical paresthesia, which is strongly correlated with no prior surgery, was significantly associated with achieving and maintaining greater than 50% pain relief ($p = 0.02$). According to the other literatures, recurrence rates at the last follow-up after radiosurgery varied from 3.3–21%.[21,48] Currently, the etiological basis and physiopathology of TN recurrences after Gamma Knife® radiosurgery still need to be clarified. The recent description of two distinct mechanisms in pain generation, ephaptic transmission and neuronal afterdischarge, will likely explain how glial processes stimulated by radiosurgery might be more efficient in blocking the ephaptic transmission, but not the neuronal afterdischarge, which is a nonsynaptic, nonephaptic transmission that could lead to painful relapses.[15]

Complications after Radiosurgery

The main complication after radiosurgery was new facial sensory symptoms caused by partial trigeminal nerve injury. Seventeen patients (7.7%) in the University of Pittsburgh series developed increased facial paresthesia and/or facial numbness that lasted longer than six months.[38] One patient (0.4%) developed deafferentation pain. No patient developed other neurological morbidities. Other reported risks include new facial sensory symptoms (2.7–10%). Brisman et al.[7,9] reported a 5% complication rate in patients treated with doses ranging between 70 and 80 Gy. Pollock et al.[49,50] reported a significant association between high radiation dose and increased risk of trigeminal neuropathy; 45% of the patients treated with a maximum dose over 90 Gy reported a trigeminal deficit compared with 15% of the lower-dose group. Increased risk of trigeminal nerve dysfunction has been reported with the use of high-dose (90 Gy) radiosurgery for TN.[42,49] Smith et al., using a dedicated linear accelerator for TN radiosurgery, reported a 25% rate of new numbness.[59] Results to date suggest that CyberKnife® SRS for trigeminal neuralgia has an increased risk of sensory dysfunction and other neurological complications (Table 1).

Table 1: Recent Outcomes of Trigeminal Neuralgia Radiosurgery

First Author	Year	Technique	% of Patients with Excellent Pain Relief	% of Patients with New Facial Numbness and Other Side Effects
Maesawa[38]	2002	Gamma Knife®	74.5%	10.2%
Longhi[35]	2007	Gamma Knife®	61%	9.5%
Chen[10]	2008	LINAC	49%	10.5%
Richards[55]	2005	LINAC	57%	14%
Lim[33]	2005	CyberKnife®	78%	51.2%
Villavicencio[65]	2008	CyberKnife®	50%	47%

Repeat Radiosurgery

Patients who experience recurrent pain during the long-term follow-up despite initial pain relief after radiosurgery can be treated with a second radiosurgery procedure.[18,21,23,47,66] At the second procedure, the radiosurgical target and dose slightly differ from the first procedure. The target is placed anterior to the first target so that the radiosurgical volumes at the second procedure overlap with the first one by 50%. Dose selection is still controversial. We advocate a lesser radiation dose (50–70 Gy) for the second procedure, because we believe that a higher combined dose would lead to a higher risk of new facial sensory symptoms. On the other hand, Pollock et al.[48] suggested a greater radiation dose to the same target at the second procedure than at the first. They updated their results in a later study and concluded that repeat trigeminal neuralgia radiosurgery at higher doses had better facial pain outcomes; however, the rate of bothersome numbness was relatively high (16%). Therefore, dose reduction is recommended to reduce the morbidity of repeat trigeminal neuralgia radiosurgery. Twenty-seven patients who had a second procedure at the University of Pittsburgh were evaluated at a median follow-up of 20 months. The mean time to recurrence was 18 months, and the mean interval between the first and second radiosurgical procedures was 22 months. After the second radiosurgery, 5 of 27 (18.5%) patients had an excellent outcome, 8 (29.6%) had a good outcome, 10 (37.0%) had a fair outcome and 4 (14.8%) had a poor outcome. The rates of excellent or good outcome (complete relief and complete or partial pain relief) were 48.1% and 85.2%, respectively. We believe that the second radiosurgery procedure is as effective as the first in terms of the initial response.

Follow-up and Medications

After radiosurgery, patients are followed to assess pain relief at three months and six months, and then at yearly intervals. Their pre-radiosurgery pain medications are continued at the same doses until pain relief is obtained. Medications then can be gradually tapered off if the patient remains pain free.

Indications for Radiosurgery

Many surgical treatments exist for trigeminal neuralgia, and long-term results have been reported. We have identified a high rate of imaging-defined pontine or cerebellar infarction (24%) in patients who had prior microvascular decompressions.[24] We recommend Gamma Knife® radiosurgery for older or infirm patients because

it is the least invasive option. The lack of mortality and the low risk of facial sensory disturbance, even after a repeat procedure, argue for the use of primary or secondary radiosurgery in this setting. Repeat radiosurgery remains an acceptable treatment option for patients who have failed other therapeutic alternatives.

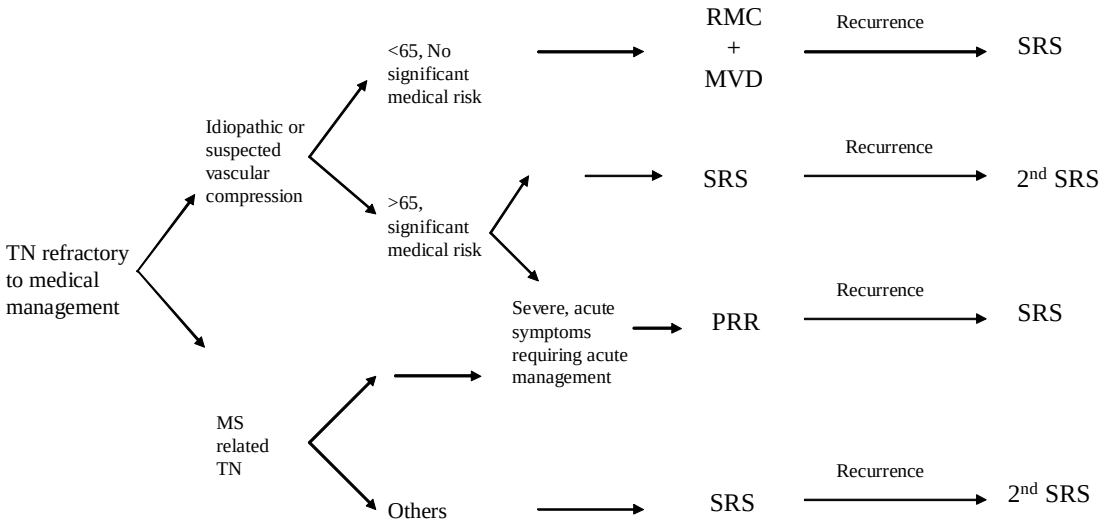
CLINICAL ALGORITHM(S):

A number of factors are considered in making a recommendation. These factors include:

1. Patient's age
2. Patient's medical condition
3. Presence or absence of multiple sclerosis
4. Presence or absence of vascular contact and/or compression on thin section MRI
5. Presence or absence of prior procedures
6. The type of prior procedure and its response
7. Severity of pain and how long the patient can reasonably wait for pain relief
8. Patient's concern and risk tolerance for dysesthesias, recurrence or complications from surgery

A broad outline of management algorithm is shown below; however, the final recommendation is usually influenced by the recommending neurosurgeon's experience.

Trigeminal Neuralgia Management Algorithm



RMC = Retro-Mastoid Craniotomy,
MVD = Microvascular Decompression,
PRR = Percutaneous Retrogasserian Rhizotomy (Glycerol / Radiofrequency / Balloon Compression)
SRS = Stereotactic Radiosurgery

References

1. Alpert TE, Chung CT, Mitchell LT, Hodge CJ, Montgomery CT, Bogart JA, et al: Gamma knife surgery for trigeminal neuralgia: improved initial response with two isocenters and increasing dose. **J Neurosurg 102 Suppl:**185-188, 2005

2. Azar M, Yahyavi ST, Bitaraf MA, Gazik FK, Allahverdi M, Shahbazi S, et al: Gamma knife radiosurgery in patients with trigeminal neuralgia: quality of life, outcomes, and complications. **Clin Neurol Neurosurg 111:**174-178, 2009
3. Balamucki CJ, Stieber VW, Ellis TL, Tatter SB, Deguzman AF, McMullen KP, et al: Does dose rate affect efficacy? The outcomes of 256 gamma knife surgery procedures for trigeminal neuralgia and other types of facial pain as they relate to the half-life of cobalt. **J Neurosurg 105:**730-735, 2006
4. 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 334:**1077-1083, 1996
5. Belber CJ, Rak RA: Balloon compression rhizolysis in the surgical management of trigeminal neuralgia. **Neurosurgery 20:**908-913, 1987
6. Brisman R: Gamma knife radiosurgery for primary management for trigeminal neuralgia. **J Neurosurg 93 Suppl 3:**159-161, 2000
7. Brisman R: Gamma knife surgery with a dose of 75 to 76.8 Gray for trigeminal neuralgia. **J Neurosurg 100:**848-854, 2004
8. Brisman R: Surgical treatment of trigeminal neuralgia. **Semin Neurol 17:**367-372, 1997
9. Brisman R, Khandji AG, Mooij RB: Trigeminal Nerve-Blood Vessel Relationship as Revealed by High-resolution Magnetic Resonance Imaging and Its Effect on Pain Relief after Gamma Knife Radiosurgery for Trigeminal Neuralgia. **Neurosurgery 50:**1261-1266, discussion 1266-1267, 2002
10. Chen JC, Greathouse HE, Girvigian MR, Miller MJ, Liu A, Rahimian J: Prognostic factors for radiosurgery treatment of trigeminal neuralgia. **Neurosurgery 62 Suppl 5:**A53-60; discussion A60-61, 2008
11. Cheshire WP: Trigeminal neuralgia: diagnosis and treatment. **Curr Neurol Neurosci Rep 5:**79-85, 2005
12. Cruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, et al: AAN-EFNS guidelines on trigeminal neuralgia management. **Eur J Neurol 15:**1013-1028, 2008
13. Dellaretti M, Reyns N, Touzet G, Sarrazin T, Dubois F, Lartigau E, et al: Clinical outcomes after Gamma Knife surgery for idiopathic trigeminal neuralgia: review of 76 consecutive cases. **J Neurosurg 109 Suppl:**173-178, 2008
14. Devor M, Amir R, Rappaport ZH: Pathophysiology of trigeminal neuralgia: the ignition hypothesis. **Clin J Pain 18:**4-13, 2002
15. Devor M, Govrin-Lippmann R, Rappaport ZH: Mechanism of trigeminal neuralgia: an ultrastructural analysis of trigeminal root specimens obtained during microvascular decompression surgery. **J Neurosurg 96:**532-543, 2002
16. Dhople A, Kwok Y, Chin L, Shepard D, Slawson R, Amin P, et al: Efficacy and quality of life outcomes in patients with atypical trigeminal neuralgia treated with gamma-knife radiosurgery. **Int J Radiat Oncol Biol Phys 69:**397-403, 2007
17. Frighetto L, De Salles AA, Smith ZA, Goss B, Selch M, Solberg T: Noninvasive linear accelerator radiosurgery as the primary treatment for trigeminal neuralgia. **Neurology 62:**660-662, 2004
18. Gellner V, Kurschel S, Kreil W, Holl EM, Ofner-Kopeinig P, Unger F: Recurrent trigeminal neuralgia: long term outcome of repeat gamma knife radiosurgery. **J Neurol Neurosurg Psychiatry 79:**1405-1407, 2008
19. Gerbi BJ, Higgins PD, Cho KH, Hall WA: Linac-based stereotactic radiosurgery for treatment of trigeminal neuralgia. **J Appl Clin Med Phys 5:**80-92, 2004

20. Guo S, Chao ST, Reuther AM, Barnett GH, Suh JH: Review of the treatment of trigeminal neuralgia with gamma knife radiosurgery. **Stereotact Funct Neurosurg 86:**135-146, 2008
21. Hasegawa T, Kondziolka D, Spiro R, Flickinger JC, Lunsford LD: Repeat radiosurgery for refractory trigeminal neuralgia. **Neurosurgery 50:**494-500; discussion 500-502, 2002
22. Hayashi M: Trigeminal neuralgia. **Prog Neurol Surg 22:**182-190, 2009
23. Herman JM, Petit JH, Amin P, Kwok Y, Dutta PR, Chin LS: Repeat gamma knife radiosurgery for refractory or recurrent trigeminal neuralgia: treatment outcomes and quality-of-life assessment. **Int J Radiat Oncol Biol Phys 59:**112-116, 2004
24. Jawahar A, Kondziolka D, Kanal E, Bissonette DJ, Lunsford LD: Imaging the trigeminal nerve and pons before and after surgical intervention for trigeminal neuralgia. **Neurosurgery 48:**101-106; discussion 106-107, 2001
25. Joffroy A, Levivier M, Massager N: Trigeminal neuralgia. Pathophysiology and treatment. **Acta Neurol Belg 101:**20-25, 2001
26. Kang JH, Yoon YS, Kang DW, Chung SS, Chang JW: Gamma knife radiosurgery for medically refractory idiopathic trigeminal neuralgia. **Acta Neurochir Suppl 101:**35-38, 2008
27. Keep MF, DeMare PA, Ashby LS: Gamma knife surgery for refractory postherpetic trigeminal neuralgia: targeting in one session both the retrogasserian trigeminal nerve and the centromedian nucleus of the thalamus. **J Neurosurg 102 Suppl:**276-282, 2005
28. Kondziolka D, Lunsford LD, Flickinger JC: Stereotactic radiosurgery for the treatment of trigeminal neuralgia. **Clin J Pain 18:**42-47, 2002
29. Kondziolka D, Lunsford LD, Flickinger JC, Young RF, Vermeulen S, Duma CM, et al: Stereotactic radiosurgery for trigeminal neuralgia: a multiinstitutional study using the gamma unit. **J Neurosurg 84:**940-945, 1996
30. Kumar GK, Vartanian AJ, Alvi A: When is facial pain trigeminal neuralgia? **Postgrad Med 104:**149-151, 155-156, 1998
31. Lee KH, Chang JW, Park YG, Chung SS: Microvascular decompression and percutaneous rhizotomy in trigeminal neuralgia. **Stereotact Funct Neurosurg 68:**196-199, 1997
32. Li K, Ma L: Selective source blocking for Gamma Knife radiosurgery of trigeminal neuralgia based on analytical dose modelling. **Phys Med Biol 49:**3455-3463, 2004
33. Lim M, Villavicencio AT, Burneikiene S, Chang SD, Romanelli P, McNeely L, et al: CyberKnife radiosurgery for idiopathic trigeminal neuralgia. **Neurosurg Focus 18:**E9, 2005
34. Little AS, Shetter AG, Shetter ME, Bay C, Rogers CL: Long-term pain response and quality of life in patients with typical trigeminal neuralgia treated with gamma knife stereotactic radiosurgery. **Neurosurgery 63:**915-923; discussion 923-924, 2008
35. Longhi M, Rizzo P, Nicolato A, Foroni R, Reggio M, Gerosa M: Gamma knife radiosurgery for trigeminal neuralgia: results and potentially predictive parameters--part I: Idiopathic trigeminal neuralgia. **Neurosurgery 61:**1254-1260; discussion 1260-1261, 2007
36. Lopez BC, Hamlyn PJ, Zakrzewska JM: Systematic review of ablative neurosurgical techniques for the treatment of trigeminal neuralgia. **Neurosurgery 54:**973-982; discussion 982-983, 2004
37. Lovely TJ, Jannetta PJ: Microvascular decompression for trigeminal neuralgia. Surgical technique and long-term results. **Neurosurg Clin N Am 8:**11-29, 1997

38. Maesawa S, Salame C, Flickinger JC, Pirris S, Kondziolka D, Lunsford LD: Clinical outcomes after stereotactic radiosurgery for idiopathic trigeminal neuralgia. **J Neurosurg 94:**14-20, 2001
39. 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 100:**597-605, 2004
40. Massager N, Lorenzoni J, Devriendt D, Levivier M: Radiosurgery for trigeminal neuralgia. **Prog Neurol Surg 20:**235-243, 2007
41. McNatt SA, Yu C, Giannotta SL, Zee CS, Apuzzo ML, Petrovich Z: Gamma knife radiosurgery for trigeminal neuralgia. **Neurosurgery 56:**1295-1301; discussion 1301-1303, 2005
42. Nicol B, Regine WF, Courtney C, Meigooni A, Sanders M, Young B: Gamma knife radiosurgery using 90 Gy for trigeminal neuralgia. **J Neurosurg 93 Suppl 3:**152-154, 2000
43. Patil CG, Veeravagu A, Bower RS, Li G, Chang SD, Lim M, et al: CyberKnife radiosurgical rhizotomy for the treatment of atypical trigeminal nerve pain. **Neurosurg Focus 23:**E9, 2007
44. 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 56:**1147-1153, 2003
45. Pollack IF, Jannetta PJ, Bissonette DJ: Bilateral trigeminal neuralgia: a 14-year experience with microvascular decompression. **J Neurosurg 68:**559-565, 1988
46. Pollock BE, Ecker RD: A prospective cost-effectiveness study of trigeminal neuralgia surgery. **Clin J Pain 21:**317-322, 2005
47. Pollock BE, Foote RL, Link MJ, Stafford SL, Brown PD, Schomberg PJ: Repeat radiosurgery for idiopathic trigeminal neuralgia. **Int J Radiat Oncol Biol Phys 61:**192-195, 2005
48. Pollock BE, Foote RL, Stafford SL, Link MJ, Gorman DA, Schomberg PJ: Results of repeated gamma knife radiosurgery for medically unresponsive trigeminal neuralgia. **J Neurosurg 93 Suppl 3:**162-164, 2000
49. Pollock BE, Phuong LK, Foote RL, Stafford SL, Gorman DA: High-dose trigeminal neuralgia radiosurgery associated with increased risk of trigeminal nerve dysfunction. **Neurosurgery 49:**58-62; discussion 62-64, 2001
50. Pollock BE, Phuong LK, Gorman DA, Foote RL, Stafford SL: Stereotactic radiosurgery for idiopathic trigeminal neuralgia. **J Neurosurg 97:**347-353, 2002
51. Regis J: High-dose trigeminal neuralgia radiosurgery associated with increased risk of trigeminal nerve dysfunction. **Neurosurgery 50:**1401-1402; author reply 1402-1403, 2002
52. Regis J, Metellus P, Dufour H, Roche PH, Muracciole X, Pellet W, et al: Long-term outcome after gamma knife surgery for secondary trigeminal neuralgia. **J Neurosurg 95:**199-205, 2001
53. 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 104:**913-924, 2006
54. Regis J, Metellus P, Lazorthes Y, Porcheron D, Peragut JC: Effect of gamma knife on secondary trigeminal neuralgia. **Stereotact Funct Neurosurg 70 Suppl 1:**210-217, 1998

55. Richards GM, Bradley KA, Tome WA, Bentzen SM, Resnick DK, Mehta MP: Linear accelerator radiosurgery for trigeminal neuralgia. **Neurosurgery 57:**1193-1200; discussion 1193-1200, 2005
56. 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 47:**1013-1019, 2000
57. Rozen TD: Antiepileptic drugs in the management of cluster headache and trigeminal neuralgia. **Headache 41 Suppl 1:**S25-32, 2001
58. Sheehan J, Pan HC, Stroila M, Steiner L: Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. **J Neurosurg 102:**434-441, 2005
59. Smith ZA, De Salles AA, Frighetto L, Goss B, Lee SP, Selch M, et al: Dedicated linear accelerator radiosurgery for the treatment of trigeminal neuralgia. **J Neurosurg 99:**511-516, 2003
60. Sweet WH: Percutaneous methods for the treatment of trigeminal neuralgia and other faciocephalic pain; comparison with microvascular decompression. **Semin Neurol 8:**272-279, 1988
61. Tatli M, Satici O, Kanpolat Y, Sindou M: Various surgical modalities for trigeminal neuralgia: literature study of respective long-term outcomes. **Acta Neurochir (Wien) 150:**243-255, 2008
62. Tawk RG, Duffy-Fronckowiak M, Scott BE, Alberico RA, Diaz AZ, Podgorsak MB, et al: Stereotactic gamma knife surgery for trigeminal neuralgia: detailed analysis of treatment response. **J Neurosurg 102:**442-449, 2005
63. Tyler-Kabara EC, Kassam AB, Horowitz MH, Urgo L, Hadjipanayis C, Levy EI, et al: Predictors of outcome in surgically managed patients with typical and atypical trigeminal neuralgia: comparison of results following microvascular decompression. **J Neurosurg 96:**527-531, 2002
64. van Loveren H, Tew JM, Jr., Keller JT, Nurre MA: a 10-year experience in the treatment of trigeminal neuralgia. Comparison of percutaneous stereotaxic rhizotomy and posterior fossa exploration. **J Neurosurg 57:**757-764, 1982
65. Villavicencio AT, Lim M, Burneikiene S, Romanelli P, Adler JR, McNeely L, et al: Cyberknife radiosurgery for trigeminal neuralgia treatment: a preliminary multicenter experience. **Neurosurgery 62:**647-655; discussion 647-655, 2008
66. Wang L, Zhao ZW, Qin HZ, Li WT, Zhang H, Zong JH, et al: Repeat gamma knife radiosurgery for recurrent or refractory trigeminal neuralgia. **Neurol India 56:**36-41, 2008
67. Young RF, Vermulen S, Posewitz A: Gamma knife radiosurgery for the treatment of trigeminal neuralgia. **Stereotact Funct Neurosurg 70 Suppl 1:**192-199, 1998
68. Zheng LG, Xu DS, Kang CS, Zhang ZY, Li YH, Zhang YP, et al: Stereotactic radiosurgery for primary trigeminal neuralgia using the Leksell Gamma unit. **Stereotact Funct Neurosurg 76:**29-35, 2001

Complete Summary

TITLE:

Stereotactic Radiosurgery For Patients With Intractable Typical Trigeminal Neuralgia Who Have Failed Medical Management.

ADAPTATION:

Not applicable: the guideline was not adapted from another source.

DATE RELEASED:

September 2003

UPDATE DATE:

January 2009

DEVELOPER AND FUNDING SOURCE:

IRSA (International RadioSurgery Association)

DEVELOPER COMMENT:

IRSA (International RadioSurgery Association) is an independent entity dedicated to promoting the development of scientifically relevant practice guidelines for stereotactic radiosurgery. IRSA is a professional organization that works to educate and provide support for physicians, hospitals, insurers and patients.

COMMITTEE:

The IRSA Medical Advisory Board Guidelines Committee and representatives in the industry.

GROUP COMPOSITION:

The radiosurgery guidelines group is comprised of neurosurgeons, radiation oncologists and physicists. Community representatives did not participate in the development of this guideline.

Names of Group Members: L. Dade Lunsford, M.D., Neurosurgeon, Chair; Ajay Niranjan, M.B.B.S., M.Ch., Neurosurgeon; Ron Young, M.D., Neurosurgeon; Ronald Brisman, M.D., Neurosurgeon; David Cunningham, M.D., Neurosurgeon; Christer Lindquist, M.D., Neurosurgeon; David Newell, M.D., Neurosurgeon; John C. Flickinger, M.D., Radiation Oncologist; Ann Maitz, M.S., Medical Physicist; Tonya K. Ledbetter, M.S., M.F.S, Editor; Rebecca L. Emerick, M.S., M.B.A., C.P.A., ex officio.

DISEASE/CONDITION:

Trigeminal neuralgia, typical (tic douloureux)

NUMBER OF SOURCE DOCUMENTS:

68

CATEGORY:

Treatment, proposed surgical management, radiosurgery

CLINICAL SPECIALTY:

Neurological surgery
Neurology
Radiation oncology

INTENDED USERS:

Physicians
Health Care Providers
Hospitals
Managed Care Organizations
Medical Physicists
Nurses
Utilization Management

OBJECTIVES:

To develop an evidence and consensus-based stereotactic radiosurgery practice guideline to be used by medical and public health professionals to make radiosurgery treatment recommendations for patients with intractable typical trigeminal neuralgia who have failed (refractory to or intolerant of) medical management.

TARGET POPULATION:

Patients with intractable (medically refractory) typical trigeminal neuralgia, often those with concomitant medical co-morbidity or advanced age.

INTERVENTIONS AND PRACTICES:

Stereotactic radiosurgery of the trigeminal nerve is performed using the following dose schedules:

- 75 Gy in a single fraction to the trigeminal nerve
- 80 Gy in a single fraction to the trigeminal nerve
- 90 Gy in a single fraction to the trigeminal nerve
- 50–70 Gy in a single fraction for repeat radiosurgery for recurrent trigeminal neuralgia

OUTCOMES CONSIDERED:

Pain control is the primary endpoint of interest. Use of pain medications, quality of life (addressed through the adverse effects of radiosurgery) and neurological outcome are also considered.

METHODS TO COLLECT EVIDENCE:

Computerized searches of published literature (primary sources); hand-searches of published literature (secondary sources); searches of electronic databases: clinical experience

DESCRIPTION OF METHODS TO COLLECT EVIDENCE:

MEDLINE and PUBMED searches were completed for the years 1966 to January 2009. Search terms included: tic douloureux, trigeminal neuralgia, stereotactic radiosurgery, Gamma Knife®, irradiation, clinical trials, research design, practice guidelines and meta-analysis. Bibliographies from recent published reviews were reviewed and relevant articles were retrieved.

METHODS TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE:

Expert consensus (committee)

RATING SCHEME:

Not applicable

METHODS TO ANALYZE EVIDENCE:

Systematic review with evidence tables

DESCRIPTION OF METHODS TO ANALYZE EVIDENCE:

Not applicable

REVIEW METHODS:

External peer review; internal peer review

DESCRIPTION OF REVIEW METHODS:

The recommendations were originally suggested by a core group of two members (AN and LDL). These recommendations were mailed to all committee members. Feedback was obtained through this mailed survey consisting of proposed guidelines asking for comments on the guidelines and whether the recommendation should serve as a practice guideline.

IMPLEMENTATION TOOLS:

Clinical Algorithm
Patient Resources

MAJOR RECOMMENDATIONS:

- Patients with typical trigeminal neuralgia who have had an adequate trial of medications can be offered stereotactic radiosurgery. Radiosurgery is typically used in patients with medical co-morbidities, patients at risk for side effects from percutaneous ablative procedures, and those in more advanced age groups.

- The optimal dose range for trigeminal neuralgia has been established. A commonly used dose range of 75–90 Gy in a single fraction to the trigeminal nerve is suggested, using a 4 mm collimator radiation field. Most centers prefer 80 Gy as a central dose targeted to the trigeminal nerve a few millimeters proximal to its entry into the brain stem; however, 90 Gy as a central dose to the trigeminal nerve near the trigeminal ganglion has also been used routinely in some centers.

- Patients who have failed other surgical procedures for trigeminal neuralgia should also receive 75–90 Gy to the trigeminal nerve. A safe interval between the initial surgery and stereotactic radiosurgery is unknown, but it is reasonable to perform radiosurgery if there is no improvement or pain recurs following the initial surgical procedures.

- After radiosurgery, patients are followed to assess pain relief at three months and six months, then at yearly intervals. Their pre-radiosurgery pain medications are continued at the same doses until pain relief is obtained. Medications then can be gradually tapered off if the patient remains pain free.

- Patients who have recurrence of pain following trigeminal neuralgia radiosurgery or who had a partial initial response can undergo a second stereotactic radiosurgery using 50–70 Gy to the trigeminal nerve (depending on the elapsed time between treatments). A generally safe interval between first and second radiosurgeries is six months.

- At present, technology to deliver focal small-volume fields is limited to Gamma Knife® by the strength of published data. (Gamma Knife® is a registered trademark of Elekta Instruments, Inc.) Current data suggest that CyberKnife® SRS for trigeminal neuralgia has an increased risk of sensory dysfunction and other neurological complications (Table 1).

TYPE OF EVIDENCE:

Class II and III

QUALIFYING STATEMENTS:

None

COST ANALYSIS:

Not applicable

POTENTIAL BENEFITS:

All of the published studies have shown a significant decrease in pain (decreased severity and reduced need to take medications).

SUBGROUP(S) MOST LIKELY TO BENEFIT:

Patients with typical trigeminal neuralgia (intermittent lancinating pain typically relieved by carbamazepine) without prior surgical procedure.

POTENTIAL HARMS:

Major adverse effects of trigeminal neuralgia radiosurgery occur very infrequently with Gamma Knife® technology.

Facial numbness < 10%
Neuropathic pain < 1%
Motor weakness < 1%

SUBGROUP(S) MOST LIKELY TO BE HARMED:

Patients with atypical facial pain (non-paroxysmal pain), deafferentation facial pain, TMJ related facial pain or orofacial pain.

GUIDELINE STATUS:

This is the full current release of the guideline.

GUIDELINE AVAILABILITY:

Electronic copies: Available in Portable Document Format (PDF) from www.IRSA.org
Print copies: Available from IRSA, 3005 Hoffman Street, Harrisburg, PA 17110

COMPANION DOCUMENTS:

None available

PATIENT RESOURCES:

Patient resources are available online at www.IRSA.org, by email at office1@IRSA.org or by calling +717-260-9808.

See "Publications" for patient resources for trigeminal neuralgia: http://IRSA.org/publications.html
Another Perspective® Volume 4, No. 3 and Brain Talk® Volume 8, No. 1.

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