Introduction and Guest Background

We found prostate cancer only when it was too late to cure it, you know, and there was not much we could do. Finding cancer so early, we don't even know what to do with it.

So we treated it and then we kind of realized that the side effects of the treatment were way worse than the cancers, right? And I think, going through the whole task force recommending against screening was an interesting exercise because it showed a few things.

One, that there is a way that you could change behavior. This is Dr. Talks. Hello everyone. Welcome once again to another episode of the Prostate Cancer Summit.

I'm your host, Dr. Gio Espinosa. And I have the great pleasure of introducing to you Dr Sanaj Poonen, who is a board certified urologist with a specialization in oncology.

He completed his medical degree at Queen's Health Science and a residency in urology at the University of Toronto in Canada. So yes. We have a Canadian, but you know, no worries.

He's now in the U S he then completed his fellowship in urology at the university of California, San Francisco, where he attained a master's degree in clinical research as well.

he treats prostate cancer, bladder cancer and kidney cancer. And as an expert in robotic surgery. Dr. Punin also has expertise in using MRI and biomarkers for prostate cancer evaluation and performing MRI-guided and transparenial biopsies of the prostate.

Dr. Poonan does a significant amount of research and is a lead investigator in several trials in at Desai Sedeurology Institute, University of Miami, Leonard Miller School of Medicine.

So you in the house, you end up go hurricanes. Now that football season, right around football. Exactly. Yeah. Thanks Sanaj so much for being on. I was super stoked to learn that you were going to be on this summit.

And I think you're one of the leading experts in the field. In terms of diagnostics and so forth, I've seen some of your lectures and I have been super impressed with your work and everything you've done in that regard.

So my first question has to do you like living in Miami more so than you liked living at Toronto? I mean, are you ever moving back to Toronto, what's the deal here?

Yeah, that's a great question. Toronto is always probably going to be home for me. You know, I've never got to a place yet where I'm considered anywhere else home per se.

And they're very different, you know. I love Toronto. It's a great city. But, working at Desai Sethi has been such a, great opportunity for, me I have grown in ways I never thought I would imagine, professionally and from a family standpoint.

We were talking about our kids earlier and my wife have raised three beautiful children here in Miami. So we're happy where we are. Your children are Miamians, aren't they?

Yes, they are. Well, actually, so it depends on how you define it. I guess one we did our fellowship is in San Juan, as you mentioned. And so my first child was born there and we moved when she was a month.

Yeah, she's a Miamian. Yeah. I tried. Exactly. And I guess you also, you know, it's also nice to enjoy some of the

tax benefits as well as a comparison to Toronto, right?

Yep. Absolutely. The sun and the sun, that's right. It's, a bit much for me, man. You know as, as Cuban, You would think, yeah, there's only a matter of time before I moved to South Florida.

That sun is a bit too much for me, man. When you get those weekends, I find myself taking naps more often than I used to. I mean, if you go out in the day, it just, It barrels you down.

Brutal. So let's talk a little bit about prostate cancer since this is the Prostate Cancer Summit. How I pigeon-holed you already as a prostate canter.

expert. So if I have a bladder cancer case or kidney case, I'm not thinking Dr. Punen anymore. I am thinking prostate cancer. I mean, so there's, there are six people in my group that do just cancer at Dysaisathy.

And all of us do pretty much whatever comes our way. Because for the most part, we're all fairly young and we don't want to just get to a point where we are only doing one thing.

PSA Screening and Prostate Cancer Diagnosis

So clinically, We do everything. Research-wise we have our areas and obviously mine is prostate cancer. I think because of that, 80% of what I see has probably been prostate, you know, radical prostatectomy, surveillance, and patients coming in for emigrated biopsies is a big chunk of my volume.

But you, know I still do bladder, I do kidney, still every now and then RPLND will come through. So I try to keep, You know still doing everything. Yeah, yeah.

You know, I find that when I talk to colleagues from around the world, only a few areas have the luxury of having this subspecialty in just prostate cancer, right?

In some, like in Colombia, not only are they treating the prostate, they're also treating incontinence in the ED that comes right after. All right. So they don't have a luxury actually, you know subspezializing in anything.

Here in U. S. Only a few areas, maybe a couple of people in New York, California, right, had the ability of just kind of sub-specializing in just prostate cancer and just do that.

Which for some people they enjoyed, other people that I know is like, yeah, I'd be bored, just doing one thing. So it's fascinating how that works. Yeah.

Diagnosis of prostate. We've come a long way. Here's where, you know, so as you, know I have a podcast. And I'm interacting with people on social media, then I see people at the clinic at NYU.

And here are their concerns, right? And, you know, as a, just as, a regular person, I can relate to that. Number one, there's a lot of information on the internet.

It's like, well, PSA doesn't matter. PSAs absolute waste. Which is not true actually, but. As it relates to PSA as a screening tool for prostate cancer, we've learned that it's not the best tool.

A lot of false positives and false negatives leads to unnecessary treatments, et cetera. People really don't wake up in the morning and are excited about getting biopsies, right?

Even when you think about it, you know, Rod, although I know you do transperoneal, which is great actually, I'm a fan, but it's still, whether it is trans perone or trans rectal.

It's a basic procedure. You've got you poking and one of the tissues. So you can start this wherever you want. Where are we now, as it relates to PSA testing, and where are now as to perhaps other tools that we have to better

assess if somebody actually needs a biopsy or not?

Yeah, great question. I mean, so, you know, I think prostate cancer, if you look at it over the last few decades, has changed so much. Right. And you talk about PSA and that really has been a game changer because before PS A, we found prostate, cancer only when it was too late to cure it, and there was not much we could do.

Now you introduce PSa in the early nineties and we're finding cancer so early, We don't even know what to do with it. So we treated it, and then we kind of realized that the side effects of the treatment were worse than the cancers.

And I think going through the whole task force recommending against screening was an interesting exercise because it showed a few things. that there was a way that you could change behavior.

You did see, after that happened, a lot of people who really got that risk versus benefit message start to push active surveillance. And I think a of the committees that said there's no benefit to screening really made that recommendation, thinking that we were never going to see the kind of uptake of surveillance that were seeing today.

The second thing is, while we add all these trials to kind of tell us that screening probably helps and more and data we get, the more it seems to tell it is.

You didn't have the actual real world experience of seeing patients coming in with metastatic disease because they never got a PSA and their doctor never talked about it with them.

And a lot of people had those stories. So, I think having that experience, has brought us back to kind of coming to a point where most people agree that screening for prostate cancer does save lives and PSA is probably the best tool we have right now to do it.

Now, we all agree it doesn't help us decide who needs a biopsy or not, it does not help decide whose got a high-risk cancer and who doesn´t, but it helps us to decide, who need to have at least some further evaluation to make sure they are going to be okay from that standpoint.

And just like, you know, anything for the heart or the chest, when you get a chest x-ray and you see a small nodule, You don't go right to pithoracotomy.

You know you got a CT scan and a biopsy and see all these things. Right in the past, we would do a PSA and run right through a Biopsi. But PSAs doesn't have that power.

A PSa just above 4 maybe, right? Yeah. Yeah, or even 2.5 at some points, right? Because they said, you know, now we're missing all this cancer below for it.

We didn't know. So, I mean, we created this huge situation where we were just having such a low threshold to look for cancer, a load threshold, to treat cancer and guys were suffering, but I think we've learned from that experience, so I thing the way I look at it now is we do screen widely because there are benefits to that.

I thin we are more selective about who we'd do it in. we aren't trying to do in older men. benefit will be, but then we intervene with evaluations and treatments selectively, right?

And I think this is where MRI has really helped. This is, where I've been biomarkers have really help to give people choices that they can use and some places the combinations of them make it an easier process.

And now we're doing better biopsies, you know? So, I, think the spectrum has come a long way. I Think we still have a, long, way to go in terms of improving our overtreatment.

And there's obviously still men that get undertreated, right? Cause we still have guys dying from prostate cancer and we're still not catching them early enough.

I know. You know, this week alone, first time ever, I mean, i've seen several in my career, you know PSAs of 20 negative biopsies, multiple negative Biopsys.

This week, alone two over 20, 23 and 25 biopsy by Samir Tanaja. So once it's Samira Tanajah, not questioning that. the quality of that biopsy, right? Yeah.

Negative, negative. And, and it's, it, this is, is a PI-RAD4 on a, on an MRI. and some years I call right, you know, even some, years, I got, yeah, know what I'm doing, but are we missing something?

So you, there's always room for improvement. So what is so speaking, taking this kind of example into account, what are the. Where do you get worried with PSA where you say, look, we know is not perfect, but look at this time we need to further evaluate.

Is there a number, I know it's age dependent. What does that look like for you? Yeah, you know, the way I look it more than anything else would be kind of an age appropriate PSa.

That's how I use it when I used it. So I look at a guy, you know, maybe in his 50s, if it's PSA, You know maybe two, that's still less than four, but for a guys in 50's that kind of on the higher side, and that is where I would think about, getting at least an MRI or something of that sort.

If it is less then one, I'm not so worried about things. I think, using it as a single cut off that way, making sure you repeat it, If did go up, because that could save you a lot of the excess cost of MRIs and other things that, once the PSAs goes back down.

But I think where I get worried about it is when we rely too much on it. Where I look at it, is this should be the signal that you're looking to kind of just pick out guys that need to look more carefully.

But the way you look them more careful is not with some PSA derivative or doing another PSa. This is where the biomarkers and the MRI really come in. And they're not perfect either.

You know, but, there are definitely a lot further along than just making a biopsy decision on the PSA, because then you biopsie a lotta people you don't need to, which ends up resulting in a lots of indolent cancer that you didn't even need And even if you manage to avoid the over-treatment, they have the burden of just being on a surveillance protocol for something that's never, ever going to hurt them.

And you'd been better off not knowing about it, you know? Right. I always say ignorance is not bliss, but sometimes it is. Like you don't want to find that Gleason 6 if don have it.

In pancreatic cancer, I guess, you wouldn't say that, but in prostate? In prostate cancer. That's right. PSA density? I find it valuable. I found it really valuable in terms of differentiating between BPH and prostate cancers.

So for the audience, PSDensity is actually a calculation that's PSa over the size of your prostate that typically would come from an MRI and somewhere around 0.15 is the cutoff.

Sometimes my cutoff, actually my caught off is 0.10 to 0.15 depending on other factors. I kind of, I want to keep it tight. What are your thoughts on PSA density and how do you use it?

Yeah, no, I think that's a great point. I, think of all the PSA derivatives that probably is the one with the strongest data behind it, because as you said, it kind of takes into effect the size of the prostate potential BPH, which is one of biggest confounders in terms of what else could be causing the PSA to go up.

So yeah, there's value. You know, use it with other factors that you're kind looking at, you know? How did you get your PSA density? Is it based on a DRE?

Well, then how accurate is that? Probably not very accurate, right? And then the ultrasound, if it's a trans-

abdominal ultrasound again, you're probably not the most accurate.

Right? So if you are talking about, um, a tritons rectal ultrasound to get that information, yeah, and that's good, but that is already, your half way here in the invasive part already.

And if your talking an MRI to it, again very good. But I would actually, I'd say the MRI itself. will provide a stronger prognostic value than the PSA density, right?

So I do think it's helpful in terms of if you see an MRI that's negative and you know there's that 10 to 20% of people that can have a missed, not so lethal cancer, but still significant that you may want to know about.

That's where I think PSD density helps you. And that is where these biomarkers can be helpful too. But PSAs density is one you get for free. So if it is high, that may alert you to something that the MRI may be missing.

Right. Right So then we have these, uh, non PSA based biomarkers, urine tests, which I've been very excited. I use probably, I used it probably several times a day, just because it's easy.

And, and I like things that are not PSa based. Uh, there are other biomARKers that PSAs based, but if we're saying that PSA is a problem, then all these other, re I don't know the algorithms, But, they, have to be some level of a, problem too, particularly if they have a high PS a from BPH.

and i've seen so high scores in. some of the other biomarkers, just my assumption is because the PSA is high from BPH, so a lot of false positives. Non-PSA based, like XODX tests.

How do you use this urine test? Tell us a little bit about it. And so we have to make the assumption that no one knows what this test is or what it looks like.

So tell us little about and how you how use it in your clinic. Yeah, so the XODX test is a urine-based test and it's a urinary collection that you actually do pre-DRE.

For a lot of urine tests, they actually require you to do a DRE first to kind of massage the prostate and get some prostate secretions into the urine itself.

PSA Density, MRI, and Biomarkers

Logistically, that can be a challenge because most patients don't like it. A lot providers don' even like. So this eliminates the need to do that. And what they actually look for is unlike a midstream urine, which most patients are used to collecting, they want the first bit of urine because that actually comes from the prostate.

So it's almost their way of doing that, getting that post-DRE prostate secretions without the DRE part. Then it really centers around this concept of exosomes or what the call extracellular vesicles.

These are little tiny packages that every cell secretes. for various purposes to communicate with other cells, to prepare the microenvironment they're in.

And we think that cancer cells secrete them about 20 to 30 times more. So they secreted them into circulation, urine, plasma, anything. You can actually identify them in there.

Localized tumors, unlike let's say CTCs or self-recirculating DNA, where you're only talking about very advanced tumors and mostly dead material, right?

These are secreted by localized tumors and they're packaged in this like little semi permeable membrane. And the importance of that is that means that all the RNA, the DNA, protein, and the fats that are in there are preserved.

So you can actually get these exosomes and get this material out. The importance to this materials, I guess, is they

serve as almost like cargo of the parent cell that secretes them.

If you're a tumor cell and you are secreting these things out, they are basically like a little repository of yourself. So you can actually get them and extract the RNA, extract, the DNA, abstract the protein.

And there's a ton of biological data available to you that is coming from the tumor. Now, we are used to kind of doing this in terms of tissue-based tests.

We were talking about decipher and things like that, where you're actually looking at the tissue, but most of that involves an invasive biopsy. Now if you can get the same information from a urine or blood test or things like that, that's very powerful.

And I think what's cool about this exosome test is what they look at is just a couple genes. They do what the call a PCR to kind of amplify some genes and they two particular genes known to be associated with prostate cancer and to see are they expressed more.

So they're really looking for a very key prostate sensor signal. But at its basic form, it's kind of a cruder version of an amazing technology because they have the ability to really interrogate the entire exosome.

I'm sure you get a lot of people talking about the future of medicine with AI and how all these other things will improve. We're going to be having so much data, RNA sequencing, proteomics, metabolomics.

All of that coming from these little particles that are secreted from the tumor. Just think about things we can learn about people's tumors, just non-invasively, serially.

So I am obviously excited about it. It's incredibly exciting. Now, and for many reasons, certainly from my end, as you know, I'm a natural doctor and holistic doctor.

Less is sometimes more for the principles and the philosophy of natural medicine. But I do think that, the fact that ignorance is not bliss. Some people come and they don't want to know.

You want know and then take action appropriately, whether it's no action. And you know what's the deal is or, or do something, you that medical treatments or whatever it is that you need to do.

Even lifestyle changes requires people to be motivated. You're a busy guy, You look very healthy to me. you're very busy, guy with three children at home.

It's impossible for you to go exercise every single day. Just the mere nature of your, what I assume is your schedule, because I know my schedule. And if my scheduled is hectic, so is yours, right?

So it's very, but now when somebody has a diagnosis, they're like, oh yeah, no, this becomes priority, Right? And so the diagnosis can even help whether to choose to be more aggressive with lifestyle or with medical treatments or both, depending on what the situation is.

The cutoff for the ExoDX test is 15.6 at this point. Meaning that if it's from zero to 15, I believe there's about a 91% chance that there is nothing there that we should worry about.

If it is above 15.6, we need to pay attention. What's your cutoff? Right? Like if it's 17, are you going to say, oh, that's it, we need a biopsy? What, you know, cause I, I I'm not exactly, and I've spoken to Dr.

Scott, the developer, uh, developer of this, of the test and a few other people. And there's some, there a little bit of margin of error. Obviously this 30 and above is a different story, but.

You know between one, between 15.6 and even 20, how do you go about that? Yeah, great question too. So I mean, you know, I think the cutoff you're going to use it depending on what you youre trying to do.

You know? So, the way I look at it is, if I'm trying figure out if someone is okay and I don't need to worry about them, then like you said, 15.6 is great.

Cause if they're lower than that, they don t need any other evaluation. The data is very strong and they've got validation studies proving that. It's what happens if their above 15 point 6. Now, If they are above fifteen point six, does that mean they definitely need biopsy because they have cancer?

No. And I think the cutoff you're going to use to decide what you do next is going depend a bit on what your doing next. If what are you doing and all you have to offer is an invasive test like a biopsy, then you may choose a higher cut off.

And for me, I would say 30. So let's say I couldn't get an MRI somewhere to look for things. Because a pacemaker or some other reason, although that's rare nowadays anyway.

Then I would probably use a cutoff of 30, because I will have a higher threshold to put someone through that type of thing. But if the next test is an MRI, you know, which is not invasive, then I think 15.6 is a great place to start that conversation, right?

And if I see something, yeah, we're getting the biopsy, but if don't see anything, that I probably wouldn't do the Biopsi unless that EXO test was above 30.

You know? Because then, I'm worried that you fall into this bucket of guys, the cancer may not have showed up on the MRI. And there is a good handful of guys that fall into that.

And that's where I think that test has value with a different cutoff. Right.

ExoDx Testing and Active Surveillance

So this is, so the test is developed for people who want to know if they have the possibility of having prostate cancer that's significant, probably higher than a Gleason 6 in their prostate.

And then to do the next thing, whether it's MRI, hopefully that, and then eventually if that shows something, biopsy. For the last couple of years, I've done a little bit, something a bit different, or I added to that.

I'm super interested, right? So my guys on active surveillance, once again, they had a biopsie. And I know they oftentimes need a confirmatory biopsy a year later to just make sure.

Some of these guys are simply not doing another biopsies unless something drastically changes. Even though most urologists are saying, look, we need one another a years later, right?

But then they disappear. I don't want them to disappear! Right? The issues that I've seen with active surveillance or men on active surveillances is when they disappear for like decades, come back, now their PSA is 100 or 200. Right.

So for me, to keep them in and to keeps them motivated, I try to do an EXO test on men, on Active Surveillance baseline, and then do it every whatever, six to 12 months to see what that says.

And maybe that indicates, yep, you need either another confirmatory biopsy or even after a confirmitory biops you need one later on. Also, selfishly, I guess, clinically I'm trying to say, man, i'm wondering if all these lifestyle modifications, very prescriptive, every exercise, everything to E, certain supplements.

I wonder if that's doing anything. i really don't have a way of measuring that. PSA, you know, tends to stabilize actually very nicely, even decrease.

But if we're saying I can't bank on that, What if this exosome test tells me something? So then I use it for those two

purposes. Why don't you take it away and tell me, Gio, you're absolutely doing the wrong thing.

I'm going to call the government on you because you utilizing this test the right way and you are harming people. Or is there some value to the way I am utilizing on men on active surveillance?

Well, you know, I obviously think you're ahead of your time because I think most of us will probably be doing something like this as we get to the future.

And I. You know in a way the, the tests somewhat need to catch up to where, where you are, so I there's a lot of truth to. what you're saying, and as we know with prostate cancer, there's so much uncertainty about the biology, whether it's going to progress all these little things, right?

And so any information that we can get that reduces the uncertainty is going help. Like if you look at the elevated PDSA setting, we saw that MRI helped us reduce the number of biopsies we do.

If you add a biomarker, you get to do an even better job there. So MRI and active surveillance, again, delaying some of the biopsy to reducing the number we need.

If you add a biomarker, I do think there'll be improvements there because what I think ultimately will happen is we're going to get AI that's going improve MRI.

We're gonna get a lot more information out of an exosome test because instead of just looking at two genes, they're entirely look at the entire panel of prostate cancer related genes because it's not that expensive to do that anymore.

They're going to be looking at the proteins and the lipids that are secreted out of that. And every six months to a year, you'll have a chance to look at how these things are changing and comparing it to all these other guys.

So I don't think we're that far away from having some app where you upload all this stuff to some cloud and metadata, AI tool feeds back to your phone how your prostate cancer is doing.

And then you only need to do biopsies like, you know, very personalized. You know? Now I get it. There's a lot that needs to be done before we get there, but you're, paving the ground for, what that's going to look like.

So I agree with you. Now, I think you were involved in a study on active surveillance using that currently is currently ongoing. Can you talk a little bit about it?

Yeah. I mean, so, you know, they're doing exactly that. They're looking at men that are newly diagnosed with prostate cancer and they are looking to see how did an exotest right before their next biopsy help pick out who needed the biopsies, who was likely to have something worse there.

So I think it's going to be very good, because I do think we are going see that this does help us pick out men that may not be the best for surveillance or men who are ideal.

I also think what's gonna be more interesting is as these men continue going on in their surveillance journey, if we're able to continue getting that urine information on them.

Because like you said, a PSA is not the most helpful. But if there's a serial noninvasive marker that we could follow that tells us a little bit about the biology of their tumors like this, then it'll be a lot more useful to us as a non-invasive marker.

And we don't have a good one right now for surveillance, so it will be welcome. All right. Some final thoughts from you on where are we going? And even where do you think we're going to go with diagnosis?

Do you there is a future? without biopsy for prostate cancer diagnosis? You know, it's a tough thing. I think we're far

from it if we ever get to that point.

But unless we get to a stage where our treatments don't cause as much side effects as they do, you know, then I think we're always going to need to know for sure that we are doing the right thing and to help us select who needs that treatment, who doesn't.

You know if we find a way to give people a pill and it melts away their prostate cancer then maybe it won't, but we aren't there yet. Dr. Sinaj Poonen, thank you so much for being on this summit.

Future of Prostate Cancer Diagnostics

I think it's incredibly valuable information. This is the one episode where we're really honed in on diagnosing prostate cancer at a higher level. How can people find you if they are interested in being your patient?

I'm not as good as you, Dr Gio, in terms of all the social media stuff, but my Twitter is at sinajpoonin. i'm at the University of Miami Health Network.

So you know, you can just Google my name and it'll pop up there. Not a lot of other Sinaj punans doing biology. So that's my favorite. I did look that up.

And I was like, wow, there's not a, lot, Sanjay, many things there are a. But not Sinanj punan. Thank you so much for being on. Anytime, Geo. Look forward to catching up with you in person soon.

That's right. Thank you everyone for coming along and watching yet this other episode, diagnosis of prostate cancer. No one wants a biopsy. I get it. And there's enough tools out there currently and it's going to get even better to perhaps possibly one day avoiding one.

Thank for tuning in. Look out for the next episode coming up next and much love. Talk to you next time. So long. Thank you for tuning in to Doctor Talks.

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