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2010 NEUROFIBROMATOSIS MIDWEST SYMPOSIUM

NF2 PATIENT CARE DELIVERY AT NORTHWESTERN

SPEAKER: DR. ANDREW FISHMAN

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>> Good morning. Ladies and Gentlemen, we're beginning our NF 2 breakout sessions. We have a small flipflop in our schedule. Dr. Ramesh will be speaking at 11. And we're beginning with Dr. Fishman from Northwestern. Thank you so

much.

>> DR. ANDREW FISHMAN: God morning. When I was asked to come speak here, the topic was for me to discuss how we deliver patient care at our center. And then I felt that the best way to describe that would be to explain a little bit first about my background, my specialty as a neurotologist and then go into how patients come into our center, describe the initial physicians that they would meet with, and then how the broader scope of care is then distributed.

I'll also speak a bit about the role of a neurotologist and why that is central to Neurofibromatosis type 2 because many of the issues that arise are within the realm or scope of practice of a neurotologist.

And then I'll describe some of the specific areas of interest, research and clinical development that is specific to our program at Northwestern.

Before coming to Northwestern, I was a partner with Dr. Roland at NYU, New York University, where we worked on a lot of NF 2 projects, patients. We also worked on some of the initial research and development of the auditory brainstem implant and cochlear implants. I've also, for the last 15 years, worked at this University in central Poland where we also treated and took care of many NF 2 patients. As well as between 2005 and 2006, I worked at the Amrita Institute in southern India where we also had a very large NF 2 population.

And here in the United States, I also have an appointment at the National Naval Medical Center. But my primary appointment is at Northwestern Memorial Hospital and the Feinberg School of Medicine in Chicago.

Now, our program is very much so physicians-centric. And what I mean by that is it is really run and guided by the three main surgeons. Because from our viewpoint, NF 2 is largely a surgical disease. Now we have other options, which include radiation and now also chemotherapy, and I'll touch a little bit on the roles that they play from our viewpoint; but many of the patients may at some point require surgery. And being surgeons, our program is largely centered on that viewpoint. So the initial contact for our program is through the physicians, specifically myself, Dr. Bernard Bendok, and Dr. Batjer, who is the chief.

What skull base surgeon means is it's a surgeon that specializes in tumors that arise from the cranial nerves. Like the acoustic neuroma. Also as a neurotologist -- now I'll talk a little bit more about what specifically a neurotologist is and how that differs from the classic neurosurgeon, skull base surgeon. But a main area of specialization in neurotology is the facial nerve. So facial nerve issues are also a very large part of NF 2 care.

So most of the patients do come through myself as a neurotologist, and very often

they come through specifically for facial nerve issues and then transition into care by this team.

And Drs. Bendok and Batjer are specific kind of surgeons, cerebrovascular skull base surgeons. Their specialty training is around the blood supply to the brain. Now, that's very important. That's the reason why I have collaborated specifically with cerebrovascular skull based surgeons is that the tumors that arise from NF 2 are not tumors located inside the brain tissue; they're tissues that surround the brain. And what is surrounding the brain is the blood supply to the brain, specifically the brainstem, and all of the cranial nerves. And that is the area where cerebrovascular skull based surgeons excel in their experience. So we feel that we have a very good collaboration in this sense because the most severe complications can arise from blood supply issues to the brainstem. And that's why I work with these specific gentlemen.

So when a patient comes to our center at Northwestern, it will typically have an initial meeting with myself as a neurotologist and usually one of the neurosurgeons, Dr. Bendok or Batjer, to sort of gain entry into our program. Sometimes a neural oncologist will be there at the first meeting. And there are two types of neuro-oncologists I'm going to discuss. One would be a radiation specialist or a chemotherapy specialist. Often it's not the first meeting; it may be the second meeting. But the initial care is taken up by a team of neurotology, neurosurgery and neuro-oncology. And neuro-oncology in the last few years has been playing a larger role in the care of NF 2.

Back when we started, in the early '90s, there was really no role for either chemotherapy or radiation. So you pretty much only saw either a neurotologist and neurosurgeon. But now with chemotherapy trials ongoing and radiation, we also involve the oncologists.

So as I mentioned, this field of neurotology, which starts off initially from ear, nose and throat, then going into neurotology as specialty training, involves neurosurgery that is around the facial nerve as well as the transtemporal skull base approaches, which I'll show a little bit about what that means. That's all surgery to go to the cranial nerves around the temporal bone regions and the extensions of that bone. And that is the techniques that we use to get in towards the tumors in the most safe fashion.

Because we also deal with hearing issues, implants, auditory implants, that's why a neurotologist is a pivotal player in the initial care in our center. And also, as I mentioned, the facial nerve. Not only surgery around the facial nerves, which is our primary structure which courses through the temporal bone, but also surgeries to reconstruct the facial nerve, facial surgery and other types of muscle

transfers all falls within the realm of neurotology.

Of course, we need a neurosurgeon, not just for the cerebrovascular protection that I mentioned, but because we are removing tumors, meningiomas and there are also spinal tumors. So most neurosurgeons, at least the ones in our center, either specialize in the cranial or spinal surgery. And you'll find that throughout the world, probably, that that is the way they divide up.

So the patients initially come to one of us, who are the cranial surgeons. And then we would involve the assistance of one of the spinal neurosurgeons. So most cases, the initial meeting would not involve the spine neurosurgeons, and then we would get them at a separate time.

And I mentioned the importance already of the management of cerebrovascular system.

We have now antiangiogenesis chemotherapy trials ongoing, which is new. It's only within the last few years. So there has been an increased role for the medical neuro-oncologist to participate in the care of NF 2 patients. And radiation therapy.

Now, radiation therapy in our center is headed by a neurosurgeon. We commonly work with Dr. Levy, Robert Levy, who is a neurosurgeon who also does radiation therapy. So patients will often consult at some point along their care with the neurosurgery radiation specialist. But I do put this under the area of oncology, because it is essentially nonsurgical.

Now, once patients either have surgery or one. Other modalities of therapy, there is what I will call sort of the broader scope of care. Because we're, as I mentioned, physician-centric, we typically call the shots, so to speak, and then communicate with our patients and arrange for them to be cared for by these other specialties, which are very important. Physical therapy is a big part of postoperative care and also post facial nerve surgery care. Ophthalmology. Many patients have ophthalmologic symptoms. Cranial neuropathies of the ocular motor system are also common issues.

We do work with -- I have Dr. Sidle, who is a facial plastic surgeon. And when we do the facial nerve reconstructive surgery, I collaborate with Dr. Sidle because there is two aspects of the repair of the facial nerve. There's the aspect of the function, and then there's also the aspect of the form or the cosmetic elements. And working with a plastic surgeon, we look at both of those aspects together. Typically there's some work that can be done around the eye, either for closure of the eye, some tightening of the lower eyelid, because with facial paralysis, there is increased tearing and laxity. So all of those things are well-handled by a facial plastic surgeon who is also in our department.

>> Can I ask you how you spell his name?

>> S-i-d-l-e. It'll appear again a little bit later.

We also, especially in patients that have either postoperative pain or spinal tumors or trigeminal involvement, there are issues with chronic pain. So we do typically collaborate with the anesthesiology department. We do have a pain center at Northwestern.

Often, these types of services, pain management and physical therapy, we outsource to more regional or local providers and centers because they may require frequent visits. Or if the patients come from far, travel to our center, we will try to find somewhere for them to go for more chronic physical therapy or pain management closer to home.

And then psychological support, genetic support, all of these things are extremely important. And those things, we ask those specialists to get involved, as well. We do have an excellent genetics department at the Children's Hospital in Chicago. And then at some point we ask the patients to have a general neurologist, because there is a phase of care that involves the surgical management, the postoperative management; but then there is, in a sense, a chronic care that needs to be administered in terms of monitoring neurological function and monitoring things, which is often best suited by a general neurologist. Some patients require seizure medications and other sorts of issues. So in having a good general neurologist also involved in the care is often helpful for some patients.

Now, I've already mentioned the importance of the neurotologist. What is a neurotologist? I think I said some of these things already, but I will try to describe to you what is a transtemporal skull based approach? The entire field of neurotology arose specifically for the development of these transtemporal approaches. And in order to understand what that is, I first need to compare it for you to a traditional neurosurgical approach, which would be coming from the back side of the skull.

So here would be the top of the head, the nose area. Here is the back of the head. And the side. This is the inner ear. The balance canals. Here is the cochlea. Here is the facial nerve. Here is the cerebellum. And then the sigmoid sinus, which is an extension of the jugular vein, the main vein that drains the brain. A traditional approach to get into this region where the tumors grow would be to go behind this sigmoid sinus. So when you may hear the term "retrosigmoid approach" or "suboccipital approach," some of these terms may be familiar to you. We're talking about opening up here.

That does require compression and retraction of the cerebellum. And that can contribute to a number of factors: Swelling of the brain postoperatively, delayed

emergence or recovery after anesthesia and surgery postoperatively because of the manipulation of the brain.

So sometime around the 1970s, the field of neurotology was borne out of surgeons that developed techniques to use the temporal bone. This is the temporal bone, which retains these structures, as a pathway to get into this region. And there are a number of those approaches, and we tailor those approaches specifically to the lesion that we are going after.

One can do what's called a retrolabyrinthian, which means staying behind the inner ear but in front of this jugular vein extension, right through the mastoid. And that lets us get to some smaller tumors. And it allows preservation of the hearing function, if there is hearing at that time of surgery in that ear.

We typically use this for some meningiomas, and we also use it for some small acoustic neuromas where hearing preservation is desired.

Then there is the translabyrinth, which is one of the more common approaches where we sacrifice the balance canal system, but that eliminates the rest of the hearing that's in that ear. So we typically use that for large tumors when there is very low probability of saving any of the residual function or in sides where there is no more hearing. And that is a very good approach because it gives not only a direct view, you can see the openings through this channel. And we get to this region without pushing back the cerebellum.

The other advantage of this approach is we find the facial nerve in the bone throughout its course. So it allows us for better control of the facial nerve on both sides of the tumor while these other approaches do not allow for that.

There is also the middle fossa approach, which is a technique that we use to preserve the hearing in small tumors. So if a patient comes to us with a small tumor, we would like to attempt removal with preservation of the residual hearing. And in order to do that, we go on top of the temporal bone. So those other procedures I showed you were going from the back or the side. And this procedure we go above. So we lift up the temporal lobe. And we work in this area. Here is where the facial nerve and the acoustic nerve is, small tumors can reside.

A patient with very small tumors with good hearing may benefit from having the removal with preservation of hearing at an early stage. And that, we believe, is a very good option in patients with small tumors that are detected early.

In some situations, we may still lose the hearing of the ear because the blood supply of the inner ear is taken up by the tumor. The small vessels go through and then the blood supply goes into the tumor. So with the removal of the tumor, the blood supply to the cochlea is sacrificed just by removing it. But in those

situations, there are some patients that are, despite that fact, we have been able to put cochlear implants in to the inner ear and still transmit signal through the acoustic nerve, which is still intact alive, even though the actual cochlea has stopped functioning.

More recently we have been using intraoperative CT scanning to allow us to take out tumors such as this, small to moderate sized, relatively localized, but not extending very far out laterally into the canal. And we take a CT scan in the operating room to just shave away as much of the bone as possible of the balance canal system and still preserve its function while opening up about 90% of the internal auditory canal. So we get an exposure very similar to a translabyrinthian approach with just about a millimeter left on the edge. And that's some of the work that we're doing at Northwestern.

Another class of lesions that we will typically operate on may be tumors that arise off of the cervical nerve movements, and that's not an uncommon place to also have tumors. Here is an MRI scan with a patient. Here's the spinal cord and here's the tumor. And this is located just at the exit point of the base of the skull. And that region is called the foramen magnum. It's the main hole where everything goes down into the spinal cord.

And I want to show this here. This is the vertebral artery. And all of the blood supply to the brainstem comes in through this vertebral artery. That's why it's essential that I collaborate with neurosurgeons who are cerebrovascular surgeons because they operate in this region very often. And we often collaborate together for not only tumors but also aneurysms in this region. So when we address a tumor in this region, we already have a lot of experience opening up this delicate area because of all of the aneurysm surgeries they do here.

Now, another aspect of our center is the research aspect. And right now, we do have a clinical trial ongoing with the antiangiogenic agents. There are a number of centers around the country, but we are able to help patients with either acoustic neuromas or patients with NF 2 into that study. This is headed right now by Dr. Jeffrey Raizer. Some of you may have met him.

We don't know yet how this is going to work out. Do you need to spell that? R-a-i-z-e-r. First name is Jeffrey.

>> Can you give us the date of that inception?

>> DR. ANDREW FISHMAN: Recent. Within the last two months or so.

>> Is it frontal therapy?

>> DR. ANDREW FISHMAN: I believe. It's intravenous. We don't know really what's going to come of this, honestly. These agents work by stopping the formation of the blood vessels to bring oxygen nutrients to the tumors. And we

believe that they may slow growth. There have been some very promising results. But the questions that still remain are going to be the duration of the therapy. Is this something that patients will need to take for the rest of their life? Is it something that we'll be able to give patients for short periods of time to regress the size of the tumor? We really don't know the answers. And we don't know really what the effects of lifelong, very long term administration of these agents is.

I don't want to speak too much about it because it is not directly in my area of expertise. Really, the neuro-oncologists, medical oncologists, would understand this and be able to tell you a lot more than I would.

But I do see that there is a role here because from a surgeon's standpoint, it is more difficult to manage and take out a tumor that is large and putting a lot of pressure on the brainstem. So one of the thoughts that we have is "well, maybe we can use these types of agents to take a very large tumor and make them more of a medium sized tumor." That would help.

Now, one of the issues with that "plan", in a sense, is there are wound healing problems that can arise after therapy. So there has to be a few months' break between any surgeries after these agents. And we don't really know what the effects of stopping it abruptly if it is really a large growth tumor.

>> But still, I keep thinking that NF 2's a genetic disorder. And I keep wondering, okay, it's like all these things are preprogrammed. Tumors to start growing, how big they're going to grow, it just seems like that even if you feed the tumors agents that are going to slow shrinking, can't the genetic process override that and continue the growth of those tumors?

>> DR. ANDREW FISHMAN: That's why our concern of this type of therapy is that we may see temporary effects. But even temporary effects may be useful in the management of a tumor if the plan is to reduce its size prior to some sort of other intervention. That is very much like what we do in some other types of tumors, specifically malignant tumors around the eye and the nasal sinuses and the brain. We do use preoperative chemotherapies to shrink them down away from other vital structures so that when we do operate on them, we have a better chance of either removing them entirely and preserving the function around them.

So, again, this is very new, this type of therapy. So what I'm telling you is sort of what I'm thinking we may end up using this for in the future. I could be completely wrong. We could see long term regression and that would be fantastic. But as you mention, I have a hard time at this point seeing that these agents are going to, in a sense, treat them as a long term curative process.

>> How long actually has it been? Everybody here's heard about it. But it's been over a year, hasn't it?

>> DR. ANDREW FISHMAN: Yeah. And that's a short period of time.

>> So we don't have any history for side effects or when they come off?

>> DR. ANDREW FISHMAN: No. We don't know. How long can we -- typical studies have gone up to about 18 months of treatment. But we don't know what the -- we need agents that are going to work for 50 years. That's what we need. So, some of the other things that we do at Northwestern is I have laser hearing research center, auditory implant research center. This is, again, some things that we apply now and some things that are going to be applied way in the future. So I'll touch a little bit about it.

We are working on using CO<sub>2</sub> laser income with flexible applications. There was a bit of news in the media publicity about that, so some of you may have heard that. It's really a tool, another cutting tool that does help us with controlling some of the bleeding. And it is also a little less traumatic than some of the other instruments. But it's really just another tool. A lot of patients call us with tumors and may have an impression that there's sort of a "magic" laser that takes them out. That's really not the case. It's just another nice tool.

We work with a company that produces it to do safety studies, safety studies around the inner ear specifically.

The other big area of research that we do, which has the potential to be applied in many years from now is with laser stimulation of nerves. And Dr. Richter, Claus Richter, is our main research PhD and myself and our team have been working on this. Right now, auditory, whether it be a brainstem or a cochlear implant, works on electricity. And as you know, if you have a whole circuit that has electric current in it, if you touch anywhere on that surface, you will get a shock, which means that electricity spreads all over surfaces that it contacts.

Laser energy is light waves that are aligned to go straight. And they only go where it's pointed.

So right now we are able to stimulate auditory responses and nerve endings with special types of laser energy. And we're hoping is that this kind of laser energy can help us develop what would be, in essence, a fiberoptic implant, where we're using light rather than electricity. And that may be a great thing in the future. It may help overcome some of the problems that there are with the auditory brainstem implant, relatively generalized stimulation is what we see. We may see great improvements there. But, again, this -- we're talking years down the line, probably five to ten years before we could actually see that in human use.

I already touched a little bit on intraoperative scanning. This is another area of

investigation and research at Northwestern using intraoperative CT scans to help fine-tune the transtemporal approach. Before interoperative CT scanning, we really had to just guess at how much bone we took off when we got close to the inner ear structures. And we got pretty good at it. Because that came with experience. But with the use of CT scanner, in very specific procedures, like either of the middle fossa or this retrolabyrinthian, we can take a snapshot right in the middle of surgery and then measure just how much more room we have. And we find that we can get very nice, delicate sections around the inner ear without damaging it.

>> Is that related to the stealth MRI that you do before surgery?

>> DR. ANDREW FISHMAN: Yes. The stealth MRI system helps us navigate through the soft tissue, brain tissue. It lets us know how close we are to soft tissue.

MRIs do not see bone. Bone on MRIs are completely black. No image. But the CT scanner shows us bone and does not show us soft tissue. So we use a combination of the two technologies.

>> Have you noted any difference in your preservation of hearing based on the use of those?

>> DR. ANDREW FISHMAN: I would say that the numbers that we have for that particular procedure is not high enough to say that it's going to be a significant change. It is relatively new. And we have managed to remove a few tumors using that with preservation of hearing where we would not have attempted that particular retrolabyrinthian procedure for that patient. And this is a really important progress.

Then there's outcome studies. This is just a sample of some of the things that I've looked at in the past, many of them also collaborating with Dr. Roland at the team at NYU. This goes back to the earlier times when there was really only surgery. So we looked a lot at our preservation of facial nerve function. We looked a lot at minimizing complications, really fine-tuning our surgical technique, also comparing different types of approaches to one another, looking at the brainstem, as well.

Now, the current work that we're doing at Northwestern in the form of a study ongoing, more of a surgical outcome is with Dr. Sidle, facial plastic surgery. And we've modified some of the traditional techniques for reanimation of the paralyzed face. Now I'll show you some examples of how that's done, but first I'll show you some of the more traditional techniques, which we still use. The hypoglossal to facial nerve grafting is a common technique that we use. But the main thing to understand about this is this can only really be done within a few

months of the onset of paralysis because up to about a year, a year and a half, the endings of the nerves where they grow into the muscle start to scar over. And even if we send a new nerve down that pathway, it won't really connect with the muscle to make it move.

So this is a common technique that we use in early facial nerve paralysis. So here's a patient who I operated with the team in Poland. And after the removal of the tumor, we knew that she had a complete loss of facial continuity. And we took her back very early on. And if this is the case, we would like to sometimes take a patient back even on the same hospitalization or in a short period of time afterwards because the sooner the grafts are in, the better off the results are. And what a facial hypoglossal graft is is we open up the front of the ear and then down a little bit into the neck. Or we can use the original incision to the extent we modify it. And then we find the hypoglossal nerve, which is the nerve that moves the tongue. And we take the nerve either from a sensory nerve behind the ear, if it's big enough, or from the side of the leg that gives some sensation to the side of the foot. Typically this nerve is not big enough, so we often use the nerve from the side of the leg. And we sew that nerve partially into the nerve that moves the tongue. So it usually does not affect the tongue movement. And then we sew it to the cut end of the facial nerve. We cut it in the cheek and sew it directly. And I'll show you a video of what it typically looks like after that's done. So you can see already -- here's her preoperative at rest. This patient has pretty good symmetry of rest after the procedure. This is one year after the surgery. Another important point about grafting procedures is that the effects take about a year to see because the new nerve grows about a centimeter a month. And it needs to travel -- the new fibers need to travel all the way the distance from that hypoglossal nerve all the way out to the muscle. That takes about a year to see the full effect.

So here she is one year later. When she swallows, -- (speaking in Polish) she's able to move.

Now, if you notice, that in a patient like that, there is still some movement across to the other side when there is speaking. And we're going to see that in just about any facial nerve reanimation surgery. When the nerve grows in, it sort of splits itself up across the muscles. And just innervates the entire side of the face. So we don't have individual muscle control.

So the goal of the surgery is to give some tone so that the patient can actively move it at will. And then counteract the movement from the other side. And the best results we see are when there is normal function on the other side. Bilateral paralysis are difficult to treat because it does require -- speaking requires an

individual movement of the muscles. It becomes a bigger challenge when there is bilateral paralysis.

This is the procedure that Dr. Sidle and myself have been doing. This is indicated when there's long-standing paralysis greater than a year or more, when there is no possibility of putting in new nerve fibers into those muscles. So even if we did a grafting procedure in a patient like this -- and this is one of my patients that was nice enough to agree that we could use her pictures. She had paralysis. She has NF 2. She had a surgery on this paralysis. She came to us from an outside center. And she had been five years without any reanimation or grafting. So after five years, it's impossible to get any nerve growth into the muscle. And this is what she was coming to us with, normal function on the other side. She also has a tumor on this side and normal hearing on this side and complete paralysis long-standing on the other side.

So what we do in this case is we make a little incision on the face here, right about where a crease would be. When there's paralysis, you also lose the crease. So by making the incision on the face, the scar is, in effect, also some of the cosmetic surgery. It gives back the crease. So it's a very nice, convenient access point. And directly through the face, we find this piece of the mandible, the jaw. This piece of the jaw is where the temporalis muscle, one of the chewing muscles, attaches and moves the jaw.

Now, you have five muscles that move the jaw. So disconnecting that muscle has almost no effect on the jaw movement. There may be a little subtle shifting of the annulation, but it's usually well-compensated over time with all the other muscles for the jaw.

This procedure does require an intact fifth cranial nerve or trigeminal nerve. So that's why we're also very conscious of preservation of the trigeminal nerve during surgeries. And there are patients that have trigeminal neuromas and have meningiomas surrounding the trigeminal nerve. So because we rely on the trigeminal nerve as a, in a sense, backup plan for the facial movement, we really gear our management plans around preservation of that system, as well.

Another aspect is that many of the surgeries done through the middle cranial fossa require movement of the muscle over that bone to get access to that area. So we also take that into consideration if we believe that a particular patient may require, in the future, some use of that muscle. So we have to balance all of these factors early on in the treatment planning.

And, again, that's why I sort of bring this all together, that our scope on you comes from this neurotology standpoint, where we know we're doing some of these procedures down the line, so we think ahead on these issues.

Now, back to the procedure. We make an incision. And then we find this bone and just separate it from the mandible. And that's done all the time by oral surgeons. And it has little impact. And then we make a small hole in the bone and take a tendon from the side of the hip, which is a very strong tendon, and suture it under the skin to the corner of the mouth above and below. And then the patient has -- initially the face is really pulled up because it always stretches down about at least 50% of the initial repair. So the first few weeks to months, it may be very pulled up. And then it eventually sags down. So I'll show you this patient how she's able to move her face with that muscle.

>> Okay. And what did we do?

>> I was wondering. Many of us have recurrent tumors. So we have successive surgeries. And I was wondering what you have shown have had several surgeries before.

>> DR. ANDREW FISHMAN: That's a good question. Many of the patients we have operated on have had multiple surgeries. So if that muscle no longer works or the fifth nerve doesn't work, there's still a benefit to the procedure because it gives what we call a "static" reanimation, just to hold the side of the face up. So in a sense, there's a cosmetic element of that just having static reanimation. So we still do it. And in some patients, we do get just static reanimation.

It's very hard to control how much of those tendons and repair slides over time. Most of the patients do see some sliding of it. And, again, if there's bilateral paralysis, it's also a very difficult problem because we don't want to overcorrect one side with a weakness on the other side and then get an imbalance in the other way. So it is a challenging issue. But there is still an advantage to doing this type of a procedure even if there isn't movement of the temporalis muscle.

>> I have a question. If you have the surgery, you said the first few months your face is really pulled up? If you have a week later -- your face is sort of pulled up, if you lose a lot of the movement, would it actually be a benefit to have the surgery again?

>> DR. ANDREW FISHMAN: That's a good question. I know we've discussed that. It's not that easy to do. The tissues are scarred in there. And it's probably not that possible to redo it.

There are other types of static type procedures that can be done. We can sling the tissues up to the arch of the cheek. But I think that if there is still some relative symmetry and some movement, that that still is probably better than what we would start to get if we start going in there and revising.

>> Do you have some kind of control studies or natural history data to show that the natural healing for people who did not have any of the procedures is worse

than having the procedures for longer term?

>> DR. ANDREW FISHMAN: Yeah, longer term. You know, that's a good question. I can't say that we have really a controlled study comparing it. But the decision to undergo that type of facial reanimation surgery and also the hypoglossal grafts is often postponed to see how much natural recovery is going to be present.

But one of the things that is an advantage to doing this temporalis sling, or this temporalis transfer, is it doesn't cut the residual facial nerve; it leaves the possibility of additional recovery over time to still be present. So we really have to make that decision based upon our sense of the likelihood of good strong recovery into the future. So we weigh those issues that we think there's a good chance, a good recovery. And we wouldn't do anything for a while. But if we think that there's a good chance of only partial recovery, then we may intervene and do this procedure because it's still not going to cut the nerve; it's still going to allow the eye to come back and some of the lower parts of the mouth to come back on their own naturally. But again it's a matter of us predicting based upon what we saw at the time of surgery.

>> What wasn't clear was that last video, the girl that came to you five years after?

>> DR. ANDREW FISHMAN: She had the paralysis five years long-standing. She came to us more recently within the last year, and that video was about three months after surgery.

So she could not have a grafting procedure because after five years, the nerve would never take to the muscles, so she needs to have this alternative technique.

>> Dr. Fishman -- do you have a question?

>> If you have the static, is there a time, like 10 years later, is it going to retighten? And is it a big deal to tighten it?

>> DR. ANDREW FISHMAN: No. Again, some of these aspects I would actually recommend consulting with my partner, Dr. Sidle. I think that it really depends on the expectations what the result is.

We have done these types of procedures in patients that have very long-standing facial paralysis and have also had prior reanimation surgery. But usually not the exact same procedure that we've not done yet.

>> The other -- you mentioned about the nerves may deaden? And you said it may take a year after that procedure for it to take place. How does that -- it's just rolling the dice a little bit?

>> DR. ANDREW FISHMAN: When we do the graft, it takes a year to see the final results because the nerve grows through the grafted nerve one centimeter

per month. And it's about anywhere from 9 to 12 centimeters depending upon the position of the graph. So you're going to see nine months. And then you'll start to see a little tone. And by a year's time, you got movement.

>> So then it's actually all new nerves?

>> DR. ANDREW FISHMAN: New nerves.

>> The existing nerves --

>> DR. ANDREW FISHMAN: Are no longer involved. The nerves have a tube, which they're sort of wrapped in. Like insulation. So motor nerves have these insulated tubes. And the new nerve runs through those tubes and then joins up with the muscle.

So I'm just going to wind down with just a couple of comments about the future directions that I see for our program. And this also goes back to some of the things that are involved with setting up a center. Because we are a relatively young program at Northwestern. I've been there for three years.

First, some of the things that I do see is we are working on developing the ABI program at Northwestern. Currently, we do send patients who are candidates, who we think are good candidates, to NYU where I was previously working.

We also are working on improved auditory prostheses. You know, the issue with the ABI and our program is: It does speak about some of the current trends in management. Because we are primarily an adult hospital, an adult program, most of our patients are patients who have had prior treatment. It's very uncommon for us to see primary diagnosed patients because they are typically presenting in as teenage years. So it's not uncommon for those patients to be first seen at a children's hospital. And that speaks to the way things are set up in some hospitals.

There are major centers that have a children's hospital separate from the adult hospital. And these more advanced, cranial-based techniques are typically from experienced surgeons in adult hospitals. So when there is a children's hospital, what we do see is a tendency to go towards radiation, early radiation. And we're not very excited about that. We do believe that that is not necessarily the best option. And we don't know that for a fact, either, because we still need to see 20 years after initial radiation, small tumors in teenagers, what's going to happen. But most of our patients are previously treated, often previously radiated patients. And that's where much of our experience is. That's why we don't typically feel that many of our patients are good candidates for ABI, because of all of the previous manipulation.

But if we do have patients that have a particular moderate-sized lesion that we

think should still be considered for ABI, then we do collaborate with my former center.

So that brings me to the future directions where we are now, in the next few years, going to integrate the children's hospital to the main campus so the two hospitals, I believe, in about two or three years are going to be right next to each other. So for our center, that should increase the access and collaboration ability between the pediatric departments, which do capture a good number of these patients, and ourselves to be able to take care of them as one team.

>> Children's Hospital as in Northwestern Children's Hospital?

>> DR. ANDREW FISHMAN: Yes. There is Children's Hospital in Chicago is affiliated with Northwestern, yes. They have broken ground on the site. And it's going to be right next door to the main campus. And I think that would be a big help in terms of caring for NF 2 patients in particular in collaboration with the children's adult hospital.

>> Is there any chance that Northwestern would be willing to become one of the clinical centers for the CTF Consortium? Our -- is that the CTF Consortium has hospitals with children with NF 1 primarily. And we're looking for a little bit of where they treat more NF 2 people, adults. And we think the statistics would promote that. Would Northwestern be interested if the --

>> DR. ANDREW FISHMAN: I think we could certainly talk about that.

The other thing I mentioned, increased multicenter collaboration. And I think this is exactly what you just mentioned. Because with the increased use of radiation as primary modality treatments, we've -- and that's not just for NF 2. That's for most benign brain lesions. In the past, really all of these patients were centralized to the major academic centers where the other smaller hospitals were really unwilling to treat them because they were too complex.

But with the advent of stereotactic radiation, it does not require a very high skill level to treat patients, so it is becoming increasingly common for patients to get their initial care scattered throughout smaller regional centers. And that is a trend that is going on all over neurosurgery issues.

So we do need -- and what happens there is that we don't really know what happens in the long run because the care of the patients is less centralized. So we need large numbers of patients that have had like treatment to be followed for many, many years to answer some of the questions. What happens after gamma is given to small tumors when you're teenagers? Unfortunately, we haven't captured all of those people to follow them closely.

>> Is it your opinion that scarring is an issue there?

>> DR. ANDREW FISHMAN: That is the main issue. Whether it's NF 2 or

others. We always counsel a patient that if you go down the road of radiation, you're going to basically have to flip the coin that you won't need a surgery in the future because it is more difficult.

That being said, I can't say that the last five or six patients that I've operated on with previous radiation, we have preserved partial nerve function, at least in part. But we don't always remove the entire tumor in order to do that. So there are -- it's just not as easy to do. So we do pay, in a sense, a price in the future. And in a disease process which has genetic predispositions to tumor development, other tumor development, we're more hesitant to use radiation as a primary treatment modality.

We also see patients develop delayed meningiomas after radiation therapy in tumors, as well. We see that as a common phenomenon. So somewhere about 10, 15 years later, we start to see those things happen. So we're a little hesitant to use that sort of knee jerk reaction as the primary treatment modality.

Though in centers which don't really have large skull based experience, the recommendation of radiation seems very appealing to not only surgeons but also to patients. And also with our changes in our health care system, which we're going down the road right now, it is considerably less expensive to treat patients with radiation. So we are going to see in the future a lot of choices made by hospitals and healthcare provider systems to use the less expensive option than to have a complex surgery, ICU and all of these things that we really were almost, in effect, taking for granted 10, 15 years ago, we're going to see a lot of those things be threatened because of the cost.

>> I'd like to bring this all back to the beginning, which is if there was centrally disseminated information for these small, very small NF 2 community about options before stereotactic radiation therapy is recommended by someone in some farm area, then you wouldn't hopefully have to repair?

>> DR. ANDREW FISHMAN: That's really what we today we're specializing in is this scenario. It's our most common scenario. It's a new field, in a sense. But that's why organizations like this are vital. Patients have access to these types of organizations to get information.

The other thing -- two more things I just want to mention. We would like to see further integration of our international centers, because our international centers provide us, myself, Dr. Bendha, we travel to these other centers, it would be nice to be able to move the patients around, or move us around in a more regulated system.

To tell you the truth, the United States is the least friendly nation towards collaboration with other centers. It's very easy for me to hop on a plane and go

operate over in India or go operate in Poland. I don't have to do anything other than a handshake and a word of mouth and reassurance that this is the professor from the United States.

But there are some excellent surgeons that I've collaborated with in India and eastern Europe with huge experiences of very specialized techniques who would be impossible to get them here in specific cases.

But we actually do shuttle patients between India and eastern Europe and back and forth. But this process, you can go to eastern Europe or India, and care is affordable. But to get a patient into the United States for care, the cost is astronomical in comparison.

And to sum this up, we really need to look to this: Philanthropy. We are entering an era where the payment from insurance and government insurers is just going on a steady decline. So we'd love to see all these services. We'd love to see patient care coordinators, full-time deaf interpreters, we'd love to have all those things; but I can tell you that those things are not going to come out of the revenues generated by hospitals for the care of such complex disease processes. But when they look at the numbers, they just can't justify the large centers, even in large university hospitals, putting these kinds of expenditures. And that was not the case 10 years ago. Because the reimbursement rates for all of these services is dropping. And when we had -- and any hospital today, do a cochlear implant, for example, we lose money. We are paid less than the cost of the device. So in a sense, there is a built-in philanthropy that the hospital has been expending. But things are going to continue to go on the decline in that area in the future, at least in the next 10 years. And the only way we're going to have really good, focused centers where all of the support services are coordinated is going to be through philanthropy.

And, again, that's where organizations like yourself are so important because we would need your help in order to get these kind of services. Because we've often been asked: Do you have the patient care coordinator that can do these things? Well, it's a salary line that is hard to justify when we look at the balance.

So, anyway, thank you so much for having me today.

[Applause.]

I wish we could stay lodger, but unfortunately I do have to go now. I know I answered a number of questions. I wish I could stay the afternoon, but we have our national meeting of neurological surgeons happens to be today, tomorrow and the next day. So I'm going to go to the airport. Thank you very much.

>> Do we have your email address?

>> DR. ANDREW FISHMAN: I have one more slide. Andrew J. Fishman,

312-695-8182, Afishman@nmff.org, www.andrewfishmanmd.com.

>> If I could make a short announcement. By the way, I'm Susie from the Midwest group. If Ladies and Gentlemen would like to get to lunch on a timely basis, we seem to be a running a little bit later today. Dr. Ramesh's presentation will begin shortly. So in order for her to be able to have her required hour, we're going to ask her to speak for about 30 to 35 minutes, then we'll retire for lunch. And when we come back, she can continue as she feels necessary.

>> Do we want to offer the other option? Or do we want to take only a half hour for lunch and let her finish?

>> How are people for a half hour? Is a half hour for lunch all right?

>> So at 12 or 12:05 and Dr. Ramesh will continue a little bit after 1:00.

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