How Will New Imaging Techniques and Genomic Tests Help In Diagnosis and Management of Prostate Cancer.

Recent advances in prostate cancer has led to the discovery of many new imaging and genomic tests.

Information on the new tests and techniques can help patients in making informed decisions regarding their prostate cancer diagnosis, treatments and management options and thereby contribute towards managing their disease efficiently and effectively.

We are talking to prostate cancer expert Dr.

David Lee of UPENN to better understand how the new techniques can help in making these decisions.

Full Transcript:

Priya Menon – Good evening and welcome to the 100th episode of CureTalks. I am Priya Menon, Scientific Media Editor, CureTalks, joining you from India. CureTalks team takes this opportunity to thank our audience and participants for supporting us through all our 100 episodes. We hope you will continue with us on our journey towards another 100 more. With that note, we will begin with today's talk. Today, we are talking about prostate cancer; and the topic of discussion is how will new imaging techniques and genomic tests help in diagnosis and management of prostate cancer. Our prostate cancer talks are conducted in association with Prostate Cancer International and Prostate Cancer Foundation.

Priya Menon – The recent advances in prostate cancer have led to the discovery of many new imaging and genomic tests. Information on the new tests and techniques can help patients in making informed decisions regarding their prostate cancer diagnosis, treatment, and management options and thereby contribute towards managing their disease efficiently and effectively. We are talking to prostate cancer expert, Dr. David Lee, of University of Pennsylvania, to better understand how the new techniques can help in making these decisions. Dr. Lee is Chief of the Division of Urology at Penn Presbyterian Medical Center and Associate Professor of Surgery, Division of Urology, University of Pennsylvania School of Medicine. He specializes in robotic surgery, including robotic prostatectomy. Dr. Lee currently serves as an active member of the American Urological Association, the Endourological Society, and the American Medical Association. Dr. Lee has published over 100 articles, abstracts, and book chapters in the field of minimally invasive urology. Welcome to CureTalks, Dr. Lee. Its a pleasure to have you with us.

Dr. David Lee – Oh, its a pleasure to be here. Thank you for the invitation.

Priya Menon – My co-host for the show is Mike Scott. Mike is Co-founder and President of Prostate Cancer International, a prostate cancer-specific and not-for-profit educational and informational organization based in Virginia. Mike is also a member of the Board of Directors of the National Organization for Rare Diseases and the International Myeloma Foundation. Supporting Mike on the panel, we have prostate cancer advocate, Paul Carpenter. Paul has contributed to dozens of online groups and forums and he co-founded a Los Angeles support group for gay and bisexual men living with prostate cancer. We also have Tony Crispino. Tony is a patient advocate at SWOG where today he works with some of the industry's finest researchers on the latest clinical trials. An advanced disease survivor himself for over six years, Tony has run online discussion forums, live support groups, and is currently the President of Us2LasVegas and a member of the American Society of Clinical Oncology. We have with us Merel Grey Nissenberg. Merel Gray is President of the National Alliance of State Prostate Cancer Coalitions, California Prostate Cancer Coalition, Mountain Foundation for Educational Research in Lung Cancer. She is an attorney by profession. Her experience and advocacy work and community involvement is extensive. I extend a very hearty welcome to all the panelists. Before I hand over to Mike to begin with the discussion, I would like to remind our listeners that you can send in your questions to me at priya@trialx.com or post it on curetalks.com website. If you would like to ask a question live, please press 1 on your keypads and let us know. With that, Mike, its over to you.

Mike Scott – Thank you very much indeed, Priya, and welcome everybody. Dr. Lee, I think what we would like to do is maybe give you about 15 minutes or so to just talk generally about how you are using new imaging and new genomic and other tests in order to give yourself and your patients the best idea of their risk factors and how that may influence their treatment and then what we'll do is we'll take questions from the panel members and for the last 15 minutes or so, we will open the floor to people who are actually on the line. So, with that, Dr. Lee, if you would like to just take that as 15 minutes and…, and give us your opening thoughts, that would be very kind.

Dr. David Lee – Oh, sure, Mike. Yeah, again, thanks for the invitation and the opportunity to talk about what's going on in prostate cancer and in my practice these days. You know, I perform pretty high volume of robotic prostate cancer surgery and, you know, I am dealing with this patient group. You know, only five years ago, it was very cut and dry, very simple. There wasn't a whole lot else to do besides react to what the prostate biopsy showed and that was typically only because somebody had an elevated PSA or an abnormal digital rectal exam, but recently there is a whole…, a whole variety of different options for patients and, you know, honestly, I think a lot of urologists included, besides patients, are trying to figure out exactly how we can best use these tools and, you know, I…, I like to think about these different tools and different baskets, so to speak, and so, you know, there is the whole arena of, you know, detection and then once detected, you have a couple different tools that can help somebody to figure out what treatment options that they might want to undergo and then there is the aspect of patient care which involves post surgery and then what tests are available besides just the pathology report which can help patients make a better and informed decision.

Dr. David Lee – So, in regards to imaging and genetic tests which I believe we are going to focus mainly on today, I think one of the big things that's happened which is, I think, a big step forward is we have a little bit better imaging test these days. I think multiparametric MRI has really helped us to fine tune our treatment decisionw and then also help us to decide in some cases whether to do a biopsy and, you know, maybe determine which patients are appropriate for active surveillance or more aggressive treatments. So, in…, in our practice these days, when we see patients with…, with more aggressive disease, so, you know, one of the pieces of information that we get from somebody's prostate biopsy is their Gleason score and so knowing what somebody's Gleason score is…, is really kind of the key to everything because traditionally that gives us the best information on what somebody's prognosis is and based on that, we can give them different treatment options. So, if somebody has lower risk disease, then we start thinking about, you know, especially if the patient is older and doesn't have very long life expectancy and a lot of talk these days is about a 10-year life's expectancy; and so if a patient falls into a little bit older category, not so healthy category with low-risk prostate cancer, then active surveillance becomes a lot more viable treatment option

and so, you know, we really only have PSA, Gleason score to help us to make that determination, but one of the tools that we are using these days is multiparametric MRI and so its a test where patients can go into the MRI scanner. The test usually lasts for about 45 minutes. There are different contrast agents involved, which can help give a picture of whether there is a solid tumor nodule within the prostate, what the blood flow characteristics are of that…, of that tumor and, you know, in…, in the realm of guise with less aggressive-appearing disease, the MRI can give us some information.

Dr. David Lee – One of the things that it can help us to do, if there is actually a sizeable tumor nodule in the prostate, then its very likely that that tumor is actually higher-risk disease, so higher Gleason score and so that can sway…, sway us to recommend more active treatment rather than active surveillance. If somebody has, you know, no tumor visible on their…, on their MRI, you know, that actually falls in line with guys with less aggressive disease. You know, even under the microscope, Gleason 6 disease really appears very similar to normal prostate tissue and so its not a big surprise that radiologically its very difficult to distinguish this and so, you know, on CAT scan, its very difficult to get that information as to whether there is any, you know, distinct cancer there, even when its high risk, but, you know, with MRI we get a much better picture and then in this kind of setting for guys with low risk disease, there are two genetic tests that are now commercially available. One is called Prolaris and that's made or run by a company called Myriad Genetics and they are based out of Salt Lake City in Utah, and then the other test is Oncotype DX and the company that provides that test is Genomic Health; and so, these tests both aim to better characterize the aggressiveness of the prostate cancer.

Dr. David Lee – So, you know, one of the constraints that we had with Gleason score is that, you know, we know that 90 plus percent of guys who have Gleason 6 disease will do very, very well with treatment, you know, either with radiation or surgery. They'll have a very high success rate and not need any extra treatment afterwards, but, you know, there is that 10% of patients who won't do well and, you know, some of those guys will go on to have metastatic disease and end up dying of their prostate cancer. So, you know, one of the things that we know is that not all men with Gleason 6 disease behave the same and so there is something else going on that we can't really put a finger on until, you know, we have the help of some of these genetic tests. So, the Prolaris test and both…, and the Oncotype DX test as well, they both work or are sampled by actually examining a piece of the biopsy tissue that was performed at the time of the standard prostate biopsy and so these very small specimens can be obtained from the slide and they only need about a 1-mm section of tumor and then they can run these genetic tests and so the…, the idea with both of these tests is that they look for RNA expression in these cells and so they can extract the RNA which, you know, I think the technology in and of itself is really amazing, but then the Prolaris test, they look at 31 genes in particular, but these 31 genes are cell cycle proliferation genes. So, they are more active or they are more up regulated in the arena or situation where the cells are more rapidly dividing and so, you know, that…, that goes along with aggressive cancer. The cells are dividing at a quicker pace and so, you know, these…, these tumors are, you know, more likely to spread. The… So, looking at that result, if somebody has a higher Prolaris score, then that gentleman will have a more aggressive prostate cancer.

Dr. David Lee –The Oncotype DX test, they look at 17 genes and…, but these tests are looking at a whole actually variety of different cell functions. Some of them are androgen receptors and so we know that prostate cancer is very sensitive to the presence of testosterone and so, you know, obviously this would be important. There are some cell cycle proliferation genes that they will get, cellular organization genes and then both of these tests also look at a set of reference genes. So, you know, its kind of housekeeping genes that are turned on all the time and so that's what you compare all of these other genes to and so, basically the higher the score, the more risk there is of an aggressive prostate cancer. The Prolaris test gives the information of actually mortality, which is interesting, because it was validated by looking at a cohort of patients from Great Britain who chose to actually not do any aggressive treatment after they were diagnosed with prostate cancer and basically underwent a watchful waiting protocol and, you know, knowing what the eventual outcome of these patients were, they were able to look at the test with the benefit of the tissue diagnosis and validate how well their tests actually function. The Oncotype DX looked at a different cohort of patients. A large cohort was from University of California San Francisco, they looked at whether a…, a little different outcome. They are looking at whether the patients are in final pathology report, you know, if patients

go ahead and get radical prostatectomy, what the chances are that their biopsy will look like what their pathology report looks like and so, you know, if you have a higher score, then its more likely that the patients will have more aggressive pathology. If you have a lower score, then that will correlate to a more favorable pathology on final pathology after surgery.

Dr. David Lee – The multi-parametric MRI, I think, is also very valuable when patients have decided that they want surgery. I use it standardly on all the intermediate-risk and high-risk patients and so these are the guys who would have a PSA greater than 10, a Gleason score of 7 or higher or high-volume disease and this can be used as a really nice planning tool as to how much nerve saving we can do for the patients. These days in prostate cancer we are dealing with a whole variety of different patients. There is a lot of the older gentlemen which, you know, we traditionally identify with prostate cancer patients, but there is a lot of younger…, younger guys too who are very worried about their quality of life, their potential for having urinary incontinence and erectile dysfunction and so having this road map, so to speak, really gives…, gives me a better idea of what kind of operation that we can do as far as nerve sparing and preserving that kind of function.

Mike Scott – Doctor, can you tell me…

Dr. David Lee – Yeah?

Mike Scott – Did…, did…, did…, did the results of these tests really…, do you feel help men to come to conclusions about whether they are good candidates for active surveillance? I mean obviously its a problem for lot of men in…, in just, you know, taking that step to say, “Oh, I don’t need to do anything yet.”

Dr. David Lee – Right. So, I think that remains to be fully proven. There have been a couple studies looking at whether it influences physicians and so when physicians are presented with case studies of patients, both with and without their genetic test results, the genetic test results actually do seem to influence the recommendations that the surgeon gives to the patient as to whether they need treatment or can do active surveillance. You know, it is a very… You know, this…, this whole, you know, situation men find themselves in when they are at this point of trying to decide what treatment options to undergo or to do active surveillance, it…, it…, you know, I…, I feel really…, I feel really bad for a lot of these guys because it…, you know, its…, its a very difficult decision to make. It has a lot of outcomes as far as their quality of life goes and then, you know, they…, they are looking at the whole issue of mortality.

Dr. David Lee – You know, is this something that’s going to kill me or not and so, you know, to choose to do active surveillance when you hear the diagnosis of cancer, its a…, its a daunting task, but, you know, I think if somebody can take the time to look at what the data means, I think the genetic tests actually do provide some really good information because, you know, looking at these validation studies, the…, the information that you get out of these studies actually has a very separate prognostic value when you compare it to Gleason score and PSA and so, you know, a…, I think a lot of…, a lot of us urologists when we first started looking at these tests, we go, “Oh, how does it compare to PSA, how does it compare to Gleason score?” and so if you see genetic test result that’s discordant from your Gleason score, then you are going to go, “Wow!” You know, this test doesn’t really work because we know that Gleason score is such a powerful predictor, but you know, these tests are actually telling us some separate information and, you know, can help us to really figure out these guys with Gleason 6 disease who look otherwise very low risk but may actually be one of these guys who goes on and does poorly. So, you know, I…, I think that’s another important point for men is that you do have to take your time and figure out, you know, what…, what the data means, what kind of tests are out there and available because prostate cancer has really changed in treatment and diagnosis and…, and testing.

Mike Scott – And…, and being based in Philadelphia, I assume you…, you see African-American patients on a fairly regular basis. Is there any distinction in the use of these tests in that population given that they do seem to be at higher risk to begin with?

Dr. David Lee – Yeah, no, that…, that's another area that hasn't been well studied. I think its a very important area for us to look at because they think most of us who treat men with prostate cancer, if you just take an African-American guy who has this…, exactly the same numbers as somebody who is Asian or Caucasian or Hispanic, the African-American guy seems to do worse, you know, even with the same Gleason score, same PSA, and so, you know, there…, there's got to be something else going on and, you know, its quite possible that one of these genetic tests can help us to pick out those guys little bit more precisely.

Mike Scott – So, if its okay with you, I…, I would like to offer the…, the panelists a chance to offer…, to ask you some questions and…, and being a gentleman, I am going to ask the lady first. So, Merel, do you have couple of questions for Dr. Lee?

Merel Gray – The patient… I hear a lot of patients telling me that…. I am sorry?

Dr. David Lee – I am sorry. Yeah. No, I…, I think I missed the first couple…

Merel Gray – Oh, okay.

Dr. David Lee – …words. Yeah, but I can…

Merel Gray – Its not a question. Its not a question per se, but its a concern. I hear patients telling me that they haven't had a biopsy, but they have got a confirmed diagnosis of prostate cancer and I take issue with that because I think its a tissue-based diagnosis and while the multiparametric MRI may be really helpful in deciding where to biopsy, I don't think its appropriate to tell a patient he has prostate caner based on simply the multiparametric MRI.

Dr. David Lee – Yeah. I…, I couldn't agree with you more. You know, it is…, its so important for us to know what somebody's Gleason score is. Even if somebody has a PSA… I am actually seeing a patient right now in my clinic who…, his PSA is 150. His MRI shows invasion of a tumor into the seminal vesicles. He has enlarged lymph nodes on MRI and, you know, we still absolutely need to have the tissue diagnosis to go ahead and, you know, start…, start the appropriate treatment and so, you know, I would never advise anybody to do anything until we have a prostate biopsy which shows what's really going on.

Merel Gray – Great! Thank you.

Dr. David Lee – So, I think that's a great point. Yeah. Thank you.

Mike Scott – Merel, do you have any other question?

Merel Gray – Nope. That's it for now.

Mike Scott – Okey, dokey. Paul, what about you?

Paul Carpenter – There is an issue. Thank you very much for being available to us, Dr. Lee. There is one question that comes up, a…, a type of question in support groups quite a lot and I think as a physician, you must face something similar and that is, how to communicate effectively with a patient who may be unable to grasp new answers of probability. They just want a black and white answer and when the actual answer is well, there is an 86% chance, they…, they will continue on active surveillance or live on into your 90s, but doesn't understand what that means. Any suggestions?

Dr. David Lee – You know, its a very… Its a tough situation. I…, I look at my role as an educator. I think its so important to spend the time that it takes to really help somebody to figure out what all of this information means, but, yeah, you know, not everybody has the same experience level with looking at these types of things and so its…, you know, it can be a challenge, but, you know, I think its…, it can be as simple as, you

know, trying to explain, you know, what somebody's batting average is in baseball.. That can be a nice kind of understandable type of corollary that can help some guys to see what these percentages mean, but, yeah, you know, I think there are a lot of guys who will really take the time to figure out, but then there are other guys who…, you know, they are just too nervous about it and so, you know, I think it is the role of the physician to give the best advice that you can, you know, if…, if…, if knowing what I know, I can help somebody to figure that out even though they don't best understand it is that's the way that I would treat my brother or myself or my dad, when I feel like that should be the best way to go, then, you know, I think that…., that behoves everybody to advise patients who have a difficult time figuring things out on their own.

Paul Carpenter – Well, I understand. Do you mind if I ask a followup question?

Dr. David Lee – No, no, no. Yeah, please do, yeah.

Paul Carpenter – I was a little surprised when you said that 90% of Gleason 6 patients will have no problem, but the 10%, well, and I had thought the figures were closer to 98% and 2% which makes quite a difference, I would think. Would you be able to comment on that or if maybe I have got my fact wrong?

Dr. David Lee – Yeah. No, I think its… I think its…, you know, Gleason score is very important, but, you know, I think it depends on what kind of time frame that you are looking at. You know, I think the 98% is very applicable for the five-year time frame, but, you know, its…, and that…, that's probably a more accurate number than the 90%, but the 90% I…, I use very often to just help patients to realize that they have a really high percentage chance, but, you know, I think sometimes that, you know, if you…, if you paint an over rosy picture, it can be difficult for patients to appreciate that, yeah, it may…, you may not have a good outcome.

Paul Carpenter – Right.

Dr. David Lee – So… Yeah. Its…, its a…. So, for those patients who do have a bad outcome, you know, its a 100% for them and so, you know, that…, that really kind of clouds everything. It makes it really difficult for those patients to understand sometimes.

Mike Scott – So, I mean we…, we are… I think, so for clarification that the audience talking was about the risk of upgrading between biopsy and actual surgical procedure if surgery is what is carried out and also quite separately the risk that a Gleason 6 cancer will progress to Gleason 7 over time. Is that correct, Dr. Lee?

Dr. David Lee – Yeah and then another… You know, I think another point that I could make to address your question was that, you know, the guys who we do the operation for, who have a Gleason 6 on their initial biopsy, when we get their final pathology reports, they will end up with a Gleason 7 afterwards, you know, a good 35% of the time. So, you know, I…, I think I am framing my reference point more to that biopsy outcome rather than the final pathology report outcome because when I…, when I talk to patients about their final pathology reports, if they have a Gleason 6 on their final pathology report, then… Yeah, then I'll tell them its at…, they are at 95% to 98% chance of being graded 10 years, but, you know, with such a significant upgrading percentage that we see for guys with Gleason 6, you know, I think that changes your overall percentage of guys who walk in your door with a biopsy report that shows Gleason 6.

Paul Carpenter – I absolutely understand. I entered the surgery with a Gleason 7 and the pathology report said Gleason 9, which was something of a shock for me.

Dr. David Lee – Yeah.

Paul Carpenter – Right. Yeah and recently…, definitely have had our share of those guys too. So, its…, its really….

Dr. David Lee – Yeah.

Paul Carpenter – Thank you.

Mike Scott – So…

Dr. David Lee – No, thank you.

Mike Scott – Thank you, Paul. Tony, do you have a couple of questions?

Tony Crispino – Yes, I do. Again, echoing Paul's comment, thank you, Dr. Lee, for coming on the show. My questions are going to run into a little bit more about genetic biomarkers that we have, the exciting, new genetic biomarkers that we have. We have seen them use and a great deal of access prior to an active therapy to make a determination that patient is maybe good candidate for active surveillance or more likely for aggressive and then also to back them around after the prostatectomy. They are in the post prostatectomy. Do you use these tests on the sample tissue and would you use that information if you do?

Dr. David Lee – Right. No. Then, thanks for asking that question. You know, I didn't… In my little opening remark, I didn't get to talk about the post prostatectomy setting and we do for, you know, all the high-risk guys, get them a genetic test afterwards and your two options in that arena right now are the Prolaris test which we talked about for the…, the biopsy situation, but then also the Decipher score and so the Decipher score I think is…, its a very interesting test. The company uses a…, a chip which actually tests for 1.4 million different gene products, but they found 22 in particular which can help stratify the guys into different, you know, chances for having metastatic disease in the long run. So, we order one or the other test for all the high-risk guys and a good number of the intermediate-risk guys when we see that on their final pathology reports and so we…, we use that information quite a bit to help guide the patients to decide whether they want to do active…, actively follow their PSA or do adjuvant radiation or do salvage radiation, you know, by continuing to monitor their PSA and see how that progresses over time.

Tony Crispino – Doc, on the…., on the genetics again here, its an exciting new field that we are finding over at SWOG where we are taking the outcomes of some of the large trials that SWOG has been able to do such as the SELECT trial, the PCPT trial, going back on over and reviewing backwards and reflecting on the outcomes and perhaps hopefully identify hypothesis for specific genes for specific patients. I…, I… Do you guys participate in that type of activity as well. I mean, I know we do on the…, on the…, on the reflection side here, but perhaps prospectively what you guys are doing.

Dr. David Lee –Yeah. So, we're…, we're keeping… So, I…, I have a database of our, you know, 4,500 guys that I have performed robot prostatectomy for and we are following all of these guys who have had the genetic testing where we have an active tumor tissue banking program as well which we could potentially get information out of and so we are trying to prospectively collect this data.

Tony Crispino – Okay. Thank you very much.

Dr. David Lee – Happy to help you.

Mike Scott – I am… I am curious you…, you mentioned the use of either adjuvant or salvage radiation in high-risk patients. The general perception seems to be that we are starting to see a great deal less adjuvant therapy and a great deal more very early salvage therapy and people being monitored with ultrasensitive PSAs. Does the Decipher test help you to tell who really does need the immediate adjuvant radiation?

Dr. David Lee – Yeah. Yeah. So, now, this is…. I think this is one of the most interesting studies that has come out regarding the genetic tests recently. The Decipher test was looked at for a group of patients from the Mayo Clinic and at Jefferson who underwent prostatectomy and then either underwent adjuvant or salvage radiation because they had high-risk features, and the Decipher score is actually able to show that guys who had very high-risk features did better when they got adjuvant radiation versus early salvage radiation. So… Yeah, so, its…, its interesting information. I think it needs to be validated on a bigger scale

because I think it was still only about less than a 100 patients in the study, but I think this is a potential…, potential aid to help guys to figure out whether, you know, they should undergo that adjuvant radiation.

Mike Scott – And the…, the other thing that interests me is we…, we are starting with the…, with the coming of…, of the 11 choline-PET/CT scans and…, and some other forms of imaging that are becoming available. We are starting to see the possibility of being able to look at patients pre-treatment to decide whether, you know, surgery is even a good idea at all, if nothing should be done in combination with hormone therapy or whatever for men who might have small…, very small amounts of…, of cancer that have already reached the lymph nodes or even other areas in the pelvis. Do you have any….

Dr. David Lee – Right.

Mike Scott – …experience yet with using some of these new tests in…, in scenarios like that?

Dr. David Lee – And so we…, so at PENN we have started using the sodium chloride PET scans on a.., on a limited basis. I think the…, you know, the pictures that we obtain are really…, they are really beautiful, but as to actually altering treatment decisions so far, we haven't really…., we haven't really come to that point yet. You know, one of the things that we are seeing recently, I think its because of the decrease in screening that's gone on over the past few years, is that we are starting to see more guys with high-risk disease pop up and so I think there is an increased interest for these guys with high-risk disease, though its a go ahead and get radical prostatectomy even in the face of low-volume oligometastatic disease or, you know, some enlarged lymph nodes which may be suspicious for metastatic disease, but, you know, with extended lymph node dissections, we can potentially remove those lymph nodes. There have been some small case reports which show that men do very well for many years even in the face of high-risk disease in this setting. So, I think the indications for surgery may be slightly expanding with this increase in high-risk patients that we are seeing.

Mike Scott – And…, and I suspect that…, that I am not the only panelist who has seen at least a couple of papers on new forms of…, of technique that will actually allow highlighting of cancer…., of cancerous areas, one might call it glowing in the dark…

Dr. David Lee – Right.

Mike Scott – …is a method to actually improve the quality of surgery. Are you familiar with any of those techniques?

Dr. David Lee – Yeah. So, you know, we…, we use a similar type of technique for kidney tumors with fluorescent. So, its called ICG. You can inject that into patients during your robotic partial nephrectomy and then with the aid of the laser fluorescence technology that's built into the robot, typically the kidney tumors will be slightly less vascular, so then you can actually see as he reports the tumor, whether you are getting too close. With prostate cancer, its…, you know, I think the benefit…., potential benefit would be if you could give somebody some type of immunofluorescence which would actually tag on to PSMA that's expressed on the surface of prostate cancer cells, inject that preoperatively and then allow that to, you know, go through the body and potentially latch on to lymph nodes that have small-volume prostate cancer and then using a similar type of laser fluorescence and actually visualize where these small tumor deposits are. I think we are still…, still ways away from that. I think there are actually other organ systems like kidney where this is actually being used clinically, but for prostate you need to have a definable target that's very reliable. We are still not there yet unfortunately, but yeah, the technology is getting there.

Mike Scott – Okay. Well, I think at this point what we'll do is we will pass the…., the mike back to Priya so to speak and…, and she can see if we can take some of the questions from the audience that's on the phone.

Dr. David Lee – Okay. Great!

Priya Menon – Thank you, Mike. Audience, if you have a question for Dr. Lee, please press 1 on your keypads and let us know and we can bring you on air to ask your question. Dr. Lee, we have got a list of questions being posted on our website as you have been talking. I will just read them off from the website so that maybe there may be some repetitions of what we have already spoken, but I will just read them out.

Dr. David Lee – Sure.

Priya Menon – The first question is Gleason… Yeah. Gleason classification is subjective. Should biopsy tissues be sent to an expert prostate pathologist to confirm Gleason score?

Dr. David Lee – We are fortunate to work at a center where we have expert pathologists. I think that that's an excellent idea. The… The more experienced your pathologist is, I think the better diagnosis you will get. I think academic centers have shown that they have a fewer incidences of upgrading at time of prostatectomy and so this…, this… Its a great idea.

Priya Menon – Thank you, doctor. The next question is, what is the rate of occurrence in these genetic tests, if any, of results indicating lower risk in the case of higher Gleason score.

Dr. David Lee – Yeah. So, that's an interesting point. You know, we have been typically reserving active surveillance for guys with Gleason 6 disease and low-volume disease, but I think there are some people who were trying to extend that indication to guys with low volume Gleason 7 disease and so, if…, if you study some of these validation tests looking at the Oncotype DX and the Prolaris test, there actually tends to be more separation between the…, the test scores for the Gleason 7 disease patients rather than the Gleason 6 disease patients and so some of these guys with Gleason 7, according to the genetic tests, are going to be, you know, as indolent as some of the Gleason 6 prostate cancers and so the relative percentage is small, but yet the test does seem to pick these gentlemen out. So, for somebody who is really considering active surveillance, they have low volume intermediate risk disease, a genetic test may be worthwhile to see if they could potentially be an active surveillance candidate.

Priya Menon – Thank you, doctor. The next one is, do those of us with artificial hip joint not qualify for the…, for the MRI scans due to the metal in the artificial hip implant, doesn't the metal scatter the MRI signal and ruin the results?

Dr. David Lee – Right. We…, we still order the MRI for patients with hip replacements. Yeah, the picture doesn't come out as…, as clearly, not as well defined, but I think we still get a really good study for most of the patients. We can get some valuable information.

Priya Menon – Yeah. The next one is that the recurrent prostate cancer, how frequently should full body bone scans be done when no mets are found? Annually, twice per year, or some other?

Dr. David Lee – So, in the situation where after treatment after surgery, we just follow the PSAs and if somebody's PSA is undetectable, then we won't usually do any further imaging. For the gentlemen who are undergoing active surveillance, we'll typically not do any bone scans. I have been ordering MRIs periodically for these guys on top of the PSAs and the regular biopsies that they should undergo, but again no regular bone scan schedule.

Priya Menon – Thank you. Where can one obtain a genomic test? Does Medicare approve it?

Dr. David Lee – So, Medicare does approve the Prolaris test and I think they are very close with the Decipher test. It may be now covered. So, as far as I know, there are no private insurances that cover either of those tests, but Medicare I think is covering both of those. As far as how to obtain one, you…, the patients can ask their physicians to order it for them. The way that it typically runs is the…, the order goes into the company and then the company will contact the laboratory where the prostate biopsy is sitting, the actual slides, and so, you know, depending on whether there is a relationship there already, there may be some lag

time to, you know, set up all the contracting that way, but if there is a…, if there is a contract set up, then, you know, the slides will go out very shortly and then we usually get turnaround in around two or three weeks as far as the test results go and then that test result comes back to the ordering physician and then the physician can review the test results with the patient then.

Priya Menon – Thank you. What is the ideal PSA number that a man should achieve before attempting either C-11 choline or acetate?

Dr. David Lee – Yeah, for…. So, for PET scans, you know, its…, its a continuous spectrum. There will probably be very few gentlemen who have a positive PET scan with a PSA less than 1. It will probably be closer to 5, where you actually see some activity on a PET scan. So, you know, it would probably be, you know, a minimum of 1, but, you know, that…, that I think makes it a little more difficult to use as a decision making tool because, you know, in the situation where somebody has an early recurrence after prostatectomy, then the guys will usually get salvage radiation, you know, well before the PSA hits 1. So…

Priya Menon – Thank you, doctor.

Paul Carpenter – Dr. Lee, I can speak to that… I am sorry, from personal experience.

Priya Menon – Yeah, sure, Paul. Please go ahead.

Paul Carpenter – Okay. Thanks. I underwent C-11 choline imaging, but I was told at the time, this was four years ago, that I needed to have a PSA of 2 or above to qualify.

Dr. David Lee – Right.

Paul Carpenter – So, I really allowed my PSA to rise to that level so that the imaging would be better.

Dr. David Lee – Right.

Paul Carpenter – That changed in the four or five years since I did that.

Dr. David Lee – So, did you have surgery first then.

Paul Carpenter – All this was after the surgery, after radiation.

Dr. David Lee – Yes. Oh, after surgery.

Paul Carpenter – Yeah.

Dr. David Lee – Okay. Yeah. Yeah. So… I think that… I think that would be what most people would recommend. You know, I have seen a study or two where they say that they can see some patients who have a positive PET scan and a PSA of only 1, but I…, I don't think we would typically or hit still in that setting. They would probably be more at a level of closer to 5.

Paul Carpenter – I see.

Dr. David Lee – Yeah.

Paul Carpenter – Thank you.

Dr. David Lee – Yeah. Thank you.

Mike Scott – So, we… we have about another 10 minutes, but do any of the panel have any other questions

they would like to ask Dr. Lee?

Paul Carpenter – Oh, you know me, I always have a lot of questions.

Mike Scott – Oh, go ahead.

Paul Carpenter – Something Tony asked caused me to think of something. How many years after a prostatectomy has been performed can genetic testing be of use? For example, my tissue is from 2007. Could I get a genetic test now?

Dr. David Lee – Its probably just a hair late now.

Paul Carpenter – Yes.

Dr. David Lee – The companies…, right, generally say that up to five years, they could still get very, very reproducible data.

Paul Carpenter – Oh, that's fascinating. Okay. Thank you. I had no idea how sure….

Dr. David Lee – Its…, its…, its really interesting…, interesting technology and I think we are going to, you know, learn to use this better and better over time and so, yeah, and then as people get more comfortable with the idea that these tests are out there, then, you know, everybody will feel more comfortable with it and figure out how to use it appropriately.

Paul Carpenter – I am sure.

Mike Scott – So, Dr. Lee, there…, there…, there are now, you know, several of these studies on the market, several more in development. Do you consent in any way that we have no head-to-head data on the relative quality of these tests?

Dr. David Lee – Right. Yeah. Still as far as these three tests go, that still isn't there yet. You know, I…, I think what is going on is, you know, like the Decipher test is really just focused at the post prostatectomy setting, but now they are starting to build their case to be used as a biopsy decision making tool. Likewise, the Oncotype test now is just for the biopsy setting, but they are working to develop their data to be used in the post prostatectomy setting. So, you know, that…, that's really what people are working on. You know, we are actually ordering a lot of these tests for the high-risk guys, both the Prolaris and the Decipher, and hope we will accrue some data which will give us some idea whether one is better than the other or more predictive than the other, but, you know, the…, the test results are still, you know, they have their own definitions as far as what they are…, what they are predicting. So, its…, its a little bit difficult to compare them one on one.

Mike Scott – Any other questions from the panel? Merel?

Paul Carpenter – Well..

Merel Gray – No. An excellent presentation.

Paul Carpenter – To that…. I am sorry. Go ahead.

Merel Gray – I was going to say an excellent presentation. Thank you so much.

Dr. David Lee – No. No. Thank you for your questions.

Mike Scott – Paul?

Paul Carpenter – I did…, I did have one followup question.

Dr. David Lee – Yeah, please.

Paul Carpenter – Okay. Do the current… Do the tests, current genomic tests currently on the market give an indication as to which drug might be more effective or less effective for those of us with advanced prostate cancer, like we have not yet progressed to extend the thalidomide, it might work, might not. Do we take the chance?

Dr. David Lee – Right. Yeah. No… I think that's…, that's a huge area of future research and then, you know, not only…, not only this, you know, because this whole…, this whole idea that President…., Vice-President Biden now is heading up as far as the moon shot for cancer cure goes…., its…, its going to be, I think a lot of personalized medicine where you really hone in on the genetics of what's going on with a particular patient's cancer and then really tailor the treatment to that patient. You know because cancer formation and proliferation is really such a personalized event, you know, there are…., there are certain genetic pathways which are mutated, but they are probably very different from patient to patient. So, looking at what the specific defect, so to speak is, I think its going to be very important and its really going to help us to figure out, you know, whether a patient may benefit from a certain type of radiation or certain dosage of radiation or, you know, what kind of hormonal therapy that they would work well with or what type of chemotherapy plus or minus hormone therapy that the patients would do best with, so…, and so this whole field for prostate cancer genetics, I think is…, you know its just starting. Its very much behind the times compared to like breast cancer where you know there is really actionable data as far as, you know, what type of therapies to administer to women based on what their genetic profile looks like, but hopefully with these new tests coming out, the…, we are going to make an impact this way.

Paul Carpenter – Understood. So, not yet but soon, we think. Thank you.

Dr. David Lee – Hopefully, yes.

Mike Scott – I think that its time we moved along. We are going to continue to see more uses of the genomics in the…, in the definitions of translational medicine and into drug sequencing. I think that's kind of what you were summarizing right there, Dr. Lee. And I think perhaps there's got to be a starting point some place. I know that its…, its back to those tissue depositories and trying to look at outcomes and see if we can find genetic markers. Let me ask you a question. Do you feel… How long do you think it would take for us to come up with perhaps a nice way to…, to break down a lot of the genetic biomarkers that we see down out there and actually start to see some of these translational medicine hitting the street?.

Dr. David Lee – Oh, it might not take that long. I…, I think that one of the big hurdles these days just is this uncertainty, you know, as to what…, what genes are really important as far as…, as far as targeting goes. You know, some of the immunotherapy agents, you know, have some promise, but then, you know, where…, where do they function, where do they target. You know, as far as the Decipher test goes, its interesting. Some of the genes if they look at, which they found, which are very correlated to poor outcomes in the long run, they are not really even certain how these genes impact the cancer and so, you know, trying to figure out this tangle, so to speak, of cellular function and where things have, you know, gone astray is…, is very perplexing and then, you know, as far as prostate cancer goes, there's such a…, such a preponderance towards low-risk prostate cancer that its hard to figure out then, you know, which of the guys who really need to be treated aggressively, the guys with high risk, you know, what are the specific, you know, genes which, you know, lend more towards less-aggressive disease and more towards the high-risk disease and then to target those things specifically. So, you know, I think its this informational gap that exists.

Mike Scott – So, Dr. Lee, I…, I…, I think we've…, we've reached pretty much the end of the hour and I would really like to thank you on behalf of all on the panel and the audience for your time, if you will. I…, I hope that you have enjoyed speaking with us, and I am going to hand it back to Priya to close up the rest of the program. So, thank you very much for your time.

Dr. David Lee – Great! Thank you. Thank you, everybody.

Paul Carpenter – Thank you.

Merel Gray – Thank you.

Priya Menon – Dr. Lee, thank you very much for that very informative session. Mike, Tony, Paul, and Merel, thank you for your participation. This talk will be made available on CureTalks' website along with its transcript. Please visit curetalks.com for details of upcoming talks. Thank you, everyone.

Mike Scott – Thank you, everyone. Good night!