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# A dosimetric comparison between Gamma Knife and CyberKnife treatment plans for trigeminal neuralgia

## Clinical article

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*Object.* The Leksell Gamma Knife and the Accuray CyberKnife systems have been used in the radiosurgical treatment of trigeminal neuralgia. The 2 techniques use different delivery methods and different treatment parameters. In the past, CyberKnife treatments have been associated with an increased incidence of treatment-related complications, such as facial numbness. The goal of this study was to develop a method for planning a CyberKnife treatment for trigeminal neuralgia that would reproduce the dosimetric characteristics of a Gamma Knife plan. A comparison between Gamma Knife and CyberKnife treatment plans obtained with this method is presented.

*Methods.* Five patients treated using the Gamma Knife Perfexion Unit were selected for this study. All patients underwent CT cisternography to accurately identify the position of the trigeminal nerve. The Gamma Knife plans used either one 4-mm-diameter collimator or two coincident 4-mm collimators (one open and one with sector blocking) placed at identical isocenter coordinates. A maximum local dose of 80 Gy was prescribed. Critical structures and representative isodose lines were outlined in GammaPlan and exported to the CyberKnife treatment planning platform. CyberKnife treatments were developed using the 5-mm-diameter cone and the trigeminal node set, which provides an effective collimation diameter of 4 mm at the isocenter. The 60-Gy isodose volume imported from GammaPlan was used as the target in the CyberKnife plans. The CyberKnife treatments were optimized to achieve target dose and critical structure sparing similar to the Gamma Knife plans. Isocentric and nonisocentric delivery techniques were investigated. Treatment plans were compared in terms of dosimetric characteristics, delivery, and planning efficiency.

*Results.* CyberKnife treatments using the 5-mm cone and the trigeminal node set can closely reproduce the dose distribution of Gamma Knife plans. CyberKnife isocentric and nonisocentric plans provide comparable results. The average length of the trigeminal nerve receiving a dose of 60 Gy was 4.5, 4.5, and 4.4 mm for Gamma Knife, nonisocentric CyberKnife, and isocentric CyberKnife, respectively. However, minimizing the dose to the critical structures was more difficult with the CyberKnife and required the use of tuning structures. In addition, the dose falloff away from the target was steeper in Gamma Knife plans, probably due to the larger number of beams (192 beams for Perfexion vs ~ 100 beams for CyberKnife). While the treatment time with the CyberKnife is generally shorter, the planning time is significantly longer.

*Conclusions.* CyberKnife radiosurgical parameters can be optimized to mimic the dose distribution of Gamma Knife plans. However, Gamma Knife plans result in superior sparing of critical structures (brainstem, temporal lobe, and cranial nerves VII and VIII) and in steeper dose falloff away from the target. The clinical significance of these effects is unknown. *(DOI: 10.3171/2010.8.GKS101002)*

**Key Words** • **trigeminal neuralgia** • **stereotactic radiosurgery** • **Gamma Knife** • **CyberKnife**

Trigeminal neuralgia is a disorder of the CN V, which causes episodes of severe facial pain. Treatment options for patients with trigeminal neuralgia include pharmacological therapy with a variety of anticonvulsant drugs, surgery (microvascular decompression), percutaneous surgical procedures (balloon compression, glycerol rhizotomy, and radiofrequency rhizotomy), and SRS. Stereotactic radiosurgery has been adopted in the management of trigeminal neuralgia since 1951, when Lars Leksell treated the first patient by irradiating the trigeminal ganglion with an orthovoltage x-ray beam.[9–11] Since then, the evolution of sophisticated radiosurgery techniques, optimization of treatment parameters, and improvements in targeting accuracy have contributed to establishing SRS as a safe, noninvasive alternative to traditional surgery for patients with medically refractory trigeminal neuralgia.[7] In particular, GKS has become the standard SRS treatment for patients unresponsive to medical therapy.[4,6,8,20,22]

*Abbreviations used in this paper:* CN = cranial nerve; GKS = Gamma Knife surgery; MU = monitor unit; SAD = source-to-axis distance; SRS = stereotactic radiosurgery.

In GKS, the trigeminal nerve is identified using specific MR imaging sequences (T2-weighted fast spin echo). Typically, a maximum radiation dose of 80 Gy is delivered to the retrogasserian cisternal portion of the nerve with a single 4-mm isocenter. Gamma Knife surgery achieves excellent rates of initial pain relief and minimal sensory loss. Despite the excellent short-term outcomes, there is a consistent rate of late failure after the procedure.[14]

While clinical outcomes vary considerably among investigators, a direct relationship between the radiosurgical parameters (target volume, target location, and maximum radiation dose), the rate of initial pain relief and its durability has been observed. In particular, higher doses of radiation and target locations closer to the root entry zone have been correlated to an improved pain relief.[15] However, the improved pain response has been accompanied by an increased occurrence of facial numbness.[16,18]

The CyberKnife system (Accuray, Inc.) is a relatively new SRS modality.[2] The application of CyberKnife to the treatment of trigeminal neuralgia was initiated by Adler's group, who, in an effort to improve the durability of pain relief, irradiated a longer segment of the trigeminal nerve to a relatively homogeneous dose.[13] This treatment was made possible by the capability of the CyberKnife to deliver nonisocentric beams.

The CyberKnife consists of a compact linear accelerator (6-MV photons) mounted on a 6-axis robotic arm. As the robot moves around the patient, radiation can be delivered from almost any direction. This results in an extremely conformal dose distribution, with steep dose gradients and minimal dose delivered to the surrounding critical structures. In the case of intracranial lesions, patients are immobilized using a thermoplastic mask, rather than a stereotactic frame attached to the patient's skull as in GKS. Submillimeter dose delivery accuracy is achieved through image guidance using 2 amorphous silicon flat-panel detectors and 2 diagnostic x-ray sources positioned at 45° angles. Camera images are automatically registered to a library of digitally reconstructed radiographs to determine the exact patient position and to compensate for any patient movement. Secondary collimators consisting of tungsten cones collimate the radiation into a pencil beam. The cones have 12 possible apertures ranging in diameter from 5 to 60 mm defined by convention at a nominal SAD of 80 cm. In the treatment of trigeminal neuralgia, the smallest cones are used (that is, the 5-mm cone at either 80 or 65 cm SAD, or the 7.5-mm cone at 65 cm SAD). The robot node set at 65-cm SAD is called "trigeminal node set" and allows achievement of a smaller effective collimator aperture (that is, 6 mm for the 7.5-mm cone and 4 mm for the 5-mm cone).

In 2005, Lim et al.[13] reported excellent pain relief results but unacceptably high treatment complication rates; 73% of patients developed facial numbness. To reduce the risk of sensory loss, they initiated a dose-volume deescalation protocol that produced encouraging results. In a recent publication, they reported complete pain relief in 85% of patients and significant ipsilateral facial numbness in 17% of patients.[1]

Although the latest CyberKnife treatment results are promising, the rate of treatment complications is still higher than that in most GKS studies. In addition, Gamma Knife studies are based on a much larger patient population, and follow-up data are available over a longer period (up to 10 years).[8] To benefit from the well-established Gamma Knife experience, some CyberKnife users might be interested in treating patients with trigeminal neuralgia using Gamma Knife–like radiosurgical parameters.

The purpose of this study is to investigate whether the CyberKnife radiosurgical parameters could be optimized to deliver a treatment that would mimic the dosimetric characteristics of a Gamma Knife plan.

## Methods

Five patients treated with the Gamma Knife Perfexion system (Elekta AB) were evaluated. Two patients had left trigeminal neuralgia and 3 had right trigeminal neuralgia. While MR images are typically used to plan the GKS, for this study we selected patients with pacemakers who underwent a contrast CT cisternography procedure for identification of the trigeminal nerve. Since a CT scan is required for CyberKnife treatment planning, this patient population allowed us to perform a systematic comparison between the 2 radiosurgery systems. However, CT cisternography is not typically required to identify the trigeminal nerve in patients undergoing CyberKnife radiosurgery. Chavez et al.[3] demonstrated the reliability of radiosurgical targeting based on T2-weighted MR imaging, and recent studies on CyberKnife radiosurgery for trigeminal neuralgia have reported on the use of MR imaging coregistered with CT scanning for target delineation.[1,5]

The Perfexion unit consists of 192 $^{60}$Co sources arranged in 8 sectors.[21] The beams of gamma radiation emanating from the sources are collimated and coincide at a fixed focal point (the isocenter). The Gamma Knife treatment plans were developed with the GammaPlan platform (version 8.3). The retrogasserian portion of the trigeminal nerve was identified using CT cisternography, and a 4-mm-diameter isocenter was located just distal to the exit of the trigeminal nerve from the pons. To protect the brainstem from radiation exposure, a second 4-mm isocenter with some sectors blocked was positioned at exactly the same coordinates as the first isocenter. While the standard procedure for treating patients with trigeminal neuralgia consists of using a single 4-mm-diameter isocenter,[17] at our institution we use the sector blocking technique to reduce the dose to the brainstem. In Gamma Knife Perfexion, this technique is equivalent to the plugging pattern technique used in Model 4C.[12] Depending on the patient anatomy (the amount of space in the ambient cistern) and the required level of dose shaping, the number of blocked sectors and the isocenter weights were adjusted. A radiation dose of 80 Gy was prescribed to the 100% point.

Critical structures (brainstem, temporal lobe, and CNs VII and VIII) and representative isodose lines (70, 60, 40, 20, and 10 Gy) were contoured in GammaPlan, and then exported via DICOM with the imaging study into the CyberKnife planning platform (Multiplan version 3.5). To reproduce the 4-mm radiation spot available in GKS, the 5-mm cone and the trigeminal node set (65-cm SAD) were selected. CyberKnife treatments were planned using the sequential optimization method. To reproduce the dose distribution of the Gamma Knife plans, the 60- and 70-Gy volume contoured in GammaPlan served as target structures, while the 20- and 10-Gy volume served as tuning structures. In addition, dose constraints were placed on the brainstem, ipsilateral temporal lobe, and CNs. The optimization was performed in high-resolution mode with the smallest possible grid including part of the brainstem, Meckel cave, and CNs VII and VIII. The maximum number of MUs per beam and the maximum number of MUs per node were constrained to increase the total number of dose-carrying beams. No beams were allowed to pass through the eyes. A final high-resolution dose calculation was performed after extending the calculation matrix to include the whole head. As for Gamma Knife plans, a maximum dose of 80 Gy was prescribed.

Since the presence of tissue heterogeneity is not accounted for in GammaPlan, the entire head was outlined in Multiplan (Accuray), and the tissue density function was disabled, so that everything inside the contour was considered as water-equivalent and everything outside was considered as air-equivalent.

Isocentric and nonisocentric treatments were evaluated. For the isocentric plans, a 5-mm isocenter was placed at the center of the 70-Gy volume, and beam weights were optimized using the sequential method.

We compared Gamma Knife plans with isocentric and nonisocentric CyberKnife plans in terms of dosimetric characteristics, delivery efficiency (number of beams and beam-on time), and planning efficiency (time required to produce the final plan).

The dosimetric parameters used to evaluate the plan quality were as follows: 1) the length of trigeminal nerve receiving a dose of 60 Gy; 2) the volume of tissue receiving a dose of 60 Gy ($V_{60Gy}$) and 70 Gy ($V_{70Gy}$); 3) the dose to critical structures (brainstem, ipsilateral temporal lobe, and CNs VII and VIII); and 4) the dose-volume histogram for the entire tissue. For each parameter comparison, statistical significance was calculated using a probability value analysis with the Microsoft Excel Student t-test function. The probability value analysis compares 2 sets of data and returns the probability (p value) for the 2 samples to have the same mean. A $p < 0.05$ indicates a statistically significant difference between mean values of the 2 data sets.

## Results

*Dosimetric Comparison*

CyberKnife plans with the 5-mm cone and the trigeminal node set provided similar high-dose coverage as Gamma Knife plans. An example showing the high-dose regions of a Gamma Knife plan and a nonisocentric CyberKnife plan is presented in Fig. 1. The mean length of trigeminal nerve receiving a dose of 60 Gy and the mean volume of tissue receiving a dose of 60 and 70 Gy are reported in Table 1 for Gamma Knife, nonisocentric CyberKnife, and isocentric CyberKnife.

While the extension of the high-dose region is similar in the 2 radiosurgical modalities, the dose falloff in GKS is steeper than in CyberKnife treatment. Figures 2 and 3 show examples of isodose line distributions in the axial

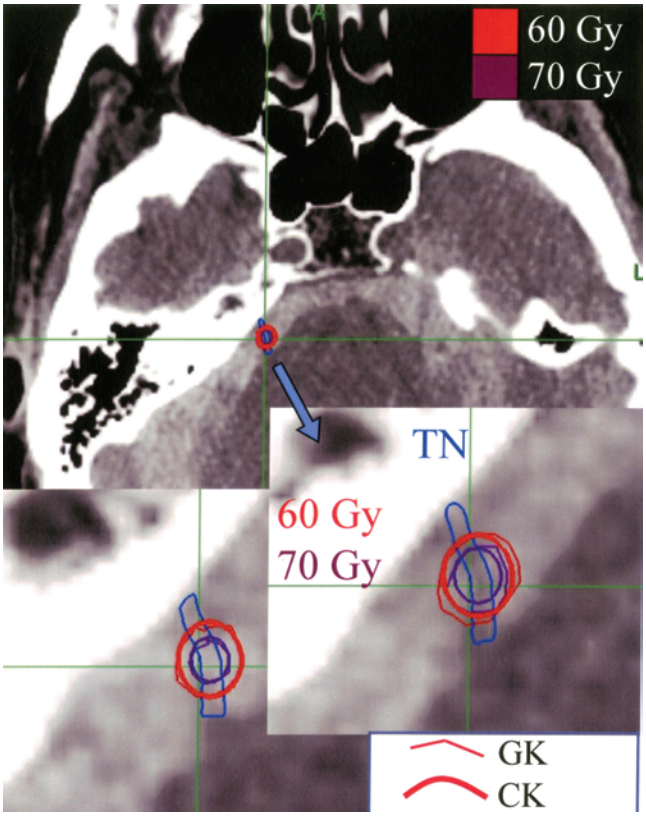


**Fig. 1.** Example of high-dose coverage for a Gamma Knife (GK) and a nonisocentric CyberKnife (CK) plan. The 60- and 70-Gy isodose lines are presented for the Gamma Knife *(thin segmented line)* and for the CyberKnife *(thick curved line)* with the same color scheme.

and sagittal plane for 2 typical cases ("easy" and "difficult" cases). For a direct comparison, the CyberKnife dose distribution is displayed on top of the Gamma Knife dose distribution. The difficulty in treatment planning for trigeminal neuralgia depends mainly on the distance between the treated trigeminal nerve and the proximal brainstem. For patients with a large amount of space in the ambient cistern, the shape of the low-dose region in the CyberKnife

**TABLE 1: The mean length of the trigeminal nerve receiving a dose of 60 Gy, and the mean volume receiving a given amount of dose for the 3 treatment modalities***

| | Mean ± SD | | |
|---|---|---|---|
| Measurement | Gamma Knife | CK Noniso | CK Iso |
| length of CN V (mm) | 4.5 ± 0.2 | 4.5 ± 0.2 | 4.4 ± 0.2 |
| vol | | | |
| at 70 Gy ($mm^3$) | 15.0 ± 0.9 | 13.8 ± 3.4 | 13.3 ± 4.7 |
| at 60 Gy ($mm^3$) | 36.9 ± 1.4 | 40.5 ± 3.9 | 40.5 ± 4.2 |
| at 40 Gy ($mm^3$) | 95.6 ± 2.6 | 147.5 ± 10.5 | 136.1 ± 8.2 |
| at 20 Gy ($mm^3$) | 274.0 ± 11.4 | 524.1 ± 25.7 | 480.7 ± 31.5 |
| at 10 Gy ($cm^3$) | 0.71 ± 0.04 | 1.5 ± 0.1 | 1.4 ± 0.1 |
| at 4 Gy ($cm^3$) | 3.3 ± 0.3 | 8.9 ± 2.7 | 7.3 ± 0.2 |
| at 1 Gy ($cm^3$) | 60.2 ± 10.2 | 266.9 ± 48.2 | 249.7 ± 38.6 |

* CK = CyberKnife; Iso = isocentric; Noniso = nonisocentric.

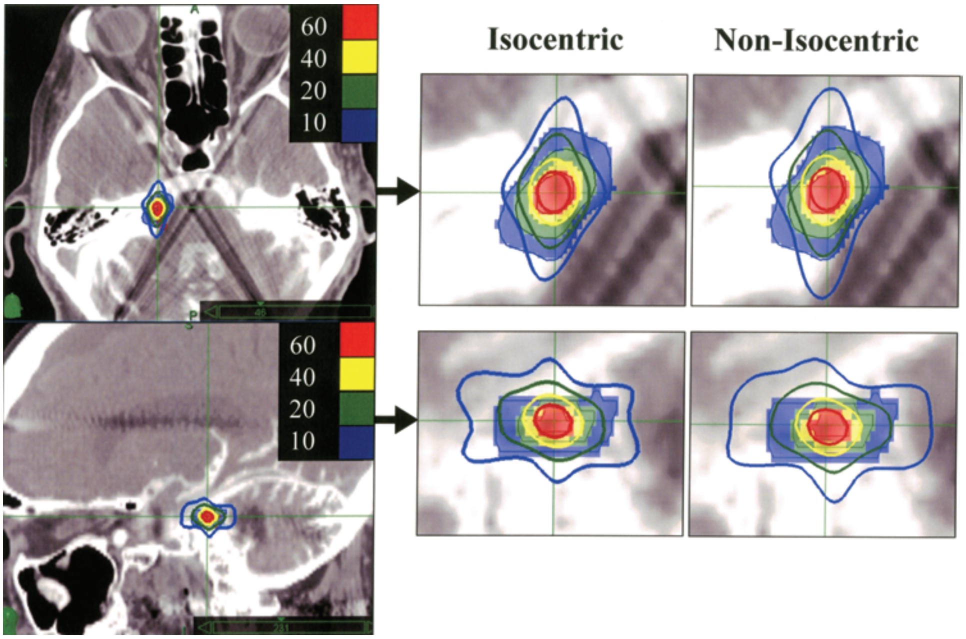


**Fig. 2.** "Easy" case. Dose distribution *(thin lines)* in the axial **(upper)** and sagittal **(lower)** planes for an isocentric **(left)** and nonisocentric **(right)** CyberKnife plan. For comparison, the Gamma Knife dose distribution is displayed as color wash.

plan resembles that of the Gamma Knife plan (Fig. 2). In particular, the 10-Gy volume extends along the anterior-posterior direction in the sagittal plane. However, while the high-dose region overlaps fairly well, the 10-Gy volume is larger for the CyberKnife than for the Gamma Knife. On the contrary, if the targeted segment is adjacent to the nerve root exit at the brainstem, it becomes more challenging to keep the dose to the brainstem below its tolerance dose. This requires constraint of the maximum dose to the brainstem, and results in an elongated dose distribution with dose "spills" into the CNs (Fig. 3). Figure 4 presents the 5-case mean dose volume histogram for each of the treatment modalities. The volume of tissue receiving a given dose is plotted on a logarithmic scale. The volume of tissue exposed to high dose ($V_{70Gy}$ and $V_{60Gy}$) is comparable among the 3 treatments. The average volume of tissue receiving a dose of 70 Gy is 15.0 ± 0.9 mm$^3$ for Gamma Knife versus 13.8 ± 3.4 mm$^3$ ($p = 0.24$) for nonisocentric CyberKnife and 13.3 ± 4.7 mm$^3$ ($p = 0.24$) for isocentric CyberKnife. The average volume of tissue receiving a dose of 60 Gy is 36.9 ± 1.4 mm$^3$ for Gamma Knife versus 40.5 ± 3.9 mm$^3$ ($p = 0.07$) for nonisocentric CyberKnife and 40.5

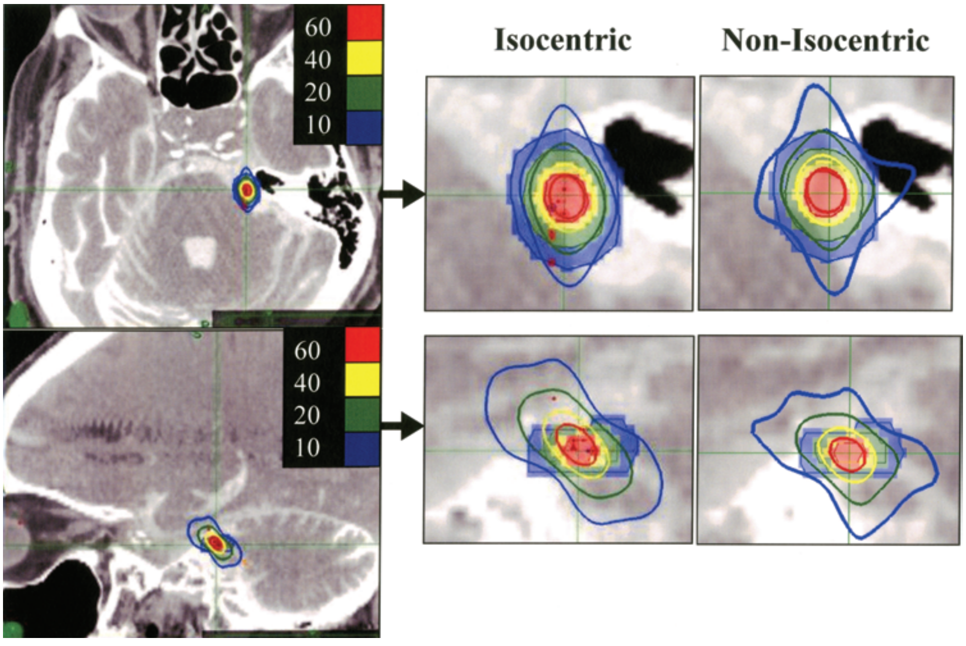


**Fig. 3.** "Difficult" case. Dose distribution *(thin lines)* in the axial **(upper)** and sagittal **(lower)** plane for an isocentric **(left)** and nonisocentric **(right)** CyberKnife plan. For comparison, the Gamma Knife dose distribution is displayed as color wash.

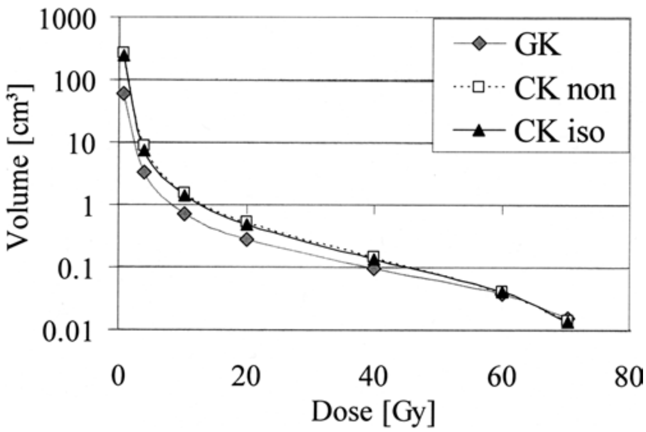


**Fig. 4.** Dose volume histogram on semilogarithmic scale for the whole tissue. Comparison between Gamma Knife *(diamonds)*, nonisocentric CyberKnife *(squares)*, and isocentric CyberKnife *(triangles)*.

± 4.2 mm$^3$ ($p = 0.09$) for isocentric CyberKnife. However, the volume of tissue exposed to a low dose ($V_{4Gy}$) is 2–5 times smaller in Gamma Knife than in CyberKnife plans. The average volume of tissue receiving a dose of 4 Gy is 3.3 ± 0.3 cm$^3$ for Gamma Knife versus 8.9 ± 2.7 cm$^3$ ($p = 0.006$) for nonisocentric CyberKnife and 7.3 ± 0.2 cm$^3$ ($p = 0.00001$) for isocentric CyberKnife.

Gamma Knife plans result in superior sparing of critical structures, including the brainstem, temporal lobe, and CNs VII and VIII. The average dose to 0.01 cm$^3$ of brainstem is 16.1 ± 2.9 Gy for Gamma Knife versus 19.4 ± 5.1 Gy ($p = 0.03$) for nonisocentric CyberKnife and 19.9 ± 4.6 Gy ($p = 0.008$) for isocentric CyberKnife. The average dose to 1 cm$^3$ of brainstem is 2.5 ± 0.3 Gy for Gamma Knife versus 3.7 ± 0.5 Gy ($p = 0.01$) for nonisocentric CyberKnife and 3.5 ± 0.5 Gy ($p = 0.02$) for isocentric CyberKnife. The average volume of brainstem receiving a dose of 8 Gy is 104 ± 35 mm$^3$ for Gamma Knife versus 205 ± 81 mm$^3$ ($p = 0.02$) for nonisocentric CyberKnife and 188 ± 78 mm$^3$ ($p = 0.03$) for isocentric CyberKnife. Figure 5 presents the dose to 0.01 cm$^3$ of brainstem, and the volume of brainstem receiving a dose of 8 Gy for the 5 patients. For the temporal lobe, the average dose to a volume of 0.1 cm$^3$ is 4.1 ± 1.4 Gy for Gamma Knife versus 7.8 ± 2.2 Gy ($p = 0.002$) for nonisocentric CyberKnife and 7.5 ± 3.5 Gy ($p = 0.02$) for isocentric CyberKnife. The average volume of the temporal lobe receiving a dose of 8 Gy is 0.9 ± 1.4 mm$^3$ for Gamma Knife versus 112.7 ± 88.4 mm$^3$ ($p = 0.02$) for nonisocentric CyberKnife and 101.1 ± 115.4 mm$^3$ ($p = 0.06$) for isocentric CyberKnife. Figure 6 presents the dose to 0.1 cm$^3$ of the temporal lobe and the volume of the temporal lobe receiving a dose of 8 Gy for the 5 patient cases. For the CNs, the average dose to 1 mm$^3$ of CN VII is 6.2 ± 3.6 Gy for Gamma Knife versus 13.4 ± 3.7 Gy ($p = 0.01$) for nonisocentric CyberKnife and 14.7 ± 5.0 Gy ($p = 0.009$) for isocentric CyberKnife. The average dose to 1 mm$^3$ of CN VIII is 3.7 ± 0.9 Gy for Gamma Knife versus 7.4 ± 2.7 Gy ($p = 0.03$) for nonisocentric CyberKnife and 8.2 ± 3.2 Gy ($p = 0.03$) for isocentric CyberKnife. Figure 7 presents the dose to 1 mm$^3$ of CNs VII and VIII for the 5 patients. The average dose to the eye was 1.06 ± 0.66 Gy, 1.13 ± 0.96 Gy, and 0.68 ± 0.51 for Gamma Knife, nonisocentric CyberKnife, and isocentric CyberKnife, respectively.

*Delivery and Planning Efficiency*

The Gamma Knife Perfexion unit has 192 beams, and the beam-on time depends on the source activity (age of the sources), the number of blocked sectors, and the relative weight of the open shot (isocenter) compared with the blocked one. Table 2 summarizes the range of the expected GKS time for new $^{60}Co$ sources (dose rate of 3.5 Gy/minute) for several treatment scenarios. For a single open isocenter and new $^{60}Co$ sources, the minimum treatment time is 28 minutes. This time increases to 45 minutes if a single shot with 3 sectors blocked is used. In addition, as the $^{60}Co$ sources decay, the treatment time increases with a doubling time of 5 years.

The number of blocked sectors ranged from 1 to 4. The average beam-on time for the considered cases was 50.1 minutes (range 38.6–63.0 minutes), and the average dose rate was 3 Gy/minute (range 2.7–3.1 Gy/minute). The patient with the longest beam-on time (63 minutes) was treated with a single isocenter with 3 sectors blocked (no open isocenter). For this particular plan, the number of dose-carrying beams was 120.

Gamma Knife plans are developed under the direct supervision of the neurosurgeon, who determines the location of the isocenter and the level of desired blocking. After the images are imported into GammaPlan and the coordinate system is defined, the planning time is generally short (< 10 minutes).

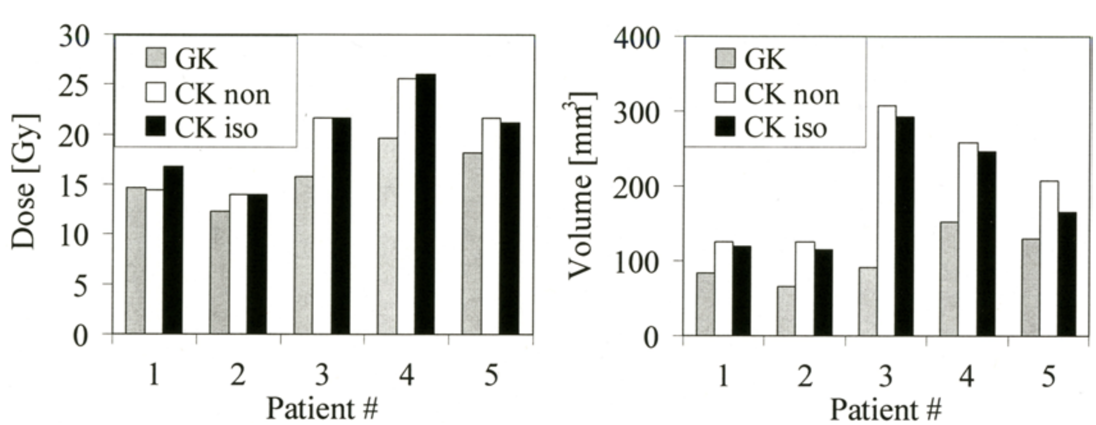


**Fig. 5.** Dose to 0.01 cm$^3$ of brainstem **(left)** and the volume of the brainstem receiving a dose of 8 Gy **(right)** in the 5 cases.

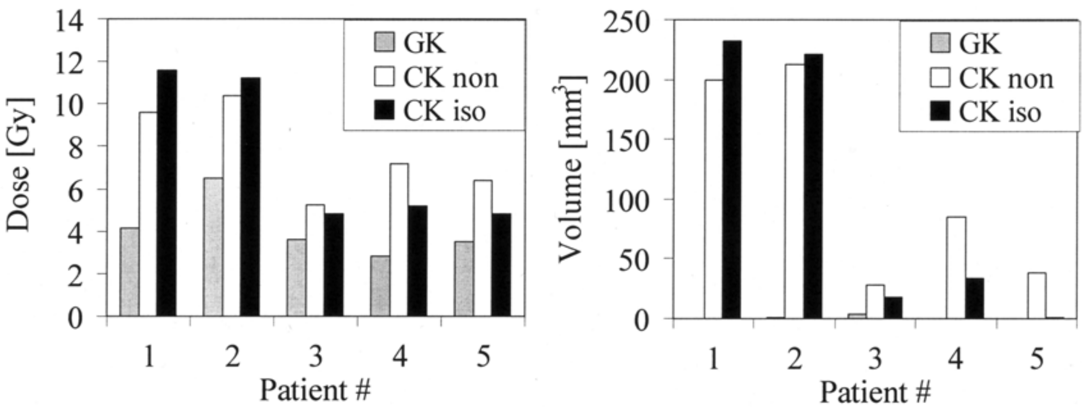


**Fig. 6.** Dose to 0.1 cm$^3$ of temporal lobe **(left)** and the volume of the temporal lobe receiving a dose of 8 Gy **(right)** in the 5 cases.

For the CyberKnife, the treatment time depends on the number of MUs, the LINAC dose rate, the total number of beams, the robot speed, and the imaging time. While the CyberKnife model G3 provides a dose rate of 400 MU/minute, newer models provide higher dose rates (600 MU/minute for the model G4 and 1000 MU/minute for the VSI System). Compared with nonisocentric plans, isocentric plans result in significantly smaller MUs. The average number of MUs was 15663 ± 344 for nonisocentric CyberKnife and 14887 ± 603 for isocentric CyberKnife ($p = 0.004$). For the 400 MU/minute G3 model (which is currently operational in our department) the average beam-on time is 39.2 ± 0.9 and 37.2 ± 1.5 minutes, for nonisocentric and isocentric delivery, respectively. However, for the CyberKnife VSI System, these times would be reduced to 16 and 15 minutes, respectively. The total treatment time (including the time it takes the robot to move from node to node, and the imaging time) is typically 1.5 times the beam-on time, that is, approximately 1 hour for the G3 model and less than 30 minutes for the VSI System. The average number of nonzero beams was 130 for nonisocentric CyberKnife and 75 for isocentric CyberKnife.

Compared with Gamma Knife planning, CyberKnife treatment planning for trigeminal neuralgia is more time consuming and requires advanced planning skills. A CyberKnife plan requires multiple optimizations using different dose constraints until the best compromise between dose to the trigeminal nerve and sparing of critical structures is achieved. Planning times vary depending on the planner's ability, and can take from a few hours to a day.

## Discussion

For over 3 decades, the Leksell Gamma Knife system has been used in the treatment of trigeminal neuralgia. Recent studies have reported rates of initial pain relief between 81% and 90% and treatment complication rates (varying degrees of facial numbness) between 4% and 36%.[4,6,8,14,19,20] While the onset of bothersome facial numbness is observed in only 6%–10.5% of patients, the occurrence of severe dysesthesia or anesthesia dolorosa is a very rare event (< 1%). Despite the excellent short-term outcomes, benefits consistently diminish over time. In a retrospective study of 503 patients, Kondziolka et al.[8] reported that while initial pain relief was achieved in 89% of patients, significant pain relief was maintained in 73% of patients at 1 year, in 65% at 2 years, and in 41% at 5 years. Other studies reported treatment failure rates of 33% 2 years after radiosurgery.[14]

The development of the CyberKnife system offers a new opportunity in the treatment of trigeminal neuralgia. The capability for nonisocentric delivery enables irradiation of a longer segment of the trigeminal nerve with a relatively uniform dose (marginal dose at 80% of maxi-

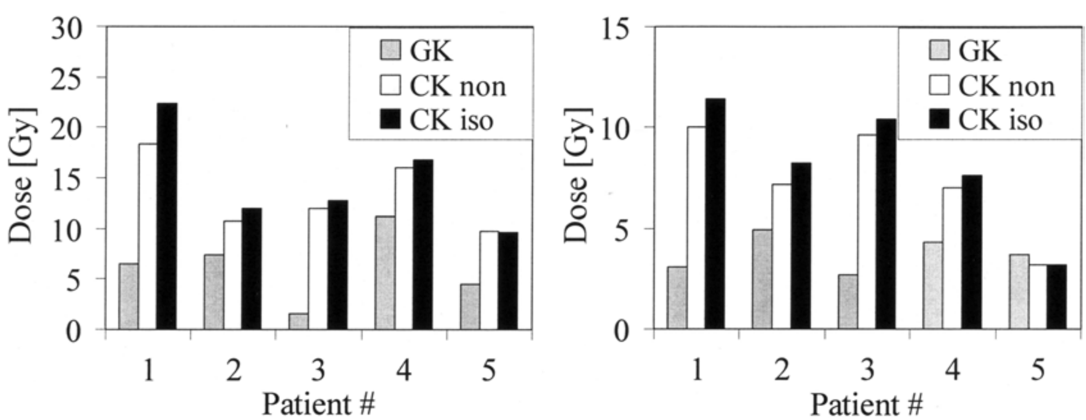


**Fig. 7.** Dose to 1 mm$^3$ of CNs VII **(left)** and VIII **(right)** in the 5 cases.

mum dose). In addition, CyberKnife radiosurgery does not require a fixed stereotactic frame, which renders the treatment less invasive and more tolerable to patients.

In the study by Lim et al.,[13] the rate of initial pain relief was 93%, and the rate of posttreatment facial numbness was 51%. Pain relief was maintained in 78% of patients after a mean follow-up time of 11 months.

In a multiinstitutional study, Villavicencio et al.[23] retrospectively analyzed radiosurgical doses and volumes in relation to pain response, complications, and recurrence of symptoms. Initial pain relief rates of 67% and facial numbness rates of 47% were reported. The authors concluded that the use of a higher dose of radiation (maximal dose range 70–85.4 Gy), and targeting a longer segment of the trigeminal nerve (range 5–12 mm) resulted in better pain relief and a higher incidence of hypesthesia. The occurrence of posttreatment numbness was predictive of treatment outcome.

To decrease the treatment-related complication rates, Adler et al.[1] started reducing the dose and the length of the treated nerve. In their prospective study, a 6-mm segment of the trigeminal nerve was treated with a mean marginal dose of 58 Gy and a mean maximal dose of 73 Gy. In terms of overall treatment response, the outcomes of this study are comparable to those reported in the GKS series (85% pain response rate). However, significant facial numbness was observed in 17% of patients.

Fariselli et al.[5] evaluated the efficacy and side effects of CyberKnife radiosurgery on the basis of 3 dose escalation protocols. Compared with Adler at al.,[1] they treated a smaller segment of nerve (length 4 mm, 2–3 mm anterior to the root entry zone) to a lower prescription dose (55–75 Gy maximum point dose). For the high-dose protocol (75 Gy maximum dose) the minimum target dose was 60 Gy and the target length was 4 mm, which is very similar to Gamma Knife treatment plans. It is therefore not surprising that their treatment outcomes were similar to those reported in GKS studies. Initial pain relief was obtained in 97% of patients, while 33% of patients experienced pain recurrence at 9 months. No facial numbness was observed.

The results of these studies underline the direct relationship between target dose, target volume, and treatment outcome applying to all radiosurgical approaches. However, the differences in treatment parameters observed in the CyberKnife series indicate that a consensus on the optimal dose and dose distribution for the treatment of trigeminal neuralgia has not yet been established for this relatively new treatment modality.

The purpose of this study was to perform a direct comparison between GKS and CyberKnife treatment of trigeminal neuralgia. If one could reproduce the Gamma Knife dose distribution with the CyberKnife, the same clinical outcomes should be expected (the assumption being that the clinical outcome is system-independent).

*Dosimetric Comparison*

Our results indicate that Gamma Knife–equivalent plans can be obtained with the CyberKnife system by using the 5 mm cone and the trigeminal node set. However, the dose to adjacent critical structures and the integral dose to the brain are lower in Gamma Knife plans, compared with CyberKnife plans. This effect is likely due to the lower beam number observed in CyberKnife plans. While Gamma Knife plans have 192 beams, an average of 103 and 75 beams were obtained for nonisocentric and isocentric CyberKnife plans, respectively. We tried to increase the number of available beams by constraining the maximum MUs per beam and by using the 10-Gy volume of the Gamma Knife plan as a tuning structure. However, the number of beams could not be more than 86 for isocentric plans or above 160 for nonisocentric plans. Our hypothesis is that the constraint on the brainstem dominates the plan quality: beams that would contribute to the brainstem doses are turned off by the optimization algorithm.

**TABLE 2: Expected Gamma Knife Perfexion treatment times as a function of the number of blocked sectors for new $^{60}Co$ sources**

| Treatment Parameters | Time (min) |
|---|---|
| 1 single open shot | 28 |
| 1 open shot & 1 shot w/ 1 sector blocked | 30 |
| 1 open shot & 1 shot w/ 2 sectors blocked | 32 |
| 1 open shot & 1 shot w/ 3 sectors blocked | 35 |
| 1 open shot & 1 shot w/ 4 sectors blocked | 38 |
| 1 single shot w/ 1 sector blocked | 32 |
| 1 single shot w/ 3 sectors blocked | 45 |

* The dose rate was equal to 3.5 Gy/minute. Assumptions: 1) The weight of open shot is equal to the weight of shot with blocked sectors. 2) The relative output factor of each sector is equivalent.

It is worth noting that our Gamma Knife plans are designed to deliver a minimal dose to the brainstem by the sector-blocking technique. Under these conditions, the CyberKnife plan was not able to match the characteristics of the Gamma Knife plans. One can expect that when the requirements on the brainstem dose are relaxed, as in the case of single-isocenter Gamma Knife plans, the differences between the two systems would be less pronounced. However, we chose to perform this comparison according to the standard clinical approach at our institution.

The clinical significance of the higher dose delivered to critical structures by CyberKnife is unknown, and only randomized trials comparing the 2 techniques in terms of clinical outcome could address this question.

Due to the different spatial resolution of dose calculation matrix, an intrinsic uncertainty is present when comparing Gamma Knife and CyberKnife doses. All CyberKnife plans were evaluated at high resolution, after expanding the calculation matrix to include the entire head. In high-resolution mode, each CT voxel is a calculation point. In GKS, the dose to adjacent critical structures was obtained by setting the resolution of the calculation matrix to 1 $mm^3$. However, to estimate the volume of tissue exposed to a low dose, the size of the calculation matrix was increased, resulting in lower resolution. To minimize this effect, we used the smallest possible grid including a given isodose volume. However, the uncertainty due to the calculation matrix is smaller than the difference between Gamma Knife and CyberKnife dosimetric parameters and does not alter the finding of this study.

*Delivery and Planning Efficiency*

While the latest CyberKnife models consistently deliver a trigeminal treatment in less than 30 minutes, the treatment time with the Gamma Knife is longer and may vary between 30 and 90 minutes depending on the source age and the degree of blocking. On the other hand, planning time is significantly longer for CyberKnife treatment than for GKS. In addition, while Gamma Knife plans are well defined and reproducible, the quality of a CyberKnife plan depends on a many parameters and may substantially vary depending on the planning ability.

## Conclusions

Gamma Knife–equivalent plans can be generated using the 5-mm cone and the trigeminal node set. CyberKnife isocentric and nonisocentric plans provide comparable results. Gamma Knife plans result in steeper dose falloff and superior sparing of the critical structures compared with both isocentric and nonisocentric CyberKnife plans. The clinical significance of these differences is presently unknown.

### Disclosure

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Author contributions to the study and manuscript preparation include the following. Conception and design: Descovich. Acquisition of data: Descovich, McDermott. Analysis and interpretation of data: Descovich. Drafting the article: Descovich. Critically revising the article: Sneed, Barbaro, Nakamura, Ma. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Descovich. Study supervision: Sneed, Barbaro, Ma. Other: McDermott (Validate contours of all critical structures in GammaPlan).

### References


1. Adler JR Jr, Bower R, Gupta G, Lim M, Efron A, Gibbs IC, et al: Nonisocentric radiosurgical rhizotomy for trigeminal neuralgia. **Neurosurgery 64 (2 Suppl):**A84–A90, 2009
2. Adler JR Jr, Chang SD, Murphy MJ, Doty J, Geis P, Hancock SL: The Cyberknife: a frameless robotic system for radiosurgery. **Stereotact Funct Neurosurg 69:**124–128, 1997
3. Chavez GD, De Salles AA, Solberg TD, Pedroso A, Espinoza D, Villablanca P: Three-dimensional fast imaging employing steady-state acquisition magnetic resonance imaging for stereotactic radiosurgery of trigeminal neuralgia. **Neurosurgery 56:**E628, 2005
4. Dhople AA, Adams JR, Maggio WW, Naqvi SA, Regine WF, Kwok Y: Long-term outcomes of Gamma Knife radiosurgery for classic trigeminal neuralgia: implications of treatment and critical review of the literature. Clinical article. **J Neurosurg 111:**351–358, 2009
5. Fariselli L, Marras C, De Santis M, Marchetti M, Milanesi I, Broggi G: CyberKnife radiosurgery as a first treatment for idiopathic trigeminal neuralgia. **Neurosurgery 64 (2 Suppl):**A96–A101, 2009
6. Han JH, Kim DG, Chung HT, Paek SH, Kim YH, Kim CY, et al: Long-term outcome of gamma knife radiosurgery for treatment of typical trigeminal neuralgia. **Int J Radiat Oncol Biol Phys 75:**822–827, 2009
7. 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
8. Kondziolka D, Zorro O, Lobato-Polo J, Kano H, Flannery TJ, Flickinger JC, et al: Gamma Knife stereotactic radiosurgery for idiopathic trigeminal neuralgia. **J Neurosurg 112:**758–765, 2010
9. Leksell L: The stereotaxic method and radiosurgery of the brain. **Acta Chir Scand 102:**316–319, 1951
10. Leksell L: Sterotaxic radiosurgery in trigeminal neuralgia. **Acta Chir Scand 137:**311–314, 1971
11. Leksell L: [Trigeminal neuralgia. Some neurophysiologic aspects and a new method of therapy.] **Lakartidningen 68:**5145–5148, 1971 (Swedish)
12. 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
13. Lim M, Villavicencio AT, Burneikiene S, Chang SD, Romanelli P, McNeely L, et al: CyberKnife radiosurgery for idiopathic trigeminal neuralgia. **Neurosurg Focus 18(5):**E9, 2005
14. 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:**915–924, 2008
15. 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
16. Massager N, Murata N, Tamura M, Devriendt D, Levivier M, Régis J: Influence of nerve radiation dose in the incidence of trigeminal dysfunction after trigeminal neuralgia radiosurgery. **Neurosurgery 60:**681–688, 2007
17. Massager N, Nissim O, Murata N, Devriendt D, Desmedt F, Vanderlinden B, et al: Effect of beam channel plugging on the outcome of gamma knife radiosurgery for trigeminal neuralgia. **Int J Radiat Oncol Biol Phys 65:**1200–1205, 2006
18. 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:**58–64, 2001
19. Régis 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
20. Régis 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
21. Régis J, Tamura M, Guillot C, Yomo S, Muraciolle X, Nagaje M, et al: Radiosurgery with the world's first fully robotized Leksell Gamma Knife PerfeXion in clinical use: a 200-patient prospective, randomized, controlled comparison with the Gamma Knife 4C. **Neurosurgery 64:**346–356, 2009
22. Sanchez-Mejia RO, Limbo M, Cheng JS, Camara J, Ward MM, Barbaro NM: Recurrent or refractory trigeminal neuralgia after microvascular decompression, radiofrequency ablation, or radiosurgery. **Neurosurg Focus 18(5):**e12, 2005
23. 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, 2008


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