Spencer Behr, MD: [Music] Thank you very much. Y'all hear me out pretty well? I'm Spencer. I'm one of the nuclear medicine abdominal imaging faculty at UCSF. Just out of curiosity, how many of you know what nuclear medicine is? I'll tell you, when I was a radiology resident, this is what I came to my mind. I was going to be working in this. It's going to be me, stating me as the Simpsons. But in reality, what is nuclear medicine? It's our ability to put radioactive material onto drugs and then watch that drug around the body. We can use it in various applications, anything from oncology, just physiology, to cardiac. We do it every day in and day out. How does it work? Well, we get this compound. It goes in and it produces radiation, and we put them underneath special machines, and those special machines allow us to see the images, or we get numbers that gives us information about a part of the body. Now, I'm going to focus in on a specific type. There's lots of different nuclear medicine. There's planar imaging, which just sees underneath a plate and makes an image. There's spec imaging. I'm going to talk about PET imaging. It's a subtype of imaging that we are tracking specific type of radiation. It stands for positron emission Tomography. It's dictated by the type of drug we inject into the patient. There's lots and lots of different choices, but we choose and tailor our application based on what we're trying to go after. In this case, let's give you an idea of all the different compounds that have been studied. I mean, the list keeps going on. I could have put dot, dot, dots there, but for years, we were going after all these different drugs. These are the ones that got FDA approved or have FDA approved imaging in prostate cancer. Why is it that we're going after all this? Well, because we're looking for specific targets. This is a cell. This is a cartoon cell prostate cancer and all these different targets in which either we've gone after from a drug perspective or from imaging perspective. Now, the story really started this is actually back when I was a fellow back in 2012, the compound that got first FDA approval, choline. Story didn't stop with choline. Then came another compound called FACBC or oximin. Then as Dr. Carroll was saying, this one really changed everything. In fact, the Germans were doing a lot of research with choline, and I was at our Society for Nuclear Medicine and they showed their graph of using choline, and then they showed their first image of PSMA PET. They literally went boom, it went off a cliff. They stopped using choline and switched right over to PSMA just because of how exquisite the imaging was. Why was all this excitement? Why was all this push for this targeted therapy? Well, back in the day, back when I was a resident in radiology, we only had a few choices for looking at patients with prostate cancer metastasis. We had CT, we had bone scan, and we had MRI. As Dr. Carroll would test data away until the PSA was almost in the '20s before they really started seeing true sites of disease. Then along comes choline. When they compared all these agents, they found that that number dropped. It went to 120th of what it was back in 2012. FACBC pushed it down even farther, and now PSMA. PSMA dropped it down to 100th of where we were. We are seeing patients with 100th of the PSA level where we were back when I was a radiology resident. What does PSMA stand for? Prostate Specific Membrane Antigen. We'll talk about that as later. Why it's a little bit of a misnomer. It's a transmembrane glycoprotein that's expressed on the cell surface of various molecules, and in this case, prostate cancer, which is 100-1,000 fold. I actually studied this back when I was an undergrad. I studied this because they knew about it. This was one of my senior thesis projects. Funny how things come back full circle. There are three FDA approved radiotracers. The one that helped with the UCLA UCSF helped bring to market was back in 2021, which was the gallium based agent. Then there's the F_18. There's another one that's FDA approved that we don't use. I don't think we use them much at all at UCSF, but the primary two that we use are these two, the F_18 and the gallium based agent. Unlike all of its precursors before it, we have the ability to treat patients. This little lutetium based PLUVICTO therapy, we have ability to knock off the imaging component and put on a therapy component, and that will be talked about in a little bit. How do you prep for these? We just ask you to be stable hydrate, drink some fluid. You don't need to fast. I don't know if any of you have ever had a FDG PET scan, but they're telling you can't eat four to six hours before your examination. Nope, take all your medications, drink your fluid, drink your coffee. You take all your medications, we give the medication IV. You wait about 50-70 minutes, and then you get your images. We only ask you to avoid prior to examination because of the fact that you got all that radiotracer going into the bladder. Show you a little schematic of what it looks like. This is the patient getting the

drug IV. You wait about 50-70 minutes. You go onto a scanner. This is our Phentermine UCSF. This is what we do a lot of our biochemical or current patients with. Then we get our images. This is where I come in as a radiologist. The technologist is the one who's going to be doing the imaging and the acquisition. I'll be the person looking at those images and trying to look for any sites of disease. This is what the normal image looks like. Lots of salivary glands uptake, liver, spleen, kidneys. Notice all the bowel and ureter. That makes it a challenge when we're looking for local recurrent disease because we're fighting what is ureter and what is bladder. Clinical indications for PSMA PET, it's really pretreatment. This used to be high risk based patients. This has been going smaller and smaller. We're moving more and more upfront in therapies. Biochemical recurrence, I think it's one of the most common indications that we do for imaging PSMA PET, either post prostatectomy or post radiation therapy, and then patients prior to getting treated because we have to make sure that it's expressing the PSMA before they get their therapy. Let me show you some examples, some images. This is a patient that was a high risk pre prostatectomy. I think it was one of Dr. Carroll's patients that showed this is what we used to do. We used to diagnose this. I'm an abdominal immature, I'm a radiologist as well. I used to do multiparametric MRI all the time. This is what a multiparametric MRI of the prostate Pyrites 5 lesion, left gland. Now, we have the ability of our pedometer to take all those pediatric images and fuse them together with our MRI images to be very confident. But then MRI is pretty confident in where the lesion is. How is this really beneficial to PSMA PET? This. This is something I made my jaw drop when we are looking at PSMA PET imaging. We would see things like this. I have to zoom it in to actually show you the finding. We see these tiny little lymph nodes that we would not see at any time or we would not call. But with the PSMA PET, it's a light. It's a clear light bulb, makes it very easy for us to make that determination of whether there's nodal involvement on the side of the cancer and helps direct therapies for that patient's. Here's another example. This is a patient. This is non-contrast CT, one small lymph node here, another one here, and a couple on the groin. Which one's positive? Well, this is what we used to have to look at when we're doing our staging CTs back in the past when we have to state, which one's cancer and which ones not. But now with PSMA PET we can go very confidently, there's our tumor. Those other lymph nodes, nothing there. We're very confident about seeing when we're seeing that, that is the tumor. That is, there is no other tumor in those lymph nodes, even though in all of our other imaging, those lymph nodes all look the same. Is that ability to go after that cell surface PSMA expression and be very confident that is where the tumor is. How good is it? Is it 100%? Are we seeing everything? Believe it or not, we're still not perfect. We're not seeing those microscopic sites of disease, 1-3 millimeter three millimeter nest of cells. Sensitivity is about 59% based some of the meta analysis, but a heck of a lot better where we were. Better than CT and MRI. Even when we had multi parametric, what is multiparametric? We're adding post contrast, we're adding diffusion, we're throwing the gambit of everything added on MRI PSMA PET still outperformed it. Here's just an example. This is a patient status prostatectomy, PSA 0.8. This is why we get our PSMA PETs. A lot of times our PET MRI because we're dealing with this. This is focus of uptake right in the middle. What exists right in the middle right there? Something when it was originally looked at in the PSMA PET, we're like, look, that's just the urethra. Nope. The urethra is more anterior there. That was actually an area of focal recurrence, but having the post contrast PET and the post contrast MR and the PSMA PET makes us very confident that's locally recurrent disease, not physiologic uptake in the urethra. Here's another example. These used to be languishing on our list because we're trying to fight all this artifact. These were all the brachytherapy seeds that we use to treat local. My dad got this for his prostate cancer. All these little seeds that are pregnant with radiation, but they cause a huge amount of artifact on the MRI. What we look for is these little wisp and ill defined areas of enhancement. But the PSMA PET made it very easy. Very confident that is the recurrence. Then we also were able to say that there's no other evidence of disease. Here's another example, another patient status post prostatectomy. On MRI, we're looking for areas of abnormal enhancement. Abnormal enhancement in this area is white. That is an area of enhancement. We're pretty confident on the MRI. PET helped. It makes us a little more confident, but where the PSMA PET really shined in this case is here. We get the full scale full body evaluation. The

patient would have probably been treated with local radiation, probably pelvic sidewall. But in this case, we saw this. This would not have been expected. Bone scan would have been negative in this patient, no doubt about it. But on the PSMA PET MRI, we could clearly say the patient go metastatic disease with an area of uptake in the rib and thoracic spine, and these went on to be radiated. PSA after this went to zero afterwards. How much is we changed impacts? This is a meta analysis, and this has been done several times. About 50% of the time when a patient gets a PSMA PET, it altered patient's management. Why is that? Well, as I showed you in that case, it included new areas of treatment, especially on radiation or surgical approach. Big thing here. Patients that would have gone on to ADT or systemic therapy, we were able to give information to either Steve or Dr. Carroll to be able to say, look, this patient can go to surgery, this patient can go to radiation and they could hold off on getting systemic therapy and try and just pluck off those lesions as they come on. Now, I want to talk a little bit some other cases. This is a 75-year-old with PSA of 10.1, so very elevated PSA. These are always struggling cases for us, this is even abdominal imagers. This is anterior fibro muscular stromal tumor. I know this can be challenging to biopsy too because it's right in the path of the urethra. On MRI, this is the classic appearance. We described this as lentiform appearance, restricted diffusion. This is all classic. The patient got a PSMA PET, and this is what it looked like. I remember my colleague, this was a case back when we really first started using a lot of PSMA PET. It was Antonio Westfaln and we sat there and we looked at this case together. Was that uptake in the bladder? Was it misregistered? We followed this one even though it had no uptake to surgery, and this ended up being confirmed surgical cancer. Why do I put this case in here? It's because of the fact that while we'd love to say this is an end all be all for staging and every patient is going to have PSMA expression. There are some types of cancers that do not have PSMA expression. While the vast majority greater than 90% of them do, not all of them do. It's not a like no uptake, we're good. Conversely, we always are challenged with this. This is a patient with biochemical recurrence. We see this uptake in the rib. We would look at these all the time in our tumor boards. See this intense uptake. This is all along the rib. As a radiologist, my first thing is to do is to look at the CT because of the fact that I'm looking for this. Rib lesions are quite common on our PSMA PET. A lot of times and most of the time, it ends up being something not related to cancer, especially low level uptake. In this case, it's an acute rib fracture. Why is there PSMA uptake? It's inflammation. When we get patients with various inflammation infection, synovitis, fractures, it can all have some PSMA uptake. That's why I'm going to come back to that as in the prostate membrane antigen. Is it really 100% specific? No, unfortunately, it is not. It is found in other things we always have to read within the context of the patient's case. We've seen lots of other malignancies. We've see lung cancer, rectal cancers, GIST, head and neck, desmoids. We've had a hepatocellular carcinoma. But we see a lot of benign things too, liver hemangiomas, schwannomas, sarcoids. We've seen fibrous dysplasia is always that frustrating one when we're dealing with the bone, trying to figure out whether it's a benign lesion or a malignant lesion. The way I always approach it if it doesn't look classic for a metastasis or a metastatic area, I always think of other potential etiologies. To show you some examples. This is a benign lesion, this is fibroelastoma, atelectasis, this is part of inflammation, lung that doesn't expand. This is why you see a low level uptake. Here's an example of a different neoplasm having uptake. This is a schwannoma and this is a head and neck cancer. In summary, PSMA PET has really changed our world as radiologists and as nuclear medicine and the clinical. It is exceptionally sensitive, even though we get the super low PSAs. It doesn't mean we're going to see it. I always think that caveat 0.2, 0.3, 0.4, 0.5. We still may not see it, but we can see disease at 0.2 and even at 0.1. Uptake is not as specific as the name would imply. There's lots of other things we have to always think about in the back of our mind when we're going through the examinations and most but not all cases are PSMA PET. Thank you very much. It was a pleasure. Thank you. [Music]