

Dr. Charles Ryan:

Hello, everybody. Welcome again. We're filming today a followup from the March 14th webinar that we did on PSMA imaging in prostate cancer. We had a great attendance for that webinar and a large outpouring of questions and comments. And so we thought it'd be a great idea to get together once again to answer online live some of the questions that we had that came in during and after the webinar.

So I'm once again happy to be joined by Dr. Phil Koo from Banner MD Anderson in Phoenix, Arizona, where we're going to go through some of these questions that have come in. And Phil, great to see you again.

Dr. Phillip Koo:

Happy to be here. Thank you, Chuck.

Dr. Charles Ryan:

So I'm going to read through some of the quick questions that have come in and we'll do some sort of rapid fire question and answer, and then we'll go through some more complex cases for the next few minutes. Question number one, what is the difference between the DCFPyL or the Gallium 68 scans?

Dr. Phillip Koo:

The biggest difference is the radial isotope that's attached to the small molecule. One is a Gallium 68 isotope, one is an F-18 radioisotope and they have differing half lives. The small molecules themselves do have subtle chemical differences, which changes a little bit of how it works.

That being said, today, I don't believe there is a significant difference between the two that justifies why one would be better than the other. So I think for the time being, whatever you can get access to, go for it.

Dr. Charles Ryan:

Interchangeable, that's what I would say as well. Are there any contraindications to having a scan such as an artificial hip, implanted device, a kidney disease, prior radiation, any medical reason why somebody should not have a scan?

Dr. Phillip Koo:

I can't really think of a medical reason why they should not get this if they were eligible to receive this. Things like artificial hips, it does give streak artifacts that make the reconstruction and the image analysis a little trickier. Some more modern scanners might have some tools that can decrease some of those artifacts.

I think the most important recommendation is just provide as much information to your physicians and the radiologists as possible so they could use all that when they are interpreting your exam.

Dr. Charles Ryan:

Great. We had a lot of questions about what to do if the PSMA PET scan is negative, especially in the post prostatectomy setting where one is trying to decide about salvage radiotherapy. How do you reconcile those rising PSA but a negative PSMA PET?

Dr. Phillip Koo:

This is an interesting question and I'd love to sort of hear your perspective on this as well. I think clearly positive studies are probably going to impact how you manage an individual case. I would think a negative scan would actually impact how you manage that patient as well. And often in that post prostatectomy setting, we're thinking about salvage therapies and I've heard various perspectives on this where some physicians might salvage early, even with a negative PSMA PET, making the assumption that the disease is recurring locally in the prostate bed, whereas others prefer to wait until the scan is positive.

Some of the data that we're seeing nationally is that earlier salvage tends to do better, especially in those who have at least one high risk factor. But Chuck, what are your thoughts here?

Dr. Charles Ryan:

Well, I think it is a dilemma, but it's a couple of things, I would say. Number one, it's always good to have a negative scan and that this is a negative scan with a very high resolution so you can be confident that you don't have tumors. So that's point number one. Point number two is in the post-operative setting, if we're talking specifically about salvage radiation therapy, a negative scan would not discourage me from doing salvage radiation therapy.

And I think what you might have alluded to also is that that's actually almost favorable and that there may be such a minute amount of cancer in the pelvic region or the prostate bed that a PSMA PET scan is not positive. If a person has had salvage radiation therapy and a prostatectomy and then has a negative PSMA PET and let's say a PSA of 2 or 3 or 1.5 in that range, then I think you need to have a conversation about what we're dealing with.

I think of this as systemic disease, but it's also heterogeneous because systemic disease with a very rapidly rising PSA is more worrisome than one with a very slowly rising PSA. So in the slowly rising PSA, I'm probably more inclined to say, "Well, let's watch and wait and repeat the PSMA PET down the road." With a very rapidly rising PSA where it's doubling every three months, four months, five months, I'm more inclined to recommend a period of hormonal therapy to try to prevent metastases from occurring.

A couple of other themes that emerge during the course of the question and answer period is, can PSMA PET imaging be used to detect prostate cancer in the first place, in the place of an MRI or even in place of a biopsy? Do you think it will ever get to that point?

Dr. Phillip Koo:

So today, I would say it's more investigational experimental. Will we get to that point? I believe so. I'm confident that it will be maybe not the primary tool, but an assistive and a valuable tool to help characterize disease better. But today, I would say it's not ready for primetime.

Dr. Charles Ryan:

Yes. And also by the way, we talked in our webinar on the 14th predominantly about newly diagnosed patients. So we might want to just quickly review the indications for sort of initial staging, but we have already gotten into some of the questions of recurrent disease and post-treatment setting. But if you could just restate the indications for PSMA PET in the newly diagnosed setting.

Dr. Phillip Koo:

In the newly diagnosed setting, it's really about the risk of having metastatic disease. So I think the guidelines sort of agree that it's patients who have unfavorable, intermediate, high or very high risk

disease at the time of diagnosis, and then you might take into consideration other genetic testing or other biomarkers that might show you're at higher risk for metastatic disease.

Dr. Charles Ryan:

Other questions we had dealt with, people who are on treatment and what the role of the PSMA PET is. So for example, somebody has a positive PSMA PET shows lymph nodes, for example. They go on hormonal treatment. Do we need to do the PSMA PET then to show that there's been a response to the treatment and what is the role for these scans and individuals after treatment has been initiated?

Dr. Phillip Koo:

So today, it is not indicated to assess treatment response. So the idea of getting a scan, putting someone on a therapy and then using another PSMA PET to determine whether that therapy worked or not is not ready for primetime. I think there's various pieces to the puzzle that we still need to clarify before it could be rolled out to be used routinely in that setting.

That being said, it is actively being investigated, so I'm optimistic perhaps in 2, 3, 4 years, this will be an expanded indication for PSMA PET in the future.

Dr. Charles Ryan:

A couple of other questions, again, comparing the different technologies, Axumin PET, we talked a little bit about the Gallium 68 versus DCFPyL, but talk a little bit about the other technologies that were out there before PSMA targeted imaging and specific Axumin and others and whether there's still a role.

Dr. Phillip Koo:

Sure. So there's sort of been a timeline. We've had sodium fluoride PET CTs, which just focused on bone disease. Those have really fallen out of favor. You had choline which looked at how the cell membrane replicated itself. That was only available at the Mayo Clinic, which really prevented sort of more widespread adoption. Axumin was FDA-approved, I forget what year, but it was available throughout the country.

I think moving forward, its role is still being defined. I would say that if you had a choice between a PSMA PET and an Axumin, the money's probably better spent with a PSMA PET. And those who might be PSMA negative, then the question becomes, all right, should I get a different test as well? And I don't really know the answer to that today because it's possible you could get another test like an Axumin or an FDG, and it could be positive.

But how does that sort of play into how we manage patients? What is the impact? What is the impact on your outcomes? These are all questions that haven't really been looked at. So really hard to say today. I think those radiopharmaceuticals on the diagnostic side that were approved in the past will likely have a smaller role now that PSMA PET is much more widely available.

Dr. Charles Ryan:

Great. A few questions about the radiation impact of the scan itself. Could patients be worried about the radiation load from these images?

Dr. Phillip Koo:

So the principle that I think we should all live by is we should try to minimize radiation exposure as much as possible, just in general. In this case with PSMA PET, the advantages of receiving it in those clinical indications that we talked about exceed any of the risks associated with that radiation exposure.

So I think from what we talked about, it's fine. But if we start talking about it repeated, repeated, repeated types of scanning, it does come into the discussion of us having to make sure that that radiation exposure is worth that risk. So today, if we just follow the way it's indicated, we're safe. Yes, there might be some exposure, but how important, how impactful that is, we don't know for sure.

Dr. Charles Ryan:

And in many instances, if radiation is going to cause a problem, it's many times decades down the road after the scans have been done. And with an older population, just to be quite frank, that's less of an issue because if a 30-year timeline is required for a second cancer to occur from that radiation, we're not going to be impacted by potentially many of our patients.

Dr. Phillip Koo:

Absolutely, and on a magnitude level, the amount of radiation exposure that you'll receive with a diagnostic scan is magnitudes lower than what you receive with anything therapeutic.

Dr. Charles Ryan:

Yes. So a number of concerns about PSMA PET scan is done, there are lymph nodes or other metastases identified at the PSMA PET. What's the decision making around who should get radiation to those metastatic sites versus systemic therapy? It's a little bit of a question we've broached during the webinar of doing metastasis-directed therapy versus not.

Dr. Phillip Koo:

Yeah, that's a really complicated question that I really can't give a single answer to. I think the best piece of advice I could provide is whenever these types of scenarios come up, it's nice when you can have a multidisciplinary discussion with a radiation oncologist who knows the radiation oncology literature the best. You have the urologist and you have the medical oncologist, and you have the radiologist nuclear medicine specialist talking together to make sure we're coming to the best conclusion. So that would be my answer today. Your thoughts, Chuck?

Dr. Charles Ryan:

Yeah, I think it's really complicated because for me it depends on where the lesions are, how quickly things are progressing, and a slow growing tumor that is recurrent after radiation or something like that. I suspect that in many cases, the metastases that show up could represent the vast majority of the cancer in the body and therefore radiating it could have a prolonged beneficial effect.

If you see that the PSA is rising rapidly and now there are three lesions, three nodes that are positive that weren't positive last time you did the scan six months ago, then I think what we're dealing with is what I call a tip of the iceberg phenomenon where the nodes are positive, but it reflects that there's an underlying burden of systemic disease in the circulation. And in those cases, I think the radiation is probably not going to be associated with great benefit.

And those observations and that bias that I have is born out by the literature where the best long-term results coming from metastasis directed therapy are those with slower growing tumors. The other thing is, one of the great advantages I see as a medical oncologist to these scans is that individuals who

previously were told you need to be on hormone therapy for the rest of your life and cure is not possible. I think that in some of these cases, it allows us to do one of two things or both.

One would be to limit the duration of hormonal therapy. So for example, as somebody who has three lesions that show up on a PSMA PET, you treat the prostate, you treat the lesions with radiation, you treat with a course of hormonal therapy. You stop that therapy, you hope that the patient may be done with their treatment and that there may be a prolonged disease-free interval or even a cure from that situation.

And that is not the way we talked a decade ago. And so that's one thing where I think we need to reimagine our perspective on the differences between localized cancer and metastatic cancer. It used to be so binary. You were localized and you'd go to the urologist, the radiation oncologist, and you try to get cured or you are metastatic. You had metastatic disease and you're on hormone therapy for the rest of your life.

And we now know because of these scans that there's a pretty significant gray zone in the middle. But it's great, and so there's lots of nuance.

Dr. Phillip Koo:

I just reviewed an article and I think a hot topic is really what you talked about risk stratification in patients with biochemical recurrence. And you're right, there's going to be those lower risks patients and those higher risk patients, and how do we sort of stratify them and figure out who's who. And I think this is where PSMA PET really helps us hopefully better define those risk categories.

Dr. Charles Ryan:

Yeah. Biochemical recurrence or serologic recurrence or PSA-only recurrence is one thing, but I'm also talking about that person who's newly diagnosed as part of his staging. He has a PSMA PET scan, which reveals that there is disease outside of the prostate. It used to be that we said no hope for cure, we're not doing surgery, you're on hormones the rest of your life.

And now there may be hope for cure. We could potentially radiate those spots, treat the prostate and potentially render the patient free of disease. But we're still working that out, who those patients are.

Good. I think the final question is one that came up on the webinar, but we can approach it again, which is what is the threshold after surgery when a PSMA PET can begin to be positive? And when is it too early? When is the right time, sort of the sweet spot where we're going to begin to see findings on the scans?

Dr. Phillip Koo:

So very tricky, hard question. So let's talk about from the perspective, here's the numbers that I've seen thrown out in a lot of discussions I've had. I've seen the number 0.2 thrown out there. I've seen the number 0.5, and then I've also heard that there is no number too low. The minute you are biochemically recurrent, you should consider getting a PSMA PET.

I think clearly there are pros and benefits to each of those approaches. What we do know is the lower your PSA level is, the more likelihood there is that it will not be able to detect disease. So if you have a PSA of 0.1, the chances of being positive compared to something a patient with a PSA of 0.5 would be much less in that patient with a PSA of 0.1.

So I think from that perspective, all patients and everyone should just sort of set certain expectations before the test to know that what the pre-test probability might be. And it's also important to sort of flip

the discussion, maybe you think about how before you even get the test results, have a discussion on how the results might impact how you're going to be managed.

And let's say it wouldn't change how you would be managed, then maybe it's not worth getting that PET at that time. But at a higher level, if it will change how the urologist or med doc or rad doc is going to manage you, then maybe that is a sweet spot.

Dr. Charles Ryan:

Yeah, this is rule number one in medical school, which is don't order a test unless you're ready to confront the results and that you are going to potentially take an action from those results. And this is a great example of that, is to kind of think ahead of time, both patient and doctor, think ahead of time of what you're trying to do by doing this test.

So thank you, Phil, for your time. I hope this has been informative for all of you tuning in to listen to these questions. And I want to thank you all for joining us for the webinar, and I want to thank you all for these really, really good questions. For obvious reasons we don't want to go into specifics, individual cases, and many of you did send in your individual cases and ask specific questions, but what I tried to do is distill the broader concept from your individual cases.

For your own individual cases, of course, you need to consult with your own doctor on that because we can't tell enough from the question to make a smart decision for you. So thanks again and be well.