



Medtronic

RECLAIM[®] DBS[™] THERAPY FOR OCD

Humanitarian Device: Authorized by Federal (U.S.A.) law for use as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive-compulsive disorder (OCD) in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs). The effectiveness of this device for this use has not been demonstrated.

Clinical summary

Rx only

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Introduction

Reclaim DBS Therapy for OCD

The clinical use of an implantable deep brain stimulation system for obsessive-compulsive disorder is supported by feasibility studies by Medtronic performed at 3 sites in the US and 1 site outside the US.

Definition of terms

Medtronic DBS Therapy and Reclaim DBS Therapy

Generic name for a medical treatment initially developed by Medtronic in collaboration with medical researchers for managing symptoms of Parkinson's disease and essential tremor. Use of Reclaim DBS Therapy for treating OCD is available under a humanitarian device exemption. The therapy uses an implantable medical device to deliver electrical stimulation to the anterior limb of the internal capsule (AIC) as an adjunct to medications and as an alternative to anterior capsulotomy for treatment of chronic, severe, treatment-resistant obsessive-compulsive disorder (OCD) in adult patients who have failed at least three selective serotonin reuptake inhibitors (SSRIs).

Anatomy

Anterior limb of the internal capsule (AIC)—The anterior limb of the internal capsule is an anatomical area in the brain that consists of white matter (nerve fibers) that lies between the head of the caudate nucleus and the lenticular nucleus.

Programmable parameters

Amplitude—A measure of the electricity intensity delivered in a stimulating pulse, measured in volts.

Electrode—The exposed end of a conducting wire (lead) where electrical current is transferred to the brain.

Parameter, programmable—A specific function with an operating range of selectable values (ie, amplitude, rate, pulse width) that enables the tailoring of a therapeutic modality for a patient.

Pulse width—A measure, in microseconds, of the duration of each stimulating pulse.

Rate—A measure, in pulses per second, that provides the numbers of times stimulating pulses are delivered each second.

Telemetry—Refers to the use of radio-frequency signals to confirm or adjust programming information from the physician programmer to the neurostimulator.

Symptoms and side effects

Akinesia—Absence of movement.

Bradykinesia—Slowness of movement.

Dysarthria—Slurred speech.

Dyskinesia—Abnormal involuntary movements that can be caused by dopaminergic drug therapy.

Hypomania—A mild form of mania, characterized by hyperactivity or euphoria.

Rigidity—Stiffness or inflexibility of the limbs and joints.

Tremor—Involuntary, regular, rhythmic shaking of a limb or other body part.

Terms

Stimulation OFF—A period of patient evaluation occurring when the neurostimulator is turned off.

Stimulation ON—A period of patient evaluation occurring when the neurostimulator is turned on.

Replacement—Any component of the system removed and replaced regardless of the time interval between explant and replacement (eg, device explanted and subsequently replaced 2 months later).

Explant—Any component of the system removed and not replaced.

Adverse events

Reported adverse events

There were a total of 347 adverse events reported in 26 of the 26 subjects (100%) in the pooled cohort. The adverse events are categorized as follows:

- Surgical/procedure-related – associated with surgical implantation of the deep brain stimulation (DBS) system
- Device-related – caused by the implanted system
- Therapy-related – caused by the electrical stimulation of the nervous system while treating the subjects' symptoms
- Disorder-related – an event that might reasonably be attributed to the patients' underlying disease state, concomitant medications or treatment regimens, or other comorbid conditions

Deaths and serious adverse events

There were a total of 23 serious adverse events reported in 11 subjects (42.3%). All serious adverse events, excluding 1 patient death, were resolved. Table 1 summarizes the serious adverse events. One death in the 26 patients at the four collaborating centers was reported. The death was identified as being related to a pre-existing condition (cancer progression) in 1 patient and was not considered to be related to Reclaim DBS Therapy.

An additional death in a patient with OCD receiving Reclaim DBS Therapy was reported in the published literature¹. Abelson et al., (2005) reported 1 suicide in their study of 4 patients, and concluded that the suicide was not related to the Reclaim DBS Therapy. This death is not included in the summary (Table 1) since it was not reported directly and did not occur in the primary patient cohort.

Two instances of intracranial hemorrhage due to surgery were reported. One was asymptomatic and resolved without further consequence. The second resulted in an increase in apathy, which resolved with time. One

¹ Abelson JL, Curtis GC, Sagher O, Albuher RC, Harrigan M, Taylor SF, Martis B, Giordani B. Deep brain stimulation for refractory obsessive-compulsive disorder. *Biol Psychiatry*. 2005 Mar 1;57 (5): 510-6.

subject suffered a single tonic-clonic seizure shortly after implantation of the leads. This subject has had no further seizures. There was 1 report of infection, which was treated and resolved.

Seven events of increased depression or suicidality and 3 instances of increased or fluctuating OCD symptoms were reported. Some of these reports occurred during periods when Reclaim DBS Therapy was actively on and several reports were associated with discontinuation of stimulation due to study design or battery depletion.

One subject was involved in a car accident and an incident of domestic disturbance. One occurrence of hypomania and 1 of violent behavior requiring medical intervention were reported. Two subjects had a broken lead or extension, which required surgical replacement. One compression fracture and 1 kidney infection occurred in subjects during the study period.

Table 1. Serious adverse events

| | Events | Patients |
|-----------------------------------|---------------|-------------------|
| Suicidality/increased depression | 7 | 5 (19.2%) |
| Increased OCD/fluctuating results | 3 | 3 (11.5%) |
| Hemorrhage, intracranial | 2 | 2 (7.7%) |
| Lead/extension failure | 2 | 2 (7.7%) |
| Aggression/violent behavior | 1 | 1 (3.8%) |
| Car accident | 1 | 1 (3.8%) |
| Compression fracture | 1 | 1 (3.8%) |
| Domestic problems/irritability | 1 | 1 (3.8%) |
| Death | 1 | 1 (3.8%) |
| Hypomania | 1 | 1 (3.8%) |
| Infection | 1 | 1 (3.8%) |
| Pyelonephritis | 1 | 1 (3.8%) |
| Seizure, post-operative | 1 | 1 (3.8%) |
| Total | 23 | 11 (42.3%) |

Summary of reported adverse events

Table 2 summarizes the adverse events reported in the Reclaim DBS Therapy for OCD clinical studies.

Table 2. Reported adverse events

| | Events | Patients |
|--|---------------|-------------------|
| Surgical/procedure-related | 46 | 14 (53.8%) |
| Pain or discomfort at incision/implant sites | 21 | 12 (46.2%) |
| General post-op discomfort | 5 | 3 (11.5%) |
| GI symptom (post op) | 5 | 2 (7.7%) |
| Hemorrhage | 2 | 2 (7.7%) |
| Infection | 2 | 1 (3.8%) |
| Apathy | 1 | 1 (3.8%) |
| Contact dermatitis | 1 | 1 (3.8%) |
| Headaches | 1 | 1 (3.8%) |
| Seizure | 1 | 1 (3.8%) |
| Other | 7 | 3 (11.5%) |
| Device-related | 5 | 5 (19.2%) |
| Broken lead or extension | 2 | 2 (7.7%) |
| Erosion of system components through skin | 1 | 1 (3.8%) |
| Sensation of shock during programming | 1 | 1 (3.8%) |
| Switched off | 1 | 1 (3.8%) |
| Therapy-related | 188 | 23 (88.5%) |
| Increased OCD symptoms | 22 | 12 (46.2%) |
| Increased anxiety | 19 | 11 (42.3%) |
| Insomnia | 18 | 12 (46.2%) |
| Increased depression/suicidality | 13 | 10 (38.5%) |
| Cognitive disturbance (clouding) | 11 | 8 (30.8%) |
| Induced muscle contraction | 10 | 7 (26.9%) |
| Hypomania | 9 | 9 (34.6%) |
| Restlessness | 8 | 3 (11.5%) |
| Stimulation induced parasthesia | 7 | 6 (23.1%) |
| Induced sensation of taste/smell | 7 | 5 (19.2%) |
| Irritability | 6 | 5 (19.2%) |
| Weight gain | 6 | 6 (23.1%) |
| Increased fatigue | 5 | 4 (15.4%) |
| Upper respiratory infection | 5 | 4 (15.4%) |
| Headaches | 4 | 4 (15.4%) |

Table 2. Reported adverse events (Continued)

| | Events | Patients |
|------------------------------------|---------------|-------------------|
| Increased tics | 4 | 1 (3.8%) |
| Dizziness | 3 | 2 (7.7%) |
| GI upset | 3 | 3 (11.5%) |
| Decreased appetite | 2 | 1 (3.8%) |
| Dry mouth | 2 | 2 (7.7%) |
| Dysarthria | 2 | 1 (3.8%) |
| Itching at surgical site(s) | 2 | 2 (7.7%) |
| Nausea | 2 | 2 (7.7%) |
| Sedation | 2 | 2 (7.7%) |
| Urinary tract disturbance | 2 | 1 (3.8%) |
| Weight loss | 2 | 2 (7.7%) |
| Acne | 1 | 1 (3.8%) |
| Cervical neck pain | 1 | 1 (3.8%) |
| Congestion | 1 | 1 (3.8%) |
| Edema | 1 | 1 (3.8%) |
| IPG depletion | 1 | 1 (3.8%) |
| Increased sleeping | 1 | 1 (3.8%) |
| Induced sensation, IPG pocket | 1 | 1 (3.8%) |
| Intermittent shocks/jolts | 1 | 1 (3.8%) |
| Left kidney area pain | 1 | 1 (3.8%) |
| Lethargy | 1 | 1 (3.8%) |
| Sore throat | 1 | 1 (3.8%) |
| Unequal pupils | 1 | 1 (3.8%) |
| Disorder-Related | 108 | 24 (92.3%) |
| Changes in mood, anxiety, or anger | 16 | 10 (38.5%) |
| Gastrointestinal disturbances | 11 | 9 (34.6%) |
| Insomnia | 10 | 6 (23.1%) |
| Headaches | 6 | 5 (19.2%) |
| Increased fatigue | 6 | 5 (19.2%) |
| Sedation | 4 | 2 (7.7%) |
| Urinary tract disturbance | 3 | 2 (7.7%) |
| Back pain | 2 | 2 (7.7%) |
| Contact dermatitis | 2 | 1 (3.8%) |

Table 2. Reported adverse events (Continued)

| | Events | Patients |
|-----------------------------------|---------------|-----------------|
| Cough | 2 | 1 (3.8%) |
| Disequilibrium | 2 | 2 (7.7%) |
| Diverticulosis | 2 | 1 (3.8%) |
| Restless limbs | 2 | 2 (7.7%) |
| Tremor | 2 | 2 (7.7%) |
| Abnormal blood sugar | 1 | 1 (3.8%) |
| Adenomyosis | 1 | 1 (3.8%) |
| Aggression/violent behavior | 1 | 1 (3.8%) |
| Ankle fracture | 1 | 1 (3.8%) |
| Attention/cognitive deficits | 1 | 1 (3.8%) |
| Car accident | 1 | 1 (3.8%) |
| Chronic cough | 1 | 1 (3.8%) |
| Compression fracture | 1 | 1 (3.8%) |
| Depersonalization | 1 | 1 (3.8%) |
| Edema | 1 | 1 (3.8%) |
| Facial numbness | 1 | 1 (3.8%) |
| Fall | 1 | 1 (3.8%) |
| Fatigue | 1 | 1 (3.8%) |
| Fever | 1 | 1 (3.8%) |
| Flu | 1 | 1 (3.8%) |
| General sense of not feeling well | 1 | 1 (3.8%) |
| Hair twirling | 1 | 1 (3.8%) |
| Hematoma, subcutaneous (eye) | 1 | 1 (3.8%) |
| Increased OCD symptoms | 1 | 1 (3.8%) |
| Increased sexual interest | 1 | 1 (3.8%) |
| Itching above eye | 1 | 1 (3.8%) |
| Memory worsening | 1 | 1 (3.8%) |
| Muscle cramps in neck | 1 | 1 (3.8%) |
| Muscle rigidity | 1 | 1 (3.8%) |
| Numbness in arm after coughing | 1 | 1 (3.8%) |
| Nystagmus | 1 | 1 (3.8%) |
| Oral paresthesia | 1 | 1 (3.8%) |
| Paresis/numbness in hand | 1 | 1 (3.8%) |

Table 2. Reported adverse events (Continued)

| | Events | Patients |
|---------------------|---------------|-----------------|
| Pneumonia | 1 | 1 (3.8%) |
| Shortness of breath | 1 | 1 (3.8%) |
| Sinus inflammation | 1 | 1 (3.8%) |
| Social withdrawal | 1 | 1 (3.8%) |
| “Spaciness” | 1 | 1 (3.8%) |
| Stomach pains | 1 | 1 (3.8%) |
| Tennis elbow | 1 | 1 (3.8%) |
| Twitching of nose | 1 | 1 (3.8%) |
| Weight gain | 1 | 1 (3.8%) |
| Weight loss | 1 | 1 (3.8%) |

Potential adverse events

In addition, one may reasonably expect the risks associated with the use of the Medtronic DBS System for the approved indications of Parkinson's disease (PD) and essential tremor (ET) to be similar in treating OCD.

Over the entire PD study duration, 12/160 patients (7.5%) had intracranial hemorrhage; 17/160 patients (10.6%) had device-related infection; 16 patients (10.0%) had paresis/asthenia; and 13/160 patients (8.1%) had hemiplegia/hemiparesis (3). The rate of stimulation related adverse events was 51.9% (83/160 patients) and the rate of ongoing stimulation-related events was 22.5% (36/160 patients). The rate of serious stimulation-related adverse events was 9.4% (15/160) and the rate of ongoing serious stimulation-related adverse events was 3.1% (5/160) patients. Ongoing serious stimulation-related adverse events included: worsening of motor impairment/PD symptoms (dyskinesia); sensory impairment (pain); and speech/ language (dysarthria, hypophonia, speech disorder). Other stimulation-related adverse events included: worsening of motor impairment/PD symptoms (worse motor fluctuations, incoordination, abnormal gait, akinesia/bradykinesia, tremor, rigidity, myoclonus, and dysphagia); sensory impairment (paresthesia, sensory disturbance, hypesthesia, hearing [tinnitus], and headache); speech/language (voice alteration); eye (visual disturbances [diplopia, abnormal vision, and visual field defect] and eye disorders [twitching]); cognitive (thinking abnormal, confusion, alteration of mentation [dizziness]); general (respiratory [laryngismus], musculo-skeletal [abnormal posture], gastrointestinal [vomiting], urogenital [urinary incontinence], metabolic/nutritional [weight loss], skin and appendages [sweating], and systemic [accidental injury]; sleep [somnolence and insomnia]; neuropsychological (psychiatric disturbances [manic reaction and neurosis]); general paresis/asthenia; internal system events (shock/jolt, positioning difficulties); cardiovascular (cerebrovascular accident); hemiplegia/hemiparesis (asthenia); and depression.

The rate of device-related adverse events was 36.9% (59/160 patients) and the rate of ongoing device-related events was 10.0% (16/160

patients). The rate of serious device-related adverse events was 17.5% (28/160 patients) and the rate of ongoing serious device related adverse events was 6.3% (10/160 patients). Ongoing, serious device-related adverse events included: internal DBS system events (intermittent continuity, electromagnetic interference, and lead breakage); infection, worsening of motor impairment/PD symptoms (worse motor fluctuations, and incoordination) due to loss of effect; and skin and appendages (erosion). Other device-related adverse events included: internal DBS system events (shock/jolt, dislodged, migration, normal battery failure, malfunction, current leak, wire breakage, kinked electrode, electrode problem, positioning difficulties, impedance low); external system events (difficult to program, printer problem); sensory impairment (pain, sensory disturbance, paresthesia, and headache); speech/language (hypophonia); skin and appendages (skin disorder); subcutaneous hemorrhage/seroma (seroma); paresis/asthenia; metabolic/nutritional (edema); and cerebral spinal fluid abnormality (pneumocephalus). One patient experienced manic symptoms (manic reaction) and attention and cognitive deficits (thinking abnormal) concurrent with exposure to an electronic article surveillance (electromagnetic interference) device.

Table 3. Summary of adverse events reported in the Parkinson's Disease clinical trial

| Major Category | All Patients (n = 160) | | | |
|---|-----------------------------|---------------|-------------------|--------------|
| | # of Events (known serious) | Study Related | # (%) of Patients | 95% CI** |
| Intracranial Hemorrhage* | 13 (8) | 13 | 12 (7.5%) | (3.4, 11.6) |
| Device-Related Infection* | 32 (23) | 31 | 17 (10.6%) | (5.9, 15.4) |
| Infection with Explant* | 15 (15) | 15 | 9 (5.6%) | (2.1, 9.2) |
| Infection without Explant* | 17 (8) | 16 | 12 (7.5%) | (3.4, 11.6) |
| Paresis/Asthenia* | 16 (1) | 6 | 16 (10%) | (5.4, 14.7) |
| Hemiplegia/Hemiparesis* | 15 (8) | 10 | 13 (8.1%) | (3.9, 12.4) |
| Worsening of Motor Impairment/ PD Symptom* | 357 (48) | 130 | 110 (68.8%) | (61.6, 75.9) |
| Dyskinesia* | 131 (22) | 64 | 60 (37.5%) | (30.0, 45.0) |
| Worse Motor Fluctuations* | 85 (15) | 23 | 56 (35%) | (27.6, 42.4) |
| Abnormal Gait* | 38 (4) | 10 | 30 (18.8%) | (12.7, 24.8) |
| Incoordination* | 33 (3) | 14 | 29 (18.1%) | (12.2, 24.1) |
| Tremor* | 22 (0) | 4 | 18 (11.3%) | (6.4, 16.2) |
| Akinesia/Bradykinesia* | 20 (0) | 9 | 19 (11.9%) | (6.9, 16.9) |
| Dysphagia* | 13 (3) | 2 | 12 (7.5%) | (3.4, 11.6) |
| Rigidity* | 13 (1) | 3 | 12 (7.5%) | (3.4, 11.6) |
| Myoclonus | 1 (0) | 1 | 1 (0.6%) | (0, 1.9) |
| Therapeutic Response, Decreased | 1 (0) | 0 | 1 (0.6%) | (0, 1.9) |
| Sensory Impairment* | 148 (14) | 59 | 79 (49.4%) | (41.6, 57.1) |
| Pain* | 71 (5) | 15 | 50 (31.3%) | (24.1, 38.4) |
| Paresthesia* | 37 (1) | 23 | 29 (18.1%) | (12.2, 24.1) |
| Sensory Disturbance* | 18 (2) | 11 | 16 (10%) | (5.4, 14.7) |
| Headache* | 16 (4) | 8 | 14 (8.8%) | (4.4, 13.1) |
| Neuralgia | 3 (2) | 0 | 3 (1.9%) | (0, 4.0) |
| Hearing* | 2 (0) | 1 | 2 (1.3%) | (0, 3.0) |
| Neuropathy | 1 (0) | 1 | 1 (0.6%) | (0, 1.9) |
| Cognitive* | 142 (21) | 61 | 72 (45%) | (37.3, 52.7) |
| Confusion* | 56 (5) | 27 | 44 (27.5%) | (20.6, 34.4) |
| Thinking Abnormal* | 39 (3) | 16 | 33 (20.6%) | (14.4, 26.9) |
| Hallucinations | 15 (2) | 1 | 11 (6.9%) | (3.0, 10.8) |
| Alteration of Mentation* | 16 (5) | 9 | 14 (8.8%) | (4.4, 13.1) |
| Amnesia* | 9 (2) | 6 | 8 (5.0%) | (1.6, 8.4) |
| Delusions* | 5 (4) | 0 | 4 (2.5%) | (0, 4.9) |
| Dementia | 2 (0) | 2 | 2 (1.3%) | (0, 3.0) |

* At least one instance was associated with the system components.
** Note: Exact 95% confidence intervals were used when the # (%) of patients was 0 (0%) because the normal approximation to the binomial does not provide a confidence interval. In every other case, the normal approximation to the binomial was used to calculate confidence intervals.

Table 3. Summary of adverse events reported in the Parkinson's Disease clinical trial (continued)

| Major Category | All Patients (n = 160) | | | |
|--|-----------------------------|---------------|-------------------|--------------|
| | # of Events (known serious) | Study Related | # (%) of Patients | 95% CI** |
| DBS System* | 93 (33) | 80 | 57 (35.6%) | (28.2, 43.1) |
| Internal* | 86 (33) | 74 | 55 (34.4%) | (27.0, 41.7) |
| External* | 7 (0) | 6 | 6 (3.8%) | (0.8, 6.7) |
| Speech/Language* | 77 (15) | 48 | 59 (36.9%) | (29.4, 44.4) |
| Dysarthria* | 47 (6) | 32 | 42 (26.3%) | (19.4, 33.1) |
| Speech/Language* | 30 (9) | 16 | 23 (14.4%) | (8.9, 19.8) |
| Neuropsychological* | 55 (18) | 6 | 31 (19.4%) | (13.3, 26.0) |
| Psychiatric Disturbances* | 25 (8) | 4 | 14 (8.8%) | (4.4, 13.1) |
| Personality Disorder | 12 (4) | 1 | 9 (5.6%) | (2.1, 9.2) |
| Hostility | 6 (2) | 0 | 5 (3.1%) | (0.4, 5.8) |
| Manic Reaction* | 5 (2) | 2 | 3 (1.9%) | (0, 4.0) |
| Neurosis* | 1 (0) | 1 | 1 (0.6%) | (0, 1.9) |
| Paranoid Reaction | 1 (0) | 0 | 1 (0.6%) | (0, 1.9) |
| Anxiety* | 25 (7) | 2 | 20 (12.5%) | (7.4, 17.6) |
| Apathy | 4 (2) | 0 | 4 (2.5%) | (0, 4.9) |
| Suicide Attempt | 1 (1) | 0 | 1 (0.6%) | (0, 1.9) |
| Depression* | 41 (10) | 4 | 35 (21.9%) | (15.5, 28.3) |
| Sleep* | 45 (1) | 8 | 37 (23.1%) | (16.6, 29.7) |
| Eye* | 48 (6) | 25 | 39 (24.4%) | (17.7, 31.0) |
| Visual Disturbance* | 33 (6) | 20 | 30 (18.8%) | (12.7, 24.8) |
| Eye Disorder* | 10 (0) | 5 | 9 (5.6%) | (2.1, 9.2) |
| Eye Infection* | 5 (0) | 0 | 4 (2.5%) | (0, 4.9) |
| Subcutaneous Hemorrhage/Seroma* | 15 (6) | 10 | 14 (8.8%) | (4.4, 13.1) |
| Convulsions | 7 (6) | 5 | 7 (4.4%) | (1.2, 7.5) |
| Death | 3 (3) | 0 | 3 (1.9%) | (0, 4.0) |
| Cerebral Spinal Fluid Abnormality | 5 (1) | 5 | 5 (3.1%) | (0.4, 5.8) |
| * At least one instance was associated with the system components. | | | | |
| ** Note: Exact 95% confidence intervals were used when the # (%) of patients was 0 (0%) because the normal approximation to the binomial does not provide a confidence interval. In every other case, the normal approximation to the binomial was used to calculate confidence intervals. | | | | |

Table 3. Summary of adverse events reported in the Parkinson's Disease clinical trial (continued)

| Major Category | All Patients (n = 160) | | | |
|--|-----------------------------|-----------------------------|-------------------|--------------|
| | # of Events (known serious) | Study Related Known/Unknown | # (%) of Patients | 95% CI** |
| General* | 312 (52) | 40 | 110 (68.8%) | (61.6, 75.9) |
| Systemic* | 75 (14) | 7 | 49 (30.6%) | (23.5, 37.8) |
| Gastrointestinal* | 55 (5) | 9 | 41 (25.6%) | (18.9, 32.4) |
| Urogenital* | 53 (7) | 3 | 43 (26.9%) | (20.0, 33.7) |
| Respiratory | 43 (10) | 8 | 30 (18.8%) | (12.7, 24.8) |
| Metabolic/Nutritional* | 36 (4) | 6 | 29 (18.1%) | (12.2, 24.1) |
| Musculo-Skeletal* | 21 (7) | 2 | 19 (11.9%) | (6.9, 16.9) |
| Skin and Appendages* | 25 (5) | 5 | 22 (13.8%) | (8.4, 19.1) |
| Ecchymosis | 1 (0) | 0 | 1 (0.6) | (0, 1.9) |
| Erosion* | 3 (3) | 2 | 3 (1.9%) | (0, 4.0) |
| Infection, fungal | 2 (0) | 0 | 2 (1.3%) | (0, 3.0) |
| Lymphedema | 1 (0) | 0 | 1 (0.6%) | (0, 1.9) |
| Petechia | 1 (0) | 0 | 1 (0.6%) | (0, 1.9) |
| Psoriasis | 1 (1) | 0 | 1 (0.6%) | (0, 1.9) |
| Rash | 7 (0) | 0 | 7 (4.4%) | (1.2, 7.5) |
| Skin Disorder* | 6 (1) | 2 | 6 (3.8%) | (0.8, 6.7) |
| Sweating* | 3 (0) | 1 | 3 (1.9%) | (0, 4.0) |
| Ear | 4 (0) | 0 | 4 (2.5%) | (0, 4.9) |
| Cardiovascular* | 64 (14) | 24 | 32 (20%) | (13.8, 26.2) |
| * At least one instance was associated with the system components. | | | | |
| ** Note: Exact 95% confidence intervals were used when the # (%) of patients was 0 (0%) because the normal approximation to the binomial does not provide a confidence interval. In every other case, the normal approximation to the binomial was used to calculate confidence intervals. | | | | |

Clinical studies

Clinical rating scale

The Yale-Brown Obsessive Compulsive Scale (YBOCS) is a 10-item, clinician-administered scale developed to assess the severity of obsessions and compulsions, independent of the number and type of obsessions or compulsions.

According to the OCD treatment consensus guideline,¹ the currently accepted definition of severe OCD, taking into account patient disability, is a score of 30 or greater on the YBOCS instrument, described as follows:

- Mild OCD (YBOCS score of 10-18) causes distress but not necessarily dysfunction; help from others is usually not required to get through the day.
- Moderate OCD (YBOCS score of 18-29) causes both distress and functional impairment.
- Severe OCD (YBOCS score of 30 or above) causes serious functional impairment requiring significant help from others.

Summary

The probable benefit of the Reclaim system in treating OCD was demonstrated in feasibility studies performed at 3 sites in the US and 1 site outside the US. At 1 site in the US and the OUS site, the pilot studies were designed as randomized controlled double blind studies.

Patient demographics

Results from 26 treatment-resistant OCD patients treated with DBS at 4 collaborating centers, 3 in the US, and 1 in Europe are summarized in Table 4. All patients met stringent inclusion criteria including disease severity (YBOCS >30), treatment refractoriness, and symptom duration (minimum of 5 years).

Mean age for the patient cohort at time of implant was 37 years, with approximately equal numbers of males and females (53.8%/ 46.2%).

¹ March JS, Frances A, Kahn DA, Carpenter D, eds. The Expert Consensus Guideline Series: Treatment of Obsessive-Compulsive Disorder. *J Clin Psychiatry*. 1997;58 (suppl 4).

Mean duration of symptoms for these patients averaged 22 years, demonstrating the long-standing, treatment-resistant nature of the disorder in this population. Treatment duration ranged from 85.6 months to slightly over 3 months for the most recently treated individuals. All patients had been treated with multiple trials of medications and had also undergone cognitive behavioral therapy. Many patients remained on multiple stable medications. A majority of the patients (89%) also reported a history of comorbid depression (major depressive disorder [MDD]) associated with their severe OCD.

Table 4. Patient demographics

| Center/ patient | Age at implant | Implant dur (months) | Gender (M/F) | Age at OCD onset | Symptom dur (yrs) | Secondary diagnosis (Axis I / Axis II) | History of depression | History of CBT |
|------------------------------|-------------------|-------------------------|-----------------|---------------------|----------------------|--|--------------------------|-------------------|
| Butler Hospital | | | | | | | | |
| BH1 | 32 | 53.5 | M | 10 | 22 | MDD (single episode), OCD/DP | Y | Y |
| BH2 ^a | 40 | 51.5 | F | 16 | 24 | MDD (hypomanic episode) | Y | Y |
| BH3 | 39 | 49.2 | M | 12 | 27 | Dysthymia | Y | Y |
| BH4 ^a | 26 | 40.3 | F | 15 | 11 | MDD | Y | Y |
| BH5 | 32 | 30.8 | M | 10 | 22 | MDD | Y | Y |
| Cleveland Clinic | | | | | | | | |
| CC1 ^b | 59 | 12.0 | F | 19 | 40 | None | N | Y |
| CC2 | 35 | 40.5 | F | 12 | 23 | MDD | Y | Y |
| CC3 | 22 | 38.8 | M | 8 | 14 | MDD, schizophrenic traits | Y | Y |
| CC4 | 23 | 34.2 | M | 7 | 16 | MDD | Y | Y |
| CC5 | 45 | 18.8 | M | 19 | 26 | None | N | Y |
| University of Florida | | | | | | | | |
| FL1 | 32 | 26.9 | F | 24 | 8 | MDD (single episode) | Y | Y |
| FL2 | 50 | 21.0 | M | 34 | 16 | MDD (recurrent) | Y | Y |
| FL3 | 38 | 17.5 | M | 22 | 16 | MDD (recurrent, in remission) | Y | Y |
| FL4 | 32 | 8.2 | M | 10 | 22 | MDD (in remission) | Y | Y |

Table 4. Patient demographics (Continued)

| Center/ patient | Age at implant | Implant dur (months) | Gender (M/F) | Age at OCD onset | Symptom dur (yrs) | Secondary diagnosis (Axis I / Axis II) | History of depression | History of CBT |
|--------------------|-------------------|-------------------------|-----------------|---------------------|----------------------|--|--------------------------|----------------------|
| FL5 | 32 | 3.3 | F | 15 | 17 | MDD (partial remission) | Y | Y |
| Luevan | | | | | | | | |
| LV1 ^c | 35 | 15.0 | M | 12 | 23 | MDD, Histrionic, narcissistic | Y | Y |
| LV2 | 52 | 85.6 | F | 24 | 28 | MDD, Generalized anxiety disorder | Y | Y |
| LV3 | 39 | 70.7 | F | 16 | 23 | MDD, Panic attacks, dependent PD | Y | Y |
| LV4 ^c | 35 | 41.0 | M | 12 | 23 | MDD (past comorbid) | Y | Y |
| LV5 | 40 | 44.9 | F | 14 | 26 | MDD (past) | Y | Y |
| LV6 | 37 | 38.8 | M | 16 | 21 | MDD (comorbid) | Y | Y |
| LV7 | 39 | 27.8 | F | 15 | 24 | MDD (past) | Y | Y |
| LV8 | 40 | 27.5 | M | 14 | 26 | MDD (comorbid), panic attacks | Y | Y |
| LV9 | 23 | 10.4 | M | 12 | 11 | MDD | Y | Y |
| LV10 | 30 | 5.3 | F | 9 | 21 | None | N | Y |
| LV11 | 57 | 3.5 | F | 16 | 41 | MDD | Y | Y |

Table 4. Patient demographics (Continued)

| Center/ patient | Age at implant | Implant dur (months) | Gender (M/F) | Age at OCD onset | Symptom dur (yrs) | Secondary diagnosis (Axis I / Axis II) | History of depression | History of CBT |
|--------------------|-------------------|-------------------------|--------------------|---------------------|----------------------|--|--------------------------|-------------------|
| Mean: | 37.1 | 31.4 | M=53.8% F=46.2% | 15.1 | 22.0 | | Yes=88.5% No=11.5% | Yes=100% No=0% |
| Min: | 22.0 | 3.3 | | 7.0 | 8.0 | | | |
| Max: | 59.0 | 85.6 | | 34.0 | 41.0 | | | |

^a Stimulators turned off at 12 months post-implant.

^b This patient died in January 2003 from pneumonia and cancer, not related to the study.

^c Number of implant months at time DBS system explanted.

Patient discontinuation

Four of the 26 patients from the 4 collaborating centers have chosen to discontinue deep brain stimulation. These patients are listed in Table 5 (including the patient death). None of these patients were reported as a YBOCS responder (based upon the 35% response criterion) in any prior analyses.

Three of the 4 patients discontinued DBS due to lack of effectiveness. One discontinued DBS because of the inability to achieve an effective level of treatment without adverse effects (hypomania).

Two of these 4 patients elected to have their Reclaim DBS System explanted and proceeded to undergo a capsulotomy.

Table 5. Patient discontinuation

| Patient | Event | Time of event (post-implant) | Reason for therapy termination | DBS system explanted | Last follow-up (outcome measures) |
|------------------|------------------------|-------------------------------------|---|-----------------------------|--|
| BH2 ^a | Stimulators turned off | 12 months | No change in OCD symptoms | N | 36 months |
| BH4 ^a | Stimulators turned off | 12 months | No change in OCD symptoms | N | 36 months |
| CC1 | Death | 12 months | Cancer | N | 6 months |
| LV1 | Capsulotomy | 15 months | Lack of DBS effectiveness | Y | 12 months |
| LV4 | Capsulotomy | 41 months | Inability to titrate DBS to effective level (between effective therapy and hypomania) | Y | 36 months |

^a Data after therapy discontinuation included in outcome measures for intent-to-treat analyses.

OCD symptoms (YBOCS)

Table 6 shows the YBOCS scores, collected over a period of up to 3 years, for the patients treated with DBS at these 4 centers. On average this patient population showed a progressive and sustained improvement in YBOCS ratings as illustrated in Figure 1.

Table 6. YBOCS scores

| Patient | Pre-stim | | Months | | | | | | |
|------------------|-----------|---------|--------|----|----|----|------------------------|----|----|
| | Base-line | Post-op | 1 | 3 | 6 | 12 | 12 (LOCF) ^a | 24 | 36 |
| | BH1 | 32 | 28 | 30 | 28 | 16 | 15 | 15 | 24 |
| BH2 | 34 | 30 | 27 | 26 | 25 | 25 | 25 | 27 | 30 |
| BH3 | 35 | 35 | 27 | 26 | 24 | 26 | 26 | 25 | 24 |
| BH4 | 34 | 30 | 21 | 19 | 27 | 29 | 29 | 32 | 30 |
| BH5 | 33 | 33 | 30 | 19 | 28 | 26 | 26 | 24 | . |
| CC1 | 38 | 38 | 28 | 30 | 31 | . | 31 | . | . |
| CC2 | 36 | 35 | 32 | 29 | 24 | 30 | 30 | 20 | 22 |
| CC3 ^b | 35 | 34 | 30 | 31 | 28 | 30 | 30 | 18 | 18 |
| CC4 ^b | 33 | 34 | 26 | 16 | 9 | 8 | 8 | 9 | 12 |
| CC5 ^c | 36 | 36 | 29 | 26 | 27 | 20 | 20 | 21 | . |
| FL1 | 37 | 21 | 36 | 18 | 14 | 26 | 26 | 12 | . |
| FL2 | 31 | 35 | 37 | 28 | 29 | 29 | 29 | . | . |
| FL3 | 33 | 28 | 35 | 26 | 31 | 7 | 7 | . | . |
| FL4 | 31 | 30 | 36 | 35 | 29 | . | 29 | . | . |
| FL5 | 32 | 26 | 30 | 20 | . | . | 20 | . | . |
| LV1 | 38 | . | . | 30 | 33 | 31 | 31 | . | . |
| LV2 | 33 | . | 25 | 20 | 14 | 25 | 25 | 21 | 21 |
| LV3 | 30 | . | 17 | 12 | 14 | 16 | 16 | 11 | 9 |
| LV4 | 38 | . | 23 | 22 | 18 | 22 | 22 | 22 | 26 |
| LV5 ^d | 34 | . | 30 | 28 | 26 | 25 | 25 | 34 | 32 |
| LV6 | 30 | . | 3 | 24 | 15 | 12 | 12 | 1 | 7 |
| LV7 | 35 | . | 10 | 14 | 9 | 7 | 7 | 3 | . |

Table 6. YBOCS scores (Continued)

| Patient | Pre-stim | | Months | | | | | | | |
|--------------------|-------------|--------------|---------------|---------------|---------------|---------------|------------------------|---------------|---------------|---|
| | Base-line | Post-op | 1 | 3 | 6 | 12 | 12 (LOCF) ^a | 24 | 36 | |
| | LV8 | 32 | . | 18 | 8 | 17 | 14 | 14 | 13 | . |
| LV9 | 31 | . | 24 | 5 | 8 | 2 | 2 | . | . | |
| LV10 | 37 | . | 18 | 1 | 5 | . | 5 | . | . | |
| LV11 | 36 | . | 13 | 6 | . | . | 6 | . | . | |
| N | 26 | 15 | 25 | 26 | 24 | 21 | 26 | 17 | 12 | |
| Mean | 34.0 | 31.5 | 25.4 | 21.0 | 20.9 | 20.2 | 19.8 | 18.6 | 20.9 | |
| Median | 34.0 | 33.0 | 27.0 | 23.0 | 24.0 | 25.0 | 23.5 | 21.0 | 21.5 | |
| S.D. | (2.5) | (4.5) | (8.5) | (9.0) | (8.5) | (9.0) | (9.5) | (9.3) | (8.3) | |
| Avg% chg | | -7.1% | -24.7% | -37.9% | -38.6% | -40.7% | -41.8% | -45.4% | -38.7% | |
| Median% chg | | -2.9% | -21.2% | -32.6% | -32.4% | -29.7% | -33.6% | -42.1% | -36.9% | |

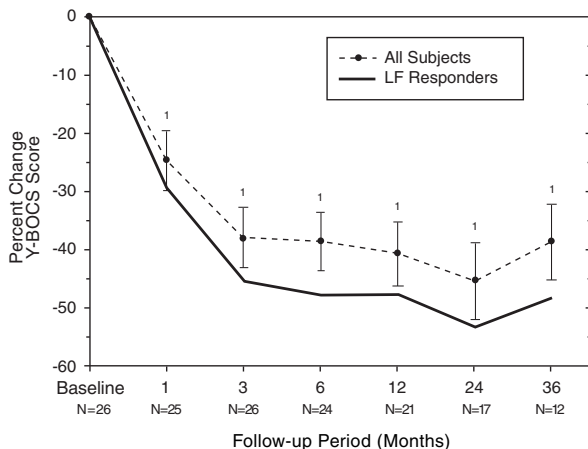
^a Last observation carried forward (LOCF) conducted for 12-month time point. Data for 5 patients (CC1, FL4, FL5, LV10, LV11) imputed using last measured YBOCS score prior to 12-month follow-up.

^b Last follow-up for patients CC3 and CC4 occurred at 33 and 32 months respectively. For analyses, the data is reported as the 36-month time point.

^c Last follow-up for patient CC5 was at 19 months. For analyses, the data are reported as the 24-month time point.

^d At the time of surgery, this patient was implanted with bilateral DBS electrodes in the anterior limbs of the internal capsule, and a second set of DBS electrodes in the dorsomedial thalamus, to investigate an alternative DBS target. At 27 months, the capsular electrodes were turned off, due to lack of therapeutic response, and the electrodes in the dorsomedial thalamus were turned on. The final data point for this patient (a non-responder) at 36 months is included in the intent-to-treat analysis.

At 12 months, data was available for only 21 of the 26 subjects. At 12 months, the average YBOCS score for the group (n=21) had decreased 40.7%, with a corresponding decrease of 45.4% for the cohort followed out to 24 months (n=17). In the subgroup of patients that met clinical response criterion (>25% or greater reduction on the YBOCS), the magnitude of these improvements were even greater (Figure 1). Using a last observation carried forward (LOCF) analysis for all patients, the average YBOCS reduction was 41.8% at the 12-month time point.



¹ Within-subject change statistically significant ($p \leq .001$, 2-sided test). LF - Last follow-up.

Figure 1. Average YBOCS scores following DBS treatment.

On average, patients treated with DBS at these 4 centers had a greater than two-thirds chance of attaining a meaningful clinical benefit (>25% YBOCS decrease at last follow-up), and if a patient reached this response criterion, the average improvement at 6 months and 12 months post-treatment was approximately a 50% reduction in YBOCS score.

According to the Expert Consensus Panel on OCD (1997), a responder is considered a subject who demonstrates a 35% reduction in their YBOCS score and a partial responder is a subject with a 25% reduction in their YBOCS score. At 12 months, 10 subjects met the 35% response criterion and an additional 4 met the 25% responder criterion (Table 7). An LOCF analysis at this time point results in 13 of 26 patients meeting the 35% response level, and 4 patients meeting the 25% level.

At last follow-up, almost two-thirds of the patient population (16/26, 61.5%) met the more conservative criterion for a clinical improvement (>35% YBOCS reduction), and another 11.5% (3/26) met the 25% reduction response criterion (Table 7).

Table 7. Responder rates: sample size (percent), and [95% confidence interval]

| Time | Non-responders | | Partial responders | | Full responders | | Full & partial responders | |
|-------------------------------------|-----------------|-----------------------------|----------------------------|------------------------------|------------------------------|-----------------|---------------------------|--|
| | No. of patients | 0 to < 25% reduction | ≥ 25% & < 35% reduction | ≥ 35% reduction | > 25% reduction | > 25% reduction | > 25% reduction | |
| 6 months | 24 | 9 (37.5%) [18.8%, 59.4%] | 4 (16.7%) [4.7%, 37.4%] | 11 (45.8%) [25.6%, 67.2%] | 15 (62.5%) [40.6%, 81.2%] | | | |
| 12 months | 21 | 7 (33.3%) [14.6%, 57.0%] | 4 (19.0%) [5.4%, 41.9%] | 10 (47.6%) [25.7%, 70.2%] | 14 (67.7%) [43.0%, 85.4%] | | | |
| 12 months (LOCF)^a | 26 | 9 (34.6%) [17.2%, 55.7%] | 4 (15.4%) [4.4%, 34.9%] | 13 (50.0%) [29.9%, 70.1%] | 17 (65.4%) [44.3%, 82.8%] | | | |
| Last follow-up | 26 | 7 (26.9%) [11.6%, 47.8%] | 3 (11.5%) [2.4%, 30.2%] | 16 (61.5%) [40.6%, 79.8%] | 19 (73.1%) [52.2%, 88.4%] | | | |

^a Last observation carried forward (LOCF) conducted for 12-month time point. Data for 5 patients (CC1, FL4, FL5, LV10, LV11) imputed using last measured YBOCS score prior to 12-month follow-up.

These changes in YBOCS scores measured in this patient group reflect a considerable reduction in symptom severity as defined by this clinical rating scale. At baseline, 100% (26/26) of the patients enrolled into the study protocols at the 4 collaborating centers met the criterion for “severe” OCD (YBOCS score of 30 or greater) as defined by the Expert Consensus Panel on obsessive-compulsive disorder (1997). Table 8 summarizes the results of the 26 subjects according to this guideline: mild 10-18, moderate 18-29, severe >30. Results at 6 months, 12 months, 12-month LOCF, and last FU, show that over 80% of the patients had decreased in severity from severe at baseline to either mild or moderate.

Table 8. OCD severity ratings

| Time | No. of patients | Range of OCD severity | | |
|-------------------------------------|-----------------|-----------------------|------------------|----------------------|
| | | Mild (10-18) | Moderate (18-29) | Severe (30 or above) |
| Baseline | 26 | 0 (0.0%) | 0 (0.0%) | 26 (100.0%) |
| 6 months | 24 | 11 (45.8%) | 10 (41.7%) | 3 (12.5%) |
| 12 months | 21 | 8 (38.1%) | 10 (47.6%) | 3 (14.3%) |
| 12 months (LOCF)^a | 26 | 10 (38.5%) | 12 (46.2%) | 4 (15.4%) |
| Last follow-up | 26 | 11 (42.3%) | 10 (38.5%) | 5 (19.2%) |

^a Last observation carried forward (LOCF) conducted for 12-month time point. Data for 5 patients (CC1, FL4, FL5, LV10, LV11) imputed using last measured YBOCS score prior to 12-month follow-up.

A majority of the treatment-resistant patients treated with deep brain stimulation obtained benefit. Approximately two-thirds of the patients met the accepted criterion for a clinical response (25% reduction in YBOCS) at 6 months, 12 months, and last follow-up, and approximately half of the patients met the more stringent criterion of a 35% reduction at these time points. A majority of the patients moved from a severe OCD rating category at baseline, to a mild or moderate rating at subsequent post-treatment time points.

There are 4 subtypes of OCD according to the Leckman¹ scheme. As seen in Table 9, subjects with the obsessions and checking subtype, had the best response, ie, 74.0%, as measured by the YBOCS. In addition, the majority of subjects had comorbid anxiety and depression which also improved during treatment. No subjects with hoarding as their primary subtype were included in the study.

¹ Leckman JF, Grice DE, Boardman J, Zhang H, Vitale A, Bondi C, Alsobrook J, Peterson BS, Cohen DJ, Rasmussen SA, Goodman WK, McDougle CJ, Pauls DL. Symptoms of obsessive compulsive disorder. *Am J Psychiatry*. 1997;154:911-917.

Table 9. OCD, depression, anxiety improvements by sub-type

| OCD sub-type | N | YBOCS | | HAM-D | | HAM-A | |
|-------------------------|----|--------|-------|--------|-------|--------|-------|
| | | Mean | SD | Mean | SD | Mean | SD |
| Hoarding | 0 | - | - | - | - | - | - |
| Cleanliness and washing | 11 | -31.9% | 19.7% | -45.2% | 33.1% | -38.5% | 33.1% |
| Obsessions and checking | 6 | -74.0% | 13.7% | -77.4% | 16.3% | -66.9% | 33.4% |
| Symmetry and ordering | 9 | -42.9% | 33.2% | -45.6% | 31.8% | -52.8% | 30.6% |

In each of these subtype categories, there were patients that responded to DBS therapy (45% responder rate for cleanliness and washing [n=11]; 56% responder rate for symmetry and ordering [n=9]; and 100% responder rate for obsessions and checking [n=6]).

An analysis of differences in prescribed medications between DBS responders and nonresponders found that patients who responded to DBS showed little change in the number of psychotropic drugs prescribed (-2.8% change) between baseline and last follow-up, compared to nonresponders, who showed an increase (15.4%) in these medications.

Two of the 4 centers incorporated a randomized blinded period of stimulation using a crossover design. As can be seen in the following tables, subjects had a greater reduction in their YBOCS and HAM-D scores during stim on as compared to stim off.

Table 10. Period 1 results - YBOCS

| STIM | N | YBOCS | Baseline (BL) | Period 1 (P1) | Diff (P1-BL) | %chg (P1-BL) |
|------------------------------|---|-------|---------------|---------------|--------------|--------------|
| ON | 9 | Mean | 34.3 | 13.1 | -21.2 | -62.1% |
| | | SD | (3.2) | (8.6) | (8.2) | 22.4% |
| OFF | 7 | Mean | 32.7 | 30.1 | -2.6 | -8.3% |
| | | SD | (2.2) | (11.7) | (11.1) | 35.7% |
| P values^a: | | | 0.253 | 0.008 | 0.003 | 0.006 |

^a Two -sample t-test assuming unequal variances (2 tailed).

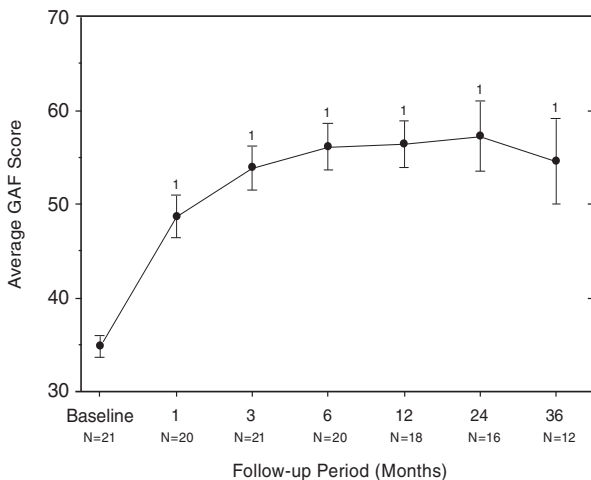
Table 11. Period 1 results - HAM-D

| STIM | N | HAM-D | Baseline (BL) | Period 1 (P1) | Diff (P1-BL) | %chg (P1-BL) |
|------------------------------|---|-------|---------------|---------------|--------------|--------------|
| ON | 9 | Mean | 24.2 | 10.1 | -14.1 | -59.4% |
| | | SD | (8.2) | (7.8) | (6.0) | 21.9% |
| OFF | 7 | Mean | 14.9 | 17.3 | 2.4 | 27.2% |
| | | SD | (5.8) | (5.3) | (6.0) | 54.2% |
| P values^a: | | | 0.019 | 0.047 | 0.000 | 0.005 |

^a Two -sample t-test assuming unequal variances (2 tailed).

Global assessment of function (GAF)

In conjunction with the YBOCS measures, 3 of the 4 centers also collected corresponding ratings of Global Assessment of Function (GAF), a measure of overall psychological, social, and occupational functioning. At baseline, the majority of patients (20/21) had GAF scores ranging between 20 and 40, indicating very severe disability. GAF scores improved over time for the vast majority of patients with the average score increasing from a baseline value of 34.8 (n=21) to 56.1 (n=20) at 6 months, 56.4 (n=18) at 12 months, and 59.0 (n=21) at last follow-up. An LOCF analysis at 12 months shows a similar level of improvement (mean=57.6) for all 21 patients. This improvement in GAF for the patient population is illustrated in Figure 2, which reflects a gradual and sustained increase in this measure of overall function, following deep brain stimulation.



¹ Within-subject change statistically significant ($p \leq .001$, 2-sided test).

Figure 2. Average GAF score following DBS treatment.

Table 12 shows the distribution of GAF scores at various time points for the 21 patients. At baseline, 20 of 21 patients exhibited scores of 40 or less, while at last follow-up only 2 patients remained at this relatively low functional level. At 12 months (LOCF) and last follow-up, 48% and 62%, respectively, of the patients scored 51 or greater at last follow-up; no patients were able to achieve this degree of function at baseline. There was a clear, progressive shift in the distribution of scores from baseline to levels of higher function over time following DBS treatment in this patient population.

Table 12. Distribution of GAF scores

| Functioning | Ratings | Number of patients / % of patients | | | | | Last Follow-up |
|--|---------|------------------------------------|-------------|------------|-------------------------------|------------|----------------|
| | | Baseline | 6 Months | 12 Months | 12 Months (LOCF) ^a | | |
| Inability to function - all areas (judgment, thinking, mood) | 21-30 | 7 33.3% | 0 0.0% | 0 0.0% | 0 0.0% | 0 0.0% | 0 0.0% |
| | 31-40 | 13 61.9% | 0 0.0% | 1 5.6% | 1 4.8% | 2 9.5% | |
| Major impairment in several areas (judgment, thinking, mood) | 41-50 | 1 4.8% | 10 50.0% | 9 50.0% | 10 47.6% | 6 28.6% | |
| | 51-60 | 0 0.0% | 3 15.0% | 1 5.6% | 1 4.8% | 4 19.0% | |
| Moderate difficulty (social, occupational, school) | 61-70 | 0 0.0% | 5 25.0% | 6 33.3% | 6 28.6% | 6 28.6% | |
| | 71-80 | 0 0.0% | 2 10.0% | 1 5.6% | 3 14.3% | 2 9.5% | |

Table 12. Distribution of GAF scores

| Functioning | Ratings | Number of patients / % of patients | | | | | Last Follow-up |
|------------------|---------|------------------------------------|----------|-----------|-------------------------------|----|----------------|
| | | Baseline | 6 Months | 12 Months | 12 Months (LOCF) ^a | | |
| Good functioning | 81-90 | 0 | 0 | 0 | 0 | 0 | 1 |
| | | 21 | 100.0% | 20 | 100.0% | 18 | 100.0% |
| | | | | | | | 21 |
| | | | | | | | 100.0% |

^a Last observation carried forward (LOCF) conducted for 12-month time point. Data for 3 patients (CC1, LV10, LV11) imputed using last measured GAF score prior to 12-month follow-up.

Treating physicians also provided an impression of the overall, global condition of these patients after deep brain stimulation, including psychological, social, functional, occupational, and quality of life considerations. Those impressions were reported on a modified Lickert scale on case report forms, similar to the standard Pippard Postoperative Rating Scale using the 5-point scale shown in Table 13. The results of those ratings were tabulated and are summarized in Table 13. Overall, the treating physicians reported that approximately two-thirds of the patients were much better following deep brain stimulation, compared to their pre-treatment condition.

Table 13. *Clinical global outcome ratings*

| Score | Rating | Number of patients | Percentage |
|---------------|-----------------|---------------------------|-------------------|
| 5 | Much better | 17 | 65.4% |
| 4 | Slightly better | 5 | 19.2% |
| 3 | No change | 4 | 15.4% |
| 2 | Slightly worse | 0 | 0.0% |
| 1 | Worse | 0 | 0.0% |
| Count: | | 26 | 100.0% |

Individualization of treatment

Best results are achieved when the patient and caregiver are fully informed about the therapy risks and benefits, surgical procedures, follow-up requirements, and self-care responsibilities. Patients who may benefit from DBS include individuals diagnosed with OCD who meet the following objective criteria:

- Have chronic treatment-resistant OCD
- Are suitable candidates for stereotactic surgery
- Have a diagnosis of OCD documented to be of five years or longer duration
- Have a YBOCS score of greater than or equal to 30
- Completed a minimum of three adequate trials of first- and/or second-line medications with augmentation
- Completed or have been unable to complete an adequate trial of Cognitive Behavior Therapy (CBT)
- Have no serious comorbid personality disorder or substance abuse issues
- Have comorbid depression and anxiety
- Meet established criteria for implantation of a DBS system
- Are 18 years of age or older

Use extreme care with lead implantation in patients with a heightened risk of intracranial hemorrhage. Physicians should consider underlying factors, such as previous neurological injury or prescribed medications (anticoagulants), that may predispose a patient to the risk of bleeding. Physicians should be aware that the risks associated with initial surgery may increase with clinical conditions such as:

- Stroke or neurological disorders
- Cardiovascular disease
- Renal or hepatic failure
- Diabetes mellitus

To help ensure maximum benefits from the neurostimulation system, long-term, post-surgical management of patients is recommended.

Stimulation parameters should be adjusted such that maximal symptom improvement is achieved with minimal side effects. High parameter values may indicate a system problem or less than optimal lead placement. Patients should be informed of the risks of higher stimulation parameters, which may result in possible excessive charge density. Refer to the *Information for Prescribers Addendum for OCD* for more information about excessive charge density.

Use in specific populations

The safety and probable benefit of this therapy has not been established for the following:

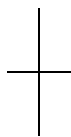
- Patients with Tourette's syndrome
- Patients with OCD with a primary subclassification of hoarding
- Patients whose diagnosis of OCD is documented to be less than 5 years duration
- Patients whose YBOCS is less than 30
- Patients who have not completed a minimum of 3 adequate trials of first and/or second line medications with augmentation
- Patients who have not attempted to complete an adequate trial of cognitive behavior therapy (CBT)
- Patients with previous surgical ablation (eg, capsulotomy)
- Patients who are pregnant
- Patients under the age of 18 years
- Patients with dementia
- Patients with coagulopathies or who are on anticoagulant therapy
- Patients without comorbid depression and anxiety
- Patients with neurological disorders
- Patients with other serious medical illness including cardiovascular disease, renal or hepatic failure, and diabetes mellitus

Use in patients with comorbid psychiatric disorders

Physicians should carefully consider the potential risks of implanting the brain stimulation system in patients with comorbid psychiatric disorders, including:

- bipolar disorder
- body dysmorphic disorder
- expanded personality impulse-control disorders or paraphilias
- psychotic disorder
- severe personality disorders
- substance abuse
- the inability to control suicidal impulses or a history of suicide attempts

The brain stimulation system may aggravate symptoms of comorbid psychiatric disorders.





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Medtronic, Inc.

710 Medtronic Parkway
Minneapolis, MN 55432-5604
USA

www.medtronic.com

Tel. 1-763-505-5000

Toll-free 1-800-328-0810

Fax 1-763-505-1000



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