Gamma knife radiosurgery for thalamotomy in parkinsonian tremor: a five-year experience

CHRISTOPHER M. DUMA, M.D., DEANE B. JACQUES, M.D., OLEG V. KOPOYEV, M.D., PH.D., RUFUS J. MARK, M.D., BRIAN COPCUTT, PH.D., AND HALLEK. FAROKHI, B.S.

The Neurosciences Institute and Department of Radiation Oncology, Good Samaritan Hospital, Los Angeles, California

Object. Certain patients, for example, elderly high-risk surgical patients, may be unfit for radiofrequency thalamotomy to treat parkinsonian tremor. Some patients, when given the opportunity, may choose to avoid an invasive surgical procedure. The authors retrospectively reviewed their experience using gamma knife radiosurgery for thalamotomies in this patient subpopulation: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Methods. Radiosurgical nucleus ventralis intermedius thalamotomy using the gamma knife unit was performed to make 38 lesions in 24 men and 10 women (median age 73 years, range 58–87 years) over a 5-year period. A median radiation dose of 130 Gy (range 100–165 Gy) was delivered to 38 nuclei (four patients underwent bilateral thalamotomy) using a single 4-mm collimator following classic anatomical landmarks. Twenty-nine lesions were made in the left nucleus ventralis intermedius thalamus for right-sided tremor. Patients were followed for a median of 28 months (range 6–58 months). Independent neurological evaluation of tremor based on the change in the Unified Parkinson’s Disease Rating Scale tremor score was correlated with subjective patient evaluation. Comparison was made between a subgroup of patients in whom “low-dose” lesions were made (range 110–135 Gy, mean 120 Gy) and those in whom “high-dose” lesions were made (range 140–165 Gy, mean 160 Gy) for purposes of dose–response information.

Four thalamotomies (10.5%) failed, four (10.5%) produced mild improvement, 11 (29%) produced good improvement, and 10 (26%) produced excellent relief of tremor. In nine thalamotomies (24%) the tremor was eliminated completely. The median time to onset of improvement was 2 months (range 1 week–8 months). Concordance between an independent neurologist’s evaluation and that of the patient was statistically significant (p < 0.001). Two patients who underwent unilateral thalamotomy experienced bilateral improvement in their tremor. There were no neurological complications. There was better tremor reduction in the high-dose group than in the low-dose group (p < 0.04).

Conclusions. Although less effective than other stereotactic techniques, gamma knife radiosurgery for thalamotomy offers tremor control with minimal risk to patients unsuited for open surgery.

KEY WORDS • thalamotomy • Parkinson’s disease • radiosurgery • gamma knife

THE use of stereotactic radiosurgery for the treatment of functional disorders dates back as far as 1951, when the father of current day gamma knife radiosurgery, Lars Leksell, experimented with an orthovoltage x-ray tube attached to his stereotactic arc-centered system to treat trigeminal neuralgia.13 Difficulties in precise targeting for functional disorders without physiological feedback, however, caused interest in this technique to wane.

By the 1980s, radiofrequency thermocoagulation of various targets within the ventrolateral thalamus had become the preferred method for the surgical amelioration of movement disorders related to Parkinson’s disease (PD).2,12,19 By this time the prototype gamma unit developed in 1968 had been used for years to treat arteriovenous malformations and trigeminal neuralgia, and more investigators had acquired a sound knowledge of the radiobiology of single fraction radiosurgery. However, no means existed to monitor intraoperative physiological feedback; and thus experience with functional radiosurgery began slowly.1,4,25

There is a subgroup of patients with PD who have conditions that predispose them to risk from invasive stereotactic neurosurgery. These are patients who are receiving a course of anticoagulant drugs, have respiratory or cardiac disease, are very elderly, or are poor risks in general for invasive surgery. In addition, some patients may choose a less invasive alternative when offered the option. Radiosurgery does not involve opening of the cranium or incisions. The risk of hemorrhage from passing an electrode to the depths of the thalamus is eliminated and so is the potential risk of meningitis from operative infection. We believe that for these reasons stereotactic radiosurgical thalamotomy has value in a small subgroup of patients. Our 5-year experience using gamma knife radiosurgery
for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgical lesions was discussed.

between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.

Clinical Material and Methods

Patient Selection

Between March 1991 and December 1996, 34 patients (24 men and 10 women) with disabling tremor due to PD that was refractory to medical therapy underwent stereotactic radiosurgery using the 201-source 60Co gamma knife radiosurgery for thalamotomy in 34 patients is described and a comparison between “low-dose” radiosurgical lesions and “high-dose” radiosurgical lesions is discussed.

This retrospective review represents the largest reported series of patients who have undergone gamma knife radiosurgery for thalamotomy with the longest median follow up. Included in this review are seven patients described by us in a previous communication.23 The goals of our study were: 1) to determine the efficacy of the procedure; 2) to see if there is a dose–response relationship; 3) to review the radiological findings of radiosurgical lesioning; and 4) to assess the risks of complications.
activity,” “activity by history,” “time to walk 20 feet,” and “20-second time tests.” These were analyzed using the paired two-tailed Student t-test. Subjective assessment of visual status and cognitive function was obtained from the patient and the examining neurologist.

Mild improvement was categorized as a change of one UPDRS grade at each independent neurologist evaluation and a subjective patient response indicating a 1 to 33% improvement. Good improvement was categorized as a change of two UPDRS grades at each neurological evaluation and a subjective patient response indicating a 34 to 66% improvement. Excellent improvement was categorized as a change of three UPDRS grades and a subjective patient response indicating a 67 to 99% improvement (Table 2).

Follow-up MR imaging was performed at 3-month intervals for the first 6 months and then at 6-month intervals thereafter. Magnetic resonance imaging protocols included 2-mm high-resolution axial and coronal T₁- and T₂-weighted images with and without gadolinium enhancement. Differences in the MR imaging lesion size between the low-dose (120 Gy) and high-dose (160 Gy) groups were analyzed using the unpaired t-test, analysis of variance, and the Wilcoxon nonparametric test.

**Results**

**Tremor Relief**

Clinical and radiological follow-up periods ranged from 6 to 58 months (median 28 months). Changes in clinical tremor as determined by the UPDRS delta score assigned by the neurologists and by the subjective patient scoring were highly correlated: 0.89 (Pearson correlation coefficient, p < 0.001).

After thalamotomy, no change in tremor occurred in four patients (10.5%), mild improvement was seen in four (10.5%), good improvement was seen in 11 (29%), and excellent improvement in 10 (26%). In nine patients (24%), the tremor was eliminated completely. The high-dose thalamotomy lesion was more effective in reducing tremor (78% mean improvement) than the low-dose lesion (56% mean improvement) (p < 0.04, Wilcoxon nonparametric test; Fig. 2).

The median time to onset of improvement was 2 months (range 1 week–8 months). Two patients who underwent unilateral thalamotomy experienced bilateral improvement in their tremor. Two patients who had initial improvement in their tremor, but who eventually returned to baseline at their follow-up examinations, were included in the treatment failure group. All other patients maintained their level of improvement throughout the course of the follow up. The four patients who received bilateral thalamotomies separated by a 6-month interval experienced no subjective cognitive or performance changes other than improvement in their tremors.

Seven patients underwent formal testing of overall function. After gamma knife radiosurgery for thalamotomy, the observed activity scores of the patients were improved (p < 0.002), as were the activity by history scores (p < 0.05). The time to walk 20 feet scores and the 20-second timed test scores did not statistically differ between patients.

There were no neurological complications. No objective adverse changes in visual fields or subjective changes in cognitive function or performance occurred as a result of the treatment.

**Radiological Findings**

Magnetic resonance imaging revealed a circumscribed spherical lesion that enhanced with administration of
The average T₁-weighted lesion size was not different for the low- and high-dose groups and ranged from 6 to 22 mm (mean 9.2 mm) at a median of 6 months follow-up time. This lesion also persisted on later MR images (Fig. 3). Although there was a trend toward more edema in the high-dose treatment group, the differences in the T₁- and T₂-weighted images of the thalamic lesions between the two groups were not significant (Fig. 4).

**Discussion**

**Tremor Relief**

This series consists of the largest number of patients undergoing gamma knife radiosurgery for thalamotomy in whom significant follow up has been obtained. Overall, 34 (89%) of 38 radiosurgically placed thalamic lesions were effective in reducing or eliminating tremor. In 24% of the patients the tremor was abolished completely, and another 55% the patients attained an average improvement of two to three grades in their UPDRS score. Evaluations by independent neurologists were highly correlated with subjective patient reports. No complications occurred.

Our results are similar to those reported in the early 1990s in which two patients were treated using the gamma knife. In the first patient, a dose of 180 Gy with an 8-mm collimator was used. This patient had complete relief of his tremor 1 month after lesioning. Unfortunately 6 months later a right-sided hemiparesis and dysphasia developed. After receiving a course of steroid medication, the patient had a mild hemiparesis and no tremor. The sec-
TABLE 2

Correlation of evaluations by independent neurologists and patient self-assessment scores

<table>
<thead>
<tr>
<th>Change in UPDRS Score Reported by Neurologist</th>
<th>Subjective Improvement Reported by Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>none</td>
</tr>
<tr>
<td>1</td>
<td>mild (1–33% relief)</td>
</tr>
<tr>
<td>2</td>
<td>good (34–66%)</td>
</tr>
<tr>
<td>3</td>
<td>excellent (67–99%)</td>
</tr>
<tr>
<td>3 or 4</td>
<td>absent tremor</td>
</tr>
</tbody>
</table>

ond patient received 200 Gy with a single 4-mm collimator and obtained only transient relief of the tremor.

Friehs, et al. treated three patients using a single 4-mm collimator with a maximum dose of 160 Gy. All three patients showed a good response 3 or 4 weeks postradiosurgery with partial or complete resolution of their tremor; however, the follow-up period was only 1 year.

Hirato and colleagues treated one patient using gamma knife radiosurgery for thalamotomy with a maximum dose of 150 Gy. The patient noted improvement in her tremor 3 months after treatment; the tremor was markedly diminished 6 months later without complications.

**Patient Selection**

Of the 900 patients treated using gamma knife radiosurgery at Good Samaritan Hospital in Los Angeles over the past 5 years, thalamotomies represent only 4.5% of the total cases. They also represent only 8% of the total number of cases of PD treated at our institution. Our treatment of parkinsonian tremor using radiofrequency lesioning with unit cell recording and physiological feedback results in 90% complete tremor relief with less than a 3% morbidity rate. This is usually our procedure of choice for this group of patients. This retrospective review proved that for a small subset of patients who are not normally considered for surgical intervention or who chose this course of treatment, gamma knife radiosurgery for thalamotomy has value.

**Target Selection**

As our electrophysiological knowledge of the basal ganglia has increased, target selection has changed to reflect this experience. Initially, the efferent pathway from the globus pallidus to the ventrals anterialis oralis of the thalamus was thought to be the prime target for tremor elimination. Since then lesions have been moved posteriorly to the VIM for selective thalamotomy for tremor.

Landmarks around the AC–PC line were used to target the contralateral VIM nucleus. In addition, subjective visual inspection of MR images and the Schaltenbrand and Wahren atlas (anatomical landmarks) were also used in the decision-making process for target placement to account for anatomical variation in individual patients. Two-millimeter-thick MR slices with T2-weighted signal change or T1 “streaking” (Fig. 3). This streaking may represent edema, radiation change, demyelination, or necrosis. It is unlikely that it represents necrosis in that the presence of the streaking within the capsule or other thalamic nuclei never correlated with neurological impairment. In addition, this streaking did not create mass effect. Only postmortem studies will elucidate the true nature of this interesting finding on follow-up images. Clinical improvement in the higher-dose group may be explained by a physiologically larger lesion in this group, correcting any target planning inaccuracies.

**Radiological Findings**

Gadolinium-enhanced T2-weighted MR sequences revealed that the sizes of radiosurgical lesions in the high- and low-dose groups were not statistically different and that they were consistent between patients. This was not the case in the T1-weighted sequences. Although the difference did not reach statistical significance, there was a trend for the higher-dose lesions to elicit a larger T2-weighted signal change or T1 “streaking” (Fig. 3). This streaking may represent edema, radiation change, demyelination, or necrosis. It is unlikely that it represents necrosis in that the presence of the streaking within the capsule or other thalamic nuclei never correlated with neurological impairment. In addition, this streaking did not create mass effect. Only postmortem studies will elucidate the true nature of this interesting finding on follow-up images. Clinical improvement in the higher-dose group may be explained by a physiologically larger lesion in this group, correcting any target planning inaccuracies.

**Conclusions**

Gamma knife radiosurgery for thalamotomy is an effective and useful alternative to invasive radiofrequency techniques in patients at high risk for surgery. The me-
Gamma knife thalamotomy for Parkinson’s tremor

Mechanical accuracy of the gamma unit combined with the anatomical accuracy of high-resolution MR imaging make radiosurgical lesioning safe and precise. Higher radiosurgical doses are more effective than lower ones at eliminating or reducing tremor and may be performed without complications.

References


Manuscript received March 18, 1997. Accepted in final form December 9, 1997. An earlier version of this manuscript was published in Neurosurg Focus 2 (3):Article 12, 1997.

Address reprint requests to: Christopher M. Duma, M.D., Neurosciences Institute, Good Samaritan Hospital, 637 South Lucas Avenue, Suite 501, Los Angeles, California 90017.