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**Moderator: Melissa Baumbick**

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Operator: Good afternoon and welcome to the 6th Annual AN Awareness Week. Today we are proud to partner with the Acoustic Neuroma Association of Canada to present another Ask the Docs webinar. This is a very popular format because it's completely patient driven and focused on your questions. We will spend the next hour answering the questions that were either submitted in advance or that come in live during the event using the chat feature.

We are honored to welcome three doctors who will share their expertise with us today. Dr. Daniel Zeitler, Otologist and Neurotologist from Virginia Mason Medical Center in Seattle; Dr. Sujay Vora, Radiation Oncologist from the Mayo Clinic in Phoenix; and (Dr. Sudan Sapaya), Neurosurgical Resident from the University of Toronto. Unfortunately (Dr. Tavon Afore) will not be able to join us today as he was called away on an emergency.

I am Melissa Baumbick, the Communication Specialist for the Acoustic Neuroma Association and your moderator today. Before we get started I want to let you know that all attendees are in listen-only mode and will remain that way throughout the webinar. There's a chat feature in your control panel on your screen that can be used to type questions that you would like to be asked during the webinar. On some browsers, the chat window is closed by default. To open it you just click the blue Talk button in the bottom left-hand corner. We will dedicate all of this webinar to answering as many questions as we can.

There will be a recording of the webinar that includes the audio and all PowerPoint slides available next week on the ANA website. There will also be a written transcript available. Please watch our website and social media sites for notification that the webinar has been uploaded and is available for viewing. We will share the webinar with the Acoustic Neuroma Association of Canada as well.

The ANA and ANAC are dedicated to providing information, education and support to those affected by acoustic neuroma brain tumors. It is our vision to continually improve the lives of acoustic neuroma patients and their families through communication, support, innovation and partnerships with the medical community.

I'd like to thank our sponsors whose funds help advance and education and support as well as increase acoustic neuroma awareness. They have been very active in our AN Awareness Week activities and we are very appreciative. Our platinum sponsors are Barrow Neurological Institute, House Clinic Acoustic Neuroma Center at St. Vincent Medical Center, the University of Cincinnati Gardner Neuroscience Institute at UC Health, UC San Diego Health Acoustic Neuroma Program and Vanderbilt University Medical Center.

Our gold sponsors are Keck Medicine of USC, USC Acoustic Neuroma Center, Neurological Surgery PC, NYU Langone Health Departments of Neurosurgery and Otolaryngology Head and Neck Surgery and Weill Cornell Medicine Dr. Samuel Selesnick and Dr. Phillip Stieg. Our silver sponsors are Facial Paralysis Institute, Rush University Medical Center and the Ohio State University Wexner Medical Center Departments of Neurosurgery and Otolaryngology Head and Neck Surgery.

Our bronze sponsors are Barrow Brain and Spine Medical Memory, Duke Skull Base Center, the Integra Foundation, Jackie Diels Facial Retraining and Mayfield Brain and Spine. And finally, our awareness sponsors are Accuray, Boston Sight, Johns Hopkins University and Oticon Medical.

Finally I'd like to introduce our speakers. Dr. Zeitler is an Otologist Neurotologist at Virginia Mason Medical Center in Seattle, Washington. His clinical interests include cochlear implantation, bone anchored hearing aids, benign and malignant tumors of the ear and skull base, facial nerve disorders, chronic ear disease, ear infections and hearing loss.

Dr. Vora is a Radiation Oncologist and has been in practice at Mayo Clinic in Arizona for more than 17 years. He currently serves as the Associate Director for Radiation Oncology as part of a multidisciplinary Mayo Clinic Neuro-oncology program. He specializes in the treatment of acoustic neuroma and other skull-based conditions.

(Dr. Sudan Sapaya) is a graduate of the University of Western Ontario. In conjunction with his neurosurgical training, he is completing landmark studies on the genomic landscape of peripheral nerve sheath tumors. (Dr. Sapaya) is also an active member of the Elisabeth Raab Neurofibromatosis Clinic.

It is now my pleasure to get started with our questions. Dr. Vora, I think we start with you and we're going to start with the topic of radiation. We have several questions on that topic but one that I got multiple times was asking about the pros and cons of having single-session stereotactic radiosurgery versus multiple sessions and then also on a different note and separately, cyber knife versus gamma knife. Would you compare all of those a little bit please.

Dr. Sujay Vora: Sure, thank you for the question and thank you for the invitation. Radiation therapy is one of the tools that we use to treat acoustic neuroma and in general we primarily use regular therapy in the setting of a tumor that's enlarging on imaging.

The treatment options are varied and there are a number of platforms or brand names that offer treatment for this type of condition. And treatments can vary from a single treatment, a single fraction of radiosurgery and you may hear the terms gamma knife for something like this. There can be treatments done over three to five treatments and the term is stereotactic hypofractionated radiation therapy and cyber knife is one of the modalities that is commonly used. And then there's a number of other platforms that can deliver very low doses but very focused doses of radiation over 5 to 5-1/2 weeks.

The preference of one treatment over another, it does vary from institution to institution but in general, for smaller tumors we tend to favor single fraction radiosurgery. For larger tumors we -

and definitely work together with our colleagues in neurosurgery and otology just to see if there are surgical options that we should be exploring where many times that is the preferred treatment. And we would treat the patients that have large tumors if they more or less would develop a recurrence after surgery or if they had residual disease after surgery. So there is some variance from patient to patient and what they may hear from center to center in terms of the preferred option.

Melissa Baumbick: Okay great. Dr. Zeitler, we've had several questions on tinnitus. Is it possible to measure how loud tinnitus is for a patient? And is it at all associated with the size of the tumor of acoustic neuroma or how advanced - basically the size of the tumor?

Dr. Daniel Zeitler: Sure, thanks Melissa. Again, to echo Dr. Vora, thanks for the invitation. I wish I knew how to answer questions about tinnitus because tinnitus unfortunately, even if you take away the topic of vestibular schwannomas, is a topic that is still kind of a black box. Typically tinnitus does vary by hearing loss so it's common in patients with tumors that are causing hearing loss for them to also complain of tinnitus so that makes sense. And there's pretty good data showing the correlations between the severity of hearing loss and the prevalence of tinnitus.

There is no good data showing any relationship, believe or not, it sounds counterintuitive, but there's no real good data showing any relationship between the size of a tumor and the amount of hearing loss, nor is there very good data showing the relationship between the growth of a tumor and the progression of hearing loss. So it's very hard, for those reasons, to use hearing loss and/or tinnitus to predict the behavior both anatomically and patho-physiologically of the tumor, specifically with regards to growth. So we tend really - tinnitus is more of a symptom and it is not any tool by which we use to predict tumor behavior.

There is, to answer the first part of the question, there's no real good - so there are what we call visual analog scales and anybody on the call who's ever been a patient probably recognizes, you know, that scale where they ask you to rate your pain from a smiley face to a frowny face or on a scale from one to ten, so there are ways for patients to subjectively rate their tinnitus.

There are also questionnaires, the tinnitus handicap index or THI is a classic one that's used which allows patients to subjectively rate their tinnitus on a numeric scale based on standardized validated questionnaires. But there is no way for an audiologist and/or a surgeon physician to actually measure tinnitus loudness because it's purely a subjective complaint.

Melissa Baumbick: Correct, okay great. And so just to answer another part of - or a part of a question that I've gotten repeatedly, can tinnitus vary in the kind of sound that people hear? Some people talked about clicking, some people talked about ringing, some people talked about whooshing. So where that's concerned, do you hear that from patients that it - is that all considered tinnitus?

Dr. Daniel Zeitler: Yes so the definition of tinnitus is simply a sound that is heard by a patient that is not heard by anyone else, that's called subjective tinnitus. There are very rare and uncommon forms of tinnitus called objective tinnitus where the physician can actually hear the tinnitus in the patient. Those typically are in patients with something called pulsatile tinnitus or tinnitus that sounds like a heartbeat. And those, when they are objectively heard, are typically due to pathologies not related to acoustic neuromas. They're typically due to other much more rare vascular anomalies which are beyond the scope of this call.

Melissa Baumbick: Okay, okay. Hi, and (Dr. Sapaya), one question that I had several times was about measuring acoustic neuroma follow up and getting multiple scans. How do you measure an acoustic neuroma on an MRI? And if the growth is only, you know, a millimeter or two millimeter from year to year or from - even from six month to six months follow up, is that considered growth? Can that just be considered subjective measurement?

(Dr. Sudan Sapaya): Thank you for inviting me for this webinar. So that's a common question we receive, especially at the University of Toronto. So from our institutional practices is that for the initial acoustic schwannomas that we use the wait and see approach. We do serial imaging approximately once a year for at least for two to three years to see if there is any interval change in the size of the acoustic neuroma.

And again, we measure the tumor based on the maximum diameter in three dimensions, so how large it is in height, width and length. And with acoustic schwannomas there is normal growth so we expect to see about two to four millimeters of growth per year and that would be considered within normal range. If there is significant growth beyond that then that is something that is more concerning.

And there's also differences within the MRI images themselves so there is some room for error in calculating the tumor size based on serial imaging. And again we say about plus/minus two millimeters is within the normal area range for MRI imaging.

Melissa Baumbick: Okay. Dr. Vora, can you talk a little bit about the fact that generally younger patients are not given radiation as an option, and I know that that's not always the case but generally. One of the patients that wrote in said, "If there is a lack of long-term research, maybe the doctors could express what specific concerns lead them to proceed with caution with younger acoustic neuroma patients and radiation."

Dr. Sujay Vora: That's a really good question. You know, in general I don't think there's a age cutoff in terms of what we would offer for radiotherapy. But our recommendations for radiation tend to be primarily in the situation where there is a tumor that's growing and many of these tend to be quite small, generally under 2-1/2 to 3 centimeters which makes them amenable to treatment.

I do always do think that there is some concern that if they do receive radiation, especially in a very young patient, there is, at least in theory, a risk of the radiation inducing a cancer that could occur 10 to 20 years down the road and sometimes that's one of the reasons why some patients are dissuaded from considering this option.

One of my colleagues up in Mayo Rochester actually looked at this question and they the incidents at 15 years to be under 1% in terms of radiation-induced malignancy related to the

radiation exposure. And that group of patients did include - many of those patients did have acoustic neuromas that was part of that analysis.

I think the second issue is while the control rates, the success rates of radiation are very high in the 90 to 93% range, if you flip those numbers around there's about a 7 to 10% risk that despite treatment that the tumor may continue to grow. And I've heard from some of my surgical colleagues that sometimes they worry about operating in areas that have seen radiation in the past in terms of tissues healing properly. So I think those are probably the two main reasons why younger patients are sometimes looked at more from the surgical perspective than the radio-surgical perspective.

Melissa Baumbick: Okay great. And Dr. Zeitler, we had actually quite a few questions on eye issues for patients that had been treated for acoustic neuroma. One in particular was about tear production and drainage. In some cases people are not able to produce tears and they suffer from dry eye and then in other cases, there is too much liquid and there's eye drainage. What are the options for patients who are dealing with this after acoustic neuroma surgery?

Dr. Daniel Zeitler: Sure, so typically, and obviously there are exceptions to the rule, but typically eye related symptoms only really occur in patients with facial nerve weakness or paralysis after surgery or even in the rare patients who presents with facial nerve paresis or weakness or paralysis before surgery from their tumor. So the first goal is to go to a center that has experience with taking these tumors out because the - it's been very clearly demonstrated that centers with experience doing these operations have lower rates of facial nerve injuries. So I would say that first and foremost is one easy way to reduce the risk of problems postoperatively.

That being said, even in busy centers there are tumors that are very sticky. Dr. Vora mentioned, you know, one way that these tumors kind of become a little more fussy is if they've been radiated previously. The analogy I give my patients which the radiation oncologist don't love, but I tell them imagine taking a marshmallow and putting it on a stick and being able to take the marshmallow back off the stick and then take that same marshmallow and put it in the fire like you're making

s'mores and then try to peel the marshmallow off the stick, it's very sticky and it kind of has webs and tangles and that's kind of the analogy of what radiation can do to these tumors, it just makes them very sticky and thick.

And so - but there are some tumors that have never been operated that also just are behaviorally problematic. And patients can have some weakness of their face, of their facial nerve which travels through the internal ear together with the hearing and balance nerves and these nerves can become weak from stretch or devascularization after surgery causing the eye to not close. And that's the majority of the reasons why people have tear production issues.

If you can't - if your facial nerve is weak then it means you have trouble blinking and blinking is the key component to tear production. Without being able to blink your eye dries out often because you're not recycling the lacrimation through the glands there. So typically for those patients we recommend a very, very aggressive hydration of the eye. This can be done with drops, you know, artificial tears. We recommend patients putting in ophthalmic ointment at night to keep their eye nice and moist. We recommend them taping their eye closed or using a moisture chamber at night which can be purchased at most pharmacies.

And then the severe cases where the nerve is either densely paralyzed or not working at all and there is the expectation that it might take the nerve some months to recover or perhaps if the nerve doesn't recover at all, then we would refer these patients to one of our plastic surgical colleagues and they can do some procedures on the eye to tighten the lids to allow the eye to close by inserting something called a gold weight into the upper lid which gives the upper lid weight and allows it to blink through the use of gravity rather than through the muscles. And these kind of procedures typically help patients substantially.

We also involve our ophthalmology colleagues very early if there is any issues with the eye because corneal abrasions can be disastrous and we want to avoid those.



Melissa Baumbick: Definitely, okay. (Dr. Sapaya) I've had several questions on tumor size and one question was, you know, how long does it take to recover from a large tumor which - or from surgery to remove a large tumor which I know is very dependent from patient to patient. But can you talk a little bit about the symptoms that are associated with acoustic neuroma and why sometimes a small tumor doesn't seem to have any effect at all and then - or very little effect. And then other times people really suffer some debilitating side effects even though their tumor is quite small. And then also is there a longer recovery time when a large tumor is removed versus a smaller tumor?

(Dr. Sudan Sapaya): So that's a very good question. So with regards to the tumor size and the length of recovery, I think it is very patient specific and it also depends on the preoperative symptomology and also how surgery went and the postoperative complications. But in general, with larger tumors there is often higher preoperative symptoms and therefore there would be significant differences in the postoperative symptomology because it takes time for the symptoms to resolve or to get better. So I would generally say that for larger tumors it would be a slightly more involved recovery time and might require additional support such as physiotherapy and other supports.

But again I think it's also very patient specific, surgery specific and also preoperative symptom specific. And - sorry could just remind us of the second part of the question again?

Melissa Baumbick: Just about, is the recovery time significantly different for the removal of a large tumor versus a small tumor?

(Dr. Sudan Sapaya): Yes so yes as I mentioned, I think for a larger tumor there - it's often more involved surgery. There's usually more cranial nerves that are either adjacent or adhered to the tumor and therefore it would require more cranial nerve manipulation so tumor size does I think make a difference in recovery time. And smaller tumors would in general have faster recoveries. But then again as I mentioned, it's very patient specific.

Dr. Daniel Zeitler: Melissa I would just add to that, interestingly enough, what we sometimes see in the neurotology clinic is patients with bigger tumors actually are less dizzy, they have less vestibular - they have fewer vestibular complaints because as the tumor has grown to a bigger size it actually very, very slowly destroys the balance system, the input to the balance systems through the vestibular nerve. And so interestingly, and it's counterintuitive, but bigger tumors, actually the patients often times recover much more quickly with regards to their balance because in many of the cases, with bigger tumors the patients have already essentially lost the balance function in the affected ear.

And in fact the patients with the smaller tumors often, again, specific to balance disfunction and specific to dizziness postoperatively, the patients with smaller tumors often times have way worse problems with regards to their balance. And the patients with smaller tumors often are the ones that require the physical therapy.

Melissa Baumbick: That is interesting. Okay let's take a couple questions from people who has catted them in here during - while we've been talking. Dr. Vora, this one is for you. There's a patient that says, "There doesn't appear to much discussion about proton therapy as an effective treatment for tumor reduction. Is it not as effective as radiation? Is it just newer? Why do you think that is?"

Dr. Sujay Vora: That's a good question. You know, proton beam therapy is a treatment modality that has gained a lot of press both positively and negatively recently. There's been a number of radiation centers that have opened around the country where they offer proton beam therapy which is a very expensive technology.

Protons is radiation so it is the same as regular radiation but the way the radiation is delivered is different. It has a very specific type of characteristic where the radiation will be sent into tissues at a certain distance. It'll drop its energy where you want it to and then basically it gives very little radiation afterwards. So a lot of people like this modality because it really allows us to spare the healthier tissues nearby to a much bigger extent.

Where this technology has really been proven is in pediatric cancers where by reducing the healthy tissue exposure, children really seem to benefit long term in terms of reducing the risk for side effect as well as reducing the risk for secondary cancers from that radiation exposure.

Now for acoustic neuromas the data is much less clear. There's very limited data showing efficacy - well I take that back. There is data for proton beam therapy that shows that it is an effective treatment in terms of controlling the tumor but there's very little data that suggests that it's a better treatment long term. One of the challenges with proton beam is that there are some inherent uncertainties when treating tumors that are very small which most of these acoustic neuromas are, so the amount of gain that you get from protons compared to our stereotactic treatments with photon-based treatment is relatively small.

Our center is actually actively looking at developing a radio-surgical type of treatment using proton beam to see if we can actually gain - use the benefits of proton beam but also be able to target very small tumors accurately and reduce the amount of surrounding tissue exposure. It's a long answer to a relatively straightforward question but I think the whole concept of using protons for this disease is still in development.

Melissa Baumbick: Still in development, okay. (Dr. Sapaya) we've had several questions on headaches. This particular patient has - experiencing a lot of pressure in the head, sometimes worse than others so not as much pain but they also have a titanium plate due to the surgery. Could that have anything to do with the headaches?

(Dr. Sudan Sapaya): So in postoperative patients after removal of acoustic schwannomas, headaches can be due to a multitude of factors. I think it's very unlikely to be a result of the titanium plate unless they're having more local discomfort near the incision site or if they feel any parts of the titanium plate protruding in the skin. But the sensation of headaches in the postoperative setting, again, could be just a result of surgery itself. And it could take time for the brain to recover from the surgical procedure.

Depending on the timeframe of the surgery, one of the other explanations could also be due to the possible leak of CSF and again that could reduce the pressure in the brain and as the brain sags a bit that can cause headaches that are more dependent on the patient's position. So the headaches get better when they're lying down and the headaches are worse when the patient's upright and walking around.

And usually if this headache is persistent and/or worsening we would recommend to get the follow up imaging, either CT scan or MRI to, again, assess for the possibility of a CSF leak or any little bit - small amounts of blood. If the imaging is negative, it's a possibility again that it's just a side effect of surgery and sometimes it gets better with time. But as I mentioned, I think it's fairly unlikely to be related to the titanium plate itself.

Melissa Baumbick: Okay, okay. And you mentioned CSF leaks, and we had a couple different questions on those. How does that happen? Why are those - why do those happen? What are the cause? And are there degrees? Are there, you know, are some worse than others? We have lots of patients that ask, you know, if I have a runny nose do I have - a consistent runny nose do I have a CSF leak? Should I be concerned? When is the time to really see a doctor about that?

(Dr. Sudan Sapaya): Okay so first off, the reason for a CSF leak is that we have to open the outer membrane of the brain which is called the dura which helps keep the CSF in the space around the brain. And then when we finish the surgical resection we have to put the dura back together which is the outer membrane as I mentioned, with stitches. And sometimes despite the best closures, there is still some gaps in the closure that can result in CSF - or the brain cerebrospinal fluid leaking through those gaps. And what - that can cause these headaches or risk of meningitis and it also reduces the effectiveness of the skin closure and fluid can leak through the wound itself.

So there's usually several degrees as the patient had mentioned. So usually our protocol is with CSF leaks, usually try to reclose the skin with extra sutures and also possible other adjuvant wound closure techniques with - such as bio glues. If that still fails then we consider putting a

lumbar drain which is a needle into the back and putting a drain in to help divert the CSF fluid from leaking through the surgical site. And if that fails then we'd have to consider going back and reopening the wound and making sure that there's a tighter closure of the dura.

And despite best efforts, this is a complication with surgery that is sometimes unavoidable given that with a patient standing upright, the amount of pressure at the site of the previous closure can be quite high. And again, despite best efforts, there can be some fluid leakage. So concerning symptoms would be worsening headaches with upright posture. If there's any signs of fever, decreased level of consciousness or any changes in neurological status, because can be concerning for meningitis and if there's obviously any leakage of CSF through the wound itself. So those would be all concerning symptoms that you should seek medical attention.

From leakage through the nose, I think if - for acoustic schwannomas themselves, the leakage of CSF through the nose is rare and I think almost might not be, you know, related to CSF leakage. Most of the time you'll have leakage of fluid either through the ear or through the surgical incision itself.

Melissa Baumbick: Okay great. And Dr. Zeitler we had many questions on hearing aids and how they help with the type of hearing loss that acoustic neuroma patient's experience where the hearing nerve is damaged. And then how do you treat - how do you deal with patients who might be older and are dealing with hearing loss in their good ear just from age related hearing loss in addition to hearing loss that is associated with acoustic neuroma treatment?

Dr. Daniel Zeitler: Sure. So, you know, the problem in many patients is they have this tumor and they get either radiation or they get surgery or they get nothing and despite our best efforts to preserve their hearing, in some cases with radiation or surgery or with watchful waiting, the hearing gradually or sometimes not so gradually declines to the point that they're clinically deaf in their ear. And that is an impossible situation to treat directly because obviously a hearing aid relies on at least some form of residual hearing to work. A hearing aid is simply a microphone so without any hearing, there's no way that a hearing aid can really work.

In these patients with deafness in one ear, or what we call single sided deafness, assuming that they have, to answer your first question first, assuming that they have normal or fairly normal hearing in their other ear, there are two options. The first - and they both kind of work the same way which is to bring sound from the deaf side of the head to the non-deaf side of the head and you can do that either with wireless FM signals - so patients can wear something called a CROS hearing aid, C-R-O-S which stands for contralateral routing of signal. And what you basically do is you wear a microphone in your deaf ear, you wear a receiver in your non-deaf ear and sound that hits the deafened ear goes through the microphone and is transferred wirelessly to your non-deaf ear.

Now what this does not do is provide any sense of localization so it's not going to allow you to tell that sound is coming from your deaf ear because everything is going to be filtered towards one side of the head. But what it does do is it eliminates something called the head shadow. So as you can imagine, the head creates a shadow and so when sound hits the deaf ear it basically hits a wall. And so sound has to then travel over your head to reach the non-deaf ear.

So by wearing the CROS aid we can at least collect the sound that's hitting the deaf side of the head and amplify it. So these are great in situations where you're sitting at a large table in a group or in a conference - in a business meeting or a conference call or things like that where being deaf in one ear could affect the way that you hear what's going on around you but again, it's not a perfect solution.

The other way to do it is a similar sort of technology, but rather than using wireless transmission over the head, you actually have an implant put behind the ear called a bone anchored implant or a bone conduction implant. The name that's often thrown around which is one of the two brands is called a Baha. And what this does is, through a very small surgical procedure that takes about ten minutes, we would implant a small titanium screw into the skull and attach, some weeks later, a little hearing aid that when it hear sound, vibrates and that sound is then taken across the skull

through vibration to the other ear. So similar idea, taking sound from the bad side to the good side, but you can either do it wirelessly or through an implant.

For the patients that you discussed in the second part of the question that may have some hearing loss in their other ear, at some point that bone anchored implant or the Baha becomes untenable because it relies on the good ear to vibrate the sound. And so at that point when the good ear becomes so bad that it can't help with the bad ear, then you're forced into a situation where you would have to use something called a BiCROS, so similar to the CROS where it brings sound from the bad side to the good side. You would have the same type of device but now in addition to having the receiver in the better ear, you would have also a hearing aid in the better ear that would both collect sound from the deaf side and amplify sound on the good side.

Melissa Baumbick: Okay great. Dr. Vora, we have several patients that are on watch and wait and the question always comes up, when do you decide to treat. But there was another question that said, how do you base your treatment decisions? Do you base it more on patient symptoms, on size of the tumor, on location of the tumor in relation to brain stem? Do you prioritize those in some way? How does that work?

Dr. Sujay Vora: Okay well, you know, in general we get patients referred to our group either at the time of initial diagnosis when they're just trying to sort out what the right answer would be. And for many of these patients watchful waiting is very reasonable to consider as many of these tumors really don't grow very much at all. But when they do grow, that many times is a trigger for making some decisions in regard to radiation or surgery.

For smaller tumors, and I say smaller as I see somebody's asked that question...

Melissa Baumbick: Yes ((inaudible)).

Dr. Sujay Vora: ...generally they're small to be about 2-1/2 centimeters or smaller, those are considered pretty ideal candidates for single fraction radiosurgery. So you'll hear words like gamma knife thrown in there as a treatment of choice.

For a larger tumors, so larger than 2-1/2 centimeters, it gets a little less clear what the right treatment is because as tumors get larger the ability of the radiation to control the disease probably goes down. So what do people do? Well they consider surgical intervention. I think that's a very good treatment option for many of these patients. And if they're not good surgical candidates or the patient just chooses that they don't want to have an operation, well then we do sometimes offer radiation.

What options do we give in these cases? We tend to do the radiation over longer periods of time because many times these tumors are compressing the brainstem or are, you know, which can lead to potential complications if you give a very high dose of radiation in a one-time setting. So many of these patients we'll tend to treat over several weeks, 5, 5-1/2 weeks rather than in just one treatment. Did I answer all your questions?

Melissa Baumbick: Okay. Yes.

Dr. Sujay Vora: Oh good.

Melissa Baumbick: I think you did, yes.

Dr. Sujay Vora: Okay great, great.

Melissa Baumbick: (Dr. Sapaya) there's a question on here that talks about growth of the tumor and it's very general. But in general do you find that if a tumor hasn't grown in two years the chances of it growing are minimal or is that, again, something that's very specific patient to patient?



(Dr. Sudan Sapaya): Again I think that is very specific patient to patient. Tumors do show - that tend to be stable on serial imaging over a few years, at least five to six years, I would say tend to have a lower risk of growth in the future. However, there are cases where tumors can change in their clinical behavior over time and that's why they require serial imaging.

For tumors that have shown stable behavior for - on serial imaging yearly over five years we can kind of - at our institution we reduce the frequency of serial imaging to every two to five years. And again, this is very patient specific and it's also trusting that the patients will come to us with any changes in neurological symptoms and also changes in hearing.

And even if we do not get serial imaging, we would continue to recommend yearly audiograms to, again, assess for any changes in hearing that might indicate that there is growth in the tumor. But again I think this is very patient specific and patient symptomology gives us a lot of information regarding the tumor growth even before we catch it on imaging.

Melissa Baumbick: Okay great. And Dr. Zeitler, we've had lots of questions -- and this is something that all of you may have some input on -- on balance. And people, at least the people that were submitting questions this week, one of the biggest questions was, "If I've had surgery or radiation to treat my acoustic neuroma and everything is going along fine and then all of a sudden, you know, a year later, 18 months later I start to have balance issues, is this - should I be concerned? Is the tumor growing again? Is that typical?" You know, what do you see when you have patients who experience something like that?

Dr. Daniel Zeitler: Yes so it's a good question and certainly something that I think all of us, both myself and the neurosurgeons and the radiation oncologist, these are questions we all have to answer because patients have these complaints, really no matter the treatment modality that they choose is. Kind of like hearing loss and kind of like tinnitus, balance is just a poor predictor of the tumor growth. It's not a good predictor of tumor behavior. I did sort of allude to the fact earlier that it's not uncommon for smaller tumors to cause more imbalance than larger tumors but I don't think

you can use worsening balance or improving balance as a sign of tumor growth or slowing of tumor growth because it just doesn't work that way.

You know, to answer the patient's question specifically, you know, is the fact that the balance is worsening when things have been kind of going along really well, I don't know. The balance, like I said, really just is a poor predictor of tumor behavior. I certainly think that in a patient who's chosen to watch and wait or the conservative approach and their balance is worsening, it probably would necessitate going in to see your doctor. And at the very least, just having a good evaluation because certainly there are other causes of balance disturbance besides the inner ear -- many causes of balance disturbances besides the inner ear. So the first thing you want to do is just make sure that it is in fact a vestibular balance disturbance.

We do see, and Dr. Vora could speak to this, patients who have had radiation, sometimes a swelling of the tumor occurs for up to a year or even 18 months after radiation. And so sometimes even after someone's been radiated, if they had no real balance problems before, the radiation can cause some acute balance changes and some more subacute balance changes.

And then for patients who have balance disturbance but don't have a growing tumor or have a tumor that they don't want to be taken out with surgery, there are some other options, there are some very non-invasive options like physical therapy. I have a lot of my patients with vestibular tumors doing yoga which they find to be extremely effective in helping with their balance if they don't want to go to a specific - to true physical therapy appointments.

There are also some things that we can do medically for their balance, both in the clinic and some - even some minimally invasive things that we can do to help with the balance that don't involve total tumor removal. So balance is hard and it certainly - we know from data, people who are on the wait and scan approach for treatments of their tumors, balance is the single most predictive factor of patients who leave the wait and scan approach and enter into the surgical paradigm because people just get so incredibly debilitated by their balance that they just want the tumor out.

Melissa Baumbick: And with that being said, do you recommend to your patients ever that they do vestibular therapy or anything like that even prior to treatment to sort of...

Dr. Daniel Zeitler: Yes.

Melissa Baumbick: ...get a handle on it?

Dr. Daniel Zeitler: Yes, there's been some preliminary evidence that was presented out of Germany where they actually showed that patients who did presurgical vestibular therapy and even patients who had had some of these non - minimally invasive procedures of specifically something called Gentamicin. So if they use Gentamicin into the ear to sort of deaden the balance system before surgery, patients required less therapy after surgery, so absolutely 100%.

Melissa Baumbick: Okay great, okay. Dr. Vora, we had a question about what specialist should be involved and should participate in a patient's radiation therapy for an acoustic neuroma.

Dr. Sujay Vora: So we usually work sort of in packs at Mayo, so we'll have the neurosurgeon involved, we'll also have an otologist involved with many of these cases because we always feel that it really provides patients a broad understanding of their disease, a better understanding of what options they have. But if the ultimate decision is radiation, the radiation oncologist tends to be sort of the leader but we always tend to involve our other colleagues because there are certain aspects of treatment planning where I do gain some insight from my neurosurgical and otology colleagues in terms of making sure that the adequate volumes covered whether, you know, if they've had surgery prior. We always want to make sure that we're covering the adequate tissues to make sure that we sterilize any cells that may be - that may have been left afterwards.

Melissa Baumbick: Okay. Okay and in addition to that, what do you recommend to your patients as far as follow up? We had a lot of questions on follow MRIs particularly after gamma knife or cyber knife,

but really any radiation I guess. Is there specific recommended follow up depending on what modality you used?

Dr. Sujay Vora: That's a great question. I don't think there's any clear consensus on the right interval for imaging. In general I'll use - get imaging at the first one at three months and then about every six months for the first couple of years and then annually thereafter. As the patients report symptoms, we get scans sooner to check of the lesion itself.

Now after radiation these lesions do, you know, they do change shape over time. So about, in our series, about half of the patients that we give radiation to where we take volumetric measurements of what happened to their tumor after treatment, we'll actually see some transient enlargement. So transient volume expansion is pretty well known in the radiation community as something occurring after treatment. And when it does expand, a lot of times patients actually report some symptoms with that.

But more or less what we do is we provide some reassurance to the patient that, yes this is something that we're seeing but this is a treatment effect. And as we continue to follow them, many times these symptoms go away completely. And the tumors themselves, instead of seeing this initial expansion where there's some concern that the tumor is continuing to grow, what we're actually seeing is just one snapshot in time. And as we continue to follow them. The tumor continues to get smaller and smaller.

Melissa Baumbick: Okay. And (Dr. Sapaya), we had a couple questions on the fact that it seems that the diagnosis of acoustic neuroma seems to become more frequent. Is there data that indicates that the occurrence is more frequent or does it have more to do with technology? (Dr. Sapaya)? Maybe we lost him. Dr. Zeitler do you have any insight on that?

Dr. Daniel Zeitler: Sorry can you repeat the question?

Melissa Baumbick: I'm sorry, it seems that acoustic neuroma diagnosis is becoming more frequent. I think we as a organization are seeing that they're being diagnosed younger. Is it - do you think that that's because there's an increase in the occurrence of acoustic neuroma or is it due to better technology?

Dr. Daniel Zeitler: The latter, 100% yes. Where, you know...

Melissa Baumbick: Okay.

Dr. Daniel Zeitler: ...a good MRI machine now is pretty - is a pretty standard piece of machinery in just about any hospital whether it's a small community hospital or a large academic institution. And these MRI machines now kind of typically can identify tumors small as one millimeter. So, you know, here in the United States we actually - we are second in the world, I think behind Sweden or Norway or somewhere in Scandinavia as far as the number of - we perform one MRI per every 11 patients here in the United States and so it is purely just a technology prevalence bias. We're just scanning more people and the technology is better and we're just finding more of these tumors.

Melissa Baumbick: Okay, okay. And while we're on the topic of technology, people are very concerned about the contrast chemical, the gadolinium and are wondering if it's okay to have MRIs without that contrast and - or even patients - there's another patient that submitted a question who has a pacemaker and isn't able to get MRIs at this point. So are there other options for diagnosis other than what we consider the gold standard which is the MRI with the gadolinium?

Dr. Daniel Zeitler: Yes so you can actually do - there have been a number of studies lately looking this exact question because people either don't want multiple series of contrast administrations or people with chronic kidney disease can't get it. Some people have allergies to gadolinium. You can actually do a non-contrasted MRI and see fairly well. It is certainly not an ideal study but it is certainly very good. A non-contrasted MRI is still actually probably a better study than a CAT scan

with contrast because a CAT scan with contrast really can only pick up a tumor about a centimeter big so, you know, there's a tenfold difference between an MRI and CAT scan.

You know, you can also do - there is an audiological test called an auditory brainstem response test or an ABR, you might see it called a BAER, brainstem evoked auditory response or auditory potential. And that is a test that can be used in someone, again, who can't have an MRI or maybe they can't even have a CT scan for whatever reason. The sensitivity and specificity of that is pretty low but it's an okay screening tool, especially if you have, say, a 75 or 80 year old patient and you're concerned about a tumor, it's going to be pretty good at identifying, through the screening process, a patient with a very large tumor. It's not going to be good at finding a patient with a small tumor but as we've already discussed, an 80 year old with a small tumor may not be such a problem anyways. That would be someone that we'd probably end up waiting and watching.

So there are other options but if you can't have an MRI with contrast, I think Choice 2 is an MRI without contrast. And if you can't have an MRI then Choice 3 would be a CAT scan with contrast.

Melissa Baumbick: With contrast, okay. And Dr. Vora, we had a couple questions about radiation on tumors that had a cystic component. Is that something, if you saw an acoustic neuroma with that cystic component, would radiation be an option? And if so, what happens, you know, with the swelling of the tumor, does the cyst tend to swell as well? How does that work?

Dr. Sujay Vora: These are tough cases. We don't see very many of them because it's not that common but it's common enough where when we see these cases we definitely talk to our surgeons in regards to their thoughts. Well the way these cysts respond after radiation is variable, some will stay dormant and some will expand and the expansion can clearly cause problems.

So many of these cases, I'll be honest with you, I tend to talk to my surgeons about potentially resecting these because I do have some concerns about post-treatment cyst expansion where

increased pressure can be caused on the brainstem. And those are the things that we just can't fix with radiation. Those are the things that really need to be addressed surgically.

Melissa Baumbick: Okay, okay. And one more question actually for both of you, there's always talk about, you know, if the tumor is radiated and then - that it's more difficult to remove surgically -- And I know you had the marshmallow analogy Dr. Zeitler -- but is it something that is commonly done particularly with not removing the entire tumor, to save the facial nerve or the balance nerve or anything like that?

Dr. Daniel Zeitler: Yes I mean, I'll speak first and then Dr. Vora can give his two cents. I think we've already kind of hit on a few of the issues which are Number 1, we're identifying more vestibular schwannomas with increasing usage and savvy ability of the MRI machines. And Number 2, people are living longer. And so you add those two things together and what's going to happen is more and more people are going to have radiation and they may live long enough for their tumor to start growing again.

And so I think it's not unreasonable to think that there may be an increased prevalence of people who have post-radiation tumor growth because most of the studies that we've looked at for post-radiation tumor growth really only go out to about 10 or 15 years. So it is absolutely all of that being said, possible. It's kind of one of those things sort of like, as Dr. Vora said, when he sees a patient with a cystic tumor he sort of shakes his head and goes to find his colleagues. It's kind of like the same thing in our clinic, if we see a patient who's had a tumor grow through radiation, we kind of shake our head and go find my neurosurgeon to help me with this case because they can be tough.

There is a slightly higher rate of CSF leak after these cases of post radiation surgery. There is a slightly higher risk of facial injury, either temporary or permanent, after cases of radiation just because the tissue planes are so difficult to discern, but they're not impossible. The other interesting thing is, I think that what's going to start happening is, and you alluded to, patients are going to come in and have surgery and maybe what we have is a subtotal resection because we

want to protect the facial nerve or other delicate structures like the cochlear nerve and we may err on leaving a little bit of tumor behind.

And we know that in the overwhelming majority of those cases, the tumor doesn't grow but I think we're seeing more and more patients -- and I'd love to hear Dr. Vora's opinion -- that may have a subtotal resection and if there's any growth of the residual tumor, they can go on and get that adjuvant radiation therapy which works beautifully in stopping that residual portion of tumor from growing.

Dr. Sujay Vora: That's definitely the much more comfortable situation to be in where there's residual disease that we can target with radiosurgery. The uncomfortable situation is when a patient's had prior radiation is starting to have regrowth. A lot of our patients are older so to consider an operation is something that they're just not very interested in. So the question gets put back to me many times is, can we offer additional treatment. And I believe a couple of people asked - sort of asked similar type of questions if they've had radiation before.

But just for the audience to know, giving a second course of radiation is problematic mainly because the body doesn't really forget the prior radiation exposure. So many times we're up against brainstem tolerances so if we try to come in a second time there's really a risk of significant or catastrophic brainstem injury with more radiation.

So that's why, you know, we really kind of rely on our multidisciplinary team to see what other options there are, whether there's a clinical trials that we can look at. There are some drugs that are on the market that are also being looked at in patients that have failed multiple core lines of therapy. But, you know, for the audience in that unfortunate situation, I would highly recommend going to a center where they treat a lot of these and do see patients back where there are recurrences and have a - at least a team-based approach in trying to address the problem because it's not simple.



Melissa Baumbick: Exactly yes, that's very important. Well we are at the end of our time today so that's going to have to be the last question. I want to thank you both Dr Zeitler and Dr. Vora and (Dr. Sapaya) I think dropped off, but we really appreciate all of you taking the time to answer our questions. I want to thank everyone that attended and submitted questions. I know that we didn't get to all of them, we tried to cover as many topics as we could and really cover on a basic level as much as we could of what was asked.

We will have a recording and a written transcript of the webinar on our website so just watch our social media for notification that that is available for viewing. And also make sure you visit our website, [www.anausa.org](http://www.anausa.org), to see how you can participate in AN Awareness Week. We have milestones stories, we have AN warrior pictures, we have lots of different things that you can do so make sure that you visit and see how you can participate. And also watch to see when upcoming webinars will be held. Thank you very much and have a great afternoon.