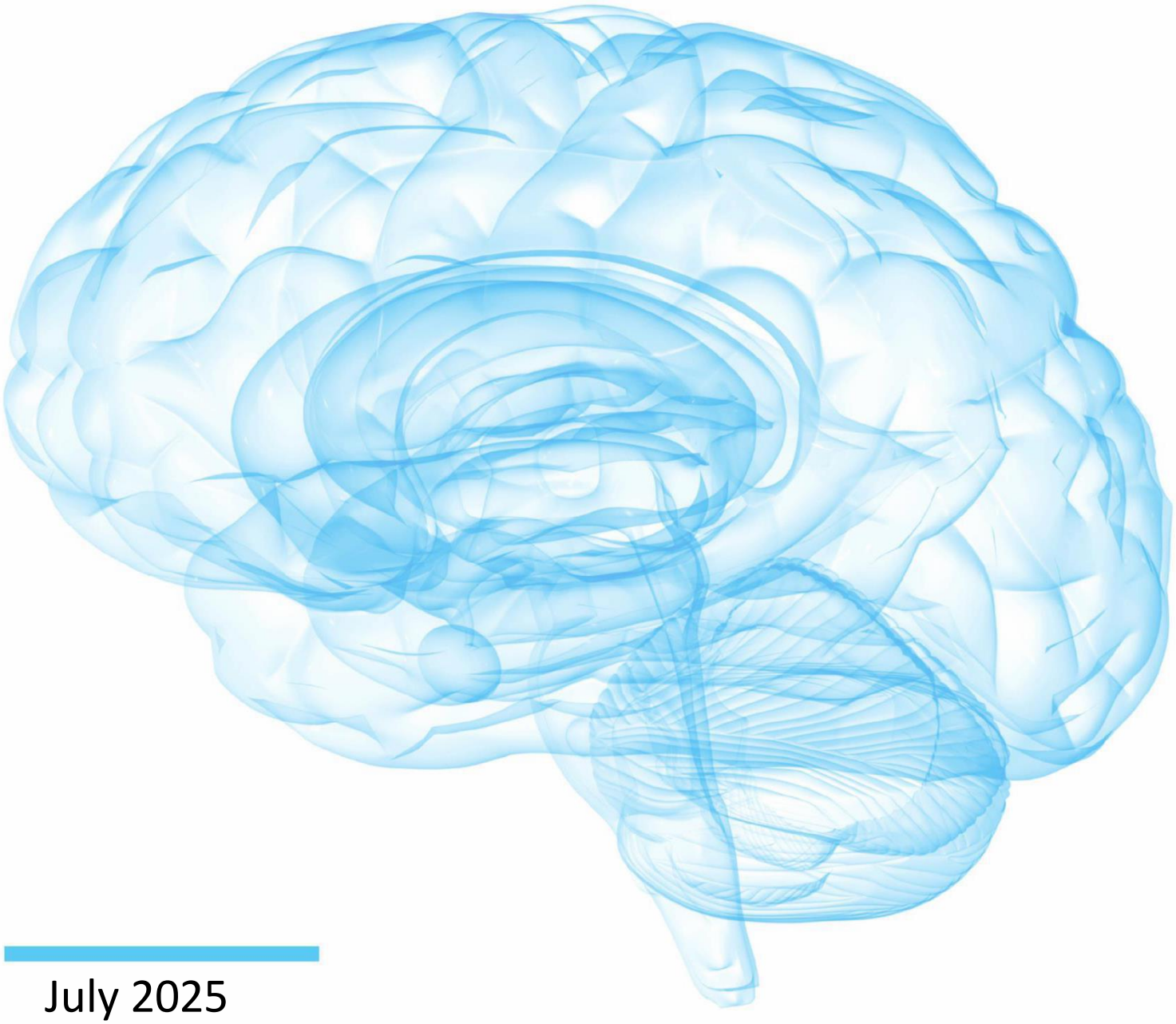

July 2025

A PATIENT'S GUIDE TO:

EXABLATE NEURO

MR GUIDED FOCUSED ULTRASOUND SURGERY FOR PARKINSON'S DISEASE

INSIGHTEC

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1. GLOSSARY

NAME	DESCRIPTION
CT or CAT Scan	Computed Tomography is an imaging technique that uses multiple cross sectional x-rays to create an internal image of a body structure
DBS	Deep Brain Stimulation is a method to control Parkinson's Disease via stimulation through wires from a generator similar to a pacemaker.
MRI	Magnetic Resonance Imaging is an imaging technique that uses strong magnetic forces to change how molecules spin so that they can be used to create an image.
MRgFUS	Magnetic Resonance guided Focused Ultrasound Surgery
Sham / placebo	Used in a clinical trial to show how effective a treatment is compared to no treatment
Randomized	Method used to assign subjects at random to a treatment arm of the study. Blinded randomization means that the individuals in the study do not know which study arm they are in until the end of the study
Pallidotomy	Type of brain surgery in which the globus pallidus (GPi), a small portion of the brain, is destroyed.
Sonication	A pulse of ultrasound energy delivered over a period of 10-20 seconds.
PD	Parkinson's Disease
GPi	Globus pallidus internus is the internal segment of globus pallidus, a key structure that regulates voluntary movement.
Thalamus	A structure in the brain's center that acts as a relay station for sensory and motor signals to and from cerebral cortex.
PTT	Is a bundle of nerve fibers that connect GPi to the specific nuclei of the thalamus. It also plays a key role in regulating voluntary movement.
Unilateral PTTractotomy	Type of brain surgery in which the pallidothalamic tract (PTT), a small portion of the tract is destroyed on one side.
Bilateral PTTractotomy	Type of brain surgery in which the pallidothalamic tract (PTT), a small portion of the tract is destroyed on both sides.

2. TREATMENT OPTIONS FOR PARKINSON'S DISEASE

PD is a disease where the symptoms include **TREMOR, MUSCLE RIGIDITY, SLOW MOVEMENTS OR FREEZING (BRADYKINESIA/AKINESIA), AND DYSKINESIAS (INVOLUNTARY MOVEMENTS)**. There are several ways doctors may treat Parkinson's Disease (PD) symptoms including medicine, brain surgery to implant a device in your brain to stimulate it (DBS), or brain surgery to destroy specific areas in the brain that cause PD symptoms including the thalamus, globus pallidum (GPi) and the Pallidothalamic Tract (PTT). While the thalamus and globus pallidum (GPi) have been used as traditional and effective targets for PD treatment, the PTT has been identified as an additional target for PD treatment.

If medication no longer works to treat PD symptoms, a doctor may suggest surgery. Neurosurgeons may use specialized equipment to precisely locate an area of the PTT. Prior to the operation, a neurosurgeon will use stereotactic technology (precise technology used to locate and map out specific areas in the brain) to identify the exact part of the brain that needs treatment by putting a metal frame on the patient's head with four pins to keep it still. The doctor will then take a detailed brain scan using computed tomography (CT scan) or magnetic resonance imaging (MRI) in order to identify the precise location for operation as well as a path through the brain to get to that specific spot. During the surgery the patient is awake, however, the area on the scalp where the surgical tools are inserted is numbed with an anesthetic. The surgeon makes a cut then inserts a hollow probe through a small hole drilled in the skull to the specific location. Different methods can be used to kill the brain cells, including circulating liquid nitrogen inside the probe destroying the targeted brain tissue, or by inserting an electrode heated up to near 200° Fahrenheit to burn (ablate) the cells.

Today, the most common approach to manage Parkinson's Disease when medications no longer help is deep brain stimulation (DBS). This form of treatment consists of staged surgeries to implant probes deep into the brain, tunnel the wires under the skin down the neck, and implant pulse generators below the skin near your collar bones. Additional surgeries may be required throughout the life of the generator(s) to replace batteries or malfunctioning parts. As with conventional pallidal brain surgery, DBS poses inherent risks.

Your doctor will discuss all your options in order for you both to decide which method is best for you.

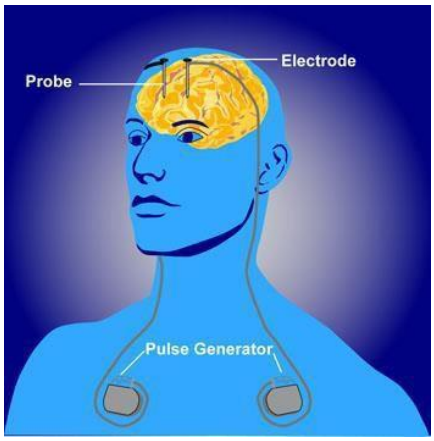

Figure 1. Illustration of a typical DBS set up.

3. WHAT IS AN EXABLATE NEURO TREATMENT AND HOW DOES IT WORK?

A new PTTractotomy technique is now available to neurosurgeons where sound waves can be focused through the skull to target the PTT without the need for incisions or holes (i.e. “non-invasive” or ‘incisionless”). Your doctor has prescribed the Exablate Neuro® procedure to treat your Parkinson’s Disease because you are a good candidate for this procedure. This is determined by evaluating whether or not medication can help control your motor symptoms and by measuring the shape and density of your skull using CT or CAT Scan. The information collected by the CT Scanner will be uploaded into the software of the Exablate Neuro device to aid it in focusing energy through the unique shape of your skull.

The Exablate Neuro® device uses sound energy that comes from an ultrasound source inside a helmet. The ultrasound waves are then focused on a specific point in the brain (e.g., the PTT) to create a tiny ablation or burn.

This focus is similar to how the sun’s rays can generate enough heat to ignite paper when focused under a magnifying glass. Just like the magnifying glass, if the magnifying glass is raised or lowered, the point of focus changes and the total effect of the energy is lost.

The Exablate Neuro system is used with a Magnetic Resonance imaging scanner (Figure 2) so that the doctor can use the images to know where to focus the device to. Only tissue at the target is heated to a level needed to kill the tissue.

The whole procedure is conducted inside the imaging scanner. During this procedure, the Exablate Neuro will use the MR imaging for planning your treatment, guiding the ultrasound energy, and determining how hot the point of focus and surrounding tissue gets.

Ultrasound is a form of sound energy that passes through skin, muscle, fat, and bone without the need for surgeries or incisions, electronic leads, or inserted probes. The ultrasound energy is non-ionizing, meaning you are not being exposed to radiation during the surgery. High intensity focused ultrasound energy, when focused on a small target volume, provides a therapeutic effect by raising the tissue temperature of the target high enough to destroy it.

Figure 2. Exablate Neuro

4. WHY DOCTORS USE EXABLATE NEURO

Your doctor has determined that Exablate bilateral PTTractotomy is the most appropriate method to treat your Parkinson's Disease symptoms. Exablate provides a non-invasive approach to performing this procedure. Based on the clinical study that served to gain FDA approval, the procedure may help your condition. Additionally, it may allow you to regain certain movements the motor complications and dyskinesias had previously impacted. It may also improve your quality of life.

Your doctor will be discussing the full risks and benefits of this procedure with you in greater detail when you discuss all your options.

5. AM I SUITABLE FOR THE EXABLATE PTTRACTOTOMY PROCEDURE? – CONTRAINDICATIONS

Exablate Neuro is not suitable for all patients. Patients who have any of the following should inform their doctor so she or he can suggest appropriate treatment options for you.

- If you have any kind of metallic implants, such as pacemakers, neurostimulator or DBS neurostimulator, spine or bone fixation devices, total joints, metal clips, screws, etc. you may not be a candidate. Any metallic implants must be non-magnetic to prevent injury to the patient from the MR's strong magnetic field.
- If you weigh more than the MR table allows, you are not a candidate for this procedure.
- If you are allergic to any MR contrast agents, you must let your doctor know so he can decide if you can be a candidate or not.
- If you are pregnant, you are not a candidate for this procedure while you are pregnant. It is not known what the effect of the procedure might be on the fetus.

- If you have advanced kidney disease or are on dialysis, you are not a candidate for this procedure.
- If you are not generally healthy enough to withstand the treatment and lie still in the same position for approximately 3 hours you may not be a suitable candidate for this treatment. Health related issues such as a recent myocardial infarction (heart attack), congestive heart failure (fluid around the heart), unstable angina pectoris (chest pain) or uncontrolled hypertension (high blood pressure) even when you take your blood pressure medications.
- If you have abnormal bleeding or clotting issues, or take medications (anticoagulants or blood thinners) that may affect these factors in your blood, then you may not be a candidate unless you can be off these medications long enough to clear your system prior to the treatment. Let you doctor know what medications you are taking.
- If you have any kind of substance abuse (alcohol or drugs), you are not a good candidate for this procedure.
- If you have extensive scarring on the scalp, you may not be a good candidate.
- If you have any brain tumors, aneurysms requiring treatment, cerebrovascular disease or other degenerative neurological conditions, you may not be a good candidate.
- If you are unwilling or unable to tolerate lying on your back for several hours, you may not be a good candidate.
- A CT of your skull will be taken to see if you have an adequate skull density ratio that will allow the acoustic energy to penetrate and focus appropriately inside you brain. If your skull density ratio is too low, then you will not be a good candidate because the target inside your brain will not receive the needed amount of energy.
- If you have psychiatric disease, severe depression, suicidal ideation, hallucinations, psychosis or delusions not controlled by medication, or other mental illness, you may not be a good candidate.
- Following an Exablate procedure on one side of your brain, if you experience significant difficulties in swallowing food or liquids, abnormal speech function, or an unusual walking pattern that are moderate to severe, you will not be a good candidate for the procedure on the other side of your brain.

Please discuss all these conditions with your physician so your doctor can properly evaluate your suitability for the Exablate therapy.

6. THINGS YOU MUST DO TO AVOID INJURY – WARNINGS

- Tell your physician of any medication allergies that you may have including and not limited to recent or past medications.
- Your physician will need to perform a full medical evaluation and full review of your medical chart to fully assess your overall condition. This is necessary to ensure a safe and effective Exablate Neuro treatment for your condition.
- Show your physician any scar on your head. Scar tissue is different from surrounding tissue and is more susceptible to heat damage and could cause pain if located in the beam pathway. Alternate beam paths may be available to avoid the scar tissue.

- You will be given a Stop Sonication button before initiating treatment. In the event of pain or patient motion, activate the stop sonication button so that you will not be harmed. If you are experiencing pain, tell your physician so he can alter the treatment, or alter the pathway to minimize the pain, slow the sonications down to allow for longer heat dissipation times, or provide medication to make you more comfortable. Failure to communicate this with your physician could result in serious injury. The Stop Sonication button is a safety feature built into the system for the patient.

7. THINGS YOU MUST DO TO AVOID OTHER HARM – PRECAUTIONS

- Tell your physician of all medications you take and of any risks or tendencies you may have for blood clots. Due to the period of immobilization required for the Exablate treatment, the risk of a blood clot forming can increase because you must lie still for so long during this treatment. If your risk for blood clots is high, your medical team may perform additional tests and prescribe additional medications during the procedure that may avert any potential problems. Compression stockings or other measures may be taken to minimize this risk which is no different than any other procedures with similar durations.
- Tell your physician of any medical conditions you have that could affect your ability to lie on the table for long periods of time. Medical conditions could include neck or back problems (herniated discs or pinched nerves), severe arthritis, claustrophobia, etc.
- After a head shave, a stereotactic frame will be attached to your skull by the neurosurgeon to prevent movement during the treatment, but it is still recommended that you remain still during each sonication. Cool water will be circulated around your skull to prevent any burning. You may also be given medication to increase your comfort during the treatment.
- You will be given a **Stop Sonication** button before the treatment starts which you will hold during the treatment. If you experience great pain or discomfort, push the button to stop the treatment and tell your physician why you stopped it. Your feedback will allow your physician to make adjustments and address your issue.

8. RISKS OF EXABLATE AND THE PROCEDURE

The following complications have been reported following Exablate Neuro MRgFUS treatments which are described below:

8.1. SHORT TERM RISKS – DAY OF TREATMENT UP TO 3-MONTHS POST- TREATMENT

The most common potential risks associated with the Exablate Neuro device and PTTractotomy procedure are listed below. These sensations are typically mild to moderate in intensity and can last as briefly as the length of the sonication or up to several days.

- transient numbness/ tingling

- poor muscle control that causes clumsy movements (ataxia),
- pain,
- dizziness, nausea, double vision (diplopia),
- difficulty maintaining upright posture (imbalance),
- rapid uncontrollable eye movements (nystagmus),
- slurred speech (dysarthria),
- warm sensation.

Headaches or head pain during sonication and imbalance or unsteady were other potential risks, but most often ended shortly after treatment.

Nausea/Vomiting were also reported in some instances. It is unclear if this is related to medications used during the treatment or the procedure itself.

You may experience bruising in the area of the intravenous (IV) catheter following the procedure similar to that experienced after blood draws. Any bruising should resolve on its own within a week.

You may experience some pain, bleeding or swelling around the pin site location from the stereotactic frame. These should resolve with a little bit of time (approximately 1 week).

8.2. LONG TERM RISKS – LONGER THAN 3-MONTHS POST-TREATMENT

Complications that have been reported following Exablate treatment include the following risks that may occur longer than 3 months after the procedure.

- numbness and tingling,
- speech or swallowing problems (dysarthria), or increased salivation/drooling,
- poor muscle control that causes clumsy movements (ataxia),
- inability to perform accurate, smooth movements (dysmetria)
- taste disorder (dysgeusia) or a reduced sense of taste (hypogeusia)
- an unusual walking pattern (gait disturbance),
- difficulty maintaining upright posture (imbalance),
- difficulty swallowing (dysphagia), ,
- fatigue
- decreased sensitivity to stimulation (hypoesthesia).

Additionally, if (unintended) brain tissue is damaged, there may be muscle weakness, numbness, or sensory loss that may resolve after several months, or it may be non-reversible.

If you experience a blood clot or deep vein thrombosis (DVT, blood clot in your leg) after the procedure that is not treated emergently, you may have long term complications related to it if it does not resolve quickly.

9. POTENTIAL BENEFITS OF EXABLATE AND THE PROCEDURE

During the study, using validated Parkinson's Disease rating scales, investigators reported improvement in motor function and reduction in dyskinesia.

In addition to possible improvements in reduced involuntary movements (dyskinesias), and improved gait function and muscle rigidity, the procedure is non-invasive (i.e., no surgical incisions or holes drilled through the skull), conducted with the patient fully awake, and may be performed on an out-patient basis.

It is possible that you do not gain any relief of your motor complications, nor improvement in your involuntary movements (dyskinesias due to meds). This procedure does not treat the underlying disease nor prevent the worsening or progression of the disease.

10. HOW TO DECIDE ABOUT THIS TREATMENT

You must explain all your medical conditions to your physician. Your physician will evaluate whether you are a good candidate for the Exablate Neuro treatment. Together, in consultation with your physician and caregivers, you will need to decide if you can tolerate the treatment and are a suitable candidate. Your physician will also discuss any other treatment options that are available to you.

11. WHAT TO EXPECT BEFORE THE TREATMENT

Your doctor will review your medications with you and tell you to skip doses of certain non-critical medications the day before and/or the day of your procedure. You will arrive to the institution at the pre-determined time "off" of your PD medications and you will be prepped for your procedure.

Once you have been evaluated to see if you are a suitable candidate as described above, and the surgeons have explained to you all the risks associated with the device and the procedure, you may be scheduled for a CT scan to determine if the shape and thickness of your skull are suitable for the Exablate Neuro device. Once confirmed and on the day of the procedure, your entire scalp will be shaved and cleaned. You will have a urinary catheter placed to drain your bladder during the procedure and you will likely wear some form of compression stockings during the procedure. Your physician may give you medication to minimize risks of DVT.

An intravenous (IV) catheter will be placed into your arm to administer fluids and medications. You will be given medications to make you comfortable. You will have the stereotactic frame attached to your head to prevent any movement of your skull during the treatment with the Exablate. A silicon diaphragm (dome shaped device) will be placed around your head to allow cool water to circulate minimizing potential heating near your scalp. Your heart rate, blood pressure and blood oxygen levels will be monitored throughout the procedure.

12. WHAT TO EXPECT DURING THE TREATMENT

You will be given a **Stop Sonication Button** to hold during the procedure. You will be moved inside the MR device (**Figure 2**If you get scared in small spaces (claustrophobic), tell a doctor or nurse so that you can receive medication to keep you calm. The procedure will be performed from a computer in the room adjoining the MR suite. A circulating nurse will be close to check on you and to administer medication.

A series of MR images will be taken for the purpose of planning the treatment. The physician will mark the area to be treated and low energy sonications can be used to cause physiological responses from your brain to ensure the doctor located the target spot in the brain.

After each time energy is applied during the procedure, a doctor (neurologist or neurosurgeon) will evaluate you to receive feedback regarding your sensations as well as determine the effect of the treatment on your body (i.e., muscle tone, finger tapping, leg lifting, etc.). You must remain still throughout the treatment session. Your procedure may last anywhere from 1 to 3 hours depending on the amount of energy that can be focused during each sonication. The time is dependent on many factors associated with the shape and thickness of your skull.

After at least 6 months from the time of the first procedure, if you qualify for the second treatment on the other side of your brain, the treatment will be repeated as mentioned above.

13. WHAT HAPPENS AFTER THE TREATMENT

You will be removed from the Exablate and MRI machine, and you will have the stereotactic frame removed. Once you have been determined to be stable, all the monitoring equipment and catheters will be removed. You will be moved to a recovery room for observation for few hours. Your physician will decide when to release you. She or he will also explain to you the post treatment care that you may need. It is important that you follow all directions from your doctor. Your physician may prescribe or ask you to take over the counter medications to help with pain or inflammation. Your physician will let you know when you can go home and when you will need to return for any follow-up visit.

14. WHEN TO CALL YOUR DOCTOR

If you experience severe pain, lightheadedness, discomfort, or fever of 100°F or higher within 48 hours of treatment, call your physician. You may receive a follow-up phone call the next day, or you may be scheduled for a post-treatment follow-up visit as routine standard of care whether you have any side effects or not.

15. CLINICAL STUDY RESULTS

The Exablate Neuro was studied in a clinical trial to show that the device is safe and effective to treat patients with motor complications of Parkinson's Disease. Patients first had the Exablate procedure on the side of the brain that was causing the most symptoms (Treatment 1). Then after 6 months or more, if the patients qualified and wished to continue, they had a second procedure on the other side of the brain (T2, bilateral PTTractotomy). The patients returned to the doctor to

assess their PD symptoms at 1 month, 3 months, 6 months, after the first and second procedures and again at 12 months after the second procedure.

A total of 54 subjects had the first procedure (T1), 40 of which went on to have the procedure on the other side of their brain (T2, bilateral).

The majority of complications (adverse events) that occurred in the study were related to speech or gait/balance disturbances. The majority were mild or moderate (94%) and 6.2% were severe or life-threatening. Of the events that were categorized as severe or life-threatening, all but one were unrelated to Exablate device and procedure. The most common adverse events that occurred in the study within 12 months are shown in Table 1.

Table 1: Common adverse events observed in the study for patients who received two treatments

Adverse Event	Incidence after 1st Treatment (% subjects)	Incidence after 2nd T. (% subjects)
Speech related (TOTAL)	**(2/40) 5%**	**(11/40) 28%**
Dysarthria	0	5 (13%)
Hypophonia	2 (5%)	4 (10%)
slurred speech	0	2 (5%)
Axial symptom related (TOTAL)	**(5/40) 13%**	**(10/40) 25%**
Gait disturbances	2 (5%)	2 (5%)
gait freezing	0	3 (8%)
unsteadiness	2 (5%)	1 (3%)
imbalance	1 (3%)	7 (18%)
Other (TOTAL)	**(1/40) 3%**	**(6/40) 15%**
Dysphagia	0	3 (8%)
increased salivation / drooling	1 (3%)	3 (8%)

To show effectiveness of the Exablate PTTractotomy, the study collected information using a validated scoring method with the *OFF medication upper and lower extremity motor score assessments from the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III*. This scoring method evaluates motor the effect of the procedure on reducing motor complications of PD for each side of the brain and the total brain (considering both sides).

At 3 months after the second procedure(T2), the median (middle value) percent improvement of the score was 32.7%. This percent improvement was significant and generally lasted through 12 months.

Patients saw more improvement after the first treatment (T1) compared to the second treatment (T2).
When considering both sides of the brain, the patients saw a median percent improvement of 35.8% after the first procedure (T1) compared to before the first procedure. The patients saw a median percent improvement of 10.4% improvement from the second procedure (T2) compared

to just before the second procedure.

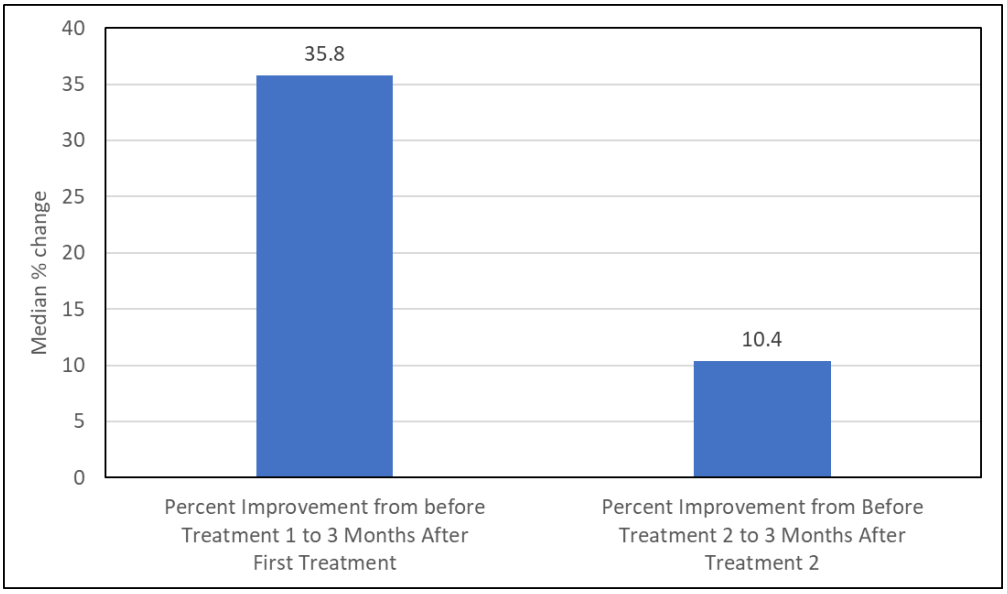

Figure 3: Median percent improvement after the first procedure (compared to before the first procedure) and median percent improvement after the second procedure (compared to just before the second procedure) This result considers improvement in both sides of the brain.

The study collected information from doctors on how much improvement they believed their patient gained from the Exablate procedure (Clinician Global Impression of Change, CGIC). At 3 months after the second procedure the CGIC showed that doctors believed that 97% of the patients that had the treatment on both sides of the brain had at least some improvement, with 70% of patients having been much or very much improved.

The study also collected self-reported information from patients on how much improvement they believed they gained from the Exablate procedure (Patient Global Impression of Change, PGIC). At 3 months after the second treatment the PGIC showed that 86% of the patients that had the treatment on both sides of the brain felt they had at least some improvement, with 43% rating themselves as having much or very much improved.

Table 2: Clinician and Patient Global Impressions of Change (percent of patients with improvement for each category)

Rating	CGIC – Percent of patients in each category	PGIC - Percent of patients in each category
1 = Very Much Improved	21.6 %	5.4 %
2 = Much Improved	48.6 %	37.8 %
3 = Minimally Improved	27.0 %	43.2 %
4 = No Change	0.0 %	2.7 %
5 = Minimally Worse	0.0 %	5.4 %
6 = Much Worse	0.0 %	5.4 %
7 = Very Much Worse	2.7 %	0 %

The study also asked the patients in the study about their satisfaction with the Exablate procedure when conducted on both sides of the brain. Patient responses at 3 months after the second treatment included **Figure 4.**

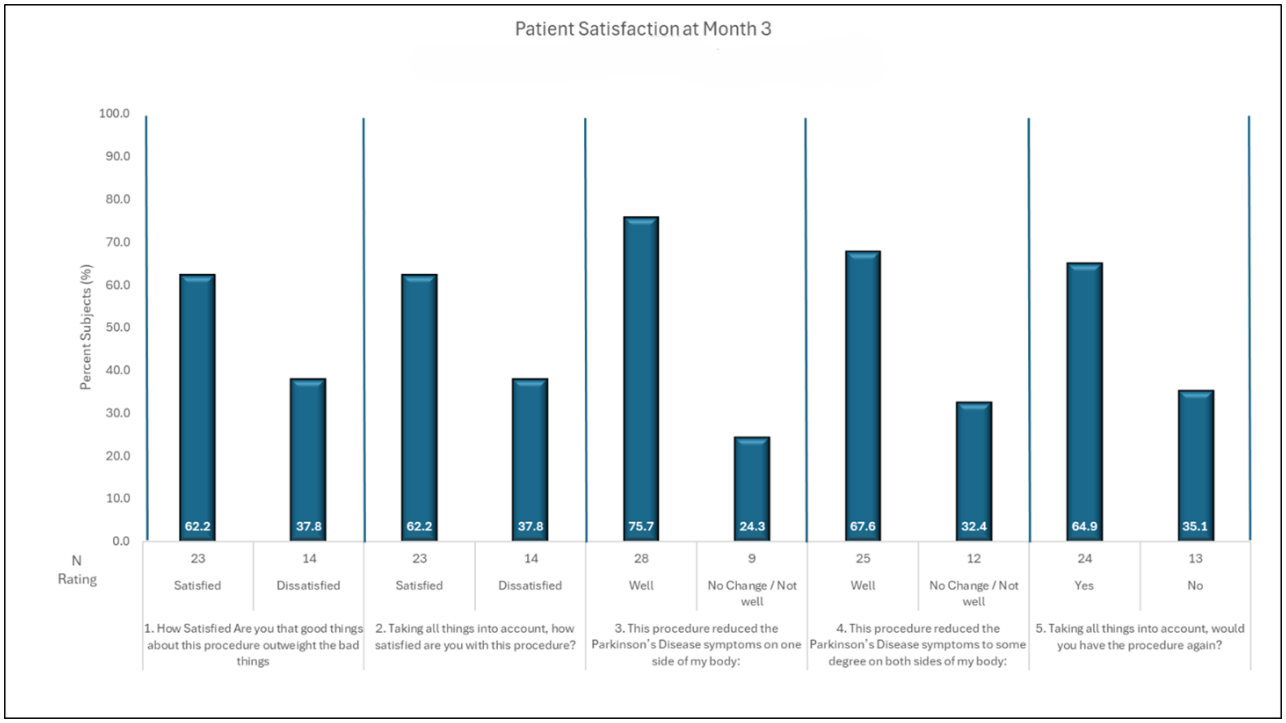

Figure 4. Patient satisfaction.

Conclusion

Exablate PTTractotomy has been demonstrated to be a safe and effective treatment for patients with advanced, idiopathic PD with medication-refractory moderate to severe motor complications as an adjunct to Parkinson's disease medication treatment. You should talk to your doctor to understand the expected risks and benefits of this treatment to understand how the results observed in the performed study may apply to you.

16. WHERE YOU CAN FIND OUT MORE

If you desire more information about this procedure, please visit the sponsor's website to learn more about the device " **www.INSIGHTEC.com**", or you may call our customer service toll-free line at **1-866-392-2528**.

You can also find out more information in the Summary of Safety and Effectiveness for the device on FDA's website.