



*Hosts*

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## State-of-the-art Treatment for Prostate Cancer

**Guest Expert:**

**James Yu, MD**

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Radiology at Yale School of Medicine*

**Yale Cancer Center Answers**

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*Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu) and the phone number is 1-888-234-4YCC. This week, Francine and Lynn welcome Dr. James Yu. Dr. Yu is Assistant Professor of Therapeutic Radiology at the Yale School of Medicine and an expert in the treatment of prostate cancer. Here is Francine Foss.*

- Foss            Could you start off by telling us a little bit about yourself and what brought you to Yale Cancer Center? What are you actually doing in terms of the prostate cancer program here?
- Yu                In our department I am considered a lifer because I did my training here and this is my first faculty appointment, and I plan on staying forever, but I am currently the leader of the Genitourinary Radiation Section of our department, and a large part of my practice centers around the treatment of men with prostate cancer, but also cancers along the urinary tract including the bladder, urethra, and also testicular cancer.
- Wilson          Tell us a little bit about some of the fundamentals, how common is prostate cancer and what age groups are typically effected?
- Yu                Prostate cancer is extremely common. In the US, almost a quarter million men are diagnosed with prostate cancer each year. Estimates for how many men have prostate cancer really depends on age, the older you are the more likely that prostate cancer is going to be found in some form in your prostate. This is why prostate cancer and how we treat prostate cancer is becoming even more and more important as our population ages. Some studies say that if you look hard enough, men in their 90s are more likely to have prostate cancer than not if you do a very fine sectioning through their prostate. So, it is an extremely common cancer. The question is, what to do with cancers that are not going to cause any problems and how to distinguish those from the cancers that will.
- Wilson          Is it a disease that sometimes happens in younger men or is it a disease exclusively of older men?
- Yu                Prostate cancer can happen as early as the 30s, and I am sure there are rare case reports of it happening even earlier, but the vast majority occur in the 50s and 60s. I think the median age of diagnosis is around 67, meaning half the people are younger than that and half the people are older than that, but that is the most common age where a cancer is diagnosed.
- Foss            Are there any differences between various ethnic or racial groups as far as the incidence of prostate cancer or the severity of the disease?

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- Yu That is a great question. We do know that African American men probably have around a 50% higher incidence of prostate cancer compared to non-Hispanic Caucasian men, and that Asian men actually have about 50% reduced incidence compared to these non-Hispanic Caucasian men. So, it does vary by race. At the same time, we do not know whether African American men actually have more aggressive disease if you take the same characteristics or whether they are just more likely to have disease and it develops earlier. I think the jury is still out on that.
- Foss And is this a disease that is genetically linked, and are there cases in families? Are there specific genes that we are looking for that might predispose to this?
- Yu I am not a geneticist, but I do know that this is a very active area of research. Two gene mutations to be aware of are the BRCA1 and BRCA2 gene mutations that we think of more commonly for breast cancer and ovarian cancer. These can also infer an increased risk of aggressive prostate cancer. So, certainly, there is a genetic component to some forms of prostate cancer. I think if you have a father or an uncle or several uncles who have prostate cancer, you probably are at increased risk.
- Wilson Aside from genetics, what are some of the other risk factors that men should be concerned about?
- Yu I think cancer is a disease of the living and prostate cancer especially is a disease of being a man and having testosterone and having a prostate bathed in testosterone. Beyond age, there really is not any major risk factor that I am aware of. Family history, I am sure, contributes to it and genetics to a certain amount, but it is really being older and being a man.
- Wilson So, things like smoking and lung cancer, for example, or diets and certain other problems, we do not see those kinds of relationships in prostate cancer? At least that we are aware of yet?
- Yu No, I am not aware of any link between smoking and an increased risk of prostate cancer. I get asked very often by my patients what diets are good, what diets will prevent prostate cancer or reduce the likelihood of having prostate cancer, and I think we have to be very careful when we counsel our patients because if I say, eat a lot of radishes, they will eat a lot of radishes, but honestly there has not been a slam-dunk study saying that one diet is better than the other. I think because prostate cancer is not as deadly in most cases, I counsel my patients to have a heart healthy diet and to exercise because they are more likely to die of heart disease or other things than prostate cancer itself, and that is what I counsel patients to do.
- Foss There is an increasing number of men out there who, like women, are using hormone replacement therapy and taking testosterone as they get older. Does this increase their risk for prostate cancer?

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- Yu That is a great point, and we do know that testosterone is like a fuel for prostate cancer, and so men who are getting testosterone replacement should talk to their urologist or talk to their primary care provider about maybe getting screened for prostate cancer.
- Foss And on that same theme, just to clarify for our audience, the use of drugs for erectile dysfunction, do they have anything to do with prostate cancer?
- Yu No, they do not. Those are non-hormonal agents and there is no link between erectile dysfunction medications and the incidence of prostate cancer.
- Wilson What are some of the symptoms that a man might present with who has not had PSA evaluation? What sort of clinical problems might they develop that would lead them to go to their care provider and then subsequently a diagnosis might be made?
- Yu Thankfully in the modern era, a lot of men have no symptoms at all when they present with prostate cancer, and we can talk about that later, but the vast majority of men in the United States are diagnosed through screening. If patients present without screening, they often have difficulty with urination, either hesitancy, which means difficulty getting the urine stream going or difficulty emptying their bladder and getting up multiple times at night. If the prostate cancer gets really big, it can start to cause some dull aching pain and discomfort in the pelvis. If it gets to the point where it is invading into the critical structures in your body, you can start to have blood in the urine and blood in the semen. If it spreads to the lymph nodes, then that starts to press on the blood vessels in the pelvis and you can start to get swelling in the legs. If it metastasizes to the bones, you can often get bony pain that is unrelenting. Thankfully, those advanced presentations are much rarer in the PSA era.
- Foss A lot of men have benign prostatic hypertrophy and they suffer from some of those same symptoms with difficulty urinating. How do those men know that they do not have prostate cancer?
- Yu The only way to diagnose prostate cancer is through a biopsy to actually have your urologist take a piece of your prostate out using a needle and look at it under the microscope. That is the only way to distinguish between prostate cancer and benign enlarging of the prostate.
- Wilson I know that over the years, and when I was a resident, we started using PSA to evaluate patients, screen patients, follow patients after treatment, and that really became something that has been very, very popular, but more recently, there has been some controversy I understand, with screening, with PSA, and asymptomatic men. Can you comment on that?

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Yu This is huge area of controversy. Recently, the US Preventive Services Task Force came out publicly recommending against PSA screening, which was a huge departure from standard practice where almost everybody is screened once you hit a certain age. They base their recommendations largely on two randomized trials; one that was here in the United States and one that was done in Europe. The United States randomized trial called the Prostate, Lung, Colorectal and Ovarian trial did not find that men who are screened lived any longer than those who were not screened. There were a lot of flaws with that study. People were actually prescreened. A good fraction of people were prescreened before they went into that study, and then a good number of people in the control arm, meaning the non-screened arm, actually did get screening. So, it is a very difficult study to interpret. The European study called the European Randomized Study of Screening for Prostate Cancer trial did show a benefit to folks who got screened, they are actually 20% less likely to die of prostate cancer than men who did not get screened. Now the problem is that there were so few, well, actually, it is a good thing, but the problem with screening in that trial was that so few men were dying of prostate cancer that it actually took the treatment of many men to prevent one prostate cancer death, and because the side effects from prostate cancer treatment can often include incontinence, erectile dysfunction, and very rarely death on the operating table, and they felt that the harms of treatment outweighed the benefit from being screened.

Foss If you go back and look at those studies, James, which patients were screened? How old were they and what were the criteria to determine who would enter those trials?

Yu I actually do not remember what the inclusion criteria were for those trials.

Foss But they were generally older men?

Yu No, they were men in their 50s and 60s. Generally, studies that have shown a benefit to screening show them before the age of 65, and so the younger you are when you get screened, the more benefit you potentially have by getting your prostate cancer treated. So, the AUA, the American Urological Association, has not agreed with the US Preventive Services Task Force, and they are recommending PSA screening for all men over the age of 50, and for African American men at the age of 40, provided these men have a 10-year life expectancy. So, this is at odds with the US Preventive Services Task Force. It is unclear right now which recommendation is "going to win" over the other. I think blanket statements about PSA screening are not helpful. I think there are men who are at higher risk either because of family history or race. I think the discussion needs to not center on whether they get screening or not for the entire country, but if you are diagnosed with prostate cancer, what would you do? What are you afraid of? Are you more afraid of having a cancer or are you more afraid of the side effects? What do you value in your day-to-day life and how can we decide whether you get screened or not based on those characteristics?

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- Foss And what is the policy at Yale Cancer Center, at Smilow Cancer Hospital, among the group of physicians that treat prostate cancer? Is there a consensus among the group as to what we are doing?
- Yu We have not come out with a formal consensus, but the feeling that I get from folks is that screening is good. The cancer mortality has declined, and that as cancer doctors we want to cure as many cancers as we can.
- Wilson So, it would be fair to say, that for any individual patients, it is probably best that they work with their primary care physician, their own team of physicians to assess what their risk might be and have an individualized discussion regarding this issue, regarding screening for any one person.
- Yu That is absolutely right. They should see an urologist, a radiation oncologist, and they should have the option of seeing a medical oncologist to discuss all potential options in their prostate cancer care.
- Wilson But in terms of the screening aspect, in terms of making a recommendation, if I was 60 years old and had one family member with prostate cancer, I should really talk to my physician about my own situation before we either embark upon or decline the screening evaluation?
- Yu Absolutely!
- Wilson We are going to take a short break for a medical minute. Please stay tuned to learn more information about prostate cancer treatment with Dr. James Yu.

*Medical  
Minute*

*The American Cancer Society estimates that the lifetime risk of developing colorectal cancer is about 1 in 20, and that risk is slightly lower in women than in men. Early detection is the key. When detected early, colorectal cancer is easily treated and highly curable. Men and women over the age of 50 should have regular colonoscopies to screen for this disease. Each day, more patients are surviving the disease due to increased access to advanced therapies and specialized care. New treatment options and surgical techniques are giving colorectal cancer survivors more hope than they ever had before. Clinical trials are currently underway at federally designated comprehensive cancer centers like the one at Yale to test innovative new treatments for colorectal cancer. New options include a Chinese herbal medicine being used in combination with chemotherapy to reduce side effects of treatment and help cancer drugs work more effectively. This has been a medical minute and more information is available at [valecancercenter.org](http://valecancercenter.org). You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.*

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- Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host, Dr. Francine Foss. Today we are joined by Dr. James Yu, and we are discussing prostate cancer. James, in the first part of the show, we talked about prostate cancer in general and some of the controversies revolving around screening. Let us talk a bit about treatment options. Let us say a gentleman has been diagnosed with prostate cancer, what should happen at that point?
- Yu So, once someone has been diagnosed with prostate cancer -- it is usually the urologist who diagnoses it by the biopsy. They should have a long and frank discussion about surgery, about what type of surgery the urologist can do and how many surgeries that urologist has done. They should then be referred for a discussion of radiation options to a radiation oncologist. At that visit with the radiation oncologist, there should be absolutely no pressure to go one way or the other in terms of cancer treatment, but they should also have a very frank discussion of potential side effects including gastrointestinal side effects, urinary side effects, and sexual side effects associated with the treatment. Both of these physicians should also discuss with the patient whether watchful waiting or active surveillance is an appropriate option for them.
- Foss As a medical oncologist, I am wondering whether or not the patient sees the oncology physician earlier or only after the other physicians have made recommendations and whether the medical oncologist weighs in on that decision as well?
- Yu Here at Yale, we have a multidisciplinary genitourinary tumor board. So, the opinions of the medical oncologists are known very early. At the same time, usually a formal consultation with a medical oncologist does not occur until either the patient needs hormone therapy at the same time or if the prostate cancer becomes refractory or resistant to hormone therapy and more chemotherapy options or more hormone therapy options need to be considered.
- Wilson James, since you are a radiation oncologist, let me ask you a little bit about that. Let us say a patient has relatively early-stage prostate cancer that is treatable, and it has not spread outside the prostate, and the patient has elected against surgery. Tell me about some of the different types of radiation that are available for the patient and talk about the potential treatment program, what it is like, how long does it take, and what sort of side effects are associated with various kinds of radiation treatment?
- Yu There are two basic families of radiation that we can do for prostate cancer. One family is called brachytherapy where the radiation is actually delivered directly inside the prostate. The other family of radiation is what is called teletherapy where the radiation is beamed in from the outside. Now, in the brachytherapy side, the most common form uses radioactive seeds that are implanted permanently into the prostate. That is something that we can do at Yale and we can discuss that option with patients. The other option, and honestly more commonly used at Yale, is the

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teletherapy option and the flavor, if you will, that we use is called image-guided intensity-modulated radiation therapy or IG-IMRT. It is a mouthful. The image guidance means that when a patient comes for their treatment, their prostate is localized in 3D space, each treatment. The IMRT or the intensity-modulated radiation therapy part of that is shaping the dose as tightly as possible around the prostate itself. Now, it is a relatively inconvenient treatment. They need to come every day for 44 treatments. Each treatment is relatively quick, usually less than 10 minutes, but it is an inconvenient treatment. Because of the inconvenience, some investigators are starting to investigate something called stereotactic body radiotherapy, or radiosurgery is another name for it. I personally think the jury is still out for that technology. I am sure there are excellent physicians around the country practicing radiosurgery for prostate cancer, but outside of a clinical trial, I think it is still in the realm of unproven.

Wilson And is that because the followup is short or just there have not been that many patients studied or both?

Yu I think it is both. The followup for how toxic the treatment is, is only 5 years, and typically that is long enough to evaluate whether a therapy is good or bad, but in prostate cancer, the emphasis now is on reducing as much as possible the long-term side effects. So, you really do need longer than 5 years to evaluate a treatment, and you also need many thousands of patients. Now we are looking into this with other collaborators. We have a pilot study looking at the quality of life of men undergoing IMRT treatment and we are going to compare that to patients who are getting stereotactic radiosurgery at other institutions, and the idea is that eventually we will be able to get a national study drawing on patient's from all around the country, prospectively comparing their patient-reported quality of life.

Foss Can you specify for us what the major issues are as far as quality of life and what the complications are from these different types of radiation therapy?

Yu I tell patients that side effects are broken up into the short-term side effects and the long-term side effects. In the short term, most patients feel tired usually around the fifth or sixth week of radiation and then lasting about a month after the radiation is done. Their urination probably becomes more frequent, again, starting around the fourth week of radiation lasting for several weeks afterwards. It is very rare to have urinary incontinence as a result of radiation therapy. On the other side of the coin, there is a risk of having some rectal bleeding from radiation. We have looked back at over 800 patients who had IMRT at Yale and our rate of major rectal bleeding was roughly 1%. It is probably lower than that now because that study was done before the advent of the image guidance. With image guidance that risk is probably closer to about half a percent. The biggest side effect is sexual dysfunction and it is difficult to put a hard number on that or even compare it to surgery because the men getting surgery are younger. The men getting radiation are

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typically order. So, it is very difficult to compare the two, but I counsel patients and say, there is a roughly 4 out of 10 chance that they are just not going to be happy with their erections after radiation is done, and it usually takes several months up to several years for that erectile dysfunction to become manifest after radiation.

Wilson And do we see the same sorts of problems and challenges with erectile dysfunction from brachytherapy? Is that an issue with the seeds as well?

Yu Yes, and again, it is very hard to compare two different populations because men getting brachytherapy are typically younger. So, the rates of erectile dysfunction are probably comparable, and I tell patients that no matter what type of treatment you get, the risk of erectile dysfunction is there, and it is real, and it is relatively high.

Wilson We have been talking about a couple of different kinds of radiation, there is brachytherapy, there is the teletherapy, and the brachytherapy is done in one session. The teletherapy is done over 44 sessions as you mentioned, and then you talked a little bit about the stereotactic radiation, which is a much shorter course of treatment, I understand, that can be given either in a week or so, and I believe there have been some studies, and you can comment on this, that have looked at a mildly hypofractionated regimen that is a little bit longer than typical stereotactic treatment but significantly shorter than the teletherapy, and I believe there was a plenary session at the international radiation oncology meeting several weeks ago in Miami. That was a large study that looked at more traditional teletherapy therapy versus a more abbreviated higher dose per day treatment, and I believe they were both clinically efficacious and equal to one another, but the side effects were slightly worse in the more accelerated treatment group. Is that correct?

Yu Yeah, that is absolutely right, and I would not even go that far and say it is significantly shorter. I think it was just several weeks shorter than the standard IMRT treatment, but there were higher complication rates with that faster course of radiation. Again, the jury is still out on these things and it is very hard to translate prospective randomized trials done in a major medical institution, like the one reported at ASTRO, out to the entire country because as we know medical practice around the country is very varied, and so just because it was shown to have slightly higher complication rates but equal efficacy in ASTRO plenary session, or this international meeting plenary session, I think it is still not ready for primetime. I think there still needs to be more studies coming out from more than one institution or more than one cooperative group showing long-term efficacy for this treatment because honestly, folks who get standard IG-IMRT treatment are doing very well, and I know it probably would be more convenient to shave a couple weeks off the treatment, but we need to make sure we do not do that and go back in time in terms of safety.

Foss The kinds of treatment that Lynn just talked about, the three different options, are those available

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in community settings as well or are those only available at large academic centers such as Yale Cancer Center?

Yu All three options are available probably within most communities. Radiosurgery is not something that we do for prostate cancer. We have been very happy with our results with the IG-IMRT program and we do radiosurgery for lung, for brain lesions, liver lesions, and spine lesions, but we have kind of shied away from prostate cancer because in that instance, to me, it seems like a hammer looking for a nail. I think the comparative studies, which we are trying to mount, need to occur before we can fully come on board with radiosurgery of prostate cancer. That said, there are fine physicians in the community doing this, and I have no problem with that, I just wish it would be on a clinical trial or have some sort of formal evaluation.

Wilson And it is certainly not for a lack of technology at Yale because I know you are involved in our stereotactic program and between the organ system sites you just listed, we are actually one of the larger centers in the United States in terms of providing stereotactic-based treatments. So, it is not a technological issue, it is really one based on your beliefs that there needs to be more study done.

Yu That is right. I think we could probably do a prostate radiosurgery treatment later this afternoon. Well, that would push the physicists a little bit, but we could probably do it tomorrow if we felt it was appropriate, but I think as a section, as a genitourinary section, we have been waiting for more data to come out.

Foss So, other than radiation therapy, can you talk a little bit about some of the other major advances that have happened in the whole field of prostate cancer?

Yu Over the past decade there has been tremendous change in prostate cancer. On the medical oncology side, the TAX-327 trial in 2004 was one of the first that showed efficacy for chemotherapy in the metastatic setting for prostate cancer. Immune therapy has come out. More advanced anti-testosterone therapy has come out. It has been amazing to see what is occurring on the medical oncology side for prostate cancer. On the surgical side, robot-assisted laparoscopic prostatectomies have become more and more in vogue and really matured I think as a technology, and that has only happened in the past decade, and then on the radiation side, image guidance, the use of intensity-modulated radiation as the standard of care now is a huge paradigm shift compared to how we were treating prostate cancer in 2001.

*Dr. James Yu is Assistant Professor of Therapeutic Radiology at Yale School of Medicine. If you have questions, or would like to add your comments, visit [yalecancercenter.org](http://yalecancercenter.org) where you can also get the podcast and find written transcripts of past programs. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.*