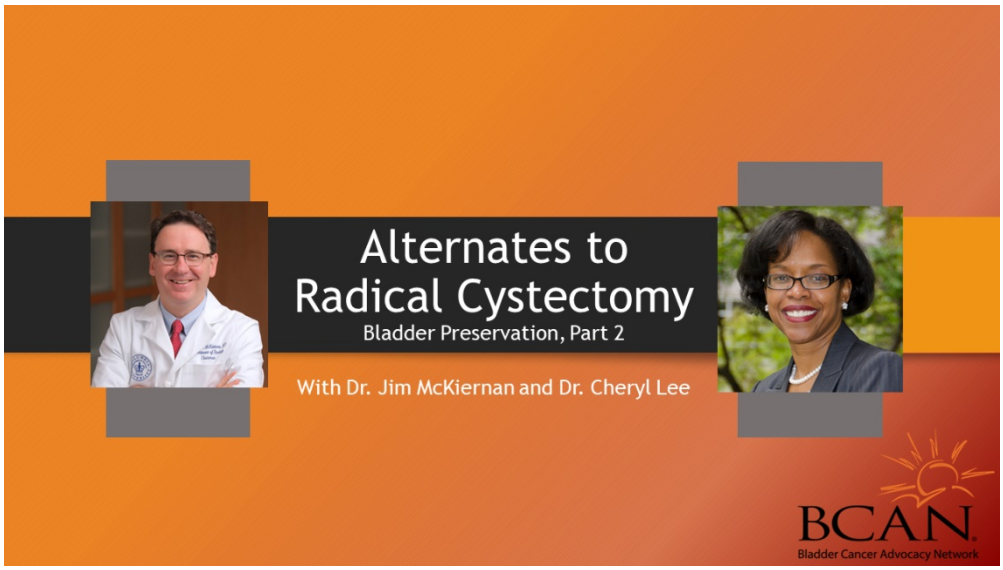


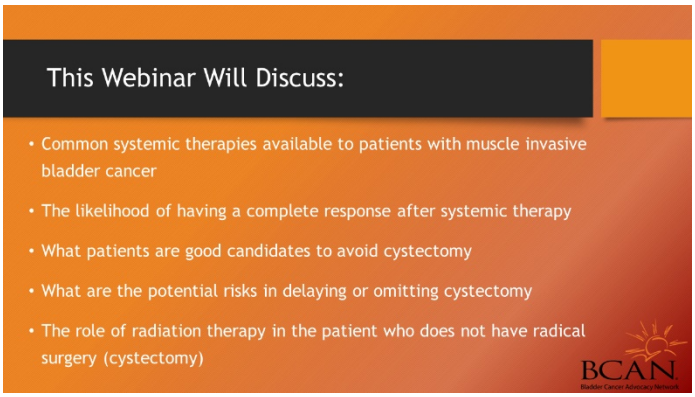
Background and Guidelines

Meet our Presenters

Dr. Jim McKiernan is the John K. Lattimer professor and chair of the Department of Urology of the College of Physicians and Surgeons and urologist-in-chief at New York Presbyterian/Columbia Presbyterian Hospital. Dr. McKiernan graduated from Johns Hopkins University with a BA in biology and received his medical degree from Columbia University College of Physicians and Surgeons. He specializes in urologic oncology, particularly surgical therapy in high-risk patients with bladder and kidney cancers.

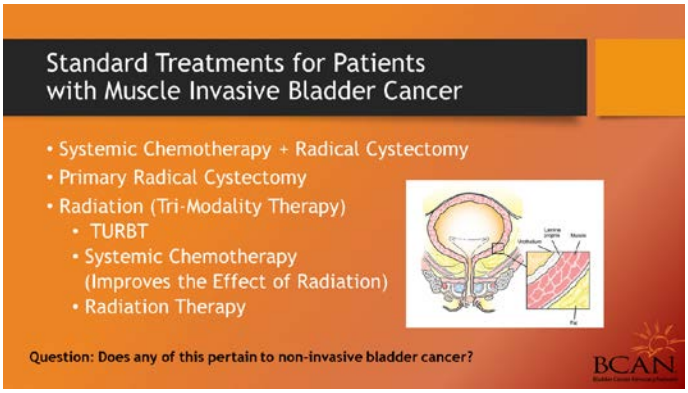
Dr. Cheryl Lee is the chair of Department of Urology and Dorothy M. Davis chair in Cancer Research at Wexner Medical Center at The Ohio State University. She is dedicated to improving the care of bladder cancer patients through advocacy, education and research. Dr. Lee is involved in more than 50 clinical research trials. Her recent research is focused on strategies to improve outcomes in quality of life for patients who've suffered impairments following bladder removal surgery. Dr. Lee is a member of the Board of Directors of the Bladder Cancer Advocacy Network (BCAN) and of the regional division of the American Cancer Society. Through her role as a member of the Education Council of the AUA, she is active in the education of urologists and urologic trainees.

Stephanie C.: Welcome to both of you. We're delighted to have you here for our program.



Cheryl Lee: Well, again, I want to welcome everybody in the survivor community to our webinar this evening. This type of program is important for patients, for their families, for caregivers because it allows us to really have a very personal conversation about important issues. Now, this particular webinar tonight is going to touch on several issues and thinking about how patient should approach bladder preservation. It's important to know about the common systemic therapies or chemotherapies or immunotherapies that are available to patients who have deeply invasive bladder cancer. In addition, we'll be thinking about what is the patient's response to those kinds of treatments. Additionally, we'll be talking about who is a good candidate to avoid radical surgery or radical bladder removal or cystectomy and we'll think about some of the potential risks that are involved in delaying or omitting cystectomy. Although this won't be the central topic in this webinar, we will touch on the role of radiation therapy in the patient who does not have radical surgery.

In the cartoon image on the right lower part of the screen, what we see is an image of a bladder, and if you look at the small box, it's really encircling the wall of the bladder, and if you took a section of the wall of the bladder and magnified it, you would see that the bladder is comprised of a series of layers.



The bladder is comprised of series of layers as we see her in the diagram. The inner part of the layer, inner part of the bladder is noted in this area and we see that there are layers deep to the surface. As cancer cells grow into the wall or invade the wall, there's a higher chance of cells spreading from the bladder and going to other organs that might be lymph nodes or lung, bone or liver. We take it very seriously when we see cancer cells in this layer of deep thick muscle and that's called muscle invasive bladder cancer and that's primary the group of patients we're going to be talking about today.

The deeper cells grow into that bladder wall, the higher the stage of the cancer or the higher the extent of the cancer. If we think about what are the standard treatments for patients with cancers that are invading the deep muscle wall of the bladder, that would be systemic chemotherapy. That means chemotherapy that's not instilled in the bladder but into the veins and being delivered to the entire body. Then ideally, we would move to bladder removal. Another standard treatment option is going straight to removing the bladder and skipping the chemotherapy and that might be important because patients may not agree to chemotherapy.

They may not be eligible for chemotherapy for example if their kidney function isn't working normally, but for those for example who are interested in preserving their bladder, a standard treatment option could be radiation treatment. In fact, we use radiation in combination with some surgery and with some of the chemotherapy and we call it tri-modality therapy. That's when we go in not doing a big open

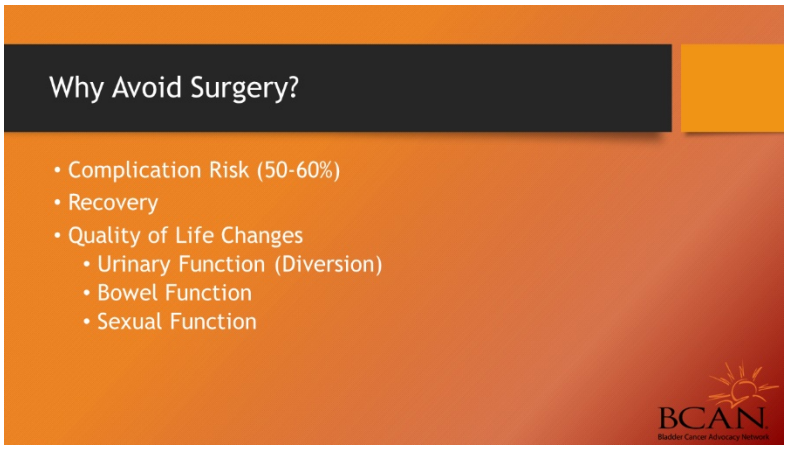
surgery but going in to scrape the tumor away as deeply as possible. That's the transurethral resection of bladder tumor or TURBT and then we move to a treatment process of chemotherapy and radiation at the same time.

The chemotherapy helps to improve the efficacy of the radiation, so that is what we would term tri-modality therapy and that's historically been the primary way of preserving the bladder. One question that came up for this webinar was, does any of this webinar pertain to noninvasive bladder cancer? Like I mentioned before, the majority of our conversation is going to be focused on people with more advanced bladder cancer invading into the deep wall or the deep muscle of the bladder. Most of what we will discuss tonight will not pertain to noninvasive bladder cancer.

Let's talk for a minute about radical cystectomy as an important treatment for bladder cancer. This is a radical surgery that involves removal of the bladder and generally the prostate in men. In women, it involves removal of the bladder, the urethra and sometimes the female organs. As we remove the bladder, we need to revise the urinary system and that might mean that the patient has to have either an ileal conduit, some type of colon or internalized diversion that still has a small stoma on the outside that needs to be catheterized, or an internalized neobladder or new bladder.

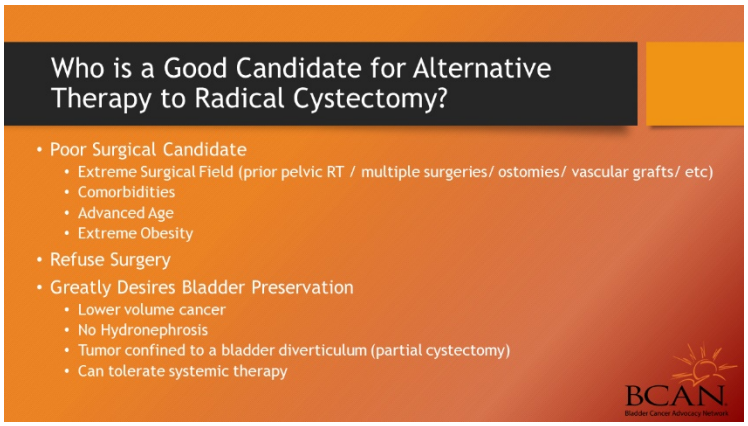
There, unfortunately, are real implications of having to have radical surgery and/or urinary diversion. As part of the considerations for having radical surgery, we must think of complication risks, tolerance for surgery and many other things. On the flip side for the person who doesn't want to have radical surgery, we have to recognize that leaving the bladder in place with a serious bladder cancer there, even after it has been treated could result in a local recurrence. In other words, the cancer could come back in the bladder. It's also possible that the cancer could come back in the bladder and then could move to other organs. Importantly when cancers return, they can result in local symptoms for patients that could involve bleeding, pain or trouble urinating. Of course, if the patients decide to preserve their bladder and undergo other treatments, we still need to make sure over time we are surveying that bladder to make sure no cancer has returned.

Cheryl Lee: Why avoid surgery anyway? Surgery is very effective in controlling bladder cancer. Why would anyone want to avoid surgery? Well, bladder removal is a major operation. It has unfortunately a high complication rate and that can be upwards of 50-60% and in some studies even higher than that. Most of these complications are going to be kind of a low-to-mid risk of a complication, but some can be quite serious and life threatening. The other reality of it is that any major surgery is associated with a



period of recovery, and particularly as individual's age, that recovery could threaten the independence of someone.

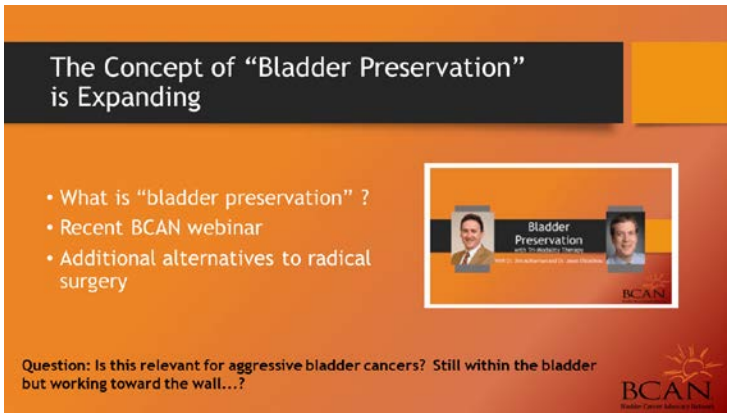
These are important considerations and I think importantly even for those patients who have a low risk of complication or for those who recover well after surgery, there are real quality of life changes that impact patient urinary function because of the urinary diversion. Some can have some changes to their bowel function and then certainly there can be implications for decline in sexual function. As we think of who might be a good candidate to seek alternative therapies for radical cystectomy, we can look at several reasons why someone would want to seek out another treatment.



Cheryl Lee: One, surgery might be risky for some patients, and this could be for a number of reasons. They might have had prior radiation. They might have had multiple surgeries in the past. They might have an existing ostomy. They may have had other vascular procedures where they have vascular graft that could be disturbed through pelvic surgery. They might just have very extreme medical conditions or comorbidities, and certainly as people age, they are at higher risk for complications and might be considered a poor surgical candidate.

Additionally, extreme obesity can make surgery very difficult and that may be another reason why one would want to avoid radical cystectomy. The other reality is that not everyone is going to consent to surgery and so refusal of surgical treatments is something that happens, not frequently, but something we must contend with. I think for many patients though, they'd rather avoid having a major surgery and associated risks and complications and preserve their bladder. There are some patients who are likely to be better candidates to have longer and better outcomes after bladder preservation strategies.

Those patients who have a smaller volume of cancer or smaller tumor volume, those patients that don't have swelling on their ureters, those patients if they have a pouch or diverticulum in the bladder with tumor confined to that area may be candidates for a partial cystectomy or a smaller type of operation, and then of course, patients who were able to tolerate systemic therapies or chemotherapy that is normally paired with other treatments to preserve the bladder. What is bladder preservation really?



I think historically we thought about bladder preservation in the context of radiation treatments and you already heard that Dr. McKiernan was part of a wonderful webinar sponsored by BCAN just about a week ago and I will refer you back to that because there was a lot of very good and detailed information

regarding radiation therapy as an alternative to radical surgery. The truth is, is that there are newer drugs being developed now. There are chemotherapies that are even more effective than they were just because of the way they are being delivered now. We're thinking that we're entering a new era of bladder preservation in which trying to avoid surgery, obtain a cure for the cancer and even avoid radiation may be possible. One question that also has come up with this webinar is, is this discussion that we're having now relevant for aggressive bladder cancers? In other words, some of those that are still within the bladder wall but working towards the deeper aspects of the wall and I would say this is exactly situation the situation that we're talking about now. These are aggressive bladder cancers that have invaded through the initial lining of the bladder wall and are growing deeply into the bladder wall.