Soon after the LGK (Elekta Instrument AB, Stockholm, Sweden) was installed at our hospital in 1991, we were interested in using it to treat movement disorders such as PD. The first case was treated in 1993. The LGK was used to perform a GKT involving the same target we used during open thalamotomy. The use of this target was based on experience with sophisticated microrecording and was located at the lateral border of the thalamic VIM. For better targeting, the percent representation of the thalamic VIM in relation to the entire thalamic length is useful. The location of the target was determined on magnetic resonance (MR) imaging and computerized tomography scanning. A maximum dose of 130 Gy was delivered to the target by using a single isocenter with the 4-mm collimator. In more recent cases, a systematic follow-up examination was performed at 3, 6, 12, 18, and 24 months after GKT.

Since 1993, the authors have treated 70 patients with PD. Throughout the series the same dosimetric technique has been used. The course after GKT was compared between the 25 cases with PD treated before reloading and the 35 cases treated after reloading. In the majority (80–85%) treated after reloading, tremor and rigidity were reduced around 6 months after GKT. In the cases treated before reloading this effect took approximately 1 year. The thalamic reaction on MR imaging showed the same two lesion types in both series: a restricted and a diffuse. After reloading the restricted lesion was more frequent and the lesion volume was smaller.

Conclusions. The shorter delay in clinical improvement and smaller lesion size may be related to an increased radiation dose.

KEY WORDS • gamma knife • thalamus • ventralis intermedius nucleus • thalamic lesion • tremor

Abbreviations used in this paper: CT = computerized tomography; GKT = gamma knife thalamotomy; LGK = Leksell Gamma Knife; MR = magnetic resonance; PD = Parkinson Disease; UPDRS = Unified PD Rating Scale; VIM = ventralis intermedius nucleus; VO = ventralis oralis nucleus.
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TABLE 1
Summary of cases after reloading of cobalt source

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>35</td>
</tr>
<tr>
<td>essential tremor</td>
<td>11</td>
</tr>
<tr>
<td>post-cerebrovascular disease (intentional tremor)</td>
<td>1</td>
</tr>
<tr>
<td>posttraumatic tremor</td>
<td>1</td>
</tr>
<tr>
<td>torticollis</td>
<td>1</td>
</tr>
<tr>
<td>neck tremor</td>
<td>1</td>
</tr>
<tr>
<td>other</td>
<td>1</td>
</tr>
<tr>
<td>total</td>
<td>51</td>
</tr>
</tbody>
</table>

open stereotactic surgery. In recent years, when a patient comes for consultation for thalamotomy, we explain the advantages and disadvantages of conventional stereotactic surgery and GKT. The patient’s own final decision is then respected. Thus, since 2002, in our center, the number of patients treated with GKT exceeded those treated with conventional stereotactic surgery. For example, in 2003 17 patients underwent GKT while 10 underwent conventional stereotactic surgery. In recent years, when a patient comes for consultation for thalamotomy, we explain the advantages and disadvantages of conventional stereotactic surgery and GKT. The patient’s own final decision is then respected. Thus, since 2002, in our center, the number of patients treated with GKT exceeded those treated with conventional stereotactic surgery. For example, in 2003 17 patients underwent GKT while 10 underwent conventional stereotactic surgery.

Treatment Data

The operative procedures are essentially the same as those reported in previous papers. Briefly, the patient is hospitalized for 3 days. On the 1st day general preoperative examinations and preparations are made. On the 2nd day the operation is performed, and on the 3rd day, the patient is discharged.

A Leksell Model G stereotactic frame (Elekta Instrument AB) is fixed to the patient’s head to ensure that the position in the Gamma Knife unit and MR imager is comfortable. Inappropriate frame application can force the patient into a position in which the throat is compressed by the jaw. This is avoided. Then, MR images are taken unless the patient has a cardiac pacemaker in which case CT scanning is used. Axial images with 1-mm slices are taken from the level of the lateral ventricle to the fourth ventricle by the FASE (hyper T₂-weighted or fast–spin echo method). Two-millimeter-thick axial slices of the thalamus are obtained using proton density–weighted images, and coronal images of the thalamus are obtained by the same method. These images are taken for use in the treatment planning. All these images are sent to the workstation for computerized image processing. In the first instance Leksell SurgiPlan (Elekta Instrument AB) is used. The target site determined there is transferred to Leksell GammaPlan (Elekta Instrument AB). Axial CT images are also sent to the workstation to superimpose on MR images to check for displacement and distortion of the MR images.

The first step is to define the intercommisural line on the FASE images. An approximate, tentative target point is then determined in keeping with the location described in the introduction. This part of the work is done in SurgiPlan. As the VIM is not visualized by modern computerized imaging methods, we depend on the standard atlas of the human thalamus and our own experience of selective thalamotomy guided by microrecording. In this regard, if the patient has already undergone a conventional thalamotomy on the contralateral side, the target planning is easier because a point symmetrical with that used for a previous lesion may be used. In the present study, nine cases had already undergone conventional stereotactic surgery on one side and GKT was then performed on the contralateral side, six cases had undergone conventional stereotactic surgery and then additional GKT on the ipsilateral side to enlarge the previous lesion, and five cases had bilateral GKT with an interval of approximately 1 year. If the major symptom was rigidity, a point located 2 to 3 mm more anterior is chosen as the target to cover the VO.

The next step is to transfer the tentative target point to GammaPlan. The isodoses are then shown to allow determination of whether this target is suitable on axial, coronal, and sagittal images. In this regard, a classic morphological study described by Brierley and Beck claims that a more reliable presentation of the thalamic nuclei can be determined by the ratio of the overall thalamic length rather than the traditional landmark of the posterior commissure. This is very useful. In practice, the VIM is located at approximately 45% of the entire thalamic length from the anterior tip of the thalamus.

Since the observation that the high signal zone surrounding a GKT lesion contains almost normal neuronal activity, the target point has been slightly modified from the previous one and lies 1 mm more medial and 1 mm more anterior than in the earlier cases. It is hoped that this is a more optimal target and will avoid capsular and VO damage. Finally, plugging of some of the beams is used to protect the internal capsule and the lenses of the eyes. The treatment lasted approximately 1 hour after the reloading of the cobalt sources. A dose of 130 Gy is used with a single 4-mm isocenter.

Follow-Up Data

In the first patients the follow-up examination schedule was fairly random. Most patients came once or twice per year for assessment of their clinical state, and thalamic lesion by MR imaging (or CT scanning in patients with cardiac pacemaker, or a deep brain stimulation electrode on the opposite side). More recently, follow up has been made more systematic. Patients return at the regular intervals of 3, 6, 12, 18, and 24 months. To date 12 cases have had a 6-month follow up and three cases have had a 3-month follow up only. Clinical studies include neurological examination and are complemented by assessment of changes in the UPDRS, electromyography, and video. The evaluation of the referring neurologist is most important. Magnetic resonance imaging is also performed at the regular follow-up time, with the Leksell MR imaging indicator without frame set temporarily over the head. At present our practice is to measure the volume of the high signal zone round the lesion on the proton density–weighted images, which are transferred to a treatment planning computer for this purpose. Because the low signal area in the center of the lesion is not always well defined, measurements of its volume are not considered here.

Results

Clinical Course

In most of the later-treated cases the clinical course was similar to that seen in the previously reported earlier-treated
cases with an improvement of tremor and rigidity.13 In most cases (~80–85%), the clinical outcome was satisfactory: tremor was reduced to less than one third of the preoperative state. This now constitutes our new standard clinical course as shown in Fig. 1. There was a difference, however, between the cases treated before and after the reloading of the cobalt. In the recent group the interval to improvement was only approximately 6 months compared with 1 year in the early series. Indeed, some patients noticed an improvement in symptoms as early as 1 month after treatment.

FIG. 1. Schematic illustration of the clinical time course of changes in tremor. In the early series, tremor decreased around 1 year after treatment (right-sided curve). In contrast, in recent series after reloading, the clinical effect appeared after 3 to 6 months (two curves in the left).

FIG. 2. Proton density–weighted MR images obtained in a representative case of early tremor reduction in our oldest case of PD. Upper: Axial view approximately 4 mm above the level of intercommissural line. Lower: Coronal section approximately the center of the lesion.
Illustrative Case

This 84-year-old man with PD had suffered from continuous severe resting tremor and slight rigidity in his right extremities for 6 years. Because the antiparkinsonian drugs did not control his tremor effectively, the patient was annoyed by the severe flapping. Because of his advanced age, open stereotactic surgery or deep brain stimulation was not indicated. A target center was chosen 6.6 mm anterior to the posterior commissure, 15 mm lateral to the midline, and 3.9 mm above the level of the intercommissural line, corresponding to a position approximately 47% of the thalamic length behind the anterior pole of the thalamus. In November 2002, he received 130 Gy, through a single 4-mm collimator, taking 50 minutes. He noticed improvement in his tremor as early as 2 weeks after GKT. This improvement in tremor continued for the following 1 month to the extent that it had almost subsided. At 5.5 months after GKT MR imaging showed a round lesion with short streaking as shown in Fig. 2. His UPDRS score decreased from 44 to 11. He had no motor paresis, weakness, or sensory disturbance. He was very happy to enjoy his daily life without motor disturbance.

In other cases, it was no longer unusual to observe a reduction of tremor, for example, within 3 months after GKT. This improvement in tremor continued for the following 1 month to the extent that it had almost subsided. At 5.5 months after GKT MR imaging showed a round lesion with short streaking as shown in Fig. 2. His UPDRS score decreased from 44 to 11. He had no motor paresis, weakness, or sensory disturbance. He was very happy to enjoy his daily life without motor disturbance.

Volume of Lesion After GKT

As indicated in previous papers, the thalamic reaction observed on MR or CT imaging varies in each case. It has been our experience that there are two kinds of thalamic lesions produced by GKT even though the dosimetry uniformly involves 130 Gy and a single 4-mm collimator isocenter. One lesion type is represented by a circumscribed round high signal area of approximately 7- to 8-mm diameter surrounding a smaller low signal area. The other is characterized by an irregular-shaped high signal zone extending into the medial thalamic area and/or the internal capsule and often accompanied by streaking along the thalamocapsular border and involving the pallidocapsular border, making raillike double streakings.

A systematic volumetric study of these thalamic lesions after various post-GKT time intervals revealed different types of volume change (Fig. 4). For the first 2 months no changes are seen. The typical time to detect an early change was approximately 3 months after treatment. It was usually a round high signal lesion with somewhat poorly defined border. The estimated volume was less than 200 mm³ or so.
in 10 of 12 patients and more than 300 mm$^3$ in the remaining two. The subsequent volume changes have been followed systematically in 11 cases observed for 6 months. During the next 3 months different patterns emerged. In two there was a marked volume increase, in three a slight increase, and in six a decreased volume or no further change. An example in which a small lesion maintained for 17 months was associated with a good clinical result is shown in Fig. 5. In this case, a 72-year-old man with essential tremor since youth underwent GKT in October 2002; however, he did not come to a follow-up examination until recently. When he attended it was to ask for GKT on the untreated side as he was so pleased with the much-reduced right-sided tremor after a latent interval of approximately 1

![Graph demonstrating changes in the volume of irradiated lesion at 3 and 6 months after treatment.](image)

**Fig. 4.** Graph demonstrating changes in the volume of irradiated lesion at 3 and 6 months after treatment.

![Proton density–weighted MR images obtained in a representative case of the smallest effective lesion, 17 months after treatment.](image)

**Fig. 5.** Proton density–weighted MR images obtained in a representative case of the smallest effective lesion, 17 months after treatment. In this case with essential tremor, the lesion size did not change for approximately 1 year since he had the first follow-up examination at 5 months after treatment (left: GKT). See text for detail. **Left:** Axial view approximately 4 mm above the level of intercommissural line. **Right:** Coronal section approximately the center of the lesion.
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year. At the time of his follow up, MR imaging revealed a small lesion in the left thalamus at the expected area of the presumed lateral part of the VIM (Fig. 5), and clinical examination showed almost normal hand writing, which had been impossible before treatment. Moreover he had regained skilled use of his right hand in daily life. Thus he was willing to accept GKT on the other side on March 2004.

As we had, in our recent cases, an impression that the thalamic reaction at 6 months was more restricted than that in the previous series, the volume of the thalamic reaction at around 6 months after irradiation was compared quantitatively. For this, suitable data were taken from seven cases in the previous study14 (thalamic volume was measured at approximately 6 months after treatment as seen in Fig. 4 of reference 14 and from 10 cases in this series (see Fig. 4 of this paper). The mean value of volume of the thalamic lesion in the previous series was 311 mm3 and that in recent series was 175 mm3. Using Student’s t-test this difference was shown to be significant. (p = 0.041). Thus, the thalamic reaction in cases treated after reloading the cobalt was less than that in patients treated before reloading.

It was also noticed that after reloading the treatment duration decreased from 120 to 130 minutes to approximately 60 minutes, in parallel with an increase of the maximum dose rate from 0.9 to 3.5/minute.

Discussion

In the present study we confirmed the previous observation that two types of thalamic lesions develop after GKT: one round and restricted and the other large and irregular. We do not understand the reason for these two varied, unpredictable reactions. It is, however, worth noting that these post-GKT thalamic lesions have been smaller in size after reloading of the cobalt sources. It is important to emphasize that no other dosimetric parameter was changed. The reason for the smaller lesions is at present unknown, but it could be related to the increased dose rate after renewal of the cobalt sources. The shorter treatment time certainly reduces patient discomfort. In theory it could also increase the radiobiological efficacy of the focused brain damage. The relevance of the dose rate in this context is considered in the literature only in relation to radiation necrosis15–19 or radiation induced cancer.18 Radiation doses of the kind given here are not reported in the general radiotherapy or radiosurgery literature cited above. Even in gamma knife treatment, the maximum dose never exceeds 50 Gy except when treating the functional disorders. Thus, the significance of increasing this parameter is difficult to assess in the present context.

It is also interesting to note that until approximately 3 months after GKT, there were no visible changes in the thalamus when using our dosimetry. The damage was always first observed approximately 6 months after GKT. We did not notice this in the previous study14 probably because the follow-up period was not systematically arranged and almost no case was examined at such a short interval after GKT as 2 or 3 months. This delayed effect of irradiation on the human nervous system is quite different from the radiofrequency lesions produced after open stereotactic thalamotomy. This induces a rather large immediate reaction, which shrinks within a couple of months. At present we know very little about the immediate or long-term effect of high-dose ionizing radiation on apparently normal thalamic neurons. We made another interesting observation. The clinical effect appeared in the majority of cases at 6 months after irradiation in the recent series whereas it was observed at 12 months or later in the early series. This might suggest a relationship with the aforementioned visible changes in the irradiated thalamic reaction, suggesting again that the dose rate may play a part. Another factor that might play a part in the shorter latent interval to clinical manifestation is the displacement of the lesion in the most recently treated patients compared with those treated earlier. The displacement is slight, only 1 mm or so, but it could still be important in relationship to the speedier clinical effect, if in fact the new lesion placement is closer to the desired target.

In this series, the clinical course did not seem to be related to the size of the lesion just as in the earlier report.15 It was more influenced by the site of the lesion, and so far as the maximum dose of 130 Gy is used, no noticeable complications have been seen. Nonetheless, while our current maximum dose of 130 Gy seems to be safe it must be kept in mind that the success rate of GKT was somewhat lower than that found after open thalamotomy. Nonetheless, the findings in this study lay to rest the criticism that GKT for PD is still immature.16 It has been shown that it is a safe and effective alternative treatment for PD and related movement disorders.

References

12. Ohye C, Shibazaki T: [Location of the thalamic Vim nucleus. Its...


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