Classic TN, first described in the early second century, is characterized by paroxysmal attacks of intense, sharp, stabbing, or electric shock–like pain in trigeminal distributions. In the past 2 decades, SRS has been established as an effective treatment modality for classic TN.\(^6,10,14,16-20,22\) Initial pain relief rates of up to 93% have been achieved in patients with classic TN after SRS.\(^6,7,13,21\) Patients with atypical TN have unilateral pain in the trigeminal distribution that is dull, aching, or burning in nature and is constant or nearly constant. Studies of most radiosurgical and surgical series have shown lower response rates in patients with atypical TN. This study represents the first report of the treatment of atypical TN with frameless CyberKnife stereotactic radiosurgery (SRS).

**Methods.** Between 2002 and 2007, 7 patients that satisfied the criteria for atypical TN and underwent SRS were included in our study. A 6–8-mm segment of the trigeminal nerve was targeted, excluding the proximal 3 mm at the brainstem. All patients were treated in a single session with a median maximum dose of 78 Gy and a median marginal dose of 64 Gy.

**Results.** Outcomes in 7 patients with a mean age of 61.6 years and a median follow-up of 20 months are reported. Following SRS, 4 patients had complete pain relief, 2 had minimal pain relief with some decrease in the intensity of their pain, and 1 patient experienced no pain relief. Pain relief was reported within 1 week of SRS in 4 patients and at 4 months in 2 patients. After a median follow-up of 28 months, pain did not recur in any of the 4 patients who had reported complete pain relief. Complications after SRS included bothersome numbness in 3 patients and significant dysesthesias in 1 patient.

**Conclusions.** The authors have previously reported a 90% rate of excellent pain relief in patients with classic TN treated with CyberKnife SRS. Compared with patients with classic TN, patients with atypical TN have a lower rate of pain relief. Nevertheless, the nearly 60% rate of success after SRS achieved in this study is still comparable to or better than results achieved with any other treatment modality for atypical TN. (DOI: 10.3171/FOC-07/12/E9)

**KEY WORDS** • CyberKnife • stereotactic radiosurgery • trigeminal neuralgia

Abbreviations used in this paper: CT = computed tomography; FIESTA = fast imaging employing steady-state acquisition; GK = Gamma Knife; MVD = microvascular decompression; SRS = stereotactic radiosurgery; TN = trigeminal neuralgia.

**Clinical Material and Methods**

Between May 2002 and December 2006, 104 patients received stereotactic CyberKnife radiosurgery for TN at Stanford University Medical Center. Patients with constant or near-constant pain in the trigeminal distribution that was reported as dull, burning, or aching in character were deemed to have atypical TN. Seven patients fulfilled these criteria and their cases form the basis of our current analysis.

**Radiosurgical Treatment Planning**

Treatment planning for atypical TN was the same as the technique previously described for classic TN.\(^13\) In brief, prior to treatment, patients received 10–12 ml of intrathecal contrast material. Iohexol-enhanced cisternography with
CT scans of 1.25-mm thick contiguous slices was utilized for visualization of the cisternal segment of the trigeminal nerve in 6 of the 7 patients. In the sagittal plane, a 6- to 8-mm length of the trigeminal nerve was included in the treatment volume. A 3-mm segment of nerve at the root entry zone was excluded from the treatment volume. The trigeminal ganglion was delineated as a critical structure to which the dose was minimized. For 1 patient who was treated after January of 2006, FIESTA magnetic resonance images were obtained and fused with 1.25-mm CT slices obtained without administration of a contrast agent. The trigeminal nerve was identified on the FIESTA sequence, and the treatment volume was contoured as just described. The treatment plan was developed using an inverse planning algorithm in which both the minimum and maximum doses to the desired target could be specified. Figure 1 depicts a treatment plan for atypical TN.

Dosage and Treatment Delivery

All patients were treated in a single session with a median maximum dose of 78 Gy (range 73.8–80 Gy) and a median marginal dose of 64 Gy (range 59–66 Gy). The mean conformality index was 2.3 (range 1.9–3.0). The dose to the brainstem was minimized by locating the 50% isodose line outside the brainstem in all patients.

Patients were placed supine on the treatment couch, and a previously constructed custom thermoplastic mask was used for immobilization. Digitally reconstructed images from the CT scan were compared with standard orthogonal skull x-rays during initial registration and periodically during the entire treatment to ensure accurate target acquisition. After registration was confirmed, treatment was carried out in accordance with the radiosurgical treatment plan.

Evaluation of Patient Outcomes

Data regarding pain relief, time to pain relief, and occurrence of new-onset dysesthesias, bothersome numbness, and other complications after SRS were collected. The Boulder–Stanford Pain Scale, as previously described,13 was used to assess pain relief. Pain outcomes were defined and reported as follows: I, excellent pain relief (> 90% pain relief with discontinuation of all medications for TN pain); II, moderate pain relief (> 50% pain relief with some reduction in the use of pain medications); III, minimal pain relief (< 50% pain relief with no change in pain medications); and IV, no pain relief.

Results

Patient Characteristics

Seven patients who underwent CyberKnife SRS for atypical TN were identified and included in the study (Table 1). The mean age at treatment was 61.6 years (range 39–84 years) and 5 of the 7 patients were women. Four patients experienced pain on the left side of the face, while 3 patients experienced it on the right. The pain was in the V2 distribution in 2 patients; in V3 in 1 patient; in V2 and V3 in 2 patients; and in the V1, V2, and V3 distributions in 2 patients.
patients. Prior to our treatment, pharmacological therapy had failed in all 7 cases and the average duration of pain was 3.4 years (range 8 months–10 years). Before treatment, all patients described their pain in the trigeminal distribution as constant or near constant and characterized it as dull, aching, or burning.

**CyberKnife Treatment**

All 7 patients were treated in a single session. A lesion was created in a 6–8 mm segment of the trigeminal nerve, with a mean lesion volume of 0.056 cm³ (range 0.031–0.121 cm³). The mean dose to the margin of the targeted trigeminal nerve segment was 63.6 Gy (range 59–66 Gy), while the mean maximum dose was 77.4 Gy (range 73.8–80 Gy).

**Treatment Outcomes**

Patients were followed for a median of 20 months (range 1.1–33.3 months). Four of the 7 patients had complete pain relief (Boulder–Stanford Pain Scale score of I); 2 patients had minimal pain relief (a score of III); and 1 patient had no pain relief (a score of IV; Table 2). Pain relief was achieved within 1 week in 4 patients and at 4 months in 2 patients. During a median follow-up of 28 months, pain did not recur in any of the 4 patients who had complete pain relief after SRS. Following SRS, 3 of the 7 patients experienced bothersome numbness. One of these 3 patients also had significant dysesthesias requiring pharmacological therapy. No other complications were noted.

**Discussion**

Treatment modalities for the management of TN include medical therapy, ablative procedures, MVD, and SRS. The efficacy of SRS in the treatment of classic TN has been established. Given that atypical TN is uncommon, however, only a few, relatively small studies have reported outcomes in patients with atypical TN after SRS. Our study represents the first report of the treatment of atypical TN via the image-guided CyberKnife SRS system.

In our study, 4 of the 7 (57%) patients who underwent CyberKnife SRS for atypical TN experienced complete pain relief and thus can be described as having had an excellent result. Excellent or good pain relief after GK SRS has been reported in 70–94% of patients with classic TN. Furthermore, we have previously reported a 90% rate of excellent outcomes in patients treated with CyberKnife SRS for classic TN. Therefore, based on this small series of subjects, patients with atypical TN appear to have a lower response rate than patients with classic TN. This finding is consistent with the findings of several other small SRS case series in which good or excellent outcomes were observed in only 9–44% of patients with atypical TN (Table 3). For example, Maesawa et al. reported outcomes after GK SRS in 204 patients with classic TN and 16 patients with atypical features and found a significantly lower rate of pain relief in the patients with atypical TN (82.3% compared with 43.8%, respectively). Interestingly, in the most recently reported and largest case series in which outcomes of patients with atypical TN were evaluated, no discrepancy in response rates between classic TN and atypical TN was reported. Dhople et al. reported outcomes in 35 patients with atypical TN after GK SRS and found good or excellent pain relief in 72% of the patients. They found no statistically significant difference in response rates between patients with classic TN (81%) and those with atypical TN (72%). They did, however, report a trend toward a longer time to pain relief and a shorter duration of pain relief in patients with atypical TN. The reason for the varied response rates (9–72%) in the published studies is not clear, but some of the variation may be explained by differences in the criteria used to define atypical TN.

Authors of previous studies have reported an average period of 5.8 weeks (range 1–24 weeks) between SRS and pain relief. Dhople et al. found a trend toward a longer time to pain relief in patients with atypical TN than in those with classic TN (5.8 weeks compared with 3.0 weeks, respectively). Similarly, Maesawa et al. reported a median time to pain relief of 2 months in patients with atypical TN. In our study, 3 of the 4 patients experienced complete pain relief within 1 week of SRS and 1 patient experienced pain relief at 4 months. Perhaps the longer segment of nerve lesioned in the present study, in comparison with the GK protocols, explains the shorter duration to pain relief. In any case, it is generally recognized that patients who do not respond to SRS within approximately 6 months of treatment have a very small chance of obtaining pain relief thereafter.

Recurrence of pain following initial successful SRS has been reported in 13–50% of patients. In our study, of the 4 patients who had complete pain relief with a follow-up of 33, 30, 26, and 18 months, none had recurrence of

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**TABLE 1**

Characteristics of 7 patients with atypical TN treated with CyberKnife SRS*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Pain Distrib</th>
<th>Duration of Pain (yrs)</th>
<th>Previous Tx†</th>
<th>Onset of Pain</th>
<th>Tx Dose (Gy)</th>
<th>Max Dose (Gy)</th>
<th>Target Vol (cm³)</th>
<th>Length of Nerve Treated (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80, F</td>
<td>V2–3</td>
<td>10</td>
<td>MVD</td>
<td>after MVD</td>
<td>66</td>
<td>79.5</td>
<td>0.037</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>54, F</td>
<td>V2</td>
<td>3</td>
<td>none</td>
<td>idiopathic</td>
<td>66</td>
<td>77.7</td>
<td>0.031</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>67, F</td>
<td>V1–3</td>
<td>1</td>
<td>none</td>
<td>after SRS for CPA meningioma</td>
<td>64</td>
<td>80</td>
<td>0.082</td>
<td>7.5</td>
</tr>
<tr>
<td>4</td>
<td>39, F</td>
<td>V3</td>
<td>2</td>
<td>none</td>
<td>idiopathic</td>
<td>64</td>
<td>78</td>
<td>0.033</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>60, F</td>
<td>V1–3</td>
<td>2</td>
<td>multi glycerol inj</td>
<td>idiopathic</td>
<td>59</td>
<td>73.8</td>
<td>0.04</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>47, M</td>
<td>V2</td>
<td>0.67</td>
<td>none</td>
<td>after acoustic neuroma resection</td>
<td>60</td>
<td>75</td>
<td>0.05</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>84, M</td>
<td>V2–3</td>
<td>3</td>
<td>none</td>
<td>postherpetic neuralgia</td>
<td>66</td>
<td>77.65</td>
<td>0.121</td>
<td>8</td>
</tr>
</tbody>
</table>

* Medical therapy had failed in all 7 cases. Abbreviations: CPA = cerebellopontine angle; Distrib = distribution; inj = injections; multi = multiple; Tx = treatment.
† In addition to medical therapy.
pain. In this regard, the longer segment of nerve lesioned in our protocol compared with the typical GK protocols may be important. In the largest study of atypical TN (median follow-up 29 months), classic and atypical TN were found to recur in 38 and 39% of patients, respectively.4 The authors also noted that pain was less likely to recur in patients who initially experienced excellent pain relief after SRS than in patients who had partial initial pain relief.

The most common complications after SRS include facial numbness and dysesthesias. Eight to 51% of patients with atypical TN have been reported to experience numbness after SRS.4,13,14,18 In our study, 3 patients experienced bothersome numbness. Of the 3 patients experiencing significant numbness, 1 had preexisting numbness and went on to develop significant dysesthesias. One explanation for our higher rate of numbness is that in 2 of the 3 patients with bothersome numbness, a longer segment of nerve was treated with a higher dose of radiation than is used in our current TN protocol. Our previous protocol for TN treated a longer segment of nerve (~7–8 mm) with a higher marginal dose (66–70 Gy). A few years ago, in order to reduce the incidence of dysesthesias and bothersome numbness, we decreased both the length of nerve treated (6 mm) as well as the marginal dose (60 Gy). Currently, we use these radiosurgical parameters to treat all patients with TN (typical and atypical). Interestingly, we did note that all 3 patients who experienced significant postoperative numbness also experienced excellent pain relief. The correlation between numbness and increased pain relief has been previously reported and is attributed to SRS causing axonal degeneration of both myelinated and unmyelinated sensory nerve fibers.3,20,23

Microvascular decompression is effective in producing durable pain relief with minor risk of facial numbness in over 70% of patients with classic TN.1,3,12 However, patients with atypical TN have been reported to have a much lower rate of pain relief after MVD.1,22 Tyler-Kabara et al.24 reported significant pain relief after MVD in 51% of patients with atypical TN and in 80% of patients with classic TN. Li et al.12 found that only 29% of their patients with atypical TN had complete pain relief after MVD. Hence, among patients with atypical TN, the 57% rate of excellent pain relief observed after CyberKnife rhizotomy is as good as or better than the response rates reported after MVD. Therefore, SRS should be considered a potential treatment option in carefully selected patients with atypical TN.

Conclusions

Compared to patients with classic TN, patients with atypical TN treated with CyberKnife rhizotomy appear to have a lower rate of pain relief. However, the nearly 60% rate of success after SRS is still comparable to or better than that achieved with any other modality in the treatment of atypical TN. Furthermore, frameless CyberKnife SRS appears to be a safe and effective treatment modality for atypical TN.

Acknowledgments

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References

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TABLE 2
Outcomes in 7 patients with atypical TN following treatment with CyberKnife SRS

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Pain Relief</th>
<th>Time to Pain Relief</th>
<th>Post-SRS bother-some Numbness</th>
<th>Recurrence of Pain</th>
<th>Off All Pain Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>complete</td>
<td>w/in 1 wk</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>complete</td>
<td>w/in 1 wk</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>complete</td>
<td>w/in 1 wk</td>
<td>yes with dysesthesias</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>complete</td>
<td>4 mos</td>
<td>no</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>5</td>
<td>none</td>
<td>NA</td>
<td>no</td>
<td>NA</td>
<td>no</td>
</tr>
<tr>
<td>6</td>
<td>minimal</td>
<td>4 mos</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>7</td>
<td>minimal</td>
<td>w/in 1 wk</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
</tbody>
</table>

* NA = not applicable.

TABLE 3
Summary of previous studies of SRS for atypical TN

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Pts w/ Atypical TN</th>
<th>No. of Pts w/ Significant Pain Relief After SRS</th>
<th>Recurrence Rate (%)</th>
<th>Rate of Numbness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rogers et al., 2000</td>
<td>11</td>
<td>1 (9.1%)</td>
<td>not reported</td>
<td>9.1</td>
</tr>
<tr>
<td>Muesawa et al., 2001</td>
<td>16</td>
<td>7 (43.8%)</td>
<td>13.6</td>
<td>10.2</td>
</tr>
<tr>
<td>Dhople et al., 2007</td>
<td>32</td>
<td>23 (71.9%)</td>
<td>39</td>
<td>19</td>
</tr>
</tbody>
</table>
CyberKnife rhizotomy for trigeminal nerve pain


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