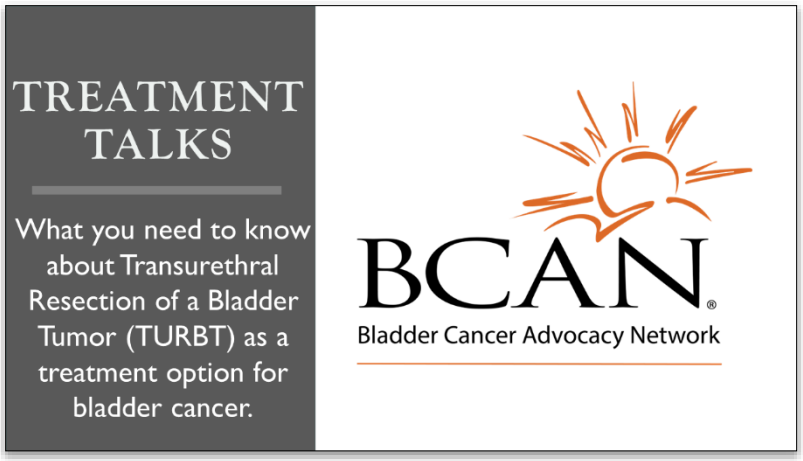

Stephanie Chisolm:

Okay. Great. So let's go to some questions that have come in from our participants. How important is drinking water and walking after that procedure? Dr. Lotan, do you want to provide some comments? You mentioned that earlier and do they do anything to rinse the bladder once you've done all of the tumor removal to get that part out, or?

Dr. Yair Lotan:

Well, for sure, we're going to remove all the cancer that's floating around there as best as we can. And we use sterile water or glycine, which lysis cells, which is hypotonic, but we'll definitely irrigate all the floating things. It's one of the rationales for putting chemotherapy wash in the bladder to kill any cells that are floating, but that's been shown to be useful in some patients. But if you have a large raw surface area, we don't want you to absorb the chemotherapy. And certainly, if there's concern that you may have made a small hole in the bladder. So it's not something that's used every single time, but just in general, yes.

Dr. Yair Lotan:

After anesthesia, when you get home, we definitely want you to drink plenty of fluid so that you make a lot of urine so that if you are having some slight oozing from the raw area, you don't form clots. The worst-case scenario is if you are not making much urine and your bladder, and if you have some oozing, then you might form some clots and we'd rather the bladder gets washed out. As far as walking. I think it's good to stay active. We don't want you lying in beds. You don't form clots or get pneumonia or something strange like that. I wouldn't walk a marathon the next day. I think it's certainly good to be up and about. But again, I would say avoiding strenuous activities, and if you normally walk five miles, I'd say one would be enough the next day and build back up.

Stephanie Chisolm:

So Ron and Lori, how about you, as far as getting back up to your normal activity levels post-procedures when you had a TURBT? Did you jump right back into life as usual when anything kind of settled down or how did you deal with that?

Ron K.:

I think I spent 48 hours or so at home and or just walking in the neighborhood. And after that, just going out for dinner was fine, and going out for a longer walk is fine. I love to play golf, but I wait about six or seven days before I do that. And within a week I'm back to normal and within a week I think every time I've had a procedure within a week, the bleeding's gone. So I really feel pretty normal after a week.

Stephanie Chisolm:

Good. And how about you, Lori?

Lori R.:

Yeah, as soon as well, I still had the catheter, no, nothing was normal. It was very uncomfortable. But once the catheter came out which was like two days later, I felt pretty good. I didn't have cramping or fatigue or bleeding and that was a big relief. So yeah, I definitely second the drinking water and moving around to the extent that you feel up to it. But yeah, the recovery was not difficult.

Stephanie Chisolm:

Okay, great. Thank you so much. Here's another question from our participants. Why do they not send the entire tumor to the pathologist? I understand that it cannot be removed in one piece. When determining mixed grade tumors, how would a pathologist determine the percentage of high-grade versus low-grade to determine the overall grade, if they don't have the entire tumor to analyze?

Lori R.:

They do.

Dr. Yair Lotan:

Well, we send the entire tumor. It's just, we send it in pieces because if you have a large tumor, it's deceptive because on the resectoscope when you look, you see, I mean, you see the entire screen, but the tube is not that wide. You wouldn't be able to fit a tumor more than two centimeters anyway, even if you tried through the urethra or through the resectoscope. So you do have to cut into smaller pieces, but we send every piece to the pathologist. Now, in terms of the question, if 50% of is high-grade and 50% is low-grade, you don't have a low-grade tumor. You have a high-grade tumor because your cancer will behave similar to the most aggressive aspect of it. If you have four tumors and three of them are low-grade, and one of them is an invasive high-grade cancer, we don't consider you as a mixed tumor.

Dr. Yair Lotan:

You have an invasive high-grade cancer. You just happen to also have some low-grade or some non-invasive component. So for us, it's not important the percentages. Now I do rarely see some patients with focal high-grade and a background of low-grade. And that sometimes does impact my decision on what to do but the pathologist will tell me that. They'll say almost every piece I saw was low-grade and I saw a small area that I think is high-grade, and I will treat that patient a little differently, but there's nothing that we, I don't take anything home with me. It's all going to the pathologist and they're going to look at all of it.

Stephanie Chisolm:

Okay. Well, that's good to know. I'm very happy to hear that. So can you talk a little bit about enhanced cystoscopy, whether it's with the blue light, with SIS view or narrowband imaging. What's the difference

from your perspective and is that better if it's available to a patient, is it going to allow the doctor to do a better job? What is the story behind that?

Dr. Yair Lotan:

Right. So normally I give a talk, I have disclosures page. So I will give you a disclosure that I do consult with Photocure, which is a company that makes blue light. And I have done research with STORZ and but, which is the company that makes the blue light scope. That aside though, there are many, many randomized trials where half the people just got white light, half got white light plus the blue light and found that the blue light improves detection of cancer especially a flat tumor called carcinoma in situ, but also improved the ability to find additional tumors. In fact, the American Urologic Association Guidelines actually recommends that if you can get blue light as urologist if you have it available, that you should use it because it does improve detection and reduce recurrence rates for patients. And the reason it reduces recurrence rate makes quite sense.

If you had three tumors and they only found two then the other tumor is not going to go away on its own. You're just going to find it later and then that's going to be considered a recurrence, but it really truly wasn't a recurrence. It was always there in the first place. And if you had removed it at the initial TURBT, you won't have to remove it as a subsequent TURBT. Now, biologically speaking, the way SIS view works and blue light is SIS view is the substance that gets taken up more often by cancer cells than normal cells. So when you shine a blue light, the cancer cells look pink. Narrowband imaging is actually incorporated with different scopes. And what it does is actually highlights blood vessels. And since cancers attract blood vessels, it's easier to your eye would naturally go to the area with more blood vessels.

So you'll see additional tumors. It's actually also recommended in the guidelines. Just has a little bit lower level of evidence because the studies that were done didn't show quite as much of a difference. But obviously, if you have a scope that has narrowband imaging, it's actually made by Olympus, then you can do that. And I do it periodically in my clinic as well. But the vast majority of TURBTs in the US are done without either blue light or narrowband imaging. But if you have it available, then I think it does help in some cases, not in every case, but in some cases, it does add value.

Stephanie Chisolm:

Great. Thank you. I have another question, a little more of a technical question. What are the indications for fulguration versus excisional biopsy and pathological examination? What you talked about with the wire was the fulguration, correct?

Dr. Yair Lotan:

Well, fulguration just means you're burning something. So we sometimes will take patients with, especially in the office setting where a patient, for example, may have eight small tumors, and they always only have low-grade cancer. So you already know that they're a person who usually makes low-grade cancers and patients who have current low-grade cancers, less than 5% of them will have high-grade cancer. So if you have a patient who's got multiple small tumors, I might biopsy one or two of them, but I won't biopsy eight of them because that will just lead to more bleeding and discomfort for the patient. So I can actually just burn the other ones, knowing that probably if they've always had low-grade, they'd probably still have low-grade. So fulguration literally just means burning a tumor. We sometimes do it in the operating room too if you have a patch of tissue that looks abnormal, you might biopsy it, but you may not resect or cut out the whole patch because you don't want to have as big a

raw area, as much bleeding as much discomfort. So you might just biopsy part of it and burn the rest of it. And that's called fulguration.

Stephanie Chisolm:

So when you're looking for a physician to do this level of examination, can a general urologist, I'm sure they could do this, is it better to go to a general urologist or to somebody who's really been doing a number of these procedures over the long term?

Dr. Yair Lotan:

So there are 80,000 cases a year diagnosed with nearly new bladder cancer. And there are about 500,000 people in the US living with bladder cancer. So as much as Dr. Smith and I like taking care of patients, there aren't enough academic urologists to do every TURBT in this country. Do I think there's a value in doing it repeatedly or having experience? Well, I'd like to think that experience helps with any procedure you do, but it's such a common procedure that people in training probably do a large number of them. And some most urologists would feel comfortable doing it. The truth is that both Dr. Smith and I see patients who have larger tumors or multiple tumors or some complexity that the urologist didn't feel comfortable doing the procedure, in which case they do refer them to us because they think that we would have an easier time. I don't know that we have an easier time. It's just, we don't really have other people to send it to. So we end up doing them, but at the end of the day for straightforward TURBT, the vast majority of urologists in the country, it should be a more than capable of doing them.

Stephanie Chisolm:

Okay, excellent. Hold on. Let's see. The pathology report on this individual's last TURBT stated muscularis propria present, but it was not the same report on their first procedure. What does that mean? Does that mean that they got a deeper sample the second time?

Dr. Yair Lotan:

Yes. In general, we would like to see that the muscle is present and not involved in the majority of patients. Now, the truth is that because we cannot see, I mean, we see what we think are muscle fibers, but that doesn't mean that we get enough muscle fibers that the pathologist feels comfortable saying that there's muscle or that when we cut through with a loop that has electricity, it causes charring that the pathologist has a hard time saying that there is muscle. Now bladder cancer does not skip through layers. So if it's not going into the lamina propria which is the layer under the lining, then it's not going to suddenly show up in the muscle typically. So if you have a noninvasive tumor that's not going into the lamina propria and there's no muscle, then we don't necessarily feel like, "Oh, we've got to back and get more tissue." But if it's going into the lamina propria and we didn't get muscle, then we usually want to go back and try to get muscle. Are we successful a hundred percent of the time? No. We don't necessarily like to go a third time. So we really try to get that tissue if we can, but it's not always so easy because like I said, visually, it's not like a Neopolitan ice cream where part of it's vanilla and part of it's strawberry and chocolate, and then you go, "Oh, I'm in the right layer. I did a good job." So we do our best to try to get the kind of tissue we need. Again, we are a little concerned because we don't want to make a hole and then have cancer cells spill out and you need a catheter for 7 to 10 days to let the bladder heal. So that's the challenge.

Stephanie Chisolm:

Another question from a participant, this person had two emergency fulguration after having their TURBT because clots had prevented him from urinating. How common is that?

Dr. Yair Lotan:

Thankfully not very common. A little more common on patients who are on blood thinners because at some point they have to resume blood thinners and many patients are taking aspirin, or Plavix, or Coumadin, or any of the variety of these blood thinners because our patients are getting older and have heart disease, or have a risk for stroke and their primary care physicians like to put them on these blood thinners. And so that is a risk. Is it common? No, it's not common thankfully, but if you do enough to TURBTs, you're certainly going to have some patients who are going to have bleeding, and sometimes it'll stop on its own. And rarely we have to go back to the operating room and to fulgurize some vessel that we didn't see or that wasn't bleeding at the time of surgery.

Stephanie Chisolm:

Okay, Let me go back to the video for a minute. What the tumor looked like on that video was very large. And what's the size of the wire, the little moon that you were talking about?

Dr. Yair Lotan:

Oh, a loop.

Stephanie Chisolm:

Was that a typical size tumor? Was that a large tumor? People were wondering about that.

Dr. Yair Lotan:

That would be a medium tumor. We don't really have a ruler. Yes. That loop probably is and Dr. Smith might correct me. I think it's about five millimeters or something. So this tumor is probably the nice thing about it was, it's not a perfect sphere. So yeah, maybe three and a half centimeters, an inch and a half in diameter, but I've seen when they're much bigger volume. We've seen tumors over five centimeters which is what we would consider large. This would not be considered large. I mean, and sometimes it's a bit of a misnomer. The whole video is about five and a half minutes from, and that's basically how long I'm scraping from start to finish. Sometimes patients, well, it's an hour procedure, but some of it's going to sleep and getting positioned and all that. Now I have scraped for 30 or 45 minutes and get a little workout. It's rare for me to be doing, so for us to have to resect for more than an hour, that would be unusual.

Stephanie Chisolm:

Right. Well, that was a very obvious tumor, because you could see all the little papillary things kind of swaying in the fluid. What do you do under somebody who's got a carcinoma in situ, so a flat tumor? How much more challenging is that from your perspective and also from the patient's recovery?

Dr. Yair Lotan:

Well, first of all, there're two issues. I would not do carcinoma in situ patient without blue light. That was a white light, not blue light. I have many blue light videos. I picked this one specifically just because I thought it was kind of a nice view of a typical TURBT. But for carcinoma in situ a blue light is for me sort of a must. So I can see where the cancer is. Otherwise, you just don't know what you're doing or where

you're doing it. Now, carcinoma in situ is also a strange cancer in the sense that we don't necessarily think we're going to be able to resect all of it and we depend on BCG or other treatments to help eradicate all the cancer. I will sometimes if it's a reasonably sized patch takes several biopsies and then burn the rest of it because I know it's not invasive. By definition, carcinoma in situ is not. But if it's occupying a third of the bladder, I'm not going to burn a third of the bladder. There's no point to it. I'll biopsy several areas to get the diagnosis and then I'll rely on BCG to get rid of the rest which actually I'm relying on the immune system to get rid of the rest. I'm going to use BCG to attract the immune system to the bladder, to fight the carcinoma in situ.

Stephanie Chisolm:

Okay, great. Thank you so much. In a follow-up TURBT, is it possible that the cuttery, effect the scarring that comes from previous TURBTs could be mistaken for cancer cells, or obviously you are a very expert in doing this. So, you know what you're looking at, but from a regular urologist who might only do one or two of these a year, or three or four, would they know the difference between potential scar tissue and another possible tumor?

Dr. Yair Lotan:

So generally speaking, my eyes are not that much better than any other urologist's eyes, but if you're going back after four to six weeks, it actually kind of looks like a volcano, the center where you resected looks kind of charred and then the surrounding area looks red and the kind of like it's just kind of swollen. The tissue is just healing. If you come back three months later, it's going to be flat and look white without blood vessels to it. And it's actually kind of, it almost has like a star pattern. So it depends on the timing. So if we go back because we didn't get muscle or because there were signs of invasion, we want to make sure there's no residual cancer, we're basically trying to get some biopsies of the floor where we resected and some of the tissues surrounding it. But I can't tell what's cancer. I can't tell what's inflammation. It just kind of looks red and angry to me. And there's nothing special about my experience that allows me to distinguish that. And in fact, if you use blue light, sometimes that will light up too because and what we call a false positive, cause inflammation can sometimes take this SIS view as well. If you come back three months later, then if it looks just like a flat area with a scar, then I think most urologists can say, "Okay, it looks like a flat area with a scar." So the timing is really important in terms of what it appears like. But in general, you can distinguish. If you come back a year later, you may not be able to tell at all where anything happened. And so, because the lining healed nicely and things like that. Sometimes you can see but you can't always see. So a lot of it has to do with the timing more than the experience of the urologist.

Stephanie Chisolm:

Okay. Okay. I think we probably have time for one or two more questions. If you have multiple tumors that are clustered close to each other, are they measured together as one or individually? And I know what we just saw was showing how you have that wire and it's only going to scrape out a certain width of tumor so you're not going to get all of those particular things at one time. So do you make a best guess when you're reporting on the tumor size to a patient if there's a lot of tumors clustered together. Do you just call it one or do you say we have multiple tumors in a small area?

Dr. Yair Lotan:

In fairness, it doesn't really matter because for us, I mean, for something a patient doesn't care, for billing purposes it matters what surface area. And then you could add it together or you could not add it

together. Let's say you had two tumors that were one and a half centimeters. If you put them together, it's three centimeters. If you count them separately, it's a multifocal tumor. It ends up in the same risk category for us one way or another. So it's just semantics. It doesn't change sort of what we do for the most part. I suppose to me, if there's a bridge of normal mucosa, I might consider it two tumors. I'm probably going to burn that little bridge because I'm going to worry that those cells microscopically may be abnormal anyway. So I'm not going to just leave a small little segment of normal lining or normal-appearing lining. I'll just take care of all of it just because that little piece of lining is not going to help the patient anyway. And I worry them leaving cancer behind.

Stephanie Chisolm:

Thank you. One more quick question. Do you ever end up removing a tumor that the pathology report says it's benign growth? Does that ever happen?

Dr. Yair Lotan:

Yes. I mean it happens more after BCG, you see a red area. I try to do more of these biopsies in clinic when I'm uncertain. And if it's a relatively small thing, I mean, what you saw today will never be a false positive. That's always going to be cancer. It's very typical. It more often in patients, like you said with carcinoma in situ or patients who've had BCG, that's have like a red patch which is not that uncommon. I usually will not take patients in the operating room and do resections. I usually will biopsy them in clinic and then I can categorize them as well. And if it turns out to be cancer. And I felt like I didn't do an adequate job getting rid of all of it, then I might say, "Well, I'm going to biopsy these two areas. And if it turns out it's cancer, we might still go to the operating room." But for the most part, it's not going to happen for a papillary or coral-looking thing it's going to happen because somebody has something that looks atypical. And in order to avoid anesthesia that's why I'll do an office biopsy in many cases, and then only go to the operating room if I'm worried that there's still a significant amount of residual cancer.

Stephanie Chisolm:

Right? So any tumor-looking material can be removed with the TURBT and then it's analyzed to determine exactly what it all is. Because I know we had somebody asking about a particular type of tumor, but are all tumors that are in the bladder removed with that TURBT?

Dr. Yair Lotan:

Yeah. I mean, those are our tools. If you have, I mean I've removed melanoma from the bladder or adenal carcinoma, or squamous cell, I mean other types of tumors, there are some benign things that you'll find as well, I suppose that are very rare but if you do enough of these, you'll find some rare things as well. But in general, it's the same type of procedure.

Stephanie Chisolm:

Well, thank you. This has been an incredibly informative program. I appreciate Dr. Lotan. You're spending the time, Dr. Smith for giving us all of the information that we used in these slides earlier. Thank you so much. And, Lori, and Ron, thank you so much for sharing your stories. It really is helpful to understand what that lived experience really is. And do you have any parting words before we end today's program?

Lori R.:

No. No. I appreciate the opportunity to participate and share my experience and anyone who I can help on this journey. I'm very happy to be able to do that. So thank you again for inviting me.

Stephanie Chisolm:

Thank you. Ron, any comments to add?

Ron K.:

I think follow-up is the most important thing I've learned in being a cancer patient, bladder cancer patient, you can't ignore it, and it can keep popping up and you have to keep up with your visits.

Stephanie Chisolm:

Well, as a lot of people have said, when you have bladder cancer you form a long-term relationship with your urologist, especially. Especially with a non-muscle invasive because it does have this ability to come back. So Dr. Lotan, thank you so much for everything that you've done to get this program together. It's been very informative. We appreciate everything. I want to remind everyone that we will be sending you a short survey so that you can give us a little bit of feedback. That's always very helpful. And we use that to plan future programs and today's program again was co-sponsored by the CISTO Bladder Cancer Study. So Dr. Smith and Lori because you're on the advisory board for that, thank you so much.