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# Gamma Knife Thalamotomy for Essential and Parkinson's Tremor

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**Summary.** *Background.* The study aims to evaluate the efficacy of gamma knife thalamotomy for the control of essential tremor and Parkinson's-related tremor when other invasive treatment modalities are not recommended.

*Materials and methods.* From June 2019 to January 2021, 27 patients with medically resistant essential tremor and 20 patients with Parkinson's disease (PD) underwent unilateral gamma knife thalamotomy. The patients were treated with a mounted Leksell G frame with modified 4 mm shots aiming to deliver 130–140 Gy to the ventralis intermedius nucleus. Post-surgical evaluation was to be performed 6 and 12 months after surgery. However, due to state-imposed quarantine restrictions direct evaluation was challenging, hence post-surgical results were evaluated via phone call.

Only 12 of 20 PD patients were reached via phone call, but 8 of them were evaluated less than 6 months after surgery. As a result, the group of PD patients was excluded from the study.

*Results.* 23 patients from the essential tremor group were assessed via phone call. One patient died from COVID-19-related pneumonia during the follow-up period. During the phone call, 16 (72%) of 22 patients reported major improvement in hand tremor or full tremor arrest on the contralateral side of thalamotomy. Meanwhile, 6 (28%) patients did not feel any improvement after the treatment. Complications were observed in 4 (18%) patients – they reported transient ataxia and hand movement dyscoordination which resolved in few months.

*Conclusions.* Gamma knife thalamotomy is safe and effective for essential hand tremor control. Main disadvantages include several months of latency period and transient ataxia.

**Keywords:** gamma knife, thalamotomy, essential tremor, Parkinson's disease.

## INTRODUCTION

Tremor is the most common movement disorder. More than 5% of the population over 65 years old complain of hand or head tremors. Large amplitude of persistent tremor raises many difficulties in daily activities, decreases work capacity, and worsens mental state which, in turn, significantly reduces the quality of life of patients. Unfortunately, medications are not effective enough, especially for those suffering from essential tremor. Over time, most patients begin developing such grueling symptoms as severe and wearisome limb pain or head tremor. Surgery is usually the only effective treatment for these patients. The goal of the surgery is to "switch off" the *ventralis intermedius* nucleus (VIM) located within the thalamus via ablation or electrical stimulation, thereby desynchronizing its activity and restoring the usual suppression of the motor cortex.

Until now, deep brain stimulation (DBS) has been considered the gold standard in managing medication-resistant essential or Parkinson's tremor. The effectiveness of DBS is 70–89% in patients who can undergo this procedure [1]. Stereotactic neurosurgery aims to destroy the VIM which is another effective invasive method for tremor control. Surgery is performed by temporally implanting a radiofrequency (RF) electrode and performing a brief electrical stimulation to identify the internal capsule and ventral posterolateral nucleus (VLP). Then thermocoagulation of the VIM is performed. The effectiveness of the RF ablation is 72–87% [2]. However, both methods are invasive and carry possible com-

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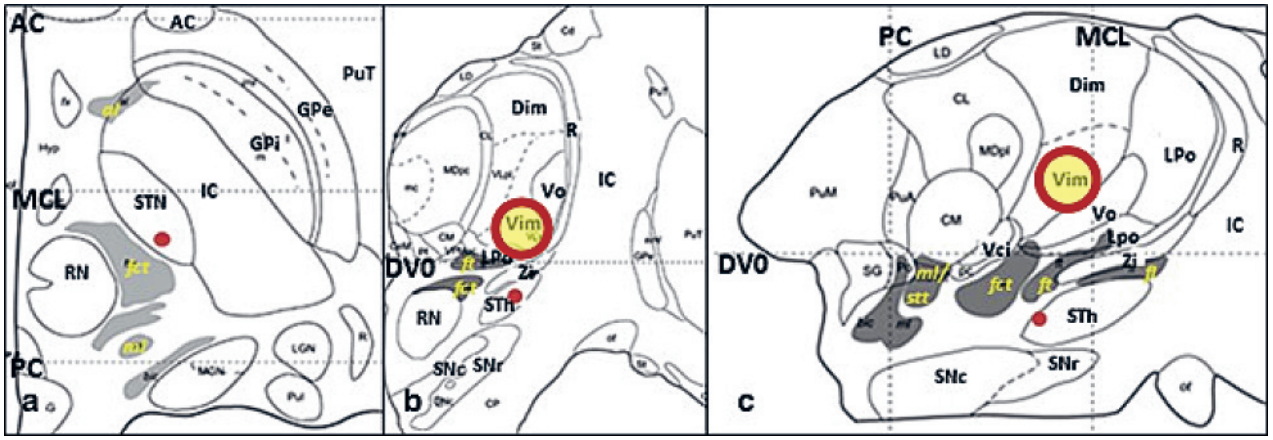


Fig. 1. **Schaltenbrand stereotactic atlas with marked VIM target**

plications, e.g., bleeding (1–2%), infection (4–5%), and epilepsy [3]. The effectiveness of the surgery is largely related to the neurophysiological identification of the VIM. Additional electrical stimulation performed during surgery helps stop tremor, induced paresthesias, and muscle contractions that allows the neurosurgeon to determine the anatomical position of the electrode. Many patients with Parkinson's disease (PD) or essential tremor (ET) are already facing problems related to diminished activities of daily life. This group of patients has many concomitant diseases, and the risk of using invasive treatment methods is significantly increased.

Gamma knife thalamotomy (GKT) is one of the alternative non-invasive methods in cases of medical-resistant tremor. The evolutionary history of stereotactic radiosurgery (SRS) and functional neurosurgery is very similar. In 1951, Lars Leksell presented a conceptually novel idea of using protons and photons crossing at the same point in a non-invasive target to treat deep brain lesions. The first gamma knife was developed in 1968 with the help of physicist Bjorn Larsson.

Until 1978, radiosurgery was limited by low-resolution imaging of intracranial structures. By that time, radiosurgery doses causing deep destruction of healthy tissues were identified via experiments with animals. Doses were reduced from 250 Gy to 100–150 Gy. Based on the clinical data, local radiological changes were observed already after 14 days. The clinical destruction effect emerged sometimes between 3 weeks and 12 months [4].

Neurophysiological information obtained during electrical stimulation using indirect stereotactic targeting is lost during SRS, making neuroradiological imaging of utmost importance. Computer tomography is used to track down even the smallest errors in stereotactic head brain imaging; however, magnetic resonance imaging (MRI) remains the best way to visualize the anatomical brain structures. 1.5T MRI machines are used to obtain the most accurate data with the least deviations caused by the magnetic field. This means that gamma knife thalamotomy can only be applied to patients who can safely undergo MRI of the head. Indirect VIM targeting requires both anterior and posterior commissures which means that magnetic resonance images must have the lowest possible isotropic spatial resolution (<1 mm).

Planning software is used to mark the anterior and posterior commissures. Based on the Shaltenbrand stereotactic atlas (Fig. 1), the 4 mm collimator sight is positioned 2.5 mm above the intercommissural line (ICL), 11 mm to the side of the third ventricle wall, and one fourth of the ICL length +1 mm towards the front of the posterior commissure. The maximum radiation dose (130–140 Gy) is then directed to the VIM. To avoid any damage to the internal capsule, the medial side of the internal capsule can be adjoined with the isodose line by 25%.

Another possible target positioning is based on anatomical studies of the thalamus. Each ventral nuclear group of the thalamus is localized using standard methods and the VIM is localized at a 45% distance from the anatomical anterior border of the thalamus in the horizontal plane. The VIM may also be localized anatomically based on MRI tractography, i.e., the anterior of the VIM is revealed by the intersection point of the internal capsule side and *tr. rubrothalamicus.*

### Gamma knife in Lithuania

The fifth generation ICON gamma knife was the first gamma knife in the Baltic states; it has been used in Kaunas Clinics of the Lithuanian University of Health Sciences since 2019. Despite the COVID-19 pandemic and "on and off" quarantine conditions, a total of 700 stereotactic radiosurgery operations were performed from 2019 to December 2020. The surgeries were mainly used to treat both benign and malignant brain tumors, vascular diseases (AVM, cavernoma), trigeminal neuralgia, cluster headache, and movement disorders (essential tremor, Parkinson's disease).

### Indications for gamma knife thalamotomy

- Parkinson's-related and medication-resistant hand tremor
- Patients >75 years old
- Heavy comorbidities
- Constant use of anticoagulants
- The patient does not consent to possible invasive treatment methods (deep brain stimulation, radiofrequency ablation)

**Contraindications for gamma knife thalamotomy**

- The patient cannot undergo brain MRI due to ferromagnetic foreign bodies
- The patient does not understand the goal and risks of this treatment method
- The patient does not consent to the placement of stereotactic frame on his head

## AIM OF THE STUDY

The study aims to evaluate the efficacy of gamma knife thalamotomy in reducing essential tremor and Parkinson's-related tremor when other invasive therapies are not recommended.

## METHODS AND PARTICIPANTS

In total, 27 patients with essential tremor and 20 patients with Parkinson's-related tremor who underwent unilateral ventralis intermedius nucleus thalamotomy were included in the study. Severity of tremor was evaluated using Fahn-Tolosa-Martin tremor rating scale prior to surgical treatment. Post-surgical evaluation was to be performed 6 and 12 months after radiosurgery. However, due to state-imposed quarantine restrictions, direct evaluation was challenging, hence post-surgical results were evaluated via phone call.

Eighteen female and nine male patients with essential tremor were included in the study. The oldest patient in the group was 91 years old, the youngest 60 years old. Mean age in the essential tremor group was 76.1 years (SD=6.1). 12 female and 8 male patients with Parkinson's disease were enrolled in the study with mean age of 73.5 years (SD=7.8).

Twelve of 20 PD patients were reached via phone call, but 8 of them were evaluated less than 6 months after surgery. It was decided to conduct analysis of the treatment results after 6 months.

All patients underwent preoperative stereotactic MRI (1,5T Siemens Avanto) with Leksell G frame which was positioned in the standard manner and under local anesthesia. Images were transferred to the Gamma Plan 11.1 planning program which was used to plan thalamotomy target points as described in the introduction (Fig. 2).

Duration of gamma knife thalamotomy is usually 70–80 minutes. After treatment, the frame is removed and the next day the patient is discharged home for ambulatory care.

## RESULTS

Main factors that influenced the decision to perform gamma knife thalamotomy: old age (>70 years) 23 (85%), advanced comorbidities 16 (60%), anticoagulant treatment 18 (67%), and medical unfitness or reluctance to undergo deep brain stimulation or radiofrequency thalamotomy.

All patients were informed about possible risks, treatment efficacy, and alternative treatment options and signed patient consent forms.

Severity of tremor was evaluated using Fahn-Tlosa-Martin tremor rating scale prior to surgical treatment. Mean tremor severity was 3.7 (SD=0.2), whereas mean

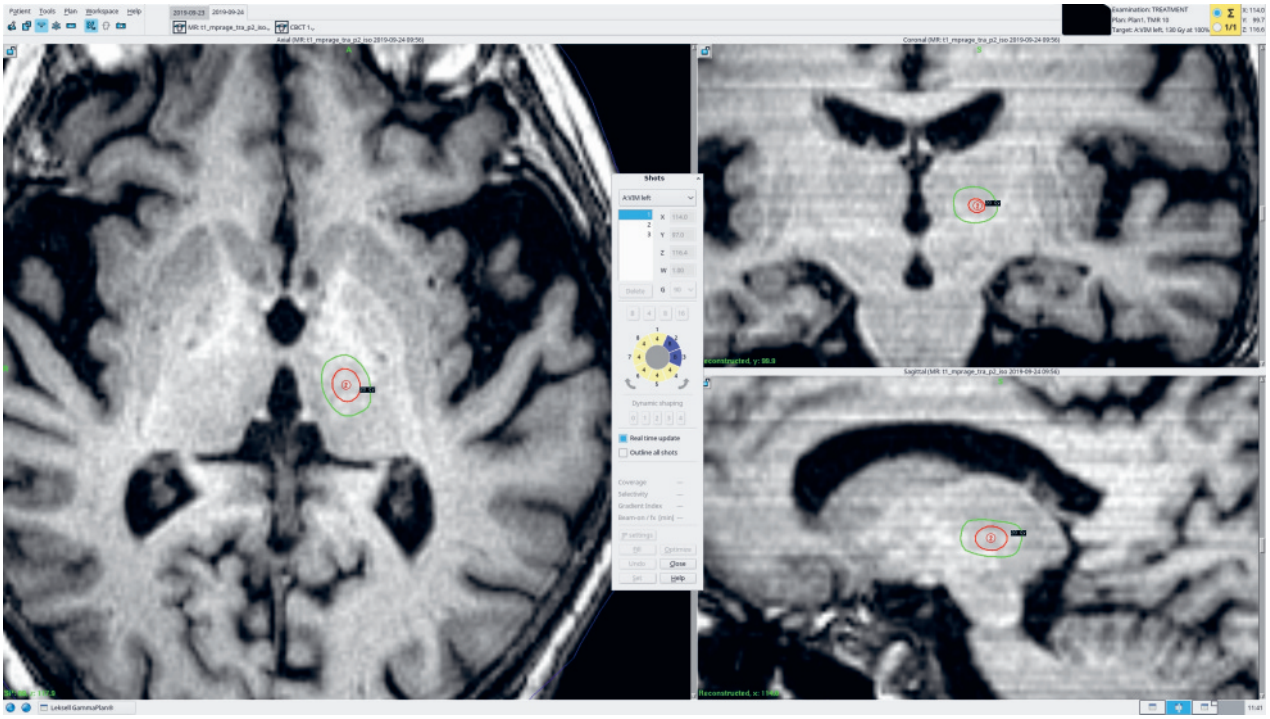

Fig. 2. **VIM target layout in Gamma Plan program**

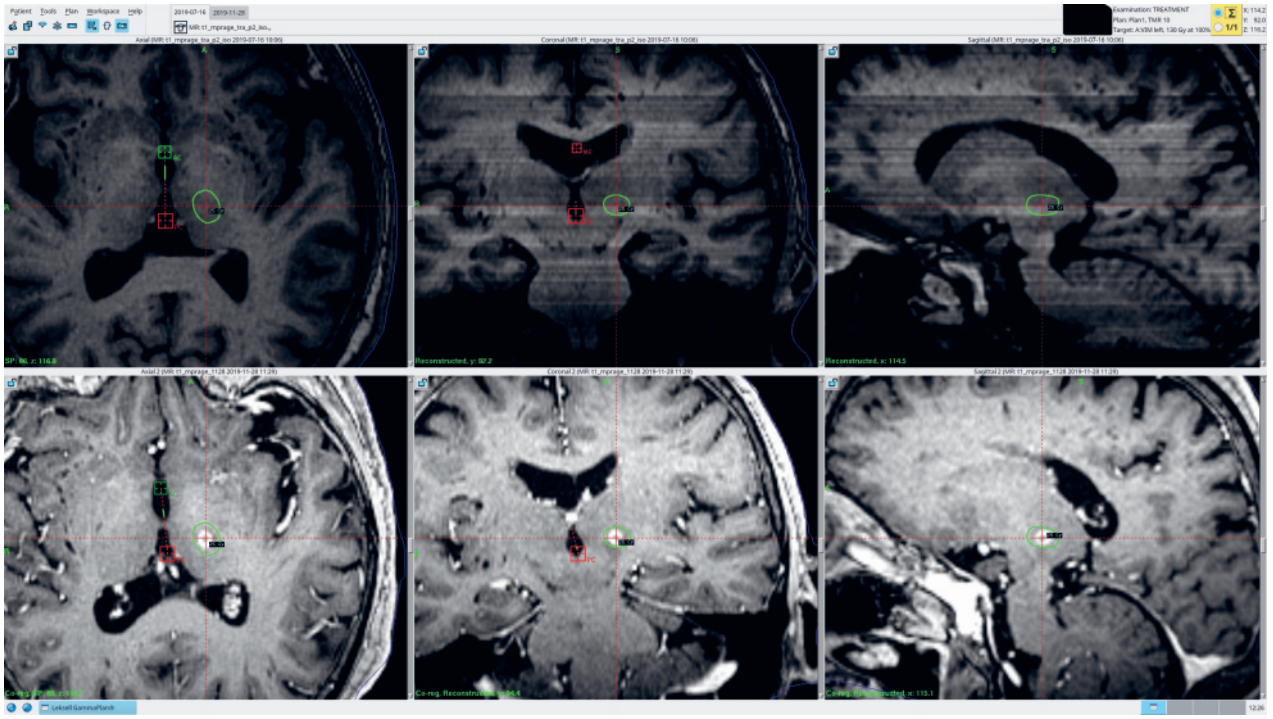

Fig. 3. **Brain MRI before and after gamma knife thalamotomy.**
Contrast media accumulation zones represent stereotactic coordinates of gamma knife shots

evaluation of handwriting was 2.9 (SD=0.1). As it was mentioned in the method section, postoperative follow-up was challenging due to the COVID-19 epidemic and recurrent quarantine restrictions in Lithuania. As a result, treatment efficacy was evaluated via phone call. The survey was conducted 4–18 months after the treatment. 23 of 27 patients were assessed via phone call. One female patient died due to COVID-19 infection during the follow-up period. 16 (72%) of 22 patients stated that they experienced significant or complete tremor reduction on the contralateral side of VIM thalamotomy. Remaining 6 patients experienced no significant change in tremor amplitude. 4 of 22 patients declared of impaired coordination and transient hand clumsiness which resolved in few months. During post-surgical consultation, 4 patients underwent brain MRI for thalamotomy target visualization (Fig. 3).

## RESULT OVERVIEW

The estimated results of our study on tremor reduction after gamma knife thalamotomy are in line with published results of other gamma knife centres. It might be assumed that efficacy rate would have been 10% higher if all patients underwent postoperative evaluation after 12 months. This assumption is plausible given that 10 (83.3%) of 12 patients who were treated for more than 12 months felt a significant or complete tremor reduction. Compared with the results of other centres, the complication rate was moderate and complications were mainly transient (4 (18%)). Results from different treatment centres with the largest sample sizes are displayed in the Table.

There are three main advantages of gamma knife thalamotomy. Firstly, this non-invasive method is suitable for patients with a high risk for surgical interventions. This

Table. **Results from studies with the largest sample sizes that analyzed tremor reduction in PD and ET patients after gamma knife surgery**

| Author | Participants, n | Follow-up period, mth | Rating scales | Improvement | Complications, n |
|---|---|---|---|---|---|
| Young [6] | 154 | 52.3 | UPDRS | 92%, 88% after 4 years | 1 ataxia<br>1 mild paresis<br>1 hand paresthesia |
| Kooshkabadi [7] | 86 | 23 | FTM | 82% | 1 paresis<br>1 dysphagia<br>2 ataxia |
| Ohye [8] | 72 | 24 | UPDRS | 81% | – |
| Young [9] | 214 | 44 | FTM | 81% | 10 motor deficit<br>5 hypoesthesia |
| Niranjan [10] | 73 | 28 | FTM | 93% | – |

UPDRS – Unified Parkinson's disease rating scale; FTM – Fahn-Tolosa-Marin clinical tremor rating scale

includes older patients under anticoagulant treatment or patients with severe comorbidities. Secondly, DBS implantation requires frequent follow-up visits, parameter optimisation, and replacement of stimulator battery. Also, kinesthetic thalamic cells are suppressed within 50% isodose volume even though apoptosis is not observed; this may result in a safe and long-term antitremor effect [5].

Although there is sufficient evidence that gamma knife thalamotomy is a safe and effective treatment method for reducing tremor in medication-resistant PD and ET, there are doubts concerning the choice of treatment method. Main disadvantages in comparison with other surgical methods are complicated neurophysiological VIM verification, the ability to observe clinical improvement only after 1 to 4 months, and a different volume of the destruction target.

Unfortunately, no clinical effect is attained in some patients who have undergone gamma knife thalamotomy. Reasons for this are poorly estimated VIM stereotactic coordinates and, therefore, a wrongly planned shot, failure to target VIM due to imaging and stereotactic frame errors, and physiological resistance to Gamma-rays. 2–8% of patients experience an insufficient or hyper-response to gamma knife treatment [5]. One 77-year-old female patient included in our study experienced no effect after thalamotomy. Therefore, brain MRI was performed 12 months after the gamma knife thalamotomy. Fig. 4 shows an insufficiently developed thalamotomy lesion.

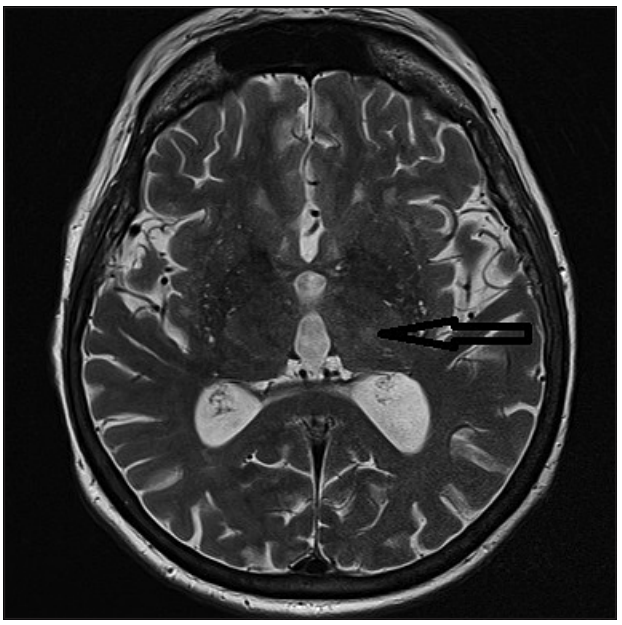

Fig. 4. **Brain MRI image which shows hyperintense lesion in VIM zone due to insufficient response to 130 Gy dose**

## CONCLUSIONS

Gamma knife thalamotomy is a safe and effective means for medication-resistant essential hand tremor control. Main disadvantages include several months of latency period and transient ataxia.

## ACKNOWLEDGMENT

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## GAMA PEILIO TALAMOTOMIJA ESENCIALINIAM IR PARKINSONO TREMORUI GYDYTI

**Santrauka**

*Tikslas.* Tyrimo tikslas įvertinti gama peilio talamotomijos efektyvumą, stabdant tremorą sergantiesiems Parkinsono liga (PL) ir esencialiniu tremoru, kai kiti invaziniai gydymo metodai nerekomenduotini.

*Tiriamieji ir tyrimo metodai.* Nuo 2019 m. birželio iki 2021 m. sausio dėl esencialinio tremoro ir PL sąlygoto tremoro atitinkamai atlikta 27 ir 20 vienpusių gama peilio talamotomijų. Naudojant Leksell G stereotaksinį rėmą, pagal standartizuotą metodiką, naudojant 4 mm diametro kolimatoriaus šūvį, į *n.ventralis intermedius* (VIM) zoną paskirta 130–140 Gy dozė.

Tyrime pooperacinis vertinimas planuotas atlikti praėjus 6 ir 12 mėnesių po taikyto gydymo. Tačiau dėl besikartojančio karantino dėl COVID-19 buvo apsunkintas ligonių kontaktinis vertinimas, todėl rezultatai vertinti telefoninės apklausos metu. Iš 20 ligonių, sergančių PL, pavyko susisiekti tik su 12, iš kurių aštuoniems gydymas buvo taikytas mažiau nei prieš 6 mėnesius. Nuspręsta PL grupės ligonių gydymo rezultatų analizę atlikti po 6 mėnesių.

*Rezultatai.* Iš 27 sergančiųjų esencialiniu tremoru telefonu pakalbinti pavyko 23 ligonius. Viena ligonė per stebėjimo laikotarpį mirė nuo COVID-19 infekcijos. Iš apklaustų 22 ligonių 16 (72 %) teigė, kad jaučia žymų tremoro rankoje sumažėjimą ar visišką jo išnykimą priešingoje, nei atlikta VIM talamotomija, pusėje. Likę 6 ligoniai (28 %) taikyto gydymo efekto iki šiol nejaučia. Iš 22 ligonių 4 (18 %) teigė, kad kurį laiką buvo sutrikusi koordinacija ir vargino laikinas rankos nevikrumas, kuris praėjo per kelis mėnesius.

*Išvados.* Gama peilio talamotomija yra saugi ir efektyvi esencialinio rankų tremoro mažinimo priemonė. Pagrindiniai šio gydymo trūkumai yra kelis ar keliolika mėnesių trunkantis latencinis periodas iki pastebimo klinikinio efekto ir laikina ataksija.

**Raktažodžiai:** gama peilis, esencialinis tremoras, Parkinsono liga, talamotomija.

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