

Selection Methodology for Inclusion in Unilateral Thalamic Stimulation for Essential Tremor and Parkinsonian Tremor Study Descriptions

The studies for inclusion as part of the evidence for unilateral thalamic stimulation were selected in the following ways:

- Studies reviewed as part of the Blue Cross Blue Shield’s technology assessment entitled, *Deep Brain Stimulation of the Thalamus for Tremor*¹.
- Studies found in a Pubmed database search using the keywords “deep brain stimulation” and “Parkinson*.” The search was restricted to publications in English about human subjects.
- The reference lists of retrieved publications were also reviewed.

Studies were excluded if there were less than 10 subjects. In reviewing the retrieved evidence, it was noted that several studies seemed to evaluate patients who had been included in previously published literature. We have included all the relevant articles for review. However, the study summary table is restricted to only the most recently published studies.

¹ Blue Cross Blue Shield Association (1997) *Deep Brain Stimulation of the Thalamus for Tremor*. Assessment Program. Volume 12, No. 20. December, 1997

Study Descriptions of Unilateral Thalamic Stimulation for Essential Tremor or Parkinsonian Tremor

Study/ Year	Study design	Patients/Treatment	Diagnosis	Results	Comments
Koller et al, 2001	Clinical series	N=49 enrolled N=25 analyzed Mean age = 72.3 yrs ± 8.9 19 men 6 women Unilateral in VIM Selection criteria: Tremor had to cause significant disability despite pharmacological treatment Tremor had to be 3 or 4 in severity utilizing the Fahn-Tolosa-Marin Tremor Rating Scale – (0) none to (4) severe	25/49 ET pts completed at least 24 month follow-up Mean disease duration = 33.3 yrs ± 15.4 24/49 ET pts without 24 mo follow-up were excluded from analysis: * 7/24 explants * 11/24 lost to follow-up * 3/24 unrelated deaths * 3/24 never implanted due to subdural hematoma and asymptomatic hemorrhage in operating room	Tremor Rating Scale with stimulation on and off (N=25) Blindly evaluated only at 3 months; with open evaluation at baseline, 12 mo post-op and then yearly (average post-op follow-up 40.2 ± 14.7 mo) Statistical analysis included Wilcoxon signed rank comparison of tremor scores for baseline and the stim on and off conditions at follow-up Histogram of tremor scores (questions 1-10 on tremor rating scale) sign. improved with stim on at long-term follow-up (3, 12 and 40 mo) as compared to baseline (p<.001) * 25 adverse surgical events including 3 asymptomatic bleeds and 1 seizure * 70 stimulation complications * 19 device complications * 18 pts received additional surgical procedures	Likely includes the 38 patients above in Koller et al (1999) Selection criteria for study inclusion not fully described Lacks intention to treat analysis for all pts initially enrolled
Krauss et al, 2001	Clinical series	N = 94 Mean age = 68.7 yrs (31-83) 68 men 26 women 65 unilateral implants 29 bilateral implants Selection criteria: “Tremor was disabling or a source of social embarrassment in all patients and was not controlled satisfactorily by medication”	45 PD 42 ET 7 Other (including multiple sclerosis, head injury, stroke, degenerative disease) Mean duration of disease not reported Prior surgery not reported	Symptomatic outcome of tremor at last available formal follow-up evaluation summarized as excellent (complete or almost complete suppression of tremor), marked improvement (70-90%), moderate improvement (30-70%), minor improvement (0-30%), unchanged, or worse Symptomatic improvement of tremor in PD pts: * 23/45 excellent * 16/45 marked * 5/45 moderate * 1/45 minor Symptomatic improvement of tremor in ET pts: * 24/42 excellent * 15/42 marked * 2/42 moderate * 1/42 minor Adverse events: 40/94 patients experienced stimulation-related side effects, generally mild and reversible, and more frequent in bilateral DBS pts	Includes 33 pts (14 ET; 19 PD) published by Ondo et al (1998) Data pooled across centers; results and complications not stratified by age or center; no description of any center effects Selection criteria for study inclusion not fully described, e.g., regarding degree of functional disability, social embarrassment or refractoriness to medications No stratification for unilateral versus bilateral implants in PD and ET patients No statistical analysis of results for subjective symptomatic improvement or interoperative test stimulation Identity of the person making assessment of symptomatic improvement not stated

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Lyons et al, 2001	Clinical Series	N = 12, analysis done on 9 Mean age = 67.8 yrs (SD 5.2) 8 men 1 woman Unilateral in VIM	9 PD with medication resistant tremor Mean duration of disease – 8.1 yrs (SD 3.5) No surgery outside of the study	Evaluation using the motor section (part III) of the UPDRS performed with meds on at baseline, 3 months, 12 months, and yearly Motor scores did not change from baseline to long-term follow- up. Tremor scores on the targeted side were significantly improved with stimulation on at long-term follow-up compared to baseline 7 patients (58%) reported global improvement, 1 indicated no change (8%) and 3 reported good long term tremor control Adverse events: * 3 patients with asymptomatic bleeds and one patient with hematoma at the implantable generator site * Stimulation events included paresthesias (12), headache (5), dysarthria (3), disequilibrium (3) and visual disturbances (2) Device complications included lead repositioning (2), lead extension wire replacement (1), implantable generator replacement due to battery depletion (2), full system explant and subsequent pallidotomy due to loss of benefit (1) 1 unrelated death at 1 year (possible MI), and 2 unrelated deaths at 2 years (sepsis and respiratory arrest)	Suggestive that the patients selected are also reported in Koller, 2001 Analysis was only done on 9 of 12 patients due to loss of follow-up (25%) Inclusion/exclusion criteria were not well defined
Obwegeser et al, 2001	Clinical series	N = 45, 4 excluded from study analysis Mean age = 71 yrs ± 8 29 men 12 women Implantation in VIM : 4 right side 22 left side 15 bilateral (1 simultaneous)	10 PD 31 ET Mean duration of illness= 8 ± 3 yrs for patients with PD; 12 yrs ± 8 for patients with ET. Previous pallidotomy in 3 patients	Tremor was evaluated 1-2 days before surgery and 3 months surgery using the Fahn-Tolosa-Marin rating scale, with stimulation on/off Unilateral: * Significant reductions in midline tremor and upper-extremity tremor contralateral to surgery. Significant reduction of upper- extremity tremor in ipsilateral arm * Contralateral lower limb tremor also improved significantly with stimulator on/off * ADLs improved for eating, drinking hygiene, writing, and working, but not speaking * Pegboard evaluations were not significantly different Bilateral: * Tremors contralateral and ipsilateral were significantly decreased	Follow-up period (3 months) short Limited description of patient selection criteria

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				<p>* ADL measurements improved after bilateral implantation</p> <p>Adverse events: No perioperative or postoperative hemorrhaging episodes or infections * 1 focal seizure intraoperatively, 1 tonic-clonic seizure 12 hours after surgery * 3 cases of broken leads (one led to loss of tremor control). <ul style="list-style-type: none"> 1 patient experienced dysarthria, emotional problems and dystonic movements in the right shoulder after bilateral placement, all alleviated by replacement and repositioning of the left electrode </p>	
Ondo et al, 2001	Clinical series	<p>N = 78</p> <p>Mean age = 71.2 yrs ± 7.1 (ET) 70.5 yrs ± 9.0 (PD)</p> <p>ET: 27 men 13 women PD: 27 men 5 women</p> <p>Unilateral in VIM</p> <p>Selection criteria: ET- dx by guidelines of Tremor Investigation Group. PD – 2/3 (tremor, rigidity, bradykinesia) Excludes dementia, prior brain surgery, comorbid disease, > age 80</p>	<p>32 PD 41 ET</p> <p>5 not included: 3 previous thalamotomy 2 not assessed prior to bilateral implantation</p> <p>Prior surgery and disease duration not reported</p>	<p>73 patients assessed</p> <p>Unblinded: Testing at 7 days preoperative and 3-6 months postoperative</p> <p>Blinded: 62 randomized to postoperative testing in either stimulator ON or stimulator OFF</p> <p>Patients evaluated using questions similar to Tremor Rating Scale and UPDRS</p> <p>ET: Unblinded: Tremor/handwriting/pouring/ADL all significantly improved contralaterally Blinded: Tremor/handwriting improved contralaterally</p> <p>PD: Unblinded: Tremor/Brady/Rigidity/ADL significantly improved contra; gait & balance didn't improve Blinded: Tremor/Rigidity sig. improved; Brady/gait didn't improve</p> <p>ET: slight improvement in ipsilateral tremors PD: no ipsilateral improvement</p> <p>Adverse events: 11 disequilibrium 6 dysarthria</p>	<p>Potentially includes same patients as Ondo et al, 1998 and Kraus 2001</p> <p>Lacks intention to treat analysis for all pts initially enrolled</p>
Schuurman et al,	RCT	N=70, 2 not treated	PD:	Patients were assessed at baseline and 6 months after surgery as	Statistical analyses not used

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2000		<p>Mean age: Thalamotomy (n = 34): 64 yrs ± 11.0</p> <p>Thalamic stimulation (n = 34): 59 yrs ± 14.2</p> <p>Thalamotomy: 17 men 17 women</p> <p>Thalamic stimulation: 27 men 7 women</p> <p>Patients for each condition were randomly assigned to undergo thalamotomy or thalamic stimulation.</p> <p>Patients with unilateral tremor underwent either unilateral thalamotomy or unilateral DBS</p> <p>Patients with bilateral tremor underwent either thalamotomy followed by contralateral DBS or bilateral DBS</p> <p>Selection criteria: Unilateral or bilateral tremor of arm due to PD, ET, or MS > 1 yr</p> <p>Exclude: <18, cognitive dysfunction (<24 on MMSE), contraindications to surgery; no evidence cerebral atrophy on CT; no previous thalamotomy</p>	<p>*23 thalamotomy *22 thalamic stimulation</p> <p>ET: *6 thalamotomy *7 thalamic stimulation</p> <p>MS: *5 thalamotomy *5 thalamic stimulation</p> <p>Mean duration of illness: *Thalamotomy: 12.6 yrs ± 12.5 yrs *Thalamic stimulation: 10.9 yrs ± 7.9</p>	<p>measured by the Frenchay Activities Index (FAI), severity of tremor, number of adverse events, and patients' assessment of the outcome</p> <p>FAI results listed as 'change in score from baseline' and 'difference between groups. No p values given. Those who underwent DBS consistently had greater changes in scores than those that received a thalamotomy. This was the case for all groups except for MS</p> <p>Tremor: Thalamotomy: disappeared in all pts immediately after & 20/26 at 6 months DBS: disappeared in all post-op and 20/28 at 6 months</p> <p>Adverse events: Thalamotomy: 16 at 6 months DBS: 6 at 6 months (1 death due to intracerebral hematoma)</p>	
Hariz et al, 1999	Clinical series	<p>N=58 (of 60 consecutively operated pts)</p> <p>Mean age: 66 yrs (24-79) ET 66 yrs (45-79) PD</p>	<p>22 PD 36 ET</p> <p>2 excluded from analysis: lack of effect during trial stimulation (1) and refusal of post-op follow-up (1)</p>	<p>At 1 yr, with 18/22 PD pts completing follow-up, motor portion of UPDRS improved from 37.2 to 26.6 (p<0.01)</p> <p>At 1 yr, with 27/36 ET pts completing follow-up, total score of Essential Tremor Rating Scale (ETRS) improved from 53.9 to 27.8 (p<0.0001)</p>	<p>No description of selection</p> <p>Incomplete analysis and variable follow-up of all pts operated</p> <p>Multiple patients had previous surgeries</p>

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		<p>ET: 26 men 10 women PD: 16 men 6 women</p> <p>Unilateral in VIM</p> <p>Selection criteria not described</p>	<p>Mean duration of symptoms for PD pts = 10 yrs (range 2-17 years)</p> <p>Mean duration of symptoms for ET pts = 18 yrs (range 2-55 years)</p> <p>Prior surgeries of PD pts: * 5 contralateral thalamotomy * 9 contralateral pallidotomy * 3 ipsilateral pallidotomy</p> <p>Prior surgeries of ET pts: * 4 contralat thalamotomy * 2 ipsilateral pallidotomy</p>	<p>Adverse events: 2 PD pts experienced previously undescribed and non-adjustable side effect of stimulation-induced ataxia, and their disability was unchanged/worsened compared to pre-op</p> <p>5/58 pts hardware complications</p> <p>10/58 pts non-adj and permanent long-term complication, include upper limb ataxia with stimulation (2), balance problems (2) and dysarthria (6)</p> <p>4/9 pts with prior thalamotomy, DBS contralateral VIM provoked some dysarthria with stimulation on</p> <p>No related deaths, hematoma, paresis or infection</p>	<p>include either ipsilateral or contralateral thalamotomy or pallidotomy</p> <p>Unable to differentiate degree to which study outcomes represent benefit from stimulation and/or prior surgery</p> <p>Authors noted decline in stimulation efficacy over time</p>

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Kumar et al, 1999	Clinical series	<p>N = 20</p> <p>Mean age: 69 ± 10 yrs ET 71 ± 8 yrs PD</p> <p>Implantation in VIM</p> <p>Selection criteria: Tremor-dominant PD or ET, both unresponsive to medical therapy and causing severe disruption of ADLs</p>	<p>Unilateral VIM DBS: 7 PD 4 ET</p> <p>Bilateral VIM DBS: 4 PD 5 ET</p> <p>Mean duration of illness= 26 yrs ± 15</p> <p>No previous surgeries</p>	<p>Evaluation by a third-party neurologist pre-op, 1 week post-op, every 3 months for the first year and every 6 months thereafter using the UPDRS, Schwab and England, Hoehn and Yahr, and the Clinical Rating Scale for Tremor (CRST)</p> <p>PD: Schwab and England and total UPDRS score improved at 1 week post-op, but not at long-term follow-up</p> <p>Contralateral arm and leg rest tremor and ipsilateral resting leg tremor were significantly improved at all time points</p> <p>No statistically significant improvements were seen in rigidity, bradykinesia, gait speech, posture or postural instability</p> <p>ET: Significant improvement in the total CRST score, total tremor score, and contralateral arm postural and action tremor at all time points</p> <p>Significant improvement in the Benabid scoring system when applied to tremor</p> <p>Adverse events: * 2 seizures * 1 patient with mild facial droop * 1 intra-op confusion which resolved * 2 ET patients developed mild persistent paresthesias in the contralateral jaw and fingertips * 2 PD patients had mild dystonia * 1 ET patient developed dysarthria, resolved with a decreased voltage and pulse width</p>	<p>Inclusion/exclusion criteria were not well defined</p> <p>Patient selection criteria not described</p> <p>Although mean follow-up time provided, no break down by time period given in results</p>
Limousin et al, 1999	Clinical series	<p>N = 111, 110 patients implanted at 13 centers in Europe</p> <p>Mean age: 63.1 yrs (SD 12.7) ET 61.5 yrs (SD 10.8) PD</p> <p>ET: 24 men 13 women PD: 47 men 26 women</p> <p>Unilateral (57) and bilateral (53) in VIM</p> <p>Selection criteria:</p>	<p>73 PD 37 ET</p> <p>Mean duration of disease: PD: 10.0 yrs (SD 5.6) ET: 26.6 yrs (SD 14.5)</p>	<p>PD patients assessed using the UPDRS, ET assessed according to the essential tremor rating scale (ETRS) at less than 1 month pre-op, 1 week pre-op, and 3, 6, and 12 months post-op both on/off stimulation</p> <p>PD: at 3 and 12-month follow-up, both upper and lower limb tremor were significantly reduced. Pts receiving unilateral stimulation had a significant reduction of contralateral tremor at both time points</p> <p>Motor score of the UPDRS was significantly reduced during “on” stimulation. Other symptoms reported as “very mild” before surgery</p>	<p>Well-described patient selection criteria and inclusion/exclusion criteria</p> <p>Effect of unilateral vs. bilateral implantation not clearly stated</p>

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		<p>Idiopathic or essential tremor with pharmacotherapy resistant tremor and tremor rating scale of at least 3</p> <p>Ability to abide by protocol. Patients were excluded if they had previous thalamotomy on the side of implantation; sig. brain atrophy; or "other disorders that may interfere with efficacy of treatment of tremor"</p>		<p>Schwab and England score improved after surgery</p> <p>Number of patients taking medications and was not changed and the mean doses were not significantly reduced 12 months after surgery</p> <p>ET: At 3 and 12 month follow-up, stimulation significantly reduced postural and action tremor of the upper limb and lower limb</p> <p>Head tremor was significantly improved by stimulation at 3-month follow-up only</p> <p>Voice tremor was not reduced.</p> <p>In patients receiving unilateral stimulation, stimulation and the procedure significantly reduced contralateral but not ipsilateral tremor</p> <p>The number of patients using meds was not changed, and the reduction in mean doses was not significant</p> <p>Adverse events: * 1 patient developed respiratory difficulty in the OR and was not implanted * 4 patients had major adverse events unrelated to surgery, including 3 deaths from unrelated causes and 1 stroke in the contralateral hemisphere 3 months after surgery * 3 patients had subdural hematomas which resolved * 2 patients had subcutaneous hematomas which were evacuated * 2 patients had infections * 5 patients required electrode replacement</p> <p>Other events were described as mild and resolved with changes in stimulation parameters</p>	
Troster et al, 1999	Clinical series	<p>N=40</p> <p>Mean age: 72 yrs ± 8.5</p> <p>Gender not reported</p> <p>Unilateral in VIM</p>	<p>40 ET</p> <p>Mean age of onset = 55 yrs ± 13.8</p>	<p>Tests: Neuropsychological test battery (not defined in methods but included all tests in results) Sickness Impact Profile (SIP) Parkinson's Disease Questionnaire (PDQ-39)</p> <p>Dementia rating scale: sig improved Hooper Visual Organization Tests: sig improved</p>	<p>Outcomes were focused on quality of life indicators</p>

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		<p>Selection criteria: Postural and/or kinetic hand tremor, in the absence of other neurological signs, inadequately controlled by medication for > 3 mo. and notable limitations of daily living</p> <p>Excluded were patients with prior thalamotomy or neuropsychological evaluations carried out in another institution</p> <p>Those with unstable medical problems, pacemakers, dementia, ect.</p>		<p>Grooved Pegboard Test: sig improved California Verbal Learning Test: sig improved except decrease in letter fluency Wechsler Memory Scale-Revised: sig improved Profile of Mood States: sig Improved SIP: sig.improved total & psychosocial but not physical PDQ-39: sig.improved</p> <p>Adverse events not reported</p>	
Hubble et al, 1997*	Clinical series	<p>N=29</p> <p>Mean age and gender distribution not reported</p> <p>Unilateral in VIM</p> <p>Selection criteria: Diagnosis of ET or PD</p> <p>Age 18-80 years with disabling medication- refractory upper extremity tremor and no other evidence of supraspinal CNS disease or injury</p> <p>Patients were excluded if they had unstable intercurrent medical problems or if they had a cardiac pacemaker, prior thalamotomy, required MRI, dementia, substance abuse, or botulinum toxin injections 6 mo. prior</p>	<p>19 ET 10PD</p> <p>Mean disease duration not reported</p>	<p>Blinded rating of randomized tremor scores by CRST and disability rating at 3 month follow-up when the stimulation was "on" and "off" via videotaped footage</p> <p>Statistically significant improvement in blinded rater CTRS videotape tremor scores ($p < 0.01$ **) for rest, kinetic, distal postural, and proximal tremor at 3 months</p> <p>One subject had no improvement in tremor</p> <p>Improvement of tremor was for most part the same between ET and PD</p> <p>Improvement in disability ratings ($p < 0.01$ **)</p> <p>Improvement of disability rating was the same between ET and PD</p> <p>Adverse events: No serious or unexpected DBS-related events</p> <p>No other cardinal symptom of Parkinson's disease was assessed.</p> <p>Side effects: All patients reported transient paresthesias when the device is first turned on</p>	<p>A subset of these patients was previously reported in Hubble et al, 1996</p> <p>This study provides additional information on patients with PD</p> <p>Relatively brief follow-up period (3 months)</p>
Koller et al, 1997*	Clinical	N=59 enrolled	29 ET	At 3 months, Pts randomly assigned to either stimulation on or	10 ET patients previously reported by Hubble

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	series	<p>Mean Age: 66.8 ± 11.5 yrs ET 65.4 ± 9.2 yrs PD</p> <p>ET: 24 men 5 women PD: 19 men 5 women</p> <p>53/59 implantation in VIM</p> <p>6/59 pts attempted surgery, but were not implanted, followed or analyzed: * 2/6 with tremor not suppressed by intraoperative stimulation * 1/6 with intercranial hemorrhage during surgery * 1/6 with persistent micro-thalamotomy effect * 1/6 with subdural hemorrhage during placement of burr hole * 1/6 with withdrawal of consent on operating table</p> <p>Selection criteria: Dx of ET or PD with tremor of marked severity resulting in significant functional disability despite pharmacological treatment</p> <p>ET dx'd by postural or kinetic tremors of hands w/out other neurologic signs</p> <p>PD dx'd by presence of 2 of 3 cardinal signs (tremor, bradykinesia, rigidity) plus sustained responsiveness to L-dopa and absence of signs of other parkinsonian syndromes</p>	<p>24 PD 6 not followed</p> <p>Mean duration of disease not reported</p> <p>However, mean age of tremor onset for ET pts = 34.9 yrs ± 16.9</p> <p>Mean age of disease onset for PD pts = 55.6 yrs ± 9.5</p> <p>Prior surgical procedures not described</p>	<p>off; one-half of pts evaluated blindly with stimulation on or off; and after blinded evaluation, all pts re-evaluated with stimulation on</p> <p>Follow-up evaluations at 6, 9, and 12 mo performed nonblinded with stimulation on and off</p> <p>Tremor evaluated utilizing UPDRS for PD patients and the Tremor Rating Scale for ET pts</p> <p>Motor performance also assessed by pt's writing and pouring liquids; and pts asked to subjectively assess change from baseline as un-changed, mild, moderate or marked</p> <p>Total tremor resolution: 9/29 (31%) ET 14/24 (58.3%) PD</p> <p>Stimulation "on" produced significant decrease in contralateral tremor at 3 month blinded evaluation, and at 6, 9, and 12 month open label evaluation</p> <p>Motor performance skills (ADLs) improved at 3 mo only in ET pts. PD pts unchanged, and no change in functional measures from 3 mo to 1 yr</p> <p>At 3 months moderate to marked subjective improvement in 90% of ET pts and 71% of PD pts</p> <p>10% of all pts thought they were unchanged or mildly worse</p> <p>Adverse events: * Surg complications among patients undergoing implantation: 1 lead dislodgment requiring reimplantation, 1 ischemic changes on EKG, and 1 generalized post-op motor seizures * Stimulation-related complications (esp paraesthesias, headache, disequilibrium and paresis of contralateral limb): 66 pts at 3 mo, 28 pts at 6 mo, and 22 pts and 12 mo * "Long-term" device complications during first year: 2 skin infections, 1 pulse generator malfunction requiring replacement, and 1 extension wire erosion requiring replacement</p>	<p>et al (1996)</p> <p>Subset of 19 ET and 10 PD pts also reported separately by Hubble et al (1997)</p> <p>Selection criteria incompletely described</p> <p>Data pooled across centers; results and complications not stratified by age or center</p> <p>Analysis did not include all pts with surg complications (see 6 pts not implanted or subsequently followed in study)</p>
Benabid et al, 1996*	Clinical	N = 117	80 PD	Patients were evaluated pre-operatively and between the 3 rd and	It is suggestive that the patients included in

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	series	<p>Mean age and sex of patients were not reported</p> <p>Implantation in 177 thalami</p>	<p>20ET 17 Miscellaneous</p> <p>Mean duration of illness not reported.</p> <p>59 patients - bilateral VIM stimulation (38 PD 13 ET)</p> <p>14 patients stimulated contralateral to a previous thalamotomy</p> <p>A total of 74 patients received bilateral surgery</p>	<p>6th months after surgery and were followed for as long as 8 years</p> <p>Tremor suppression for as long as 8 years in PD but no suppression of bradykinesia or rigidity</p> <p>Satisfactory results in essential tremor, with deterioration with time in 18.5%</p> <p>Much less favorable results for other dyskinesias (except MS: 2 of 4 have good to fair benefit)</p> <p>Adverse events: * No operative mortality. * No permanent morbidity. * Paresthesias (9%) usually induced at intensities of stimulation higher than those that suppressed tremor * Foot dystonia (9%) seen after 12 months of stimulation, reversible when stimulation discontinued dysarthria in 23 patients (19.6%), 4 of whom had previous contralateral thalamotomy, and 14 of whom had bilateral stimulation</p> <p>Side effects: 37 patients (31.6%) experienced minor side effects, always immediately after surgery</p>	<p>this study were included in Benabid et al, 1991 and 1993</p> <p>No information on selection criteria for inclusion into the study</p> <p>No statistical analysis of results</p>
Alesch et al, 1995*	Clinical series	<p>N=27</p> <p>Mean age = 65 yrs (41-77)</p> <p>25 men 8 women</p> <p>27 patients received unilateral implantation (total 33 thalami)</p> <p>6 patients received bilateral implantation</p>	<p>23 PD 4ET</p> <p>Mean duration of illness = 13 yrs</p> <p>Previous thalamotomy in 5 patients</p>	<p>Evaluation of the patients occurred pre-operatively and after 3, 6, and 12 months</p> <p>The Tremor Rating Scale was used to assess tremor: * Complete suppression of tremor seen in 21/33 (64%) implanted thalami * Major improvement occurred in 6/33 sides (18%) * Marked tremor remained in 4 sides (12%) a minor improvement * No improvement in 2/33 sides (6%).</p> <p>Patients under stimulation showed a mean improvement of 45% during ADL and 43% for motor performance test measured by the UPDRS.</p> <p>No significant effect on any other exiting symptoms of Parkinson's disease, such as rigidity and akinesia, as measured by the UPDRS.</p>	<p>36 patients were screened for inclusion in the study and 27 were selected. However, there is no information as to what criteria was used to select these patients for inclusion</p> <p>Patients severely impaired in most routine activities due to persistent tremor refractory to conservative treatment</p> <p>All side effects reversed by turning off stimulator</p> <p>No statistical analysis of results</p>

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				<p>Adverse effects: * In 27 cases, turning on the IPG led to paresthesias which lasted about 5 seconds and disappeared; * In 2 cases, paresthesias were permanent; * Mild dysarthria in two patients implanted bilaterally * Marked dysarthria in 1 patient implanted bilaterally * Disequilibrium- one case</p> <p>Complications one patient suffered subdural hematoma at time of drilling of the burr hole</p>	
Caparros-LeFebvre et al, 1993*	Clinical series	<p>N=14</p> <p>Mean age = 62.5 yrs</p> <p>Distribution by sex not reported</p> <p>Implantation in VIM</p>	<p>10PD</p> <p>Mean duration of illness = 10.4 yrs.</p> <p>Group 1: 5 patients without levodopa-induced dyskinesia</p> <p>Group 2: 5 patients with levodopa-induced dyskinesia</p>	<p>Tremor was assessed by 3 neurologists according to the UPDRS before and after thalamic stimulation on videotape recordings</p> <p>Dyskinesia was rated on a 4-point scale before surgery and after implantation and with and without stimulation</p> <p>Follow-up was for average of 27 months.</p> <p>Group 1: Tremor suppression in 4/5 (one patient, with previous thalamotomy, not controlled by stimulation)</p> <p>Group 2: Tremor suppression and suppression of levodopa induced dyskinesia in 4/5 patients (one patient with previous thalamotomy derived only transient tremor relief and no dyskinesia relief)</p> <p>No effect on other cardinal symptom of Parkinson's was reported</p> <p>Peak-dose dyskinesia was improved in all 5 cases where L-dopa induced dyskinesia was observed</p> <p>No neuropsychological side effects were noted</p> <p>There was no effect on L-dopa dosing before and after implantation</p> <p>Adverse events: Mild dystonic hand posture related to stimulation observed in one case</p>	<p>Patients included in this study were part of the selection of patients previously reported in Blond et al, 1992</p> <p>This article provides additional information on the differences in effect of stimulation for patients with and without L-dopa induced dyskinesia</p> <p>No statistical analysis of results</p> <p>Only a brief description of the patient selection method was included</p>

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Blond et al, 1992*	Clinical series	N = 14 Mean age: 62.5 yrs (54-74) ET 62.2 yrs (42-76) PD Distribution by sex not reported Implantation in VIM	10 PD 4 ET Mean duration of illness = 10.4 yrs PD and 36.8 yrs ET 3/10 PD cases had previous contralateral thalamotomy	Tremor was assessed before and after stimulation by means of clinical evaluation, surface electromyography, accelerometer, and video tape recordings PD patients were followed on average for 19.4 months ET patients were followed on average for 11 months Complete suppression of tremor in 9/14 patients (64%) Marked functional improvements in 11 patients (78%) L-dopa induced dyskinesia improved in 5 PD patients Akinesia was not changed by stimulation. Residual rigidity was difficult to assess, but seemed to improve No postoperative memory, speech, or praxis skill disorders with neurophysiological testing a few days after surgery Adverse events: Tonic posture of fingers during stimulation in one patient with PD Persistent slight paresthesias during stimulation in one patient with ET	Patient selection method was described and stated that age was not part of the criteria because of the presumed safety of the procedure Description of the assessment and results of all other cardinal symptoms of Parkinson's, except tremor, were vague and inadequate. No statistical analysis of results

Notes:

* These summaries included text from a Blue Cross Blue Shield review of these articles in their technology assessment, *Deep Brain Stimulation of the Thalamus for Tremor (1997)*.

Abbreviations:

ET- Essential tremor

PD- Parkinson's disease

MS- Multiple sclerosis

CRST-Clinical Rating Scale for Tremor

DBS – Deep brain stimulation

UTRA - Unified Tremor Rating Assessment.

UPDRS - Unified Parkinson's Disease Rating Scale

MMSE - Mini-Mental State Examination

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