

Bibliography

# Gamma Knife radiosurgery for Tremors

December 2016–July 2021

Vim stereotactic radiosurgical thalamotomy for drug-resistant idiopathic Holmes tremor: a case report. Acta Neurochir (Wien). 2021 Jul;163(7):1867–71. DOI: 10.1007/s00701-020-04489-1.

Tripathi M, Mehta S, Singla R, Ahuja CK, Tandalya N, Tuleasca T, Batish A, Mohindra S, Agrahari A, Kaur R.

We share our experience with stereotactic Gamma Knife thalamotomy (GKT) for medically refractory Holmes tremor (HT). A 22-year-old patient underwent Gamma Knife thalamotomy at the ventral intermediate nucleus to disable HT of the right upper limb. A single 4-mm isocenter was used to target the ventral intermediate nucleus with 130 Gy irradiation. At 4 months follow up, we observed an 84% improvement in his Fahn-Tolosa-Marin (FTM) rating scale with significant improvement in the right upper limb

dystonic tremor. There was only subtle improvement in the ataxic component of the right lower limb. At one-year post-stereotactic GKT, there was sustained neurological improvement with no side effect. We present stereotactic GKT as a treatment modality for drug-resistant HT. Moreover, it may be considered an alternate treatment modality, especially in reluctant patients or those for whom any invasive surgery is contraindicated.

Gamma Knife thalamotomy for medically refractory tremors: Longitudinal evaluation of clinical effects and MRI response patterns.

**Acta Neurochir Suppl. 2021;128:127–32. DOI: 10.1007/978-3-030-69217-9\_14.** Ochiai T.

#### Objective

The present longitudinal study evaluated the results of Gamma Knife surgery (GKS) for medically refractory tremors.

#### Methods

The outcome after Gamma Knife thalamotomy targeting the ventral intermediate nucleus (VIM) was analyzed in 17 patients (9 men and 8 women; mean age 72 years) with either Parkinson's disease or an essential tremor, who were followed up for at least 2 years after treatment. Clinical and magnetic resonance imaging (MRI) examinations were done before and every 3 months after GKS.

#### Results

The mean rates of symptom improvement (a decrease in the tremor frequency) were 6%, 39%, 63%, and 64% at 3, 6, 12, and 24 months after treatment, respectively. The defined MRI response patterns included a minimum reaction (in 3 patients), a normal reaction (in 11 patients), and a hyperreaction (in 3 patients). They were not associated with any evaluated pretreatment, radiosurgical, or outcome parameter, although 2 patients with a hyperreaction exhibited mild-to-moderate motor weakness in the contralateral limbs. Linear contrasting of the border between the thalamus and the internal capsule adjacent to the lesion site was noted on follow-up MRI in 13 cases and was associated with a higher symptom improvement rate.

#### Conclusion

GKS allows effective and safe management of medically refractory tremors. The treatment is characterized by variable MRI response patterns. Some imaging findings during follow-up may be associated with clinical effects.

Ventralis oralis anterior (Voa) deep brain stimulation plus Gamma Knife thalamotomy in an elderly patient with essential tremor: A case report.

Medicine (Baltimore). 2021 Apr 16;100(15): e25461. DOI: 10.1097/MD.0000000000025461. Oh BH, Park YS.

#### **Rationale**

Deep brain stimulation (DBS) of the ventralis intermedius nucleus (Vim) provides a safe and effective therapy for medically refractory essential tremor (ET). However, DBS may be risky in elderly patients and those with ischemic brain lesions. Gamma Knife radiosurgery (GKS) is a minimally invasive procedure, but bilateral thalamotomy is dangerous.

#### Patient concerns

We report a case of ventralis oralis anterior nucleus (Voa) DBS for dominant hand tremor plus Voa GKS for non-dominant hand tremor in a very elderly patient with medically intractable ET.

#### Diagnosis

An 83-year-old right-handed woman visited our hospital with a medically intractable ET. Because of the ischemic lesion in the right basal ganglia, we decided to perform left unilateral DBS instead of bilateral DBS.

#### Intervention

We chose Voa as the target for DBS because, clinically, her tremor was mainly confined to her hands, and Voa had better intraoperative microelectrode recording results than Vim.

#### **Outcomes**

After 2 years, her right-hand tremor remained in an improved state, but she still had severe tremor in her left hand. Therefore, we performed GKS targeting the right Voa. One year after surgery, the patient's hand tremor successfully improved without any complications.

#### Lessons

Salvage Voa GKS after unilateral Voa DBS is a valuable option for very elderly patients and patients with ischemic brain lesions. We suggest that Voa GKS thalamotomy is as useful and safe a surgical technique as Vim GKS for dystonic hand tremor. To the best of our knowledge, this is the first case report using salvage Voa as the only target for ET.

The brain connectome after Gamma Knife radiosurgery of the ventro-intermediate nucleus for tremor: Marseille-Lausanne Radiobiology Study Protocol.

Stereotact Funct Neurosurg. 2021;99(5):387-92. DOI: 10.1159/000514066. Epub 2021 Mar 8.

Tuleasca C, Witjas T, Levivier M, Girard N, Cretol A, Levy N, Thiran J-P, Guedj E, Van de Ville D, Régis J.

Essential tremor (ET) is the most common movement disorder. Deep brain stimulation is the current gold standard for drug-resistant tremor, followed by radiofrequency lesioning. Stereotactic radiosurgery by Gamma Knife (GK) is considered as a minimally invasive alternative. The majority of procedures aim at the same target, thalamic ventro-intermediate nucleus (Vim). The primary aim is to assess the clinical response in relationship to neuroimaging changes, both at structural and functional levels. All GK treatments are uniformly performed in our center using Guiot's targeting and a radiation dose of 130 Gy. The MR neuroimaging protocol includes structural imaging (T1-weighted and diffusion-weighted imaging [DWI]), resting-state functional MRI, and 18F-fluorodeoxyglucose-

positron emission tomography. Neuroimaging changes are studied both at the level of the cerebello-thalamocortical tract (using the prior hypothesis based upon Vim's circuitry: motor cortex, ipsilateral Vim, and contralateral cerebellar dentate nucleus) and also at global brain level (no prior hypothesis). This protocol aims at using modern neuroimaging techniques for studying Vim GK radiobiology for tremor, in relationship to clinical effects, particularly in ET patients. In perspective, using such an approach, patient selection could be based upon a specific brain connectome profile.

Gamma Knife stereotactic radiosurgery as a treatment for essential and parkinsonian tremor: Long-term experience. Neurologia (Engl Ed). 2020 Sep 8;S0213-4853(20)30217-6. DOI: 10.1016/j.nrl.2020.05.014.

Pérez-Sánchez JR, Martínez-Álvarez R, Martínez Moreno NE, Torres Diaz C, Rey G, Pareés I, Del Barrio A, Álvarez-Linera J, Kurtis MM.

#### Introduction

Unilateral Gamma Knife stereotactic radiosurgery on the ventral intermediate nucleus of the thalamus is a minimally invasive neurosurgical option for refractory tremor. We describe the experience of Gamma Knife thalamotomy (GKT) in patients with essential tremor (ET) and tremordominant Parkinson's disease (PD) at our specialized stereotactic neurosurgery unit.

#### Methods

We reviewed the cases of patients treated with GKT between January 2014 and February 2018 with a minimum of 12 months follow-up. We analyzed clinical and demographic variables, indication, radiation dose, effectiveness (based on subscales of the Fahn-Tolosa-Marin [FTM] scale and the Movement Disorders Society-Unified Parkinson's Disease Rating Scale [MDS-UPDRS] motor score), and adverse events.

#### Results

Thirteen patients were registered, 6 with a diagnosis of tremor-dominant PD, four with refractory ET, and three with ET and PD. Median age was 78 years (range, 62-83), with seven patients aged over 75 years. Four patients were receiving anticoagulants and two had a history of stroke. The maximum radiation dose administered was 130 Gy. Mean (standard deviation) follow-up duration was 30.0 (14.5) months. Significant tremor improvement was observed on the FTM subscales: 63.6% at 12 months and 63.5% at the end of follow-up; MDS-UPDRS tremor items showed improvements of 71.3% at 12 months and 60.3% at the end of follow up. Eleven patients reported significant improvements in quality of life, and 3 reported mild and transient adverse effects.

#### Conclusions

This is the largest series of patients with essential and parkinsonian tremor treated with GKT and followed up in the long term in Spain. GKT can be safe and effective in the long term in patients with refractory tremor, including in elderly patients and those receiving anticoagulants.

Stereotactic radiosurgery for medically refractory multiple sclerosis-related tremor.

J Neurosurg. 2018 Apr;128(4):1214–21. DOI: 10.3171/2017.1. JNS162512. Epub 2017 Jun 30.

Raju SS, Niranjan A, Monaco EA, Flickinger JC, Lunsford LD.

#### Objective

Multiple sclerosis (MS) is a neurodegenerative disease that can lead to severe intention tremor in some patients. In several case reports, conventional radiotherapy has been reported to possibly exacerbate MS. Radiosurgery dramatically limits normal tissue irradiation to potentially avoid such a problem. Gamma Knife thalamotomy (GKT) has been established as a minimally invasive technique that is effective in treating essential tremor and Parkinson's disease-related tremor. The goal in this study was to analyze the outcomes of GKT in patients suffering from medically refractory MS-related tremor.

#### Methods

The authors retrospectively studied the outcomes of 15 patients (mean age 46.5 years) who had undergone GKT over a 15-year period (1998-2012). Fourteen patients underwent GKT at a median maximum dose of 140 Gy (range 130-150 Gy) using a single 4-mm isocenter. One patient underwent GKT at a dose of 140 Gy delivered via two 4-mm isocenters (3 mm apart). The posteroinferior region of the nucleus ventralis intermedius (VIM) was the target for all

GKTs. The Fahn-Tolosa-Marin clinical tremor rating scale was used to evaluate tremor, handwriting, drawing, and drinking. The median time to the last follow-up was 39 months.

#### **Results**

After GKT, 13 patients experienced tremor improvement on the side contralateral to surgery. Four patients noted tremor arrest at a median of 4.5 months post-GKT. Seven patients had excellent tremor improvement and 6 had good tremor improvement. Four patients noted excellent functional improvement, 8 noted good functional improvement, and 1 noted satisfactory functional improvement. Three patients experienced diminished tremor relief at a median of 18 months after radiosurgery. Two patients experienced temporary adverse radiation effects. Another patient developed a large thalamic cyst 60 months after GKT, which was successfully managed with Ommaya reservoir placement.

#### Conclusions

Gamma Knife thalamotomy was found to be a minimally invasive and beneficial procedure for medically refractory MS tremor.

Is staged bilateral thalamic radiosurgery an option for otherwise surgically ineligible patients with medically refractory bilateral tremor?

J Neurosurg. 2018 Feb;128(2):617-26. DOI: 10.3171/2016.11.JNS162044.

Niranjan A, Raju SS, Monaco EA, Flickinger JC, Lunsford LD.

#### Objective

Unilateral Gamma Knife thalamotomy (GKT) is a well-established treatment for patients with medically refractory tremor who are not eligible for invasive procedures due to increased risk of complications. The purpose of this study was to evaluate whether staged bilateral GKT provides benefit with acceptable risk to patients suffering from disabling medically refractory bilateral tremor.

#### Methods

Eleven patients underwent staged bilateral GKT during a 17-year period (1999-2016). Eight patients had essential tremor (ET), 2 had Parkinson's disease (PD)-related tremor, and 1 had multiple-sclerosis (MS)-related tremor. For the first GKT, a median maximum dose of 140 Gy was delivered to the posterior-inferior region of the nucleus ventralis intermedius (VIM) through a single isocenter with 4-mm collimators. Patients who benefitted from unilateral GKT were eligible for a contralateral GKT 1-2 years later (median 22 months). For the second GKT, a median maximum dose of 130 Gy was delivered to the opposite VIM nucleus to a single 4-mm isocenter. The Fahn-Tolosa-Marin (FTM) clinical tremor rating scale was used to score tremor, drawing, and drinking before and after each GKT. The FTM writing score was assessed only for the dominant hand before and after the first GKT. The Karnofsky Performance Status (KPS) was used to assess quality of life and activities of daily living before and after the first and second GKT.

#### Results

The median time to last follow-up after the first GKT was 35 months (range 11–70 months). All patients had improvement in at least 1 FTM score after the first GKT. Three patients (27.3%) had tremor arrest and complete restoration of function (noted via FTM tremor, writing, drawing, and drinking scores equaling zero). No patient had tremor recurrence or diminished tremor relief after the first GKT. One patient experienced new temporary neurological deficit (contralateral lower-extremity hemiparesis) from the first GKT. The median time to last follow-up after the second GKT was 12 months (range 2-70 months). Nine patients had improvement in at least 1 FTM score after the second GKT. Two patients had tremor arrest and complete restoration of function. No patient experienced tremor recurrence or diminished tremor relief after the second GKT. No patient experienced new neurological or radiological adverse effect from the second GKT. Statistically significant improvements were noted in the KPS score following the first and second GKT.

#### Conclusions

Staged bilateral GKT provided effective relief for medically refractory, disabling, bilateral tremor without increased risk of neurological complications. It is an appropriate strategy for carefully selected patients with medically refractory bilateral tremor who are not eligible for deep brain stimulation.

#### Stereotactic radiosurgery for tremor: systematic review.

J Neurosurg. 2018 Feb 1;1–12. DOI: 10.3171/2017.8.JNS17749.

Sahgal AS, De Dalles A, Hayashi M, Levivier M, Ma L, Paddick I, Régis J, Ryu S, Slotman BJ, Martínez-Álvarez R.

#### Objective

The aim of this systematic review is to offer an objective summary of the published literature relating to stereotactic radiosurgery (SRS) for tremor and consensus guideline recommendations.

#### Methods

This systematic review was performed up to December 2016. Article selection was performed by searching the MEDLINE (PubMed) and EMBASE electronic bibliographic databases. The following key words were used: "radiosurgery" and "tremor" or "Parkinson's disease" or "multiple sclerosis" or "essential tremor" or "thalamotomy" or "pallidotomy." The search strategy was not limited by study design but only included key words in the English language, so at least the abstract had to be in English.

#### Results

A total of 34 full-text articles were included in the analysis. Three studies were prospective studies, 1 was a retrospective comparative study, and the remaining 30 were retrospective studies. The one retrospective comparative study evaluating deep brain stimulation (DBS), radiofrequency thermocoagulation (RFT), and SRS reported similar tremor control rates, more permanent complications after DBS and RFT, more recurrence after RFT, and a longer latency period to clinical response with SRS. Similar tremor reduction rates in most of the reports were observed with SRS thalamotomy (mean 88%). Clinical complications were rare and usually not permanent (range 0%–100%, mean 17%, median 2%). Follow-up in general was too short to confirm long-term results.

#### Conclusions

SRS to the unilateral thalamic ventral intermediate nucleus, with a dose of 130–150 Gy, is a well-tolerated and effective treatment for reducing medically refractory tremor, and one that is recommended by the International Stereotactic Radiosurgery Society.

#### Radiosurgical pallidotomy for Parkinson's disease.

**Prog Neurol Surg. 2018; 33:149–57. DOI: 10.1159/000481083. Epub 2018 Jan 12.** Cahan LD, Young RF, Li F.

Deep brain stimulation (DBS) has been widely accepted as a tool for treating many symptoms of Parkinson's disease (PD); pallidotomy has been nearly abandoned. Concerns about both the safety and efficacy of pallidotomy are based on small series, isolated case reports and techniques that would now be considered obsolete. The senior author recently reviewed long-term follow-up of a series of patients who had Gamma Knife pallidotomy (GKP) for advanced PD. GKP leads to durable, clinically significant benefit. Bilateral GKP adds incremental improvement. The complication rate

was 4% when calculated on a per lesion basis. GKP is not quite as effective as DBS for tremor and bradykinesia; the results of GKP and DBS are equivalent for dyskinesia. GKP should be considered in patients who are not candidates for DBS. GKP is not as invasive as radiofrequency pallidotomy and avoids the problems and expenses associated with DBS. Patients on anticoagulants, with cognitive deficits or with other contraindications to DBS can be offered GKP to alleviate many of the motor symptoms of PD.

## Assessing the clinical outcome of Vim radiosurgery with voxel-based morphometry: visual areas are linked with tremor arrest!

Acta Neurochir (Wien). 2017 Nov;159(11):2139-44. DOI: 10.1007/s00701-017-3317-7.

Tuleasca C, Witjas T, Najdenovska E, Verger A, Girard N, Champoudry J, Van de Ville D, Cuadra MB, Levivier M, Guedj E, Régis J.

#### Introduction

Radiosurgery (RS) is an alternative to open standard stereotactic procedures (deep-brain stimulation or radiofrequency thalamotomy) for drug-resistant essential tremor (ET), aiming at the same target (ventro-intermediate nucleus, Vim). We investigated the Vim RS outcome using voxel-based morphometry by evaluating the interaction between clinical response and time.

#### Methods

Thirty-eight patients with right-sided ET benefited from left unilateral Vim RS. Targeting was performed using 130 Gy and a single 4-mm collimator. Neurological and neuroimaging assessment was completed at baseline and 1 year. Clinical responders were considered those with at least 50% improvement in tremor score on the treated hand (TSTH).

#### Results

Interaction between clinical response and time showed the left temporal pole and occipital cortex (Brodmann area 19, including V4, V5 and the parahippocampal place area) as statistically significant. A decrease in gray matter density (GMD) 1 year after Vim RS correlated with higher TSTH improvement (Spearman = 0.01) for both anatomical areas. Higher baseline GMD within the left temporal pole correlated with better TSTH improvement (Spearman = 0.004).

#### Conclusions

Statistically significant structural changes in the relationship to clinical response after Vim RS are present in remote areas, advocating a distant neurobiological effect. The former regions are mainly involved in locomotor monitoring toward the local and distant environment, suggesting the recruiting requirement in targeting of the specific visuomotor networks.

Treatment of the ventral intermediate nucleus for medically refractory tremor: A cost-analysis of stereotactic radiosurgery versus deep brain stimulation.

**Radiother Oncol. 2017 Oct;125(1):136–39. DOI: 10.1016/j.radonc.2017.07.030.**McClelland S III, Jaboin JJ.

#### Introduction

Medically refractory tremor treatment has evolved over the past half-century from intraoperative thalamotomy to deep brain stimulation (DBS) of the thalamic ventral intermediate nucleus (VIM). Within the past 15 years, unilateral radiosurgical VIM thalamotomy has emerged as a comparably efficacious treatment modality.

#### Methods

An extensive literature search of VIM DBS series was performed; the total cost of VIM DBS was calculated from hospitals geographically representative of the entire United States using current procedural terminology and work relative value unit (RVU) codes. The 2016 Medicare Ambulatory Payment Classification for stereotactic radiosurgery (SRS) was added to the work RVU to determine the total cost of VIM SRS for both Gamma Knife and linear accelerator

SRS. Cost estimates assumed that VIM DBS was performed without intraoperative microelectrode recording.

#### Result

The mean unilateral VIM DBS cost was \$17,932.41 per patient. For SRS VIM, the total costs for Gamma Knife (\$10,811.77) and linear accelerator (\$10,726.40) were 40% less expensive than for unilateral VIM DBS.

#### Conclusion

Radiosurgery of the VIM is 40% less expensive than unilateral VIM DBS in treatment of medically refractory tremor, regardless of radiosurgical modality. This finding argues for increased radiation oncology involvement in the management of medically refractory tremor patients.

Stereotactic radiosurgery for intractable tremor-dominant Parkinson's disease: A retrospective analysis.

Stereotact Funct Neurosurg. 2017;95(5):291–97. DOI: 10.1159/000479236. Epub 2017 Sep 2.

Raju SS, Niranjan A, Monaco EA, Flickinger JC, Lunsford LD.

#### Objective

The purpose of this study was to retrospectively analyze the outcomes of stereotactic radiosurgery for patients suffering from medically refractory Parkinson disease (PD) tremor.

#### Methods

We retrospectively studied the outcomes of 33 patients who were treated with Gamma Knife thalamotomy (GKT) over a 19-year period. Twelve patients were ≥80 years. A median dose of 140 Gy (range, 130–150 Gy) was delivered to the nucleus ventralis intermedius through a single 4-mm isocenter. We used the Fahn-Tolosa-Marin clinical tremor rating scale to score tremor, handwriting, drawing and ability to drink fluids. The median time to the last follow-up was 23 months (range, 9–144 months).

#### Results

After GKT, 31 patients (93.9%) experienced improvement in tremor. Twenty-three patients (70.0%) had complete or nearly complete tremor arrest. Nine patients (27.2%) noted tremor arrest and resolution of impairment in writing, drawing and ability to drink fluids. One patient (3%) improved in bradykinesia, three patients (9%) improved in rigidity, and three patients (9%) decreased their dosage of dopa after GKT. Tremor relief was fully maintained in the last follow-up for 96.8% of responding patients. Two patients (6%) experienced temporary adverse radiation effects.

#### Conclusions

GKT is a safe and effective treatment for medically refractory PD tremor, especially for the elderly or those not suitable for deep brain stimulation or thermal thalamotomy.

Equivalence of cell survival data for radiation dose and thermal dose in ablative treatments: analysis applied to essential tremor thalamotomy by focused ultrasound and Gamma Knife.

Int J Hyperthermia. 2017 Jun;33(4):401-10. DOI: 10.1080/02656736.2016.1278281. Epub 2017 Jan 31.

Schlesinger D, Lee M, Haar GT, Sela B, Eames M, Snell J, Kassell N, Sheehan J, Larner JM, Aubry JF.

Thermal dose and absorbed radiation dose have historically been difficult to compare because different biological mechanisms are at work. Thermal dose denatures proteins and the radiation dose causes DNA damage in order to achieve ablation. The purpose of this paper is to use the proportion of cell survival as a potential common unit by which to measure the biological effect of each procedure. Survival curves for both thermal and radiation doses have been extracted from previously published data for three different cell types. Fits of these curves were used to convert both thermal and radiation dose into the same quantified biological effect: fraction of surviving cells. They have also been used to generate and compare survival profiles from the only indication for which clinical data are available

for both focused ultrasound (FUS) thermal ablation and radiation ablation: essential tremor thalamotomy. All cell types could be fitted with coefficients of determination greater than 0.992. As an illustration, survival profiles of clinical thalamotomies performed by radiosurgery and FUS are plotted on a same graph for the same metric: fraction of surviving cells. FUS and Gamma Knife have the potential to be used in combination to deliver a more effective treatment (for example, FUS may be used to debulk the main tumor mass, and radiation to treat the surrounding tumor bed). In this case, a model which compares thermal and radiation treatments is valuable in order to adjust the dose between the two.

Stereotactic radiosurgery for essential tremor: Retrospective analysis of a 19-year experience.

Mov Disord. 2017 May;32(5):769-77. DOI: 10.1002/mds.26925. Epub 2017 Mar 20.

Niranjan A, Raju SS, Kooshkabadi A, Monaco 3rd E, Flickinger JC, Lunsford LD.

#### **Background**

Essential Tremor (ET) is a common movement disorder that can be disabling. Initial treatment is in the form of medical therapies. Patients with medically refractory ET seek surgical intervention, which include radiofrequency thalamotomy, deep brain stimulation and radiosurgical thalamotomy. Radiosurgical thalamotomy is a minimally invasive surgical option which is especially valuable for elderly and high surgical risk patients.

#### Objective

The purpose of this study was to retrospectively analyze the outcomes of stereotactic radiosurgery for patients suffering from medically refractory essential tremor.

#### Methods

During a 19-year period (1996–2015), 73 patients underwent Gamma Knife thalamotomy for intractable essential tremor. A median central dose of 140 Gy (range, 130–150) was delivered to the nucleus ventralis intermedius through a single 4-mm isocenter. We used the Fahn-Tolosa-Marin clinical tremor rating scale to score tremor, handwriting, drawing, and ability to drink fluids. The median time to last follow-up was 28 months (range, 6–152).

#### Results

After Gamma Knife thalamotomy, 93.2% improved in tremor. Forty-four patients (60.3%) experienced tremor arrest or barely perceptible tremor. Eighteen patients (24.7%) noted tremor arrest and complete restoration of motor function. Tremor improvement was sustained at last follow-up in 96% of patients who experienced tremor relief. Mean tremor score improved from 3.19 before to 1.27 after Gamma Knife thalamotomy (P < 0.0001). Mean handwriting score improved from 2.97 to 1.25 (P < 0.0001). Mean drawing score improved from 3.16 to 1.26 (P < 0.0001). Mean drinking score improved from 3.14 to 1.56 (P < 0.0001). Imaging follow-up showed three types of lesions: enhancing lesion, streaking along internal capsule on fluid-attenuated inversion recovery, and significant reactive changes. Three patients (4%) experienced temporary adverse radiation effects.

#### Conclusion

Radiosurgery is a safe and valuable treatment option for medically refractory essential tremor, especially for the elderly or those with high surgical risk for DBS or radiofrequency thalamotomy. © 2017 International Parkinson and Movement Disorder Society.

Gamma Knife radiosurgery in movement disorders: Indications and limitations.

Mov Disord. 2017 Jan; 32(1):28-35. DOI: 10.1002/mds.26625. Epub 2016 Mar 31.

Higuchi Y, Matsuda S, Serizama T.

Functional radiosurgery has advanced steadily during the past half century since the development of the Gamma Knife technique for treating intractable cancer pain. Applications of radiosurgery for intracranial diseases have increased with a focus on understanding radiobiology. Currently, the use of Gamma Knife radiosurgery to ablate deep brain structures is not widespread because visualization of the functional targets remains difficult despite the increased availability of advanced neuroimaging technology. Moreover, most existing reports have a small sample size or are retrospective. However, increased experience with intraoperative neurophysiological evaluations in radiofrequency thalamotomy and deep brain stimulation supports anatomical and neurophysiological approaches to the ventralis intermedius nucleus. Two recent prospective studies have promoted the clinical application of functional

radiosurgery for movement disorders. For example, unilateral Gamma Knife thalamotomy is a potential alternative to radiofrequency thalamotomy and deep brain stimulation techniques for intractable tremor patients with contraindications for surgery. Despite the promising efficacy of Gamma Knife thalamotomy, however, these studies did not include sufficient follow-up to confirm long-term effects. Herein, we review the radiobiology literature, various techniques, and the treatment efficacy of Gamma Knife radiosurgery for patients with movement disorders. Future research should focus on randomized controlled studies and long-term effects. © 2016 International Parkinson and Movement Disorder Society.

#### The role of diffusion tensor imaging tractography for Gamma Knife thalamotomy planning.

J Neurosurg. 2016 Dec;125(Suppl 1):129-38. DOI: 10.3171/2016.7.GKS161553.

Gomes JGR, Gorgulho AA, de Oliveira López A, Saraiva CWC, Damiani LP, Pássaro AM, Salvajoli JV, de Oliveira Siqueira L, Salvajoli BP, De Salles AAF.

#### Objective

The role of tractography in Gamma Knife thalamotomy (GK-T) planning is still unclear. Pyramidal tractography might reduce the risk of radiation injury to the pyramidal tract and reduce motor complications.

#### Methods

In this study, the ventralis intermedius nucleus (VIM) targets of 20 patients were bilaterally defined using Iplannet Stereotaxy Software, according to the anterior commissure-posterior commissure (AC-PC) line and considering the localization of the pyramidal tract. The 40 targets and tractography were transferred as objects to the GammaPlan Treatment Planning System (GP-TPS). New targets were defined, according to the AC-PC line in the functional targets section of the GP-TPS. The target offsets required to maintain the internal capsule (IC) constraint of < 15 Gy were evaluated. In addition, the strategies available in GP-TPS to maintain the minimum conventional VIM target dose at > 100 Gy were determined.

#### Results

A difference was observed between the positions of both targets and the doses to the IC. The lateral (x) and the vertical (z) coordinates were adjusted 1.9 mm medially and 1.3 mm cranially, respectively. The targets defined considering the position of the pyramidal tract were more medial and superior, based on the constraint of 15 Gy touching the object representing the IC in the GP-TPS. The best strategy to meet the set constraints was 90° Gamma angle (GA) with automatic shaping of dose distribution; this was followed by 110° GA. The worst GA was 70°. Treatment time was substantially increased by the shaping strategy, approximately doubling delivery time.

#### Conclusions

Routine use of DTI pyramidal tractography might be important to fine-tune GK-T planning. DTI tractography, as well as anisotropy showing the VIM, promises to improve Gamma Knife functional procedures. They allow for a more objective definition of dose constraints to the IC and targeting. DTI pyramidal tractography introduced into the treatment planning may reduce the incidence of motor complications and improve efficacy. This needs to be validated in a large clinical series.

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