

Yale CANCER
CENTER
answers

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Hosts

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**Screening Options for Prostate
Cancer**

**Guest Expert:
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Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Anees Chagpar. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale-New Haven. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This week, doctors Foss and Chagpar welcome Dr. James Yu. Dr. Yu is Assistant Professor of Therapeutic Radiology at Yale School of Medicine. Here is Francine Foss.

Foss Can you start off by telling us about your background and how you came to Yale Cancer Center, how long have you been here?

Yu I have actually been in New Haven on and off since the mid 90's as I went to college here, and then I went to medical school at the University of Michigan, and came back for my radiation oncology residency training and never left and right away my practice was treating folks with prostate cancer, with cancers of the genitourinary tract, and I also treat patients with brain tumors along with my colleagues in neurosurgery, folks with brain metastases using Gamma Knife.

Chagpar Tell us a little more about prostate cancer in particular, since it is an area of expertise for you, and the role that radiation plays and all of the different options that people have. You mentioned Gamma Knife and we hear about all of these new-fangled technologies, set the plate for us of what the options are for people and what role radiation plays in the treatment of prostate cancer?

Yu Radiation is a local treatment, sort of like surgery in the sense that it treats an area of your body, but unlike surgery there is no cutting, it is also not as specific as surgery. It is kind of in between a whole body treatment and a very specific treatment like surgery. Radiation is used in an attempt to cure prostate cancer. Traditionally, it has been used in folks who are not eligible for surgery because of their advanced age and are not likely to tolerate surgery as well, but radiation is also used in combination with androgen deprivation therapy, otherwise known as pulling away the testosterone of the patient in higher risk disease. So, those are the two main areas where radiation has been traditionally used. Folks who are older, who cannot tolerate surgery, or folks who have disease that may be outside of the prostate, so removing the prostate may not be as helpful as treating the specific region of your body.

Foss You mentioned older people, can you tell us the average age of patients with prostate cancer and is that changing?

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Yu The average age of the patient who has prostate cancer is roughly 65 or 66 and that is in the current era, and I'll foreshadow our discussion about screening, but in the current era, in the current screening climate, men in their mid-60's are the most common age at diagnosis, but because prostate cancer is so common and so prevalent, I am sure if you looked hard you could find prostate cancer in even earlier ages than we currently do, and if we do not screen as much, I am sure that age at which folks are diagnosed will get older.

Chagpar I want to get to the screening issue in just a second, but tell us a little bit more about radiation because some of us think of radiation as sitting outside in the sun and getting radiation, and that is one form of radiation, but you hear about all of these new-fangled technologies and you wonder, is this all the same stuff or are they different? Which ones are the best, and can you give us some insight into this because we hear about all of these new technologies, and I do not know about the rest of the world, but I am still a little unclear on what all of these things are.

Yu At the core, therapeutic radiation is the breaking of a cancer cell's DNA with a particle, either a photon, proton or an electron, or in certain places in the country a neutron or a carbon ion, regardless, it is a beam of energy, and what you are trying to do is the break the DNA of the cancer cells so that the next time it tries to divide it cannot, and that is the primary way that radiation kills cancer. 99% of beam radiation is delivered with photons, megavoltage photons, with a machine called linear accelerators; that is the way it is done throughout the country. At a few select places around the country, there are huge proton machines that can beam high energy protons at the prostate in an attempt to kill the cancer and then beyond that, there is brachytherapy, which is also very commonly done where radioactive seeds are inserted inside the prostate itself. The photons that are emitted from the radioactive sources are much lower energy than the beamed in radiation, so the energy deposition is more localized to the prostate, but the goal is the same, to break the DNA of the cancer cell and we could go on and on.

Foss Does the prostate particularly lend itself to radiation therapy because of the location? Are there good things and bad things about radiating the prostate?

Yu I think radiation has been popularized for prostate cancer because you do not have to cut the connection between the bladder and urethra and you do not have to cut through tissue to get there, but radiation itself can cause local side effects to the urethra, which follows through the prostate or to the rectum immediately behind it or the bladder immediately above it. But, compared to the other places in your body, it is both a location that you have to be very careful about, but it is also

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not in your brain, for example, so there are no long-term neurologic side effects with radiating the prostate and it is not near your heart, so you are not going to die of a heart attack because you had your prostate radiated. So it is both a good and bad place to get radiation.

Chagpar James, I can imagine that there may be some men out there who have just been diagnosed with prostate cancer, because as you say with the era that we are in now where so many men get screened and so many people get diagnosed with prostate cancer, I would bet you there are people out there who are wondering, okay he is talking about photons and then he is talking about protons, then he is talking about this brachytherapy, and what people really want to know is which one is the best?

Yu If someone asks me which one is the best, the answer always is, it depends, it depends on what your own personal values are, how far you want to travel, how much you want to spend, for example, how convenient you want the treatment to be, and what side effects you are most worried about and helping patients make a decision about what treatment to get is an intense area of study. There are a lot of people out there trying to build these decisions tools, and I met with a wonderful group of men who were trying to ask the questions that prostate cancer patients are asking, and one of those things we are trying to do is to develop a tool that can help folks match the treatment that is best to them, because if you ask a physician what is the best treatment, there is no study that definitively says, treatment A is better than treatment B, which is better than treatment C. It really depends on who asks and sadly sometimes it depends how much the physician is invested in the piece of equipment too.

Foss That brings us back to a very fundamental question. A man is diagnosed with prostate cancer, what are the next steps and do all men with prostate cancer see a radiation therapist? Can you step us through the whole process from the time of diagnosis?

Yu Currently in this day and age the most common way that someone is diagnosed is through screening, so they are usually relatively asymptomatic. Their primary care provider, or if they have a urologist, they check their PSA, prostate specific antigen, which is a routine blood test, then the urologist biopsies the prostate and then that is when you have a diagnosis of prostate cancer. At that point, studies have shown that the urologist is the primary determinant of whether the patient then goes on to get what type of treatment and in an ideal world though they would have a conversation with a radiation oncologist, or two, and have a conversation with a urologist, or two, and really take their time thinking about the options. My group of men that have informed me about what they like in terms of decision help, also point to online forums of other prostate cancer patients as being very helpful, and reaching out their friends and family who have had prostate cancer, really just getting comfortable with a treatment is best.

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Foss You talked about time and a lot of cancer patients think, I do not have a lot of time, I have to make a decision very quickly about this. Can you talk about the time issue with prostate cancer, how much time do you have to make these decisions?

Yu Prostate cancer patients, the vast majority of them, can take months to decide on a treatment, particularly with the low risk prostate cancers where the Gleason score is 6 or the PSA is changing very, very slowly and it has been watched for years, those folks can take a long time to think about their options, and really discuss it with their friends and family, do research. We found that Wikipedia is actually one of the more reliable sources of information, believe it or not, rather than the industry websites and even sadly some academic websites that have their own investment in machinery. The American Cancer Society, Wikipedia, those types of things are very helpful.

Foss So, Wikipedia for medical information, who knew?

Chagpar That brings us back to the whole screening topic because as you point out a lot of people now are getting diagnosed at a really early stage and in general, we say that is great. The earlier you are diagnosed, the more treatable cancers are, and so the more time you have to think about what you want to do. But recently the screening recommendations for prostate cancer have changed and I think that this has caused some men perhaps a fair amount of angst because now if I understand it correctly, recommendations are that you do not need to get screened quite as much as we had previously advocated, can you speak to that?

Yu The big controversy was put out there by the US Preventative Services Task Force that basically came out and said that you do not need to routinely screen men for prostate cancer, now that is a group of physicians that have looked at all the data, but there was not a urologist, or a radiation oncologist, or a medical oncologist involved in that study group as far as I could tell and then competing guidelines came out from the American Urological Association, and The American Society of Clinical Oncology, which said yes, you need to screen, but you do not have screen as often as you used to, every two years is fine and folks, before they get screened, should have a conversation with their physician about what they will do should there be a prostate cancer diagnosis, and also it should be men over the age of 55 and under the age of roughly 70 to 75 with good health who are expected to live 10 to 15 years and so will benefit from a small decrease in the likelihood of dying from prostate cancer. If you are in your 80s and you are smoking 8 packs of cigarettes an hour and you not in the greatest health, prostate cancer screening is likely to cause more harm than good. If you are in your early 60s, you are a marathon runner, you have a father who died of prostate cancer early, then maybe you should get screened, maybe you should have

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a conversation with your primary care provider and talk about the implications of prostate cancer, the types of prostate cancer, and I think it really should be individualized and that is what our society is recommending.

Chagpar We are going to take a short break for Medical Minute. Please stay tuned to learn more information about screening options for prostate cancer with our guest, Dr. James Yu.

*Medical
Minute*

The American Cancer Society estimates that over a 1000 patients will be diagnosed with melanoma in Connecticut each year. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable and new treatment options and surgical techniques are giving melanoma survivors more hope than they have 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 melanoma. The specialized programs of research excellence in skin cancer grant at Yale, also known as the SPORE grant, will help establish national guidelines on modifying behavior and on prevention as well as identification of new drug targets. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Chagpar Welcome back to Yale Cancer Center Answers. This is Dr. Anees Chagpar and I am joined today by my co-host Dr. Francine Foss. Our guest tonight is Dr. James Yu and we are discussing screening for prostate cancer. James, right before the break you had told us that there were two sets of competing guidelines, one that came out from the USPSTF and one that came out from the AUA and ASCO. Both seemed to recommend against doing prostate screening as frequently as we have done it before and some advocating even less than that. Can you talk about what the excepted guidelines are, what should men who are listening to this program be thinking about in terms of screening and what were the motivating factors for those changes in screening recommendations? Some argue that it was all cost driven and not quality driven, can you speak to that as well?

Yu The screening guidelines were driven by the fact that there is not strong randomized trial evidence supporting screening as lengthening men's lives on a routine basis. There were two major screening trials that came out a couple of years ago, one in the United States and one from Europe. The United States trial, called PLCO prostate, lung, colon, ovarian group basically found no survival benefits to folks who were recommended routine screening compared to best practice

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and I do not think the audience can see me waving my fingers in terms of the quote sign, but best practice in the United States at that time was screening so the trial was flawed to begin with because a lot of folks in the screening arm obviously got screened, but also a lot of folks in the best practice arm got screening. It was kind of a given that there would not be a big survival difference between the two arms. In Europe, they did the same trial, the ERSPC randomized trial and they did find a benefit to prostate cancer screening, but it was small and because of that the USPSTF, the US Preventative Services Task Force said, the evidence is pretty modest, there are lots of side effects associated with treatment and because of that we do not think screening routinely makes a lot of sense. Those of us who treat prostate cancer would take a step back and say, yes, screening does make sense but screening in moderation and screening with eyes wide open and having a discussion with the patient about what it means should they want screening and what it means to be diagnosed with the cancer, that is very unlikely to cause their death. Now prostate cancer is a very expensive cancer for the United States as a whole, one in six men will be diagnosed with prostate cancer during their lifetime and each year almost a quarter million men are diagnosed with prostate cancer, so as a burden on the US health care system, it is huge, it is about the second leading cause for cancer deaths in American men. So any time you talk about prostate cancer you have to think about it from a national standpoint and what it means to treat a quarter million men every year and pay for their side effects and pay for all of the things that happen to them with only a modest benefit in survival.

Chagpar You talked about one in six, is that correct? One in six men, is that one in six men that are screened or is that one in six in the population?

Yu That is in their lifetime, one in six men, and honestly as you get older and older there are some studies, for example, one done with Japanese men in their 90s, where it was found that at the time of autopsy, almost 80% to 90% of those men had prostate cancer in their prostates. So if you screen intensely enough in the oldest men you are going to find prostate cancer.

Foss We talk about screening costing money and you have alluded to the PSA, but can you tell us what the whole screening process is like, are there things that are done other than the PSA?

Yu So after the blood test, if you have an elevated PSA, which again there are a lot of studies looking at what the ideal cut off is, but routinely the cut off is 4, if your PSA is above 4.0 you get a prostate biopsy. A prostate biopsy is done by inserting long needles into your prostate and typically 12 cores are obtained by the urologist. These cores are sent to a pathologist and they are examined under the microscope for evidence of cancer.

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- Chagpar James, I want to get back to talking about cost, because I know, but maybe our audience does not know, is that one of James' fortes is actually in health services research and you have done a great deal of work looking at cost and quality and so on, and I think that that is particularly relevant today and thinking about the Affordable Care Act and the sequester and the deficit and everything else, can you speak a little bit more about the balance between the cost of screening and the cost of treatment because I am sure that the men out there who are thinking about health care cost are thinking, well it is fine to save on other people's health care cost but when I get my cancer, by golly, I want the Rolls-Royce.
- Yu Well the cost of prostate cancer treatment is enormous and different treatments cost more than others. Radiotherapy, particularly a technique called intensity modulated radiation therapy, which is the type of therapy that I apply to men is particularly expensive and then beyond that proton radiation which is delivered by these \$100-\$150 million machines is even more expensive. So at a certain point, I think both Medicare and the insurers are going to stop paying for these treatments without evidence of efficacy and that is part of the research that we do and there are many studies out there trying to compare the impact of the treatments on men's lives, the efficacy of those treatments and the cost of those treatments, but honestly, a complex decision analysis cannot take into account an individual patient's preference. So yes, those studies are interesting from a macroscopic standpoint and I participate in those studies too, but ultimately it just goes back to a closed door with the physician and the patient talking over the options.
- Foss When you talk about the decision being made based on efficacy, can you clarify for the audience, are we talking about a patient responding to the treatment, or are we talking about a patient living longer or an improvement in quality of life? What is the actual measure that is going to help them to determine whether they should continue paying for this?
- Yu In health economics people use a term called quality adjusted life year, which is a combination of how long folks live, but also the quality at which they are living, and when people do cost effectiveness analysis they try and calculate that for a treatment. So if you have a treatment where you live 100 extra years, but you are living with terrible side effects, that may not be as good as the treatment where you live 90 years, but have no side effects whatsoever. So quality adjusted life years is the typical measure.
- Chagpar Can you put into context when we were talking about cost and quality, a lot of people sit there and think, maybe the cost of treatment will actually be lower if we detect this early and therefore the cost of screening may be worth it? Certainly in some cancers, like breast cancer, for example, that applies. How does it in prostate cancer?

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Yu People have not really looked at the cost of screening per se. Although our research group, the Cancer Outcomes and our Public Policy and Effectiveness research, of which you are a member, we are looking at the cost of cancer screening but it is very difficult to separate right now from just the lab tests, just the biopsy because there is more cost than that. There is the psychological cost, there is the impact of lost days of work if you working etc., but early indications are it is not really the cost of this screening it is what you do with that screening that really costs a lot more.

Foss Should most men in the audience when they are thinking about prostate cancer and they are thinking about treatment, should they be thinking that this treatment is going to cure them and prolong their life, and should they be worried that say if they decide not to get treatment that their life would be shortened from this cancer?

Yu It depends on how aggressive their prostate cancer is, but certainly if they have a favorable risk for prostate cancer, meaning their Gleason score is 6 or less, their PSA is less than 10, none of their physicians can feel a big tumor in their prostate, if those three things are true then it is extremely unlikely that that cancer would cause the patient to die. They could have their PSA followed over time under technical active surveillance where they get a PSA very regularly and also a biopsy every one to two years to make sure that the cancer does not change. That is a very reasonable way to go. Now the caveat though is there are men out there who no matter how much you reassure them that they just have a favorable risk prostate cancer, that knowledge impacts their quality of life and is extremely anxiety inducing. Those folks, despite their favorable risks, despite the fact that the cancer is not going to kill them, they may benefit from treatment at least just to get the cancer off of their minds as, and that may sound silly, but it is really a patient-to-patient discussion.

Chagpar Well it is the big C word and that is scary for a lot of patients, but I think that the thing that those patients should think about as well is the balance between, is this treatment going to save my life, and all of the side effects. James can you talk a little bit about the side effects, the side effects of surgery, the side effects of radiation and what people who pursue aggressive treatment may have to look forward to?

Yu Absolutely, so both surgery and radiation can cause erectile dysfunction, significant erectile dysfunction. The number I quote to men is that roughly 40% of men, regardless of the treatment they get are not going to be happy with their erections after treatment. With surgery that impact is right away and then there is some recovery, with radiation, it is an accelerated but overtime erectile dysfunction and in the end it is the same. Studies comparing the two groups are very difficult to do because surgery patients are younger and usually more potent, and study after study has shown they are roughly the same, so erectile dysfunction is the most common. Surgery can cause

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urinary incontinence, usually it is a little bit of dribbling stress incontinence, coughing, lifting heavy objects will cause a little leakage and sometimes it is much worse than that, but rarely. There are usually no rectal side effects associated with surgery. For radiation though, the side effects are short term and long term. In the short term, they typically have increased urination, increased urgency of urination, and increased frequency of urination, very rarely requiring a catheter because the prostate has swollen to the point where men cannot urinate, but usually overtime after about a year to two years they come back to where they were before the radiation started. More common in radiation than in surgery are the rectal side effects. Rectal bleeding is a rare but real side effect from radiotherapy. Some men do report increased urgency and frequency of bowel movements and very rarely there is fecal leakage that can happen after radiation, typically years after radiation. So it is a mixed bag of side effects and again it points to the individuality of making a choice. If men are extremely worried about their sexual function, then they should get active surveillance for as long as possible.

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 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.