CURE Epilepsy Webinar
Advanced Imaging in Epilepsy: How MEG Can Assist in Surgery
Presenter: Dr. James Wheless
(Transcript)

Dr. Laura Lubbe...: Welcome, everyone to today's webinar. I'm Laura Lubbers, and I'm the Chief Scientific Officer of CURE Epilepsy. I want to thank you for joining us today. Today's webinar is entitled Advanced Imaging in Epilepsy: How MEG Can Assist in Surgery, and it's intended for everyone, including persons with epilepsy, caregivers, and physicians. In the United States alone, approximately 4,000 surgeries are performed each year to treat epilepsy in comparison, an estimated 100 to 200, 000

[00:00:30] people may benefit from epilepsy surgery.

This significant gap between the number of people who could benefit from surgery and the number of surgeries performed could be reduced by procedures that can more easily identify patients who are good candidates for surgery. Magnetoencephalography, or MEG for short, is the newest, most advanced

[00:01:00] technology that can help close this gap. MEG can pinpoint the source of abnormal brain activity associated with seizures. It's painless, safe, and requires only one and a half to two hours to perform. Ultimately, MEG can help surgeons decide if someone should pursue surgery.

Use of MEG may allow more patients to be identified for surgery and potentially lead to greatly reduced or no seizures for people. This webinar is brought to you in partnership with our friends at MEGIN as a part of CURE Epilepsy's 2022 Leaders in

[00:01:30] Research Webinar Series, where we highlight some of the critical research that's being done on epilepsy. Today's webinar, like all of our webinars, is being recorded for later viewing on the CURE Epilepsy website. You can also download transcripts for all of our webinars for reading.

For over 20 years, CURE Epilepsy has raised millions of dollars to fund epilepsy research that supports our mission, which is to find a cure for epilepsy by

[00:02:00] promoting and funding patient-focused research. CURE Epilepsy provides grants that support novel research projects and that advance the search for cures in more effective treatments. Today's webinar attendees will learn how MEG is a key part of epilepsy surgery evaluation, including information about how MEG works, and hear about how MEG can help surgeons by mapping key functions such as those involved in speech, motor, and vision for use in the operating room.

[00:02:30] Today's webinar will feature Dr. James Wheless. Dr. Wheless is a neurologist and researcher whose work is focused on pediatric anti-seizure drug development, the ketogenic diet, epilepsy surgery, and noninvasive brain mapping. Dr. Wheless is a professor and the Le Bonheur chair of pediatric neurology at the University of Tennessee Health Sciences Center in Memphis, Tennessee. He also serves as the director of the Neuroscience Institute and the Comprehensive Epilepsy Program for

[00:03:00] Le Bonheur Children's Hospital. Dr. Wheless is also an adjunct faculty member at the Department of Pediatric Medicine at St. Jude Children's Research Hospital.

Before Dr. Wheless begins, I'd like to encourage everyone to ask questions that we'll address during the Q&A portion of the webinar. You may submit your

[00:03:30] questions for Dr. Wheless anytime during the presentation by typing them into the Q&A tab located on your Zoom panel and click send. We'll do our best to get through as many of the questions as we can. While we do want this webinar to be as interactive and informative as possible, we do want to respect everyone's privacy, so we ask that you make your questions general and not specific to a loved one's epilepsy. With that, I will turn it over to Dr. Wheless.

Dr. James Whele...: [00:04:00] Thanks, Laura. It's great to be here and great to be part of this wonderful series that CURE is involved with and the driving force behind. It's an organization that I've been involved with for 23 years, so I'm happy to still continue that involvement. It's great, like I said, that you're getting this information out to a lot of the families and patients that really otherwise wouldn't be able to access it. It's a wonderful undertaking.

[00:04:30] But what I hope to do over the next 30 minutes or so, I want to leave enough time for some questions, is take this very sophisticated imaging technology that has really improved dramatically in the last, I would say, five years, and a lot of that is to tell folks the same reason that few of us have the same cell phone that we had two or three years ago, or even especially five years ago, is because the technology has jumped ahead. Just like in our personal technology that we all love, medical technology is benefiting from that as well.

[00:05:00] It's a little bit slower maybe sometimes to jump because of the regulatory hoops that it has to go through that personal technology does not have to jump through, but it still has made impressive advances because of the advances in electronics and technology that really makes some of these things that in the past maybe seem like they were a little bit out there, really practical and part of what we're using every day to help figure out what's best for patients. Obviously, today, what I'm going to talk about is magnetoencephalography. That's a mouthful, so often we shorten it and just say MEG.

[00:05:30] [00:06:00] I'll show you where that comes from as we get into this as well and how that fits in with evaluating patients for surgery. Before we get into MEG, I thought first step is to just briefly highlight why epilepsy surgery. Laura gave away most of my talk in her two-minute summary. I was like, "Oh, we could be done almost." Then I'll just quickly show you some of the kind of underpinnings, if you will, of how MEG works and then actually some real life kind of patient examples of how we fit it into the streamlining, as she said, the evaluation for surgery and making it work for our patients. Having said that, let's see, we'll get things moving forward here.

[00:06:30] There we go. That should work. There we go. Yes. Everybody's familiar with this, but once you're diagnosed with epilepsy, medicine is where almost universally everybody goes from the get-go. If that works, great. If it does, you probably wouldn't be listening today. But if it doesn't is when we have to look at our other options. I'll just remind folks that we have kind of four categories or four buckets, I guess if you want to think of it, of options as we sit here today. We probably have a fifth one that's going to hit some of our patients that's not far off, but that'll be another CURE seminar down the road maybe next year sometime.

[00:07:00] But as we sit here today, we have medical therapy, surgery, which is what we're going to talk about today, device therapy, and dietary therapy. The only thing I want to say upfront is while I'm talking about epilepsy surgery, keep in mind that these four different treatment options are not mutually exclusive. We have many patients that have hard-to-control epilepsy that need combinations of these. They may need a device surgery and medicines to get to that seizure free stage. Don't interpret this as these are exclusive. I always kiddingly tell folks this is not. Let's make a deal. You don't have four doors and you only get to pick one and you're off the show.

[00:07:30] You can keep going back and pick another door if you're better or if you're not as good as you think you need to be. But for today's talk, we're mainly going to be focusing on surgery. Why is that? You've heard a little bit about this, but just to remind you, we see patients with epilepsy. Our goal really, medicines is where we go. Ideally, one medicine or a couple well-tolerated, minimal side effects to get to that seizure freedom or cure them of their seizures. I'm going to use cure here in [00:08:00] the sense that they're seizure free, tolerating their medicines well. That's maybe a little bit different than you might think about traditional cure.

If I had a bad let's say ear infection and pneumonia, got put on antibiotics, when I finish them, I hope that I'm done with my medicine and I'm cured to my pneumonia, if you will. That's not quite the same implication here, but we're still trying to cure the patient other ongoing kind of symptoms, in this case, the [00:08:30] seizures. That's still where we'd like to get to. Someone with refractory or hardware control seizures, refractory epilepsy, we're still trying to get there. We're evaluating them, and then we're making that decision. For those folks that we do the evaluation... Let me see. There we go. Surgery as an option.

The reason that we're talking about that is because of all of our options, once medicine is not working for you, surgery has the highest rate of getting you and [00:09:00] keeping you on our goal of seizure free. That's why people sometimes ask me why the emphasis on surgery, it seems dramatic, and the emphasis is because that's what gets us there. If you can have surgery... I'll mention today, obviously, not everybody can have surgery. Sometimes our testing helps kind of make that decision as well too so that those families can move on with other options, which is important for those families as well too.

[00:09:30] If you're not surgery, we talked about devices, dietary therapy, and then we're still trying to do well by the patient, improve their seizures, their quality of life. Surgery is what we're going to be focusing on and where MEG fits in with that. I just want to remind you, once a patient has hard-to-control seizures and we're thinking that, okay, we've got to do something other than medicines, where do we go? Basically, our testing goes from noninvasive, what we as physicians would call it. I think with [00:10:00] patients would view this as non-painful hopefully, easier to do, not painful, whatever term you want to attach to that.

If we have to make a decision, we get into invasive testing, which could be painful because that involves usually placing electrodes either on or within the substance of the brain. If we can make a decision with our noninvasive test, as you heard from Laura the numbers, the more patients that we can figure out without going to [00:10:30] invasive tests, then the quicker we can put patients from evaluation to surgery, which then helps with that big backlog of patients that she was talking about. Because if I have to do noninvasive and then bring that same patient back for invasive, I've basically taken up a spot, if you will, twice.

Whereas if they could go straight to surgery, I've not done that. At the heart of our noninvasive protocol, there's a lot of other tests, but video EEG just with scalp [00:11:00] electrodes, so electrodes on the surface of the brain, sorry, on the skull, on the skin, not on the brain, are imaging, are MRI, and usually some kind of testing of intellectual abilities, how you think, neuropsychologic testing. We may do other tests. It depends on the patient and on the center, but those are kind of a minimum. MEG we're going to talk about today. And then there's some other noninvasive imaging and functional tests I've talked about here that maybe for another day.

[00:11:30] But MEG, at least, has now jumped up into what I've kind of called the Phase 1A here. We use it a lot with our Phase 1 because it's so easy and noninvasive. Sometimes at the same time. Some immediately afterward. It depends a lot on the site and kind of availability and how that works. But the benefit I think is that if that tells us... Once we do this type of testing or noninvasive testing, it may say, "You know what? You're good for surgery, but we're still going to need to do a Phase 2," which is often stereotactic EEG, electrodes within the brain. It could be electrodes [00:12:00] on the surface, so still intracranial EEG.

But the hope is that if we do our noninvasives, we have enough information that we can say, "You know what? We're good. We can go directly to surgery and kind of bypass this step. We've got all the information we need because our noninvasives have given us that." It's both easier for the patient, but it also allows [00:12:30] us to kind of throughput patients more efficiently. The other side of this is that there are some patients that between our noninvasives and MEG, we say, "You know what? We've got all the information we need to say. Unfortunately, epilepsy surgery is not going to help you.

It's not that it couldn't be done, but there's no point in going through surgery to have three seizures a week before surgery and three after surgery. We need to look at other options." If we can make that decision earlier on, we've actually helped

[00:13:00] folks as well too. Sometimes you know that yes/no, should we be going forward, is a critical branch point and that's where MEG can really assist with our other testing. It's not a standalone test. But with other testing, it can really help make that decision. Let's now switch gears and we're going to look at MEG a little bit here. Before we get into how does it fit in, let me just walk you quickly through what's involved with MEG.

You see the long name there, which is why we call this MEG as well. MEG is [00:13:30] traditionally done. It has its own kind of area, if you will, in the hospital or outpatient. Much like if you went for MRI, there's kind of an area in radiology, if you will, where that's done. This is outside the room here. In the far left, you see the monitors that our PhD is kind of looking at brain activity. There's a monitor over here where they can visually identify the patient during the test. There's also [00:14:00] microphone. They can talk to the patient. This wall here, which is this same wall, backs up to this MEG room. It has a very impressive door on it.

It looks a lot like a bank vault door, but it's very different. This door looks that way because it has to magnetically shield the room. We're measuring very small changes, we'll get to that in a minute, in magnetic current or flux in the brain. These are teeny compared to what is in the environment, so compared to your car, [00:14:30] elevator, you know name it, the earth's own magnetic field. We have to have this room with all the shielding built into the wall, the rooms, the doors, the ceiling, everywhere to shield our patient from the magnetic noise, if you want to think of it that way, that's around them, so what we're measuring is just from the patient.

It's kind of like if you were going into a soundproof room to do a recording and you [00:15:00] wanted no noise from the outside world, because you're going to do a pristine recording of your music group or your voice or whatever you're recording. This is the same concept, but we're not doing a voice recording, we're doing a brain recording, if you will. The patient then is in the room. They can be lying down, as you see here, on their back. Their head would be up here surrounded by this device. This is the MEG machine. It's plastic here. Right below the plastic are our sensors, and I'll come back to those in a minute.

[00:15:30] The sensors actually detect the brain activity. I'll come to that in a minute. They're kept at about minus 270 degrees cooled with liquid nitrogen. That's not cold to the patient, so you can touch us with your hand. They're just on the other side of it. There's a lot of electronics involved with this, but that has to be that way for them to measure successfully brain activity. That's why I said there's a lot of technology [00:16:00] and this uses super conducting technology, the same technology that kind of allows the bullet train to exist, if you will. It's the same technology nowadays that's in airport security.

It's not the x-ray machine that when you walk through, you kind of have to put your hands up and it gives you that ghostlike image of you. But when you walk through, I

[00:16:30] guess, the old fashioned one where you just walk through and it sees if you have any metal, that's using the same technology, because metal generates a magnetic field too, if you have it anywhere. It's the same technology in other areas. All right, so how does MEG work and the advantages of MEG? I'm going to scroll these out. You've heard a lot of these from Laura in the intro. This also shows you what a patient looks like in the machine.

[00:17:00] Here, their head is about to be slid up a couple inches, if you will. It's actually surrounded by that. It's just a little bit below it, but it rests on a pad. You can see, you're not kind of a hidden in the machine like you are in MRI. Your head's covered, but your body is kind of out, if you will. It's not as claustrophobic, I guess is a good way to put it. But there's no needles involved, so it's painless. The machine is actually recording your own brain activity. It's not giving you any x-rays. It's not subjecting you to any magnetic field. It's recording from you, so it's safe. The nice part about that means that you can repeat this.

[00:17:30] If we do a MEG study and we get information and we say, "Gosh," we look at it and we say, "Oh. After the fact, if we would've known we were going to see this, it'd be nice to do this," we can bring the patient back and re-look at it. Now, we don't need to do that a lot, because we try and get it correct, if you will, their first time. But if we have to, it's an easy test to repeat because there's not anything involved as far as needle stick, anything. We're trying to detect these very small signals from the brain, and we actually are tracking those signals in real time as they go through

[00:18:00] the brain, literally a fraction of a second at a time.

[00:18:30] We can divide a second up into hundreds of a second intervals or less, if you will, and look at that activity, so much like if you were tracking a signal through a computer, think of the brain as a computer, the same thing. And then I'll show you that when we combine this with MRI, we can not only track it, but then we can place it in the brain exactly where that's occurring as well. That's a quick little overview. Let me just highlight some of that, the instrumentation. I won't try and make anybody here a physicist, because I am not one either, keep that in mind, but just to give you an idea.

[00:19:00] The plastic shielding that I was talking about, if you strip away that plastic that's there that the patient's head's going into, you see all these little tiny sensors. Typical machines will have several hundred of these, anywhere from a couple hundred to 500. There's lots and lots of them. They're literally this size, about an inch or so across. These are detecting this very weak magnetic field in the brain from the area that's underneath them. One of the advantages you can probably see from this already is we're detecting all the brain areas. If you had EEG electrodes, you probably wouldn't have them going this low on the head or this far down on the forehead.

We really are able to cover, if you will, the whole area of the brain with these.

[00:19:30] There's lots of them. We cover it pretty thoroughly as well. This is what it's doing. On the left side, I'm kind of a cartoon here, but it's showing you the cells in the brain, if you will, that are in a group. I mean, we're not recording from single cells. Typically if you have epilepsy, if you have an abnormal area that's generating seizure activity, it's hundreds of thousands to millions of cells. It could still be a small area, but it's a lot of cells. For the purpose of this picture, I'm just showing you how they line up. The electrical field is there. That electrical field will be generated by that group of neurons.

[00:20:00] And then what we're trying to do is measure that outside the head. Here, now we've got our head involved. Here's our electrical field. It's going to spread and spread and spread. If it gets outside the head, that's where we are trying to measure it. Our probe or our detector in our MEG is measuring that kind of flux of that electric current. The technology takes advantage of something we all learned, [00:20:30] depending on how old you are, either in college, high school, middle school, or nowadays grade school probably, which is what's called the right-hand rule, which means that if electricity is throwing in the direction of my thumb, the magnetic current is flowing in the direction of my curve fingers like this.

That's always flowing around electricity in something, in this case, electricity in the brain. This is our electricity and we're measuring it. That magnetic field that's there [00:21:00] is why sometimes if you're at a public event, you'll hear that squeaking noise or high pitch squealing noise we all hate when microphones get too close to other electrical things because their magnetic fields are overlapping from the wire and they're creating that feedback within the system as well. This will give you an idea once we put all our sensors on our head and then our patient now is sitting up with this surrounding their heads so we can record a whole head activity.

That gives us a recording, but it's in space, if you will, around our patient's head. [00:21:30] The next step is to say how do we get that onto their actual MRI? The way we do that is by registering it with kind of three points, if you will, on the patient. We use the patient's actual MRI, so we can register a point right above their nose, between their eyebrows, same point the back of their head, just in front of their ears on both sides, and then the crown of the head. If we know those when they go to MRI, then all of our MRI images are linked to those coordinates.

[00:22:00] And then when they come in for MEG, we can register those points just by touching them with the MEG probe and then the computer knows where those are in relationship to the activity it's recording. When we do our MEG, we basically kind of say, okay, we've got our functional data from the MEG. We can then combine that with our MRI, so our high-resolution pictures, if you will. And that gives us the data I'm going to show you, which technically is called a magnetic source imaging. We [00:22:30] tend to just refer to it as our MEG image and leave it at that. But that's how we get to an actual image of a patient.

[00:23:00] These are real image patients. That may be more than you wanted to know about the MEG physiology and some of the physics, but let's look at what do we do with that with real patients and how do we put it into our evaluation. I would say the two primary roles are to help localize or determine where are the seizures coming from, where is that spot in the brain that we can say, "You know what? This is really telling us your seizures are coming from this area." Typically, we're looking at activity between seizures. It's very uncommon we record a seizure, because as Laura mentioned, our entire MEG study may only last an hour or two.

[00:23:30] Even some with frequent seizures, it's pretty unlucky or lucky, however, you want to think of it, that they would have one during MEG. Some have been recorded. If that happens and the patient doesn't move enough that they move out of the recording field, that's helpful, but it's not common. Usually, that's the rare, rare exception that we get that. And then we also use it to do some of the functional mapping, which I'll come back to. Let's look at the epilepsy side. I want to just kind of highlight how we do this. The MEG will have hundreds of channels. I've not listed them all because you can't see them all here.

[00:24:00] You could have several hundred up to 500. We have usually scalp EEG at the same time. You don't have to have that, but we do. Here, I've just taken a snapshot to show you and highlighted it in color, but this is our abnormality between seizures, what's often called epileptiform discharge, highlighted nicely on MEG. If we look on scalp EEG down here, you can say, "It looks like something's different there than these other channels, but it's not as clear." Here, it really stands out. The reason it really stands out is because when we record scalp EEG, it has to be filtered through the brain, through the skin, through the skull, get up to my electrode, and all those [00:24:30] could modify it.

[00:25:00] When we record the magnetic waves associated with it, they're not affected by all that tissue. In other words, they go out without being dampened, if you will, whereas the scalp electrical change is. And then you can see, we can then figure out where that is on the brain. We then put that on the MRI I showed you and we can say, "Okay, all of these are nicely lining up in this particular patient right along their perisylvian gyrus, where on MRI we saw a structural change. This is a family that literally just having this MRI and the MEG, we're still going to record their seizures, but we're really pretty confident that we can tell them, "You know what? We know where your seizures are coming from. These all are lining up there.

[00:25:30] You've got a structural abnormality. Usually, they are the cause of your seizure until proven otherwise. And that's the only spot we're seeing in abnormality more importantly." This really would make us encourage this family to say, "You know what? Surgery is something that looks like could be really beneficial to you and should be really thought of from a practical standpoint." What about somebody like this? This is a patient where MEG really helps us because our EEG does not do as well sometimes. This is someone who's had prior surgery. You see this kind of big black hole here? This side should look like our other side here.

[00:26:00] This is our left temporal lobe. Most of our right was taken out. If we look over here, you can see the remnant on the top at the right kind of and there's some at the back. This is a patient that had surgery, was dramatically better, but then had a recurrence of seizures. They were still not as bad as before surgery, but still were happening. Came back for repeat evaluation and we were able to nicely show, yes, there's a nice what we call cluster or grouping of the abnormalities on the little piece of temporal lobe that was not removed at the top, but probably as important [00:26:30] is there was this cluster at the back end that was distinctly different and that's why I've color coded them to help you with that.

They were kind of independent or different than this group here. In other words, this group here didn't happen and then just spread to here. This group happened at times, and then clearly independently, this group happened back here. When we record from scalp EEG on the skin, by the time this one spreads out through the [00:27:00] scalp and the skin to our electrodes, or this one spreads out, they're close enough that the seizure looked identical. There was no difference in the recording. Plus, they have to spread through all this lake of fluid, if you will, had to get out to our electrodes here too, which also makes them kind of look the same, the signal change we see.

This was a nice example especially where prior surgery has happened. MEG is not kind of susceptible to some of the changes that are now there for our electrical [00:27:30] activity because of the prior surgery where it was really helpful because we could talk to the family and say, "Yes, we can safely remove this right temporal lobe that's remaining at the top, but we also need to do about another half inch up the back, which is what happened to this patient, and then we can get rid of all your seizures." It really was helpful in kind of guiding that surgical decision and allowed us to go to surgery without having to do any more than scalp recording and the MEG and the MRI.

[00:28:00] We didn't need to go to any kind of intercranial EEG. All right, finally, this is one of the ones... I almost hate to bring it up, but I would love everybody to have a good surgical option, but we know there are patients that surgery is not going to fix, unfortunately. And like I said, I think in those patients, it's equally helpful to say, "Can we figure that out sooner rather than later in the decision-making?" This is a patient that had intractable seizures, had more than one brain abnormality, and [00:28:30] was sent for possible surgery. The question was, we knew they had more than one kind of abnormality in structure of their brain, but were the seizures only coming from one spot, which sometimes they are.

When we did MEG, what did we see? I kind of color-coded these so you could appreciate it. We saw that actually there were three different areas that we're worried about. The most prominent one was this one on the left in the back that

[00:29:00] you can see in the yellow. There was a separate less prominent one on the right side in the back here, and then there was even a one in the left temporal lobe sitting up here. You could make the argument, well, gosh, if this one is, let's just pick numbers, the yellow is 70% of their current seizures and this is 15% and this is 15%, does this still not help you? Because you could go after this because the yellow was much more prominent on MEG.

[00:29:30] When we recorded seizures, unfortunately, that was not the case. We said, you know what? Even if these were 70%, I think we'd still have enough seizures here, we'd be refractory, so we wouldn't be seizure free. And then the concern was this was also overlapping with vision. Do we want to even dare risk a change in vision if we cannot become seizure free? It really helped with that equation for balancing [00:30:00] what's the risk, what's the benefits, which we have to do with every surgery and saying, maybe we should look at other options. We could always revisit this down the road. But for the time being, maybe we should say what else is an option there as well.

It can really help with that. With some of our patients, it can help guide placement of where we place stereotactic EEGs. Some patients we may still need to go onto that, but the MEG data may help even figure out where we put those, where we place those. Just for sake of time, I didn't want to go into that a lot, but clearly [00:30:30] that's an area that can help us. Let's switch gears and look at the other use here, kind of the second half, which is the functional mapping component, both for language, what we call sensory motor, so my feeling and my moving, and then vision as well. I'll just highlight some of these for you as well.

We can look at all these different functions, so sensory motor I've kind of marked here, vision, auditory, auditory is just do we even hear it, but we can get that, [00:31:00] receptive language, so my understanding of speech if you say something, expressive is me talking. We can map those areas out and literally put them on top of the patient's MRI like this so that our surgeon can know to avoid those areas in the operating room. Because unfortunately, while we can color code them on the imaging for the surgeon, when they get in the operating room, the brain is not color coded. And that would be so nice if it was, but it's not.

We kid our surgeons that that would be great. All right, so let me maybe start off [00:31:30] with the one that was the first one that was done, which was looking at what we call sensory motor function. What we do and you'll see, I'm going to roll a short video here. This is a patient's hand. There's an electrode that's placed here. And much like when I tap someone's knees and do a reflex, there's a nerve that's really close to the wrist there. That with a very mild and non-painful electric signal, we can trigger that nerve and it'll make my thumb twitch. The thumb twitch is not important other than telling me that I'm in the right spot.

[00:32:00] The reason I want to be there is I want to then see when that signal goes up the

[00:32:30] arm, into the brain, where is the part of the brain that ties into that thumb because we need to know where the hand is. And that's where we actually record. Let me see if I can get my video. Okay, let's see. Oops, let me see if I can get that. I lost my video there for a second. Okay, I thought we had that a minute ago. Can anybody behind the scenes... Oh, there it is. Sorry, it just wasn't right over it. If you watch, you'll see we get a slight twitch. It's kind of like when I'm doing someone's reflexes. That slight twitch will be carried upstream, if you will, to the brain.

[00:33:00] We can look at our signal change in the brain, and then we can put that right on top of the patient's MRI and literally get this down to a teeny, teeny area, that small area, and say, "This is hand area. Do not touch that because people do not losing their hand function. At the time of surgery, avoid that." We can stick it on the patient's MRI and our surgeon can pull this up in the operating room so they know exactly where they are as well. How do we use this? Let me just kind of give you a patient here for example. This was a patient that from imaging, it's buried underneath all my markings here, but we knew had seizures and they had what we call focal cortical dysplasia, abbreviated here FCD.

[00:33:30] We knew that was the cause of their seizures, their pattern fit with what we'd expect. Their abnormalities between seizures just on scalp EEG fit. When we recorded their seizures, they seemed to be coming from that area. Our concern was that that was close to hand area. You can see when we did our MEG, this is hand area, these are all our abnormalities basically totally overlapping and surrounding it. We knew that, okay, if we remove this to get rid of your seizures, [00:34:00] you're going to lose your hand function. I can tell you, no one is happy when that happens and no one wants to trade their seizures for that.

[00:34:30] It does help us with other things. I know we're talking about surgery today, but in this particular case, we actually used a device, the RNS device. We put electrodes over this so we weren't using it and then used that to treat the patient's seizures. It can still guide us. This is a patient that was able to have surgery. They had a very low grade tumor back here. We knew from imaging this was likely a tumor. We knew it was close to hand. Here was hand function. Our surgeon said, "It's close, but I can do this and get by without problems." This patient had resection just very temporarily postop for a couple of weeks.

[00:35:00] They had some slight decrease use of their right-hand clumsiness, but it all came back to where they were, which is what we had thought would happen. But this allowed our surgeon to have that discussion with the family in advance without doing any more invasive testing as well. Just a couple other examples to show you. This is a patient that had a known prior surgery again. Felt to be probably in front of motor area on the right side and we want to document that. This is where hand was in the right. We thought it's close, but it's there. We did our epilepsy, our dipoles. One of the things you can see is these were almost all on the front side of that abnormality.

[00:35:30] In other words, they were really more up here in the bottom edge. They, luckily, were not pushing back in the backside, which made us feel even better that we can offer you surgery because most of the remaining seizures are coming from the front end of this, which is further away from hand and from kind of the deep end and we don't have to go back here towards hand. It really gave us that combination of function and epilepsy to go on without having to do anything more evasive. All right, let me just finish up with language. I'll show you the task we do. It's an easy task. We tend to do a listening task.

[00:36:00] The patient has earplugs in. They hear a word. They're just asked to raise their finger when they hear it. The finger raising is not important for the MEG processing. It just helps us know the patient is still awake and they haven't fallen asleep during the task. We give them a few second break. We give them another word. The words are kind of appropriate to the patient's language skills, if you will. Those then generate activity in the brain. You go from hearing it, just like we all [00:36:30] hear noise, if you will, kind of to then understanding what that noise is. In this case, our brain part that is tied into language figuring out that that noise is a word and what is that word.

We can track that in real time through the brain and say, where is language function, and then put that on the imaging. I want to show you this is a patient. You can see about getting ready here. Our device here, it hasn't been lowered. In this case. They're actually doing a visual task, looking at words, but we typically do it playing into the words. With the visual, you can see kind of in cartoon form here, [00:37:00] but the area of the brain that sees things kind of lights up first. We can then track it to an area that's kind of saying, "Oh, that's a language related process. I'm seeing it. It's not a figure," that then will track to both receptive, my understanding of speech, and expressive.

And that happens once you get to be a certain age automatically. You can't say. "I'm not going to do that." It's so automatic that even if patients are lightly asleep, [00:37:30] you can do this because their brain is still trying to figure out what that sound is as well. Your brain just can't help itself. Once it knows how to process language, it hears language, that's what it tries to do. The nice thing is you can look at multiple languages. These are bilingual patients. In this case, English and Spanish. We looked at Chinese, English, Spanish, multiple languages. But for sake of this, these are all Spanish/English and you can see the language maps for three different patients.

[00:38:00] In the first two, the maps kind of overlap a lot. In the third one, it's kind of like someone drew a line in the sand. Spanish is down here, English is up here. This is the border, if you will. You can guess maybe why these are different. These are patients that grew up in households. These are children speaking Spanish and hearing English from all their friends. These are their parents that grew up speaking Spanish, moved to the US, learned English. Their languages are close, but they're

[00:38:30] not mixing. This is why you do so much better when you learn language at a young age as well. Not that you can't learn it at old age, but your brain kind of by then is partitioned it off some, but you can look at the very unique aspects.

[00:39:00] It really can help you with that as well. How do we incorporate this? Language is obviously a key function, so we don't want to mess with that with surgery. Again, this is just an example. This is a patient that had a very low grade brain tumor outlined here. These are the language areas sitting back here. In the past, we would have put a big electrode on the surface of the brain, monitored them for a couple days, done language mapping, and then gone back to surgery. With this patient nowadays, we say, "You know what? We're pretty comfortable going directly to surgery based on our MEG data with our other stuff. You just have one surgery instead of two, if you will."

[00:39:30] This is a patient that actually had a congenital stroke. You can see big holes here in the brain. Usually, that's where the seizures are coming from. It was their left side of their brain though. For most of us on the planet, that is where language resides. Very few people is on the right side. There are some, but it's few. The question was, do we have to worry about language here? You can see, there's a teeny bit, but the vast majority is on the right side. In this kind of unevenness, if you will, racial language is normal in all of us and this told us that, you know what? Most of the language is all over here. They will do fine with surgery over here.

[00:40:00] They're not going to drop any at all. What little is here, the other side will compensate for, if you want to think of it that way. There won't be a problem. It allows us to move forward the surgery. Now, let me just finish up with this one. This is a tough one because this was a patient that was known to have seizures. The imaging showed this abnormality. The challenge was left hemisphere, normal 15-year-old, normal intelligence, sitting right by language areas. Everybody kind of said, "You know what? You should not have surgery. Don't touch this," but they

[00:40:30] persisted in having seizures. We kind of said, "Let's look at MEG."

[00:41:00] And sure enough, they were pretty close, right? Here's our tumor, here's our receptive language function, here's our expressive. Our surgeon was able to use this, talk to the family and say, "I can approach this in a way that will only get the tumor. I will not interfere with language function," and could literally sit down with them calmly like we're doing now, have that discussion, show them the pictures and answer questions before surgery without any invasive testing. This is someone that went to surgery and is now tumor and seizure free. Just a huge advantage in these kind of patients to be able to do it.

The other thing we've done, I alluded to this, but you can look at these with someone asleep even too. We realized that not all of our patients can lay still for an hour to two hours on their back in a machine and cooperate. That's the ideal. But for some of our patients, that's challenging, even though they're kind of not in a

[00:41:30] claustrophobic MRI-like room. If we need to have them lightly asleep, we can give medicine to help with that. We can still record the epilepsy component. In a lot of patients, we can get language and usually sensory too. We can still get many of these even without "patient cooperation" with them asleep.

If we can do it awake, that's our preference, but we don't have to. The vast majority we can get this even asleep. Let me just finish up, take home message. [00:42:00] You heard it's a very safe, user-friendly way to get functional data, but also our epilepsy data. We can marry those two together and use that to help make surgical planning and assist in that. Part of that assistance can be directly going to surgery. Part of that can be if we need intracranial electrodes is guiding placement of those so we do better even with those as well. The beauty is we can actually look at brain function in real time as it's happening.

[00:42:30] In some of our patients, this may even tie into treatment response. I'm going to stop there. I appreciate your attention. This is where I normally am, and I'm actually across the street now in the office building, but where I reside. Happy to answer questions.

Dr. Laura Lubbe...: Wow! Wonderful, Dr. Wheless. That was fascinating. What an amazing technology and what an amazing way to use it to help our epilepsy community. I didn't realize how finely it could identify regions of the brain like that. That's truly amazing. We [00:43:00] will now start with our Q&A portion of the webinar. I know we already have some questions queued up, but if you have additional questions, go ahead and put them in the Q&A portion of the Zoom panel and click send. We will do our best to get to as many of them as we can. Some great questions here already. One is, can a MEG scan identify a misconnection with a hemispherectomy?

[00:43:30]

Dr. James Whele...: Yeah, great question. If someone's had a hemispherectomy, just to make sure everybody understands that, it's a big surgery, but basically what you've done is you've disconnected, if you will, one half of the brain and parts of that brain from the other half. You may have abnormal tissue that's still in place. It can still generate a seizure. But the way I describe it to patients, it's kind of like it's on an island. It can't spread from there to the rest of the brain or to the body, so it's not really causing a seizure, even though it may have nothing but abnormal activity. It's [00:44:00] been disconnected, if you will, from the rest of the brain.

Usually, the best strategy for saying are we confident that's disconnected is to do what we call a tractography. It's a type of MRI imaging where they actually look at the pathways from those disconnected areas and they can see have they all been cut. And that's probably the best way to look at those, because MEG picks up abnormal electrical activity, and that abnormal electrical activity is still going to be [00:44:30] sitting there because it hasn't left that area. The question is, is it confined there, and that's where the tractography helps us better.

Dr. Laura Lubbe...: Addition of another test, but great. This individual writes about having a pacemaker and also having a MEG test. One of the concerns is that the device may cause too [00:45:00] much noise for the MEG and how well can the MEG reading be cleaned up if a device like that is present?

Dr. James Whele...: Yeah, that's a great question and an area that I didn't touch on that I probably should have for purpose of the time. But their question is great because they've picked up on what I was saying at the beginning that the MEG is detecting these magnetic signals and anything that's metal generates a magnetic signal, which is why we all know if you take a magnet, you go around, you can pick up other things that are metal, right? Pacemaker nowadays, most modern pacemakers and other [00:45:30] metal implants, if you think about dental fillings, more common than pacemakers even, as well could have an associated magnetic field with them.

The brain is small by comparison. They can overshadow, if you will, the brain. In the past, those were a huge problem. With modern software, we usually, I almost say 100%, but we usually can filter the noise out from those and still get the data that [00:46:00] we want in patients that have those. Whereas in the past, we kind of said, "Gosh, that's a deal breaker, unfortunately." Nowadays, we say, "You know what? Let's look at it. Let's get you in the room. Let's see what we're recording." Even if it's somebody that we can just kind of... I guess you would say get in the room and try it.

We're not doing the full recording, but just say, "Let's make sure we're not overwhelmed by the noise," we can just test them, if you will, to see because it's easy to do. You just go in the room and lie down. It's pretty simple to do. But most [00:46:30] of the time, nowadays with our current machines and the software improvements, we're able to record.

Dr. Laura Lubbe...: Wonderful. Wonderful. Great advancements. Here's a question. I'm not sure if it's something you can answer, but I think it's a great question to ask. Is having MEG done something that insurance will cover if a patient is not wanting surgery, but wants to identify where the seizures are coming from? I think this is really [00:47:00] fascinating and an amazing research tool as well. I can understand where this person is coming from. They don't want surgery. They want to know where the seizures are coming from.

Dr. James Whele...: Yeah, no. I will say MEG has been utilized... Obviously, today's focus was on patients with surgery, but many patients get MEG that are not surgery candidates where it's still helpful. For example, for some patients that we say, "Gosh, we think we know your seizure type, but you're responding a little bit differently than the normal person with this." Sometimes using the MEG with EEG really helps refine, [00:47:30] are we on the right track for what we think is the type of seizures that they have? It's been used there.

[00:48:00] It's been used some in folks that have seizures, probably mainly in childhood where the seizures also may be associated with kind of developmental or language changes that are negative to say, "Okay, let's see if we can tease out the relationship of these two to each other." Obviously, today's focus was surgery, but has it been used in other aspects of epilepsy aside from surgery? Yes, as well. The question they asked about insurance, at least at our center and I think most centers, obviously like any test we do pre-approvals so somebody's not out of pocket, a surprise. None of us like that.

[00:48:30] I get it. I don't like that either. Usually, that's not a barrier. I know when we see patients, even if they're from other centers, I mean, I didn't mention this either, but the nice thing is the MEG data can all be kind of put on disk, if you will, or printed out in picture form. It can go back to referring neurologists, neurosurgeon, whoever, for them to pull up. We can even put it on disk so they can pull it up on their own inter-operative equipment to register in their own OR as well. It's portable from that standpoint.

Dr. Laura Lubbe...: [00:49:00] Wow. Wow. Amazing. Here's another, if seizures are coming from scar tissue left from a Gamma Knife surgery in middle age following an AVM removal at 15, so long time ago, could MEG be useful?

Dr. James Whele...: Yeah, I think MEG could be, because a couple things with that kind of surgery is, one, if it was near critically functional areas, so language, motor, vision, it could help figure out that relationship. Even if it was not in one of those areas, if around where the prior abnormality is on MRI, if all of those make dipoles line up all around that, it's really telling you, it's like a big arrow saying, "This is the problem. [00:49:30] This is why you're still having seizures." And then obviously that's a discussion with what are my options to get rid of that problem.

Dr. Laura Lubbe...: I think you addressed this. Again, I'm amazed at the resolution that MEG has. This person is asking about the precision. I mean, clearly, it's very precise, but is it ever inconclusive?

[00:50:00]

Dr. James Whele...: There are times. Just like any test, can you have an inconclusive test? Sure, you can. I would say the benefit of the MEG is that that happens. I will say I've not done this a lot, but we've done this some, we've had patients, their first has been inclusive. We really thought, gosh, we really need to get this data. We've literally brought back the patient a little while later and said, "Let's just redo it and see for whatever reason we can get better data that day," and we've got wonderful data that's fit.

[00:50:30] The analogy I would give folks, it's kind of like many of our patients that have seizures have gone for EEGs and at some point in their life they say, "I have several normal EEGs or inconclusive, if you will, and then I finally got the one that showed my doc, yes, I have epilepsy. This is an abnormal EEG." Can that happen to us? Yes, it can. But the nice thing is, especially if the person can do it without sedation or anything, is it's an easy test to repeat.

[00:51:00]
Dr. Laura Lubbe...: Right. Very good. Great points and great comparison for sure. I always love our audience. They have amazing questions and interesting and deep knowledge of neuroscience. This person asks, are you able to see the dendrites from the machine to determine damage to these after prolonged seizures?

Dr. James Whele...: [00:51:30] We don't visualize the actual structure, which is what they're asking. We're looking at function, if you will. We can get an idea if function has been changed in some other ways that I didn't talk about today. There's other ways we can use the MEG technology to look at function if it's been altered. In the example I would give folks, again, if we look at analogies is I could give my car detail, take a picture of it, make it look great and show it to you, and then say, "Do you want to buy it?" You'd probably say, "Well, wait a minute, can I drive it first? Can I see if the air conditioning works?"

[00:52:00] But if some of those functions weren't quite so hot, that might change your thinking, right? They're looking for, is there a change in structure? Whereas often what we really want to know is, is the function different in the patient, right? I mean, structure, yes, but we want to know how things are functioning.

Dr. Laura Lubbe...: Right. Right. Great point. Great point. You've talked about how you can use MEG, different ways to work with patients who may struggle to sit in the machine for that long, and there seem like a lot of opportunities for people to participate in this kind of testing. But are there patients that cannot have MEG?

[00:52:30]
Dr. James Whele...: They're rare in the modern era. The biggest ones I would say, and they're pretty rare because the technology has shifted for a lot of our implants, I would say if a patient has had, gosh, probably like a really horrible head trauma where they had to have some kind of large bone flap that was metal plate because their head trauma was so bad and they had seizures from that. Even in the modern era, a lot of the ways that surgeons are doing that are compatible because they've gotten [00:53:00] away from some of the older fashion kind of metal ones, because even with MRIs that's a problem. They've kind of had to adapt for more current imaging where that's less of an issue for us as well.

There are rare folks, to be candid. Even some of our patients that have cognitive issues that make it hard for them to understand the testing, if we can do sedation, unless they're just behaviorally and cognitively so challenging that literally the [00:53:30] parents tell us, the caregivers, it's hard to even get them in a car to get to a hospital. Short of that, we can do it. There really are pretty rare exceptions in the modern world. I mean, we call patients, we kind of say, "Here's what's going to happen. Tell us about you," most of those, if there's any odd one there, we can tease it out before a patient's driven to get a MEG or gone through the process, if [00:54:00] you will.

Dr. Laura Lubbe...: I think we have time for one last question. Can you use prior MRI to superimpose the MEG or do you have to have sort of coincident testing done?

Dr. James Whele...: Prior MRI, I will say, sometimes can be used. Political answer here. The reason I say sometimes is it depends how it was done. To get the degree of resolution I showed you, we need what are called really thin cuts of the MRI to be done. Sometimes if they're just doing what I would call a regular run-in-the-mill MRI, say you have [00:54:30] headaches and got MRI, the cuts are much thicker. They don't give us the details that we need to put our data on top of the structural picture.

That's when we end up just saying we can just do part of the MRI over. We just need to do our structural part. We don't need to do the whole 45-minute to hour MRI. It may just take us 10 minutes to do our part, for example. But if they've had a good structural MRI and we look at it, yeah, we can use that. Even my own [00:55:00] patients, if they've had one six months, a year ago, as long as it wasn't so long ago that we say, "Okay, things may have changed," we can use those.

Dr. Laura Lubbe...: Okay, great. Great. Thank you so much. There are a few more questions, but I think we will hold off on asking them. We'll take a look and perhaps send them to you in case we can get a response and then post it on our website is that's okay.

Dr. James Whele...: That works for me. Yes.

Dr. Laura Lubbe...: Fabulous. This has been an incredibly informative webinar. We thank you so much [00:55:30] for your time. I'd learned a tremendous amount about an amazing technology, and I know our audience did as well. If others who have been listening in would like more information about MEG and understand the surgical impact from the patient perspective, please visit our website at cureepilepsy.org/seizinglife, because we actually have a Seizing Life episode with one of our CURE Epilepsy Champions, Kate [00:56:00] Neale Cooper. She talks about how MEG led to a successful epilepsy surgery for her daughter, Virginia.

That's another great perspective to get. As always, we have an amazing audience with great questions and I thank you for submitting those. If you do have questions, we will try to get those addressed. Please send them in. If you'd like to learn more about CURE Epilepsy and our research programs or webinars, you can visit our website or email us at research@cureepilepsy.org. Finally, actually, Dr. Wheless [00:56:30] alluded to this, there's some really exciting opportunities coming forward and we want to share the information that we've had.

Be sure to register for our next webinar, which will be presented by Victoria Titoff from the State University of New York, who will discuss regenerative cell therapies for epilepsy, a new approach for treating epilepsy that holds at least a lot of hope. [00:57:00] This webinar will take place during Epilepsy Awareness Month in November. Stay tuned for more details, which we will release shortly via email and social media. Thank you all again and be well. See you soon.