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A Look at the Utility of PSMA PET Scans in Prostate Cancer

**Host Intro**

You're listening to *Project Oncology* on ReachMD. I'm your host Dr. Jennifer Caudle, and today, I'll be discussing the utility of prostate-specific membrane antigen, or PSMA, PET scans in prostate cancer with Dr. Geoffrey Johnson, who also presented this at the Society of Nuclear Medicine and Molecular Imaging 2024 Annual Meeting. He's a Nuclear Medicine Specialist and Radiologist at the Mayo Clinic in Rochester, Minnesota. Dr. Johnson, thanks for being here today.

**Dr. Johnson:**

Thank you. Pleasure.

**Dr. Caudle:**

So, Dr. Johnson, can you start us off by explaining what PSMA PET scan is and how it's being used to treat prostate cancer?

**Dr. Johnson:**

Yeah. So PSMA PET scans are basically a method by which we, as physicians, can see if a patient suffering from prostate cancer has the ability to target their cancer with our medications. So in other words, we can inject a radioactive medication or a radiopharmaceutical into the patient's vein, it goes to their cancer, and sticks to it, but it only sticks to their cancer if their cancer is expressing the PSMA target, so it's basically a whole-body pathologic stain. We're going to see all the places where their tumors are and whether or not those tumors are expressing the target.

And in addition to that, the scan allows us to measure how much of the medication we get on to that cancer target, so it gives us an idea whether or not we can use a therapeutic version of the PSMA injection after the PET scan and whether it looks like it's going to be effective in the patient. So it's a patient selection tool. That's the primary first use case for it or one of them, or to say I'm going to choose, to use the PSMA therapy for my patient based on whether the PSMA PET scan shows that the drug actually gets to the tumors.

**Dr. Caudle:**

Turning to your recent presentation on the use of PET scans for biochemical reoccurrence after a radical prostatectomy, can you explain why this was a significant area of investigation?

**Dr. Johnson:**

You may use a PET scan for staging, for diagnosis only. So if you have a patient who had a prostatectomy and you know

that their cancer is back because you can see the PSA expressed by the tumors in the blood it's, unfortunately, a fairly common scenario. And a lot of patients have prostate cancer, so there are a lot of patients out there who they and their physicians know that somewhere in their body the prostate cancer has come back after their initial surgery, and the question is where?

And we used to just radiate the prostate bed where the prostate was resected assuming that that's where the cancer is most likely to come back, but we now know that a lot of patients whose cancer has come back comes back not only in that location but also elsewhere, maybe in their bones or their lymph nodes, and so radiating the prostate bed isn't going to affect their long-term benefit much because they have got cancer outside the prostate cancer bed. So we used to use scans like CT scans or bone scans to try to identify where the cancer might be, but they're just not very sensitive. In other words, we can't see small amounts of cancer very well. There's a lot of false positives, and therefore, PSMA PET scans are just far superior in this population of patients to see exactly where the cancer is and see it sooner.

We have a few other scans that we could use. Like at Mayo Clinic, we actually got an NDA for C-11 choline PET, which was something you could use in this setting, and still can. There's also fluciclovine PET, which is out there as an alternative. But both of those are metabolic agents, meaning you only see it when there's enough metabolism in the tumor to see the activity, and PSMA PET scans in general are significantly better in most patients than either of those scans. So it's just changed our ability to properly manage patients in that group, and so when they have recurrent PSA in their blood, you do the exam with a PSMA PET scan, and you much better target the appropriate therapy to the patient.

**Dr. Caudle:**
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host Dr. Jennifer Caudle, and I'm speaking with Dr. Geoffrey Johnson about his research on PSMA PET scans for prostate cancer.

Are there any challenges or limitations to PSMA PET scans?

**Dr. Johnson:**
It is possible that a PSMA PET scan doesn't get what the patient and referring physician want when a patient has biochemically recurrent prostate cancer after their prostatectomy. In other words, maybe the PSA is showing the cancer has come back, you do the PSMA PET scan, and you don't confirm where it is. And sometimes you don't confirm where the cancer is because it's too small. Even with this really sensitive PSMA PET scan, which maybe is the best way to detect the cancer in most locations in the body, maybe it's just too small, or maybe it's spread out thinly along the peritoneal lining, and there's just tiny cells, and it's just not grown in any one location big enough to see. Sometimes it's invading the bladder, and unfortunately, when we do the scan, the patient's body is secreting the PSMA radiopharmaceutical into the bladder. So they haven't had a chance to urinate all of that excess PSMA, and there's all of this activity going to the scanner from the urine, and therefore, the radiologist or med physician reading it really struggles to see cancer right along the bladder. And so sometimes you need an MRI or other scans to add to the PSMA PET scan to better localize.

**Dr. Caudle:**
What impact could the use of PSMA PET scans have on the diagnosis and treatment of prostate cander, and how could this affect patient outcomes?

**Dr. Johnson:**
So when you have a patient who has metastatic prostate cancer, currently, in clinical trials we'll commonly use things like CT

scans and bone scans by the working group criteria to see whether the systemic therapy, hormonal therapy, chemotherapy, or even these new PSMA radiopharmaceutical therapies are working. Those technologies are old, which is fine if they work great, but we've got newer ones. So can't we look at a technique like a PSMA PET scan itself to confirm whether their systemic metastatic cancer is responding to a systemic therapy? We commonly do that with FDG PET, and it's a standard clinical practice. The problem is we don't have much data to confirm in these different populations whether a follow-up PSMA PET scan is going to give us accurate information to tell us whether the patient's responding or not. So this is an emerging field, and there's a lot of debate about that.

It would be great if you could because the PSMA PET scan changes dramatically and quickly, so we get a very fast answer as to whether or not the tumors look like they're responding, whereas CT scans and bone scans require a much longer delay before you actually see changes on those scans that you can reliably say are real. For example, the cancer may be dead, but it's still sitting there. It hasn't resolved yet. It hasn't shrunk yet. So the PSMA PET scan allows you to say, 'Well, if the cancer is dead, it's probably not expressing PSMA on its surface anymore, and it's not really a target, and it's not going to light up on the PET scan. But can we confirm what kind of changes in these scans actually predict a good outcome?' And so I went through a whole bunch of different criteria that people are debating about using right now, but we're still debating about whether insurance companies should pay for it, how often do we use it, where is it appropriate because these are expensive scans.

It's very clear that in certain cases they look very useful, and there's emerging data from a number of institutions on that, but which criteria do you use and where and how do you standardize that is still being debated.

**Dr. Caudle:**
And what are the ongoing efforts to improve care for these patients?

**Dr. Johnson:**
I think when we look at the question, we have a new technology, we know we can use a metabolic PET scan like FDG to say whether a cancer is dead, minor changes get more debatable—and we can also pretty well predict if it crosses a threshold whether it's progressing. That gives you a sense of how much energy the tumors are consuming.

PSMA is different. PSMA is a cell surface receptor. So the concern that we would inappropriately use it in the same way as a metabolic PET scan for follow-up was the following; If you have a cancer and you give it a hormonal signal, we know that that can change the expression of the receptor without changing the number of cancer cells. So we know that in certain settings hormonal suppression or medical castration as we call it, can affect the expression of the PSMA receptor independent of whether the cancer is responding or progressing. And since we knew that, we were concerned that maybe a change in the amount of activity on a PET scan on a follow-up would just reflect the up or downregulation of the receptor and not true progression or response.

Luckily, as we look at this unless the patient is changing from going on or off of a hormonal therapy, I predict—although we need to prove it—that in many of these scenarios, we can use a PSMA PET scan to very accurately early predict the patient's outcome in terms of whether the tumors are responding or progressing, and that emerging data is very exciting because it tells us that we can pivot therapy much sooner. We can say, 'Okay, you're responding. We want to continue this therapy,' or, 'You're not. We've got to shift our gears and go somewhere else.' Or maybe even, 'You've got 10 tumors, and nine of them are responding, but one is progressing. We need to radiate that one tumor. But then if we do, we can continue on with your systemic therapy.' And that's pretty cool if you don't have any other options for the patient. So those new ideas

are really emerging, and we're really debating about where we can rely on them, and where we're reaching outside of the lines and in trouble of potentially putting a patient in harm's way because we don't have enough data yet.

**Dr. Caudle:**
Before we end today, Dr. Johnson, what additional research is needed?

**Dr. Johnson:**
So to validate being able to use a PET scan, especially a PSMA PET scan, or even what we call a therapy-monitoring PSMA SPECT scan, which is the imaging of the actual therapy if they're going on PSMA therapy, you need prospective trials where you're given the opportunity to see how those changes on those scans correspond to outcome. We're getting a lot of good data there. It gets a little more questionable if you said, 'Okay, what happens if, as a physician, I act on that data?' For example, let's say you've got a patient and you've got them on PSMA-617 lutetium therapy, and you're monitoring them in follow-up before you finish all the cycles with either SPECT scans or PSMA PET scans, and you say to yourself, 'You know what, I think we have a complete response.' Maybe we should pause the therapy. Maybe we shouldn't continue the therapy because with that particular therapy we think that, when the tumors are small, it becomes less effective, which is different than chemo; but with this particular therapy, the way the radiation is delivered to the tumor is with the medication. As the tumors get small, the radiation doesn't concentrate on the tumor cells as well. In theory, doesn't work very well. So we think that doing a pause would be beneficial, but we don't yet know whether that actually results in a better outcome or at least an equivalent outcome with less medication.

Having said that, there are many other scenarios where you want to use an imaging study like a PSMA PET to do an early change in the course of therapy. At some point, I think there has to be collective understanding that this is effective in enough scenarios that we can allow physicians to use them intelligently based on what we know and really try to iterate a little faster in the care of these patients.

**Dr. Caudle:**
And with those final insights in mind, I want to thank my guest, Dr. Geoffrey Johnson, for sharing his research on PSMA PET scans for prostate cancer. Dr. Johnson, it's been a pleasure speaking with you today.

**Dr. Johnson:**
Oh, it's been wonderful. Thank you for highlighting this field and helping us to communicate it to our colleagues.

**Dr. Caudle:**
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