

DR. BILLIE A. SCHULTZ: For those of you here on time, we're actually going to get started on time because we have a lot of stuff to cover, and we want to make sure we finish. And so when it's the brain practice's turn to give their presentation for Friday conference, and different ideas were floated around, and we thought this might be a good opportunity to talk about some of the current clinical research that's going on in the department. So Scott and I'll be talking about one of the studies, and then at the end, we'll just do a quick blurb on a couple of other studies that we're recruiting. So in case anybody sees any patients that might be appropriate, they can send them our way.

So first, Scott and I-- if anybody doesn't know Scott Miller, he'll be doing the second half of this. We have no disclosures, no financial disclosures, and we're not talking about any off label usage of any products or medications. And objectives. We're going to talk about stroke rehabilitation, past and present, what that entails. We're going to talk about the actual therapy technique that we're utilizing in this study, called repetitive facilitative exercise. And then we're going to review our protocol itself and inclusion/exclusion criteria, as well as the status of where our study stands right now.

So how does this affect you all? Well, therapists, physicians, you all see patients in clinic. You see the typical 78-year-old gentleman who's seeing you for knee osteoarthritis, or seeing you for some other reason, gait dysfunction-- who come in, and, oh gosh, by the way, they had a stroke about four years ago. And they had all their rehabilitation, and they're doing really well, but they say, hey doc, or hey Ms. [INAUDIBLE], or whoever they're seeing, I still have left arm weakness after my stroke. Is there anything new? Is there anything you can do for me?

And back in the day, we would have said, no. More recently, we say, yes. In fact, going back, the historic approach-- this is from Dr. Rusk's autobiography. The historic approach was the old wives' tale was that you had one stroke, and then you sat around waiting for a second one, or a third one, or however many it took to kill you. If you had any type of brain injury at all affecting your locomotive function, everybody assumed your life was finished. Obviously, Dr. Rusk and others have changed that philosophy over time, and we no longer think that. In fact, right now about 800,000 people annually have a new or recurrent stroke. There's about a 3% prevalence of people living with stroke in 2011, and it's one of the leading causes of long term disability.

The other thing that's a little unique about stroke is kind of how the practice has changed over time. So back in 1990-- so not that long ago-- average length of stay for inpatient rehabilitation following stroke was 32 days, a month or so. Now we've slowly decreased over the years. 2007 was the last actual documentation in a study, and it was 16.5 days. Here on the rehabilitation unit, it's about two weeks now-- how long people are on inpatient rehabilitation after stroke. And so the actual practice has changed a lot, and a lot of the practice philosophies have changed.

This makes outpatient therapy very, very important. So I was going to briefly discuss some of the thoughts around stroke rehabilitation and rehabilitation in general. These are going to be a really general. I'm not going to spend a lot of time on this, because I want to leave time for the actual study and the practice that we're using now, but some of the techniques that have been used and are still being used kind of in combination with each other. You won't see a lot of these used in isolation, but proprioceptive neuromuscular facilitation utilizes resistance to facilitate movement. So within a movement, there's resistance of the stronger muscles, and in theory, that will help facilitate the weaker components of the muscle movement, and this is best for use in the flaccid or hypotonic patient, not for the spastic patient, because it can actually worsen spasticity.

Along the same lines, Brunnstrom's technique is best for use in the same patient population. In this technique, we utilize resistance with the stronger muscles, as well as utilizing some primitive postural reactions to facilitate some growth synergistic movement and pattern. The idea is that we utilize these synergies, and that activation will transition into a voluntary activation out of synergy, and we'll be able to develop isolated movement and control further along in the Brunnstrom stages.

So Brunnstrom actually has stages, and over in Europe and in Asia these stages are used a lot more than we utilize these stages here. Going from one to six-- six being normal, one being flaccid-- there's an increase in specificity, an increase in synergistic movements, and then a decrease in spasticity and movement out of-- and then isolated movements out of synergy that develop. The reason I'm bringing this up is a lot of the studies with this particular protocol-- with this particular technique that we're using utilize the Brunnstrom stages to actually characterize who can be included in the study and who can't, and utilize the Brunnstrom stages for progress. So they say, gosh, our average change was from Brunnstrom stage 2 to 4, and so we had to go back and look at these, because it's not something that we actually use very often here.

Bobath technique is actually kind of with the opposite type of patient. This is best used in more of the hypertonic or spastic population, where they're utilizing flex inhibitory movement patterns to inhibit that increase in tone, and the focus of it is beginning with postural control and then beginning to develop more coordination of movements to develop movement initiation, body alignment, to decrease abnormal tone and improve muscle weakness.

And lastly, constraint induced is going to get us into the next phase of stroke rehabilitation. So the constraint induced treatment-- the idea was we're combating the learned disuse of those weak muscles. So we've all seen our patients compensate for the weakness that they have on one side by utilizing the other side, and patients are fairly easily able to adapt to this and able to learn different techniques for dressing, different techniques for feeding utilizing their other hand. The idea behind this is that, well, if we restrain that unaffected side and force them to utilize the affected side, we, in theory, should be better able to incorporate that weaker side and potentially improve some strength.

The initial studies-- the EXCITE trial was the big one that people quote. It's very different than our therapy that we do here, mostly because of the dose of the therapy or the timing of the therapy. These patients-- they had 14 days of therapy, 10 days of supervised training with the unaffected limb restrained. And in each of those 10 days, there was a total of six hours of the supervised training, which is very different from what we can actually provide. They did do one study looking at that dose to see if they made a difference-- three hours versus six hours of that supervised training. And both made improvements, but again, six hours made more, and this just kind of reaffirms that which we know that dose makes a difference when it comes to therapy techniques, as it does with a lot of other things in life.

The one thing that's a little unique about this is the Bobath and Brunnstrom techniques-- they're really focused on the impairment and improving the impairment, or the weakness of the limb, or the spasticity of the limb. This seems a little bit more task oriented or functional oriented, and so it gets into what is currently recommended, which is task oriented training. 2006-- a recommendation was that therapy should be task oriented training, and the buzz words are willful, repetitive, task specific activity. And so when you see patients in therapy a lot of times, they're not just working on getting some strength back. They're working on doing something with that. This addresses more of the activity limitations aspect of their disability, as opposed to the actual impairment.

According to the stroke recovery and rehabilitation textbook by Stein, there are three ingredients that are needed for the perfect task specific training exercise. And that is the task needs to be challenging. The task needs to be progressive and optimally adapted for that patient. And we need to have active participation from that patient in the task.

So how does this affect me? And now I'm talking about me, not you. These are my patients. I work in a brain division. These are the patients that I take care of, and these patients ask me about whether or not anything has changed in the field, especially when they get out from their stroke, and they're like, gosh, I had my stroke 5 years ago, 10 years ago. Has anything changed? Is there any new technique? Are there any new advances?

So how I got involved in this-- I was minding my own business in Virginia. These are just some stills from a documentary that was produced where I did my fellowship. Taking care of great patients, good patient population, and if anybody has any free time, the documentary is about a half hour long, but it's great. I did not make an appearance. I stayed far, far away from the camera crews when they were there.

Then I moved to back here. I'm still all packed up. I hadn't unpacked anything, and Dr. Basford-- I think it was my first or second day back here, and Dr. Basford was like, Billie, would you like to go out to dinner? I have some people I'd like you to meet. So I thought, well, great. I haven't unpacked my pots or pans yet. I'm going to get a free dinner out of this. It's going to be fabulous.

Well, I did get my free dinner, but it wasn't just that. I got a chance to meet [INAUDIBLE] who's a physician from Japan. This is his wife, as well, and a lot of you had the chance to meet Dr. S while he was here. He visited us for a total of eight months during his second visit to really help us get this program off the ground and train the therapist in the technique and everything that we did.

So what I got actually-- free dinner and a crash course on repetitive facilitative exercise. So this particular technique was developed Kagoshima University in Kagoshima. My Japanese is not that great.

AUDIENCE: Kagoshima.

**BILLIE A.
SCHULTZ:**

Yes, thank you, Dr. O-- Japan. And it utilizes the stretch reflex and the skin-muscle reflex, but the unique part of it is the intensive repetition part of it. So a lot of these therapy techniques-- they've been studied. Bobath-- there are numerous studies, as well as the others-- and have not been shown to be any better than conventional therapies. So you just do see this isolated therapy technique. It hasn't been shown to be any better than kind of just doing conventional therapy-- conventional task specific therapy.

Their argument was, well, we still think that these are very beneficial. We just don't think the repetitions are there to show a difference. And so what they did is they actually developed a technique that was suitable for this repetitive facilitation that wouldn't tire out the therapist, in theory, that wouldn't tire out the patients. The patients were in a comfortable position for-- and they could actually do 100 repetitions of each one of these movements in a timely manner. So their hypothesized mechanism is that they actually stimulate the patient simultaneous to the patient actually making effort to move in the direction described or instructed to them. In theory, it elevates the excitation of the descending motor tracks to overcome that decreased excitation due to the stroke.

And so they've published four papers about this. The first paper was in 2004, and this was in hemiplegic lower extremities that they developed the technique for initially. So they had 24 patients in this study, and 22 of them had stroke, and this other two were tumor resections if I remember correctly. And they all had hemiplegia of one lower extremity. Upper extremity was affected in most of these patients, too, but the technique didn't address that.

And they did a multiple baseline study. And so they found that the greatest slope of improvement in the patients was when they were getting the RFE treatment, as opposed to when they were getting conventional treatment. And what they were testing was toe tapping, strength of knee extension, and strength of knee flexion as some of their outcome variables.

And so if you look at-- this was specific for the toe tapping exercise, but if you look at this, you can see that the largest slope of improvement correlates with the RFE treatment in both cases. These were acute patients. These were patients about 1 to 12 weeks following their stroke, and these were patients who were inpatient, so they got the therapy five days a week.

So they said, gosh, that seems really exciting, and they further developed the techniques to involve upper extremity, as well. And so the second paper they published was in 2009, and it was just the case report-- and again, looking at starting with conventional treatment, then going to RFE, then conventional treatment, then RFE, a similar design of study. And this patient was a patient with limb apraxia secondary to corticobasal degeneration.

And so for this particular patient, again, it's just a case report. So I can't say, gosh, is this better than anything else we could have done? Is this just one patient? Would the patient have done this without RFE? I don't know, but the patient recovered the ability to dress, recovered the ability to carry dishes to and from places they needed to go, recovered the ability to chop and peel foods, all of which are important to our patients.

The Barthel Index score did improve from 65 to 90, and they did notice that the finger tapping activity that was one of their outcome measures seemed to increase in speed and frequency more so during the RFE treatments, as opposed to the conventional therapy, but that's all you can say about that. You can't say that RFE was better than conventional treatment in this particular study.

The third study is more recent. It's in 2010. It was published in *Brain Injury*, and this is looking at upper extremity. And this is the study that we're kind of focused on for our project. So 23 patients with upper extremity impairment secondary to stroke. It was a crossover study design, and so the patient had conventional treatment, then went to RFE, or the other group had RFE fee, and then went to conventional treatment. And then they flipped back and forth a couple times.

So in both the conventional treatment group and the RFE group-- so we know therapy is good is what we're getting at-- there were improvements in manipulation of objects. There were improvements in a couple of other areas, but the RFE group-- during the first session of RFE, regardless of which group they were in, the improvements in isolated movements from synergy seemed to be seen. And that's when we're talking about that improvement in Brunnstrom stage that they were talking about.

So my concerns about this is, gosh, are we moving backward? How is this-- those 2006 recommendations of doing a task specific training, which is what we're supposed to be doing-- how is this doing that? Because this seems like it's looking more at the impairment again.

So looking back at their studies, they actually included 40 minutes in each one of their sessions. 40 minutes of the RFE treatment, and then 20 minutes of task specific training. So they did incorporate that in there, as well. So my concern was, are we looking at the impairment and not the limitation? Again, well, not really. We still are looking at the activity limitation.

This is one of Scott's quotes. We need to prime the pump before watering the flowers. We need to actually get the movements before we can do some of those activities. And so the study that we're currently enrolling for-- and like I said, this kind of a recruitment tool for you all, so keep this all in mind, but we're investigating the use of this particular technique, but we're changing the population. All of these studies have been done on acute patients, so we're looking at chronic patients, patients with chronic stroke who have upper extremity impairment and whether or not we can see any benefit of this technique in that patient population.

So inclusion criteria-- we're looking at adult patients. We're looking at patients who had a stroke greater than six months ago. We're looking at patients who have at least 10 degrees of MCP and IP extension and 20 degrees of wrist extension. The reason for this particular criteria is there are a number of different techniques for different muscles. I think there were 16-ish techniques, and the way they're doing this technique in Japan is that therapists are assessing the patient and deciding which technique to use.

We wanted to make our patients look a lot more alike so that we could just say these are the eight techniques that we use, regardless of the patient, so that our therapist wasn't making any decisions about this. Again, trying to keep everybody the same, so hopefully it's a better study design for us. We are excluding patients who have upper extremity contracture, pain, orthopedic, neurologic issues that would keep us from mobilizing that shoulder. We are excluding patients with a higher BMI. We are excluding patients who cognitively, or linguistically, or visual-spatially can't really do the therapy technique. They need to be able to provide consent, and then we are kind of screening-- do they have any active medical issues? Do we think that they're going to be able to be in therapy for the full month?

The technique is actually pretty labor intensive for the therapist. So the therapists wanted to make sure that they weren't going to injure themselves. And we'll show you video of the technique, so hopefully it will explain a little bit more. So the study design is we're getting 40 patients. The patients first undergo an evaluation, and the evaluation includes Fugl-Meyer Arm Score, 9-Hole Peg Test, Box and Blocks, and grip strength, the motor activity log, which is looking more at that activity limitation-- it is a scale that measures does the patient use the arm, and then how well do they use the arm on a zero to five for activities such as cutting food with a fork and knife, drying off their face with a towel? And there are a lot of daily activities that you would use the arm for. We're looking at range of motion, and then just, is the patient satisfied or not?

Then they're put into one of two groups-- either the conventional treatment group, which is everything but electrical stimulation [INAUDIBLE] robotics and then this particular treatment-- and the RFE group, which is the treatment that Scott's going to describe in detail. If they get randomized into the conventional treatment group, following all their evaluations, they do have the option to jump up into the RFE group at that point and go through that, as well.

So the therapy sessions themselves are three days weekly for a total of four weeks. So this is a huge time commitment on the patient's part. The duration of each session is an hour. 40 minutes are spent in the actual treatment, and then 20 minutes are spent in a task specific training activity. Because all the patients who were done in Japan were in the acute setting, they had five day a week therapy, and so in order to kind of make ours as similar as possible, we did provide a home exercise program for the patients. And we asked the patients to do that an additional two days a week. And there are specific instructions. They're taught how to do it, and they get all the supplies they would need to do the home exercise program.

So I'm going to play a short video of the technique, and then Scott's going to take over. There's no sound. And so this particular part is more for looking at the shoulder, but there are-- and Scott will show you-- movements for the elbow and the fingers, as well. So it is kind of labor intensive, and you can see, if you could have a heavy arm, that that might injure the therapist's shoulders if they weren't using proper body mechanics.

**SCOTT A.
MILLER:**

Thank you all for coming this afternoon, and thank you, Dr. Schultz, for including me. I didn't get the dinner out. I got invited to a conference room, and maybe there was a cookie in there. I don't remember. Dr. Basford and Dr. Schultz were like, you want to jump in on this research, and try this? And it became a real big thing.

So we have quite an extensive team of therapists [INAUDIBLE] that have gone through either the training for the RFE or conventional therapy technique. And then we have some blinded therapists that are actually the evaluators that aren't involved in the treatment arm of the study. So these are from our OT and physical therapy staff on the [INAUDIBLE] unit. Oh, there's a group picture of them.

The training specifically involved 10 plus hours with Dr. [INAUDIBLE] from Japan this past spring, where we had very intense training because this is a very specialized manual technique that is used with stroke patients. And so he came last spring. We learned the initial technique. We began patients in the research study, and then he returned here this past fall actually to kind of troubleshoot and problem solve some questions the therapists had.

So as Dr. Schultz mentioned, there are multiple techniques that are used in Japan for RFE. For our study, we specifically were focusing on five patterns that we wanted to address, starting proximally with shoulder flexion, working down towards the elbow, the wrist extensor, and then the hand with the fingers and the thumb. The repetitions are of 100, and that we'll usually-- in most cases, if the therapist and the patient tolerate, we'll do 50 repetitions very simultaneously, give them a short one to two minute rest, where we'll be doing some stretching and relaxation techniques for usually the tone in their arm, and then we repeat the last 50 repetitions of that joint, and then move down. And so it's kind of a sequential progression from shoulder to hand, coming up with 800 repetitions for that session of 40 to 45 minutes. Once that patient's done, then we have them sit up and proceed to working on some functional activities.

The theory behind RFE is actually multi-faceted. We're trying to produce a stretch, or, through tapping and rubbing, a tactile stimulation, as well as then providing auditory cues, encouraging patients to have visual attention to their limb, and then also attending, and trying to volitionally move while the therapist is helping them move. And because of that, we're hoping there's enough stimulation to those movement patterns to elicit more volitional movement. And over time, as they get stronger, you'll see more active movement from the patient.

So this is one of our clinicians just kind of starting to work with a patient. So the first moment we address is shoulder reflection, or shoulder flexion with adduction. We're trying to avoid the synergy pattern that we typically see in the upper extremity after a stroke. Positioning is critical for the patient and the therapist. We're assessing initially their subluxation in the shoulder to make sure we're adequately positioning that joint, so that RFE if he isn't hurting them, causing pain or trauma. Though we do, then, ask the patient to volitionally participate in the flexion or flexion and action motion.

And we proceed down to the elbow, where we're initially working on extension and flexion. And usually, if they have quite a bit of tone for the flexors, we will specifically focus on extension. We're producing a quick stretch in supination and then trying to have the patient actively assist in extending the elbow. We can, at times, use rubbing or tapping of the triceps to also facilitate that. Then if they don't have a lot of tone in their biceps, we will engage them in trying to, through pronation-- quick probation work on that bicep in working on flexion of the elbow.

From there, we proceed down to the wrist. In this slide, it shows that we're using kind of the thumb as an access point, and then through that pronation and supination motion of the forearm, we're providing tapping through the fourth and fifth metacarpals and facilitating that motion, and then trying to assist the patient in wrist extension. So it's that quick stretch and trying to avoid stimulation into the palm so they're not developing a flexor stimulation-- that we're encouraging extension.

Down in the fingers, it's quite a technique that requires a lot of practice, because it is a very highly coordinated activity where you're working specifically on the index and the middle finger. You place the patient's wrist in full flexion, as well as fingers in as much flexion as possible. You're providing then that quick stretch to the extensor muscles and then encouraging the patient. Extend your finger. Extend your finger. Extend your finger.

So we do 50 repetitions to the index finger, rest, and do some stretching. Then we finish the last 50 repetitions. Then we move down to the middle finger and do the 100 repetitions there with the rest in between. After those two fingers, then we go down to the thumb, and we're working on the thumb, working on abduction, as well as flexion. Here's a picture of Carol providing that volar abduction, and then also working on kind of an initial lateral pitch. And so the concept is to really-- I mean, you're doing that quick stretch, move your thumb. Quick stretch, move your thumb. And actually it's surprising how well the patients do engage in that.

Well, this is kind of a collage of the different procedures that the therapists are using during the treatment. So as I mentioned, the goal is to always perform that joint motion and provide 100 repetition. We do provide-- at least after 50-- a short rest for one to two minutes, where we're working on stretching, especially if there is some flexor tightness, flexor tone. We're working on number one there, where we're positioning the wrist in extension, trying to facilitate and stretch that tightness. There's also a facilitatory technique we call scissoring to inhibit the flexors and work on stimulating the extensors, or brushing-- that's another technique that they use along the extensor surface of the fingers, trying to stimulate, of course, the extensors. And then also, if the patient is showing a lot of spasticity or tightness in their elbow, we will use the process of reciprocal inhibition to try to inhibit the bicep by using tapping on the triceps and trying to inhibit that tone during the rest time.

And then in Japan, they also during the break time really feel it's important that, if the patient especially hasn't been able to utilize their hand in a functional task for any period of time after their stroke-- that they lose the arches that are so important in the hand. So this is actually a technique they showed us on how to kind of stretch the palmar area of the hand and work on breaking the tone up in the hand, trying to improve the transverse arches that are really critical for hand function and motor control when they start showing active movement.

So again, as mentioned, we do 40 minutes of RFE. We're targeting that 100 repetitions for each joint motion, and then after the patient gets up, they're usually not very tired after this because we're not asking them to work at their maximum resistance level. We're asking them to try to assist with the motion, but we're not asking them to work at their maximum exertion. And so they're able to get up right away, and then we use what active motions we've noted during their treatment, and provide at least 20 minutes of task oriented activities that are very critical to them, and then reinforce the home program because they really need to be doing that on a regular basis.

So these are some of the suggested activities, especially if they still are having some flexor tone. We will kind of make sure that we're instructing them in weight bearing support through the wrist and hand, and then also work on tabletop activities where the table was kind of a stationary surface where they could work on small movements with the washcloth across the table to maybe a gross motor activity with stacking objects. Here, we're using the cups. If they have a little bit more active motion-- and this gentleman actually had sufficient strength to work with, then, some weighted balls. [INAUDIBLE] some great at strengthening. This gentleman actually had enough fine motor skill to then work with some fine dexterity activities and active movement of the shoulder and elbow, reaching forward, trying to break up that flexor pattern and to stimulate more active reaching.

So and then these are some additional task oriented activities. We try to teach-- have the patient actively help. During the treatment session, the therapist will be there assisting them, if they are weaker, to still complete the motion. At home, we teach them how they do them bilaterally so they're using their stronger arm to actively assess.

So what has been some of the feedback since spring time? This is some of the feedback that initially the therapists were experiencing as we started seeing research patients are performing 800 repetitions on the upper extremity. There was concern related to back strain, proper body mechanics, avoiding injury. And we were feeling somewhat fatigued in that. Not that we're out of shape, but just that we're not used to doing that many repetitions in a therapy session.

Sometimes patients had extremely heavy arms. How did we best manage that? As well as, when tone became an issue and spasticity was present, were we using the best strategies to reduce that to help the patient? So Dr. Megumi actually returned in the fall, and we worked on these techniques. I mean, he helped us to kind of strategize were we sitting correctly next to the patient, how are we standing when we were doing some of the procedures? He really stressed that good positioning and making sure we were close to the patient-- I mean, this is really a manual technique. You're really close to the patient, and you're engaging the patient. Those were really important when you were doing the procedure.

So he showed us how to work at height adjusting our tables and our therapy gyms, using the correct stools, chairs to best work with the patient. So we have a few pictures of that. The first picture is-- I mean, of course, if you had to do 800 repetitions and you were kind of in that kyphotic posture-- and that I'm sure each of us would experience a lot of back discomfort. So he showed us how to kind of work with the mat height, and that modified how close we were working with the patient to, of course, work on our body mechanics. And then because we felt we were OK having the patient work on strengthening and that they were working so hard that we were really tiring ourselves out, he reinforced that they should be submaximal exercises and repetitions.

And then some additional photos of just how to, by adjusting the proximity at the table-- adjust just the chair height, use a foot stool. I mean, it really does help the therapist improve their body mechanic. He also showed us some strategies for using our thigh, our torso to best support when we're doing the exercises and reduce the strain from the repetition.

And then he also specifically worked a few days with some patients that had very heavy arms and high tone, and how we could modify the sequence of the repetitions. And ultimately they would get their 100 repetitions during the session, but maybe you did 25 to the shoulder. Then you did 25 to the elbow. Then you rested. Then you went back and did the next set. So we were able to modify the sequence of the RFE exercises, as well as the number of repetitions, ultimately at the end coming up with their 800 repetitions, but reducing the strain to the therapist, as well as the positioning, and then going into greater detail about that principle of reciprocal inhibition.

What was the client feedback? This is our last slide, and it's been really amazing to hear what the patients actually have said after their month of RFE. There have been little to no pain with that number of repetitions. They felt that, after that, their arm was less tight throughout, and that-- at the session, after the session, less spasticity, and that actually lasted for hours of time after they left their treatment.

And some of the quotes that they were able to share with us-- I can use my arm and hand more in daily activities. My speed of moving my weaker arm has improved. My hand does something more now. So they were able to use their hand and that a little bit more actively. And this one was the one I like the best-- from one of the first patients that was a very high level patient-- active, working, out in the community, and that. With better hand control, this patient noted, my golf is better, because the coordination has improved. So he had gotten enough return in his affected arm and that that he was much better at that. Thank you.