Stereotactic gamma knife surgery for trigeminal neuralgia: detailed analysis of treatment response

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Objective. The purpose of this study was to assess the durability and completeness of pain relief in patients treated using stereotactic gamma knife surgery (GKS) for trigeminal neuralgia (TN).

Methods. Thirty-eight patients with refractory TN were treated with stereotactic GKS. All patients received a prescription radiation dose of 35, 40, or 45 Gy to the 50% isodose surface through a 4-mm collimator helmet. The group was assessed regularly based on physician-directed interviews for a median follow up of 24 months (range 6–27 months). Pain relief was classified as excellent (no pain without medication), good (well-controlled pain with continued medication), fair (decreased but residual pain with continued medication), or poor (unimproved or increased pain with the same or increased medication).

Three months after treatment, pain relief was good or excellent in 71% of patients. By 24 months post-GKS, 50% of the original cohort had poor pain relief, 21% continued to have either excellent or good relief, 3% had fair relief, and 26% had not reached the 24-month follow up. Based on their status at the last follow up, 29% of patients had excellent and 16% had good pain relief. Thirty-seven percent experienced facial numbness, which was dose related. In addition, there was a significantly higher rate of complete pain relief in patients who had facial numbness following treatment (p = 0.003).

Conclusions. Stereotactic GKS is an effective treatment in patients with TN; however, the durability of pain relief and the time to treatment response are limiting factors. As with other types of ablative treatment, facial numbness is strongly associated with better treatment response.

Key Words • facial pain • gamma knife surgery • radiosurgery • tic douloureux • trigeminal neuralgia • pain

TRIGEMINAL neuralgia is a paroxysmal pain syndrome that frequently arises in association with vascular contact between arteries or veins and the trigeminal nerve at the REZ.29,10,15 Patients with this condition may eventually fail to respond to medical treatment, thus necessitating invasive measures such as MVD and ablative procedures such as RFR, glycerol rhizolysis, stereotactic GKS, percutaneous balloon microcompression, and various peripheral nerve blocks. Stereotactic radiosurgery with x-rays was first used to treat TN in 1951. Subsequently, treatment with cobalt-60 as a source of gamma radiation was reported in 1971. Although radiosurgery has emerged as a minimally invasive mode of treatment for TN with few complications,18,21,29,34 questions remain regarding its efficacy, the patient subgroups best served by the treatment, and the durability of the pain relief provided. Several studies have demonstrated complete pain relief following stereotactic GKS in 56 to 64% of patients on a long-term basis without medication.17,18 A proportion of patients, however, does not respond to stereotactic GKS or experiences recurrence of pain after an initial treatment response.3 We report on our experience in a cohort of 38 patients who underwent stereotactic GKS for the treatment of TN. In an effort to determine the durability of pain relief and the factors associated with an optimal treatment response, we assessed our patients directly by physician interview and examination every 3 months during a median follow-up period of 24 months after therapy.

Clinical Material and Methods

Patient Population

Between November 1998 and March 2002, 42 patients with facial pain underwent stereotactic GKS at Roswell Park Cancer Institute in Buffalo, NY. All patients included in this investigation had TN with typical clinical symptoms (Table 1). The majority of patients had been treated with more than one pharmaceutical agent and all were refractory to medical treatment. Patients with atypical facial pain and TN associated with multiple sclerosis or tumor were excluded, thus leaving 38 patients for the final analysis. In addition to medical therapy, 11 patients (29%) had previously undergone interventional procedures. Following stereotactic GKS, patients who experienced no treatment response or
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A recurrence of intolerable pain were considered to have had treatment failure. All who underwent additional surgical intervention or repeated GKS were considered to have treatment failure, regardless of whether the treatment was initially effective. Note that three patients underwent a second stereotactic GKS procedure.

Radiosurgical Technique

The radiosurgical procedures were performed at a single center (Roswell Park Cancer Institute) by using a Leksell Model B gamma knife unit (Elekta Instruments, Atlanta, GA). The stereotactic headframe (Elekta Instruments) was applied following administration of a local anesthetic agent together with light sedation (2 mg intravenous midazolam). Thirty-five patients were treated using one isocenter and three patients were treated using two isocenters. Doses of 35, 40, or 45 Gy were prescribed for the 50% isodose surface and were delivered through a 4-mm collimator helmet. In each case, the REZ was targeted so that the 30% isodose surface contacted the edge of the pons. The output factor for the 4-mm collimator was changed from 0.80 to 0.87 after the third patient. This adjustment was made based on revised measurements reported in the literature.22

Imaging Parameters

Imaging of the trigeminal nerve was performed using a 1.5-tesla MR imaging unit (Signa Horizon 5.8; GE Medical Systems, Milwaukee, WI). Localization was performed based on T1-weighted images, and targeting was accomplished with T1-weighted and fast–spin echo T2-weighted axial and coronal images of the trigeminal nerve. The parameters for the axial T1-weighted images were TR 400 msec; TE 11 msec; excitations 2; matrix 256 \times 192; FOV 15 cm; section thickness 1 or 2 mm; and no section gap. The parameters for axial fast–spin echo T1-weighted images were TR 3600 msec; TE 85 msec; excitations 3; matrix 256 \times 192; FOV 16 cm; section thickness 1.5 or 2 mm; and no section gap. Coronal sections of 3-mm thickness were obtained with 1-mm gaps. Imaging was performed from the lower pons to the dorsum sellae. The T1-weighted images were repeated after administration of intravenous gadopentate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) at a dose of 0.2 ml/kg. Flow compensation pulse was added to the contrast-enhanced imaging sequences. The T1-weighted images with an FOV of 25 cm were obtained to accommodate the fiducial markers required for stereotactic GKS.

Patient Follow-Up Evaluation

Follow-up data were obtained by direct physician interview and examination of each patient every 3 months during clinic visits (Fig. 1). Information obtained during each encounter included the following: presence or absence of pain, degree of pain relief, continuation of medical therapy (both dose and number of different medications), need for further interventional procedures, and presence of any side effects (including facial numbness, and paresthesia). Patients’ families were interviewed to determine the presence or absence of specific pain behaviors as well.

Response to treatment was categorized as excellent, good, fair, or poor. Patients with an excellent treatment response had complete resolution of their pain without medication. Within this category, we distinguished between those with complications and those without. Because the side effects of treatment were generally rated as acceptable by patients in light of pain relief, the presence of complications was not used to downgrade a patient’s result. Patients with a good outcome included those whose pain was well-controlled but who continued on medical therapy. Patients with residual facial pain that was significantly, but not completely, reduced in intensity and who managed to remain off medications were also considered to have a good outcome. Those who experienced modest pain relief and who continued on medications were categorized as having a fair outcome. Patients assigned a poor outcome had treatment failure and included all those who either experienced no pain relief or who required subsequent invasive therapy (including a second stereotactic GKS procedure). Furthermore, those with increased or different medical therapy or hospitalization for pain control were included in the poor
outcome category. Once a patient was placed in the poor outcome group he or she remained there for the entire follow-up period, regardless of the outcome of additional invasive procedures or significant modifications in drug therapy. No patient was considered to have treatment failure until at least 3 months had elapsed since stereotactic GKS, and no patient was lost to follow up.

Statistical Analysis

Univariate analysis was used to assess variables predictive of complete response on long-term follow up as well as those predictive of poor initial response to stereotactic GKS. The following variables were assessed: patient age, sex, pre-GKS duration of pain, number of trigeminal divisions affected, laterality (sidedness) of pain, prior surgical interventions, prior ablative procedures, radiation dose, post-treatment facial numbness, and paresthesia. With categorical data (nominal or ordinal) the two-tailed Fisher exact test was used for group comparisons. The unpaired Student t-test or analysis of variance was used for continuous variables. The response analyses were first performed by right imputation of the 3-month interval follow-up data, followed by nonparametric actuarial analysis by using the Kaplan–Meier product-limit method. The durability of four different levels of pain relief was separately assessed in ascending order: 1) any pain relief; 2) complete pain relief with or without medication; 3) complete pain relief with no medication, with or without complication; and 4) complete pain relief with no medication and no complication. Durability of pain relief was further assessed as a function of the presence or absence of new facial numbness. The log-rank test was used to compare durability of pain relief between groups. All statistical analyses were performed using commercially available software (Statview, version 5.01 for the Macintosh; SAS Institute, Cary, NC; and InStat, version 2.01 for the Macintosh; Dr. Harvey Motulsky, GraphPad Software, Inc., San Diego, CA). In all cases, two-tailed probability values were calculated and statistical significance was defined as a probability value less than or equal to 0.05.

Results

Patient Population

Pertinent characteristics of the study population are summarized in Table 1. Of 38 consecutive patients with TN who underwent stereotactic GKS, 16 (42%) were men and 22 (58%) were women. The median age at the onset of symptoms was 64 years (range 20–84 years). The median age at treatment was 70 years (range 29–88 years). The median duration of pain before GKS was 6.5 years (range 0.3–31 years). Twenty-six patients (68%) had right-sided pain and 12 (32%) had left-sided pain; no patient had bilateral pain. The majority of patients had pain in the V2 and V3 of the trigeminal nerve; one (3%) had involvement of V1 only, two (5%) V2 only, seven (18%) V3 only, 13 (34%) V2 and V3, 12 (32%) all three divisions, and three (8%) V1 and V2.

Pain Response and Durability of Pain Relief

Following stereotactic GKS, pain relief was recorded with direct serial assessment by the treating neurosurgeon at 3-month intervals. The greatest number of patients with excellent pain relief was noted at 3 months (Fig. 1). At this time point, 70% had either excellent or good pain relief (44 and 26%, respectively), whereas 21% had treatment failure. Six months following treatment, 61% of patients had

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Fig. 1. Graph of follow-up assessments of pain relief at 3-month intervals following stereotactic GKS for TN.
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excellent or good pain relief (37 and 24%, respectively). By 24 months post-GKS, only 21% continued to experience excellent or good pain relief (16 and 5%, respectively), and 50% of the original cohort had treatment failure. Three percent of the patients had fair pain relief, and 26% had not reached the time point of 24 months post-GKS.

Factors Associated With Pain Response

Several pretreatment predictors of poor response to stereotactic GKS became apparent (Table 2), including two or more previous surgical procedures (including MVD) for TN (p = 0.004, OR = 29), a previous ablative procedure (p = 0.012, OR = 14), and an age less than 70 years at the time of GKS (p = 0.049, OR = 6). Men with right-sided TN had a greater chance of responding to stereotactic GKS than the group as a whole (p = 0.032, OR = 8). In contrast, women with right-sided pain were less likely to respond to GKS than the group as a whole (p = 0.039, OR = 7).

Two factors were significantly associated with durable pain relief. New trigeminal nerve dysfunction (numbness or paresthesia) post-GKS was strongly associated with a better long-term response (p = 0.013, OR = 11). The degree of pain relief achieved was directly related to the development of new facial numbness following treatment (Fig. 2). In general, patients with facial numbness had a better chance of obtaining benefit from the procedure than those without numbness (Fig. 3). Durability of pain relief was also better in those who had trigeminal nerve dysfunction (Fig. 4). Sixty-four percent of patients with new numbness had excellent pain relief without medication at 18 months, whereas only 11% without numbness experienced excellent relief. The relationship between numbness and pain relief was most striking in the group of patients that experienced the greatest degree of pain relief. Hence, patients with excellent pain relief were significantly more likely to experience new facial numbness (p = 0.003, log-rank test). This relationship was evident at multiple time points throughout the follow-up period. Although there was a strong indication that numbness was more common in those who obtained any degree of pain relief and in those with good pain relief, these associations were less statistically significant (p = 0.043 and p = 0.089, respectively).

Radiation Dose and Treatment Response

In this study, we were unable to detect a significant difference in pain relief based on radiation dose. There was no significant difference in the percentage of patients who obtained any measurable degree of pain relief (excellent, good, or fair) regardless of whether they received 35 or 45 Gy (p = 0.32). Among patients with complete pain relief with or without continued medication, there was no difference in the response to the treatment based on radiation dose (p = 0.45). There was an indication of greater durability of pain relief (continued complete response at 18 months without medication) in those who received a dose of 45 Gy, although this trend did not reach statistical significance.

**Fig. 2.** Graph depicting the percentage of patients with complete pain relief (without medication). Patients with new facial numbness have a significantly higher rate of pain relief.

**Fig. 3.** Graph demonstrating results of a Kaplan-Meier analysis of the relationship between pain relief and the development of new trigeminal nerve dysfunction following stereotactic GKS. Pain relief is strongly associated with the development of postradiosurgical numbness (p = 0.003). GKSR = stereotactic GKS.

**Fig. 4.** Graph depicting results of an actuarial analysis of pain relief durability by initial degree of pain relief.
Radiation Dose and Complications

Although the relationship of radiation dose to the degree and durability of pain relief is uncertain, dose did have a direct relationship to complication rate. Thirty-seven percent of patients experienced minor complications, including some degree of facial numbness (37%) or facial paresthesia (13%). All patients with facial paresthesia also suffered facial numbness. No patient experienced either loss of the corneal reflex or anesthesia dolorosa. Trigeminal motor function was not routinely tested. The median time to numbness was 8 months (range 3–18 months). Patients who had received a radiation dose of 45 Gy had a higher rate of complications than those who had received a dose of 35 Gy. Only three (23%) of 13 patients receiving a dose of 35 Gy suffered complications (median follow up of 27 months). In contrast, nine (60%) of 15 patients who received a dose of 45 Gy experienced complications (median follow up of 24 months). These results, although not statistically significant because of the small number of patients, indicate a linear correlation between radiation dose and complication rates and are similar to those reported in other series (Fig. 5). Two (20%) of 10 patients treated with a 40-Gy dose experienced complications (median follow up of 6 months). Given that this subgroup was mostly treated later in the series and that numbness generally occurred much later than the treatment response, there was insufficient long-term follow-up data to determine the exact rate of complications or whether these patients had intermediate levels of sensory complications. All patients with numbness or paresthesia stated that their adverse symptoms did not significantly interfere with daily life and were acceptable in light of the pain relief provided.

Discussion

Pain Response and Durability of Pain Relief

Pain relief is the most important treatment outcome for patients suffering from TN. Although often producing initial pain relief, stereotactic GKS has definite rates of pain recurrence and morbidity. Early data on the procedure revealed some degree of pain relief in more than 80% of patients together with a very low risk of trigeminal nerve dysfunction.17,18,34 Rates of recurrence were reportedly low and ranged from 6 to 19%, which compared quite favorably to those reported for other surgical interventions.26,28,34 With most follow-up periods ranging from 1 to 12 months, the percent of patients becoming pain free following a single stereotactic GKS procedure ranges from 35 to 47%.6,11,26 In comparison, 70% of patients have excellent facial pain control 10 years following MVD and 75% have similar results 15 years after RFR.11 Thus, when the published results are closely examined, it appears that the efficacy of stereotactic GKS is not directly comparable to either MVD or other available percutaneous procedures.2,3,26,31

Results of previous series on stereotactic GKS indicate that recurrence of TN remains a major challenge.2,8,11-14 In a series of 220 patients reported on by Maesawa, et al.,19 complete pain relief was achieved in 64.9% of patients at 6 months, 70.3% at 1 year, and 75.4% at 33 months. Atypical facial pain was present in 7.5%, and 61.4% had previously undergone surgery before stereotactic GKS. Only 55.8% experienced complete or partial pain relief 5 years after an initial favorable response. The rate of obtaining and maintaining complete pain relief was 60% at 2 years and 40% at 5 years. In a series of 54 patients described by Rogers, et al.,29 96% experienced initial improvement of their pain during a mean follow up of 12 months. Only 41% were able to stop medications, and the overall recurrence rate was 21% (median time to recurrence 6.7 months [range 1–20 months]). The actuarial 2.5-year pain recurrence rate for the entire group was 36%. Note that 100% of patients with new numbness following radiosurgery experienced pain relief, compared with 35% of patients without new numbness. In a report on a mult-institutional study of 50 patients with a median follow up of 18 months, Kondziolka, et al.,17 described 39 patients (78%) with excellent pain control and 18 (36%) with good pain control (50–90% pain reduction). At the 2-year follow up, 54% remained pain free and 88% had good pain control. In another series with a mean follow up of 9.6 months (range 2–29 months), Kondziolka and colleagues18 reported on 37% of patients with excellent pain control and 41% with 50 to 90% pain relief. Subsequently, these same authors published a follow-up study18 of 106 patients, 77% of whom maintained pain control above 50% at a median follow up of 18 months (range 6–48 months). In a series of 112 patients, Petit, et al.,34 reported 77% pain relief at a median follow up of 3 weeks. Actuarial analysis
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demonstrated 1-, 2-, and 3-year recurrence rates of 23, 33, and 39%, respectively. In a series of 51 patients, Young, et al., reported a 74.5% rate of complete pain relief following a latency period of 1 day to 4 months. After a mean follow up of 16.3 months, 80.4% remained pain free or had marked pain reduction. In a subsequent update, these authors reported on 435 patients with a median follow up of 4.8 years (range 1.5–9 years). At the 6-month follow up, 397 patients (91%) had excellent (64%) or good (27%) results. At the last follow up, pain recurred in 62 patients (14%), leaving 335 (77%) with excellent or good results. Recently, Massager, et al., reported on a series of 47 patients with a mean follow up of 16 months. These authors used a central radiation dose of 90 Gy in all patients together with a target immediately posterior to the gasserian ganglion. Six months after radiosurgery, pain relief was excellent in 68%, good in 15%, fair in 6%, and poor in 11% of the patients. At 42 months, the actuarial curve displayed a 59% rate of excellent pain control and a 71% rate of excellent or good pain control. Although the rates of initial pain relief in patients treated at our facility were similar to those reported by others, only one third of the evaluable patients in the original cohort had an acceptable degree of pain relief when assessed at 24 months after stereotactic GKS.

Pitfalls and Selection Bias in Stereotactic GKS Series

Stereotactic GKS outcomes vary considerably with respect to several factors. A lack of standardization of these factors can potentially be misleading when comparing different studies. For example, although several authors use an output factor of 0.87 with the 4-mm collimator helmet, others continue to produce treatment plans featuring a factor of 0.80. Given that the value of the output factor has a direct effect on the delivered dose, ambiguity in reporting the actual delivered dose may arise. Similarly, there is significant variation in the way that the durability of treatment response has been reported, with most authors describing the percentage of patients with continued pain relief either at the last follow up or on an actuarial basis. Some authors have included in the excellent group patients who are pain free with or without medication, whereas others have included in the excellent outcome group only patients having a greater than 90% reduction in pain. Thus there may be difficulty in comparing study data. Several other factors contribute to problems in evaluating methods in the stereotactic GKS literature. Numerous investigators have mostly reported pain control at a limited number of time points without much consistency between studies, rather than at specific and serial time intervals. Thus, a clear picture of the degree and durability of treatment response is hard to derive from the literature.

A number of authors have based their results on subjective outcome measures, for example, mailed questionnaires or telephone interviews. Although this methodology might be satisfactory in following up TN, for which pain relief can be defined in terms of decreasing severity and number of attacks, it is less accurate for evaluating possible side effects that are best detected on direct neurological examination. In our series, new numbness was observed at a median follow up of 8 months (range 3–18 months) following stereotactic GKS. This finding concurs with the results of Maesawa, et al., who reported a median time to the development of paresthesia of 8 months (range 1–19 months). Thus, the true complication rates may have been underestimated in series with short-term follow ups. Our results indicate that 1.5 years should elapse before accurately defining the subgroup of patients with side effects. As such, it is difficult to draw firm conclusions about complication rates based on studies with relatively short-term follow ups.

The variable natural history of TN also increases the difficulty in analyzing results of case series. Trigeminal neuralgia is characterized by periods of partial or complete spontaneous remission in many patients. This characteristic waxing and waning as well as the subjective nature of symptoms like pain, sensory loss, and paresthesia points to the necessity of conducting prospective studies for accurate evaluation of results. In addition, patient selection should be considered when comparing results of stereotactic GKS. Most GKS series include patient groups with a high frequency of prior failed surgical interventions and pretreatment trigeminal deficits. In addition, most patients undergoing this treatment modality are elderly, and several series have included patients with typical and atypical pain as well as those with mass lesions impinging on the trigeminal nerve. Furthermore, stereotactic GKS series may not include patients with the most severe symptoms. Given that time to treatment response is usually measured in weeks, patients with a TN crisis may be selected to undergo other techniques that provide faster responses.

Predictors and Prognostic Factors for Pain Relief

Several factors have been reported to be associated with a better response to stereotactic GKS, including the absence of multiple sclerosis, greater radiation dose, no previous surgery, absence of atypical features, and proximity of the isocenter to the brainstem edge. Kondziolka and colleagues examined the influence of radiation dose on procedural safety and efficacy. They demonstrated a relationship between dose and efficacy but no relationship between dose and the incidence of facial numbness. A radiation dose of at least 70 Gy (35 Gy to the 50% isodose surface) was associated with a better outcome than were lower doses. In a series of 54 patients, Rogers, et al., described five patients (9%) with new facial numbness who were all pain free after radiosurgery, compared with only 35% of 49 patients without facial numbness. These authors also found that patients with classical TN were more likely to have no need of medications than were those with atypical features: 49% (21 of 43) compared with 9% (1 of 11), respectively. In a series of 179 patients, Brisman, et al., reported 41% with an excellent outcome (no pain with no medication) and 17% with a good outcome (90–100% pain relief with medication). The best prognosis was found in patients without prior surgery who had evidence of contact between blood vessels and the trigeminal nerve on high-resolution MR imaging studies (35 [60%] of 58 patients had an excellent outcome). Only 39 (32%) of the 122 remaining patients achieved this level of pain relief. In the same series, 16 (94%) of 17 patients who had experienced facial numbness had an excellent outcome, compared with 58 (36%) of 163 patients who had not suffered numbness (p < 0.0001). Other study data have confirmed the association between new trigeminal dysfunction and the achievement and maintenance of pain relief after stereotactic GKS. Con-
versely, the low rate of facial sensory dysfunction with stereotactic GKS has been implicated in the lower rate of complete pain relief with this technique.

Other treatment factors have been reported to be associated with better stereotactic GKS outcomes. Brisman and Mooi\textsuperscript{1} reported that close proximity of the isocenter to the brainstem is associated with a greater chance of an excellent outcome at 6 and 12 months follow up. It has also been asserted that patients with TN who are treated using stereotactic GKS as primary management have better pain relief than those treated using the procedure as secondary management. Vascular contact with the trigeminal nerve revealed on MR imaging and the absence of preoperative sensory disturbance may also portend a favorable response to stereotactic GKS.\textsuperscript{5,10}

The correlation between trigeminal nerve dysfunction and the success rate of stereotactic GKS has been noted by several authors.\textsuperscript{25,26,31} According to Pollock, et al.,\textsuperscript{26} higher doses of radiation are associated with an increased risk of trigeminal nerve dysfunction as well as with a better outcome. To elucidate the imaging characteristics of TN following stereotactic GKS and to examine its relationship to treatment response, we previously reported on a series of 22 patients who had undergone MR imaging with intravenous contrast from 6 weeks to 6 months following the radiosurgical procedure.\textsuperscript{1} Enhancement of the target site within the fifth cranial nerve was demonstrated in 77.3\% of cases. There was no statistically significant association between postradiosurgical contrast enhancement of the REZ and the likelihood of obtaining an initial treatment response. In fact, patients with good or excellent treatment responses were as likely to have enhancement of the nerve as patients with fair or poor treatment responses.

In the current study, we identified several predictors of a poor initial response to stereotactic GKS, including more than two previous procedures for TN and a younger patient age (< 70 years). In addition, women with right-sided pain tended to respond less well than the group as a whole. In contrast, men with right-sided pain had a statistically better chance of obtaining a durable response. Individually, neither sex nor sidedness of pain was associated with initial treatment response or durability. Although difficult to explain, this same observation was made in a large series of patients who had undergone MVD.\textsuperscript{12}

\textit{Complications of Stereotactic GKS}

The clinical outcome following ablative treatment for TN is assessed in terms of the degree and durability of pain control along with the presence or absence of complications such as facial numbness, paresthesia, masseter weakness, and anesthesia dolorosa. In several clinical series, the occurrence of facial numbness ranged from 6 to 66\%.\textsuperscript{17–19,25,26} Only a few authors have indicated that complications were troublesome to patients.\textsuperscript{5,14,15,21,26} In a series of 33 patients with a mean follow up of 13 months (range 3 to 36 months), Matsuda, et al.\textsuperscript{25} reported a 17.1\% complication rate. The authors reported seven patients (21\%) with facial numbness and three patients (9\%) with dry eye and diminution or absence of the corneal reflex. Pollock, et al.\textsuperscript{26} reported on the association between a high radiation dose and an increased risk of trigeminal nerve dysfunction. Fifty-four percent of the patients treated with 90 Gy radiation (central point) experienced a trigeminal nerve deficit, whereas only 15\% of those treated with 70 Gy had such a deficit. In the present series, 37\% of patients experienced complications directly attributable to stereotactic GKS. All of these patients experienced some degree of facial numbness and 13\% had facial paresthesia. We used a dose range of 35 to 45 Gy prescribed to the 50\% isodose surface and adjusted for the output factor changes from 0.80 to 0.87. Three (23\%) of 13 patients who had received a radiation dose of 35 Gy experienced complications, whereas nine (60\%) of 15 patients who had received 45 Gy experienced facial numbness. Paresthesia was severe in only one patient, who required treatment with gabapentin. All other patients indicated that their sensory loss and paresthesias were mild to moderate. These deficits did not appear until months after pain relief had been achieved. Our complication and failure rates were similar to those reported by Pollock, et al.\textsuperscript{25} The rates of facial numbness relative to dose were also similar to those reported in other series.\textsuperscript{12,26,30}

The serial 3-month follow up in all of our patients is unique among stereotactic GKS studies. Several investigators have reported pain relief at the last follow up based on actuarial analysis, mailed questionnaires, and telephone interviews. In addition to reporting subjective results at one point in time, rather than serially over time, this last follow up was poorly defined. Our study is different in terms of reporting more comprehensive data based on serial assessment through direct physician interviews. We believe that direct serial follow up provides a more complete picture of treatment response for a condition that is notoriously variable in nature. This type of evaluation also helps to determine the true rate of complications, which require objective neurological testing to be detected fully.

Most of the patients with recurrent pain in our study subsequently underwent further interventional procedures, including MVD in four cases. Only three patients underwent a second stereotactic GKS procedure, making any conclusions about the value of repeating this surgery impossible. Nonetheless, recurrence of facial pain continues to pose a difficult clinical challenge, as illustrated by recent reports of several clinical studies on repeated stereotactic GKS.\textsuperscript{14,23,25,30}

\textbf{Conclusions}

Stereotactic GKS is one of the least invasive treatment options for patients with TN. Although MVD remains the treatment of choice for this disease entity, stereotactic GKS is a safe and effective technique especially in older patients with significant comorbidities that are refractory to medical therapy. Although the initial response rates are comparable to those of other ablative procedures, close serial follow up reveals that the durability of the treatment response is limited, with half of all patients experiencing treatment failure within 24 months after stereotactic GKS. The time interval from treatment response to the low durability of pain relief continue to represent major limiting factors. As with other ablative techniques, our results strongly indicate that obtaining excellent pain relief may require the acceptance of some degree of facial numbness. Nevertheless, the technical factors responsible for producing numbness, other than radiation dose, are not as clearly defined, or perhaps as controllable, as for other ablative techniques such as RFR.
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References