Dr. Jason Barnes:

Hey there. Welcome to another episode of ENT In A Nutshell, my name is Jason Barnes. And today, I'm joined with head and neck surgeon, Dr. Kate Van Abel, and we will be discussing melanoma. Dr. Van Abel, thanks so much for being here.

Dr. Kathryn Van Abel:

Thank you, Dr. Barnes. It's my pleasure.

Dr. Jason Barnes:

When we talk about melanoma, we're talking about skin cancer, and this can be broken down into melanoma and non-melanoma, so we'll be focusing on the melanoma side of things. And when you see a patient who presents to your clinic with melanoma, how do they typically present?

Dr. Kathryn Van Abel:

Most of our patients are going to come in saying that they or their significant other noticed a change or a lesion on their skin that seemed abnormal. In my practice, most patients have been seen by somebody else at that point, but most of the time, patients are the ones who are identifying the abnormal lesion and bringing it to their physician's attention. The things that I'm looking for really are signs for how long it's been there, whether this is an early lesion or a late lesion. Things I might be asking them about are whether there's any itchiness, whether it has been bleeding, whether there's any ulceration, because those might be a sign that it's more of a late presentation.

And then when I'm asking patients about it and when I'm thinking about it, I have to have the A, B, C, D, and E's of melanoma in my mind. And honestly, as a non dermatologist, the one that matters the most to me is evolution. So if somebody tells me, "I'm a conscientious person, I know that this is different than it was a year ago," that really raises the alarm bells in my mind a lot more than a slight asymmetry, a change in border, a darker color, or multiple colors, or a particularly larger lesion. That evolution is really key in my mind.

Dr. Jason Barnes:

And in terms of the epidemiology, who are the types of patients who are presenting with melanoma?

Dr. Kathryn Van Abel:

Well, in my practice in Northern Minnesota, that's frankly almost everybody. But the thing that we want to keep in mind is, skin cancer is the most common type of cancer overall. And while melanoma is the least common of the three that we think of; squamous cell carcinoma, basal cell carcinoma and melanoma, it's the most lethal. And the people that I am concerned about who are going to be coming in with this type of tumor or who are at risk are going to be men, they're going to be in their 50s, 60s, something like that. And while I find this question to be a little bit difficult to interpret, somebody who has a history of a peeling or blistering sunburn is at higher risk. I think that's almost everybody, and am surprised when people tell me they've never had that type of sunburn before, but that's borne out in studies.

People who have a family history can be at higher risk. Anyone with a personal history of melanoma is going to have a sustained lifetime increased risk, someone with multiple clinically atypical moles or those dysplastic nevi. The medical student question, of course, you're always going to be thinking about things like xeroderma pigmentosa or Cowden syndrome. Those are much less common,

but something that you have to have on your radar. Again, something that I see a lot of are immunosuppressed patients, somebody who's either got on some medical immunosuppression, has had an organ transplant or a bone marrow transplant for some reason, those folks are going to be at much higher risk.

And then finally are Fitzpatrick skin type, is something we have to think about. And we can go into that in our physical exam. Basically, you want to think about your Fitzpatrick skin type from one to six. You can think of type one as always burns, never tans, and type six as never burns, always tans. And while type one through three are going to be the most common skin types affected by melanoma, you can develop melanoma in any skin type so you need to make sure that you're thinking about it regardless of the skin type that you're evaluating.

Dr. Jason Barnes:

And when you evaluate these patients that you suspect melanoma, what are some questions that you ask in clinic and what are you looking for on physical exam, maybe even apart from just the lesion that you see on their skin?

Dr. Kathryn Van Abel:

So the lesion is the easiest thing to look at, it's typically right there on the head and neck. When we look at all melanomas, about 25% of all melanomas are in the head and neck area, and so I want to take a look at that and get my impression of the size and what it's next to, what I need to remove in order to clear it. And then I want to look for lymphadenopathy, so I want to look in the basins that typically drain the lesion that I'm looking at, so whether that's parotid basins, suboccipital nodal basins, or in the neck itself, and so you do your typical neck exam. And then I think one of the harder things is assessing for distant metastatic disease, and that's certainly something I think a lot about for melanoma is how do I get at those questions.

And things that I like to ask that I think are somewhat helpful are asking about new or different symptoms. So somebody who comes to me with a diagnosis of melanoma is certainly going to be anxious. They probably are losing a little weight, they're a little nauseous, that kind of thing. But a new headache that's really different than something they've had before, and it's been going on for a little bit, new back pain or trouble with their bowel or bladder or something like that. And I think that someone who's got a new, easy bruising or difficulty stopping bleeding, something like that. The things that are easier for our patients to answer in a meaningful way are the questions that I try and focus on for metastatic disease.

Dr. Jason Barnes:

So we talked about presentation, and next I wanted to move on to pathophysiology. Could you tell us a little bit about the pathology that we see in melanoma?

Dr. Kathryn Van Abel:

When we think about melanoma, we have to take ourselves back to medical school where we really learned about the different layers of the epithelium and the dermis, and thinking about where those melanocytes really live, down near the basal layer of the skin. And we are going to need to understand what different slides would look like. If we were asked to look at a biopsy of melanoma, and this is helpful because when we are interpreting the pathology reports from our pathology colleagues after we've taken a biopsy, it's nice to be able to read more than just the diagnosis, to be able to delve into a

little bit about what they actually saw, especially if there's some a little bit of confusion or some nuance to it.

And so the things that you really need to be looking at when you're thinking about reading a path report for a biopsy for melanoma is, you're looking for these large, atypical melanocytes, you're looking for some melanin granules, hyperchromatic nuclei. Sometimes you can see ness of the melanocytes within the epidermis. And once you start seeing that breaking through the basal layer or the basement membrane, that's when you're really going to be calling it an invasive malignant melanoma. We can also see things such as spindle or oval shaped cells. Sometimes pathologists will refer to certain patterns of invasion as pagetoid in pattern, so you may see those words.

And I think that having a good understanding helps you work hand in hand with your colleagues in pathology.

Dr. Jason Barnes:

And what kind of stains are involved with this?

Dr. Kathryn Van Abel:

Yeah. So the most important stands that we think about when we're talking about a melanoma are S100, MART-1, HMB-45 and Melan-A. It's often a combination of a few of those stains that really proves the diagnosis of malignant melanoma. And one thing that is helpful to understand is whether or not your frozen section lab or your moss colleagues have access to those stains, that can be done in a moss style fashion while you're doing a wide local excision in the operating room, because for some of the more nuanced melanomas, having those stains available can really make the difference between taking that next set of margins or not. And so I think that all of us as surgeons need to understand what our pathology colleagues have in their tool set at whatever institution you're at.

Dr. Jason Barnes:

And can you speak to the relevant genetic genetics surrounding this?

Dr. Kathryn Van Abel:

Yeah. We're learning more and more about the genetics of melanoma. And it's really interesting that there's some differences in melanomas that form in chronic sun damaged skin versus those that form and non chronic sun damaged skin. The most common mutation that we're thinking about is our BRAF V600 mutation. And this is helpful to know about if you test positive for that, there may be some immunotherapy options that are available for those patients.

Dr. Jason Barnes:

Now, occasionally when I'm looking through or studying melanoma, I'll see a list of different subsets of melanoma. Could you speak to these subsets, maybe briefly describe them and how it applies clinically?

Dr. Kathryn Van Abel:

Sure. When I was learning about melanoma way back when in medical school, we really focused a lot on the WHO designation for different types of melanomas. And it became confusing because there's things like nodular or superficial spreading, or lentigo maligna. And while this terminology is still important to know, it is not used in our staging system, it's not used to define our treatment approach. And the reason is because it's very challenging for dermatologists to agree, one dermatologist to the next, with a

high level of certainty. And so the WHO has recommended that while we still provide some of this information on our pathology reports, and there are certain types of melanomas for which the subset classification is important. For example our desmoplastic melanoma, whether it's pure or mixed, something like that really does make a difference, we think.

For the most part, that's a part of our pathology report, but we're not using it to guide treatment decision making, and I think that takes some of the stress off of really understanding what each of those different subcategories mean.

Dr. Jason Barnes:

And when we talk about pathophysiology, one of the questions I like to ask is, what's the natural history of this disease? Why do we need to treat it? And why do we tell patients we need to treat it?

Dr. Kathryn Van Abel:

That's a good question. A lot of patients want to know, "Well, what if I don't do anything?" This is a deadly disease. This is a life-threatening disease. And as I said at the beginning of our discussion here, melanoma is the most lethal of the skin cancers that we see and treat. And so typically, it'll get larger, it'll bleed, it'll be painful, it becomes harder to remove. We would expect nodal metastatic disease and we would ultimately expect distant metastatic disease commonly to the lung, the brain and the bones. And that's why when we start getting a large bulk of disease, we'll talk about it in a little bit, but a large bulk of disease, or something that's really concerning. When we think about our imaging, we also have to get brain MRIs to make sure that we don't have intracranial metastasis.

Dr. Jason Barnes:

And what else do you put on the differential diagnosis for this?

Dr. Kathryn Van Abel:

So I think I'd always start with a skin lesion with our top three. So squamous cell carcinoma, basal cell carcinoma and melanoma. Melanoma is not always darkly pigmented, you can have amelonitic melanoma. You could have certainly a benign nevus, you could have some just funny looking freckle and you could have a junctional nevus. The list can get quite extensive. I would also strongly recommend everybody when you're thinking about preparing for going into a head neck cancer clinic where you're going to have different skin lesions, to really understand that there's more than just squam, basal cell and melanoma. You can have a cancer that forms from any of the subunits of the hair follicle, for example, or surrounding structures within the skin unit.

And so having a broad differential is important, but most commonly, I think of those top three.

Dr. Jason Barnes:

Sure. So you see this patient in clinic and you suspect a malignancy. I think I'll just let the cat out of the bag, I think the first step is going to be biopsy or trying to figure out what this is. How do you approach when you decide to biopsy, how you biopsy, and if you do it in the clinic versus in the operating room?

Dr. Kathryn Van Abel:

I have a pretty low threshold for biopsying things, and that's because of the nature of what I do. I think a biopsy is fairly low risk. Leaving an undiagnosed melanoma is very high risk. And so I think it's worthwhile to biopsy. There are lots of different ways to biopsy and I will stop and emphasize that

getting a diagnosis of melanoma, no matter how you do it is better than not getting a diagnosis of melanoma. So we have a lot of angst about, "Oh gosh, this was cut off at the deep portion of the tumor, or we don't know how deep it is." While I always wish that we could do the exact right biopsy for every patient at the exact right time, sometimes our ability to appropriately diagnose these things is an evolution. And so we get folks that have all different types of biopsies.

So number one, just getting the tissue under the microscope and finding those things we talked about to start with is the most important. But, if I had my preference, I would advocate for a narrow margin excisional biopsy. This leaves the door open for reconstruction, this leaves the door open for wider margins. And most importantly, this leaves the door open for sentinel lymph node biopsy, which we'll talk about shortly. It would allow us to be able to assess the depth of the lesion, and that's one of the most important things when we're talking about staging. You can also think about a punch biopsy, a deep shave biopsy or an incisional biopsy. One of the challenges I have with some of those is, you don't always know what is the deepest part of the tumor.

And when we talk about depth of invasion, we need to compare that to the normal layer of skin. And so, if you're always punching on the border, you may not be getting the deepest part of the tumor, but again, at least you would know that it was a malignant melanoma and you need to do more, and you haven't burned any bridges.

Dr. Jason Barnes:

And you've mentioned staging. And since we talked about biopsy, I thought I'd ask, what will be reported from the pathology when you do the biopsy, and how does this inform T-staging?

Dr. Kathryn Van Abel:

It gets reported depends on your pathologist. The American Academy of Pathology, I may be saying their organization name wrong, but basically the governing body for pathologists in the US has recommended that they include a lot of the details that aren't necessarily a part of the TNM staging system but for example, include the margin status, perineural invasion, lymphovascular invasion, whether they see any of these specific WHO subtypes. They want them to include things like their mitotic rate, which if you look at the newer staging system, is no longer a part of the T stage because all of those things are taken into context, and if we have a lot of red flag, high risk features, we may push for something that we wouldn't have based on just the T stage, for example.

Dr. Jason Barnes:

Can you talk to us about Breslow thickness?

Dr. Kathryn Van Abel:

Sure. So again, when we look back to the classic teaching of melanoma, you're thinking about Breslow thickness, and you're thinking about Clark's Level. Clark's Level is no longer a part of the staging system. You may still see that in your pathology report, and it gives you some information, but it's no longer a part of the T staging. Breslow thickness is still a part of our T staging, although you don't always see it as that full word anymore, you may just see thickness or depth of invasion. And when we look at our T staging system, you can see that the two most important features for a T stage include thickness and ulceration. So thickness is basically your Breslow depth.

And what you're doing is you're looking at the normal epithelium, and then you're measuring the distance from that to the deepest portion of the tumor. And that's different than measuring from the mound of tumor that's sitting out top to the deepest portion of the tumor. So it has to be from that

adjacent normal skin and that will drive the T stage. So the overall T stage T1, two, three, four is driven by depth of invasion. The A or B sub categorization for T stage is driven by ulceration. So ulceration always upstages it to a B categorization, whereas the depth is really what's driving the number of the T stage.

Dr. Jason Barnes:

Sure. And what are those numbers?

Dr. Kathryn Van Abel:

So for T1, you can think about this. I think of T1, less than one, T4, greater than four. Then you can go T2 is one to two, T3 is two to four. So if I can get those T1, T4 in my mind, then I can place the other ones. The only one that's really tricky is our T1 stage. So T1a is less than 0.8 millimeters, and this is all driven by whether or not we should do a sentinel lymph node biopsy or not. So less than 0.8 millimeters, no ulceration, that's going to give you And typically you don't need to do a sentinel lymph node biopsy for these folks, unless you see some other high risk features because you were astute and you read your pathology report and identified some of those.

T1 B is going to be 0.8 to 1.0. And basically, anyone greater than 0.8 an on if there's no clinical evidence of nodal disease, we're going to be thinking about sentinel node biopsy.

Dr. Jason Barnes:

And once you get a positive diagnosis from a biopsy here, I imagine patients are going to wonder what stage they're in. How do you counsel them on staging, overall staging in melanoma?

Dr. Kathryn Van Abel:

Sure. So I think melanoma, again, unfortunately it's a very common disease, but that means that we've had a lot of research on it and we've got a lot of data. And when we have a lot of data on a cancer diagnosis, it means that our staging system can get more complex because we know more about it, and that's certainly the truth with melanoma. And patients always want to know, "What stage am I?" Because that's sort of, what's driven home to them as the most important thing. Are they advanced or did they catch it early? And basically, I can't tell them exactly what their stage is until we've done their operation, because for the most part, we're doing our sentinel lymph node biopsies because we think that the volume of nodal disease will be undetectable with any of our current imaging modalities.

So remember that a PET-CT scan, its inferior limit of resolution is somewhere around five to seven millimeters in size. And so if you think that you're going to be detecting microscopic disease on a sentinel lymph node biopsy, it's not the time to be doing a PET-CT scan. And so that's what makes melanoma a little bit confusing because you can have a decently large or deep primary tumor and not necessarily be able to see anything on your PET-CT scan. And so when patients are asking me what stage they're at, I have to paint broad strokes to start with. And I think it's helpful to break up the staging system into something that at least resonates in my mind. And then when I need to get very specific about exactly what stage, I can pull up the staging system and look.

But basically, stage one is going to be localized, thin melanoma, so T2a or less, and no lymph nodes. Stage two is also no lymph nodes, but we're getting into a little medium thick or thicker melanomas. So T2b to T4b. But basically, stage one and stage two are localized disease. Stage three has metastatic disease to lymph nodes, so regional disease, and then stage four is going to be metastatic disease. So stage three regional disease, stage four metastatic disease, and I can generally give people

an idea of what their staging is, but I always have to tell them, "There's no way I'm going to be able to give you a final answer until we're completely done with your surgery and your workup."

Dr. Jason Barnes:

So if that's the case, how do when to obtain imaging and how does it apply in this context?

Dr. Kathryn Van Abel:

Yeah, I think that this is something where it's really helpful, at least when you're starting off in practice, to keep your guidelines up and available that help you through this, but up to stage two, remember we said that includes T4b tumors, but no obvious lymphadenopathy, so nothing you can feel with your hands, they do not need imaging preop. And I think that this is a really uncomfortable realization when you're starting off in practice, that you can have a pretty deep, nasty looking tumor on the top of someone's head and you don't necessarily need any imaging. If you can't get a good exam, for some reason, you could consider an ultrasound or something like that, but you have to recall that that's not a substitute for a sentinel lymph node biopsy.

Our sentinel lymph node biopsy is actually part of our diagnostic workup. So while it's an invasive procedure and it is not exactly the same as an imaging modality, it is something that we use as a diagnostic tool. So no, we don't necessarily need any imaging for up to stage two disease. Anyone though that has symptoms, something that's concerning you, something that raised a flag for you that you were worried about, if you can feel any lymphadenopathy or if we're down the road a little bit and you did have a positive sentinel lymph node biopsy, for those folks, we're going to be thinking about imaging. So anyone with regional disease, anyone with a clinically palpable disease or any symptoms you're worried about.

And so for what imaging to consider, you have a few options available to chest, abdomen, pelvis, CT with IV contrast are very acceptable as is an acceptable route to go. I often go with a PET-CT scan because it's a single study, it's done quickly. But I have to remember that with both of those; chest, abdomen, pelvis CT, or a PET-CT scan, I have not adequately imaged the brain. And so if I'm worried, if there's a big bulky disease, if there's regional lymphadenopathy, if someone's complaining of a new headache or some intercranial or CNS related finding, we need to get a brain MRI scan in order to fully work that up. And then the last thing is, if I'm going to do a PET-CT scan and there's a node that's a bit funny in there, I'd like to see the anatomy of it better.

I do have the ability to get a CT neck with contrast as well which will help me with my surgical planning.

Dr. Jason Barnes:

And one more question, while we wrap up the workup part of this discussion, what are some other considerations for melanoma that don't always apply to other lesions like in-transit mets, microsatellites, macro mets.

Dr. Kathryn Van Abel:

So before we can even answer that question, we have to define those terms a little bit. An in-transit metastasis is a nodule of tumor that you can see with your eyes typically on your physical exam that's more than two centimeters away from the primary tumor site, but not beyond the nearest lymph node basin. So let's say you have a vertex scalp lesion, this in-transit met would be somewhere between that lesion and the parotid basin somewhere in the skin. Well, let's say we have that same lesion and it's down in the neck, it's in the neck, skin biopsy, it's melanoma. That's a dermal metastasis, that's not an

in-transit metastasis. And the reason that those things have to be differentiated is because the treatment's different or the staging is different. We would not consider someone with in-transit metastases as having distant metastatic disease.

If you look at the nodal staging system, it's very complex and the in-transit metastasis increase the amount of nodal burden and go into the N-staging system, not the M-staging system. So that's what we think about for in-transit mets. For microsatellitosis, this is something that you're not going to be able to see with your eyes, you're going to have to rely on your pathologist to look at this during their assessment of the primary tumor. And basically, this is a nest of tumor cells that are greater than 0.05 millimeters in diameter, located in the reticular dermis or near the panniculus, or vessels, and it's separated from the primary tumor by at least 0.3 millimeters.

And again, you're never going to see that, it has to be looked at with a microscope when you hear the word macrometastasis, just think you're going to feel these, or you're going to be able to see them on imaging. So macrometastasis or something that you can see or feel with your hands, micrometastasis, you need a microscope to see.

Dr. Jason Barnes:

Next, I wanted to move on to treatment, but I like what you said about the sentinel lymph node biopsy, because although we're moving into treatment, we'll start to talk about the resection of the primary lesion. Also, when we're in the operating room, we'll be doing some diagnostic work as well with sentinel lymph node biopsy. So to start, how do you plan on approaching the resection of the primary tumor?

Dr. Kathryn Van Abel:

Sure. So I think that that's helpful because, especially as a resident or as for myself, I have to think about what am I going to list this patient for surgery? What things do I need to be thinking about? And it starts with where the tumor is in their head and neck. And based on that and my understanding of the lymphatic drainage patterns, I can have a pretty good idea of where the tumor is likely to drain to. And so, with that in mind, I may consent someone for a superficial parathyroidectomy, possible total parotidectomy possible neck dissection. So those are the three things that are most commonly on my listing for that case.

I want to be thinking about how I'm going to get that person to a lymphoscintigraphy, and in our institution, we can do that the afternoon before, as long as I put that patient on fairly close to first case the next day. Sometimes that can be nice because you don't have to delay your operation or I'm doing same day lymphoscintigraphy. So they go to the lymphocytic review suite that morning, and then I'm taking them to the operating room later that afternoon. And basically, what's happening there is the radiologist is injecting a material that goes through the lymphatic system, goes to the sentinel node.

So that can be one or two lymph nodes or grouping of one or two lymph nodes. And it's going to show you what drains that region first. And this is why, again, it's helpful to do a narrow margin excisional biopsy instead of a wide excisional biopsy because hopefully you're disrupting those local lymphatics, the least amount possible. So I would think about, when I'm going to get that person their lymphoscintigraphy, I'm going to get that scheduled for them, I'm going to take a look at the results from that lymphoscintigraphy. And typically, I don't have that tiller in the operating room.

And then we will put an X on their skin so that I know approximately where anatomically those nodes sit, and I'm going to have the images up so that I can reference them as well. And what I want to emphasize is that the sentinel lymph node biopsy, the goal of it is to be as minimally invasive as possible to get the information that we need and to do it as safely as possible. So if I need to do a superficial

product activity to get that one sentinel lymph node biopsy out, because I can't do it safely without working around the facial nerve, I'll go ahead and do that operation. Whereas if I can get to the sentinel node without doing that, that's preferable. But I think before you engage in going in to do the sentinel node biopsy, you have to be prepared to do all of the next steps.

Dr. Jason Barnes:

And how do when to perform a sentinel lymph node biopsy?

Dr. Kathryn Van Abel:

That's a great question because I think it also emphasizes whether we should be taking somebody to the operating room or not. In my mind, what I can offer as a head neck surgeon is that I can complete the lymph node assessment at the same time as the wide local excision. But, if sentinel node biopsy is not necessary, it's often nice for our patients who are often a bit older or immunosuppressed or something like that, to have MOSE, and then they don't have to go under general anesthesia. So I think it's really hand-in-hand operation with your dermatology colleagues.

But when we're thinking about sentinel lymph node biopsy, basically if we look at back at our T-stage, anyone that who's T1b or higher, meets criteria for a sentinel lymph node biopsy, if they don't have any obvious metastatic disease or obvious nodal disease. If they have either of those things, it doesn't make any sense to be offering that person a sentinel lymph node biopsy, because we already know they've metastasized. What about T1a?That's the one that often is the head scratcher. And basically, our risk of having a pathologically positive node and a clinically node negative neck is about less than 5% or less.

The things that would drive up my concern for those patients are if there's perineural invasion, lymphovascular invasion, if this is a recurrence lesion, something like that. Those would make me a little bit more concerned and maybe think about a sentinel node biopsy for a T1a patient, but typically T1B or higher. I'm thinking about that.

Dr. Jason Barnes:

And as a resident, I always ask myself the question, how do you know what your margins are on your primary tumor? Do you have a general rule that you follow for this?

Dr. Kathryn Van Abel:

Absolutely. So, we've thought about what we're going to do when we go into the operating room. We're going to take out the primary tumor, we're going to do a sentinel node biopsy, we've prepared the patient by setting them up for lymphoscintigraphy either the night before or the morning of. We've prepared to do the completion lymphadenectomy, if our pathologist's notes melanoma on their frozen pathology. And that's something we can talk about a little bit here in a second, because that's different institution as well. But, now we're standing in the operating room, looking at the patient, what do we do next?

The first thing we're going to do is we're going to inject methylene blue because the sentinel lymph node biopsy is a two stage or two signal-type procedure. And our radiologists, thankfully I've injected our radio isotope for our lymphoscintigraphy, and now it's our turn to inject the methylene blue. There are specific procedures that we can go through to talk about that, but it's a little bit challenging just over audio. But basically, what we want to do is create a visual marker for ourselves. And so before I do the methylene blue, I want to look at the tumor and make sure that I can see the edges.

I want to mark out the edges of the actual tumor, because it might be a little bit hard to discern for some lesions after I inject the methylene blue, I'm going to go ahead and inject the methylene blue and then continue doing my prep work for however long it takes, just because that'll give me time if I do the methylene blue upfront to allow it to reach the sentinel node ideally. Some people will talk about having the patient in a little bit of a head up position to have gravity help us get the methylene blue to the nodes, I don't think that's always necessary, but it certainly something you could think about.

Then we get to our margins. So now I've injected my methylene blue, I'm letting that percolate, and now I have to think about where I'm going to mark out these margins. We have some data that can drive our decision making, and I think there's a really nice systematic review that was published by Dr. Zenga and colleagues, which I think is helpful to me for head neck melanoma. And basically, bottom line is I aim for somewhere between one and two centimeters, if at all possible, but if I have an in situ melanoma, I'm typically not taking that person to the operating room, but if I did, it would be somewhere between five millimeters and a centimeter.

And if I have a really thin melanoma, so a T1b, T1a, T1b a tumor that I'm taken to the operating room, I could potentially get away with one centimeter margins. There's some data to suggest that that may be safe, but there's more and more literature out there that perhaps there's a higher risk of local recurrence when we start pushing the envelope on that one centimeter margin, as you know when we're operating in the face, there are critical structures that are hard to resect or unacceptable to resect. So we're always trying to balance oncologic cure with acceptable aesthetic and functional outcomes. But I feel comfortable if I'm somewhere within that one to two centimeters leaning towards the two centimeter mark for margins, if at all possible.

Dr. Jason Barnes:

And you mentioned positive neck nodes, how do you approach either clinically positive neck or when you do have a positive sentinel lymph node biopsy?

Dr. Kathryn Van Abel:

Okay. So for a clinically positive neck, I would have gotten some imaging that would also help me understand whether there's any other lymphadenopathy in the adjacent regions, but typically, you're looking at the involved nodal level and you want to clean out at least the levels in front and behind it, and the levels that make the most sense as draining the lesion of interest. So let's say you had a cheek melanoma, and I have a parotid nodal metastasis, I need to clean out that whole parotid nodal basin. Now, that includes the superficial and the deep lobe.

There was some data where people were talking about these being two separate nodal basins, that's not accurate. It's a single nodal basin with 80 to 90% of the nodes in that basin sitting lateral to or superficial to the facial nerve, and 10 to 20% of the nodes sitting deep to the facial nerve. And so, the NCCN guidelines recognize this now that if you have the skillset and comfort to be able to do a total parotidectomy, that is beneficial to the patient to prevent regional recurrent disease. And then you would go ahead and do probably level two and three, because those would be the next two logical levels underneath the parotid, but it really depends on where the lesion is.

And then as far as what to do with the positive sentinel lymph node biopsy, that really comes down to whether or not you're going to get that result at the time of your initial operation or whether it resulted back to you in a delayed fashion. Most institutions are going to have that come out in a delayed fashion because there's some risk of having a false negative sentinel lymph node biopsy at the time of your frozen section analysis. Our typical practice is that we still will look at it under frozen section, and

we have a pretty low rate of needing to do a revision operation, but it's still something that I counsel my patients on, revision being that in a delayed fashion, we identified a positive sentinel node biopsy.

But then I would say, once you get that sentinel node, you really need to think, "If I had gotten this in the operating room, what was my plan going to be?" And you should still do the plan that you had in that first operative day. So if I get a positive sentinel node, I'm going to go back and try and do a completion lymphadenectomy unless there's something that is restricting me being able to do that, is the patient too sick? Are they absolutely against it? Something like that. The last thing I'll point out is there's some growing literature that the volume of disease in that sentinel node matters.

And so, if you have less than 10% of the node involved with tumor, is pretty unlikely that you're going to have any other nodes when you do your completion lymphadenectomy that have tumor in them. And so you could potentially make a case for observing a patient with a very small volume micrometastatic positive sentinel node.

Dr. Jason Barnes:

And what's the role of radiation therapy in melanoma?

Dr. Kathryn Van Abel:

Interesting, there's not a huge role for radiation, and if we do a good operation with a good margins, there's almost no role for adjuvant radiation therapy to the primary site. And this is helpful to think about when you're thinking about your reconstruction, especially on the scalp, because if we're ever thinking about adjuvant radiation therapy, we don't want to be skin grafting over the calvarium or leaving exposed calvarium to granulate in. In that case, you would want to be putting some vascularized tissue over the bed, but for the most part, we don't need to be thinking about adjuvant radiation therapy to the primary site, unless there's some extenuating circumstances or large caliber perineural invasion, something like that.

But typically, we are only thinking about this if we can't operate on the patient or too sick, resecting the disease would incur to high morbidity to the patient, or they're not willing to accept it, or if we end up with positive margins and we just can't resect any further, those would be reasons to think about adjuvant radiation therapy to the primary site.

Dr. Jason Barnes:

What about radiation therapy to regional disease?

Dr. Kathryn Van Abel:

There are some pretty specific guidelines available for our radiation oncologists and for us as to when adjuvant therapy is indicated, I would say whenever you have a question, reach out to your radiation oncologists, we are better when we work together as a team, but typically, any time you have extra nodal extension and if you have one or more lymph nodes within the parotid of any size and two or more lymph nodes within the neck, or if you have a three centimeter or greater volume of tumor within a neck lymph node, then those would all be indications for adjuvant radiation therapy to the nodal basin.

Additionally, you can think about radiation and palliative settings when you can't do any additional operation.

Dr. Jason Barnes:

Can you speak a bit to the systemic therapy that's sometimes offered in folks with melanoma?

Dr. Kathryn Van Abel:

I think there's a lot of exciting things happening in melanoma. We're learning a lot more about immunotherapy, we're learning about vaccine trials, and I think that there's going to be a lot changing in our lifetime of treating this disease. And again, when in doubt, reach out to your medical oncologist, there may be trials that you're not aware of, that our patients can qualify for. Typically, these are going to be stage two or higher patients, but typically, we're thinking about immunotherapy for patients or adjuvant therapy for patients for metastatic or unresectable disease. It really doesn't play a major role in adjuvant therapy for local regional disease

And our two most common areas that we're thinking about for immunotherapy are drugs that target the PD-1, PD-L1, ligand like pembrolizumab or nivolumab, or we have some targeted therapy towards that mutation, that'd be BRAF-V600, mutations such as dabrafenib or vemurafenib, those are both interesting drug choices as well.

Dr. Jason Barnes:

And one other question I wanted to ask going back to the treatment of the neck and as we move into prognosis and outcomes, how does treatment of an effected neck affect outcomes?

Dr. Kathryn Van Abel:

That is a very challenging question, and it's unsettling to answer in some ways. So you could say, "Well, gosh, I did such a great job. I did my sentinel lymph node, I found this positive note, I took it out. I should have affected their long-term survival." And the answer unfortunately to date is no, we don't affect their cancer specific or overall survival by doing our lymph node dissection. But, by identifying this lymph node is being involved, you've done a great service to identifying the most important prognostic factor for that patient and perhaps getting them on a closer surveillance schedule or opening the doors to immunotherapy.

But we do know that doing your completion lymph node dissection or doing your sentinel lymph node biopsy and identifying the tumor sooner rather than later, decreases our regional failure, so it increases our local regional control. And you might say, "Well, if I find it today versus if I find it two years from now, what difference does it really make?" And in the head and neck, it can make a difference. If you have tumor growing in the deep lobe of the parotid, and all of a sudden the patient's face is paralyzed, that's not something that we should be saying is okay.

Identifying that lymph node during your total parotidectomy, and being able to get that out and preventing that sequela from progression of disease and the local regional nodal basins, I think offers a benefit to our patients. But we have to be very clear that we have no evidence that doing any of our lymph node management affects long-term cancer specific or overall survival

Dr. Jason Barnes:

And regarding outcomes in survival for melanoma, how do you counsel patients on what they should expect, depending on the extent of their disease?

Dr. Kathryn Van Abel:

This is also something that's changing, and I think as again, as we learn more of better treatment options, that'll be changing, but typically, a gestalt view, T1 tumors do very well, five-years survival

should be somewhere in the 90% range. We know that as tumors get deeper and have more aggressive features, so T2 to T4 against LN(0), so no nodal disease, we're going to drop our five-year survival. We've got reports anywhere from 50 to 90% five year survival for those patients. As soon as we have a node present, this significantly drops our overall survival. So you'll see ranges now, 20 to 7%. So historically, we were taught that a patient walking in the door, if you can feel an involved lymph node, it drops their survival to 50% off the bat.

That doesn't hold true for all tumors, but it certainly holds true for melanoma. So it is the most important prognostic feature. And then for somebody that presents with distant metastatic disease, they're five-year overall survival was typically 10% or less, but again, that is hopefully going to be changing here.

Dr. Jason Barnes:

And how do you follow up with these patients?

Dr. Kathryn Van Abel:

Again, you always think, "Well, I should be getting imaging, I should be getting PET scans," those types of things. And the answer is no for a lot of our melanoma patients. For all melanoma patients, we really need to do some education and emphasize these common follow up recommendations. So patients should be getting at least annual skin exam for life. And we really need to advocate or educate our patients about that because they often say, "Well, I got my melanoma treated. I don't ever have to go back to the dermatologist," or their primary care physician who does their skin exam. That's not true. They really need to be doing this annual skin exam for life.

If there are certain risk factors, if this is recurrent, if they've had a couple melanomas, if there's something really concerning, they're immunosuppressed, you're going to want to follow those folks up a lot closer. I have some patients that have skin exams every quarter, so every three months or so. If for some reason you offer sentinel lymph node biopsy and the patient didn't want to do it, or you tried to do it, but it just didn't drain anywhere, their lymphatics, who knows what happened, but it didn't drain, didn't work, or you had a positive sentinel lymph node biopsy, but for some reason, weren't able to go back and do your completion, lymph node dissection, you can offer regional lymph node ultrasounds.

And typically, those are offered every three to 12 months for their first two to three years. Now, that's a pretty broad range and you'll have to adjust it for your patient and your concern, but that's something that you can offer. A lot of patients want to know, should they go see a geneticist? Should they send their family to see a geneticist? And really, there's pretty strict recommendations on when we should make that consult. So for folks who have three or more invasive melanomas, if they have any history of pancreatic cancer or a diagnosis of astrocytoma in their family, then I'd send them over to the geneticists. But again, we're all a team, I think that if you have questions, you can reach out and call your local geneticists and see if they have anything to offer.

Dr. Jason Barnes:

Well, this has been a super helpful discussion, Dr. Van Abel, thank you so much. Before I go into my summary, is there anything you'd want to add?

Dr. Kathryn Van Abel:

No. Just remember that melanoma's tricky, it's confusing. It's okay to reference the literature. It's okay to have a cheat sheet for your staging system available, even being in practice where we're taking care

of these patients frequently, you still need to be able to reach out to your reference. And things are changing, we're learning things, so staying up-to-date on your literature is going to be important.

Dr. Jason Barnes:

Great. In summary, melanoma commonly presents in those who are older with significant sun exposure, and they have a lesion that classically follows those A, B, C, D, and E's. Pathophysiology includes invasive, large atypical melanocytes that stain for S-100, MART-1 and HMB-45. Workup includes biopsy and possible imaging for more advanced disease. And treatment includes, resection of the primary lesion, as well as possibly addressing the lymph node basin, either with lymphadenectomy or sentinel lymph node biopsy in stages, 1B or 2 disease. Systemic therapy is also rising, this could be in the form of PD-1 or PD-L1 inhibitors or BRAF activating medications.

And prognosis is generally very good for early stage disease, but become significantly worse with advanced disease. Dr. Van Abel, anything you'd like to add?

Dr. Kathryn Van Abel:

Thank you so much for having me, Dr. Barnes. This has been a great review of melanoma in a nutshell.

Dr. Jason Barnes:

Well, thank you. And now, I'll move on to the question asking portion of our time. As a reminder, I'll ask a question, wait a few seconds and then give the response. So the first question is, describe some of the common features of the histopathology of melanoma. There are a lot of buzzwords for the histopathology of melanoma, and these include large atypical melanocytes, melanin granules, hyperchromatic nuclei, and nests of melanocytes and the epidermis. They can have a pagetoid pattern, but most importantly, there are atypical melanocytes that are invading beyond the basal layer, which makes this malignant. And these will stain positive for S-100, MART-1, HMB-45 and Melan-A.

Our next question is, describe the T-staging of melanoma. T-staging of melanoma is as follows; T1a is less than 0.8 millimeters, T1b is 0.8 to 1.0 millimeters. However, if it's less than 0.8 millimeters with ulceration, that would fall into a T1 big category. T2 is one to two millimeters, T3 is two to four millimeters, and T4 is greater than four millimeters depth of invasion. Our next question is, when is sentinel lymph node biopsy warranted? Sentinel lymph node biopsy is indicated in T1b disease or greater when there is no clinically evident neck disease.

And for our final question, what are the desired margins in melanoma resection of the primary lesion? As Dr. Van Abel said, we usually shoot for a one to two centimeters, but to be more specific in our margin resection, if it's melanoma in situ, we're looking for 0.5 to 1.0 centimeters. If it's less than one millimeter, we're looking for one centimeter. If it's one to two millimeters, we're looking for one to two centimeters of margins. And if it's greater than two millimeters, we're looking for two centimeters of margins. Thanks so much, and we'll see you next time.