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Original article

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

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A R T I C L E I N F O

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ABSTRACT

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.

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The treatment of medically refractory tremor has evolved over the past half-century from intraoperative thalamotomy to deep brain stimulation (DBS), which was first explored in humans for multiple sclerosis tremor by Brice and McLellan in 1980 who targeted the midbrain and basal ganglia with electrodes [1]. Subsequently, the pioneering work of Benabid et al. used the hypothesis-driven target of the thalamic ventral intermediate nucleus (VIM) beginning in 1987 to treat refractory tremor [2,3]. VIM DBS has proven efficacious for patients with essential tremor (ET), tremor-dominant Parkinson's disease (PD), and less common causes of tremor including multiple sclerosis and orthostatic tremor [4-6]. Within the past 15 years, unilateral Gamma Knife radiosurgical VIM thalamotomy has emerged as a comparably efficacious treatment modality, particularly for ET and tremordominant PD patients, utilizing a mean dosage of 130-140 Gy [7–10]. Compared to DBS, radiosurgical thalamotomy has the

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http://dx.doi.org/10.1016/j.radonc.2017.07.030 0167-8140/© 2017 Elsevier B.V. All rights reserved. advantage of reduced patient burden, due to the absence of inpatient hospital stay and elimination of intraoperative complication risks such as infection, hemorrhage, and/or cerebrospinal fluid leakage which have been reported following DBS [8]. Despite extensive investigation of these treatment modalities, there has been no cost-comparison of unilateral DBS versus radiosurgery of the VIM.

Materials and methods

Determination of mean operating room time for VIM DBS

The estimated operating room (OR) time of unilateral VIM DBS was acquired from a literature search using the PubMed database (http://www.ncbi.nlm.nih.gov/pubmed) and associated references from VIM DBS publications. The results of the search are demonstrated in Table 1, as of the 17 studies, only one included the mean intraoperative time for VIM DBS [2–6,11–22]. This study also happened to be the only study to report VIM DBS performed without intraoperative test stimulation, and notes that all VIM DBS cases were performed without intraoperative microelectrode recording (MER) assistance [22]. From this study, the mean intraoperative



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Table 1

Literature review of operating room time in deep brain stimulation of the ventral intermediate nucleus for medically refractory tremor.

Study	Number of VIM DBS patients (electrodes)	Mean OR time for unilateral VIM DBS (minutes)
Benabid et al. [2]	32 (43)	NR
Benabid et al. [3]	87 (126)	NR
Caparros-Lefebvre et al. [11]	10 (10)	NR
Alesch et al. [5]	27 (33)	NR
Benabid et al. [4]	117 (177)	NR
Hubble et al. [12]	10 (10)	NR
Koller et al. [13]	24 (24)	NR
Ondo et al. [14]	33 (33)	NR
Koller et al. [15]	38 (38)	NR
Caparros-Lefebvre et al. [16]	73 (96)	NR
Schuurman et al. [17]	22 (22)	NR
Lyons et al. [18]	12 (12)	NR
Ondo et al. [19]	21 (42)	NR
Pilitsis et al. [20]	27 (31)	NR
Parihar et al. [21]	8 (8)	NR
Coleman et al. [6]	2 (2)	NR
Chen et al. [22]	57 (89)	146.4

NR = not reported.

time of 146.4 min was used as the estimate operative time for VIM DBS for the present study, since the vast majority of VIM DBS cases reported have been performed without the use of general anesthesia [2-6,11-22]. The use of general anesthesia increased the mean intraoperative time to 192.5 min [22].

Calculation of time-dependent operating room costs for VIM DBS

Extrapolation of cost calculations to the entire United States involved amalgamation of OR costs per minute from four geographically representative academic hospitals as previously described [23]. Costs were averaged from representative Eastern (Cornell Medical Center, New York, NY), Midwestern (Ohio State University Medical Center, Columbus, OH), Southern (Emory University, Atlanta, GA) and Western (University of California at San Francisco, San Francisco, CA) medical centers; OR and anesthesia costs were obtained from the billing departments of each hospital as previously described using current procedural terminology code 61863 (DBS without MER) (Table 2) [23]. The geographically averaged OR cost per minute was then multiplied by the previously calculated average OR time of VIM DBS.

The total anesthesia cost was calculated by multiplying the cost per anesthesia unit by the total number of anesthesia units for VIM DBS. For CPT code 61863, the anesthesia base unit was 11 units, plus an additional unit for every 15 min of OR time. The final cost of VIM DBS dependent on OR duration time was then calculated by combining the total OR cost with the total anesthesia cost.

Time-independent costs of VIM DBS

The neurosurgeon reimbursement for VIM DBS without MER was calculated via relative value unit (RVU) and CPT codes using the CodeCorrect program (MedAssets, Inc., Alpharetta, GA). As in previous work, only the work RVUs were calculated due to their

Table 2

Time dependent United States operating room cost estimate (anesthesia, nursing, staff, setup) for CPT code 61863.

Geographic region	OR cost per minute	Cost per anesthesia unit
East	\$60.78	\$150
Midwest	\$131.44	\$85
West	\$119.44	\$124
South	\$90.71	\$102
Average	\$100.59	\$115.25

* Each anesthesia unit represents 15 min of OR time.

approximation of reimbursement to the surgeon (not to transition facility practice or malpractice expenses) and because they are the least variable geographically across the United States; the 2016 work RVUs (which include stereotactic frame placement as well as electrode implantation) were multiplied by a previously published conversion factor of \$37.942 per RVU to obtain the neuro-surgeon reimbursement [23].

Costs of radiosurgical VIM thalamotomy

The estimated radiation oncology cost of radiosurgical VIM thalamotomy (Gamma Knife or linear accelerator) was derived from the 2016 Medicare fee schedule, due to its relative resistance to geographic and hospital variations in billing. Practitioner costs were derived from treatment planning, devices, and management (from CPT codes 99205, 77263, 77470, 77295, 77334, 77300, and 77432) based on the 2016 Oregon Health & Science University Department of Radiation Medicine mean payment per intervention.

The neurosurgery cost was derived from the work RVU for VIM SRS, based on CPT code 61796 rather than 61798 since the lesion target was less than 3.5 cm. The 2016 work RVU for this code was 13.93. The work RVU for stereotactic frame placement in Gamma Knife SRS (which unlike for DBS is billed from a separate CPT code) is 2.25, corresponding to CPT code 61800. These work RVUs were then multiplied by the conversion factor to obtain the neurosurgeon cost for VIM radiosurgery.

Results

Unilateral VIM DBS

The cost of OR time for unilateral VIM DBS (including initial setup charge, use of room, and nursing) is equivalent to 146.4 min \times \$100.59 per minute = \$14,726.38. The anesthesia cost of 146.4 min of VIM DBS (CPT code 61863) is 21 units, equivalent to \$2420.25 (\$115.25 per unit). The neurosurgeon reimbursement for CPT code 61863 is equivalent to the work RVU, which is 20.71 multiplied by the previously published conversion factor of \$37.942 per RVU = \$785.78. Consequently, the total unilateral VIM DBS cost = \$14,726.38 + \$2420.25 + \$785.78 = \$17,932.41.

Radiosurgical VIM thalamotomy

Based on the 2016 Medicare hospital outpatient prospective payment rates, the comprehensive Ambulatory Payment Classification (APC) for Gamma Knife single-session cranial radiosurgery reimbursement is \$8827 which is inclusive of delivery and ancillary codes but exclusive of co-insurance and other adjustments. This rate is equivalent to reimbursement for linear accelerator radiosurgery. For Gamma Knife, the estimated neurosurgeon reimbursement is equivalent to: (work RVU for radiosurgery + work RVU for stereotactic frame placement) × RVU conversion factor = $(13.93 + 2.25) \times $37.942 = 613.90 . The radiation oncology reimbursement is equivalent to \$1370.87 (Table 3).

Table 3

Estimated radiation oncology practitioner cost for stereotactic radiosurgery.

Intervention	CPT code	Mean payment
Consult	99205	\$198.30
Clinical treatment planning	77263	\$201.87
Special treatment procedure	77470	\$130.14
3D plan	77295	\$280.04
Device: per collimator	77334	\$73.46
Radiation dosimetry calculation	77300	\$38.18
Radiosurgery management	77432	\$448.88
Total		\$1370.87

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Consequently, the total radiosurgery cost was \$8827 + \$613.90 + \$1370.87 = \$10,811.77 for Gamma Knife SRS. This total is 40% less than the cost of unilateral VIM DBS. Since linear accelerator SRS does not require frame placement, its cost is \$8827 + neurosurgeon cost of \$528.53 + radiation oncology cost of \$1370.87 = \$10,726.40 total radiosurgery cost, which is also 40% less than the cost of unilateral VIM DBS.

Discussion

Treatment of medically refractory tremor over the past quarter century has predominantly involved VIM DBS, yet VIM radiosurgery has proved efficacious, making it an attractive alternative for patients who either are not medical candidates for surgery or refuse operative intervention. The cost of each treatment modality had not been previously explored, which this study sought to address.

Although theoretically VIM SRS can be performed by either Gamma Knife or linear accelerators, the vast majority of the radiosurgery thalamotomy literature has been performed using Gamma Knife; prior to 2016 only a single study involving three patients has examined linear accelerator thalamotomy, and none of those patients had VIM as a radiosurgical target [7-10,24-30]. Anecdotally this makes sense, given the extremely high target dose (130–140 Gy) and the fact that Gamma Knife is frame-based for optimal head immobilization, a feature that linear accelerators do not share. Furthermore the potential morbidity of Gamma Knife is tracked and registered in a central database given the stricter monitoring standards of the Nuclear Regulatory Commission due to its cobalt source, while linear accelerators are not subject to such database reporting of morbidity and have historically been monitored by a less stringent regulatory body (the Food and Drug Administration) [31]. While such differences may not make much clinical difference in morbidity for most conditions, the extremely high doses used for this condition coupled with the proximity of critical structures has led to significant morbidity in linear accelerators during treatment for other functional disorders, such as trigeminal neuralgia [31]. However, a recent study involving a linear accelerator-based frameless system and quality assurance procedures examined 20 patients treated with VIM SRS to a median prescription dose of 140 Gy and found a mean error of distance to be only 1.1 mm based on post-treatment MRI [32]. Although no clinical outcomes have yet to be reported by this group, should their accuracy become reproducible by other centers, linear accelerator VIM SRS may increase in popularity. Recent advances in diffusion tensor imaging technology may also result in improved targeting accuracy, which could potentially increase the feasibility of linear accelerator VIM SRS even further [33].

It is important to note that both the mean operative time and anesthesia costs were calculated assuming that VIM DBS was performed without intraoperative microelectrode recording (MER) assistance. This is noteworthy, since in Parkinson's disease patients where the DBS target is the subthalamic nucleus (STN) rather than the VIM, MER has been shown to improve targeting accuracy over image-guidance alone at the cost of increasing unilateral STN DBS operative time by 3 h, increasing the total cost of STN DBS by 158%, and increasing the risk of intracerebral hemorrhage without improving patient outcomes or preventing suboptimal DBS placement [23,34-39]. As MER is associated with a 60% increase in neurosurgeon reimbursement in STN DBS, it is possible that some neurosurgeons may use MER for VIM DBS despite the absence of evidence supporting any contribution to clinical outcome improvement [22,23]. From a cost-effectiveness standpoint, any use of MER intraoperatively for VIM DBS would only exacerbate the increased cost of DBS versus radiosurgery for medically refractory tremor patients. Consequently, the surgeon preference regarding MER utilization should be communicated clearly to these patients when deciding between operative versus radiosurgical intervention.

Limitations of this study include its retrospective nature, the dearth of published reports of intraoperative OR time in VIM DBS, and the inability of the numbers presented in this study to be more than estimates due to the differences between hospitals in OR costs, costs per anesthesia unit, and RVU conversion factors. Furthermore as stated above, any use of MER during VIM DBS would lead this study to underrepresent the true cost of DBS for medically refractory tremor. Finally, because hospitals can arrange their own reimbursement rates for Gamma Knife SRS, the model described in this study is more stable for linear accelerator-based SRS. Nonetheless, this study provides the first systematic cost comparison of VIM DBS versus radiosurgical VIM thalamotomy for medically refractory tremor.

In conclusion, radiosurgery of the VIM is 40% more costeffective than unilateral VIM DBS in treatment of medically refractory tremor, regardless of radiosurgical modality. This finding provides another important aspect to be considered for treatment modality decision-making, and argues for increased involvement of radiation oncologists in concert with movement disorder neurologists and functional neurosurgeons in the management of medically refractory tremor patients, particularly those who may not be able to medically or financially tolerate the stresses of operative intervention. Such involvement will be all the more important as newer methodologies, such as focused ultrasound, become employed in the treatment of medically refractory tremor [40].

Conflict of interest statement

No author has any conflict of interest.

Financial disclosure statement

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Author contributions

Conception and design: Dr. McClelland. Data collection: Dr. McClelland and Dr. Jaboin. Data analysis and interpretation: Dr. McClelland and Dr. Jaboin. Manuscript writing: Dr. McClelland and Dr. Jaboin. Final approval of manuscript: Dr. McClelland and Dr. Jaboin.

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References

 Brice J, McLellan L. Suppression of intention tremor by contingent deep-brain stimulation. Lancet 1980;1:1221–2.

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- [2] Benabid AL, Pollak P, Gervason C, et al. Long-term suppression of tremor by chronic stimulation of the ventral intermediate thalamic nucleus. Lancet 1991;337:403–6.
- [3] Benabid AL, Pollak P, Seigneuret E, Hoffmann D, Gay E, Perret J. Chronic VIM thalamic stimulation in Parkinson's disease, essential tremor and extrapyramidal dyskinesias. Acta Neurochir Suppl (Wien) 1993;58:39–44.
- [4] Benabid AL, Pollak P, Gao D, et al. Chronic electrical stimulation of the ventralis intermedius nucleus of the thalamus as a treatment of movement disorders. J Neurosurg 1996;84:203–14.
- [5] Alesch F, Pinter MM, Helscher RJ, Fertl L, Benabid AL, Koos WT. Stimulation of the ventral intermediate thalamic nucleus in tremor dominated Parkinson's disease and essential tremor. Acta Neurochir (Wien) 1995;136:75–81.
- [6] Coleman RR, Starr PA, Katz M, et al. Bilateral ventral intermediate nucleus thalamic deep brain stimulation in orthostatic tremor. Stereotact Funct Neurosurg 2016;94:69–74.
- [7] Duma CM, Jacques D, Kopyov OV. The treatment of movement disorders using Gamma Knife stereotactic radiosurgery. Neurosurg Clin N Am 1999;10:379–89.
- [8] Niranjan A, Jawahar A, Kondziolka D, Lunsford LD. A comparison of surgical approaches for the management of tremor: radiofrequency thalamotomy, gamma knife thalamotomy and thalamic stimulation. Stereotact Funct Neurosurg 1999;72:178–84.
- [9] Young RF, Jacques S, Mark R, et al. Gamma knife thalamotomy for treatment of tremor: long-term results. J Neurosurg 2000;93:128–35.
- [10] Kondziolka D, Ong JG, Lee JY, Moore RY, Flickinger JC, Lunsford LD. Gamma Knife thalamotomy for essential tremor. J Neurosurg 2008;108:111–7.
- [11] Caparros-Lefebvre D, Blond S, Vermersch P, Pécheux N, Guieu JD, Petit H. Chronic thalamic stimulation improves tremor and levodopa induced dyskinesias in Parkinson's disease. J Neurol Neurosurg Psychiatry 1993;56:268–73.
- [12] Hubble JP, Busenbark KL, Wilkinson S, Penn RD, Lyons K, Koller WC. Deep brain stimulation for essential tremor. Neurology 1996;46:1150–3.
- [13] Koller W, Pahwa R, Busenbark K, et al. High-frequency unilateral thalamic stimulation in the treatment of essential and parkinsonian tremor. Ann Neurol 1997;42:292–9.
- [14] Ondo W, Jankovic J, Schwartz K, Almaguer M, Simpson RK. Unilateral thalamic deep brain stimulation for refractory essential tremor and Parkinson's disease tremor. Neurology 1998;51:1063–9.
- [15] Koller WC, Lyons KE, Wilkinson SB, Pahwa R. Efficacy of unilateral deep brain stimulation of the VIM nucleus of the thalamus for essential head tremor. Mov Disord 1999;14:847–50.
- [16] Caparros-Lefebvre D, Blond S, Feltin MP, Pollak P, Benabid AL. Improvement of levodopa induced dyskinesias by thalamic deep brain stimulation is related to slight variation in electrode placement: possible involvement of the centre median and parafascicularis complex. J Neurol Neurosurg Psychiatry 1999;67:308–14.
- [17] Schuurman PR, Bosch DA, Bossuyt PM, et al. A comparison of continuous thalamic stimulation and thalamotomy for suppression of severe tremor. N Engl J Med 2000;342:461–8.
- [18] Lyons KE, Koller WC, Wilkinson SB, Pahwa R. Long term safety and efficacy of unilateral deep brain stimulation of the thalamus for parkinsonian tremor. J Neurol Neurosurg Psychiatry 2001;71:682–4.
- [19] Ondo W, Almaguer M, Jankovic J, Simpson RK. Thalamic deep brain stimulation: comparison between unilateral and bilateral placement. Arch Neurol 2001;58:218–22.
- [20] Pilitsis JG, Metman LV, Toleikis JR, Hughes LE, Sani SB, Bakay RA. Factors involved in long-term efficacy of deep brain stimulation of the thalamus for essential tremor. J Neurosurg 2008;109:640–6.

- [21] Parihar R, Alterman R, Papavassiliou E, Tarsy D, Shih LC. Comparison of VIM and STN DBS for Parkinsonian resting and postural/action tremor. Tremor Other Hyperkinet Mov (NY) 2015;5:321.
- [22] Chen T, Mirzadeh Z, Chapple K, Lambert M, Dhall R, Ponce FA. "Asleep" deep brain stimulation for essential tremor. J Neurosurg 2016;124:1842–9.
- [23] McClelland 3rd S. A cost analysis of intraoperative microelectrode recording during subthalamic stimulation for Parkinson's disease. Mov Disord 2011;26:1422–7.
- [24] Young RF, Li F, Vermeulen S, Meier R. Gamma Knife thalamotomy for treatment of essential tremor: long-term results. J Neurosurg 2010;112:1311–7.
- [25] Lim SY, Hodaie M, Fallis M, Poon YY, Mazzella F, Moro E. Gamma knife thalamotomy for disabling tremor: a blinded evaluation. Arch Neurol 2010;67:584–8.
- [26] Ohye C, Shibazaki T, Ishihara J, Zhang J. Evaluation of gamma thalamotomy for parkinsonian and other tremors: survival of neurons adjacent to the thalamic lesion after gamma thalamotomy. J Neurosurg 2000;93:120–7.
- [27] Niranjan A, Kondziolka D, Baser S, Heyman R, Lunsford LD. Functional outcomes after gamma knife thalamotomy for essential tremor and MSrelated tremor. Neurology 2000;55:443–6.
- [28] Friedman DP, Goldman HW, Flanders AE, Gollomp SM, Curran Jr WJ. Stereotactic radiosurgical pallidotomy and thalamotomy with the gamma knife: MR imaging findings with clinical correlation–preliminary experience. Radiology 1999;212:143–50.
- [29] Young RF, Shumway-Cook A, Vermeulen SS, et al. Gamma knife radiosurgery as a lesioning technique in movement disorder surgery. J Neurosurg 1998;89:183–93.
- [30] Frighetto L, De Salles A, Wallace R, et al. Linear accelerator thalamotomy. Surg Neurol 2004;62:106–14.
- [31] Walt Bogdanich, Kristina Rebelo, "A Pinpoint Beam Strays Invisibly, Harming Instead of Healing", The New York Times; 2010.
- [32] Luo G, Neimat JS, Cmelak A, et al. Margin of error for a frameless image guided radiosurgery system: direct confirmation based on posttreatment MRI scans. Pract Radiat Oncol 2016. pii: S1879-8500(16)30156-4.
- [33] Jakab A, Werner B, Piccirelli M, et al. Feasibility of diffusion tractography for the reconstruction of intra-thalamic and cerebello-thalamic targets for functional neurosurgery: a multi-vendor pilot study in four subjects. Front Neuroanat 2016;10:76.
- [34] Binder DK, Rau GM, Starr PA. Risk factors for hemorrhage during microelectrode-guided deep brain stimulator implantation for movement disorders. Neurosurgery 2005;56:722–32.
- [35] Gorgulho A, De Salles AA, Frighetto L, Behnke E. Incidence of hemorrhage associated with electrophysiological studies performed using macroelectrodes and microelectrodes in functional neurosurgery. J Neurosurg 2005;102:888–96.
- [36] Patel NK, Plaha P, O'Sullivan K, McCarter R, Heywood P, Gill SS. MRI directed bilateral stimulation of the subthalamic nucleus in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 2003;74:1631–7.
- [37] McClelland 3rd S, Ford B, Senatus PB, et al. Subthalamic stimulation for Parkinson disease: determination of electrode location necessary for clinical efficacy. Neurosurg Focus 2005;19:E12.
- [38] Ellis TM, Foote KD, Fernandez HH, et al. Reoperation for suboptimal outcomes after deep brain stimulation surgery. Neurosurgery 2008;63:754–61.
- [39] McClelland 3rd S, Ford B, Senatus PB, et al. Typical variations of subthalamic electrode location do not predict limb motor function improvement in Parkinson's disease. J Clin Neurosci 2009;16:771–9.
- [40] Elias WJ, Lipsman N, Ondo WG, et al. A randomized trial of focused ultrasound thalamotomy for essential tremor. N Engl J Med 2016;375(8):730–9.