Dr. Jason Barnes:

Hey there. Welcome to another episode of ENT In A Nutshell. My name's Jason Barnes. And today, we are joined by Dr. Matt Carlson and we will be discussing vestibular schwannoma. Dr. Carlson, thanks again for being here.

Dr. Matthew Carlson:

Thanks for having me.

Dr. Jason Barnes:

I do just want to say before we start that vestibular schwannoma can be seen in a couple of subsets of patients. We typically describe them as sporadic or involved with NF2. And this episode will only focus on the sporadic side of vestibular schwannomas with another episode dedicated to NF2. So, Dr. Carlson, when you have a patient with a vestibular schwannoma present to your clinic, what types of symptoms do they usually have when they present?

Dr. Matthew Carlson:

Being in a tertiary center, very commonly, patients are actually referred in with the diagnosis established based on an MRI, but there are very typical symptoms that most patients have. Approximately 90% of patients will have some degree of asymmetrical sensorineural hearing loss, where the affected ear has poor hearing. And with that, about 70% of patients will have concomitant tinnitus, either bilateral, but more commonly affecting just the side with the hearing loss. Even though these tumors are called vestibular schwannomas and they arise from the vestibular portion of the eighth cranial nerve, surprisingly, dizziness is not a common feature or a prominent feature for many patients.

If you really ask a patient about it, maybe up to 50% will say, "Yeah, I feel a little off balance, particularly when I turn my head quickly," or if you've got vestibular testing, you see a chloric deficit, but the number that would say that they're actually vertiginous is typically less than 10% by most series. And those are some of the more common symptoms. Less commonly, and this is primarily based on tumor size, when a tumor exceeds about two or three centimeters in particular, you can have fifth nerve symptoms, and most commonly that's facial numbness affecting the same side.

And less commonly, you can have trigeminal neuralgia, which is distinctly different, where you have facial pain on the same side that's typically described as lancinating or lightening like or shooting pains. Less commonly, in less than 5% of patients with vestibular schwannomas, they'll present with some level of facial nerve paralysis that's clinically significant. It's so uncommon in vestibular schwannomas that when a person presents with facial nerve paralysis, our suspicion for something else more sinister is raised. So for example, you worry about it potentially being what's very rare, and that's a malignant peripheral nerve sheath tumor, for example.

Or, even a little bit more common would be something like a facial nerve schwannoma that is mimicking of a vestibular schwannoma because of its location in the IC and the CPA, for example. But overall, among vestibular schwannomas, certainly less than 10% and most series would say less than 5% have facial nerve weakness. Interestingly, there's been a growing number of patients that have been incidentally diagnosed, and that's based on our current era where we use MRI very frequently for many different symptoms. So head MRIs are frequently obtained for many different indications; headache, dementia screening, or memory impairment, etc.

In a 20%, at least in Olmsted County, up to 20% of vestibular schwannomas are actually diagnosed incidentally when the patient presents and gets an MRI for seemingly unrelated or

unattributable symptoms. Most of the time now, a patient who's diagnosed with a vestibular schwannoma presents with some level of asymmetrical hearing loss, and that's what leads to the MRI. There's been a greater understanding of the need to obtain an MRI for asymmetrical hearing loss. There's more MRIs around and access to MRIs has increased, and that's what's driving a rising incidence of the disease overall.

Dr. Jason Barnes:

And when you see these patients in clinic and perform a physical exam, what are you looking for or what could you find?

Dr. Matthew Carlson:

So really, the money's on the MRI and seeing the size, but if you're looking for specific symptoms, you will check a facial malfunction appraised using the House-Brackmann system. You'll look for facial numbness, particularly if the tumor is larger than about two centimeters, you can check your V1 through V3 distribution on the ipsilateral side to see if that's present. And of historical interest, not really talked about much now, is the Hitselberger's sign, and the facial nerve carries some sensory twigs that innovate the posterior external auditory canal, and as well as some skin on the posterior aspect of the pinna on the posterior aspect of the conchal bowl and involvement of the facial nerve vestibular schwannoma can actually because numbness in this distribution, but again, not really commonly talked about.

Dr. Jason Barnes:

And could you speak a little bit more to the epidemiology of this disease? Who are the patients who are most commonly affected by this?

Dr. Matthew Carlson:

So there is no strong gender or sex predilection compared to some other tumors that involve the skull base. It's pretty close to equal between men and women in presentation. It generally presents between the ages of 40 and 60 years, although certainly presenting outside that is common. Whenever we see a patient who's presenting at a much younger age, particularly if they're in their teenage years, 20s, or even early 30s, our suspicion for a possible developing condition of NF2 is heightened. So we'll calmly scrutinize the contralateral ear care very carefully an MRI to make sure we don't see another concomitant, very small vestibular schwannoma, and we'll always be aware of this when we're following the patient with additional scans.

And in some cases, if the patient's very young, we might even get genetic testing in a person, for example, under the age of 30, depending on the circumstances. There are some risk factors for the development of a vestibular schwannoma. And as you already alluded to, one of the things you always ask about is the history of developing a vestibular schwannoma in other family members. And specifically, you're looking for the condition of NF2. Again, today we're talking about unilateral sporadic vestibular schwannoma, but having a family member with NF2 increases your risk, of course, for getting NF2.

Very briefly, NF2 is an autosomal dominant condition. So half of offspring would inherit and half wouldn't. And half of people with NF2 have a family history of disease, and the other half do not have a family history of disease, they're the originator of the disease in that mutation, which I think is a very important thing to think about. But when we get back to sporadic tumors, what are risk factors for that? Well, there's, in most cases, there's no identifiable risk factor. Early life exposure to ionizing radiation is

a risk factor, but again, that's quite rare that people have that these days. But for example, the person at a very young age who received radiation for tinea capitis, or adenoiditis or somebody who is perhaps exposed from another country to Chernobyl or World War II atomic bomb blast could develop vestibular schwannomas from that.

They can also develop other sequela, delayed sequela from radiation, including other tumors, including meningioma. I think that probably summarizes the risk factors. You'll read in some manuscripts or some publications that cell phone use and loud noise exposure are risk factors for vestibular schwannomas. I don't really buy it personally, and I think that if you really understand the literature well, you'll probably come to the realization that these are in fact, just screening tools or they increase your detection of the tumor, but probably don't actually cause the tumor. If you have a long standing history of noise exposure, if you have hearing loss, you're more likely to have some level of asymmetry and you're more likely to get an MRI, so you're more likely to have a tumor detected.

The same thing for a cell phone. A cell phone is in essence, a screening tool. If you have only mild hearing loss in one ear, you may not notice that normally, but if you're using your cell phone in that ear, very quickly you might realize that you're developing some level of hearing loss, you could present to the doctor, get an audiogram, find asymmetrical hearing loss, get your MRI, then you have your diagnosis. So I don't think they're causative, I think they're associated.

Dr. Jason Barnes:

And when you see folks who present to your clinic and you have the suspicion of vestibular schwannoma, what else is in your differential diagnosis here?

Dr. Matthew Carlson:

So when we break down the differential diagnosis, we're essentially looking at the radiological differential diagnosis of an internal auditory canal and cerebellopontine angle lesion. There are a lot of different lesions that can affect this area of anatomy, but by far and away, the most common tumor of the IC and CPA is a vestibular schwannoma and collectively, they encompass about 90% of all cases of posterior fossa CPA lesions. The second most common lesion to affect the CPA is a meningioma. A vestibular schwannoma with regard to radiological characteristics, there are some distinguishing features that will separate that from these other pathologies we're talking about.

Vestibular schwannomas or isointense on T1 pre-gadolinium, isohyperintense on T2, and one very characteristic thing is they will avidly enhance with gadolinium. They typically have a more heterogeneous enhancement pattern because they contain microcysts, and less commonly, they may actually have macrocysts, which can be within the tumor substance itself or in the periphery of the tumor. They are generally centered very much on the porous acousticus, which is the medial opening of the internal auditory canal. And they almost always, not always, but almost always have extension within the internal auditory canal.

Meningiomas in contrast typically are eccentric or off-center from the porous acousticus. They may or may not have extension into the internal auditory canal. They may have ossification or calcifications within the tumor itself. They may have hyperostosis of the base of the tumor, and they tend to be extremely homogenous on T1 post-gadolinium imaging, which those features really separate meningioma from vestibular schwannoma. In most cases, you can separate them just on the scan features alone. There are other cranial nerve schwannomas, aside from the vestibular schwannomas, that can affect the area.

The one that can be mistaken most commonly is a facial nerve schwannoma. So facial nerve schwannomas can affect the facial nerve anywhere from the ponds where it exits all the way to the

peripheral branches of the face. But if it only involves the CPA or IC, they are almost indistinguishable in most cases from a vestibular schwannoma, they have the same enhancement pattern and everything else. There are a couple clinical clues that's a facial nerve schwannoma. Commonly, you could have a medium sized tumor, and you may not have any degree of hearing loss because it's affecting the facial nerve primarily and not the auditory nerve or eighth nerve.

Less commonly, you could have hemifacial spasm. In about 20 or 40% of patients, you might actually present with a history of "Bell's palsy," facial nerve paralysis on that side. But to really distinguish a facial nerve schwannoma versus a vestibular schwannoma, you have to have extension of the enhancement and nodularity of the tumor extending beyond the IC into the labyrinthine segment or beyond. If you cannot see enhancement beyond that, then your suspicion for a facial or schwannoma will be pretty low. You can also have a lipoma. A lipoma is a congenital lesion that typically does not grow significantly after puberty.

A tip off for a lipoma and also an epidermoid is the nerve fascicles will actually often travel through the substance of the tumor, blood vessels and nerves will do that, and that's in sharp contrast to other neoplasms such as meningioma and vestibular schwannoma, where the nerve fascicles and arteries are pushed on the periphery of the tumor capsule. So very different from that standpoint. You can see it on the scan. But most characteristically, a lipoma will be a hyperintense on pre-gadolinium T1, which is in sharp contrast to vestibular schwannomas that basically shouldn't have any significant hyperintensity pre-gad T1. And they should also subtract with fat saturation technique on an MRI.

The next lesion is an epidermoid, also a congenital rest of essentially a cyst of keratin debris in the center with a capsule of keratinizing squamous epithelium. And just like a cholesteatoma, they tend to grow over time as the cyst wall deposits more and more keratin. Imaging features are pretty characteristic. The center of the lesion is hyperintense on T2 and, actually very much isointense too, or it has similar intensity to CSF, so it almost looks like a CSF pocket, which is why they're commonly confused with arachnoid cysts.

They generally do not enhance on T1, except sometimes the peripheral capsule may enhance with contrast. It's important to understand that how you differentiate an epidermoid from an arachnoid cyst, because those two look very similar on T1 and T2. The distinguishing feature of an epidermoid is that it will restrict on a diffusion weighted imaging, so specifically, non-echo-planar diffusion-weighted imaging, the lesion will appear very bright compared to an arachnoid cyst. Hemangiomas infecting the IC or CPR are relatively rare. They can present like this tuber schwannomas radiographically, but clinically, they often manifest with symptoms that are out of proportion to what you'd expect based on the tumor size.

So they'll commonly present with very advanced hearing loss or facial nerve paralysis with even a small tumor, which is uncommon. Glial heterotopia is commonly under-recognized, but it's where you have an ectopic rest of normal brain [prankerma 00:13:07] along the course of the eighth cranial nerve. And historically, people have called these "burned-out acoustic neuromas," because they don't enhance with gadolinium, but they, from every other standpoint, look very much like a vestibular schwannoma. We already talked about arachnoid cyst, which are essentially an arachnoid area that has a loss of the circulation of the general CSF, surrounding CSF, and you create a cyst wall there.

Osteomas are quite uncommon, but they can involve the internal auditory canal. Choroid plexus papilloma are also rare. And then you can have metastasis, and there has been case reports of bilateral melanoma metastasis to the bilateral ICs, for example.

Dr. Jason Barnes:

And moving on to pathophysiology, can you tell us exactly what is a vestibular schwannoma?

Dr. Matthew Carlson:

That's a really important question. So there's historically people would call these acoustic neuromas. More commonly now, or more accurately, we call them vestibular schwannomas, but you'll even hear people talk about them as being acoustic schwannomas or vestibular neuromas. The anatomically correct term for this disease is a vestibular schwannoma because the great majority of these lesions arise from the vestibular portion of the eighth cranial nerve. Depending on the source, some sources will say they're more common to arise from the superior division, some people say the inferior division. I'd say the jury is still out on that, but they come from the vestibular nerve generally in the area close to Scarpa's ganglion, where there's a increased density of Schwann cells. That's at the peripheral and central nervous system junction.

They arise from Schwann cells. So Schwann cells are the insulating fibers of the peripheral nervous system. That distinguishes schwannomas from neurofibromas. Neurofibroma are different, and they typically are more common to develop in neurofibromatosis type one. Histopathologically, neurofibromas have dense tangles of axons within the tumor with a haphazard organization. That's in contrast to schwannomas that typically don't involve the axonal portion of the nerve, but affect primarily or only affect the portion of the periphery comprised of Schwann cells. Histopathologically, there are some buzzwords that you'll commonly hear and that you should recognize, and specifically, Antoni A and Antoni B.

That's the histological appearance that these tumors can take on. Typically, they're heterogeneous. And when you look at them under a slides and you'll have these areas of Antony A fibers, which are dense, hypocellular palisading spindle cells. And Antoni B fibers, which are loose hypocellular microcytic structures or patterns. The Verocay bodies are dense bodies that are commonly intermingled within the hypercellular palisading spindle cells of the Antoni A variant. Despite what you'll read in several publications, it's not that one type, Antoni A versus Antoni B predominance predicts more aggressive growth or any other type of clinical behavior, but just histological findings that you can see.

Dr. Jason Barnes:

And one question that I like to ask is, what's the natural history of the disease? If we diagnose this and decide not to treat it, what would happen?

Dr. Matthew Carlson:

I'd say there's very few questions that are more relevant to vestibular schwannoma than that question. The natural history of the disease and understanding the natural history of the disease has substantially changed our treatment paradigm overall. Historically, with all skull-based lesions, the mantra was, see tumor, treat tumor radically with surgery, and it would be only rarely that you'd observe a patient because it used to be that we thought all of these tumors grew and they always cause some neurological incapacitation or demise. And over time with MRI, we've seen a growing number of small tumors being diagnosed and we've seen that when, if you are a very aggressive in treating a small tumor, you'll often make a patient worse.

Following patients over time on MRI and CT have led us to find out that about half of small to medium-sized vestibular schwannomas do not grow at all within the first five years. In a small subset, maybe three to 5% will actually regress in size. There's nothing about the imaging features of a tumor that can help you predict if it's going to grow fast, or if it's going to involute or if it's going to stay the same for a long time. And there's no way to know how long it's been there. We don't think that anyone's

really born with a vestibular schwannoma. So certainly, it had to grow at some point to get to the size it was at diagnosis, but oftentimes, they'll enter a period of quiescence and not grow.

It is unpredictable though, when they will start growing. Most of the literature says that if it hasn't grown by five years, you're free to not necessarily follow it as closely, or perhaps not even follow it anymore if the patient's older. But we have seen in our series that there are people with late growth, people that didn't have any growth for five or 10 years, and maybe 15 years later we'll have a more rapid growth. And so from our perspective, we never tell a patient that you're released from care and you never need any additional imaging. We'll still follow them indefinitely even though we'll space the imaging intervals farther out.

I think it's worth mentioning that with the amount of people who are undergoing just observation without treatment because of the greater understanding of natural history of disease, the number of MRIs we're getting is going up. And you'll probably read about it in the news sometimes, that there's some issue with contrast accumulation, gadolinium accumulation in the body can a can deposit within the kidneys, within the brain and other areas of the body. And that's led several groups to use just heavily-weighted T2 imaging to perform surveillance of tumors after they've established a diagnosis with their first scan using gadolinium.

And certainly following an observed tumor, or even after radiation, just using T2 imaging, as long as it's thin slice CISS/FIESTA type imaging, is certainly adequate in most cases. I think whenever we think of any disease process that involves a skull base, particularly when it's benign, we have to think of what I call the golden rule of skull based management, and that is you should never impart more harm on the patient than what the natural history of the disease is expected to do during their lifetime.

Dr. Jason Barnes:

So you see a patient in clinic with a vestibular schwannoma, you have the MRI that's pretty classic for it. What's your workup?

Dr. Matthew Carlson:

As you had said, most people come in with an MRI, and that helps establish the diagnosis. Sometimes the diagnosis is in question because the MRI was just a course, had MRI without contrast and so you might repeat it. But by far and away, MRI is the workhorse for diagnosis and the gold standard for diagnosis now. CT is rarely obtained, it might be for the person who can't have an MRI because they are pacemaker dependent, etc, or you might be using it to decide between surgical approaches. For example, if you're thinking about doing a middle fossa approach, but overall CT scans are rarely used in the workup for vestibular schwannoma.

Dr. Jason Barnes:

Any role for vestibular testing?

Dr. Matthew Carlson:

So you can't get vestibular testing. Vestibular testing, some groups will commonly obtain vestibular testing on everybody and other groups will basically obtain it on nobody. We'll typically obtain it for two different scenarios. The first is if the patient's really reporting a lot of dizziness, we want to make sure that it's actually the vestibular schwannoma causing the dizziness. And of course, the response from the patient is, of course the vestibular schwannoma is causing the dizziness. You're saying it's a tumor on the dizzy nerve, but there are a lot of other causes of dizziness besides vestibular schwannomas. And a lot of vestibular schwannomas actually don't result in significant dizziness. So we'll get it for that reason.

But then secondly, if it's a very small tumor, there are some groups that will obtain vestibular testing to help further refine or define the nerve of origin. And there is data to show that a superior vestibular nerve tumor, you're more likely to save hearing on a hearing preservation microsurgery attempt compared to an inferior vestibular nerve tumor. And so sometimes the tumor is so small on an MRI, particularly on a coronal, you can see where the tumor is emanating from, the superior or the inferior vestibular nerve. However, when it's a little bit bigger, it can be a little more tricky, and so some groups will use a caloric testing to ascertain whether or not it's coming from the superior vestibular nerve and cervical vamp testing to see if it comes from the inferior vestibular nerve.

Separately, ABR is of historical relevance. I will say that most groups in the United States and other developed countries don't use ABR for screening or workup. The one caveat might be if you're considering a hearing preservation approach and your approach is dependent on ABR testing during surgery, you might obtain a preop to make sure they have a good way for them for testing. But I think that is a main discussion as it pertains to work up.

Dr. Jason Barnes:

And then just one final question for that. In terms of the audiogram, what are you looking for on the audiogram? And can you tell us about what rollover is?

Dr. Matthew Carlson:

Yeah. So when you look at the audiogram, I think there's several really important things to talk about, and thank you for bringing that up. So you'll read in the literature that vestibular schwannomas may have some characteristic pure tone patterns, but I'll tell you that most of the time, it primarily involves the middle and high frequencies, but it can also involve the low frequencies, but there's no characteristic pattern on an audiogram that will tip you off. For example, in Meniere's, you look for the low frequency sensor or hearing loss and familial hearing loss. You look for that cookie bite for noise notch, noise exposure, you look for the 4k.

There's nothing like that that's really characteristic for vestibular schwannoma pure tones, but there are a couple of things that I do think are true. The first is you'll often see a disproportionate loss in your word recognition score compared to your pure tone, what you'd expect based on your pure tones, and that's the so-called retro cochlear pattern of hearing loss. The other phenomenon that's commonly discussed is the idea of rollover. Whenever an audiogram is performed, typically the audiogram with speech audiometry, the sound or voice has presented at a comfortably audible level above a person's reception threshold, meaning they can hear the sound pretty comfortably and easily when the words are presented.

With the vestibular schwannoma, as you present that sound louder, a person may actually get worse where in most people they don't experience that. So there's a paradoxical, worsening in word recognition score with increasing loudness at presentation of words. The last thing that is sometimes talked about for the workup in a vestibular schwannoma, again, I would say this is, in my opinion, completely historical relevance, although some people might still use it today, and that's looking at stapedial reflex decay. So to perform stapedial reflex testing, what the audiologist will do is they'll present a noise or sound, tone, that's typically about 70 decibels above a person's hearing threshold.

That should elicit a stapedial muscle contraction or a stapedial reflex response. That sound is generally sustained for 10 seconds, and the stapes muscle or stapedial tendon should contract that entire time and not change. In a pathological situation such as with the vestibular schwannoma, you may see decay. That means during the course of it, it might lose some of its contraction and you'll see a

drift off and that's stapedial reflex decay, again, primarily of historical relevance, but still, maybe worth mentioning.

Dr. Jason Barnes:

So once we have the diagnosis made, or at least were highly suspicious given the MRI findings and some of the audio metric findings, what's your treatment and how do you counsel patients for treatment options?

Dr. Matthew Carlson:

I'll say there's probably nothing more controversial in all of skull-base surgery or skull-based disease management than the treatment of a smaller, medium-sized vestibular schwannoma. I'll try to acknowledge some of the controversies as we go through it and I'll talk about our preferences or my preferences. Overall, when you approach a person with a vestibular schwannoma, there are some overarching features of the patient and of the disease that might push you towards a surgical versus nonsurgical treatment, factors including the patient's age, the tumor size, tumor features, whether or not it's cystic, for example.

Patient preference is very important for this disease, patient's symptoms, particularly those that are related to mass effects, such as facial pain or facial numbness, hydrocephalus, for example, the hearing status of the patient, do they still have useful hearing in their ipsilateral ear? And also very importantly, what is their hearing in their contralateral ear as well? You'll look at their general health. There are some geographic biases and provider biases. If you go to certain centers, you might be more likely to walk away with the recommendation of surgery versus others, you might be recommended radiosurgery, just even for the same type of tumor.

But by far and away, the very most important feature of a tumor to help determine what treatment trajectory you're going to go toward is tumor size. So there's nothing more important when you're talking about management. And broadly, I think it's best to divide tumor size into three different categories, and even before that, we should define how you measure a tumor. So when you're talking about tumor size for a vestibular schwannoma, the first division is you say, "Is this a purely intracanicular tumor or is this a tumor with cerebella pontine angle extension?

An IC tumor can be just described as an IC tumor, or you could give its maximal length within the IC. When it grows into the CPA, typically, most people will measure it in its single largest linear dimension in the axial plane. There are other ways to measure it, but pragmatically in clinic, that's how most people will define them. So understanding that definition and how to measure tumors, we'll talk about the different size categories. Generally speaking, we call small tumors, anything that has less than 1.5 centimeters in the CPA on maximum linear dimension, medium-sized tumors categorized as anything from 1.5 to 3.0 centimeters, largest dimension in the angle, and anything greater than three centimeters, that would be considered a large.

So you have small, medium and large at 1.5 to three, and over three. When we talk about a small tumor, you really have three very good management options, and there is no data to say that one is unconditionally better than the rest, they all have their advantages. The options are observation with serial imaging over time, meaning you don't treat the tumor, but you just watch it to see if it grows. You can do microsurgical resection, and you can do radiosurgery. For tumors that are between 1.5 and three centimeters, we generally say, observation is not usually on the table anymore, and it's only a microsurgery or radiosurgery.

And again, a little controversial, but most people would agree that any tumor that's over two and a half or particularly three centimeters in size and the ankle, radiosurgery and observation are off

the table and only microsurgical resection is performed. When we talk about observation, the advantage of observation is there's very little risk incurred, just with observing a tumor. We'll typically get a scan, and if it's a smaller tumor, we'll have a repeat scan about six months and that's to catch those fast growing tumors. During that time, the patient has an opportunity to think about their options and they don't feel forced or rushed into a treatment.

The other thing that's beneficial is it can help determine whether or not the tumor is growing or not, because if the patient knew it was growing, they might be much happier about or much more willing to enter a treatment versus somebody who has a non-growing tumor, for example. And they might also be more willing to accept a complication of a treatment if they knew that they had to have it because the tumor was growing. We would typically get an MRI at six months and then a yearly for at least three years, then go every other year for a period of time, but we will follow patients indefinitely, spacing out their MRIs more and more over time and being more likely to use just T2-weighted imaging.

Another aspect, it's really important to mention about observation and what's commonly not discussed in textbooks, for example, is the idea that the patient themselves cannot rely on their symptoms to determine if their tumor is growing. They have to get an MRI, there's no other way to do it. I'll always tell patients, "Don't use hearing loss or other symptoms as a barometer for growth." There's an issue of noncompliance or non-follow up for patients who elect observation, meaning they were just saw doctor, they were told they had a three millimeter tumor, tiny tumor, they were told it was benign, and they were told that there's a good chance it's not going to grow.

Naturally., some patients are just going to take that to believe that they don't have to get additional imaging. And so we always emphasize that's important. And specifically, I'll outline that if you have a tumor that doesn't grow, your hearing can still get worse, and conversely, you can have a growing tumor we're hearing stays the same. So I'll say that if for example, if the patient experiences a sudden hearing loss during their course of observation, which does happen in 10 or 20% of vestibular schwannomas, I'll tell him not to develop a lot of anxiety, it doesn't mean the tumors doubled in size. And the converse is true, if they feel like they're hearing hasn't changed, I'll still urge them to come in for their next regularly scheduled MRI study.

Dr. Jason Barnes:

And the next treatment option, it sounds like is radiotherapy. Can you tell us a little bit more about that?

Dr. Matthew Carlson:

Radiotherapy and within that umbrella is radiosurgery, is the second treatment option. That's a good management option for tumors that are generally less than two and a half to three centimeters in maximum CPA dimension. I think it's good to understand the nomenclature before we discuss this all, but typically, radiosurgery implies that the patient's being treated with a single fraction of radiation, meaning one single treatment. There is some latitude in its definition, some will include up to three or five fractions, but for the most part, people describe this as a single fraction of treatment.

The benefit of radiation is that it's an outpatient treatment, patients generally feel the same they do several days after, as they did several days before. There's no post-treatment restrictions, and there's essentially no recovery time, so people can resume work right away. The goal of radiation is to make the tumor not grow. So you'll get six sequential scans and the tumor will probably still remain the same size, even up to 10 or 20% of cases, you'll see something called pseudoprogression where the tumor gets a little angry from getting the radiation, we'll have some swell, but that's well, we'll stabilize within the first two or three years. And we generally don't call that a radiosurgical failure.

Most literature would support that with radiosurgery, radiosurgery provides tumor control and up to 90 or 95% of patients at the 10-year mark. Currently, most platforms for radiosurgery in the United States employ the Gamma Knife. The Gamma Knife is the most common platform, but also people will use CyberKnife, which uses something called LINAC or Linear Accelerator. Less commonly, and I would say there's only a couple centers in the United States to do this, but you can also consider proton beam therapy and even much more rarely, would you use something less focused such as IMRT. I think just describing one of the platforms will be beneficial to understanding what radiosurgery is.

Again, the most common platform is Gamma Knife radiosurgery. Gamma Knife uses cobalt-60 for a radiation source, and Gamma Knife employs a headframe that rigidly fixates to the person's head that can provide very precise radiation. Again, the Gamma Knife uses a 200 different radiation sources that can all be optimized to stereotactically or very precisely and accurately treat just the tumor and significantly limit the amount of radiation that's obtained by other areas that are unaffected by the tumor. So in that way, the side effects are very few. When we talk about outcome with radiation besides tumor control being about 90% at 10 years, radiosurgery will advance or accelerate the rate of hearing loss over the natural history, but generally, is gradual over time.

If you look at most serious, if you start off with what we call functional hearing, being greater than 50% word recognition scores in the affected ear, by about five years, 50% of people will lose functional hearing. And by about 10 years, only about 25% of people will retain functional hearing if they had it at the beginning of when they were treated. The risk of facial nerve paralysis with Gamma Knife radiosurgery when you're using a conventional dose of 12 or 13 grades the tumor margin, is less than 1%. And the risk of other sequela such as malignancy or stroke or hydrocephalus are also very, very low. I think it's worth briefly mentioning the issue of malignancy because this is commonly discussed about, but rarely occurs.

When you talk about the risk of developing malignancy after radiosurgery, you have to put it in the context of the general risk of spontaneously having malignancy, but also you have to separate out sporadic in NF2 patients. Patients with NF2, most patients have a germline mutation or constitutional mutation, the NF2 gene, which is a tumor suppressor gene, which predisposes them to developing tumors to begin with. In this population, the risk of malignancy is higher, it's still relatively rare compared to the sporadic group. If you look at the literature, most publications will say that the rate of developing a malignancy after radiosurgery is less than one in 5,000 or one in 10,000 overall. So rare event, even though it's commonly talked about.

Dr. Jason Barnes:

So, we just discussed radiation. Can you now tell us about the surgical option for this tumor?

Dr. Matthew Carlson:

Microsurgical resection can be used for any size tumor and it can be used for cases where you're trying to preserve hearing. So I think those are the two things to think about at the beginning. There are three surgical approaches that are commonly employed for microsurgical resection of a vestibular schwannoma. There's the translabyrinthine approach, which goes through the labyrinth, and as a definition of the procedure, a patient will lose hearing if they still have it with that surgical approach.

It allows you to identify the lateral portion of the facial nerve at the labyrinthine segment or at the distal fundus, which is reliable. It also is advantageous because all of your drilling is extradural, so you're not drilling and disseminating bone dust intracranially. Its risk of at least short term headache is probably lower than for example, the retrosigmoid approach. And it provides you with a more lateral to medial corridor for tumor resection in a shorter distance for tumor resection. There are some

disadvantages of the translab approach, besides just causing profound hearing loss, there is more limited exposure with very ventral portions of the tumor and tumors that go on below the juggler ball, for example.

You can still overcome that by wide decompression, but compared to the retrosigmoid approach, for example, it is more difficult. The retrosigmoid approaches, the second surgical approach. The reason it's popular is it's very familiar, particularly for neurosurgeons. The retrosigmoid approach is the workhorse approach to the posterior fossa for neurosurgeons. Although there are subtle differences between the retrosigmoid approach in general, they're essentially synonymous terms, it's a synonymous term with the suboccipital approach. The retrosigmoid approach allows you to see all the way from the frame and magnum to the tentorium, so you can see very small tumors and very big tumors and surrounding anatomy quite well.

It does allow you to see the Meckel's cave and the fifth nerve very well or better than translab approach in general. And that might be advantageous for a patient who has trigeminal neuralgia, can comment with having a vestibular schwannoma. It also allows you to see lower, so for tumor that's extending below the level of the juggler bulb, you could see this better. The primary disadvantage or quarter disadvantage of the retrosigmoid approach, at least in the short term is a possibility of greater headache risk. The etiology of a greater post craniotomy headache risk is not well defined, but there are several theories.

One is that you have bone dust dissemination because after you remove a lot of the CPA portion of the tumor, you're drilling on the IC, and you're doing intracranial drilling. The second is that if you don't put a bone flat back, some of that muscle, suboccipital muscle will insert on the dura, and that traction can cause pain. There's the occipital nerve that goes to this area, so you can have occipital neuralgia or neuroma in this area. And those are the main reasons why some people hypothesize that there's a higher short-term risk with headache, but we found that long-term risk of headache with this approach and other approaches is pretty comparable.

You'll also read in the literature that perhaps the facial nerve outcomes are better with one approach compared to another when you're compare the retrosigmoid and translab approaches, that has not been our experience at all, for us, the number one factor is tumor size. And probably the second factor is the course of the facial nerve, more than anything. And in our experience, the translab approach and retrosigmoid approach provide similar outcomes in that respect. As I mentioned too earlier, with the retrosigmoid approach, you can use it for hearing preservation approaches, but you can also use it for very large tumors.

When you're talking about hearing preservation approaches, classically in a textbook you'll read that medial tumors that are more in the cerebellar pontine angle are more amenable to a retrosigmoid approach compared to tumors that are more laterally based in the IC are more amenable to middle fossa approach. And that's theoretical benefits of each, but I'll tell you that most centers use what they're most comfortable with. If you're really good at a retrosigmoid approach, you can get the tumors that extend out laterally. And if you're very good at a middle fossa approach, you can get tumors that stand up to half a centimeter, or maybe even a centimeter if you're really pushing it in the CPA using a middle fossa approach.

That brings us to our third approach, and that's the middle fossa approach. That's a transtemporal approach. So you're going through the squamosal of the temporal bone, extradural subtemporal. So you're elevating the dura and you're lifting up the temporal lobe and there is some level of retraction, that allows you to drill out the internal auditory canal. The middle fossa approach is essentially only used for small intracanalicular tumor. Generally, the patient has to have very good

hearing to begin with. And as a general rule, the tumor shouldn't extend more than about half a centimeter within the ankle.

And the reason is you just don't have good control of the posterior fossa through this limited approach, so if you got into bleeding or something else, it might be difficult to access the area. The one thing that's I think very important to mention with the middle fossa approach is that at least the temporary risk of facial nerve paralysis goes up compared to the other approaches. And the reason is oftentimes the facial nerve will cause over the top of the tumor. And so the facial nerve is between you and the tumor. So as you're pulling out tumor, you're dissecting it off the nerve and pulling it around, and that can cause some level of stretch injury.

Most publications would say the long-term risk of facial or paralysis when you're comparing the same size tumor compared to the different approaches is not significantly different, but certainly the short term risk is different. So I think that encompasses the three different surgical approaches. One last aspect that I think is worth mentioning because it has become more of a hot topic is the idea of extent of resection. So historically, gross-total resection was the goal, but more commonly now, we're performing more conservative resections to limit cranial nerve morbidity or risk of stroke. So there has been a couple of recent publications that show some pretty staggering data, I think, that up to a third or even half of tumors over two centimeters undergo subtotal resection nationally across the country.

And of course, that varies a lot by different centers. Some people intentionally enter a case, performing a very subtotal resection with the intent of performing radiosurgery right away afterwards for the remnant. Most other centers will enter the surgery with the intent to performing gross-total resection, but can see to subtotal resection if they feel they need to because the facial nerves are becoming splayed, overly here into some of the blood vessels are very stuck to the tumor, for example. So I think that summarizes microsurgical approaches.

Dr. Jason Barnes:

That was a great overview of treatment and respective outcomes. Do you mind just quickly summarizing all of those treatment modalities and what we can expect for outcomes?

Dr. Matthew Carlson:

Absolutely. So very briefly, the benefit of observation is it allows the patient more time to think about their condition, allows the patient to know if it's growing or not. But typically, observation is only used for tumors are less than about 1.5 centimeters in the angle. The risk of facial nerve paralysis during observation is low. There is a risk that the patient will develop progressive hearing loss during that time, and maybe perhaps lose an opportunity to perform hearing preservation surgery, but overall, it's very low risk in the short term.

Radiosurgery, the primary benefit is there's no recovery time, it's a single-outpatient treatment, patient can resume all of their daily activities shortly thereafter. It has a 90% tumor control rate and a 1% risk of facial nerve paralysis and a very low risk of other much more significant side effects. It does accelerate hearing loss over what you'd expect with the natural history. The last is microsurgery, microsurgery can be used for any size tumor. Generally, tumor over three centimeters is primarily only treated with microsurgery. Microsurgery can be used for hearing preservation approaches and also larger tumors that are resulting in brainstem compression.

The risk of facial nerve paralysis is very largely dependent on the size of the tumor, but generally, for a small to medium-sized tumor, the risk of long term permanent facial nerve paralysis is 10%. And the risk of temporary facial paralysis is probably 10 to 30%, depending on several different factors. The risk of recurrence for microsurgery is heavily dependent on your extent of resection. If you

perform gross-total resection, your risk of recurrence is less than two or 3%, similar or close to the same risk for near total resection, where less than a five by five by two millimeter pad of tumor's left behind.

When you leave greater amounts of tumor behind, we define that as subtotal resection and your risk for recurrence is heavily dependent on the volume of tumor that you've left behind.

Dr. Jason Barnes:

And I know it's probably different depending on which treatment modality a patient receives, but can you talk to us about how you follow up with these patients?

Dr. Matthew Carlson:

Yeah. That's a very important question and something that's controversial. So as we alluded to earlier, after observation, after a person has been diagnose initially, we'll get a scan typically at six months later to catch a fast growing or atypical tumor. And then we'll do annual scans for at least two to three years, and then we'll often go to biennial after that. And we'll always emphasize the importance of lifelong follow up. You can increase your intervals after that, but you should never release a person from getting imaging except in rare circumstances.

With radiation, typically you'll get an MRI post radiation about nine months to a year thereafter. And depending on the tumor size and features, you'll see on the MRI, such as pseudoprogression or a peritumoral edema, you may get imaging more or less frequently. The imaging intervals are less frequent than with observation, but you do need lifelong follow up. Finally, with microsurgery, with gross-total resection, your follow up is the least, and with subtotal resection, your frequency of follow up is the greatest. We at our center usually get an MRI three months after a microsurgical resection and then at a year.

And then our follow-up schedule after that is highly dependent on the findings. If it looks like all the tumors got and our interoperative impression was gross-total resection, then we'll get another scan approximately three years and five years, and then less frequently thereafter. If there's significant disease left behind, we'll get more frequently imaging intervals.

Dr. Jason Barnes:

Well, Dr. Carlson, that was a very comprehensive review of a very interesting topic. Before I move on to the summary, is there anything else you'd like to add?

Dr. Matthew Carlson:

No, I think that covers everything well.

Dr. Jason Barnes:

In summary, the vestibular schwannoma is a benign tumor of the eighth cranial nerve, patients presenting with vestibular schwannoma most commonly have hearing loss and can also have tinnitus, dizziness and symptoms of the fifth nerve and the seventh nerve. In terms of epidemiology, this doesn't have a predilection for gender and incidentally found tumors are becoming more and more common. Risk factors include genetics such as NF2, and prior radiation. The differential diagnosis should include meningioma and facial nerve schwannoma as well as many others.

In terms of pathophysiology, the pathology demonstrates Antoni A regions with Verocay bodies and Antoni B regions. When we work up these patients, the MRI is really the workhorse here. T1 is isointense without gadolinium, but avidly enhances with gadolinium and can have some heterogeneity,

and T2 is isointense. Audiogram will demonstrate hearing loss, and there are also historic findings, such as rollover. In terms of treatment, we talk about observation, radiosurgery and microsurgery, and we usually make our decision based on size, which can be divided into small, medium and large tumors.

Small tumors are anything less than 1.5 centimeters, medium tumors are generally categorized as 1.5 to three centimeters, and large tumors are greater than three centimeters. Outcomes and expectations are dependent on the size of the tumor and the treatment that's followed. Dr. Carlson, is there anything else you'd like to add?

Dr. Matthew Carlson:

No, I think that really sums it up well.

Dr. Jason Barnes:

Well, thank you so much for being here.

Dr. Matthew Carlson:

Thank you for having me.

Dr. Jason Barnes:

We'll now move into the portion of our episode before we close that I'll ask a few questions, as a reminder, I'll ask a question, pause, and allow you to think about the answer or pause this podcast yourself, and then I'll give the answer. So the first question is, what are the most common presenting symptoms for vestibular schwannoma? The most common presenting symptom for vestibular schwannoma is hearing loss. This can also be accompanied by possible tinnitus, vestibular symptoms and other more sinister symptoms, such as fifth or seventh cranial nerve findings. It is worth noting that incidental diagnosis is rising with up to 20% of these being found incidentally.

The next question is, what are the common histopathologic findings in vestibular schwannoma? The buzzwords for pathology for vestibular schwannoma are Antoni A regions with Verocay bodies, and these include dense hypercellular palisading spindle cells and Antoni B regions, which are loose hypercellular microcytic tissue. For our next question, what are some of the classical descriptions of an audiogram in vestibular schwannoma? Some of the more commonly described audiometric findings are as follows; patients will have mid to high frequency hearing loss, word recognition is worse than suspected for the given pure tone averages. Stapedial reflexes will show decay, and rollover will be present here. And that's when word recognition is worse when it's presented at a louder volume.

Next question, describe the classic MRI findings of a schwannoma. Again, vestibular schwannoma will be isointense on T1 without contrast, hyperintense with some heterogeneity on T1 with contrast, and they will be isointense on T2. Finally, describe the treatment options and how you categorize them based on size, and the types of surgery offered. Intervention offered is largely based on the size of the tumor. If you have a small tumor, which is less than 1.5 centimeters, you can offer observation, radiosurgery or microsurgery. If you have a medium-sized tumor, which is 1.5 to three centimeters, you can offer radiation or microsurgery. And if they're greater than three centimeters, we often only offer microsurgery.

Microsurgical options include the translab approach, the retrosigmoid approach and the middle cranial fossa approach. Thanks so much for listening, and we'll see you next time.