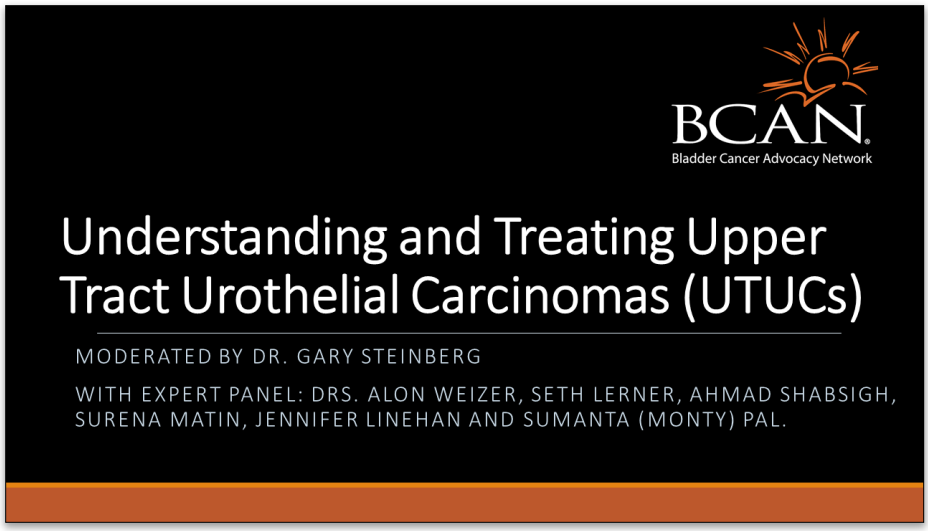
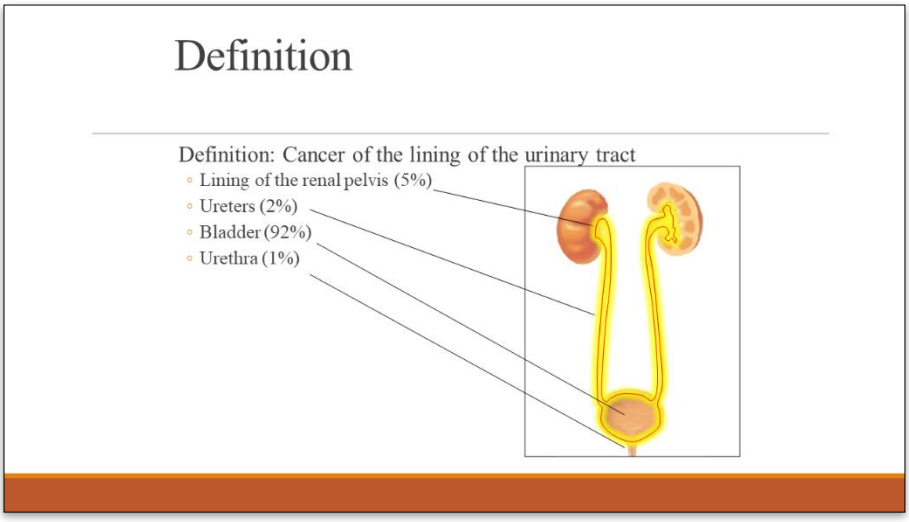


Meet Our Presenters:

Moderator: Dr. Gary Steinberg from NYU Langone Health

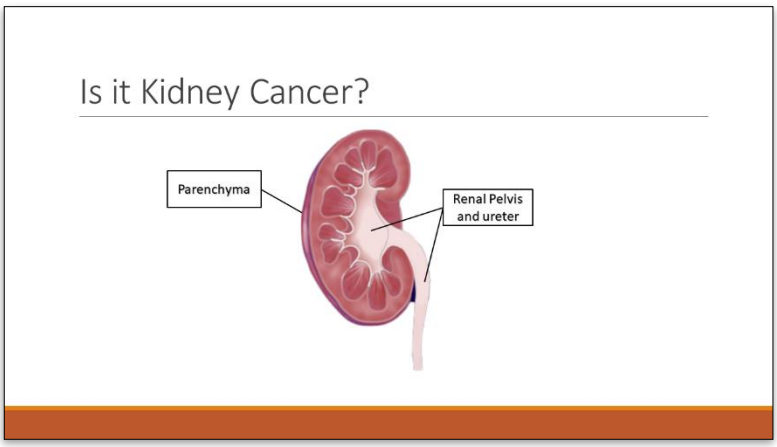
Panelists: Dr. Ahmad Shabsigh from the Ohio State University, Dr. Alon Weizer from the University of Michigan, Dr. Seth Lerner from Baylor College of Medicine, Dr. Jennifer Linehan from the John Wayne Cancer Institute, Dr. Surena Matin from MD Anderson Cancer Center, and Dr. Monty Pal from City of Hope. Read more about our panelists and moderator.

Dr. Shabsigh: I'm going to go over the natural history, the definition of what's new to UTUC, upper tract urothelial carcinoma, and how does it resemble bladder cancer, and what are the differences between the two, and what kind of challenges our patients and the physicians have in managing this disease.

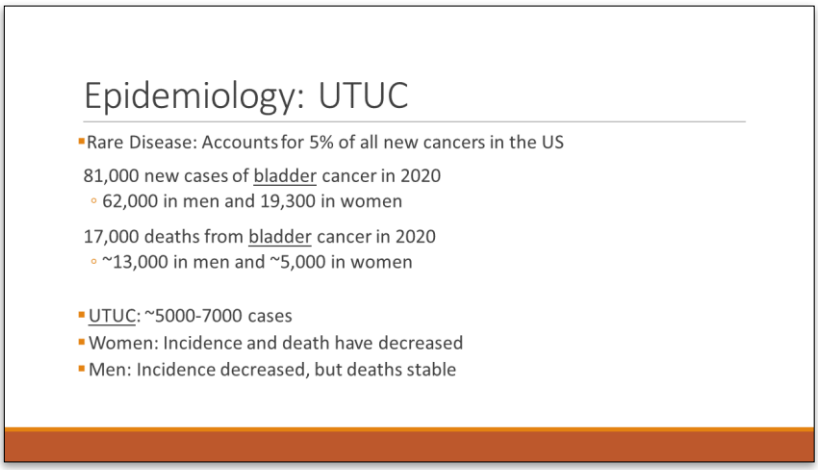


Upper tract urothelial carcinoma is a disease that includes cancers that develop in the pelvis of the kidney, in the ureter- the tubes that connect the kidney all the way to the bladder. Lower tract urothelial carcinoma is what we usually call when its affect the bladder and the urethra, and upper tract is on top of the bladder, the ureters on both sides, and the pelvis of the kidney. This is a rare kind of disease; it's around five to seven percent, as was mentioned before, compared to the vast majority of urothelial carcinoma happening in the bladder itself.

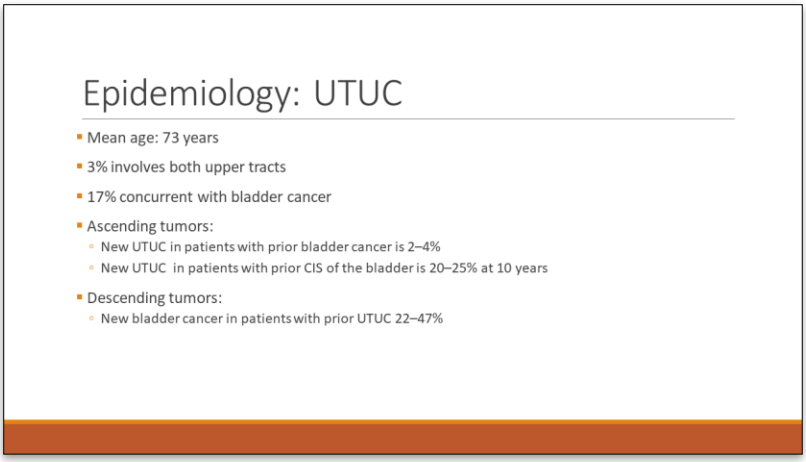
So is it kidney cancer? We get that questions quite a lot. Well, it's not exactly. There are two main cancers that starts in the kidney. One that start in the parenchyma, or the meat of the kidney; that's the functional part of the kidney, that's the part that makes urine, gets rid of extra fluid in the body, electrolytes, toxic materials, all kind of stuff, makes the urines, and this parenchyma dumps the urine into the pelvis of the kidney, and the urine goes down through the ureter. Well, there are cancers that originate from the parenchyma, the meat of the kidney. That's not what we're talking about. We're talking about the cancer that starts in the pelvis or the ureters. So is it kidney cancer? Not exactly, but can it be in the kidney itself, in the pelvis of the kidney? Yes, it can.



How common is this? Again, it's very rare. Its account for five percent of all new cancers in the United State. It's 81,000 new cases for bladder cancer. On the other hand, bladder cancer has around 17,000 death. Now out of all these cases, upper tract urothelial carcinoma is around five to 7,000 cases. It's more common in men. The women incidence and death have decreased over time. On the other hand, the incidence in men decreased but the death stabilized over a couple of years now.



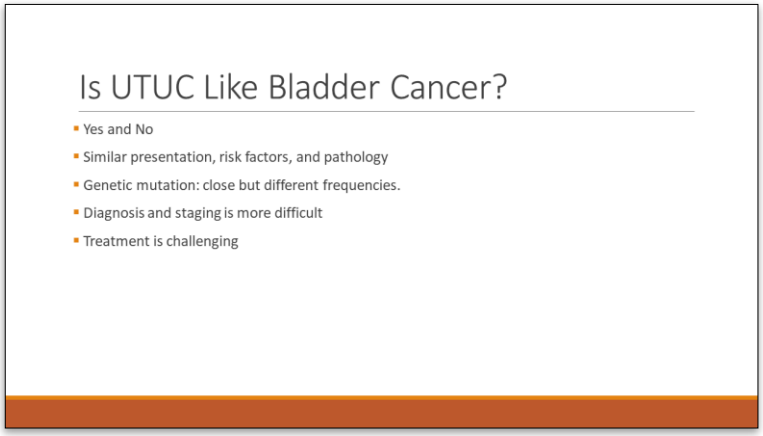
The average age for our patients with upper tract urothelial carcinoma is 73 years. Three percent involves both ureters when they're diagnosed, and 17% concurrent with bladder cancer. In other words, 17% of patients who have upper tract urothelial carcinoma are diagnosed at the same time when they are diagnosed with bladder cancer.



When you look at it, it's interesting. If a patient has already bladder cancer, depending on a lot of different risk factors, they have around two to four percent chance that they can develop upper tract

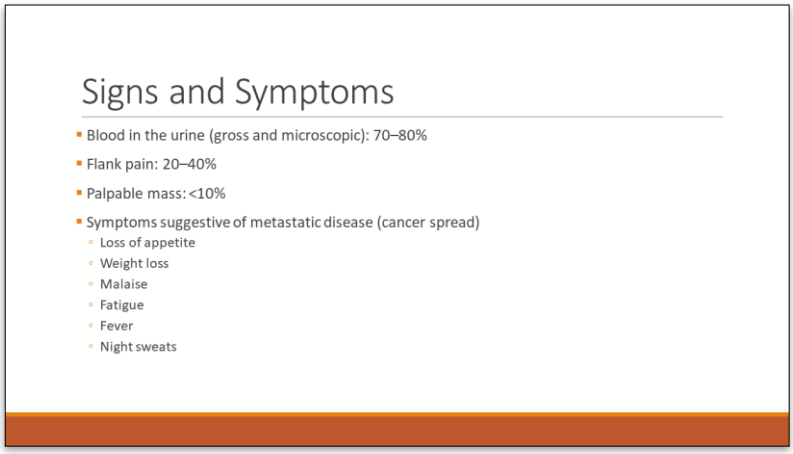
urothelial carcinoma. On the other hand, this can be different if the patient have some risk factors, such as prior carcinoma and such. This is a more aggressive type of superficial non-invasive bladder cancer. On the other hand, if the patient had upper tract urothelial carcinoma, the chance that they eventually will develop bladder cancer is much higher, and depends on what study you read, it's between 20, 22% to 47%.

The question that comes again is: is it like bladder cancer? Well, yes and no. There are a lot of similar characteristics and features between the two diseases. They have very similar presentations. There are a lot of risk factors that are shared between the two, and under the microscope they look alike most of the times. On the other hand, we do know that genetically they're not completely the same. There are slightly different genes and gene changes percentages between the two diseases.

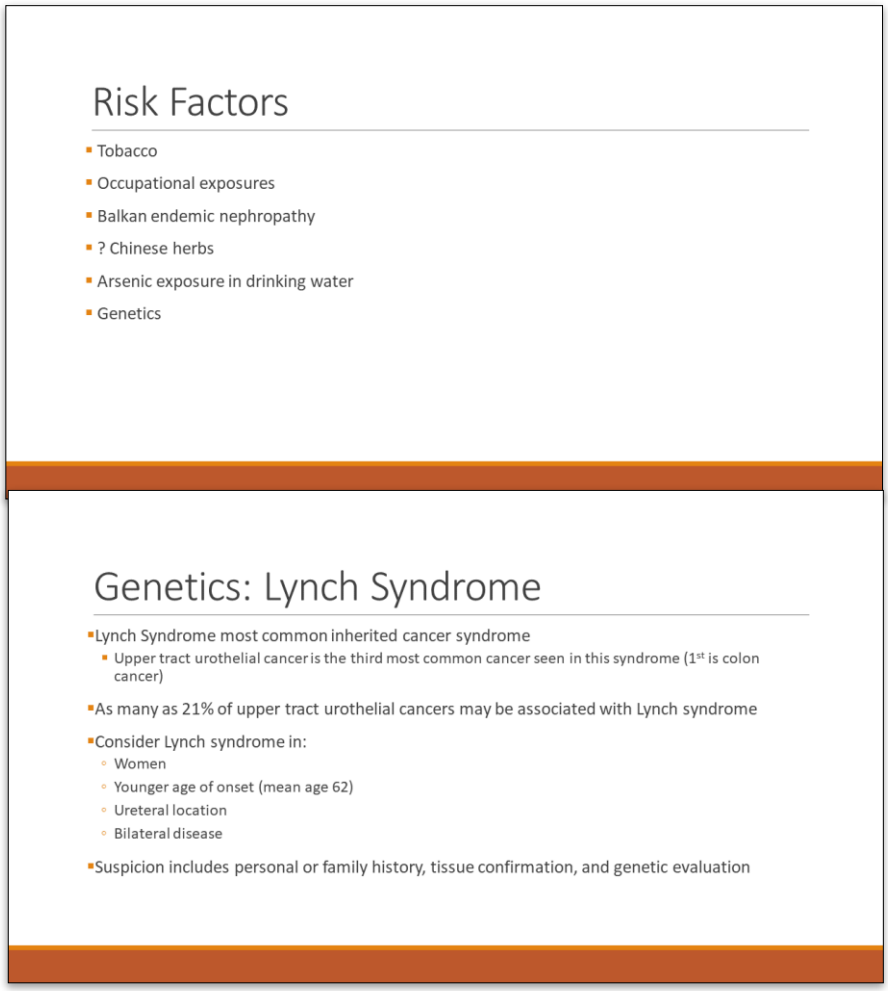


What's also important to understand is the fact that diagnosing and staging, or correctly staging, UTC is much more difficult. In addition to that, treating upper tract urothelial carcinoma has its own challenges, and sometimes it's more difficult to do than bladder cancer.

The most common symptoms for the disease is blood in the urine. It's either something that's seen by our patients, they come complaining that they see blood in the urine, or sometimes they are found on urinalysis, urine testing. Some patient will develop flank pain, or back pain. And in rare cases, especially now with more imaging studies being done, it's very unusual for us to feel a mass, but sometimes in thin patients you can feel that. If the patient has metastatic disease, in other words the cancer has spread from the ureter or the pelvis of the kidney to somewhere else, they have symptoms of metastatic disease that includes loss of appetite, weight loss, fatigue, fevers, even night sweats.



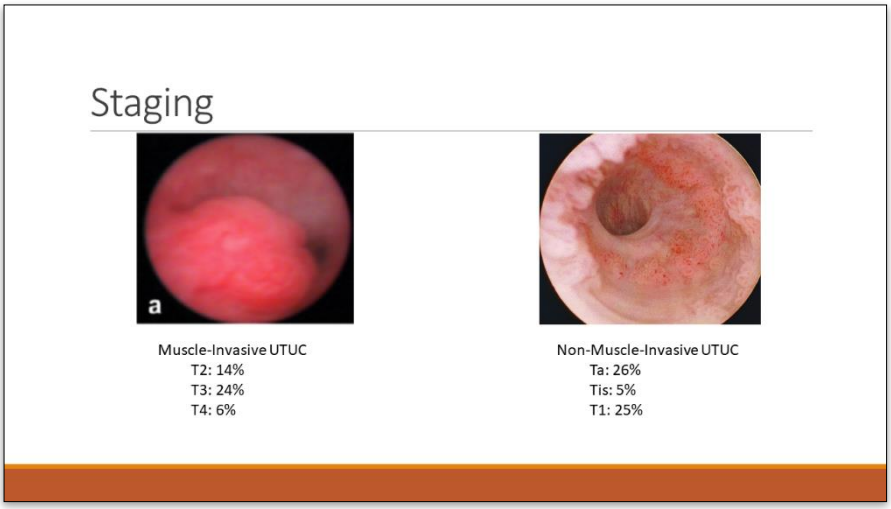
What are the risk factors? Just like bladder cancer, tobacco is the most common cause of upper tract urothelial carcinoma. In addition to that, exposure to certain chemicals; being from a certain part of the world and having some genetic changes and familiar diseases can expose you to upper tract urothelial carcinoma. There are some also chemicals that can exist in water and in rare cases, can be a link to the disease.



For example, one of the most common syndromes or genetic changes that runs in family that can cause this rare disease is Lynch Syndrome. It's one of the most common, if not the most common, inherited cancer syndrome. It includes a lot of different diseases, and upper tract urothelial carcinoma is one of them. As many as 21% of upper tract urothelial carcinoma may have actually Lynch Syndrome. And it depends what study you read; there's actually some thoughts that some of these genetic changes can be more prominent and more common in upper tract urothelial carcinoma.

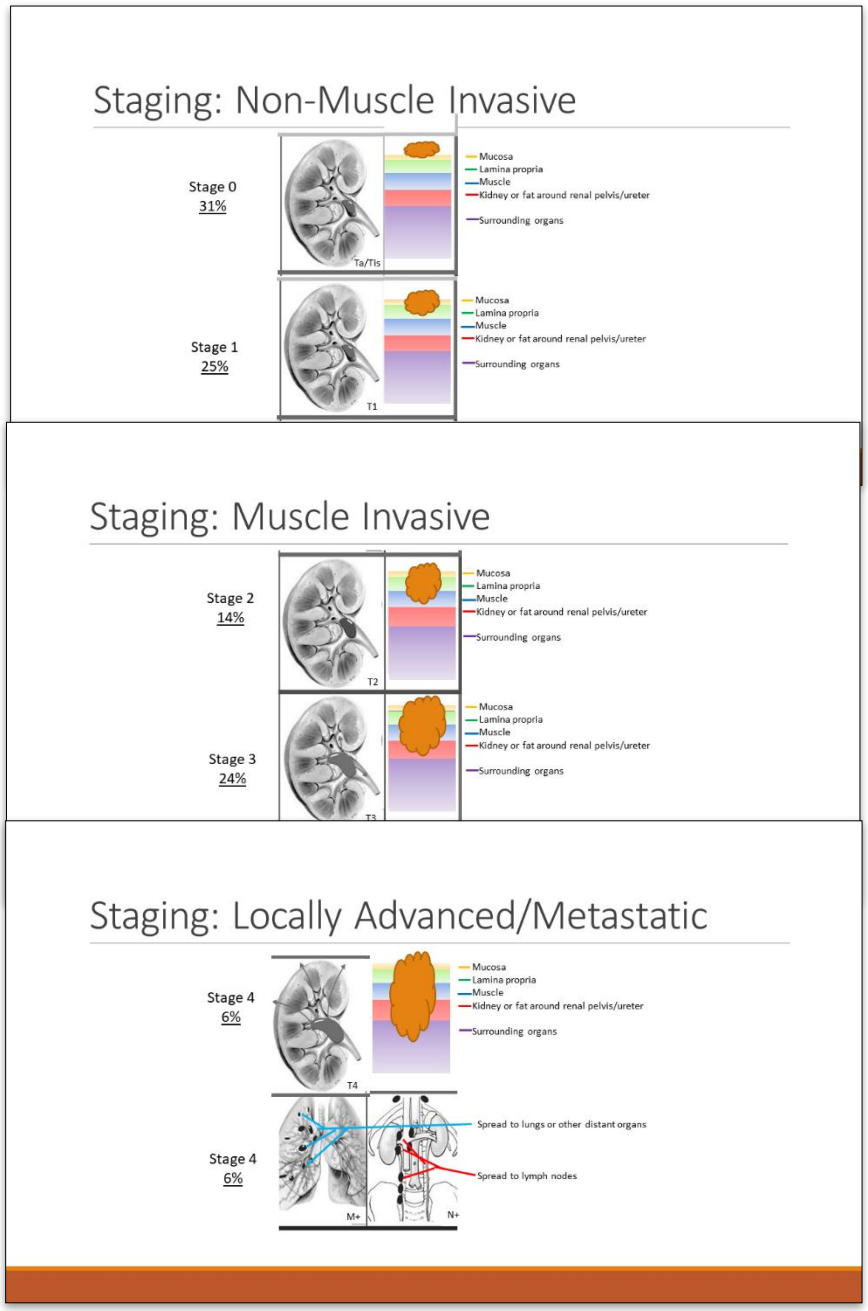
The criteria to consider this changes a lot. The most common things is for women, younger patients who have this disease. It's only in the ureter without bladder cancer, or if there's bilateral disease.

There are some recommendations, some guidelines where they actually recommend testing every patient for this. It may be important to find out for the family and everyone else. In this syndrome there are a lot of other cancers that can come with it.



How do we stage the disease? How do we find out? So the staging of the disease is similar to bladder cancer. It can be superficial, just like on the right side, and that includes disease that's in the lining of the ureter, or CIS, just like what can happen in the bladder itself, or down to

stage one disease. And it can be also invasive disease, where it goes into the muscle or outside the ureter to the tissue around it, or invade other organs. But usually, if you look at non-invasive disease compared to invasive disease, it's around 50 and 50%.



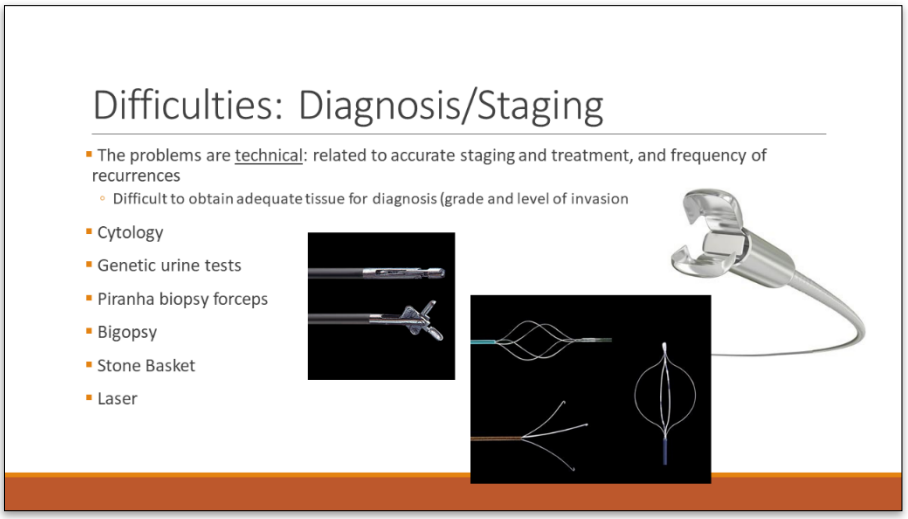
So the staging of the disease also can be related to what kind of pathology we can get. Again, these are pictures that show us exactly what are the stages, so this is the stage where it's only in the mucosa, STA or CIS. Or it can be stage one, where it's invaded into the first layer underneath the lining of the ureter and the kidney pelvis, it's the lamina propria. In stage two, it's invasive into the muscle. Stage three it goes in the fat or to the kidney itself, if it was in the renal pelvis. And finally, unfortunately, there is a small percentage of patient where the cancer is more aggressive and it's spread outside the pelvis of the kidney, and goes to other organs, such as lungs, lymph nodes, liver, even bones.

What kind of difficulties do we have in diagnosing the disease? The vast majority of this is related to technical issues. The ureter is very small, the lumen is tiny, and our ability to be able to go up the ureter is much better than before. We have flexible scopes that give us excellent access. However, we're still talking about very small amount of tissue that we can get when we do a biopsy.

When we do the staging, we rely on a lot of different things. We rely on urine tests to look for cancer cells. That's called cytology. Sometimes we do genetic testing on the urine itself if cytology wasn't conclusive, or if we are suspecting still that there's disease even without seeing the disease for sure. We do biopsies using different instrument, and in general they give us very tiny, small specimen.

These are the three most common ways to do biopsy, and sometimes we use laser to resect some of the tumor and take it out and send it to the pathologist. This is a piranha biopsy, this is a big biopsy, and this is a basket that we use.

In addition to that, we use imaging studies. IVP used to be used commonly in the United States, not anymore. We mostly use CT scan with special read, reconstruction, to see the renal pelvis and the ureter. Sometimes we use MRI, and there has been some studies of using ultrasound, but it hasn't panned out to be very useful at this point, and it's not commonly used.



What kind of treatment difficulties we have? Well it's difficult because it's difficult for us to know the stage of the disease. In addition to the fact that our patients are older in age, and they have a lot of other medical problems. Sometimes we have to take the kidney out, and that can impact their kidney function and can impact their quality of life. In addition to that, we think about a lot of different factors that help us decide what kind of treatment, which will be covered by my colleagues, including the stage, the grade, the location, the number of the lesions.