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CLINICAL INVESTIGATION **Brain**

DEDICATED LINEAR ACCELERATOR RADIOSURGERY FOR TRIGEMINAL NEURALGIA: A SINGLE-CENTER EXPERIENCE IN 179 PATIENTS WITH VARIED DOSE PRESCRIPTIONS AND TREATMENT PLANS

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Purpose: Dedicated linear accelerator radiosurgery (D-LINAC) has become an important treatment for trigeminal neuralgia (TN). Although the use of gamma knife continues to be established, few large series exist using D-LINAC. The authors describe their results, comparing the effects of varied target and dose regimens.

Methods and Materials: Between August 1995 and January 2008, 179 patients were treated with D-LINAC radiosurgery. Ten patients (5.58%) had no clinical follow-up. The median age was 74.0 years (range, 32–90 years). A total of 39 patients had secondary or atypical pain, and 130 had idiopathic TN. Initially, 28 patients received doses between 70 and 85 Gy, with the 30% isodose line (IDL) touching the brainstem. Then, using 90 Gy, 82 consecutive patients were treated with a 30% IDL and 59 patients with a 50% IDL tangential to the pons.

Results: Of 169 patients, 134 (79.3%) experienced significant relief at a mean of 28.8 months (range, 5–142 months). Average time to relief was 1.92 months (range, immediate to 6 months). A total of 31 patients (19.0%) had recurrent pain at 13.5 months. Of 87 patients with idiopathic TN without prior procedures, 79 (90.8%) had initial relief. Among 28 patients treated with 70 Gy and 30% IDL, 18 patients (64.3%) had significant relief, and 10 (35.7%) had numbness. Of the patients with 90 Gy and 30% IDL at the brainstem, 59 (79.0%) had significant relief and 48.9% had numbness. Among 59 consecutive patients with similar dose but the 50% isodoseline at the brainstem, 49 patients (88.0%) had excellent/good relief. Numbness, averaging 2.49 on a subjective scale of 1 to 5, was experienced by 49.7% of the patients,

Conclusions: Increased radiation dose and volume of brainstem irradiation may improve clinical outcomes with the trade-off of trigeminal dysfunction. Further study of the implications of dose and target are needed to optimize outcomes and to minimize complications. © **2011 Elsevier Inc.**

Dedicated linear accelerator, Radiosurgery, Trigeminal neuralgia, Stereotactic.

INTRODUCTION

Trigeminal neuralgia (TN) is a syndrome characterized by severe, stabbing facial pain. This is most commonly idiopathic in nature; however, tumors of the posterior fossa, demyelinating disease of the nerve root entry zone (REZ), and infection can also produce symptoms (1–3). In most, it is believed that the genesis of disease is abnormal vascular loops, abutting and compressing the trigeminal nerve root (4). Several treatment options exist. Microvascular decompression (MVD) was developed for direct neural decompression (5). This surgery has produced excellent and sustainable pain relief (6). Treatment options also include percutaneous routes, including glycerol injection, balloon compression, or thermal rhizotomy (1, 7, 8). The role of radiosurgery continues to evolve for patients who are poor candidates for craniotomy or those who prefer a less invasive approach (9–11).

We previously reported our experience with D-LINAC-based radiosurgery in 60 patients (12). We now report the outcomes of 179 patients treated at our institution during the last 12 years. During this period, we sequentially increased both the radiation dose and the fraction of radiation received by the brainstem. In this study we have evaluated the effects of modifying dose and radiosurgery target.

METHODS AND MATERIAL

Diagnostic criteria

Diagnosis was based on a description similar to that of recently published clinical criteria (2). Patients with the diagnosis of

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idiopathic trigeminal neuralgia had classic symptoms of the disease, including attacks of unilateral, stabbing, and intense pain confined to one or more divisions of the trigeminal nerve. Secondary causes of trigeminal pain included infection, demyelinating disease (multiple sclerosis), and neoplastic disease affecting the trigeminal root. All treated patients failed conservative management, including use of antiepileptic and neuropathic agents.

Patient population

Between August 1995 and January 2008, 179 patients were treated. Ten patients (5.58%) were lost to follow-up. The study includes patients with essential TN (ETN) (130 patients), secondary TN (28 patients), and TN with atypical features (11 patients). The median age was 74.0 years (range, 32–90 years); and there were 68 men and 101 women. Sixteen patients (9.5%) had repeat SRS. Secondary causes of trigeminal neuralgia included 9 patients with multiple sclerosis, 7 with pain secondary to herpetic infection, and 9 with infiltration of the nerve by a neoplastic lesion. Two patients had trigeminal pain from a brainstem stroke. One patient presented with trigeminal pain resulting from cutaneous manifestations of Sturge-Weber. Patient characteristics are listed in Table 1.

Radiosurgical procedure

All patients were treated with the Novalis LINAC unit (BrainLAB Inc., Heimstetten, Germany). Before the procedure, magnetic resonance imaging (MRI) and computed tomography (CT) were performed. Planned targets for radiosurgery were obtained with MR fused to CT scans for correction of MR image distortion and dose calculation. In 169 patients, the doses administered were 70 Gy (16.5%), 75 Gy (3.6%), 80 Gy (5.9%), 85 Gy (0.6%), and 90 Gy (83.4%), prescribed to the 100% normalization point. A single 5-mm collimator was used in 151 patients (89.3%), and a 7.5-mm collimator was used in 18 (10.7%). In all patients, the target was located at the base of the trigeminal nerve at the junction of the nerve and brainstem (Fig. 1). The target was localized such that the brainstem surface was located near either the 30% or 50% prescription isodoseline.

Table 1. Characteristics of 169 clinically followed patients who underwent radiosurgery for TN*

	Idiopathic TN			
Characteristic	Initial op	Prior ops	Secondary cause	Atypical pain*
No. of patients	87	43	28	11
Mean age (y)	66.1	63.0	62.7	60.0
Mean prior operations	0	1.60	0.93	0.45
Nerve div affected (%)				
V1	11 (12.6)	1 (2.3)	7 (25.0)	0 (0.0)
V2	17 (19.5)	12 (27.9)	0 (0.0)	1 (9.1)
V3	16 (18.3)	7 (16.3)	4 (14.3)	3 (27.2)
V1 and V2	9 (10.3)	14 (32.6)	1 (3.6)	3 (27.2)
V2 and V3	18 (20.7)	9 (21.0)	4 (14.3)	0 (0.0)
V1–3	16 (18.4)	0	12 (42.8)	2 (18.0)
Mean f/u (mo)	26.6	36.2	26.7	35.8
Range	5–89	5–128	5–107	5–80

Abbreviations: div = division; f/u = follow-up; no. = number; op = operation.

* Two patients (1.8%) had facial pain that poorly correspond to dermatomes.

From August 1995 until April 1999, our standard treatment was 70 Gy with a single isocenter localized such that the brainstem surface was at the 30% isodose line. A total of 28 patients (16.5%) were treated with this protocol. The next 82 patients (48.5%) were treated with an increased dose of 90 Gy, using the same 30% isodose line at the brainstem surface (May 1999 to September 2003). Planning was further modified in late 2003 with the goal of increasing the dose at the root entry zone. From October 2003 until January 2008, 59 patients (34.9%) were treated with the same 90 Gy dose prescription, but with the 50% isodose line moved toward the brainstem.

Three patients in the lower-dose treatment period had individualized treatment plans. In two patients with pain secondary to squamous cell invasion of the nerve, the radiation dose volume contained both the REZ as well as the infiltrating mass. A 5-mm collimator was used to concentrate a high dose of radiation at the trigeminal nerve root and either a 20- or a 28-mm collimator was directed at the infiltrating lesion (13). A single patient with a cavernous sinus meningioma was treated with a 7.5-mm collimator and a 70 Gy dose directed at the REZ of the trigeminal nerve.

Radiosurgery equipment

All patients underwent CT (General Electric, Milwaukee, WI) with a stereotactic localization system and 1.5 Tesla MRI scan (Siemens, Erlangen, Germany). The images were transferred to the workstation after processing in the Digital Imaging and Communications in Medicine (DICOM) and planning with the BrainSCAN planning system (versions 3.5 and 5.3, BrainLab, Heimstetten, Germany). The target was drawn based on three planes, as coronal and sagittal reconstructions could be displayed in smaller windows in the same screen. A detailed description of planning is available elsewhere (14). The dedicated linear accelerator used in all patients was a Novalis D-LINAC, dedicated to radiosurgery, which provides mechanical dose delivery to the isocenter with a precision to 0.4 mm. The technique and application of this device have been previously described (15, 16).

Patient outcomes and follow-up

Patient outcomes were reviewed retrospectively following approval from the institutional review board. These were obtained by standardized clinical questionnaire, which included the current state of facial pain, degree of facial numbness on a five-point scale (Table 2), presence of possible clinical complications, and presence or absence of any subsequent procedures. All patient information was collected by two individuals (Z.A.S., A.G.) independent of clinical care.

Facial pain outcomes were modeled upon the outcome scale that we have previously used and that has been established in the literature for pain relief after Gamma knife surgery (12, 17). Facial pain outcomes were graded as excellent (complete pain relief, no medications), good (>50% pain relief with decreased medications or complete pain relief with decreased medications), marginal (minor pain relief), or poor (no change from baseline). Both marginal and poor outcomes were considered failures. Criteria for improvement included a reduction in both severity and frequency of trigeminal pain attacks. Outcomes were assessed at 3 months, 6 months, and 1 year after treatment, and then subsequently at 1-year intervals.

Ten patients (5.6%) were lost to clinical follow-up. Of these patients, nine had idiopathic trigeminal neuralgia and a single patient presented with trigeminal pain following a brainstem stroke. Eight of the patients lost to follow-up were treated in 2002 or before, and only a single patient was lost to follow-up after treatment with 90 Gy using a 50% isodose line (IDL).