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Date: July 21, 2016

Event: United Spinal Webinar

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>> Thank you for joining us today for United Spinal Associations Webinar. All you need to know about direct nerve stimulation. Today's expert presenters are Miss Jennifer French, MBA and Kimberly Anderson-Erisman, this is Bill, director of the resource center, I'll be your moderator for today's presentation, one of continuing series of United Spinal Association education Webinars. Archived at spinalcord.org. Please use the chat window for your questions, the window you'll find on your control

panel. We will try to get to the questions at the end of today's presentation. For any questions remaining unanswered please e-mail them directly to the presenters, the addresses are displayed upon the last slide. Further, closed captioning instructions wills appear on chat window of your control panel. Jennifer French became a quadriplegic from a C6/7 incomplete spinal cord injury in 1998. She is an active user of the implantables stand and transfer system, provided by the Cleveland FES center, the first woman to receive such a system. She is co-founder and Executive Director of the 501C3 non-profit organization, Neurotech Network, with a focus to educate about and navigate for access to neural technology. French is also associate publisher and senior editor of neurotech Reports, a leading news and analysis publication for the neurotechnology industry. She is a silver medalist from the 2012 Paralympic games and the 2012 Rolex Woman of the year, the first woman with a disability to receive this distinction. Co-founder and development officer of the Warrior Sailing Program for wounded, ill and service members of the sailing foundation. Dr. Anderson-Erisman is a Research Associate Professor and the director of education for Miami project cure paralysis at the University of Miami Miller School of Medicine. Her research is focused on translational investigations and bridging the gap between basic science, clinical science and the public community living with a spinal cord injury. Her training stands the spectrum of resource from Cellular and molecular studies to whole animal and behavioral studies, to human clinical research. She has conducted a multicenter clinical study evaluating the reliability and validity of the spinal cord independence measure in the US health care setting. Several of studies focused on the perspective of people living with spinal cord injury on various aspects of research, including priorities, acceptable benefits and risks, preference for prosthetics and exercise. Her current project focused on aging related changes in bladder health after SDI, determining the minimum amount of exercise and locomotor training required for clinical trials targeting SCI and identify with facilitators and barriers to clinical trial participation from SC icon assumer perspective. In addition to pursuing own research to chronic injury, she is part of the leadership team with the transplantation CNN trials at the University of Miami and collaborating with Dr. Levi to lead participation in industry sponsored cell trial. I would like to hand it off to Jennifer French to begin the presentation.

>>Jennifer: Thank you for the great introduction Bill and thank you all for attending this presentation about direct nerve stimulation. As Bill had mentioned in the introduction, you can ask questions while we are going along this presentation. Please be sure to put that in, any questions we are not able to answer at the end of the presentation we will be able to address those. Also, we will be presenting quite a bit of information and providing quite a few links during this presentation, so don't feel obligated to write everything down. You will find in your, little control box there, an area that says handouts and that's this presentation in a PDF format and you'll be able to have the live links that you'll be seeing online today. So please use those resources as well. We wills have this presentation uploaded as a PDF both on the spinal cord.org website as well as the Neurotech Network and Miami project website. So definitely resources available for you to be able to follow along and be able to reference back to this at a later date. So just a little, couple disclaimers we have to do before we get into the presentation. One is that please the information is presented in this Webinar is not meant to be replaced by advice by medical professional, consult your health care professional who is aware of your particular case. The representatives do not support, sell, administer or recommend any products, procedures or services, but we highly recommend for you to take this information to a trained medical professional familiar with your case to discuss the options that are best for you. Wooh -- so there are our disclaimers and now we can get into the fun part of the presentation. First we would like to introduce you to our two organizations, Kim would you like to introduce the Miami Project?

>>Kimberly: Yes, it is based within University of Miami and we do research and the main goal of our research is to define more effective treatment and ultimately cures for paralysis resulting from a spinal cord injury.

>>Jennifer: Thanks Kim and the Neurotech Network is non-profit organization and we focus on education and advocacy for neural technology devices and treatments, caregivers and the medical professionals who care for them. We have lots of free resources on our website, visit neurotechnetwork.org. So now I would like to hand it over to Kim, she will talk about our objectives tore this presentation and start to dig into some of the details. Kim?

>>Kimberly: Okay, thank you Jen. So today we're going to go over some basic information about the nervous system and use that to introduce purposes of stimulation for nerves. And then we will try to explain the differences between external stimulation and internal implanted stimulation. Then we will go through various examples of different types of technology that are out there, either available for clinical use or for research use and they are for different applications, peripheral nervous system, brain and spinal cord. We will end with several different resources we can provide to you for more information for those interested about specific things. So first we are going to talk about the human nervous system, get my computer to work here. Okay. So the human nervous system is quite complex, but it can be broken down into two parts. The first part is the central nervous system and the other part is the peripheral nervous system. So if you look at these little figures to people, the central nervous system is the brain up here and the spinal cord that goes straight down inside the spinal column. So the brain and the spinal cord are connected and they communicate with one another and the two are considered the central nervous system. And over here, if you look at all of the other nerves that are coming out in the body in this diagram, that's considered the peripheral nervous system. Everything outside of the brain and the spinal cord is considered the peripheral nervous system. And the peripheral nervous system is divided into two parts and we call one of those the autonomic portion and the other one the somatic portion. And somatic portion is the peripheral nerves that go out to muscles, your skeletal muscles. So those that are involved in movement and in sensation from those skeletal muscles. The autonomic nervous system is further divided into two different components called the sympathetic and parasympathetic and an easy way to think about those two components are the fight or flight response, so fight is sympathetic nervous system component of the autonomic and that arouses the body so that if you do need to fight you got all of that um energy and the parasympathetic is flight, meaning that it calms the body after an arousal and allows escape. So the autonomic nervous system is very involved with things like bladder control or bowel control, how you regulate your body temperature, how you regulate your heart rate and your ability to sweat. So those people that have injuries above thoracic level 6 can have autonomic dysfunction related to the damage of the autonomic portions of the peripheral nervous system. So if we go to our next slide we are going to explain, just a little bit more, about how the peripheral and the central nervous system interact. So we start down here in this diagram at the bottom, we are going, your body is going to take any kind of sensory information that comes in from the external world. So the peripheral nervous system, sensory component has many different receptors or sensors in the skin, in the muscles, in our different organs, so that they can interpret what comes into our body in regards to sensation. That information, from the peripheral nervous system, comes in, into the central nervous system spinal cord and it goes up to the brain here. The brain processes what that information means and almost always it produces a motor output back down to the somatic or the autonomic nervous system. So your body is constantly sensing,

interpreting and outputting actions based on what our nervous system experiences. So we can use nerve stimulation to alter the way that our nervous system reacts. So there's two main x or three main categories of nerve stimulation in there outlined here. So the first one is using nerve stimulation to promote plasticity. And plasticity refers to almost like adaptive connections and we can do that with peripheral stimulation, brain stimulation, or Spinal Cord Stimulation and plasticity can really be promoted in people that have any complete spinal cord injury, if some degree of motor sensory sparing across the lesion, a lot of things, including electrical stimulation, can promote plasticity of those parafibers. The second way that you can use nerve stimulation is to modulate activity, which is another way to say that you could regulate activity that's going on in the nervous system. So one very common way of using Spinal Cord Stimulation or deep brain stimulation is to control pain. And you can do this by interrupting or altering the signals that are coming out so they can be interpreted in a different way that is not as painful. You can also use modulation or regulation to suppress tremor movements or seizures, it is often used for obesity and in bladder control. And then the third way that you can use nerve stimulation is to actually induce movement and you can use this in a couple different ways. You can use it as a rehabilitation component, and augment the movement, the physical movement that is seen then. You could use it for functional electrical stimulation, that's what FES stands for, and that is providing a movement that you cannot necessarily initiate on your own by stimulating that and then you can also use it to regulate movement and how strong those movements might be. So we have a couple other things that we want to differentiate and we can go, you can have stimulation that is external or internal. So external means that the device is outside your body. Internal means that components of the device are actually surgically implanted and there's pros and cons to both of them. Here we have an example of external electrodes and these are sticky, you can put them on the skin over different muscles and the benefits of external stimulation are that there's very low risk -- it is very easy to implement and the cost is quietly. But some of the risks are that if you stimulate too much you could burn the skin, you are stimulating a large muscle group rather than a specifically targeted area and it can be -- the results can be difficult to duplicate across people or even across one person across time. And therefore compliance might not be as well maintained. Now implanted devices have stimulators or leads that can be implanted into the body, different locations and we will show you examples of these different types. And there are pros and cons to this as well. So the benefits are that you can really target the stimulation as opposed to with external you are just stimulating a very large group of muscles. The stimulation and the results can be very consistent across time and across people. It is easy to use and you can be more mobile, you don't have to be connected to a stationary device. The risks though are that they do involve surgery and surgery is risky in and of itself. And with these components permanently implanted in your body there will always be some chance of infection. You can develop scar tissue around the electrodes or the leads and obviously there are higher costs and they can be more complex. So going to take us through examples.

>> Thanks Kim, first we are going to start off talking about different types of technologies, peripheral nervous system, application to the brain as well as applications to the spinal cord. First we want to kick this off by talking about stimulation to the peripheral nervous system and Kim very eloquently described the peripheral nervous system and how it impacts many functions within our body. This chart is looking at what types of applications there are for stimulation to the peripheral nervous system and whether they are commercially available, they are available in the markets for purchase or if it there is being further investigation into those devices as well. So just to run through these, through these quickly. So when we look at stimulating facial muscles, this really applies to people that have some nerve damage in

their face, also those living with Bells Palsy and possibly even ALS, there are commercial device out there, two commercial devices out there, one from Neuro-4 another one from Biomation for stimulating those facial muscles. There is also some investigation device of called a Blink prostheses, for those unable to blink their eyes. Swallowing, can be a problem for those with ALS also stroke survivors as well, looking into that there are commercially available devices that are stimulating the peripheral nervous system again Neuro-4, Biomation as well Stem device are available commercially, that means that they can be purchased on the market or through a prescription. Also there is devices being investigated at Case Western Reserve University in terms of implanting electrodes for, for the function of swallowing. For sleep apnea, believe it or not sleep apnea is a really big problem in the unfortunately S and several people are impacted by that. In fact several people use C-PAP machines, now stimulation of peripheral nerve system for sleep apnea is alternative to C-PAP, we are looking at stimulating the hypoglossal nerve, currently a commercial device out there offered by a company called Inspire Medical and that stimulating the hypoglossal nerve and there is also an investigational device that's, that has a an industry partner, very close to commercialization by a company called Inphera, so there are some alternatives available for those out there using C-PAP machines. We are also looking at peripheral nervous system for the treatment of depression. Now we will be going into some brain stimulation for the treatment of depression, but for the peripheral nerve system isn't a lot available commercially for the treatment of depression, however, there is a device that's under investigation that's typically used for the treatment of epilepsy called the vagus nerve stimulator and it is currently being investigated to see if it can be a potential treatment for what's called treatment resistent depression. Moving on, for stroke and spinal cord recovery, this is a topic we will go into more later in the presentation, using stimulation for actually recovery of upper extremity function. So there is investigation, but believe it or not there are some devices currently available for stim stating the peripheral nervous system temperature and using it to potentially gain some upper ex-tremendously fee function. A lot are used for, this is typically sold as a prosthetic or FES device to restore growth function in the hand. It has also been used for a therapeutic effect as well. There is also a device currently available in Canada, they are working on making it available here in the United States called Mindtech and it is using surface stimulation, stimulating peripheral nerves as a treatment coupled with rehabilitation to restore voluntary function for stroke survivors as well as those with incomplete spinal cord injury. There is also quite a bit in terms of looking at investigational devices for stimulating the peripheral nerve. One I would like to point out again is looking at the vagus nerve stimulator, device called the Serenity system provided by a company called MicroTransponder out of Texas, it is currently available in Europe, they are working on making it available here in the United States. There is current clinical trials going on at this point and again that's to restore a hand in upper extremity function for stroke survivors and those with incomplete spinal cord injury. Blaire management, there is a lot going on in terms of and what's available commercially for stimulating the peripheral nervous system for restorations of bladder function and being able to manage the bladder, such devices as the device, the sacral nerve, tibial nerve stimulation, are just to name two. And also looking at investigational devices, we're looking at the pudendal nerve, the sacral magnetic stimulation and several others that are available. On this topic, while we are on it I would like to refer those that are here to um a Webinar that Kim and I did earlier in the year regarding bladder management and stimulation and you can find a lot more details on that in that presentation is archived on the spinalcord.org website. Going on to nerve repair, when we are looking at nerve repair it is actually using peripheral nerve stimulation to regain function of damaged peripheral nerves. So when we are looking at this they are actually a lot of research institutions as well

as commercial firms that are really pursuing this type of technology to restore peripheral nerve damage. Now we always thought that peripheral nerve damage will definitely grow back and sometimes that damage does not and it requires surgery. So what a lot of these investigational devices are looking at, how they can apply stimulation to restore function and restore those peripheral nerves. There are several large companies such as striker and integral neural sciences that are looking into this and building certain types of devices to restore peripheral nerves from damage. For pain management there is quite a few out there and now we will go into that in just a little bit more detail as well as I would like to refer those to, those that are on here to a Webinar that we will be doing in October specifically for pain management and alternative therapies. And finally for gate for Dropfoot stimulation, there is quite a few devices out there from Odd stock, now Hanger that are commercially available. There is also investigational devices looking at in terms of improving Gait for Drop Foot. So just to take another step further in terms of the pain side of things and function there is quite a few devices that are available for what's called Percutaneous Neuromodulation Systems and typically when we see those these are external devices commercially available, the uniqueness of this which is different from a PENS unit, the percutaneous systems they penetrate the skin with minute needles, if you look at the this device, this is using acupuncture with electrical stimulation, used quite frequently actually over in Europe, you don't see it as much here in the United States, but again another way in terms of treating pain, if you will. Device called Biowave, a surface device for pain, again the reason it is in category of PENS and peripheral nerve stimulation is because the electrodes have unique design of penetrating the surface and you can see that here in the electrodes that we have on the screen. And finally there is a device called the smart patch by SPR therapeutics, this device again is a patch you put on the skin, has needles within the electrodes to penetrate deep into the tissue and this in particular is being used for a stroke recovery. So moving on to the brain there is quite a different types of stimulation to the brain, there is a bunch of alphabet soup but I will go through quickly so we can start to understand how we stimulate the brain differently and how the brain plays a key role when we're looking at regaining function as well as applications and modulating, if you will, systems in the body. So starting off in the upper left there is something called DBS or deep brain stimulation, electrodes that are implanted deep into the brain. Moving to the right we're looking at what's called TMS or rTMS and that's transcranial magnetic stimulation, again it is using magnetic stimulation or the r in front of TMS is referred to as repetitive transcranial magnetic stimulation, again external treatment not an implanted, which is an alternative to deep brain stimulation. Moving down there is a treatment called tDCS, that's transcranial direct current stimulation. Again this is an external treatment, but it is using alternating current to be able to apply stimulation. Finally in the bottom left-hand corner you'll see that the abbreviations of BCI and BMI, which stands for brain computer interface or brain machine interface and that is actually taking, sensing electrodes, sensing neural activity that's happening in the brain and being able to convert that into actionable, actions if you will in terms of controlling a robotic arm or even controlling a computer and applying that brain activity to a specific function. So let's get into the external stimulation options first. So when we look at what TMS here, if you look here on the left-hand side an external treatment using magnetic stimulation outside the body and it is really looking at using magnetic pulses to produce the changes in neuron activity. When Kim described the different applications earlier in the presentation she talked about plasticity. This is really kind of the cornerstone of what this external brain stimulation is doing. It is really exciting that neural activity that's happening inside the brain. On the right-hand side you'll see what we previously described as transcranial direct current stimulation, so this is direct current stimulation to the brain, you can see it in this picture where you have electrodes on either side

of the brain and what this uses is low level current between an annode electrode which is considered the positive stimulation and producing a current to the negative electrode, which is called the cathode. With that the stimulation goes between those two and again producing changes in neural activity. So again it is an external stimulation to the brain and in terms of applying it for changing the neural activity. Now when we look at brain stimulation that's interim or implanted we are looking at what we call deep brain stimulation and deep brain stimulation has been used for quite some time for Parkinson's disease, central tremor, but also being investigated for several other uses as well. So typically when looking at stimulating the brain we are looking at stimulating abnormal or affected cells and chemicals inside the brain. So we are really trying to not only influence the neural activity, but also trying to influence some of the chemical activity that's going on in the brain, which is much the case for those living with Parkinson's disease with dopamine. Now we are looking at various types of targets they have in the brain and a lot of investigation is going on in terms of trying to understand what targets you go after when we're looking at deep brain stimulation, but most commonly, particularly for those that are commercially available, you are looking at stimulating the subthalamic nucleus, excuse me, subthalamic nucleus you can find right here where that electrode is inside the brain and the Globus pallidus interna, again this middle one right here where they are stimulating that section of the brain also called the GPI. Moving on to what type of brain stimulation is actually available commercially, as you can see from this slide it has grown quite a bit and a lot of commercial devices available. So starting from the left we have here the big three, Medtronic, Boston Scientific, St. Jude all offer devices that are applicable to deep brain stimulation. There is also a new company called Aleva Neurotherapeutics that is offering deep brain stimulation device. Why do we think this is important for consumers to know? Even though these are surgically implanted devices, it is really important as a consumer and a caregiver to understand what features are of those devices and what the risks are as well as the benefits. Not all devices are the same, so it is really important to be able to investigate these devices. So moving on to TMS or transcranial magnetic stimulation, quite a few devices out there, Neurostar TMS has been around for some time now, these devices are used particularly for depression as well as pain treatments. Also if you look at eNeura or suspect Spring TMS, as well as Cefaly, two devices being used for the treatment of migraine headaches and also there is Nexstim, Brainsway and Rio Grande Neurosciences, just taken over by Endodura, another company, they offer different options for external stimulation for TMS and various treatments. Now TDCS or transcranial direct current stimulation, there is a lot of devices available for this and a lot of controversy around this as well that I want to make sure we touch on. So for TDCS there are two commercially available devices, the Fisher Wallace as well as Halo Neuroscience, FDA cleared or FDA approved. These devices are being used for such treatments as insomnia, for anxiety, for depression, and you can get those either to be reimbursed by insurance or to pay out-of-pocket. Now there is also a lot of press and a lot of talk about how to use TDCS for performance enhancement and that's where you see all of these companies coming into play that are not FDA approved. You can buy online, direct consumer as we have them listed here. But just be aware that those devices are not FDA approved, that means they haven't gone through rigorous investigation of the FDA in terms of safety and in terms of efficacy, to show that what they're saying, that the device does is actually a true and has met the scientific requirements if you will, the regulatory requirements. So when we look at TDCS for performance enhancement, meaning it is being investigated actually quite a bit in terms of improvement of memory, improvement of brain function, really hasn't been any conclusive evidence as of yet. There are several studies that are investigating it, but just keep in mind if you are looking at that and investigating this for your own personal use, understand the risks that are behind

using a device to stimulate your brain that is not FDA approved. So let's move on to investigational devices, we are using these same applications but we are looking at how effective they are in different applications. Now the exciting thing, at least I think, is that the TMS and tDCS has really been investigated quite a bit and there is a lot of investigation going on applying these types of brain stimulation coupled with rehabilitation and being able to augment or improve the therapeutic effect. So for instance a company that we mentioned earlier called Nextim has active double blind study going on in terms of looking at the therapeutic effect of using rTMS, again repetitive transcranial magnetic stimulation for stroke rehabilitation, as well as some investigation out of Imperial College looking at using rTMS again for both motor and sensory, regaining of function, for people with incomplete spinal cord injury. Also a study going on in terms of looking at using rTMS for incomplete spinal cord injury for preserving that corticomodal for chronic spinal cord injury, for those injured for quite some time. Also some pilot studies going on using tDCS, coupled with robotic assisted training to restore upper extremity function for those with incomplete tetraplegia or high level spinal cord injury, if you will. Also again for Parkinsons disease using rTMS to restore hand function and gait function, as well as for ALS is being investigated right now to see if it can slow the progression of ALS using rTMS. Finally quite a few clinical trials going on right now in terms of deep brain stimulation, not only for chronic pain, Tourette'ss, Huntington's disease, for multiple sclerosis as well as several different types of psychiatric conditions, particularly those that are treatment resistance, such as schizophrenia, anorexia, dementia, bipolar disease as well as addiction to see if that can help treat those types of conditions. And finally, real quickly, to go over brain stimulation in terms of brain computer interface as well as brain machine interface, there is three really big landmark studies going on in the US that in terms of using brain computerized or brain interface to restore function. So notably Battelle and Ohio state University has one going on with brain stimulation, brain computer interface with surface stimulation to see if someone can just think by the movement of their hand and being able to stimulate that hand just by thought. Also the Brain Gate Study being led by Brown University using this interface to control a robotic arm, as well as University of Pittsburgh, again using brain computer interface to control a robotic arm. So at this point I would like to hand it over to Kim to talk about Spinal Cord Stimulation. Kim?

>>Kimberly: Great, thank you Jen. So you've already heard about different types of peripheral stimulation and brain stimulation, so now we're going to close out this seminar with information about Spinal Cord Stimulation. So there are things that we can, we will show examples of for cervical Spinal Cord Stimulation, thoracolumbar Spinal Cord Stimulation and we're not going to go into it but you can also have intrathecal that provide drugs or medications in the intrathecal space, spinal cord and canal. So let's talk a little bit about um the types of devices that are available for Spinal Cord Stimulation and just advance this slide here. Jen, you may have to help me advance this slide here.

>>Jennifer: Let me try it again, there you go Kim, try that.

>>Kimberly: There we go. So Spinal Cord Stimulation devices, they have three components that you can see here examples on the screen. One of the components, an example up here, includes the implanted electrode and what I'm describing here are all implanted devices. The implanted electrode, you have the implanted postgenerator or the stimulator and there are six different examples here. One is Medelectronic, Boston Scientific, St. Jude and Nuvectra, these are all different variations that provide different types of stimulation and then you have an external component of it, which is an example here with this black remote control basically. This is external controller of the internal implanted device. So we call these hybrid systems because you have the implanted devices and external control unit and for

um the most popular use of Spinal Cord Stimulation is for pain management and it uses the electrical stimulation over the spinal cord to block or interfere the pain pathways that go up to the brain through the spinal cord so different signal is produced. Spinal cord stimulation has also been used to try to decrease plasticity and when you are going to use these in addition to if you were going to use intrathecal pump for plasticity or drug delivery, you need to do a trial, an initial trial first with a physician and if the results are effective for you, then they will actually do the full surgery to implant the device in. And the user has the ability to keep the system on permanently or use as needed per the different parameters of the device. So now we're going to talk about a particular application of Spinal Cord Stimulation that has received quite a bit of press over the last couple years. And that's called epidural stimulation. And I want to describe this figure here first because what this diagram shows here on top is that almost every traumatic spinal cord injury is not really completely cut in half. There are these areas of fibers around the industry site. So even though somebody may be called neurologically complete or functionally complete they are not necessarily anatomically complete unless there was an extreme trauma that cut the actual spinal cord physically in half. These fibers are important because they create a substrate or platform that you can promote different types of functional recovery. So you can use stimulation to try to interact with these or other types of interventions with drugs or therapies to try to interact around here. So what happens though is with epidural stimulation you are going to try to modulate or influence the activity of these fibers and the way that epidural stimulation works is to try to modulate the sensory input to create a different motor output and we already know that with past specific training, for example standing, doing locomotive or sitting to stand or stand to sit, if you do those without any kind of epidural stimulations this is providing sensory input to your spinal cord. So from this peripheral nervous system into the central nervous system of the spinal cord that creates sensory input. What epidural stimulation does is to use that sensory input in a way that makes the amount of information needed to target these motor fibers, so decrease the amount that it takes to activate those motor fibers. So from what we know so far from the data, epidural stimulation is not necessarily permanently changing the connections inside the spinal cord. Now that's also difficult to gather data on in living human beings because the only way you would actually be able to look inside the spinal cord is if someone were to pass away and donate their spinal cord to research or an autopsy. So it will always be difficult to know whether or not epidural stimulation is making permanent changes inside the spinal cord. But the group at the University of Louisville that has been doing the epidural stimulation in motor complete spinal cord injury for a few years now is using an electrode that lays on top of the membrane that surrounds the spinal cord down in the lumbosacral area of the spinal cord. Then they do different task specific training with the simulator on and uniquely programmed for each person to try to alter the activity in the spinal cord, lower the threshold it takes to induce motor activity and create output that way. So we have a couple different research studies that we want to talk about and the first two are clinical trials that are ongoing at the University of Louisville using epidural stimulation and the first one here, which you can look up on www.clinicaltrials.gov, you can enter this number in which will take you straight to the page that talks about this particular trial and this trial is recruiting cervical injuries and thoracic injuries to implants epidural stimulator to see whether or not that influences the ability to stand and step along with path specific training. The other study they are doing, for cervical spinal cord injury, is also using the implanted epidural stimulator to see whether or not they can actually improve cardiovascular and respiratory function. So cardiovascular is actually part of the autonomic nervous system temperature that I explained and then respiratory system is your breathing ability, your lung capacity. Is we know that locomotor training can have many effects aside

from walking and so it is important to test whether or not the epidural stimulation also has this other thing. So there are a couple other trials that are ongoing, this particular trial here is University of California in Los Angeles and you can look up that specific trial with this number on clinical trial.gov and this trial is using an implanted spinal cord stimulator to modulate the signals in the spinal cord to see whether or not they can improve the ability to move arms and hands in individuals with cervical spinal cord injury. And then we also have another study that is being done at Case Western Reserve University in Cleveland that you can look up the trial information with this number again and they are using implanted Spinal Cord Stimulation to try to restore effective cough in those individual watershed chronic cervical spinal cord injury. Then we have a couple trials that are using external stimulation and these are both at the University of California in Los Angeles again and the first one is using transcutaneous, which means across the skin from the outside in, electrical spinal stimulation to try to measure one, whether or not there is any spared activity in individuals that cannot walk with spinal cord injury. That's the first component. And then in those individuals, in that transcutaneous stimulation, actually be a useful rehabilitation tool. And that trial was taking cervical and thoracic spinal cord injuries. Then finally we have the other trial at UCLA that is using external spinal stimulation to try to improve the ability to enhance arm and hand function in those individuals with cervical spinal cord injury. I encourage you to go to www.clinicaltrials.gov and read more information on each of these different studies. So finally here we are going to wrap-up with some of the resources or things to consider when participating in any clinical trial, either with nerve stimulation or any other types of intervention, is to really know your rights and know your risks. You have to be informed and you need to read the details. You should understand what commitments you are actually making to the research team, how much time, how many days do you have to go and get evaluated and you should expect to be evaluated here, should expect follow-up. You should know what kinds of improvements, finance, in a research trial you may expect. Remember research trial is an experiment that needs to be done prior to something becoming commercially available and also you really need to be aware of trials or ''treatments" that are not really being approved. For example, for any legitimate clinical trial you should not be asked to pay for treatment, it should be free to you and you should expect the follow-up that is free as well. So always do your research, you know, get a second opinion or a third opinion. Contact people at the different research centers or hospitals. Contact United Spinal and they have connections to different research centers. So you can always get extra information about different research trials. And the clinical trial website really is a wonderful resource. Not only do they have this listed here that you can learn blood pressure studies and about clinical trials and what you should expect. We also have a few other resources here, when you go on to clinical trials.gov you can use many of these different search terms to find out more information about nerve stimulation trials that are out there. We also have, this project we do have a clinical trial ongoing using deep brain stimulation for severe pain resistent to treatment. Then the Neurotech Network has fact sheets you can look at for different conditions as well. And you can go to the website, go back here real quick and download this information booklet about types of questions and what you should know for different experimental treatments for spinal cord injury. In the back there is a table that has several different questions that you should ask and expect answers for and you can download that at our website here. So we're going to conclude there and we would like to just mention that we will be giving another Webinar in October on management. We would like to open up for questions now.

>> Bill: Thank you Jen and Kim, we do have a couple questions, I will categorize as one brain related and a couple that are not surprisingly spinal cord related and you did sort of address this, but it's maybe

there would be more to add, I'm not sure. Has there been any progress in the spinal cord stimulator trials of type used in paraplegic I can't in Louisville Kentucky and my take on that, it was a surprise at the time and there may be follow-up research in that area. I was wondering if you, either of you had heard about any progress towards a follow-up trial after the somewhat surprising discovery of this motor function during stimulation.

>>Jennifer: Either you or me. [LAUGHTER]

>>Kimberly: Go ahead and start.

>>Jennifer: Okay sure the study looking at those four gentlemen in regard to epidural stimulation for chronic spinal cord injury, that is an ongoing study and they have opened it up to more participants from the last presentation we saw it was I believe nine participants they have now. Nine or eleven I think Kim, either one of those. But it is an ongoing study where they are still looking at more participants and the results of those. Kim you want to add --

>>Kimberly: Yeah I would just say that it is what we might consider to be a Phase 1 trial because they are still looking at the different safety parameters of different types of stimulation and how effective those are in different situations. So it will take a little while for it to open up to large numbers of people. From my understanding they are still recruiting.

>> Bill: Okay, that part is good information to know of course we get speculation and we get the questions that are speculative in nature. In the resource center, you know, understanding in a laymens view that the spinal cord stimulator was affecting one leg, would there be a model of stimulator that would affect both legs purportedly for stimulating the walking action, but possibly that's far off from what I'm hearing between the lines, would that be accurate?

>>Jennifer: It is, again like Kim had mentioned it is a Phase 1 trial, so Phase 1 trial start looking at safety and effectiveness or efficacy. So that's really the goal of those studies, so the anecdotes that come out of it that we have seen a lot in the press are, are really encouraging. However, they still are collecting that data to really truly understand the safety and true effectiveness. So trying to use it on multiple participants and that's why the participation in the clinical trials are so important.

>> Bill: Okay, thank you. The brain related question has anybody looked at changes produced in the brain from peripheral nerve stimulation I guess long-term changes?

>>Jennifer: Those are ongoing studies to truly understand what is going on inside the brain and particularly a lot of that is coupled with the studies that are using brain stimulation coupled with rehabilitation. So that in terms of being able to monitor the brain to see the impact of it in terms of rehab, those are still ongoing studies, so I don't think there is any conclusive evidence yet of what is going on. We do understand changes in neural activity in the brain, but we are not sure exactly what. Now in being, in terms of monitoring the brain coupled with rehabilitation without stimulation and just rehab, I don't know of any results off the top of my head. Kim, do you know of any?

>>Kimberly: No, no, uh-huh.

>>Jennifer: I hope that addresses the question.

>> Bill: I believe it does and if anyone has questions we have time for maybe one more question at the end there was, really a lot of fascinating detail on the basic nerve function and the progress and basic nerve stim research as well as in the areas of the brain and the area of the spiem cord, so thank you both for that great detail. I may have one more comment, not so much of a question person comments that I had an implant done, honestly had no luck with it. So sometimes these procedures are um noticeably effective and sometimes apparently not.

>>Kimberly: I would say that is particularly true with pain modulation. It is not, the pain stimulation for pain is kind of dependent upon each person and don't really understand why yet.

>>Jennifer: It's true, thanks for bringing that up Bill, not all stimulation is good for every case and also what else I would encourage as well is that there is a lot of parameters that you can play with or you can, you can tune if you will, the system, to be able to change for instance frequency or pulse and to see if that would improve the stimulation that's actually being delivered. So the new systems that are coming out are much more robust to allow to be able to adjust those parameters. Maybe if it is not working, for instance the first trial, it is worth going back to see if you can change those parameters to see if you can come out with a more effective treatment.

>> Bill: So I have a two-fold question, two-part question from the same audience. Why the designation of complete versus incomplete if we recognize complete doesn't really mean that and doesn't that harm that designation, doesn't that harm the ability of patients considered complete for recovery, treatment, participation and trials? So the completeness versus incompleteness diagnosis versus, you know, the ability to participate in certain trials. Would one of you wish to address that?

>>Kimberly: I can address that. The complete versus incomplete has become used very popularly and it is really only in reference to one specific examination and American spinal injury examination. It looks at ten muscles, five in each arm and five in each leg and then it looks at like touch and pinprick sensation in the different dermatomes of the body and the designation of complete versus incomplete is based only on those parameters and that tool helps clinicians with different types of treatment plan and it is not, it has become very popular, you know, as a result of many different things. Now when it comes to being screened to determine your eligibility for a clinical trial, that examination may be one component and most likely it is not going to be the only thing. Investigators do a lot of different assessments to see really what your whole picture looks like. And depending on what the trial is for then, you know, they may look at many different other types of evaluations to determine your appropriateness for your trial. It doesn't really harm people's ability to qualify for trial.

>> Bill: That's excellent, thank you I did not know the answer to that and I'm informed by your answer there as well Kim. We have time for one more question um does the benefit decrease with passage of time? Now we have no more detail there, recently here we are talking about epidural stem or really I guess the question could be answered on basis of all of the types of treatments that you've mentioned today but the question does benefit increase with time?

>>Jennifer: It might of been reference to using stimulation for rehabilitation and I think that's still an unanswered question as to what the long-term affect is. For instance the going study going on in the US but it is approved over in Europe using vagus nerve stimulation for the restoration of upper extremity function um there is still truly trying to understand what long-term affect of that is. Now they know it has a therapeutic effect meaning we can apply stimulation, apply a treatment, take it away and there is

still voluntary function remaining, the question is how long is that voluntary function remaining. We know that it has been a year or two, but they don't really know from a long-term stand point how that will stay. So I think that's what that question is alluding to, typically if you have something implanted and use it on a regular basis constantly it is applying a treatment, if you will.

>> Bill: Sure. Well thank you. On behalf of United Spinal Association I'd like to thank Jen French and Dr. Anderson-Erisman for sharing professional knowledge today on important topic of what you need to know about direct nerve stimulation. Thank you so much Kim and Jen.

>>Kimberly: Thank you, it was a pleasure.

>> Bill: Please join us for coming Webinar presentations including third in series on employment with a disability. That presentation will be August 18th from 2 to 3 pm eastern time with Barbara Cornblau. To join up and receive Webinar announcements Advocacy Alliance, visit spinalcord.org or publication site Newmobility for coverage of everything active wheelchair users need to know. This will conclude today's presentation and thank you for your time and attention to this important topic.