Frequently asked questions: Deep Brain Stimulation for Parkinson's Disease at UCSF

Contents

When should one consider surgical therapy?

For patients with early Parkinson's disease, levodopa (sinemet) and other antiparkinsonian medications are usually effective for maintaining a good quality of life. As the disorder progresses, however, medications can produce disabling side effects. Many patients on long-term levodopa develop troublesome dyskinesias, excessive movements that often cause the limbs and body to writhe or jump. In addition, their dose

of levodopa no longer lasts as long as it once did. This may lead to "on-off fluctuations," a condition in which the ability to move changes unpredictably between a mobile ("on"), state when medication seem to work, and an immobile ("off") state in which little effect of medication is apparent and normal movement is very difficult. When patients no longer have an acceptable quality of life due to these shortcomings of medical therapy, surgical treatment should be considered.

What are the different types of surgery for Parkinson's disease?

There are several different types of surgery for Parkinson's disease. The first surgical procedures developed were the ablative, or brain lesioning, procedures. Examples of lesioning surgery include thalamotomy and pallidotomy. Lesioning surgery involves the precisely controlled destruction, using a heat probe, of a small region of brain tissue that is abnormally active. It produces a permanent effect on the brain. In general, it is not safe to perform lesioning on both sides of the brain.

We continue to perform some lesioning surgeries for patients who desire it, although in our practice lesioning has been largely replaced by deep brain stimulation (DBS). DBS surgery involves placing a thin metal electrode (about the diameter of a piece of spaghetti) into one of several possible brain targets and attaching it to a computerized pulse generator, which is implanted under the skin in the chest (much like a heart pacemaker). All parts of the stimulator system are internal; there are no wires coming out through the skin. To achieve maximal relief of symptoms, the stimulation can be adjusted during a routine office visit by a physician or nurse using a programming computer held next to the skin over the pulse generator. Unlike lesioning, DBS does not destroy brain tissue. Instead, it reversibly alters the abnormal function of the brain tissue in the region of the stimulating electrode. DBS is the procedure most often recommended in the UCSF Movement Disorders Surgery Program. Although deep brain stimulation is a major new advance, it is a relatively complicated therapy that may demand considerable time and patience before its effects are optimized.

Many patients inquire about the "restorative" therapies, a category of procedures which includes transplantation of fetal cells or stem cells, growth factor infusion, or gene therapy. These procedures attempt to correct the basic chemical defect of Parkinson's disease by increasing the production of dopamine in the brain. In the future, restorative therapies will hopefully emerge as effective and possibly curative interventions for Parkinson's disease. Growth factor therapy for Parkinson’s disease (using brain injection of modified viruses to deliver the growth factor) is an experimental therapy recently studied in several phase II clinical trial at UCSF and seven other centers. Thus far, none

of the trials of growth factor therapy have shown a major benefit.

What are the possible brain targets for DBS?

There are now four possible target sites in the brain that may be selected for placement of stimulating electrodes: the internal segment of the globus pallidus (GPi), the subthalamic nucleus (STN), the pedunculopontine nucleus (PPN), and a subdivision of the thalamus referred to as Vim (ventro-intermediate nucleus). These structures are small clusters of nerve cells that play critical roles in the control of movement. Thalamic (Vim) stimulation is primarily effective for tremor, not for the other symptoms of PD. Stimulation of the globus pallidus or subthalamic nucleus, in contrast, may benefit not only tremor but also other parkinsonian symptoms such as rigidity (muscle stiffness), bradykinesia (slow movement), and gait problems. All three of these targets are now approved by the U.S. Food and Drug Administration, which oversees medical devices. The PPN is a new, investigational target that may be appropriate for patients with gait freezing, but there are currently few clinical studies of this. For most patients with Parkinson's disease, DBS of the globus pallidus or subthalamic nucleus are the most appropriate choices because stimulation at these targets affects a broad range of symptoms.

How does DBS work?

The exact way that DBS improves movement in PD is not known but is under intensive study. About 25 years ago, it was discovered that in Parkinson's disease, loss of dopamine-producing cells leads to excessive and abnormally patterned brain cell electrical activity in both the GPi and the STN. "Pacing" of these nuclei with a constant, steady-frequency electrical pulse is thought to correct or override this abnormal activity. DBS does not act directly on dopamine producing cells and does not affect brain dopamine levels.

How is the surgery performed for awake microelectrode guided surgery?

There are several available surgical methods: awake microelectrode guided surgery, and interventional MRI guided surgery.

In the microelectrode guided method, implantation of the brain electrode is performed with the patient awake during the middle part of the surgery using only local anesthetic. Intravenous sedation is used to make the patient sleepy at the beginning and end of

surgery. The basic surgical method is called stereotaxis, a method useful for approaching deep brain targets though a small skull opening. For stereotactic surgery, a rigid frame is attached to the patient's head just before surgery, after the skin is anesthetized with local anesthetic. A brain imaging study (MRI or CT) is obtained with the frame in place. The images of the brain and frame are used to calculate the position of the desired brain target and guide instruments to that target with minimal trauma to the brain. After frame placement, MRI/CT, and calculation of the target coordinates on a computer, the patient is taken to the operating room. At that point an intravenous sedative is given, a Foley catheter is placed in the bladder, the stereotactic frame is rigidly fixed to the operating table, a patch of hair on top of the head is shaved, and the scalp is washed. After giving local anesthetic to the scalp to make it completely numb, an incision is made on top of the head behind the hairline and a small opening (1.5 centimeters, about the size of a nickel) is made in the skull. At this point, all intravenous sedatives are turned off so that the patient becomes fully awake.

To maximize the precision of the surgery, we employ a "brain mapping" procedure in which fine microelectrodes are used to record brain cell activity in the region of the intended target to confirm that it is correct, or to make very fine adjustments of 1 or 2 millimeters in the intended brain target if the initial target is not exactly correct. The brain mapping produces no sensation for the patients, but the patient must be calm, cooperative, and silent during the mapping or else the procedure must be stopped. The brain's electrical signals are played on an audio monitor so that the surgical team can hear the signals and assess their pattern. The electronic equipment is fairly noisy, and the members of the surgical team often discuss the signals being obtained so as to be sure to interpret them correctly. Since each person's brain is different, the time it takes for the mapping varies from about 30 minutes to up to 2 hours for each side of the brain. The neurological status of the patient (such as strength, vision, and improvement of motor function) is monitored frequently during the operation, by the surgeon or by the neurologist.

When the correct target site is confirmed with the microelectrode, the permanent DBS electrode is inserted and tested for about 20 minutes. The testing does not focus on relief of parkinsonian signs but rather on unwanted stimulation-induced side effects. This is because the beneficial effects of stimulation may take hours or days to develop, whereas any unwanted effects will be present immediately. For the testing, we deliberately turn the device up to a higher intensity than is normally used, in order to deliberately produce unwanted stimulation-induced side effects (such as tingling in the arm or leg, difficulty speaking, a pulling sensation in the tongue or face, or flashing lights). The sensations produced at high intensities of stimulation during this testing are experienced as strange but not painful. We thus confirm that the stimulation intensity needed to produce such

effects is higher than the intensity normally used during long-term function of the device.

Once the permanent DBS electrode is inserted and tested, intravenous sedation is resumed to make the patient sleepy, the electrode is anchored to the skull with a plastic cap, and the scalp is closed with sutures. The stereotactic headframe is removed. The patient then receives a general anesthetic to be completely asleep for the placement of the pulse generator in the chest and the tunneling of the connector wire between the brain electrode and the pulse generator unit. This part of the procedure takes about 40 minutes.

Why are patients awake for microelectrode guided DBS surgery?

Using the standard, microelectrode guided technique for DBS surgery, brain mapping is performed using microelectrodes. The brain mapping procedure is much harder to do if the patient is under a general anesthetic or a strong sedative. In addition, the procedure is safer if the patient's neurological function (speech and voluntary movement) can be checked periodically during the procedure, which is only possible in an awake patient.

For patients undergoing surgery using our interventional MRI method, general anesthesia is used for the whole procedure, as the MRI images take the place of electrical mapping and monitoring of neurological function.

How is surgery performed for interventional MRI guided surgery?

At UCSF, we have also developed an alternative method for DBS electrode placement, in which the surgery is performed entirely within a high resolution MRI scanner. The method is referred to as "interventional MRI" or iMRI. One advantage is that patients may be under general anesthesia for the entire implantation procedure, since no physiological testing is required. The iMRI protocol started in 2004 and has been used for 200 patients thus far. In 2010, we launched a new generation of hardware and software to improve the accuracy of the procedure, the "Clearpoint" system manufactured by MRI interventions, Inc. Currently, all children requiring DBS for a movement disorders are implanted under general anesthesia using iMRI and about 1/3 of our adult patients with PD choose to have their surgery using iMRI.

For iMRI guides surgery, patients are placed under full general anesthesia before any part of the procedure, in a room adjacent to our MRI. A standard stereotactic head frame is not used. Instead, skull mounted aiming devices are used after the incisions are made, and these are aimed at the selected brain target using frequent, real time MR imaging. MRI is also used to confirm appropriate electrode placement before the surgery is

complete.

What are the differences between the two types of surgical methods for DBS?

We believe that the risk and benefits of our two methods of DBS surgery (awake microelectrode guided surgery versus asleep interventional MRI-guided surgery) are the same in adults with PD. The method is selected by patient preference. Patients with major anxiety about the awake procedure, or patients who have severe pain in the off-medication state tend to choose iMRI guided surgery. The following table compares the two types of surgeries.

	Microelectrode guided surgery	iMRI guided surgery
Risks and benefits	Same for both methods	
Anesthesia for the brain lead implant	Sedation for beginning and end of DBS implant surgery, patient awake for middle part of surgery with local anesthetic in scalp	General anesthesia for whole procedure
Where is surgery performed	Regular operating room	Interventional MRI suite
Hair shave	1-2 inch wide strip	Larger, 3-4 inch patch
When can the pulse generator be inserted?	Can be done same day as the DBS implants, in the regular operating room	Performed 1-4 weeks after the DBS lead implantation, usually in our ambulatory surgery center as an outpatient surgery
Stopping anti-PD medications	Stopped the evening before surgery	OK to take anti-PD medications the morning of surgery with a small sip of water

What are the cosmetic considerations with DBS surgery?

Complete shaving of the head is not necessary for surgery. However, patches of hair on top of the head and behind the ear are shaved immediately before surgery when the patient is sedated. Many patients elect to get a short haircut after surgery (must be at least 2 weeks afterwards) so that the hair grows in evenly.

There are generally 3 incisions made on each side for DBS surgery: a 5-8 cm (2-3 inches) incision on top of the head, a 2.5 cm (1 inch) incision behind the ear, and a 6 cm (2.5 inches) incision in the chest just under the clavicle. For patients with receding hairlines, a slight scar from an incision will be visible on top of the head, but is not especially prominent. The cap used to anchor the DBS electrode (under the scalp) forms a slight bump, which again may be visible in the case of a receding hairline.

There is often puffiness around the eyes for a few days after surgery, but this goes away rapidly.

All parts of the device are internal (under the skin), so there are no wires sticking out. In a thin person, the connecting wire running down the neck may be visible as a slight bulge when the head is turned all the way to the opposite side. The incision for the pulse generator in the chest is closed with particular attention to minimize scar formation; this incision would be visible with the shirt off, or in a swimsuit, or in a low-cut evening gown. In thin persons, the pulse generator itself forms a bulge under the skin in the pectoral area that may be apparent if the area is uncovered, but is not visible through clothing.

Would both sides of the brain be done at once, or only one side?

DBS on one side of the brain mainly affects symptoms on the opposite side of the body. Most patients have symptoms on both sides of the body and thus require both sides of the brain to be implanted for maximal benefit. In the first several years of our DBS program, most implant surgeries were "staged," that is each side done in a separate surgery separated by several months. As this surgery has become more rapid and routine, we are now offering "simultaneous bilateral" procedures, or implantation of both leads in a single surgery, to many patients. The brain side opposite the most affected body side is implanted first. Then, if the patient and anesthesiologist agree to proceed, the second side is then implanted. Staging the procedures (performing the two lead implants about 3 months apart) is often done for patients >75 years old, or for patients with some cognitive (thinking or memory) dysfunction, or for any patients who might have increased risk from a longer operation.

What are the benefits of DBS surgery?

The major benefit of DBS surgery for PD is that it makes movement in the off-medication state more like the movement in the on-medication state. In addition, it

reduces levodopa-induced dyskinesias, either by a direct suppressive effect or indirectly by allowing some reduction in medication dose. Thus, the procedure is most beneficial for Parkinson's patients who cycle between states of immobility ("off" state) and states of better mobility ("on" state). DBS smoothes out these fluctuations so that there is better function during more of the day. Any symptom that can improve with levodopa (slowness, stiffness, tremor, gait disorder) can also improve with DBS. Symptoms that do not respond at all to levodopa usually do not improve significantly with DBS. Following DBS, there may be a reduction, but not elimination, of anti-Parkinsonian medications. At present, we believe that DBS only suppresses symptoms and does not alter the underlying progression of Parkinson's disease. Tremor is usually reduced a lot, but may not be totally eliminated, after DBS.

What are the risks of DBS surgery?

The most serious potential risk of the surgical procedures is bleeding in the brain, producing a stroke. This risk varies from patient to patient, depending on the overall medical condition, but the average risk is about 2%. If stroke occurs, it usually occurs during, or within a few hours of, surgery. The effects of stroke can range from mild weakness that recovers in a few weeks or months to severe, permanent weakness, intellectual impairment, or death. The second most serious risk is infection, which occurs in about 4% of patients. If an infection occurs, it is usually not life threatening, but it may require removal of the entire DBS system. In most cases, a new DBS system can be re-implanted when the infection is eradicated. Finally, hardware may break or erode through the skin with normal usage, requiring it to be replaced.

In the first few days after surgery, it is normal to have some temporary swelling of the brain tissue around the electrode. This may produce no symptoms, but it can produce mild disorientation, sleepiness, or personality change that lasts for up to 1-2 weeks.

What makes a patient a good candidate for DBS for Parkinson's disease?

In determining whether a patient is a good candidate for surgery, we look for the following:

Good intellectual function and memory. Dementia (significantly impaired memory or thinking) is a major contraindication to surgery, since such patients have great difficulty tolerating the surgery, may have further loss of intellectual function due to the surgery, deal poorly with the complexity of DBS therapy, and realize little overall functional benefit.

History of significant benefit from taking levodopa (Sinemet). Good mobility, with the ability to walk, in the best "on-medication" state is important for a good outcome. In general, surgery makes the "off" medication state more like the "on" state but rarely does better than the best "on" state, so a patient with poor function in best "on" (for example, unable to walk at any time) is a poor surgical candidate

Certainty of diagnosis. A number of neurological illnesses can mimic the symptoms of Parkinson's disease but do not respond significantly to levodopa. Such illnesses are often called "atypical parkinsonism" or "Parkinson's plus syndromes." These illnesses are different from classic Parkinson's disease, and they do not respond to DBS surgery. If there is a strong possibility that the patient has atypical parkinsonism rather than classic Parkinson's disease, surgery should not be performed.

Lack of other untreated or inadequately treated illnesses. Serious cardiac disease, uncontrolled hypertension, or any major other chronic systemic illness increases the risk and decreases the benefit of surgery.

Realistic expectations. People who expect a sudden miracle are disappointed with the results, and they may have difficulty with the complexity of the therapy.

Patient age. The benefits of DBS for PD decline with advancing age, and the risks go up. We rarely offer surgery to a person over 80 and would only consider it if they are in otherwise excellent health, are cognitively intact, and have good function in the “on” state.

MRI of the brain should be free of severe vascular disease, extensive atrophy, or signs of atypical parkinsonism.

Degree of disability. DBS is a poor procedure to rescue someone with end stage Parkinson's disease who is wheelchair bound or in a nursing home, although these may be the most desperate patients. It is an excellent procedure for Parkinson's patients who are still employed but may be just at the point where disability would stop them from working.

Where is the surgery performed?

For patients referred to the Movement Disorders Surgery Program at UCSF, surgery is performed at the UCSF Medical Center (Moffitt Hospital) at 505 Parnassus Avenue. This campus is about 1 mile from our outpatient clinic, located at 1635 Divisadero St. Our surgical team also performs DBS surgery for patients in the Veterans Health Care system, at the San Francisco Veterans Affairs Medical Center at 4150 Clement Street.

What are the results and complications of DBS at UCSF?

Since beginning our DBS program in 1998, we have performed over 15000 implants for movement disorders. Over 1000 of these have been STN or GPi implants for Parkinson's disease. A subset of our patients has had formal neurological evaluations on and off of medications, with the stimulators on and off. For bilateral DBS, the evaluations showed a 45-70% improvement in the scores on standard rating scales, off of medication, as a result of DBS. This is similar to the results from other major centers and represents a major improvement in mobility. In our series, the risk of stroke is 1.0%, the risk of severe stroke with death or permanent major disability is 0.5%, and the risk of device infection that requires further surgery for device removal is 3%.

What clinical trials are available at UCSF for Parkinson's disease, and what are the advantages of participating in them?

We have several research studies available to PD patients having DBS surgery:

1) Trial of a new DBS device with the capability for "fractional programming" (Boston Scientific "Intrepid" study)
2) Chronic brain recording using a novel pulse generator that senses brain activity as well as delivers stimulation therapy (Medtronic Activa PC+S)
3) Brain physiology during microelectrode guided DBS implantation
4) Clinical outcomes of iMRI guided DBS surgery
5) Noninvasive study of brain physiology in PD using scalp electroencephalography

If you meet entry criteria for any of these studies, we will provide further information. Patients in a clinical trial may have more detailed neurological follow up than if he/she were not in the study. The main benefit of participating in a study, however, is contributing to advances in the understanding and therapy of Parkinson's disease. No patient is required to participate in research.

What determines the choice of STN versus GPi as the target?

Four large randomized trials of STN versus GPi stimulation for PD have been completed in the past 5 years. Most data show that the two targets offer similar benefits for improving PD motor problems, but may differ in their possible side effects. At UCSF, we recommend a target based mainly on the patients' neuropsychological study (a set of tests for thinking and memory).

What tests are needed prior to surgery?

Patients should have a brain imaging study (MRI or CT) to determine if there are problems in the brain that would pose excessive risk for surgery, unless one has been done within 5 years. Patients will have a formal neurological exam in the off-medication condition, following by re-assessment after a test dose of medication, by one of our neurologists. Patients should have formal neuoropsychological testing, which is normally done by our own neuropsychologist. All patients must have a blood test (mainly for blood clotting ability) and visit or phone call with the anesthesiologists in the week prior to surgery.

How should the patient prepare for surgery?

For 10 days prior to surgery, patients must not take aspirin, any aspirin containing drugs, related drugs such as ibuprofen (Advil, Motrin) or naproxen (Naprosyn), or Vitamin E. These drugs can increase the risk of bleeding. The evening before surgery, patients should wash their head, neck, and chest with hibiclens (or other soap containing chlorhexidine) in the shower. Care must be taken to not get hibiclens in the eyes. The morning of surgery, if having standard microelectrode guided surgery, the patient should not take their antiparkinsonian medications. However, the patient should take any medications they normally take for other problems, such as high blood pressure, as instructed by the anesthesia clinic at the preoperative visit. For iMRI guided surgery, patients may take their morning medications.

Patients should inform the surgeon if they develop a cold, cough, or any type of infection in the days prior to the surgery. Patients should hydrate (drink a lot of non-alcoholic, non-caffeinated drinks) prior to surgery.

What type of follow-up is needed after surgery? Who will program the DBS unit?

Patients normally leave the hospital two days after surgery. We ask patients to return to our clinic 1 week later for suture removal and check of the incisions by our DBS nursing specialist, and approximately 4 weeks later to see the surgeon and neurologist in the Movement Disorders Surgery Clinic. The initial programming is done at UCSF usually at the one week or 4 week postoperative visit. Some patients have temporary disorientation or sleepiness for a few days after surgery due to temporary brain swelling, and if this occurs programming is deferred until the mental state completely returns to baseline. For subsequent programming needs after the initial stimulator activation, the patient is welcome to continue in our Movement Disorders Clinic. For patients who have neurologists outside of UCSF who are comfortable with programming, it is often most

convenient to return to their regular neurologist. We are happy to advise referring neurologists regarding programming strategies, and we have close working relationships with our major referring doctors around the Bay Area, West Coast and Hawaii.

In the first month following DBS implantation, some patients may develop an infection of the device or of the skin over the device. This would present as drainage, increasing redness, increasing swelling, or increasing pain starting a few days to a few weeks post-surgery. It is very important to let our office know IMMEDIATELY if such signs are noted, since early wound care may be effective at salvaging the device. If such symptoms are ignored for even a few days, however, the patient will usually have to have all of the hardware removed.

Patients will typically require replacement of the pulse generator after 3-4 years, depending on the exact settings of the device. This is an outpatient procedure that takes about 30 minutes. In 2009, a rechargeable pulse generator became available, described further below.

How long does it take before the full benefit of DBS is apparent?

For reasons that are not fully understood, the improvement in parkinsonian symptoms may take a few hour or days to reach its maximal level following a programming change. Some problems may respond more quickly than others. In addition, to realize the full benefit of DBS, medication changes and multiple programming sessions may be needed. Thus it is usually 4-6 months after surgery before the final degree of benefit is actually realized.

What types of pulse generators (implanted DBS control unit) are available?

As of 2013, we are implanting 3 types of pulse generators in PD patients, all made by Medtronic, Inc.: Activa SC, Activa PC, and Activa RC (devices from other manufacturers may be available within a formal research study). The choice of pulse generator for an individual patient is based on considerations of size of the device, desire for patient control over the stimulation level (see below), and need for recharging.

The Medtronic Activa RC is a re-chargeable pulse generator. It has the advantage of a very long interval (estimated at 9 years) prior to the need for surgical replacement. It has the disadvantage that the patient must charge it with a device strapped over the pulse generator, for a few minutes every day or for a few hours each week. At this time, we are

recommending the Activa RC only for patients with existing DBS systems who have used up their non-rechargeable system less than 2 years from implantation. Patients must have a teaching session preoperatively about the recharging requirements, to make sure they are willing to do this.

Can patients control the DBS device themselves?

Following surgery, the patient is given the Medtronic Access Review unit, a hand-held battery-operated unit that can be used to determine if the device is on or off, to turn it on or off, and to check battery life. Other aspects of stimulation, such as voltage level or frequency of stimulation, can also be controlled by the patient under limits programmed in by the physician.

Are there any restrictions on a person's activity after a DBS system is implanted?

For at least 4 days after surgery, the patient should refrain from flying in commercial aircraft. For one week after surgery, the incisions should be kept dry, so for showering in the first week incisions must be covered with an occlusive dressing. Tight clothing or tightly fitting hats should be avoided in the two weeks after surgery. After the incisions are completely healed (2-3 weeks), the patient may return to all normal activities, including exercise. Normal physical activities will not harm the device. Security devices (such as those in airports or stores) will not harm the device or the patient, although in rare cases they may activate the on-off switch, thus turning off a DBS system that had been on. The loss of benefit to the patient may take minutes or hours to be apparent. When traveling extensively away from home, patients should carry their Medtronic Access Review unit so that they can easily re-activate the DBS system if it is de-activated by a security device.

Can I have an MRI scan after DBS?

After DBS implantation, patients should avoid most types of MRI exams, as the exam may produce heating of the brain electrode. At UCSF, we have developed a specialized, low energy protocol for brain MRI, allowing us to perform postoperative brain MRI safely. However, we do not recommend any other forms of MRI (such as spine or chest MRI), because safe conditions for performing these have not been worked out.

Updated August 2013

Is DBS surgery covered by health insurance?

Medicare and almost all private insurers in California now cover DBS for Parkinson's disease. Insurance approval is sought prior to hospital admission.

Summary

There are more medical and surgical treatment options for patients with Parkinson's disease than ever before. Deep brain stimulation surgery offers important symptomatic relief in patients with moderate disability from Parkinson's disease who still retain some benefit from antiparkinsonian medications and who have good cognitive function. Patients who fluctuate between "on medication" and "off medication" states are usually good surgical candidates. The major risk is a 1% risk of stroke, due to bleeding in the brain. DBS is a relatively complex therapy requiring regular neurological follow-up and battery changes every 3-4 years. It reduces, but does not eliminate, symptoms of Parkinson's disease. The time to consider DBS surgery is when quality of life is no longer acceptable on optimal medical therapy as administered by a movement disorders neurologist.