Chuck Ryan:

Greetings from the headquarters of the Prostate Cancer Foundation in Santa Monica, California. I'm Chuck Ryan and glad to see you all. We have a very special webinar tonight. We're going to be talking about PSMA PET imaging, doctor and patient perspectives. And this event tonight is generously supported by Lantheus. So PCF has been involved in funding research on the discovery of the prostate-specific membrane antigen and its subsequent use in the clinical setting for both diagnostic use and therapeutic planning. The mission of the Prostate Cancer Foundation is to reduce the death and suffering from prostate cancer and to fund transformational research that accelerates progress towards this goal.

We started funding research on PSMA back in 1994, which was the second year of the Prostate Cancer Foundation's existence. The man shown up in the upper right corner of your screens, Dr. Neil Bander is at Weill Cornell is accredited with the discovery and much of the characterization of this important molecule. We've invested no less than $28 million in research on PSMA biology, molecular imaging, and therapy. And we are now, in 2023 and 2022, beginning to see the use of the importance of this molecule in its use in the day-to-day clinic in the initial staging and treatment of men with localized and even metastatic prostate cancer.

For further information on PCF resources in our community for patients and families, I remind you all to go to pcf.org where you can sign up for updates, download our guides, view past webinars, and register for our upcoming webinar in April, which will cover clinical trials and even join one of our online support group Facebook. We have several thousand members, and you see some of the titles of some of our resources shown below.

It's my pleasure to welcome a friend and colleague, Dr. Phil Koo from the Banner MD Anderson Cancer Center in Arizona. Dr. Koo is the chief of Diagnostic Imaging and a physician executive of oncology. He's a diplomat of the American Board of Radiology and the American Board of Nuclear Medicine. He has an academic interest in PET imaging in prostate cancer and many years of experience, not only interpreting these images, but in developing them as national standards. He's known internationally for his education and lecturing on these topics related to imaging and radiopharmaceutical-based therapies in prostate cancer. And he is the editor of the Imaging Center of Excellence on UroToday. And I encourage you all to visit eurotoday.com where there is also educational material. Much of it is doctor-to-doctor, but we have some other nice pieces of information and a nice interview with Dr. Bander who discovered PSMA that was filmed a few months ago. Dr. Koo was awarded the 2022 Society of Nuclear Medicine and Molecular Imaging Presidential Distinguished Service Award.

Our two guests tonight are Dr. Ike Credle and Dr. Sharron Credle. And Ike Credle is a prostate cancer patient. He's a retired major in the US Army, served in Operation Desert Storm and Desert Shield, and served as a professor of military science, and American military history of Virginia State. He holds a doctorate of education organizational leadership, and he works as a senior training specialist at Fort Belvoir, in Virginia. Dr. Sharron Credle is founder and CEO of the Sharron Credle Corporation, has extensive experience in organizational leadership training and development. We're delighted to have both of them with us tonight to talk about this important area. And for the first time on our webinar, we are joined by a patient and a caregiver who can give us their perspective on these advances.

I'm going to now welcome Dr. Koo. Phil, good to see you. Thank you for joining us, and we're going to talk about diagnostic PSMA PET imaging tonight, and you are a nuclear medicine specialist who does this every day. So tell us a couple things. Tell us first of all what you do in nuclear medicine in terms of the scope of the work, and then let's talk about what is a PET scan and what is a PSMA PET scan?

Phillip Koo:

Great. Well first off before I get started, wanted to congratulate you and thank you for the amazing work that PCF does with regards to supporting research discovery and education. And I think this idea of empowering patients with knowledge so that they can make the right decisions for their care is really priceless and just kudos to PCF for really taking the lead with this.

So if I could just level set, maybe what I'll do, is I'll show a few slides just to give the audience a little bit of background on what we're talking about today. So PSMA stands for prostate specific membrane antigen. On the first slide, what we see is this is a protein that sits on the surface of the prostate cell. And in prostate cancer patients what happens is those cells proliferate, they grow, and this small molecule that was developed by Neil Bander can target that protein, and then give off some light that we could capture on a camera.

So if we go to the next slide, we dive in a little deeper and we see the target, which is PSMA. And then what we do is we can create these links, but eventually at the end what you see is the payload. So in this case, if we want it to serve as a flashlight, if we want this to help us see disease, we attach something like a gallium-68 isotope or an F-18, a fluoride isotope, and it helps us visualize the disease. And on the flip side, if we want to treat disease, we put something on it like a lutetium that gives off radiation that actually can kill the disease. We see then at that point it can serve as a missile. But today we're really just focusing on prostate specific membrane antigen as a flashlight. How do we detect disease better?

Chuck Ryan:

And Phil, just let me stop you, ask you a couple questions here just for those listening. This is different from PSA number one, and number two is it is not something that we can detect in a blood test necessarily. Correct?

Phillip Koo:

Correct. We have to target it and exactly. It's not in the blood test and it's very different from PSA.

Chuck Ryan:

So this is really something that exists almost solely on the surface of a prostate cancer cell.

Phillip Koo:

Correct. It does exist in some other areas, but for our discussions today, pretty much just on the prostate cells.

Chuck Ryan:

Great.

Phillip Koo:

And when we're talking about PSMA PET, we're really talking about two pieces to the process. We're talking about PET CT, which is the camera, and we're talking about what we're injecting into your body. So the metaphor or their analogy I like to use is like a smartphone. So your smartphone, your iPhone is the hardware and the applications you run on your smartphone are what allows you to do certain functions. So the analogy back to PET is, PET is the hardware, and what we inject into your veins is what really changes the output.

So if you get a PSMA ordered, you're going to go to the center, the technology usually is going to get access, an IV access, intravenous access. They're going to inject the PSMA radiopharmaceutical, which is in very, very small amounts. So this idea of having an allergic reaction to what's injected is pretty much unheard of. And then once it is injected into your system, it circulates, and it starts accumulating in those sites where there are prostate cells. And that helps us detect disease. And then after maybe an hour or so, you go and you lay on the camera, and it captures some of that light that's being admitted from that isotope. And then that helps us create that picture, which tells us where exactly in the body your prostate cancer is living.

Chuck Ryan:

Now, for those not familiar with PET scans, you might want to give a little primer on what is a PET scan in general, because there are other types that don't detect PSMA. And I think it's important that when people go and they talk to their doctors about this, that they know that this is different from an FTG PET or others that people get with other cancers or in other settings.

Phillip Koo:

Absolutely. So when we talk about imaging technologies, you hear a lot about CT, MRI, ultrasound, all different types of hardware that can image the body. When we talk about PET, we're really talking about... It stands for positron emission tomography. Again, you could inject multiple different radiopharmaceuticals into your system, and that's going to tell us things about what's going on in your body. So the most common one is something called FTG. It's a glucose analog that helped us understand cancer better. In this case, it is prostate-specific membrane antigen, which again is going to circulate your body and be much, much more specific for prostate cancer in your body.

Chuck Ryan:

And how much radiation are we talking about here? And are people safe after they get the scan? Or what kinds of precautions do people need to take when they get these scans?

Phillip Koo:

You're absolutely safe after you get the exam to go home and go about your normal activities. We do give general recommendations to patients just to stay hydrated, drink lots of water and flush it out of your body over the next day or so. It does expose your body to radiation, and it's something that's important that we have to be aware of. So this is a study that we don't always want to get in patients all the time, but clearly in certain instances, the benefits far outweigh any of those risks.

Chuck Ryan:

So you're a nuclear medicines physician, and tell us a little bit about the scope of your work and how this has impacted what you do. And then we'll talk about specific instances in which this test is indicated.

Phillip Koo:

So I'm a nuclear medicine physician, also a radiologist. Our job and our training has really been focused on making sure we diagnose disease in patients the best way we can. And a lot of that has to do with what types of tests we're doing, how we conduct the tests. And then oftentimes, most importantly it is how we interpret the images that we see. So the images that are generated from this PSMA PET are put into a series, and we can scroll through the body, and look at all the different parts of your body, look at

how it's distributed throughout your body, localize those area where it's accumulating, and then provide the medical oncologist like yourself or the surgeon or whoever it might be with our impression, our interpretation of what we're seeing in the images.

Is the disease just in the prostate gland, has it spread outside of the prostate gland? And if it has, is it in lymph nodes? Is it in the bones? Is it in your lungs? Is it in any part of your body? And then help guide and provide that information to the medical oncologist or surgeon so that they could then make the best decisions on how to treat you next.

Chuck Ryan:

So hugely important advances in how we image the disease. We'll talk to the talk about that, but tell us right now there are a few different types of these scans, a few different companies that make them, and they have an FDA approval for certain uses. Tell us on label right now when one can get a PSMA PET scan, and who is the appropriate patient to be getting one.

Phillip Koo:

So if someone gets diagnosed with prostate cancer, it's obviously very terrifying. This is not meant for every single person who's diagnosed with prostate cancer. If you get the diagnosis of prostate cancer, and before you might get surgery or definitive radiation, your physician might recommend this if you have what we call unfavorable intermediate, high-risk or very high-risk disease. And again, there's various criteria that's used to determine that, but before you undergo one of these types of definitive procedures, it could be indicated to get this test before we make that decision.

And then the second space where it is indicated is if you have... Your PSA, usually after treatment will go down. If the your PSA levels start coming up after definitive therapy, again, radiation or a surgery, then that's another indication to get this test so that it could tell all of the physicians that are working with you, where is that prostate cancer coming back from? Is it just in your prostate bed? Is it in your pelvis, or has it spread far out throughout your body? And obviously that's going to help all of us make the best decision on how to treat you next.

Chuck Ryan:

Excellent. And so it's really at the time of diagnosis for intermediate or high-risk disease to help plan the initial therapy. And then in relapse management, and I'm a medical oncologist. My most common source of referral is a patient who had a prostatectomy for example, or had radiation therapy. Now, their PSA is rising, what we call serologic relapse or rising PSA. This stage of the disease has many indications. When should we get a PSMA PET? I think a lot of patients are out there wondering, "My PSA is 0.01, or 0.9, or 1.5, which at what point does the PSMA PET actually become useful in that setting?"

Phillip Koo:

That's a very tricky question, and it's a question that's being actively discussed in a lot of our scientific societies today. In my opinion, I think as soon as your physician who's managing you labels you as biochemically recurrent, I think we need to start having that discussion of should we get the PSMA PET? And if we get it, is the team that's treating you ready to take action based on its results? So if it's negative, are they going to consider salvage therapies, or if it's positive, would they consider chasing some of the meds with what we call meds-directed therapy?

So I think it really requires a thoughtful approach. I don't want to necessarily give a definite cutoff on the PSA level because I think it can vary, and it really depends on how aggressive, and how the team wants

to treat you. But in my opinion, as soon as you are biochemically recurrent, I personally would want one, and then I'd like that to help the team make the decisions on how to go next.

Chuck Ryan:

So do you have some pictures you can show us?

Phillip Koo:

I do. I think what we're learning, and we're still learning because this is a new technology and every day... And what's great is we share this knowledge globally. And some of these cases come from the literature where a lot of wonderful physicians have taken the time to publish these and share some of this, share this knowledge with the world.

So in this patient, what you see is A and B, they show a typical bone scan, which is what we call conventional imaging. And what you see on that is you see some areas of activity that look abnormal, and what we would most likely classify as metastatic disease. But what we're learning is that oftentimes bone scans are not the true representation of how much metastatic disease you have in your body. So if you go to column C, what you see is a PSMA PET. And I don't think it takes a microscope or magnifying glass for anyone in the audience to know that you see a lot of areas that have that PSMA activity, that shows that this disease has spread much greater than what we had thought when we used our traditional technologies. And again-

Chuck Ryan:

These look pretty scary. Is this a common scenario for those out there who just had a normal bone scan? Is this something they should be worried about?

Phillip Koo:

I agree. I wouldn't say it's common. That being said, it does happen relatively frequently where we get surprised by something like this. So this is something you have to be prepared for. So this-

Chuck Ryan:

And just to be clear, in the current era when a doctor refers a patient to have a PSMA PET scan, do you get a bone scan as well?

Phillip Koo:

So the great news is it is not required. In fact, it's not recommended that you get that bone scan CT before PSMA PET.

Chuck Ryan:

Should we be doing bone scans anymore?

Phillip Koo:

I do think for the time being and for the near future, it does have a role, but it's evolving, and it's changing, and I think the utility will decrease over time.

Chuck Ryan:

Right. So I think that's a sense that's happening in the field, but I know a lot of people are asking that question. Just before we leave this slide, do you want to point out the pink arrows? Are they something we should know? And what are some of the other things on here that we see that are not cancer?

Phillip Koo:

So the pink arrows just show areas of disease. What you also see is you see normal organs that have activity. So earlier we talked about some other areas that might have uptake with PSMA, and you're clearly seeing that a little bit in the liver, a little bit in the spleen, more intense in the kidneys, some in the glands up here by your cheeks and under your jaw. So there are areas that have normal activity that the radiologist or nuclear medicine physician need to be aware of.

Chuck Ryan:

Yeah, I don't know if you're able to point those out. You mentioned the spleen in the liver, but it's just something where if folks are not as proficient in anatomy, they might want to know because the two kidneys stand out as the darkest spots. So those are the liver right there. The two kidneys, there's the spleen, and the two kidneys are where the tracer is ending up after it circulates in the blood. It is being filtered out into the kidneys and then down into the bladder.

Phillip Koo:

Absolutely.

Chuck Ryan:

And then when I show patients their scans, I say, "The first thing you need to train your mind when you look at scans is eliminate the intestines because that's just a lot of artifact." And so you can see in this case below the kidneys there, there's what looks like a lot of intestine artifact that I think you and I are pretty adept at a erasing, but that's not cancer in there for the most part, right?

Phillip Koo:

Yes, absolutely. And I think one of the messages you see from this is most of the diseases in the bones, and that could obviously inform the medical oncologist that maybe some bone-targeted therapies might be more appropriate in this patient.

Chuck Ryan:

And then finally, the salivary glands worth pointing out here.

Phillip Koo:

Absolutely. It's the cheeks and the stuff right underneath.

Chuck Ryan:

So those are not tumors. Those are the salivary glands just showing up. Great.

Phillip Koo:

So this is a good example of how conventional imaging underestimates disease, and then PSMA shows that you have more disease than what we had suspected. So if we go to the next case, it shows the

opposite, which is just as important. So on the next slide, we're going to show a case of a patient who had a bone scan performed, showed some areas of activity, which the radiologist might have interpreted as might be metastatic disease, suspicious for metastatic disease. And they went on to get a PSMA PET CT, which shows that area of activity in one of the ribs on the right that has low-level activity. And what we've learned through practice now is that single rib lesions typically are benign. So this patient went from potentially having metastatic disease that was said in the report on a bone scan to now having non-metastatic disease. And obviously, that downgrading of that patient is going to have a very big impact on how the patient is managed next.

Chuck Ryan:

And in teaching and in training people over the years, I've always said never give a patient a diagnosis of metastatic prostate cancer based solely on a rib metastasis. And this demonstrates why. And by the time you get into your 50s, 60s, or 70s, you may have had some rib trauma, that can lead to some bone remodeling, that can lead to some false positivity on the scan. So great. So those are your two pictures. And so just tell us a little bit more about if somebody has a rising PSA as we talked about after surgery, you do a PSMA PET and it's negative. How do you follow them? What's the next step? Do you continue to wait for it to rise? Do you do them every three months? What's the standard?

Phillip Koo:

This is an area that's being actively discussed as well. Again, because we're learning. And in my opinion, I think we should consider early salvage therapies. There's a paper that was just published I think a week ago in the Journal of Clinical Oncology that talks about salvage therapies after prostatectomy with a PSA less than 0.25, actually has a decreased risk of dying later on. So that to me says, "If it's negative, the disease is probably in the prostate bed. Maybe we should look at salvage options there." But I'd love to hear your opinion on this, as a medical oncologist.

Chuck Ryan:

This is tricky because what can happen is you can do the PSMA PET scan. Of course, if you have a negative scan entirely, that's reassuring for the patient, for reasons that are obvious. And as you point out, one can conclude if they've recently had, or even not recently, if they've had a radical prostatectomy, there's a reasonable likelihood that the remaining disease is in the bed of the prostate, and they can be cured with radiation therapy. So this brings up the subsequent dilemma, which is I see a lot of people who have already had radiation therapy of the prostate bed, their PSA is rising, and you either see a positive...

You see one of three things. You either see a positive PSMA PET scan indicating that the cancer is spread to the lymph nodes or to the bones or somewhere like that, or you see a negative PSMA PET scan, in which case you have a long conversation with the patient and you have to say, well... What I tell them is that there's not enough cancer to form tumors yet, but that doesn't mean that there's no cancer in the body. And I sometimes refer to it as a liquid phase of the cancer.

But then the other thing that we see, which is tricky, is people who've had a prostatectomy, they've had radiation to the prostate bed, now they have a single area of positivity on the PSMA PET in the radiated field. And in general, that's a situation where we have a difficult time doing any focal therapy or local therapy. We generally don't do radiation again to the same part of the body because of toxicity reasons. And so it creates somewhat of a dilemma. So sometimes we get these scans and we conclude that we're just going to watch, and we'll repeat the scans down the road. I don't think there's really a standard in terms of the interval that one should get one. I would say that it depends on how quickly the PSA is

going up. But yeah, so that's something where we very frequently are doing these scans and left scratching our heads as to what to do.

But I'm from the school of thought that more knowledge is always better, and knowing that a scan is negative is sometimes very useful. In many cases, when I'm talking with patients, I'll cite them a really interesting piece of data that came out of Johns Hopkins many years ago where through a whole series of complicated a math problems, they determined that it takes something like 1.7 billion cells to create a tumor that one can see. And so when a scan is negative, what that means is you could have 1 billion cancer cells circulating in the body, and they haven't yet formed a tumor, and so are not showing up on the scans.

I use this sometimes to talk about the other angle on therapy, which is systemic therapy, and in many cases that's required. So in many cases, we're looking at these scans trying to make a decision about whether we should do focal therapy like radiation, and we can even do focal therapy to metastatic lesions of course, or should we do systemic therapy like hormone therapy? Or should we do a combination of the two? And just in the final question on that front, when are these situations where you could see a PSMA PET leading to a focal, a metastasis-directed therapy where you send them to a radiation oncology colleague or even sometimes a surgeon to remove what tumors are there, and what are the outcomes we expect?

Phillip Koo:

So that's the beauty is there's this really hot topic called oligometastatic disease. And I think what a lot of us hope and believe, and there's data that shows, that if we can actually treat some of these patients with this transitional state of disease, maybe we can cure them. So patients, if the PSMA shows a smaller number of metastases in the pelvis or just throughout the body, maybe there's an opportunity for us to use radiation to zap those, potentially cure or potentially delay the progression of disease. And there's other benefits too. Some studies in Europe have showed maybe we could delay the start of ADT. We know androgen deprivation therapy is not something that's pleasant, and if we could delay the initiation of that, that's a very important quality of life endpoint for patients as well. So better imaging has helped us really think about pursuing these roads that we couldn't travel down before.

Chuck Ryan:

This disease really exists on a spectrum. So if I'm looking at a patient who had, let's say surgery five, 10 years ago, and now I do a PSMA PET and I see one spot on the bone or something like that, I'm thinking this person has a slow growing form of the disease. I'm more likely to think I can probably do radiation to that spot and save that patient maybe ever needing hormonal therapy, or I can delay that from happening. By contrast, if a patient had a negative PSMA PET six months ago, and now it's positive on multiple fronts, and the PSA is going up quickly, I'm thinking more systemically here. I'm thinking that this is something where radiation to all these spots may just be too much and not curative.

So clinical judgment comes in here, lots of experience comes in here. But I think Dr. Koo's point is a really important one, which is we are now beginning to change our frame of reference on how we think about metastatic disease, metastatic prostate cancer. It used to be if you had cancer that spread outside of the prostate, you were getting hormone therapy for the rest of your life, and we didn't talk about curing you, and we didn't talk about eliminating prostate cancer as a cause of death. Well, now, I think we can have that conversation. We're still doing a lot of research. We're still seeing a lot of publications on this topic, but it's really changing how we look at this disease. Final question in the last minute before we go on, where is this available? Does insurance cover it? How hard is it to get one? Tell us a little bit about that.

Phillip Koo:

Sure. At this point, it should be available almost all throughout the country. Maybe if there's a PET CT scanner in your area, they should be able to get delivery of the radiopharmaceutical PSMA that they would inject into your veins. Insurance is always tricky. I think clearly all of the national and international guidelines have recommended this, and the FDA has approved this in these two spaces at initial diagnosis and biochemical recurrence. And Medicare reimburses this as well. So we fully expect all the private insurers to pay for this as well. That being said, they might put up a little bit of a fight, and that's where I think together with patient advocacy groups, with physicians, patients, and whatnot, we could hopefully, make this a little bit more easy to get across the board.

Chuck Ryan:

Agree, and I would say we're still in the early days of this, and we're still doing bone scans a lot and trying to sort out the exact place for this to be placed in the spectrum of the disease to be done, but it certainly changed my perspective on this disease. So as we think about new perspectives on prostate cancer and being a prostate cancer doctor, let's talk about being a prostate cancer patient, the more important perspective.