How PSMA PET Can Help Guide Your Care

Phillip Koo, MD [00:00:00] So thank you all for joining. The topic of PSMA PET is not new to all of us. In fact, of the 90% of the people who are on this call tonight, I'm sure many of you have received a PSMA PET. But I think it's really, really great that people continue to sign into these types of presentations, because we keep learning a lot more about this, and I think a lot of this is something that is still relatively new in the prostate cancer community. And to discuss this, we have two experts, Drs. Chu and Tagawa to talk about this.
Before we get into the detail, we're just going to do a little bit of level setting and explain what PSMA PET is and how that PET-CT technology works. And just for those of you out there, I'm actually a nuclear radiologist by background, so this is sort of the bread and butter of what I do with regards to my clinical practice. Becky will bring up those slides. So, you hear this all the time, PSMA stands for prostate-specific membrane antigen, and in prostate cancer cells, there's greater expression of this PSMA protein on the cell surface that can be targeted. This is very different from PSA, which is prostate- specific antigen. So, PSA and PSMA are very different. So, the way in which it's targeted is that there are these small molecules, we can go to the next slide, that have been developed that attach to the PSMA protein. And then at the end of it, you could attach either a beta part- a beta emitter, which sort of lights it up. It's like a flashlight which tells the camera, hey, I'm here, this is where the prostate cancer cells are.
And then you could switch it and put like a beta emitter or an alpha emitter which is more like a missile where it could actually start killing those cells. So, one is about seeing, and one is about destroying the cell. There's a lot of flexibility there and that's why this area of theranostics or whatnot is so exciting because you could see something and treat it as well. We'll go to the next slide.
So PET, there was a question in the chat about PET/PET-CT. So, this is a PET-CT scanner. There's a PET machine and a CT scanner next to each other. And it's able to image the radiotracer and do a CT scan. So, in many ways, this is the CT plus. So, it's, I mean, I guess I'm biased, but I think it's much better than just the CT. So, the analogy I'd like to make is, It's kind of like your smartphone and the apps. So, the hardware, so your iPhone, is similar to the PET-CT machine. And then what you're running, the apps that you're running are similar to the radiopharmaceuticals that you are injecting into the patient. And based on what you are injecting, you're imaging different processes. In this case, we're gonna be talking about PSMA. So, we'll go to the next slide.

We're just going to do quick examples. This is a good example of how you do see some metastatic disease on this traditional bone scan, so marked A and B. But you get a PSMA PET, and you see many more sites of disease that light up than what you had seen on the traditional bone scan. And I will speak on behalf of Drs. Chu and Tagawa that they've seen cases like this in their practice. We'll go to the next slide.

And this is just an example of how everything that lights up isn't always prostate cancer. That was another question that was in the chat. Some non-cancerous things can light up. And these foci of activity that show up in the ribs are one of those problematic areas. But I will say that where we were when this was first introduced versus where we are today is very different. And now many more physicians are comfortable seeing findings like this. And sort of ignoring it as it being benign and not necessarily metastatic disease. And this is one of those examples of that learning curve and experience that has really helped all of us with this new technology.

All right, so now we're going to get into some questions and learn more about how this is used. So, we're gonna start off with Dr. Chu. And can you tell all of us when you would order a PSMA PET?

Carissa Chu, MD [00:04:20] Thank you so much for having me. So as a urologist, I see patients sort of as they're working through their initial diagnosis of prostate cancer. A lot of my patients are actually men who come in with an elevated PSA, undergo a workup, a biopsy. And so, I get to be the person kind of across the desk from them to tell them about their disease, what the risk stratification is. And a part of that workup, a part of that staging can include a PSMA PET scan. And so, these are men now who are prostate-intact, who hopefully have a diagnosis of early prostate cancer. And so, based off of important clinical features such as how high is your PSA? What does the tumor look like on your MRI? Is it close to the capsule? Is it growing past it? Is it invading the seminal vesicle? That's the tumor stage or the T stage. What's the T stage? What's the Gleason score? So, when the pathologists look at the cancer under the microscope, how aggressive do those cells look? You put all those things together and people kind of fall into these different levels of risk. And so, for men who have higher risk prostate cancer driven by any one of these four features, there's a role for PSMA PET scanning and those patients to understand, are we dealing with disease that's just confined to the prostate or am I worried about potential areas of spread outside? And so, it completes that staging, you know, for someone just initially diagnosed.

Phillip Koo, MD [00:05:55] So let's say a patient comes into your office, what specifically, you know, are there criteria that they would meet that you say, hey, you should get a PSMA PET, and perhaps others where you say oh, you don't need to get one.

Carissa Chu, MD [00:06:09] Yeah, so it's really a kind of a composite risk stratification. So certainly, patients who have tumors that look like they're trying to escape the prostate already, T3 disease, so extra capsular extension, seminal vesicle extension, you're already thinking, let's make sure there's not cancer outside of that. So those are patients that I don't even need to really think about necessarily, their Gleason score or their PSA, I'm like we should go ahead and get that PSMA PET scan. For men who have PSAs that are sort of 10 or higher, high PSA densities, you know, you're worried that there could be other areas producing that PSA. And so, you know I'd get a PSMA PET scan for those patients as well. And then you know generally Gleason 8 or higher. And so, yeah, that's sort of diagnostic imaging in the primary setting.

Phillip Koo, MD [00:07:01] You know, there was a question that came up about… could a PSMA PET be used to detect the primary tumor, to detect the prostate, in the prostate itself.

Carissa Chu, MD [00:07:15] Yes, it can. So, anything that expresses PSMA would light up with a PET scan. And that includes tumors within the prostate. And so, it can help localize areas of disease within the prostate itself. So certainly, I would expect to see some signal in the prostate.

Phillip Koo, MD [00:07:36] I imagine though it's not being ordered routinely for that type of indication, is that correct?

Carissa Chu, MD [00:07:42] It's not, it's not because, you know, the test really is about trying to understand how it might change management. So, for higher risk disease, if there's nodes involved or bone or other soft tissue, it changes what you'll do. For lower risk

cancer, where you know the likelihood that there's cancer outside the prostate is extremely low. Those are risk levels where our guidelines don't recommend using PSMA PET and often insurance companies won't cover it for lower risk primary cancer.

Phillip Koo, MD [00:08:19] And then one other question that came in, is there a role for PSMA PET in patients who are on active surveillance?

Carissa Chu, MD [00:08:28] That is a great question and currently actually being studied in a couple of other, you know, a couple different prospective trials. I would say currently standard of care, we don't use PSMA PET for active surveillance because MRI gives you a lot of great soft tissue definition and those are the changes that you're really hoping to see for a small, localized tumor on surveillance. You know that PET scan is a full body scan so actually your cuts of that prostate are….the resolution may not be as high. But what we're interested in understanding is, are there potential areas that are PSMA PET-avid or have some uptake outside of the primary tumor, what are potential implications for focal therapy, for example. So, there are ways to play around with PSMA PET in these low-risk groups that are sort of separate from staging, but under investigation, and so not really approved or used routinely.

Phillip Koo, MD [00:09:26] So let's sort of move forward, Scott. You know, these questions, I'll start with you. So, we've covered the use of PSMA PET in patients who have initial diagnosis. We know, so it's a huge area and Dr. Chu clearly outlined those patients who need to get a PSMA PET. The other sort of big bucket where patients will often get a PSMA PET is if they have a biochemical recurrence. So maybe you could help us and sort of help us define and understand what is biochemical recurrence.

Scott Tagawa, MD, MS [00:10:00] So, biochemical recurrence to me means several factors that kind of need to be checked to get into this box, if you will. So, prior diagnosis, as well as prior treatment, and as a general, I would say that prior treatment is either surgical removal of the prostate, i.e. a prostatectomy, or radiation to the prostate. Whether that is shooting it in or putting something in, seeds or rods, things like that. So, treatment there, generally speaking, it's nearly 100% where after that, either one of those PSA goes down, and then there's a subsequent rise. So, all those boxes I would say need to be hit to fall into this biochemically recurrent population. And that's at a high level the most important information.

We do have some very specific definitions of what a true biochemical recurrence is in terms of the level of PSA following surgery, which is different than the level of PSA following radiation, but this is where PSMA PET is sometimes useful even before we hit those kinds of criteria. So, 0.2 when there's no more prostate, and then however low the PSA went after radiation and/or hormone therapy, we call that nadir, the lowest point plus 2, not 0.2 but 2, is the other true definitions, but, and I saw, I'm gonna cover the initial thing, Phil, that I saw a couple times in the chat or the Q and A.

Sometimes we want to get some information at even lower thresholds. So sometimes after surgery, PSA is undetectable and rises. Sometimes 0.1 is where we might want to intervene. And I agree with Carissa that we want to do tests when it might make a difference, so even though there is a lower likelihood of seeing anything significant with lower PSA values. I have not seen a PSA value where there is zero chance of seeing something on a PET scan, so it's all in kind of perspective. I've seen plenty with PSA that are detectable, but those start with metastatic disease, so don't want to kind of put those together. But we and others have done some of these initial studies where any PSA value

was okay to come into it as long as it was detectable and we've seen as high as 30% we see something when it is 0.06 or 0.05 and above you know up to 0.2.

And then when someone has radiation as the primary treatment, we know that some of the time there can be active cancer below the threshold of 2. For both these situations, there's curative therapy. And whether we're talking about radiation after surgery or surgery or some sort of ablation after radiation, those are generally more successful at lower levels of PSA. It makes sense when there's fewer number of the tumor cells. Answering your question, Phil, there are definitions of biochemical recurrence, which is a certain number after prior treatment, but on monitoring there are times where it might be indicated to get a scan early and we just need to interpret that in the optimal way.

Phillip Koo, MD [00:13:24] So, you know, this brings up a lot of great points and questions. So I think it's really not as simple as oftentimes people think. So, if someone has had surgery, you sort of mentioned [PSA level of] 0.2, maybe even 0.1, or maybe even lower, depending on the scenario. So, oftentimes, Carissa - you can hop in here - you know, our goal here is to cure the patient, even though the PSA is coming up, and that would be ideal, you know. For some reason, there are some leftover cells. Somehow, we could use radiation or whatnot to cure that patient. And you mentioned, Scott, earlier that earlier is better. So, Carissa, from your standpoint, someone who's had surgery, at any point if the PSA starts rising, when do you start thinking about what we call salvage therapies, where you try to zap things so you could cure the patient?

Carissa Chu, MD [00:14:13] It is a really important question, such an important question. And we're operating on higher risk disease. We've shown that because we have more patients on surveillance than ever before. And, you know, we know a certain percentage of these patients will experience a return of their PSA post-surgery, where you expect the PSA to go to zero. So, a quarter to a third of patients with high-risk features will have a PSA recurrence within the first three to five years.

And so, the decision to kind of pull the trigger on next salvage therapy, whether it's radiation to the pelvis, metastasis-directed therapy, etc., is sort of driven by, of course, how they're doing and also any really worrisome features of their primary cancer that was removed, right? So... Um, if that cancer had, you know, a very high Gleason score, you know, 8 or higher, if there was obvious lymph node involvement, if, there is, like I was mentioning before, extraprostatic extension of the tumor, seminal vesicle invasion, or big positive margin, those are patients where you're thinking, okay, there's probably cancer still left in this body. And so, you know, we should be aggressive about treating it if it's what the patient wants and if their urinary and sexual function have recovered adequately after surgery.

And so, I think the PSA doubling time, so how quickly the PSA is coming up and how soon after surgery that PSA goes up, are reasons for me to push towards, you know, having that patient treated sooner rather than later.

Now where the PSMA PET scan falls into that though is interesting because I'm not quite sure we've really defined that space yet well with PSMA PET and so if someone gets a PSMA PET scan at a detectable PSA post-operatively and localizes a metastasis, let's say, in the arm, or in the liver, or somewhere that you don't typically expect inside the pelvis, you want to deliver additional treatment to that area, metastasis-directed therapy. And so, we're changing the way we're doing - not we, but our radiation oncologists, our

medical oncologists, they're changing the way that they think about biochemical recurrence because PSMA PET is being used now in that setting.

Phillip Koo, MD [00:16:43] Great. So, you know, Scott, we just heard the term metastasis-directed therapy. I think there's a lot worth still learning about how you zap these mets that have gotten outside of the prostate. Oftentimes, we hear numbers thrown around where, or if you have more than five mets, you shouldn't get them zapped. If you have less, you should. We hear these terms called oligometastatic disease. Can you just simplify all that for us? We know there's not a simple answer because it's a complicated topic but just break it down for us a little bit.

Scott Tagawa, MD, MS [00:17:16] So, to kind of get a little bit of background and level set, so we've had for decades a very sensitive test in terms of the PSA blood test. And that, as a general rule, even today, remains more sensitive than any imaging. It sounds scary, but 100,000 cells in one area, we're probably not going to detect on almost any test that is there. So, we've had that. In the past, when we saw something, let's say in a bone scan, we saw one place on a bone scan, or on a CT scan. You know, we call that the tip of the iceberg. Especially if, Carissa used the term PSA doubling time, how fast is the PSA going up? Especially when that's going up, we knew it's highly likely that we take it out or radiate, that PSA might go down a little bit, but it's going to come right back up because we're missing stuff.

PSMA PET is way more sensitive. So, there's some pictures that were shown and you all can look up the internet, and you know bone scan shows one thing and a PSMA PET shows five or 10. So we can see much more. But we're not necessarily seeing everything. That's kind of the background. I agree with one of the things that, well, actually most of the thing or maybe everything that Carissa said.

But one thing that she said is, is going to be based on what we think about the cancer risk. And another thing is going to be based upon the patient / family wishes. So, when it is what I would call high risk. So some of the same things that Carissa mentioned, including a PSA high, going up very fast, even if I see only one thing in a very sensitive test like a PSMA PET, I'm thinking that there's more that's out there, and I'm thinking that if a patient wants to be the most aggressive in terms of treatment, we might consider metastasis-directed therapy, some treatment to that area, because that's the biggest area. But they probably need something else to back that up for the other parts of it. So often that would be hormone therapy with radiation, for instance. And, you know, there's interesting factors like the hormone therapy can actually make the radiation work better, but I don't want to get into that so much.

That being said, when someone has more [metastases or areas of cancer], and we don't know the right number, some of you are aware that there's something called NCCN. It's a group of NCI-designated Cancer Centers. And the current definition of oligometastatic is 10. And the three of us all know the chair, we joke, because the chair is a radiation oncologist, so it's now 10. But it's also because of more sensitive imaging, where oligometastatic first starts, oligo meaning few, ….. The idea was that it's enough that we can go in and take it out, or radiate it, or ablate it or something else, with less worry of other things. Because we have more sensitive imaging, that number has gone up, but it is a decision to make. So, some patients have a lot, but their primary goal is not necessary to live longer. It might be to maintain a testosterone level. And we'll have a discussion and maybe going after whatever we see, whether it's one or whether it’s 10, even if there might

be, you know, a detriment in duration of life, but the amount of the better quality of life at least upfront might be better, and we'll have that kind of discussion.

So, there's no exact number, and I don't think there's ever going to be a set number for a patient sitting in front of us in kind of the real world. Because is 5 really different than 4 or is 11 really different than 10? But we'll take a look at the entire picture, what is the pace of the disease, how fast are we seeing things grow or appear, what's the PSA, and then very importantly, let's say equally importantly are the patient's wishes, and you know, our job is to give guidance. When I think the patient's wishes are not in his best interest or the family's interest, I'm going to voice that, but I'm not going to force myself on anyone. I'm just going to say, I really think this, go home and think about it, come back, you know another day to kind of make that decision. Sometimes I'll call for "reinforcements," for family, just to kind make sure that everyone's on board. But we want to put everything into perspective, both the tests that we have, talking about PSMA PET, as well as the treatment options and what the patient's interests are.

Phillip Koo, MD [00:22:00] So, you know, just to summarize, we've talked about initial diagnosis, and as we learned, if there's a suspicion of the disease getting outside the prostate, PSMA PET really helps, and this is for those higher-risk patients who, obviously their disease might be a little more aggressive. And then in biochemical recurrence, this tool can be used early. There's no definite set cutoff on how low [the PSA level], but it really depends on how the physician plans to manage your care based on those results, whether you're going to do salvage therapy, mets-directed therapy, or perhaps it's spread to multiple parts of the body where you might need more systemic therapies.

There are some other indications, which we're going talk about later. And there's also close to 1,000 people who've signed on tonight. And you've asked so many great questions. And we're going to try to get to those questions later on tonight as well. But before we do, we have a special guest, Ron Piela, a patient who's been through this journey. And specifically, you know, the PSMA PET had really impacted his care.

Ron Piela Thank you, Dr. Koo, I appreciate it.

Phillip Koo, MD So, Ron, thank you so much for joining us. So, for those of you, Ron lives in Wisconsin. He just said that the temperature was, was it minus 19, you said?

Ron Piela [00:23:20] Yeah, with a wind chill of 31...

Phillip Koo, MD [00:23:23] So yeah, you look warm though, so that's good.

Ron Piela [00:23:27] It is, yes, yes.

Phillip Koo, MD [00:23:29] So tell us a little bit about yourself and your journey with prostate cancer, how you were diagnosed.

Ron Piela [00:23:36] Sure, so I was 61 when I was diagnosed. I don't have any history of prostate cancer in my family. I have a history of cancer, my father, mother, and brother all died from cancer, but no prostate. So, I was just going through my regular annual physicals. My PSA had risen from about 1.8 to about 4 in an 18-month period. And so, my urologist said we really should get that checked out. So, we did an MRI and MRI did not show what we wanted it to show. And so that was the initial diagnosis, um, just through general PSA, through general physicals every year is how we found out.

Phillip Koo, MD [00:24:22] And then what was the plan to get surgery or was the plan to get radiation?

Ron Piela [00:24:27] Uh, so I, I spent a ton of time, and I guess one thing I could offer to patients is just do a lot of research, a lot of research, lot of research. And so, uh, I probably took three months, uh and a lot of time on the internet, talking to physicians, talking to nurses, talking to other patients. I finally decided to do radiation. And so that was the route I was going to go. Um, and they scheduled a bone scan for me and a CT scan just to confirm that everything was in the prostate, and that's where things got interesting.

Phillip Koo, MD [00:25:02] Alright, so let's get into that. So, you got a bone scan and a CT, which, you know, we often call conventional imaging in our world because it's sort of the basic what we used to use. So, tell us how PSMA came into play and how that changed sort of the course of your care.

Ron Piela [00:25:18] Yeah, so exactly. And, and I apologize after the MRI, I had a biopsy and so had pulled, uh, 18 biopsies, 6 were, uh cancerous and my Gleason score was only 7. So, due to the low PSA and due to low Gleason and only 6 out of 18, um, and I was seeing three different teams, uh at given the fact that I'm in a rural community, I was saying a regional hospital center, a regional cancer center, and then I'm about three hours from Minneapolis - St. Paul. I was seeing a major oncology group there. So, I had three teams working for me. They all assured me, things look good, we'll do the bone scan, we'll the CT scan. We think this is all contained within the prostate. If you wanna do radiation, you certainly can. It shouldn't be a problem.

So, I was scheduled to have the CT scan and the bone scan on a Friday. Prior to that - it was out about two months. Prior to that….and I've spent 30 years in the business side of the medical community, working for pharmaceutical companies and medical device companies, getting them to have their products paid for by the insurance companies like United or Aetna or Cigna. So, I had done a ton of research, as I said, and I found out about the PSMA. I think it was approved very late December 2020. This was April, May of 2022. So, I talked to my doctors at the regional center and the cancer center. They had heard of it, but they didn't do it there. And so, the only place I could get it done was Minneapolis - St. Paul. And so, when I went and talked to my oncologist there, he said, yeah, you can do it, he says, but your insurance isn't going to pay for it. And I said, well, I said I've got some experience in that area, let me see if I can try. And he said go right ahead. It was not a part of any, even in Minneapolis - St. Paul, they were not doing them because insurance wouldn't pay for them. And I had one of the biggest insurers in the Twin Cities.

So fortunately or not, unfortunately, there was some, I got the criteria from the insurance company. Um, and there was, some imaging on the MRI that showed some darkening by the border. Because of that, I was able to convince the insurance company to pay for the PSMA. My doctors were shocked. They couldn't believe it. So, they said, well, you know, we really don't think you need it. The bone scan, a CT scan, we'll have them done. And then they were going to be done on a Friday, and I had a PSMA scheduled for one week later.

So, I get the bone scan, I get CT scan, and I get my results in MyChart two or three days later. Everything is perfectly fine. Talk to my doctors, everything's perfectly fine, they said no issues. So, I go to the PSMA that Friday, and lo and behold, the following Tuesday on MyChart I see that I have five lymph nodes in the groin area, pelvic area. That are all

lighting up due to the PSMA. Talked to my doctors, they were shocked, some of them were shocked. And that, to your point, changed my entire treatment plan. Radiation as the primary solution was out the door. And so that started, I went from stage 2 to stage 4a overnight.

Phillip Koo, MD [00:28:41] Great. So, you know, I think there's a lot of lessons to be learned here. Number one, the advocacy piece. You did the research, you did the learning, and then you fought for what you felt like you needed. And I think we can't talk about that enough. And that's one of the reasons why we do these types of webinars is we want patients to feel empowered so they can advocate for themselves.

Another topic I'd like to mention is, I will say today, arguably, the access to PET is much greater than it was in 2022, and that's for a variety of reasons, and I think it's wonderful that more patients have access, and, I believe, more insurance companies are reimbursing for this routinely.

So, alright, you mentioned this upstaging. So, you went from stage 2 to stage 4. And this is a common story that we hear often with PSMA PET is you see more and you end up getting staged higher. So, how did your treatment change? So, you went from radiation, to what now?

Ron Piela [00:29:39] So I went from radiation to eventually radiation plus hormone therapy. So, I did 25 sessions of radiation therapy. And within probably two weeks after that, I started on hormone therapy, Eligard shots, and I…my oncologist wanted me on those for three years. So, I stayed on Eligard for a year, and then I convinced him to allow me to go to Orgovyx. And so, I went to Orgovyx for another year. At the end of two years, my PSA had dropped to 0.01. And it was at 0.01 for roughly 18 months of the 24 months of therapy. And so, at that point, I convinced him to allow me to go off the hormone therapy. The hormone therapy is…it might be fine for some people. I found it very debilitating and did not like the side effects. So, after two years on hormone therapy, I was then taken off of all medication at that point, and that was 17 months ago. And since then I get my PSA tested every six months. I have another test coming up next month. It has remained at 0.01 for the 17 months post-drug.

Phillip Koo, MD [00:31:00] That's wonderful, that's great to hear. So, Carissa, I'm going to turn to you and get your perspective, and we're not going to talk about Ron's case specifically, but oftentimes you'll have a patient that presents to you with a new diagnosis, maybe you think it's localized, and then you see a couple findings, let's say, lymph nodes or whatnot. How do you sort of assimilate all that information, because we still are trying to figure out what does this all mean, and how does it really impact long-term outcomes?

Carissa Chu, MD [00:31:30] Yeah. Yeah. I mean, two things I'll say about Ron's case that I'll move on, is one, you got to listen to your patients. And two, I hope you're feeling better off of the ADT. You know, it can be really tough. So hopefully you're feeling' better.

Ron Piela [00:31:42] Thank you.

Carissa Chu, MD [00:31:43] You know PSMA PET has certainly caused sort of this stage migration, right? Where, in the past, with conventional CT scan with bone scan. You didn't see these little lymph nodes light up because you just didn't have the sensitivity for it. So, you know, all - everything we know about prostate cancer, we learned from that era, right, where we didn't have PSMA PET. So, someone like Ron, you know, five, 10 years ago

would have had just radiation or just surgery and just kind of hope for the best and watch the PSA, right?

So, we've sort of defined this new space where we're having these patients with just lymph nodes positive, with the bulk of their cancer being in the primary [i.e. in the prostate]. And so, the question becomes, you know, how maybe what is the role of surgery still in these patients coming from, you know, a urologic perspective, but also what is, what's your first move? You know, and my first move is always to send them to medical oncology and to send them to radiation oncology, because I think, you know, in 2026 now, I guess, for patients who've got node-positive disease, a high-risk primary cancer, you know, there's more evidence to have radiation with longer-term hormone therapy.

Now the hormone therapy is really tough, as you know, Ron and many, many other patients have said, you know two years, three years. And so, you know, we're still actively looking at whether or not surgery can have a role in these patients to remove as much of the tumor as we can, with the understanding that additional treatment is likely going to be necessary - radiation and / or hormone therapy.

And the last piece I'll say is, we have a number of clinical trials open here at UCSF, but also across the country, looking at these patients who have small amounts of nodal disease in the pelvis, primarily large burden of primary cancer, maybe symptomatic, from obstruction, seeing if we can give them some form of treatment to shrink the cancer, to render it more resectable, and then still take them to surgery if that's what they want to do. But the first thing I'll say is that I always get my colleagues on the phone and talk to radiation oncology, talk to medical oncology when I see that the lymph nodes are positive.

Phillip Koo, MD [00:34:03] Great, so you know, just because a PSMA PET is positive doesn't mean surgical options are off the table. So, there could still be roles for surgery even though it's positive. And I think a lot of patients often think, oh, if they see something outside the prostate, surgery has no role. So, I think that's a good lesson for all of our listeners out there. Scott, you probably see this scenario often. Before I get to that, number one, if someone's getting a PSMA PET, do you still even bother getting a CT and a bone scan?

Scott Tagawa, MD, MS [00:34:40] Sometimes, I guess is the answer. So, I would say that in the setting that we're mostly talking about, you know, initial workup, I would say MRI and PET scan are going to be the two main ones. But occasionally we'll want some clarification, and then occasionally we'll also want to know, based on the available data, what the volume status is. So more specifically, so Carissa mentioned that the current data that we have is based on, 10-year-old data, is based on patients from 10 years ago. And to have 10-year follow-up, we have to go by that. So, in the setting of metastasis or spread disease, particularly to bone, some of our treatments are tailored based upon the volume of disease. Especially one of the common questions, should we give chemo or not, and that's based on bone scan. You know, 4 or more [metastases] in a certain distribution is going to be high-volume disease, but a PET scan might show 10 things that is only 3 on a bone scan. And we just didn't have these tools. Well, some of the tools were available. It's still investigational and not done in some of these trials. So, we don't know.

So, in answer to the question, sometimes at initial diagnosis or shortly thereafter, I am getting a bone scan. Many of my patients, as Carissa mentioned, might go into clinical trial, and the clinical trial still mandates some of these tests, so the answer is yes, but it's not as universal as it was before. And to, you know, one of my pet peeves, is conventional

tests at conventional times. So, I think, I would say that PSMA PET is conventional, depending on the certain, certain situations, and the same situation the bone scan may not be the most conventional today, but we're still using that, you know, that terminology. So maybe "modern imaging."

Phillip Koo, MD [00:36:39] All right, I like that. All right Ron, let's go back to you. Great story, I think your healthcare background probably helps understanding some of these different situations and how to navigate the insurance piece and whatnot. What advice do you have for all the patients on the webinar today regarding your story, and how to sort of fight for what you need?

Ron Piela [00:37:05] So a couple of things. I guess the biggest thing is to be your own advocate and you had mentioned it previously.

I'm a big football guy. So, I guess I use the football analogy is - you need to be the quarterback for your healthcare. So, in this situation, you know, I had a urologist, multiple urologists, radiation oncologists, regular…medical oncologists. There's a lot of people that were looking at the situation. And I think what people need to realize is physicians are very, very busy. You've got lots and lots of patients. Patients need to be responsible for learning as much as they can and then determining and making sure all of their physicians and everyone on their team is on the same page.

Don't be afraid to talk to your oncologist about what your urologist said. And don't be afraid to talk with your medical oncologist about what your radiation oncologist said. Don't assume that they're all talking about your case, you know, when you're not around. You need to advocate and you need to research, which is number two, is research, research, research. There are tons and tons of studies out there. I was fortunate because I could read clinical studies from my training in pharmaceuticals and medical device, but they're not that hard to read if you get through one or two.

All kinds of online information. You know, PCF is a great organization. There's other great organizations. There is a ton of information on the internet. I would encourage folks to get absorbed and learn as much as they can. Tons of great books, because it's really, it's your life at the end of the day. I mean, your physicians are there to help you, but they see lots of patients. You need to be your own quarterback. You need fight for what you want. You need find doctors that will match what you're looking for. They should listen to you. They should take the time, they should help explain things to where you understand them, but you really need to drive. That's the number one thing. You need to the drive the team, you need to make sure everybody's on the same page as you and you can't just be a bystander.

I mean, you can, but like, for example, in my case, I didn't know anything about a PSMA until I started to research. And when I talked to my doctors about it, I said, isn't this much, much more specific? He said, if you have any concerns whatsoever that it's outside the prostate, why won't you use the best test? Is this not much more specific? And they said, absolutely, it's much more specific. I said, then why can't we use that test? Why would we take that chance? Because the other thing that is, I don't understand how patients could have radiation and surgery and then have a high recurrence rate. Well, I think one of the reasons was, that they were metastatic that wasn't being caught by a bone scan or a CT scan. So, you need to educate yourself. You need to be your quarterback. Those really are the top two things. If you can do that, you can feel confident that you're going to get the best care.

Phillip Koo, MD [00:40:14] You know, I think those are wonderful points. It's interesting. Dr. Chu earlier talked about how she talked to her colleagues in rad onc and med onc. And at a place like UCSF, you might sort of see them in the hallway, see them eating lunch or whatnot. You're sort of all in close proximity most of the time. Ron, you received the bulk of your care in like a regional, sort of rural setting, in which case, yeah, those connections and those conversations probably don't occur as frequently, in which case the patient needs to sort of help facilitate some of those conversations. And I think that's a great point.

And then research, you know, you're right, there's tons of information out there. You obviously need to be very careful about the credibility of the information that you're ingesting. And that's why we'll put a plug in for the PCF website. Obviously, we have very curated, vetted information on our website.

So, you know, we're going to move on a little and talk about other applications for PSMA PET. So, we talked about initial diagnosis. We talked about biochemical recurrence. Scott, this is kind of your wheelhouse with regards to using PSMA PET to identify patients who could get radioligand therapy, like a drug like Pluvicto. Tell us more about that.

Scott Tagawa, MD, MS [00:41:29] Yeah, you gave a nice, for those of you that remember or that were joined at the beginning, there was a kind of a structure of the PSMA, well, PSMA targeting agents. So, there's part of it that's going to attach to the PSMA and just kind of very briefly for those that missed it, same three words in PSA, just M for membrane. So, PSA is inside the cell, comes out, PSMA is stuck to the cell. So, we can have something that targets that. And there's different things that can attach to it.

So, the flashlight, as Phil gave the analogy, can light things up like a PET scan. But we can also attach things that can treat the cell, and the only currently FDA-approved treatment in terms of PSMA targeted therapy has what Phil mentioned, a beta emitter, lutetium-177. It's approved for certain gastrointestinal tumors with a different target, and for prostate cancer with the PSMA targets. Very similar molecule as for the PSMA PET scans, except what's attached to it, that's able to kill cells…that specific cell, plus cells around it. Currently FDA approved for patients with tumors that have grown despite hormonal therapy, might get approved for initial treatment of patients with metastatic disease, and you know, maybe even earlier. And just kind of loosely, besides radiation, we can attach chemo or you can attach things that are more immune in nature. So, we have the first set of PSMA imaging agents. So, several that are out there that are not all exactly the same, but similar. And we have a first therapeutic - that's radiation, with more to come.

Phillip Koo, MD [00:43:15] Great, thank you. So, Dr. Chu, from your perspective, there's a lot of questions about getting PSMA PETs serially, maybe looking at treatment response, maybe after surgery, maybe after ADT. What's your perspective on serial or use of PSMA PET for treatment response?

Carissa Chu, MD [00:43:35] So in a post-prostatectomy setting, so after surgery, the goal is for your PSA to go to zero. There are things that can influence that. And if there's a detectable PSA after surgery, suggests that there could be cancer somewhere in the body. Okay, there are other things that could be going on, such as sometimes you have some benign prostate tissue at the margin that can produce some PSA as well after surgery. But when the PSA starts to come up after, you know, after the prostate's been removed or if it's been radiated, assuming all the cancer is gone and been treated, it makes you think that there's some residual cancer somewhere that's producing that PSA.

Now, how sensitive is the PSMA PET scan in that particular setting? Let's say your PSA is 0.1 or 0.2, still very, very low levels of a PSA. We know the sensitivity is around 30 to 40%. Okay, so, if you were to get a PET scan at a low but detectable level of PSA, it may not show you anything after the prostate's been removed, okay? And so, in those situations, you kind of have a choice with that patient. You could get serial PET imaging while you're watching the PSA to see if you could localize any areas of recurrence for directed therapy okay. That's one model, in the patients who aren't eager or aren't hungry for additional treatment.

Or you could say, you know, the PSMA PET's negative, but you know your cancer at surgery looked like this, you know, it had some aggressive features, I think we should start treatment sooner rather than later. So, in that situation, I would counsel my patient, you know….That it's probably time to start thinking about the next line of treatment, even if the PSMA PET is negative. But if people are comfortable with surveillance, and watching, that's a situation where maybe you could get repeated PSMA PET scans just to see if you can detect where that cancer might be coming from. Let's say it's something slow-growing or indolent that isn't really going to cause symptoms, isn't going to cause problems, where the treatment might be worse than that disease. Those are scenarios where you can still do surveillance with serial PSMA PET post-surgery.

Phillip Koo, MD [00:45:55] So there's a question about, so there's several PSMA agents that are actually approved. So, several of those apps that you'd be running on your iPhone. I guess for the time being, as long as you're getting one of the approved ones, you should be good. There's some subtle differences, but I haven't seen convincing data that says one's better than the other. There was another question about why would you still get surgery if you have nodes that show up on a PSMA PET? Do you wanna sort of tackle that briefly?

Carissa Chu, MD [00:46:22] I can tackle that. You know, it's a little controversial. There's practice variation across the country. You know, the short answer is that surgery can be offered for patients who are healthy, fit, good candidates for it,and understand that they're likely going to need some additional therapy afterwards, okay? The lymph nodes, like Scott was saying, usually is sort of the tip of the iceberg. So, if you're seeing some lymph nodes on the PET scan, those patients are likely to recur somewhere. They've probably got microscopic cells of disease elsewhere. And so, you know, hormone therapy probably is going to be more effective at really shutting that down early on.

But there are men who have large prostates, obstructing tumors, have other urinary symptoms, want the prostate out, or are young and have a long time of follow up ahead of them. And so, you can make a strong argument for getting rid of the primary cancer, knowing that there is a likelihood that they'll still need some additional treatment. Not always though. There are a percentage of men who have durable PSA responses despite having node-positive disease on their PSMA PET scan after surgery. We just don't have a good way of predicting who those men are. So, I tend to tell people, you're likely going to need something more if you embark down the surgery path.

Phillip Koo, MD [00:47:34] Great, so we have five minutes left. I'm going to ask the same question to all three of you. And Ron, I'm going to give you the final word. The question is, what has PSMA PET meant to you? So obviously for the physicians at your practice, Ron, for you it's a little bit more personal. So, Scott, I want to start with you. How has PSMA

PET sort of transformed your medical oncology practice? What has it meant for you and the patients that you treat?

Scott Tagawa, MD, MS [00:48:00] Yeah…I realized I forgot to introduce myself, because the introduction said, which is true academically, professor of medicine and urology, but you don't want me operating on you, you want Carissa operating on you, it's an academic appointment.

So, in the setting of me being a medical oncologist, I see a lot of patients with metastatic disease, and if someone's going to die of prostate cancer it's a metastatic disease. So early identification of that, coupled with the therapeutic option of targeting PSMA, I would say. And part of this is my bias from working on targeting PSMA therapeutically for little less than 20 years, but almost 20 years. So, to me, that has been the number one biggest thing from a combination of a research point of view, plus for the patients that have traditionally run out of options, another therapeutic option. But just a second, a quick one, a very common question, where's my PSA coming from? I can answer that much of the time if there's a PSA rise. So that's probably the most common that I've seen over the last, we've been using PSMA PET for about a decade.

Phillip Koo, MD [00:49:08] Uh, Carissa.

Carissa Chu, MD [00:49:10] PSMA PET, what has it meant for me? So, I think it's added some complexity, but it's added precision. And I think, it's given more information that we can discuss together with the patient to help make an informed decision. And so, I think actually is very empowering of the patients in that way. It has added complexity because how we practice now is different than how we would have practiced 10, 15 years ago based on what we thought we knew about prostate cancer then. But we're learning a lot more about the disease. We're learning more about how it recurs, how it spreads. And so, we've added on that sort of theranostic component to it, which is a nice model for treatment for cancers across the board. Um, so I think it's, you know, it's been a practice changing addition for sure.

Phillip Koo, MD [00:50:02] You know, I think that complexity comment's really important. A lot of patients sort of in the chat are saying how, oh, why isn't it being used for everything? It's much more complex, and you're right, it does raise some questions that we still need to answer as a community, which is why we continue to fund research in this area as well. So, Ron, final word.

Ron Piela [00:50:20] So I think personally it has saved me multiple years of my life. If I had not done the PSMA, they would have only radiated my prostate. They would not have radiated the other 5 areas in my pelvic region, which means by the time they found out as the PSA rose over the next 6 to 12 to 18 months, that cancer could have spread and could have metastasized to bone and could have gone from a 4A to a 4F. So, I think it's a godsend that I had the PSMA. I think it's added years to my life.

Phillip Koo, MD [00:50:56] That's the perfect way to end this webinar, using great technology to really improve outcomes. And we appreciate you sharing your story with us. I know it's going to really help so many of the patients who are listening today and who are going to watch this later. And to Drs. Tagawa and Chu, thank you very much for sharing your knowledge and wisdom and expertise. So, thank you both and we'll see all of you next time.

Carissa Chu, MD [00:51:21] Thanks for having us.

Scott Tagawa, MD, MS [00:51:21] Thank you.

Carissa Chu, MD [00:51:21] Take care.