Yale CANCER CENTER answers

WNPR Connecticut Public Radio

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Targeting Biopsies for Prostate Cancer

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Yale Cancer Center Answers
is a weekly broadcast on
WNPR Connecticut Public Radio
Sunday Evenings at 6:00 PM

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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, Dr. Anees Chagpar welcomes Dr. Preston Sprenkle. Dr. Sprenkle is Assistant Professor in the Department of Urology. Here is Dr. Chagpar.

Chagpar Let's start off by having you tell us a little bit about what prostate cancer is?

Sprenkle Prostate cancer is the most common cancer in men and we have a recent problem with the U.S. Preventive Services Task Force and their recent findings that recommended against prostate cancer biopsy, or prostate cancer screening, and it has been a challenge for urologists because PSA and prostate cancer screening is really the only the way that we have to detect prostate cancer. Before screening prostate cancer was detected when men had metastatic disease. It was too late for cure and often too late for treatment that was anything other than palliative. So with our recent screening efforts the pressure is on to decrease the morbidity of the screening efforts and to really treat men appropriately. We have new program now such as active surveillance which is a nonsurgical and non radiation way of treating men with prostate cancer that is low risk. Before we even get to treating though, we have to diagnose prostate cancer. Prostate cancer screening with PSA and a physical prostate exam are still the only ways that we have to be able to diagnose prostate cancer. There are no real symptoms of prostate cancer in its early form that men should look out for to be able to identify and that is why we continue to stress that screening is a good idea. Once screening is done with PSA, a blood test, or biomarker blood test and/or rectal examination to examine the prostate and identify suspicious lesion or the PSA is elevated, the definitive next step for diagnosis is a biopsy, and prostate biopsy is the only way that we can accurately stage prostate cancer. We have a new device at Yale, which we are pretty excited about, that allows us to take MRI images of the prostate and fuse them with an ultrasound and when we put these two images together we can get all of the benefits of an MRI, which allows us to identify lesions within the prostate. Over the last several years MRI imaging has become better and better at identifying these prostate cancer lesions and we can take that and instead of having a patient in a huge MRI machine and trying to do biopsies there, we are now able to do them in our office, which is much more comfortable, and use an ultrasound probe, which we use anyway for biopsy, and we can take the images from the MRI, which are better than the ultrasound images in detecting cancer, and fuse them with our ultrasound images and we can then in real time identify the lesions that were visible on MR and biopsy those using an ultrasound. So it really takes the benefits of MR and the benefits of ultrasound and puts them together.

Chagpar Let's go back a half a step, so here you are, you are one of our listeners and you are thinking about prostate cancer and the first question that you have is, should I even get a PSA test? So your

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recommendation is to continue to get PSA test because without them you get advanced disease, is that right?

Sprenkle Well not necessarily, so the current recommendations from the American Urological Association, our national body as urologists, and the National Cancer Society, are that men should be screened for prostate cancer from about the age of 45 until the age of 75, or earlier if they have less than 10 years of life expectancy. Prostate cancer is a slow growing disease and so we do not want to be screening everyone, and that is one of the problems with prostate cancer screening, and one of the reasons that the USPSTF made its recommendations, because men who were 30 were being screened without reason and men who were 85 and only had two years left to live were being screened, so there was definitely an overuse of the test. So, who should be screened? Men over the age of 40 if they are African American or if they have a first-degree relative, meaning a father or a brother, who has been diagnosed with prostate cancer. Those men should be screened starting around age 40 to 45. Otherwise, age 45 to 50 until about the age of 75 depending on their health status, and at that point it has to be individualized a little bit more depending on how healthy someone is.

Chagpar So you are a guy, you are 65, you are relatively healthy, you go to your family doctor and your doctor does a PSA and lo and behold does a digital rectal exam and feels a nodule. What happens next?

Sprenkle Typically they are referred to see a urologist and the urologist would repeat the exam and see what the PSA values were, but usually the PSA and the prostate exam are independent of each other. We only need one of those to be positive, so if you felt something abnormal on a prostate exam, it does not really matter what the PSA is, versus if the prostate exam is normal, but the PSA is elevated, either one of those is enough for a biopsy to be recommended.

Chagpar At that point, is your first test an ultrasound or it is an MRI?

Sprenkle MRI and ultrasound and are not used by themselves currently to detect prostate cancer. There is not enough experience and if there is a lesion that we see on an MRI, we cannot say, okay you have this cancer and we know what the grade is, so they can only be used with biopsy.

Chagpar Right.

Sprenkle In fact, if the MRI is negative and does not show anything, it does not mean that there is not cancer there. We do not have enough data or information yet to be able to say that. Our goal is to be able to do that eventually, but an MRI or ultrasound can be used to target your biopsies. So typically a

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biopsy is done in the urologist's office with a hand held ultrasound and an ultrasound of the prostate is done to measure the size of the prostate and to look for anything that appears abnormal on the ultrasound. It is difficult to read an ultrasound, abnormalities are not always that common. So what you then do is use the ultrasound to look where the prostate is and try to distribute random biopsies throughout the prostate using the ultrasound. There is a recent study out of Korea and Johns Hopkins University, that showed that the hand held ultrasound-guided biopsy does an okay job, but often the biopsies are clustered and they can miss entire portions of the prostate altogether. So they are random, but they are not evenly distributed throughout the prostate and they compared this to a robotic arm-guided biopsy, which showed a systematic or very even distribution of biopsies throughout the prostate. What we are doing here is sort of a combination of that, we actually take the MRI images, which are much better at identifying lesions in the prostate, and we combine that with a real time ultrasound, which is typically what is done, but we have a robotic arm that holds the ultrasound probe, so not only does it help steady the biopsy, it allows us to do that in an evenly distributed way throughout the prostate.

Chagpar But it sounds to me that this is even better because if I understood you right, and correct me if I misunderstood, historically ultrasound helps you to see the prostate itself, but does not necessarily help you to exactly visualize where the lesion is, and so you would take these "random biopsies," but if the MRI actually helps you to see the target and now you are able to fuse seeing the target with the ultrasound that you have in your office, one would presume that you now have this way to definitively sample not just the entire prostate, but the actual target right in your office. Is that right?

Sprenkle That is correct, and we feel that is one of the major leaps forward with this technology, and in a recent article that was published by a group at UCLA who has been using this device, they found that the targeted biopsies were three times more likely to have cancer than the random biopsies. So it increases our yield, that does not say that this creates more positive biopsies, but if something is there and was potentially missed before, we are now able to identify that. That is one of the problems with biopsies, if you miss something and things are still abnormal, we do repeat biopsies. This ideally will decrease the number of repeat biopsies that are necessary and it definitely increases our ability to hit or target and sample the lesions that are identified.

Chagpar It would seem that, that was the whole purpose of the screening program, you screen a guy and you say, your PSA is through the roof, and I either feel or do not feel a nodule, I am pretty worried, but then you do these biopsies that are a little bit in the dark if you did not have this targeting system, but now you are able to say, guess what, I hit the target and this is what it is.

Sprenkle Yeah, so that is definitely a big help in what we hope to do and we are still evaluating it to see how much better it is. There are some limitations in that it is an additional device and there is a little bit of training to be able to use it, but we think that it could revolutionize the ability to do a biopsy and really help identify where lesions are and biopsy those lesions that are high risk.

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Chagpar It sounds like this is very hi-tech with the MR and the 3D ultrasound and fusing these images. This is not something that I would think you would find in your friendly neighborhood urologists office.

Sprenkle I think there are about 10 centers around the country that currently have it in clinical use. UCLA is one of the oldest, they have been doing these biopsies since 2009, but they are the only group that has published their results with this specific technology. There are other groups doing MR fusion technology where they take the MR images and fuse it with ultrasound and do the biopsies. The NIH has had a program there for many years, but they are using a different technology, but again, they see the same results where they are able to target lesions and get much higher yield in the targeted biopsies.

Chagpar So now are you using this universally on all patients who present to the urology program at Yale?

Sprenkle We are trying to, we are in the process of implementing that, yes. Right now I am the only one who is doing them fulltime, but the other physicians are in the process of either getting them engaged or having referrals, so that I can do the biopsies for them.

Chagpar That is fantastic. Have you found that with this technology, when you actually see the lesion, that you are getting more positive results? Are you finding these cancers earlier and are you able to treat more men with prostate cancer?

Sprenkle Those are good questions. The biopsy is not necessarily going to help us find cancer earlier, and there is actually a question of do we want to find prostate cancer earlier in men with low risk prostate cancer? What we hope, and what we see some evidence of is that men who have a high risk lesion, the men where the prostate cancer will likely affect the course of their life, those are the patients that we are detecting with MRI and those are the patients that we are able to biopsy and identify the prostate cancer and even if the prostate cancer is in a difficult location that we would not get on a regular screening biopsy, those are the people that are really benefited by this.

Chagpar That sounds excellent. We are going to take a short break for a medical minute. Please stay tuned to learn more information about prostate cancer with Dr. Preston Sprenkle.

Medical Minute *Breast cancer is the most common cancer in women. In Connecticut alone approximately 3,000 women will be diagnosed with breast cancer this year. But there is new hope. Earlier detection, noninvasive treatments, and novel therapies provide more options for patients to fight breast cancer. Women should schedule a baseline mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection, and a healthy lifestyle breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make innovative new*

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treatments available to patients. A potential breakthrough in treating chemotherapy resistant breast cancer is now being studied at Yale combining BSI-101 a PARP inhibitor with the chemotherapy drug irinotecan. This has been a medical minute brought to as a public service by the Yale Cancer Center. More information is available at 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 guest Dr. Preston Sprenkle and we were discussing biopsies for prostate cancer and some new technology that is being utilized fusing MRI images with ultrasound helping to target prostate cancers. Preston, right before the break, I had asked you about whether this targeting technology allows you to find cancer earlier and you said it allows you to more accurately target these cancers, but you do not necessarily want to go whole hog and treat these early prostate cancers really aggressively. Tell me a little bit more about how people who may have a really early prostate cancer are managed and how you use this technology to help you with that.

Chagpar With prostate cancer there is low grade and high prostate cancer. We use a Gleason score to differentiate how cancer is graded and typically the most common and lowest grade that is considered cancer currently is Gleason 6, and it goes up to a Gleason 10, and what we found is that there have been many studies of trials called active surveillance and this is different than the historic watchful waiting that many patients' parents or even grandparents had where watchful waiting was you were diagnosed with prostate cancer, but you are old and sort of sick, so you were told you have prostate cancer and you were sent home until you had symptoms of disease that had spread to the bones and you had pain and then you would come back and we would give palliation with some treatment. Active surveillance is a very difference sort of treatment. What we do is we identify patients that have low risk disease. So what that typically means is Gleason 6 prostate cancer in a small amount of the biopsy cores. It can be 5%, it can be 25% of the core, typically it is less than 3 cores involved and less than 40% in any one of those cores that makes someone a candidate for active surveillance. What we are able to do with these patients is identify those who have a low likelihood of progression of their prostate cancer, and the reason this is really important is that prostate cancer is a bad disease, but the treatment is also very bad. While we can cure a cancer, the side effects such as urinary incontinence and sexual dysfunction are major and they significantly impact quality of life. Good surgical technique can minimize that a fair bit, but still it can happen to a large number of people. Our active surveillance protocol, which we have instituted here at Yale, allows us to identify patients with low risk disease, so a very low likelihood that disease is going to advance quickly, and we can put these patients on active surveillance. We can delay or perhaps prevent forever them needing definitive therapy and the associated problems with urinary and sexual function. So if you can give someone an additional five or six years of their normal urinary or sexual function, that is a tremendous advantage over early treatment. What we have seen in other studies is that there is no decrease that we have been able to identify in long term survival by doing active surveillance appropriately. Now surveillance, like I said, we are not sending you home, we keep a close eye on the patients, we do a PSA test and a prostate exam

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usually every six months and we repeat biopsies about every two years with the possibility of doing it earlier if anything in the PSA or the rectal examination feels abnormal, but by doing this, in general, we are able to keep patients pretty happy with their current sexual and urinary function and allow them to have a prolonged course of their natural life.

Chagpar That is really cool. So you could be a gentleman who comes in, gets screened, has this MR ultrasound fused targeted biopsy and then is told that their cancer is really low risk, we are going to see you back in six months, repeat your PSA and in two years we will do a whole biopsy again. If things look the same then, and they can live with this cancer, and know that they are at low risk.

Sprenkle That is correct and actually while we do use the fusion biopsy to diagnose this, it is not required that you have that biopsy to be a candidate for active surveillance. Any biopsy could make someone a candidate for active surveillance. So it is not only for those people. We often will repeat a biopsy at around six months from the first one, because it is a random biopsy, so that we do not miss anything in the prostate and by doing that we are able to confirm that this really is low risk disease. We feel more comfortable that this is low risk disease and continuing active surveillance is a good idea. Now for patients with high-risk disease, there are very good treatment options and surgery and radiation are definitely important and should be thought of as treatment options because they do give very good cure and survival rates. Unfortunately in those levels of prostate cancer the risk of prostate cancer affecting their quality of life and longevity of life is high enough that definitive treatment for cure is recommended.

Chagpar So you have this kind of weighing of risk and benefit. What are the risks of the cancer being very aggressive such that the risk of surgery and radiation outweighs the benefit that you would get with those treatments? I want to come back to the targeted biopsy just for a minute in terms of this active surveillance. One of the things that struck me about this targeted approach is that it is harder to miss when you see the target right there because the MRI sees it so well and you are able to fuse it with the ultrasound, one would think that would be particularly useful in the active surveillance rather than the random biopsy that they may have gotten initially because then you would really be able to say, I know that this is low risk, I know that I am not missing something by doing a random biopsy.

Sprenkle You are absolutely right, and that is one of the benefits of the fusion biopsy and why even if someone is a candidate for active surveillance with an outside biopsy, I will repeat a fusion biopsy before they go into active surveillance so that we can follow it and exactly as you mentioned, we can record exactly where on a three-dimensional model our biopsies went. So we can see where prostate cancer was and we can biopsy the exact same place when we do the repeat biopsies, which is impossible without a technology similar to this.

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Chagpar You mentioned the higher risk people, so if somebody came in, they had screening and now they actually have a higher Gleason score, what Gleason score or what criteria would you kind of say, you know, that tilts the balance a little bit against active surveillance and more towards active treatment.

Sprenkle There are a lot of variables and a lot of them are personal in addition to just the cancer. A patient's age makes a difference. Again, we know prostate cancer is rather slow growing, especially the low risks types. High risk we think of as more aggressive, but for someone diagnosed in their early 70s with a Gleason 7, that is a low intermediate risk Gleason, that is small volume. Some people do consider and do put those people on active surveillance versus a 52-years-old gentleman with a small amount of prostate cancer or even the same amount of cancer. It becomes difficult because there is no cookie cutter that fits everyone and we try to personalize based on what the patient wants as well. Some people are not comfortable with knowing they have a diagnosis of cancer and watching it and being on active surveillance. They would rather be assured that everything is done and the tumor is removed, the prostate is removed and they are free of that cancer. While others really are concerned about their quality of life and would rather try to take a risk of having some cancer in their prostate and actively survey it. Currently, we do not include many intermediate risk patients in active surveillance. We do not have enough long term information or understanding yet to think that it is safe to include those people, but in general, to qualify for active surveillance, I mentioned the Gleason criteria for the number of biopsy cores, a PSA less than 10, and 3 cores or less involved with prostate cancer. And typically almost all age groups are now considered eligible for active surveillance.

Chagpar If there is a gentleman who says to you, I am 52 years old, I have a high risk Gleason score and I want my prostate out. One of the things that you mentioned before we went to break was that while treatment is associated with some side effects, some of that can be minimized with good surgical technique and there is a lot of talk out there now about different kinds of surgical techniques, particularly for prostate cancer using robotics. Is that type of thing available? Are you doing that? How does that play into the paradigm?

Sprenkle We do have robotic surgery available at Yale. I do perform robotic surgery. The caveat with robotic surgery is that it is a tool. The robot is not better than a surgeon's scalpel at cutting out prostate cancer. It really depends on your surgeon and the surgeon's skill level, that is what is going to determine how good your outcomes are and that is part of it. It is also unfortunately the physiology and just the way the person's body is put together. So we can do the same surgery every time and people have different outcomes. All surgeons do their best every single time they go in there to preserve as much function, both urinary and sexual as they can, but the main goal is a cancer operation and to cure the patient of cancer and the technology, whether robotic or open, is not as important as the skill of a surgeon.

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Chagpar I guess it is something that I am not sure that everybody always understands, when we talk about robotic surgery you think of R2-D2 or C-3PO taking out your cancer, but in reality there is a surgeon running that robot making the robot do what the surgeon wants them to do, right?

Sprenkle Correct, these robots are very hi-tech, but there is no artificial intelligence. They do not have their own brain. They are tools. They are a machine that the surgeon drives and it allows the surgeon to not have his hands in the patient's body, but the extension of his hands, the robotic arms, are in the patient's body. So the main benefit of robotic surgery is that it has lower blood loss than open surgery. This has been well accepted and the incisions are individually smaller. Long term outcomes seem pretty similar between the two, after about six weeks the recovery is pretty much the same, maybe 12 hours or earlier on discharge with robotic surgery versus open, but I can say that having operated with expert open surgeons and expert robotic surgeons, their outcomes are pretty equivalent.

Dr. Preston Sprenkle is Assistant Professor in the Department of Urology 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.