DEEP BRAIN STIMULATION
VANDERBILT UNIVERSITY
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ANNOUNCER: Welcome to this OR-Live webcast presentation live from Vanderbilt Medical Center in Nashville, Tennessee. During the program, it's easy for you to make referrals, make appointments, or request more information. Just click on the buttons on your webcast screen and open the door to informed medical care. OR-Live: the vision of improving health.
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PETER E. KONRAD, MD, PhD: -- of our team here, the deep brain stimulation and surgery team at Vanderbilt University. We're first of all grateful to the simulation technology program at Vanderbilt to allow us to host this program in our simulated operating room environment. And today we want to talk to you about deep brain stimulation and surgery, implants, who's eligible for it, how's the surgery done, what's involved after the implant's received, and how you can learn more about this new, exciting procedure. First of all, let me introduce the rest of the panel here that's with us today. This is not all-inclusive of the team, but key members of the team are here. My name is Dr. Peter Konrad, I'm director of function neurosurgery at Vanderbilt. And starting at this end is Dr. Joseph Neimat --
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JOSEPH S. NEIMAT, MD: I'm Joseph Neimat, another functional surgeon here.
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PETER E. KONRAD, MD, PhD: And we have our two neurologists, one -- two members of six neurologists involved in the surgery here.
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THOMAS L. DAVIS, MD: I'm Tom Davis, director of movement disorders.
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FENNA T. PHIBBS, MD: And I'm Fenna Phibbs, one of the assistant professors in the movement disorders division.
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PETER E. KONRAD, MD, PhD: Several other members of the team that you don't see here today is Dr. Tramontana from the neuropsychology group here, as well as Dr. Chris Kao and Dr. Mike Remple, who are clinical neurophysiologists that are involved in the operating room. And also Ms. Cissy Voight from Star Physical Therapy, who does our assessments. Let's begin by initially setting the stage for what a deep brain stimulator is by looking at an actual deep brain stimulating electrode implant, and I'm going to ask the camera to focus in on this. This is actually an implant that is used to control symptoms for patients with Parkinson's disease, a central tremor, or dystonia, and this is the actual -- what the actual implant looks like. You can see, there's four contacts on here. And what's

absolutely remarkable about this implant is that we're able to treat a patient's symptoms by essentially delivering electrical stimulation through just one of these four contacts. Each of these contacts is only a millimeter and a half big, and one contact will essentially, if placed in the right location, be able to provide significant benefit for the patient. So to use this device, it's important, obviously, that we select the right patients. And maybe we can ask Dr. Davis briefly to go over reasons as to why choose deep brain stimulation over medical therapy.
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THOMAS L. DAVIS, MD: Well, deep brain stimulation is FDA-approved for the treatment of Parkinson's disease, drug-resistant essential tremor, and dystonia. Like any invasive procedure, it's reserved for patients who do not respond to medication adequately and is for patients who want enhanced symptoms response. For patients with essential tremor, roughly 5-10% are resistant to medication, they would be considered candidates. People with Parkinson's disease who have an initial good response to their medicines but then later develop motor fluctuation would be considered potential candidates. And then finally, patients with dystonia who don't respond to medications or injections of botulinum toxin again would be potential candidates.
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PETER E. KONRAD, MD, PhD: Okay, very good. That's a brief outline, and we'll go into this more towards the middle of the program and the end of the program. What -- maybe perhaps another key question I wanted to bring up front here, we'll get Dr. Neimat to comment on, is you see -- we mentioned all the members of the team here. Why is it important to have so many people involved in deep brain stimulation surgery? Why can't the surgery be done just at any local hospital?
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JOSEPH S. NEIMAT, MD: Sure. I think deep brain stimulation surgery is a tremendously precise procedure that involves a number of checks and double-checks. It involves imaging that we'll show you, we'll get an MRI and a CT on each patient. It involves intraoperative physiology, where we're using microelectrodes to listen to individual cells. And then it involves stimulation in the O.R. and a neurologic assessment performed by the neurologists where we sort of check and double-check to see that the areas that we've recorded are the best areas to stimulate. So each of those is an important facet, and the whole team together gives us a much more precise and effective surgery.
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PETER E. KONRAD, MD, PhD: Absolutely true. And then also perhaps I can ask Dr. Phibbs, basically we go through all this process involving very precise placement of the brain stimulating electrodes, and a lot of patients wonder, well, what happens after the implant's in? And I know you're going to be talking about this a little bit later, but after the implant's in, that's really just the beginning of the use of the device, right?
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FENNA T. PHIBBS, MD: It is. What happens after surgery is the patients come to clinic and we evaluate their response to the stimulation and also adjust the medications to really optimize their treatment. And it usually takes several visits -- you know, three to six months or so -- before we get people really optimized with their treatment.
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PETER E. KONRAD, MD, PhD: Okay, great. So that sets the stage of essentially the steps involved in putting a deep brain stimulator in and then using it. To go back in time a little bit, if somebody were to look up deep brain stimulation implants on the internet presently and today, many people would find that to be able to put this electrode in a very precise location, the type of equipment that's routinely used at many medical centers is a stereotactic frame. And this is a subspecialty training required by many people to do this surgery in neurosurgery, and it involves understanding how to use one of these devices. And basically, what you're seeing in front of us here is a standard stereotactic frame. It's a CRW frame. And up until about four or five years ago, this was the frame we used to place deep brain stimulating electrodes. And it's probably still used in a majority of centers around the world today. The frame's very rigid, it's literally bolted to the head, and the reason for that is because we're trying to hit a very precise target and to be able to manipulate a device like this, we have to be able to move it in millimeter or less distances to accurately get that electrode placed precisely within the brain at the exact location. The targets that we're trying to hit are on the order of about four to six millimeters, which is a little bigger than a green pea, and it requires that amount of accuracy. About four years ago, we changed this method because a lot of our patients found it very uncomfortable to wear this frame all day for a procedure, and we went with a newer process using computerized rapid prototyping technology, and we've gone to a custom-made frame that's made individually for every patient. And you're seeing, I'm holding it up next to the frame here, and this little frame now, which is manufactured for each patient individually and it contains the coordinates that we planned for the surgery, is now manufactured for us by a company in Maine. And we use this instead of the big frame these days. We've found this has been much more comfortable for patients to wear during the surgery, and it contains as much accuracy or even better than the standard frames in studies that we've performed. In addition in the program today also, we want to highlight some newer technologies that we've been able to utilize from a grant from the National Institutes of Health with Dr. Dewant from the college of engineering, developing computerized atlas-based techniques and how can we target more accurately. And the whole goal of the surgery, I think Dr. Neimat will agree, is to put the electrode ideally in the right spot the first time. And why can't we do that initially right off the bat, Dr. Neimat, based on our targeting, on the scans?

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JOSEPH S. NEIMAT, MD: Yeah, when we talk about getting this in the right spot, what we're really talking about is not just the STN nucleus, the nucleus that we're aiming at, but really getting it into a submillimetric area of that nucleus. And so the scans that we have, which give us a certain measure, don't give us the amount of precision that we need, so we have to sort of approximate it with the scan, approximate it even closer with microelectric recordings, and then finally see what the stimulation does in that spot and adjust based on that to get really the best effect.

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PETER E. KONRAD, MD, PhD: Exactly right. So comparing the traditional way that stereotaxy is done with this type of frame, this is usually placed the day of surgery by taking the patient to the x-ray department, where either an MRI or CAT scan or perhaps both is obtained with this frame mounted on the head using local anesthesia. And one other important facet to the surgery that you'll learn about is that patients really do need to help us get that implant in the right spot, and the only way to do that today anywhere is really keep the patient awake and comfortable during the procedure and ask them specific questions so that we know we're placing it with that amount of precision. This frame is mounted in the x-ray department. Usually then the patient is brought to the CAT scan or MRI image with this frame in place with some markers on it, and then the images are then used that day to plan out the trajectory, that's fed through a program which then gives us the coordinates to use this frame and dial in the exact location for the target, much like you would look up a star in the sky based on an atlas of some sort or find a location using a map of some sort, we use the computer and atlases of the brain to actually help us dial in the exact precise location we want to go to. This is all done usually in one day with one of these frame systems. And we've found that we spent a lot of time in the morning initially putting the frame on, acquiring the images, doing the plan, and weren't really able to get ready for the actual surgery where we mapped it and put the implant in till late in the morning at best and the surgery was then fairly long throughout the day. What we'd like to go through now is actually the method of using this type of system, which is the STarFix system as our method of performing deep brain stimulation surgery at Vanderbilt University, which is again unique to most centers in the world. And we were the first center actually to use this system about four years ago and have implanted over 250 patients using this system without any problems in the last four years, so we're quite pleased with this and especially the flexibility it gives us. And what it's allowed us to do is break the surgery up. Instead of an all-day procedure where we use one of these devices, to break it up into three different parts. And we'll go through those parts here now to show you exactly what's involved in the way we do deep brain stimulation surgery at Vanderbilt. So if we can have the first section of the video run here, it shows the first step, called Stage One, which are these little bone markers. These little anchors that you're seeing on the screen are actually used to loo-- to apply the platform the following week. And this patient that you're seeing here has been put under anesthesia in the x-ray department, in the CAT scan room. Dr. Neimat here is placing four of these little small markers -- you saw they were about maybe four millimeters big. They're actually literally screwed into the skull through a small puncture site in the scalp with some anesthetic there. And these little markers are left implanted for about a week or two under the scalp with a small staple left in the scalp. These are the attachment points for the platform that we are going to have custom-made for the patient. So they are temporary anchors used to mate with the platform. Once the markers are placed, the patient, while still asleep, is scanned with the CAT scan and an MRI scan, and we feel this is very important to obtain images of the patient without motion. This allows us the most accurate imaging we feel when the patient's asleep. It allows us to target more accurately without having any movement on the images. And then we'll explain to you a little bit later how we use those images and manufacture a platform. Okay, so that was a video section or video segment of the markers and how they got put in. The patient essentially goes home after this. This is an outpatient procedure usually performed about a week before the actual intended surgery for the implant. And again, the patient just has four little markers in their scalp with a staple over each area. There's not much to really maintain with this. And then we take those images and we use that to plan the targeting. And maybe Dr. Neimat, you could lead us through how we take those pictures and get one of these made.

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JOSEPH S. NEIMAT, MD: So during that week between the time that you have the screws implanted and the time that we actually do the implantation, what we do is we take these images -- and I'm going to show you on a computer here -- this is the actual planner that we use. And this has been made here for us at Vanderbilt. If you can see that on the screen. So what I'm showing you is that those scans that have been obtained, the CT and the MRI scan, are fused together. And we're looking at both here mapped on top of each other. And we're going to use that first to identify where those anchors are. That gives us sort of our reference point. And the computer will automatically find that. And we just simply verify it. You'll recognize the shape from the video that you just saw, that sort of hexagonal screw. And we can see that the computer has found all four of them. And that's going to serve as the anchor for our platform. And then what's left for us to do is to decide, okay, what do we think is the STN, what's the target that we're going to aim for? And we can do that a number of ways. We can do it using standard coordinates from a Shelton-brand atlas, from a map that's used typically in neurosurgery. And then we can also look at that scan and we can kind of fine-tune it, so we can adjust and -- and see what -- if that doesn't seem quite right to us, we'll just move it a little bit here and there. when we're happy with it -- we can go ahead and add the trajectory. And we also, a very important part of this process is picking an entry point. And what I like about the fact that we've separated out the planning from the day of surgery is that I have all the time in the world to sit and really plan what I think is the safest way to do this, going past blood vessels, avoiding targets that are -- areas that are maybe more dangerous, and really getting right to the target. So I might select this as an entry here. This computer won't let me. And it doesn't want to show it to me today.
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PETER E. KONRAD, MD, PhD: Also I think one of the other important features, too, that planner -- that we have been able to utilize has also shown us the ability to assimilate the data from successful implants prior to this surgery, so we take the last 100 patients, for instance, in which we've had successful implants, and that data is collated into one master atlas contained on the computers within the engineering department, all funded by this research grant from the National Institutes of Health, and we use that data for more accurate targeting. And again, the more accurate we're able to pick our first target at, the less we have to customize that for a given patient. The computer atlas actually is able to adjust for the dimensions of an individual brain and size and scale that in a way that's much more thorough than we used to do as a surgeon planning it with his own view of the brain on the MRI study. So this has been a huge addition and a help for us that's again a very unique aspect to the type of surgery we do. We actually build on the success stories of previous patients and make that process more and more accurate all the time. And again, if we had the ability to see the target as a little red dot on the MRI scan, this wouldn't be a very hard surgery to do. It's just a matter of how accurate you could get it there, but today, even with the best images, we can see outlines of perhaps some of the targets we want to hit, but some of the targets are just not visible on the MRI. And until that happens, we really have to make our best estimate coming into the surgery and then we rely on the patient to actually help us tune that implant into their own customized best-functioning implant. So that kind of discusses how we take the pictures and the images and the markers and basically assemble an instruction so that the company then

can manufacture one of these. And as you can see, this particular platform has four legs on it, and it would mate with four little markers on the scalp for this particular patient. And it has two apertures here in which these would hold microdrives, and in particular, one of the advantages of this type of system over the other stereotactic frame system is we can actually be more efficient. We can do both sides of the brain in terms of recording or testing in one sitting. And many of the diseases we treat actually are bilateral, meaning the patient has symptoms on both sides of the body. And that allows us then to work much more efficiently during the procedure by being able to do recording simultaneously on each side. We send off the instructions, we typically order a bilateral platform, or a two-hole platform like this for a Parkinson's patient, for instance. And then this platform takes about three days to make and ship and test and make sure that it's accurate to the specs that we need. And then it arrives here at Vanderbilt in time for the surgery. And the actual surgery then starts off with all of our coordinates built into the frame, and it custom fits for the patient and we're able to start the surgery now at 7:30 in the morning rather than 10 or 11 later in the morning like we used to with the other frame. So let's go into the next video here, which actually shows a surgery in which one of these platforms has been built for us and is used in a surgery. This patient has Parkinson's disease, and you can see the little white platform. In this case, the platform is shaped more like a cross rather than in a square pattern. The item that's being assembled there is a microdrive. That's what these two apertures hold, one microdrive in each side. And essentially, the first thing that we do is we take the platform, and you can see the patient sort of vaguely behind the drapes there, but the patient's awake during this procedure. We're able to actually perform the surgery on a patient awake mainly because of the fact that the place where people feel pain is on the scalp only. They don't feel pain in the brain. And if we give enough novocaine or lidocaine as we use it and marcaine in the scalp, we can numb up the scalp. And essentially the rest of the surgery is painless for the patient. Once we've done the initial injection and numbed up the scalp and made sure the patient's comfortable and we will not proceed unless the patient tells us they're comfortable with that. Then the first thing we do is we find those little markers we put in, and we initially mount the platform to see where those apertures sit over the skull and allow us to identify where we want to make our two entry points into the skull. So what you're seeing on the video here is initially mounting the platform and attaching it to the little markers that have been implanted a week previously.
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JOSEPH S. NEIMAT, MD: Let me just add the fact that we're putting the frame on now at this point, all of the trajectories have been dialed in, this is much faster. We're usually about at this stage in the operation at 8:00 in the morning, very early, whereas previously the first couple hours that morning were spent going down to radiology, having the larger frame placed on the head, and waiting, all that time with the patient off medication and often uncomfortable during that. So this is a much better way, I think, to start the operation and get a move on quickly while the patient is still comfortable and alert.
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PETER E. KONRAD, MD, PhD: Correct. It's really probably saved at least, I would say, two to three hours of time in the morning, and we can certainly use that much better by doing the planning and everything else the week prior to this, just starting in with the surgery first thing in the morning. So here the platform's been initially mounted and

there's been no incisions in the scalp yet but we've marked on the scalp exactly where we want to make the entry points. Then we take the platform off again just as simple as that. It's screwed to the markers, the markers sit in the skull, and it allows us to apply and remove and reapply the platform without any loss of accuracy. We're now outlining the incision. If a person is to receive two implants, they'll get two incisions on their head typically, one on each side for each electrode system. And again, this would be because a patient has symptoms on both sides of their body. For instance, if both arms had tremor or both sides were rigid, we would put an electrode in for each side. You can see the patient laying there. He's quite comfortable during the case and is able to talk to the anesthesiologist, and the anesthesiologist is there more to monitor and make sure the patient is comfortable and the blood pressure and oxygenation is correct and that the patient's needs are addressed throughout the case.

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JOSEPH S. NEIMAT, MD: You'll see as they pan around the room that it's a fairly large team. So it's not just the surgeons in the operating room. There's the surgeon, surgical assistants, there's the anesthesia team that's paying close attention to see how the patient is doing and if they're comfortable. There's a team of physiologists that are going to be looking, once the electrodes are in, to analyze the signals from the cells and give us an idea of where exactly we are inside the brain, inside the STN when we reach that nucleus. And then the neurologist is there at the end once we are stimulating to show us exactly what the best spot is based on that stimulation. So it really is a team effort, and we think that makes for a much better result at the end of this.

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PETER E. KONRAD, MD, PhD: Everybody certainly has their role during the case and knows it well. So at this point you can see two incisions have been made in the scalp. Briefly, you saw the drill used there. We make two small holes through the skull that are about the size of a dime each, and again, this is not painful to the patient because the scalp and skull has been numbed with the novocaine or the lidocaine medications. Once the holes are made, we make a small nick in the lining of the dura and then the -- this is the passageway through which the electrodes are passed. The first part of the procedure involves mounting the platform and passing test electrodes, so we make these small punctures here for the test electrodes to pass, and then once the test electrodes are passed and we gather the information we need to understand the anatomy in a very small scale in the brain, then the final electrode is just dropped through a tube where those microelectrodes are at. What you're seeing here is the mounting of a locking ring. And the locking ring is what will hold the final implant securely to the skull without allowing it to move. Obviously if we go through quite an effort to locate an implant to within a millimeter or two, we don't want it to move later on. And so this little locking ring is a -- a mechanism by which it clamps on the electrode once it's in place. It's literally a circular piece of plastic initially screwed to the skull, and you're seeing us just attaching it to the skull around the hole that was made. And then the electrodes are passed through that ring and at the end of the procedure, when we have the final implant passed down, we basically put a little clamp in that locking ring and it holds it tightly to the skull. It's a very nice little device that assures us that the electrode, once positioned, doesn't move. Obviously, we have to put this circular ring on before we pass the electrodes through the skull, so that's why we do this at the beginning of the procedure. And again, the patient

here is awake, able to tell us whether they're uncomfortable or not. They're really not perceiving any pain here. They will perceive -- the patient will describe either pushing or tugging during the case, but again, there's not any pain associated with this. And I know Dr. Neimat and myself go through quite a bit of questions with the patient throughout the case to make sure they are indeed comfortable through the procedure, and that's what you're seeing here. The patient's quite happy. The other thing maybe Dr. Neimat could comment on here is the luxury of not having a large frame in the way of working here, the movement that we get with this particular system.
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JOSEPH S. NEIMAT, MD: Sure. I think both for the patient and for the surgeon, it's nice to have the smaller frame. With the older frames, you used to have to hold it to the table with a special sort of a clamp apparatus, and so the patients couldn't move at all. So I think for the patients, given that even with the shorter operation, it's still several hours sitting in the same place, it's nice to be able to turn your head a little bit and move and make yourself a bit more comfortable. We go through some adjustments periodically to make sure the patients are comfortable. Also for the surgeon, I think it's a bit easier to work around the smaller frame. And I think that the shorter distance of the frame also increases its accuracy and lets us do both sides at the same time, which shortens the time of the surgery and usually patients complain about the length of the surgery more than anything, and this has helped us shorten that time.
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THOMAS L. DAVIS, MD: And for patients who had involuntary movements of their head or trunk, you know, like the dystonia patients, it was impossible to do those awake with the traditional frame.
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PETER E. KONRAD, MD, PhD: Absolutely correct. Once that big frame goes on and it's locked to the bed, if the patient has a lot of uncontrolled movements, they're basically struggling within the frame, and that just makes it difficult for the patient as well as the surgical team. Here's the microdrive, which is being calibrated. And it's about ready to be mounted on this little platform. And these are the drive units that we use to drive the small microelectrodes, which you'll see in a minute, into the region of the brain where we want to listen, first of all, to the nerve cells that are firing abnormally in the area of interest. One other final comment regarding mobility with the frame was I know that if a person has a chance to talk to someone who's had this surgery with the large platform on, one of the biggest comments we heard when we were using it and others have commented that have been through it is that it was probably the most uncomfortable part of the whole surgery was wearing the large frame. And I don't think we've ever had a patient complain of wearing this platform during any of our surgeries. Is that correct, Dr. Neimat?
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JOSEPH S. NEIMAT, MD: That's true. And we've had a few patients who, for whatever reason, had had a surgery done previously elsewhere with the larger frame and then had a second surgery with this frame on, and I think universally, they preferred this just for the comfort and ease of having the procedure.
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PETER E. KONRAD, MD, PhD: Okay. So here you see not one but two microdrives placed, and again, the reason we do this is so it allows us more efficient use of our time. We can actually map and record from both sides of the brain at once. And the reason we'd be interested in doing that is because most of the problems we treat affect a person differently on one side versus the other. And in fact, in Parkinson's disease, typically we'll see patients with much worse symptoms on one side than the other side, and we will need to understand a little bit what makes the one side different versus the other, and it allows us also to ask research questions regarding why -- why is it different in a Parkinson's patient and perhaps not so different in an essential tremor patient. The use of a bilateral platform like this, or one that we can record from both sides simultaneously, gives us the unique advantage of being able to get that phase of the surgery done in half the time as opposed to the use of a standard frame, where you can make only one pass at a given time. And the second thing is it allows us to answer perhaps some key questions of how Parkinson's disease progresses over time and affects one side of the brain more than the other.
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JOSEPH S. NEIMAT, MD: The other thing I would point out here is that we're using not just a single electrode trajectory but an electrode array, which can be four or five electrodes on each side. And what that does, we feel, is that it gives us a comparative measurement, so we're not looking at just one snapshot, one little window into the nucleus that we're aiming at. We're actually seeing a span of it and we're able to compare across that nucleus where are we getting the best signals, where are we getting the best stimulation. And in the end, that'll let us pick really an optimal target as opposed to just an adequate target.
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PETER E. KONRAD, MD, PhD: Okay. Here you're seeing one microelectrode contained within its little tube, and this is one of those four or five electrodes Dr. Neimat was just talking about. And if we extend the electrode out, you'll see the tip of it. That tip of that microelectrode is sharpened to about 40 microns, which is actually about five or six red blood cells thickness, and the whole dimension of the tube is under about a half a millimeter. So it's a very small electrode. We use this initially to listen for the abnormal firing patterns associated with the area we want to find. And again, this is one of the first key steps we use in targeting accurately to an incredibly precise dimension our target, our final target. The actual implant is probably four times fatter than this test electrode, and when we put that implant in, we would like to put that in once and know that it's in the correct place rather than multiple times. So this is one reason when people read about deep brain stimulation surgery, they read about microelectrode recording, or MER, and that's what this is. And we like to do several measurements while we're there so that it helps us to detect that area with much more precision. You can see the microelectrodes now being connected up to the wires, and we're going to actually listen to multiple points at once. And this is done through our neurophysiologist. And perhaps we can stop this video at this point and ask Dr. Neimat to show us a little bit or talk a little bit about what's involved in microelectrode recording and what are those -- what do those abnormal cells sound like to us in the operating room?
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JOSEPH S. NEIMAT, MD: Sure. So I'm going to go ahead and show you some samples we have from the operating room. Again, in the operating room we rely on a team of physiologists -- Chris Kao and Mike Remple -- who do this work for us, and they are experts at looking at the cells from neurons specifically and measuring which cells tell us where we are in different parts of the brain. So if we can go to the computer again, I'm going to show you, here on the left side, we have a map from a Shelton-brand atlas, and this dotted line here is showing us the trajectory, the direction that we're coming through the brain from the skull. And what we're going to go through is first the thalamus, then an area of -- without a lot of cells beneath the thalamus, followed by the subthalamic nucleus, the STN, which is our target, the area that we want to eventually stimulate. And I'm going to show you samples of each of those areas. So first we start with the thalamus. And here you can see we have sort of irregular firing spaced out pretty far compared to some of the other things we'll see. And it has a particular sound, a kind of static-y sound, which hopefully you're able to hear at home. After that, we'll come through the thalamus and we'll end up in an area that's quiet. And you can see, just looking at this trace, it looks very different. You don't have these cells spiking out of it. You really just have sort of background static. And if we hear that, it has sort of a different sound to it, kind of an emptier, hollow sound. And then now as we get to the STN, this is really the very exciting part of the operation where you see very dramatic changes in the signals that you're getting. The STN has a very rapid, chaotic sort of a firing with an increased background. And so you can see that just looking at how much thicker this is compared to the traces we've seen. And when you hear that sound...
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PETER E. KONRAD, MD, PhD: It sounds like an old radio.
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JOSEPH S. NEIMAT, MD: It has that kind of a brisk static-y sound that you get with an old radio or really, when you've heard enough of these, it sounds very specific for the STN. The other thing we want to pay attention to, we measure exactly where we entered the STN and we see how many millimeters we traverse before we fall out. And all that time we're seeing signals like this. And what that tells us is whether we've kind of hit a nice thick part of the nucleus where we might get five or six millimeters or if we get just a little bit, it means we might be just at the edge of it, where we've sort of skimmed the STN and then we have to think about whether one of the other trajectories might be better.
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PETER E. KONRAD, MD, PhD: That would nec-- that would probably be a reason why we would make an additional pass if we had one electrode. By using four electrodes, it allows us to make that assessment all in one pass down through the brain.
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JOSEPH S. NEIMAT, MD: And then here when we've come out of the STN, we again get an area that's kind of quieter without a lot of brisk spiking over the baseline. And then finally, we always look to see that we're hitting the substantia nigra, which is this larger nucleus beneath. And that, too, has a characteristic sound, which is a bit like the STN in that it has more rapid firing, but it, too, has sort of a distinct static-y sound that tells us when we've come through the STN nucleus and went beyond it. And this again, so looking at this in a number of electrodes, in an array of electrodes, gives us an idea of

where we are relative to the nucleus and gives us some sense of which of those trajectories might be the one that we want to select for our eventual -- our eventual implantation. To really decide between those, we turn to our neurologists and get their opinion of what the best way is and do that by stimulating. Maybe they'll tell us about that.
00:37:28
PETER E. KONRAD, MD, PhD: Okay, very good. before I go on to ask Dr. Phibbs to talk about the next section of the surgery, we do have an interesting question that came in, and that is the risk of brain injury from patients moving in the operating room. I know this is a concern, and again, it's the whole reason we actually mount the platform on the head. And as the patients move, the platform moves with them. So actually, there is no movement of the electrode with respect to the brain. And it's absolutely key that that's true. So there's actually no risk for electrode movement once it's mounted accurately on the frame and secured there. It's the reason we can't do the surgery holding the electrode by hand. We have to use some secured device to the skull so that it actually will hold it still. And one other thing is, for those of you watching here, please feel free to e-mail in or type in your questions as prompted on the screen. And now let's move on to the next phase of the surgery. The first part you heard us where we talked about mapping and understanding the environment in a small area around the electrode, and now the second part, more important part honestly to me, and I like to see is what happens when we actually use the electrical stimulation to affect the person's disease. And, Dr. Phibbs, can you walk us through this next part?
00:38:46
FENNA T. PHIBBS, MD: Yeah, as you've heard so far, it's really important that the patients are awake during surgery so they can interact with us and tell us the symptoms they're having as far as side effects of stimulation but also symptomatic benefits they're having from the surgery itself. And -- and as you've seen, it's very precise surgery, but everybody's brain is a little bit different, so it's important that we have the stimulation in the O.R. and the cooperation of the parent-- excuse me, of the patients, but also the interaction with the neurologist. So what you'll see in this video that we're about to show is the neurologist, Dr. Charles, also part of the team, explaining to the patient some of the side effects that they might experience during the surgery. Let's go ahead and start.
00:39:29
MAN: I'm ready whenever you are.
00:39:32
DR. CHARLES: Okay, so that's your baseline, okay? Try it again?
00:39:33
PATIENT: Will we ever change that baseline?
00:39:35
DR. CHARLES: That's what we're going to work on. So if you -- if I have you do this again and it feels different to you, I want you to let me know. So I'll probably ask you, going along here, to do this again. And I'll say, "Tell me if it's worse." Could be worse, could be better, could be no change. Another thing that you might feel to be tingling down in your leg and your hand, could be on your face. And you may feel, too, a change in the way your eyes feel. Look over to your left, look to your right, look up.
00:40:07

FENNA T. PHIBBS, MD: So here we're actually increasing the voltage to see what symptomatic benefit the patient has but also what side effects he may be experiencing.
00:40:14
DR. CHARLES: Hold right there. What do you feel?
00:40:15
PATIENT: It's -- very good.
00:40:19
DR. CHARLES: What does it feel like?
00:40:21
PATIENT: Speech very slurred all of a sudden.
00:40:24
DR. CHARLES: Okay, repeat after me: the fire engine is red.
00:40:27
PATIENT: The fire engine is red.
00:40:29
DR. CHARLES: Okay. Off.
00:40:30
MAN: Off.
00:40:31
DR. CHARLES: Okay. What else did you feel?
00:40:33
PATIENT: Just a flattening, if you will, of my speech ability.
00:40:38
FENNA T. PHIBBS, MD: And you'll see, these symptoms are very difficult to describe, and that's why it's important that we have the patients awake and as interactive as possible to be able to describe the symptoms that they're having to us.
00:40:48
DR. CHARLES: Stimulator's off. This is --
00:40:51
PATIENT: The fire engine is red. It's definitely better.
00:40:43
DR. CHARLES: Yeah. So it'll be that quick, sort of off and on. So if you start to feel something...
00:40:58
FENNA T. PHIBBS, MD: And here he's describing how quickly the symptoms can develop, but as we turn the stimulation off, the symptoms disappear. And here, Dr. Charles is examining the patient to see if there's changes in stiffness or rigidity that we see with Parkinson's disease or, with our tremor patients, we'll look for a reduction in their tremor. And you'll notice as we increase in voltage that the patient reaches a threshold where his symptoms improve.
00:41:25
DR. CHARLES: You feel something?
00:41:28
PATIENT: I hate to tell you, no.
00:41:29
DR. CHARLES: That's fine. I'm not trying to get you to feel something. Don't --

00:41:36
PATIENT: It's just not there.
00:41:45
DR. CHARLES: Oh, that's fine. Okay.
00:41:51
MAN: Four twenty-five.
00:41:52
PATIENT: This feels great.
00:41:53
DR. CHARLES: Hold right there. This feels different?
00:41:56
PATIENT: Yeah.
00:41:57
FENNA T. PHIBBS, MD: And again, you see Dr. Charles actually doing his exam and feeling the reduction in stiffness in his arm.
00:42:03
DR. CHARLES: Okay, hold it up just --
00:42:05
FENNA T. PHIBBS, MD: And here the patient's actually feeling and noticing that his movement's easier to do.
00:42:11
MAN: You can tell the difference here?
00:42:12
PATIENT: Indeed.
00:42:13
FENNA T. PHIBBS, MD: And what we like to replicate with our Parkinson's patients is that this sensation is very similar to what their medication is like.
00:42:21
PATIENT: Just then, it was a good feeling on the right side of the bed, feelings on the left side.
00:42:26
FENNA T. PHIBBS, MD: So we take all this information from the different electrode passes that we have, and this allows us to choose the best electrode placement of the three to four that we take in the O.R. Here, Dr. Charles is describing the percent efficacy and the side effects the patient has developed, again, allowing us to choose the best spot to leave our electrode.
00:42:52
PATIENT: A lot better. A lot better.
00:42:54
DR. CHARLES: All right, let it down. All right, let it go.
00:42:57
FENNA T. PHIBBS, MD: I think we can move on from here to explain the rest of the surgery.
00:43:03
PETER E. KONRAD, MD, PhD: Okay. So there's basically three things that we use to target the correct target in any given patient, and again, it's one of the examples we use,

it's like going to an eye doctor and having a pair of glasses fit. You'll get a lot of questions about "better," "worse," and essentially we want to focus on getting that implant in the optimal spot for the patient. So the use of the microelectrode recordings, the use of the stimulation to determine side effects, and most importantly, to determine effective therapy. And based on those three criteria, the neurologist and the neurosurgeon and the neurophysiologist meet, discuss where the ideal target is, and then we put the electrode in. And maybe we can just have a brief section of the next video showing the implant going in in that particular patient. So let's pull the next video up, please. So again, just to recap, this is a four-contact lead implant that's available today. We want to locate this implant so that it's middle two contacts, shown here, are centered around the ideal target. And again, that target is usually no bigger than one of those contacts will cover. And the contact's about a millimeter and a half. That whole length of all those four contacts is seven and a half millimeters, and we'll capture the target within that implant there. Once we've determined the actual target depth and exact location based on the previous mapping that we've done, we essentially trade out the microelectrodes or the small test electrodes for this implant. And again, this implant is about four times as thick as the microelectrodes. This is how the implant's calibrated to the exact depth that we want to leave it at, and then the video here shows, basically all we do is we mount that electrode and we insert it in through a small tube. And once it's in place, we perform a test stimulation to just double-check that the implant is working correctly. And as I mentioned earlier, then the tubes are all withdrawn and the electrode is locked to the skull. And the remaining part of the wire or the electrode lead is buried under the scalp and the incision is closed and those small markers removed. And the patient is basically allowed to recover that evening and sent home the next day. So this is the major part of the surgery, and we usually finish the surgery around noon with both electrodes going into the brain. If we have just one electrode going in and we're just treating one side, we'll usually be done in two or three hours. And I think we can stop this video here so that we can go on to the next section and just briefly discuss -- once we have the wire in place, then that's only part of the system. It has to be hooked up to the device that actually runs the electricity through the device, and we call that the generator. Dr. Neimat, can you show them what a generator looks like?
00:46:15
JOSEPH S. NEIMAT, MD: Sure. So I'll tell you briefly about Stage Three, which is putting in the generator and connecting it to the DBS leads. These two devices here are -- if you can see those there, these are two generators: one for a single side and this if you have two electrodes, this controls both of them. And within this system, what you have is not just a battery, but you also have a computer device that allows you to stimulate at different frequencies, at different pulse widths, at different voltages so that the stimulation can be fine-tuned once the leads are in. To put this in is a fairly simple operation. The patient is asleep for this one. We simply access the ends of those DBS leads that we had previously buried under the scalp, we make an incision there, we make another incision right here sort of just beneath the collarbone, and we implant this battery and we run, beneath the skin, a wire between them. So all of the system -- and you can see here, here's a picture of the incision after a patient has had one of these placed in. There's a small protuberance where this has been placed, but all the wires and the battery are all underneath the skin. And the programming can then begin.

00:47:23
PETER E. KONRAD, MD, PhD: One other small point is the fact that the patient really has to be asleep for this part of the procedure. And rather than put them to sleep at the end of this second stage surgery, we prefer at Vanderbilt to let the person recover from the initial mapping experience, go home for a few days, and then return to have an outpatient procedure done in which this generator is implanted. We find that most patients transition through this very easily. So those are the three stages of the surgery: the bone marker placement and imaging and what we call image acquisition and creation of one of these platforms, the second stage is the actual overnight stay when the patients come in, get the area of the brain mapped and the actual electrodes placed. This is probably the most delicate, complicated part of the surgery. And then the third stage, which is performed as an outpatient procedure about a week after the second stage in which we put the patient to sleep and hook up the generator. But at this point, the -- all the pieces are all hooked together but nothing's turned on yet. So perhaps we can hear about what happens in the next phase of the proc-- of the process of getting a deep brain stimulator to work.
00:48:40
THOMAS L. DAVIS, MD: Sure. So once everything is in place, approximately three to four weeks after the surgery, when the swelling's gone down -- because a person can have or typically has some symptomatic benefit just from the mild amount of trauma from electrode patient -- the patient's asked to come back to clinic off their medications -- and maybe we can roll the video -- and we try and program each individual electrode. So this is a patient who underwent surgery. This is, again, about four weeks after his electrode placement. And Dr. Charles will use a portable programmer that will lay over the pulse generator here, and with that, the programmer can adjust the frequency, pulse width, amplitude, and electrode configuration. And as Dr. Konrad mentioned, it's kind of like getting your spectacles fitted. We typically hold the frequency and pulse width constant and then individually stimulate off each of those four electrodes with increasing voltages, examining the patient, having the patient go through various fine motor movements, and reporting any side effects. And along with our examinations and the patient's report, pick the single electrode that provides the patient the most symptomatic benefit with the least amount of side effects. Now, typically when the device is turned on, we'll start at a relatively low voltage. And depending on the pulse generator that's been implanted, either program the patient a range of voltages that they can slowly adjust at home -- so they're given a schedule to increase the voltage at home using a hand programmer -- or the voltage will be set and they will go home and come back to clinic at relatively frequent intervals and have the voltage slowly increased by us. This is a very dynamic process, usually takes three to six months to get a Parkinson's patient optimized, because as they're going up on their voltages, they are also coming down on their medicine. So on average, a Parkinson's patient would reduce their medication by 40 or 50% by the time they're optimized. So we first do the right side, do the left side, and then bilaterally stimulate and check for side effects. This is Dr. Charles increasing the voltage using the programmers. The patients are also given a device that they can interrogate the stimulator at home. Again, depending on the pulse generator. These vary a little bit, but they all can tell if the device is on or off and turn it on or off if they need to. For the vast majority of patients, they run the device 24 hours a day. They may electively turn it off if they're undergoing,

say, an EKG and it's providing some electrical interference, but most patients run it 24 hours a day. So we can clip that video there.

00:52:00

PETER E. KONRAD, MD, PhD: Okay. Let's spend a little time addressing some of the questions you all have sent in to the program here. And again, I think several of these questions center around indication. So can one of you just give us the three FDA-approved indications for deep brain stimulators?

00:52:18

FENNA T. PHIBBS, MD: So currently the three conditions that DBS is FDA-approved for is for dystonia, Parkinson's disease, and essential tremor.

00:52:28

PETER E. KONRAD, MD, PhD: A couple of the questions asked about whether or not this might work for traumatic tremors, athetotic tremors, depression, Alzheimer's. What's the role -- we hear a lot of this on the internet and also through medical news articles and things. What's the role of DBS in those applications?

00:52:50

THOMAS L. DAVIS, MD: The traumatic tremors, the athetotic tremors -- what we would all secondary movement disorders -- where a fixed lesion of the brain is the cause of the involuntary movements, those are relatively rare disorders, and they're very heterogeneous. So there are certainly reports in the literature of deep brain stimulation helping those. I don't think it'll ever be FDA-approved for that indication because it's just too rare to do formal studies. I think currently that is, you know, an individual group choice, considering, number one, the nature of a person's movements, number two, what the cause is, what their scan looks like, how much brain damage has been done, and, you know, how functionally disabling the movement is.

00:53:39

PETER E. KONRAD, MD, PhD: Even though this would be an off-label use of the device, there have indeed been reported significant successes with the use of this. The difficulty then becomes in using a device not for what it was initially indicated, but deciding whether the risk/benefit ratio is appropriate. And that's an individual decision the team needs to make. And that's one reason to run this by a group of people who have experience in this field. Dr. Neimat, can you comment on the state of use of deep brain stimulation for Alzheimer's or depression?

00:54:09

JOSEPH S. NEIMAT, MD: Sure. Well, there have been a number of studies looking at both of these things, looking both at depression, other psychiatric diseases, even Alzheimer's, I think, more recently. These studies are still in the very early phases for the most part. We're probably going to be looking at a multi-center study for depression in the next year or two, but they're not quite here yet. But certainly there's a lot of excitement about these things, and we're -- we're eager to see what the results of these studies will be.

00:54:35

PETER E. KONRAD, MD, PhD: Yeah, thank you. I appreciate your comments being short and to the point. Another important question that came up, I'd like one of our neurologists to answer, is whether or not there's any indication for deep brain stimulation in patients who don't respond to dopamine or who have Parkinson's plus syndromes.

00:54:55
FENNA T. PHIBBS, MD: You know, ideally the patients that respond best to stimulation that have Parkinson's disease are patients that really show a good response to dopamine. And in part, we see this with our preoperative evaluation, where we test patients both on and off medication to make sure that they do indeed show a good response to dopamine replacement. And Parkinson's plus syndromes traditionally don't show a dramatic response to dopamine and therefore aren't a very good surgical candidate. So it's not an FDA-approved treatment option for those patients.
00:55:27
THOMAS L. DAVIS, MD: Yeah, I would say that the only medication-resistant treatment -- the only medication-resistant symptom in Parkinson's disease that we would really consider treating at this time is tremor, which does respond very well.
00:55:42
PETER E. KONRAD, MD, PhD: Speaking about tremor, there was one question regarding is the targeting for essential tremor the same as for Parkinson's disease? We've been talking a lot about STN. Dr. Neimat, can you enlighten us on targeting options?
00:55:57
JOSEPH S. NEIMAT, MD: Sure. For the most part, essential tremor is -- it's a thalamic target. We saw the thalamus sort of on the way to the STN, but it's a slightly different area that we aim for in essential tremor, so they are different targets. That said, there are multiple targets that have been used in the past and even currently for Parkinson's disease. And when tremors, the worst symptom that a Parkinson's patient has, it may be that a thalamic stimulator like the essential tremor target would be the best for them.
00:56:26
PETER E. KONRAD, MD, PhD: Thank you. There's also a question about whether or not there's an age limit for deep brain stimulation. And typically, for Parkinson's disease and essential tremor, this is a disease that affects adults, and primarily, although there's not specifically a lower age limit, we tend to think of this as more of an adult disease. The upper age limit is debated perhaps by some people, and it really is determined by the patient's medical conditions and their health conditions. We certainly have not operated on people who were only 60 years old, mostly because they had other medical conditions that would make the surgery too risky for them, and yet we have implanted patients in their 80s with an implant for disabling tremor or for medically refractory Parkinson's disease that are otherwise healthy and living a fairly active life. And so the age limits can be quite varied. For dystonia, the FDA-approved indication for dystonia is from 9 years old on, because dystonia is a disease that can affect children. And so this is the one disease in which DBS is indicated in childhood also. And the results of this can be quite remarkable. Let me move on to some other technical questions we've gotten here. How long does the generator battery last, typically? Dr. Neimat?
00:57:57
JOSEPH S. NEIMAT, MD: Typically, with normal use, it lasts about five years right now. And so we're having to change them about ever five years.
00:58:03
PETER E. KONRAD, MD, PhD: And one particular question about the connector device: where does it actually sit in a person or where does the selector device sit? Where exactly do we put this?

00:58:16
JOSEPH S. NEIMAT, MD: Sure. I can show that. In both cases, what we're doing is we're implanting it underneath the skin or underneath the muscle right here, just a few inches below the collarbone. So mostly like a normal pacemaker that you would see in a patient with cardiac disease, it's very similar.
00:58:30
PETER E. KONRAD, MD, PhD: Sometimes if there is some limitation and we can't fit it here, we can occasionally put it down here. It requires a longer extension lead to route it down to the abdomen, but most patients prefer to have the unit sitting up just below the skin below the clavicle. There was a question about what's the future for these devices. Is there a rechargeable? There's no rechargeable battery or rechargeable implants yet available to us on the market, but we feel that that's -- that's going to be available shortly. I'm hearing perhaps in the next year or two that we'll see a rechargeable deep brain stimulator device. And this would certainly lengthen the expected battery life. Can you also explain to the audience briefly how we go about changing out a dead unit?
00:59:19
JOSEPH S. NEIMAT, MD: Sure. So there's no battery within this, per se, that can be removed. Really the whole unit is changed out. So what we do, we plant it under the skin here, we make a small incision reopening the same incision that we put it in through, we remove the battery, we reattach the extension leads to a new battery and then insert that in the same spot. It's very quick, it takes about 30 minutes.
00:59:42
PETER E. KONRAD, MD, PhD: Yeah, and that's also as an outpatient procedure. And we're now probably in second-generation replacements in some of our patients who've gone through two sets of generators already, find the device still quite helpful in their symptoms, and they've come back for a third unit to be replaced out. Once we place the brain electrode in, we really don't like to make any changes with that. We're not -- once we do the whole procedure to put the electrode in place, there's really no reason to move that wire if it's functioning correctly. One other question that we had was what are actual physical limitations of the patients with this device after the surgery? Dr. Davis, have you seen anything that patients can or can't do once they have one of these?
01:00:30
THOMAS L. DAVIS, MD: Well, the package insert says you're not allowed to scuba dive greater than 70 meters, so, you know, if you're a deep-sea -- you know, if you're a pearl diver, it might be -- but the device is titanium, and it's generally pretty sturdy, so I tell patients they can do, you know, physically, any kind of activity that they want. It is metal and it will conduct heat, and so diathermy, which is the therapeutic ultrasound, this kind of deep heat, is contraindicated because of the potential of transferring heat through the unit. Also because of its metal, currently except in very few exceptions, MRI is contraindicated. So if a patient needed to have regular MRI scans --
01:01:22
PETER E. KONRAD, MD, PhD: This would be the same concern patients would have having a pacemaker. So if a patient has a pacemaker, we know they're not allowed in an MRI scanner. We tend to think of the brain stimulator as having very limited options with an MRI, if any at all. But there are certainly other pictures we can obtain besides an MRI scan to work a patient up, so it's not really a serious limitation, we just have to be

cognizant of it. Another question here was how often do I need to follow up once I have this implant in or what sort of time frame do we expect to see results and how long are they going to last? What's sort of the -- what happens after the implant goes in and is this a visit with a doctor every week or two or a month or how does it go from there? Dr. Phibbs, can you...

01:02:12

FENNA T. PHIBBS, MD: Yeah, Dr. Davis alluded to this a little bit as well. So initially after you get your unit turned on for the first time, you do have to come back on a fairly frequent basis until we get the stimulator fine-tuned but also reduce any amount of medications that patients are on. And once patients are stable, they can usually return to the clinic about every six months or so for just routine check of their battery and maybe a minor adjustment of their stimulation up or down. And often can follow up with their local neurologist, since a lot of our patients do have a long way to drive to come all the way here to be seen.

01:02:45

PETER E. KONRAD, MD, PhD: And then one final question I know is very important. A lot of patients look at this as a replacement for medications. Is that true? Either... anybody.

01:02:54

THOMAS L. DAVIS, MD: Well, I mean, for essential tremor, those patients are generally not taking any medication for their tremor, as -- because the medications didn't work. And a similar situation for dystonia. So often for the essential tremor patients and dystonia, it is their only therapy. For Parkinson's disease, it is extremely rare for somebody to go off medicine, and so most of those patients continue to require adjustments of both their medicine and the stimulator throughout their life.

01:03:26

PETER E. KONRAD, MD, PhD: Terrific. Okay, I think that's going to wrap up our session here learning about deep brain stimulation surgery and how we do it at Vanderbilt. If you're interested in learning more about this surgery or want to look into receiving a brochure about deep brain stimulation surgery or how we perform it here at Vanderbilt, please follow the cues on the screen to submit your questions and requests for more information. Again, we want to thank you for taking your time to learn about deep brain stimulators and how this surgery can help potentially many people and how we perform it here at Vanderbilt. Thank you.

01:04:20

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