

Okay, so I'm going to talk, I'm going to try to stay on time here and look at my watch and give an overview of the course and a general overview of brain stimulation. So we really are going to talk mostly about deep brain stimulation today, even though the closed loop device for epilepsy for which there will be a talk by Dr. Popescu later in the afternoon is not thought of in the same way as traditional DBS is thought of because it can also stimulate the cortical surface. So most of the time when we are talking about deep brain stimulation we are talking about stimulating subcortical structures and most of the experience with that is in movement disorders as you can tell from the program it's highly movement disorder oriented.

So DBS is not the only type of brain stimulation. I mentioned responsive neurostimulation which is a closed loop device for epilepsy, can stimulate cortical and subcortical structures. Here is an example of those two devices. So when we talk about DBS and please no question is - the point of this course is to orient you in this technology and basic indications and surgical techniques and outcomes. So please if you have any basic questions write them down on the cards we have to address those, so that's why we are here today.

So it's cut off from the picture but the actual stimulator is the pulse generator that's implanted in the chest. I have a picture of that again later. But the business end in terms of the brain surgery part is in the brain. This would be for instance a movement disorders patient who has an electrode planted deep in the brain, there is a 14 mm opening in the skull, typically there is one on each side through which a DBS electrode is placed. We'll talk about how that's done later. There is a plastic base for a locking cap so there are two locking components that keep the electrode secured in place on the

skull. And this is typically done in one surgery and then in a second surgery we open up another incision here, find the other end of the DBS lead and connect that to an extender wire that then goes down to another incision that's open in the chest where we place the pulse generator.

That's in contrast to this other stimulation system which is the Neuropath system. In that system the pulse generator is actually implanted in the skull. So one makes a pocket in the skull for the device. There is a holder that's secured and the device is placed there. There can be a deep stimulating electrode, typically these will go in the temporal lobe but they don't have to they could go anywhere a seizure focus has been detected. And then there is another electrode that could also be a deep - in a deep structure or could be on the cortical surface and these electrodes can both record and stimulate and so we'll have some more information about that later.

Now there are - so there are types of brain stimulation that are not invasive. We are going to talk about invasive brain stimulation today but transcranial magnetic stimulation actually has an FDA approval for some use in depression as well as migraine headache. The efficacy studies however are not great, a lot of insurance companies do not cover this therapy. DBS has a much longer history of efficacy but we should mention that there is TMS and there is also transcranial direct current stimulation, so the TDCS some of this is voodoo that you kind of see out there, these little devices that people make and they you know put it on You Tube and sell them out of their garage. And then there are some real studies in transcranial direct current stimulation that are interesting. But that is not FDA approved and not really in clinical use.

Okay, so what is DBS? We've talked about this. So a little bit about deep brain stimulation. Here is a picture of that pulse generator and this is true relative size. So I tell patients that it's not as big as a hockey puck but it's pretty close. It does protrude from the chest, there is a visible you know incision that is going to heal pretty well but you know always someone is going to notice that if you are at the beach. For ladies we do try to make the incision so that if they are wearing a deep V shirt it sticks off to the side so it's not as apparent. But it is certainly visible and patients can feel this under the skin. Typically they get used to it, acclimate to it pretty well but there is a range of how long that takes. And we can hear from the patients later about that in particular.

What our neurologists and physician assistants do in the clinic with programming the patients is done through this telemetry device. So this is a telemetry head that's placed over the pulse generator, it's connected to a wire, by wire to this handheld computer and using this computer one can program different characteristics of stimulation. And I would like to point out that we'll see in a second this therapy is not experimental, at least not for primary movement disorders and some of you may have seen that the Lasker Prize was recently awarded to a neurosurgeon and a neurologist jointly for their work in deep brain stimulation for Parkinson's disease. So this is an important point about the nature of this treatment and its use and it really does require a team approach between neurologists and you'll also see psychiatrists for other indications outside of movement disorders where these two subspecialties really need to work together to both identify patients and to treat them and maintain treatment with the therapy. Dr. Benabid was the first neurosurgeon, he is French, to implant the DBS system. He did that in 1987 and this is Mahlon DeLong who is a movement disorder neurologist at Emory University in Atlanta.

Okay, so DBS is not new. Here is the proof of that. First implant in 1987, that is basically with the same technology that we are using today by the way. The European Union has always been ahead of the United States for approving both devices and pharmaceutical treatments so you can see they were a couple of years ahead but DBS has been FDA approved for use in the United States since 1997, so this is you know over 15 years now and there is a lot of good safety and efficacy data. It was 2002 when the FDA approved this for treatment of Parkinson's disease although it was being used off label for some before that in the United States so there is actually a much longer history than just 2002.

A humanitarian device exemption was granted for dystonia in 2003, so that's actually a pretty longstanding history of treatment of dystonia now over a decade, and then in 2009 also a humanitarian device exemption was granted for the treatment of obsessive compulsive disorder and we'll have a talk about obsessive compulsive disorder in the afternoon. So humanitarian device exemption is granted for indications where it's felt that there will not be enough patients to generate multicenter large randomized controlled trial data.

Quickly to wrap up, how does DBS work? These are the electrodes that are available to us. These are the two that are typically used in movement disorders, so the electrodes themselves are 1 1/2 mm long with either a half mm gap or a 1 1/2 mm gap. This is the electrode that's approved for obsessive compulsive disorder because it stimulates over a longer region in the brain and also is used to stimulate some white matter pathways. And each of these can be programmed independently and

you can program 3 different parameters so one is the amount of charge or the amplitude, one is the rate so how often you get pulses of electrical stimulation and then you can set the duration of each of those pulses. So these settings have different effects on improving symptoms and they also have different effects on creating side effects that may be unwanted. So these are things that we can tinker with in terms of getting the stimulation correct.

Okay, so how does DBS work? Well it's essentially based on this concept of loops, segregated loops, functional loops within the brain and we think of these as basal ganglia which is the target for most of our indications for DBS, thalamocortical basal ganglia loops. And these are - have a little bit of an overlap but for the most part they are segregated into a motor system, a limbic or kind of emotional system, and an associative or executive system that maybe is more important for kind of putting information together and decision making. So for instance this is why we can put a DBS electrode within the motor circuit and not affect we hope these other regions. When we do get side effects that may be associative or limbic it's because of spread of electrical current or in some cases the electrode could be not in the optimal position. But 99% of the time we put it in the right place and get a nice benefit with motor symptoms.

So just to summarize, a lot of neurologic and neuropsychiatric diseases are known to be associated with different problems in some of these individual nodes. And Dr. Homayoun who is going to talk next will talk to you about how that happens in Parkinson's disease. But essentially any diseases that we are trying to treat with brain stimulation we are trying to alter a network and there is a specific part of that network that's known to be affected. So when that happens communication that's

important for the initiation of movement and also important for sitting still is thrown off and electrical stimulation in the way the DBS is delivered in some way resets abnormal communication in the brain and generally speaking I think Dr. Homayoun is going to talk about this too, there are different bands of oscillatory activity and neurons fire signals at different rates and communicate with each other in that fashion.