CONDOR Trial and PET Scan Technology

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Welcome to Yale Cancer Answers with doctors Anees Chapgar and Steven Gore. I am Bruce Barber. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about Nuclear Medicine and PET Scan Technology with Dr. Lawrence Saperstein. Dr. Saperstein is an Assistant Professor of Radiology and Biomedical Imaging and Chief of the Nuclear Medicine Program at the Yale School of Medicine, where he is also the Program Director of the Nuclear Radiology Fellowship. Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital.

Gore That is a bundle of titles you have got there. Biomedical imaging, nuclear medicine, sounds very, very complicated.

Saperstein I am a nuclear radiologist.

Gore What does that mean?

Saperstein Nuclear medicine or nuclear radiology is a subspecialty of diagnostic radiology. It is a little different than what most people think about radiology. Nuclear medicine involves imaging based on physiology or how structures are functioning rather than purely anatomy when we think of CAT scans or MRIs; those images are primarily based on anatomy. In nuclear medicine, we inject a substance into patients’ bodies, in the vein, and they are taken up differentially by areas of the body based on function. So, we are generating images based on physiology rather than anatomy.
Gore: And the stuff that you are injecting tends to be radioactive right?

Saperstein: That's right. In essence, it is radioactive. It is a small amount of radiation. Some people think of it as comparable to a CAT scan, that puts it in a perspective that patients can understand. So, it is a small amount of radiation.

Gore: Aha. And then, you have got some camera that is counting, that is detecting the radiation like Geiger Counter basically?

Saperstein: There is a camera and it detects the radiation that is omitted or comes out of the patient, and from that information, we generate the images. We also treat patients in nuclear medicine, commonly thyroid cancer - the most common forms of thyroid cancers are treated with radioactive iodine. Patients ingest radioactive iodine and the activity goes specifically to the thyroid cancer cells and kills the tumor cells. So, nuclear medicine is a combination of diagnostic imaging and therapy.

Gore: That's very interesting. So, we hear a lot about PET scanning and that is one of the nuclear medicine tests, right?

Saperstein: That's right. PET scanning is becoming more and more important in nuclear medicine. PET stands for positron emission tomography.

Gore: I am so glad you told me that.
I haven't done physics in a few years.

Right. So, basically it involves again an injection of a radioisotope and the difference with PET scanning is that it is a 3-dimensional relatively high-resolution clear image of the function of bodily structures. So, we do PET scans for a variety of reasons in nuclear medicine, but most commonly for cancer. We can image a number of cancers. The most common cancers that we image in PET scanning are head and neck cancers, lymphoma is a big one, lung cancer, esophageal cancer, pancreatic cancer, colorectal cancer and more recently the prostate cancer and neuroendocrine tumors. that is a particularly exiting area of nuclear medicine.

Well, how does the PET scanning thing work? Let's say, I mean, I have patients with lymphoma and I order a PET scan and I get some pictures back with some bright dots, like what is going on there?

It is a great question. So, the most common form of PET scan utilizes the injection of basically an analog, something very similar to sugar or glucose. So, the idea is that tumors take up more sugar or glucose than normal cells. We call this metabolism. So, tumors are more metabolically active than regular non-cancerous cells. So, we inject this analog of sugar and it is taken up by tumor cells more readily and they look brighter on a PET scan and that is how we can identify the lesions. So, we use PET primarily to diagnose cancers and assess treatment response after therapy. It can be very helpful in that sense.

Yeah. It is really fascinating, and you know, I don't know if our listening audience has ever seen them, but I mean, the degree of detail that can be seen is really astonishing right?

Yeah. It is remarkable. And in addition, with the PET scan at the same time, a low-dose CAT scan is obtained. So, again remember, CAT scan is for more anatomy and PET scan for physiology. And what we do is, we have the computer fuse these into a single image, which is a PET-CT scan and that really helps maximize our ability to localize lesions. So, we see the activity on the PET scan and then we can determine exactly it is on the CAT scan. We call this fusion imaging.
Gore Well, I can say out of recent patient experience just to put this in perspective, we had a patient who we did not really know what was going on, we did not know if there might be a lymphoma going or an infection and we did a PET scan and the person did not really had anything localize symptoms wise and 2 bright spots popped up in lymph nodes in the chest and surprisingly it turned out to be infection when we biopsied them and it was really a spectacular find, and we could not have done without the PET scan I think.

Saperstein Right. You know, we are finding that PET is extremely sensitive, so we are able to detect smaller and smaller lesions. What is interesting is, it also can detect infection as you noted. So, we may in the future be using it actually to detect areas of infection in patient’s bodies in addition to cancer.

Gore So, how does PET, you mentioned that CAT scan is more anatomic, then we have MRIs as well, I mean do you make the decision about what tests patients should have or you talk with the clinician or the clinician just decides?

Saperstein Yeah. In general, it is sort of a multi-disciplinary approach. You know, the patient has a particular problem, let us say it is lung cancer, sometimes they work it up with a CAT initially, but really PET-CT is probably the best way to evaluate and stage cancers of that nature. So, it is a discussion that goes on between the radiologist, the oncologist and other members of the clinical care team.

Gore Gotcha, and I presume that the procedures are mostly covered by insurance similarly?

Saperstein Yes. You are lucky enough, most cancers are covered by all types of insurance. At this point, it is really the standard of care in the imaging of many tumors. So, I think it is, you know, over the years, it has become a very important part of our ability to image and stage tumors. You know, PET has not been around as long as some of those other modalities. It was actually created, discovered in the 1970s, but it did not really enter the clinical arena until about 20 years ago on a regular basis. It is
striking the number of PET scans that we do every year is really increasing. So, I think the role that it plays in cancer management is big.

Gore  So, where do you get the radioactive chemicals from? Like, is there a radioactive pharmacy or?

Saperstein  Well, it has to be produced in a cyclotron. So, most of these agents are produced off-site, even though we do have a cyclotron at Yale.

Gore  Is this like some kind of a nuclear reactor, am I right?

Saperstein  Nuclear reactor-type setting. And the agents have a very short half life. So, what that means is there is not much time between when the agents are created and when they do not have any more radioactivity. So, we have to work relatively quickly. The good news is that the radioactivity does not stay in patients very long. So, that is usually a common question because people get concerned about radiation when they are having any type of scan.

Gore  That really sounds scary.

Saperstein  You know, it sounds scary but it is not that scary. The amount of activity is small, again kind of like a CAT scan and by the time the patients leave the department for these imaging studies, most of the activity is out of their body.

Gore  Well, I can tell you that I have a nuclear stress test last year and you know, I did not think much about it, but when they brought a little vial or a syringe with the radioactivity and it is like in a lead case and stuff, like wow! this is like serious business.
Saperstein Right. You know, I think it is serious business. Imaging again deals with smaller doses, nuclear medicine also treats patients and when we treat patients, we do use higher activities and that is when we are more cautious. So, you know, that sort of leads to a couple of exciting developments in nuclear medicine. I do not know if we have time to discuss those today.

Gore Go right ahead.

Saperstein Well, I think more recently, Yale as a site in the recent CONDOR study, which is a very exciting trial that deals with prostate cancer and an agent has been created that specifically binds to something prostate-specific membrane antigen or PSMA. I will try not to use too many acronyms today. But, PSMA is an interesting protein. It is on all prostate cells, but it is over-expressed or it is more abundant in prostate cancer cells. So, what is really exciting is, this is a small molecule that binds specifically to PSMA. So, we are able to image prostate cancer much more accurately than ever before. So, the hope of this trial is earlier detection and the initiation of the best therapy for patients obviously with a goal of improved outcome. So, we are really excited about the CONDOR trial.

Gore So, which patients are eligible for such a trial? Do they have to have a diagnosis of prostate cancer?

Saperstein The way we are using these agents now is in patients who have a diagnosis of prostate cancer, so have had some form of treatment, either surgery or radiation, and then their PSA, which is an element of the blood that is followed closely by doctors in patients who have prostate cancer is starting to go up.

Gore Okay. So, they have been rendered cancer free as far as anybody knows and then there is some hunch that maybe things are getting worse based on this blood test and so you are using this nuclear test to see if you can visualize the occult cancer?
Saperstein: Exactly. So, right. The situation is that the PSA in the patient's blood is rising, all of the conventional or standard imaging such as a CAT scan or a nuclear medicine bone scan are negative. They are not showing the tumor but we know that the patient has a recurrence on some level, whether it is in the prostate area or outside of that. And that is really important in terms of treatment. So, these agents, at least preliminarily have shown that they are much more accurate in detecting recurrence at a much lower PSA level and a much smaller degree of tumor burden. So, it is really exciting. We can treat these cancers, know exactly where they are before, earlier than we were ever able to do before.

Gore: Do you have any anecdotes of the kind of things that you have found on those scans?

Saperstein: Well, again, it is a trial in progress, but some of the preliminary data is quite striking. These agents are very sensitive and remarkably specific.

Gore: So, do you find small lesions in the bone that could not be picked on a bone scan or are they most finding things in the prostate?

Saperstein: Both, actually both. And what is amazing is that the lesions we are finding are smaller than would be normally detected on any other imaging study.

Gore: That is so interesting. I remember, you know, I deal mostly with leukemia, so I do not have to, you know, isolate tumors that often, but sometimes I do of course, but I remember when I was in my fellowship training quite a few years ago and I was caring for somebody, I do not remember what kind of cancer she had but it was something that we used one of these markers - CEA, I think is the one that we were following and it was just going up and up and up...we visualized her and visualized her and visualized her, and could never find the cancer until she was really almost on death store eventually, and it was way before the PET scan days, and I wonder have we had access to these diagnostics, whether we might have, should have been able to localize whatever was going on.
Saperstein       That's right. Right and I think what we have seen is a real change in the development of our ability to see things earlier and in much smaller size than ever before. But what is also particularly exciting about nuclear medicine is, not only are we using these agents for imaging but we are now starting to use them for treatment. I would love to tell you about that if we have time.

Gore       Well, we might have time in the second half of the show, but right now we need to take a short break for a medical minute. Please stay tuned to learn more about nuclear medicine in cancer diagnostics and apparently therapeutics with Dr. Lawrence Saperstein.

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This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable. And as a result, it is recommended that men and women over the age of 50, have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents resulting in more patient-specific treatments. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

Gore       Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest Dr. Lawrence Saperstein. We have been discussing nuclear medicine imaging and in particular PET scanning among others for cancer diagnostics and research. You know, this is so exciting for me because I am not really a total geek, but I do love, you know, running by these pictures and you know that we can download on our patients, right? You know, the old days, which was also fun, we used to go down to the, you probably were too young, we used to go down to the radiology reading room where they had all these films from x-rays and CAT scans on these readers and we had to go, you know, find the grace of the radiologist, you know, pull up your scan and we always felt a little bad, but they were always happy to show you around, but you know, nowadays, we just go on the computer and we can look at the pictures ourselves which for some things that I can do now, MRIs - I cannot do that at all, but it is pretty cool technology I have to say this - this nuclear medicine stuff.
Saperstein  You know, that is one of the things I really love most about -- radiology and nuclear medicine is it’s constantly changing, developing new technologies, really every year - there is something exciting that is coming through the pipeline and what is really wonderful is that a lot of these agents are developing into therapeutic modalities where we can use the imaging technology and harness it to treat patients with cancer.

Gore  When you told me about the iodine story in thyroid cancer, what else is new in that?

Saperstein  Right. Iodine has been around for a while treating, differentiated with the most common types of thyroid cancer.

Gore  Because thyroid cells like iodine, they need to make the hormone right?

Saperstein  Right. So, iodine-131 is the radioactive agent and it emits a beta particle that treats the cancer. Along the same lines, there is recently FDA approved agent called Netspot.

Gore  Netspot? Sounds like something you get, you know like, on your TiVo or on your Roku. You get a Netspot...

Saperstein  I am always amazed how they come up with these names. I think the Net is really derived from the fact that it images neuroendocrine tumors.

Gore  What is a neuroendocrine tumor?
Saperstein Right. So, neuroendocrine tumors are uncommon tumors, the most common type that we see is something called carcinoid tumor, and what it is is an agent that binds to the somatostatin receptor. I know I am using a lot of big terms. Let’s keep it simple - so neuroendocrine tumors express the somatostatin receptor.

Gore So, they want to be like gland tissue, right? They want to be like endocrine gland tissue kind of?

Saperstein That’s right partially. So, what we have now is this Netspot compound that uses again a small amount of radioactivity and binds specifically to these tumors so we can see them more accurately than ever before. So, Netspot is another imaging agent.

Gore Gotcha. To find these carcinoid tumors.

Saperstein That’s right.

Gore And if I recall, these carcinoid tumors - they have all sorts of weird effects on people like making them diarrhea and flushing and very difficult to live with. They are not so terribly malignant right, but they really wreck havoc on a person's life?

Saperstein They can and they can be challenging to treat. So, I think that is the really breakthrough. So, now that we have Netspot to image these tumors, here comes another one, we have Lutathera. Okay, so, Lutathera and Netspot together really comprise a very exciting area of nuclear medicine called theranostics okay, and let me explain..
Gore That sounded something you go to like Sedona, Arizona and get some new AG theranostics.

Saperstein Right. So, theranostics is a term that was coined by combining the words therapy and diagnostics. So, there we have theranostics. But what's really exciting about theranostics is that we can take the binding site that we use for imaging, change the radioactive compound to something that can treat patients rather than image them and we are treating them specifically with the Lutathera, which kills the cancer and does not really harm a lot of the tissue around the cancer.

Gore And this is an FDA approved drug?

Saperstein This is the first FDA approved agent of this nature. We are doing this routinely now in patients. So, I think that is particularly exciting area in nuclear medicine, which I find fascinating.

Saperstein Well, there is a protocol for Lutathera. Right now, we are treating patients 4 times every 8 weeks.

Gore Four times once a week or?
19:58.800 --> 20:04.900
Gore Gotcha. I see. So, one dose and then another treatment 2 months later, like that?

20:04.900 --> 20:05.800
Saperstein That's right.

20:05.800 --> 20:07.900
Gore Okay. And then, then what happens?

20:07.900 --> 20:24.500
Saperstein Well, that's a great question because since we have just started doing this, we are still in our first round of treatments. So, patients have responded very well and you know hopefully they will not have to have another course of Lutathera, but we are not there yet.

20:24.500 --> 20:31.400
Gore And are they able to get re-treatment with Lutathera if the numbers start getting worse, or you can only treat it?

20:31.400 --> 20:41.200
Saperstein You know, I think the jury is still out on that. These are, you know, again insurance does cover Lutathera, they are expensive treatments but it is the first FDA-approved agent of this nature. So, I think we will just have to see.

20:41.200 --> 21:26.800
Gore That's very interesting. You know, during the break, you and I were talking about an area in which your group coordinates with our group for very resistant leukemias and in a study called Iomab, patients are getting radioactive antibodies that basically wipe out the bone marrow in the context of a stem cell transplant and as I was telling you during the break, I send some patients out to Seattle where this was originally developed quite a few years ago when they were early in the development of this agent, and I know of at least one patient who is probably cured 10 or 15 years later, so it is really cool. That is another iodine-based, would that be considered as theragnostic or?
Saperstein   You know, I think it would be a form of theragnostics right.

Gore       Because they have to get imaged first too right?

Saperstein   That's right. So, the imaging defines the extent of the tumor and then we swap out just the radioactive particle from something that is used for imaging to something that is used for treatment.

Gore       It's interesting. And for leukemia, that is important because leukemia is all over the body and they want to make sure, I guess that you know, they are not delivering too much radioactivity to sensitive areas like the liver or something like that.

Saperstein   That's right. And you know, these types of dosimetry is the word that we use. It is the amount of radiation that normal tissue is exposed to. So, these have been worked out and really there is not a lot of damaging effect to normal tissues in the body. But in Lutathera, it is here what is particularly exciting is that this is really just the beginning - you know, we are going to harness the power of this modality to hopefully treat cancers in a way that they have never been able to be treated before.

Gore       So, do you have anything next on the horizon that you can tell us about?

Saperstein   Well, actually yeah. Moving along with the CONDOR trial, which is an imaging trial...

Gore       That was that prostate one?
Saperstein: Right. So, that one binds to prostate-specific membrane antigen. There are agents being developed again not to image but to treat prostate cancer. So, we are about to initiate a trial which used the same concept with just treatment rather than imaging. Same idea as Lutathera and it is linked to the small molecule that binds to PSMA which is overexpressed or more abundant in prostate cancer cells. So, really, I mean it is a wonderful exciting time in nuclear medicine and you know, I am thrilled to be involved with it, I must say.

Gore: I have to say I am just a pointed in the choice of the CONDOR for something for the prostate, where I might have preferred platypus or porcupine?

Saperstein: Yes, that would be reasonable.

Gore: I think you should give them feedback about that.

Saperstein: The last study we did was the osprey trial.

Gore: Really. So, is it the same company?

Saperstein: Same company.

Gore: So, they like birds of prey?
Saperstein     I think they like birds of prey.

Gore        And osprey particularly nice for Connecticut.

Saperstein     Is that right?

Gore        Well there is a lot of osprey here. At least in Branford, we get a lot of osprey in the right season.

Saperstein     But, you know, it is really like a brave new world of nuclear medicine. It is a revolution or it is a really exciting time and the hope is that patients will really do well with this new agent.

Gore        Well, it sounds to me like to do your job, you need to understand a lot of physics right?

Saperstein     You know, there is a decent amount of physics in nuclear medicine.

Gore        I would hate that. I like physics really, but it is hard.

Saperstein     I think it is interesting. For me, what I love most about radiology and nuclear medicine are the images. You know....
Gore You know, I am saying the same thing with the geekiness, you know that.

Saperstein Just more of a visual way of looking at disease. You know, now it is really fun and exciting because we get to interact directly with the patients and we are seeing great results with these compounds. So, it is very exciting.

Gore So, do people who are going into nuclear medicine, do they have to do a regular training in diagnostic radiology to start or?

Saperstein Most people go through a standard diagnostic radiology residency, so it is 1 year of internship in either medicine or surgery or subspecialty, 4 years of diagnostic radiology and then most people do at least a year of a fellowship and in this case, it would be a nuclear radiology fellowship.

Gore I see and they probably had some exposure to nuclear medicine during their radiology residency?

Saperstein Yes, nuclear medicine training is part of the curriculum for diagnostic radiology residency with that extra year just sort of they are inundated with more nuclear scans and PET scans and therapies so they are ready to take the helm.

Gore A year is enough? It does not sound like a year would be enough.
Saperstein    We are busy.

Gore    And do people in nuclear medicine subspecialize then, I mean are there some people in your group who do more one thing than other or you all kind of generalize right now.

Saperstein    You know, we all are able to read and interpret nuclear medicine studies on all levels. We all treat patients, you know, everyone has their little niche, some people are more inclined to study cancer therapies and imaging, others maybe neurological disease and other big area is the evaluation of dementia patients that is something that is developing in nuclear medicine.

Gore    Really?

Saperstein    There are a couple agents that are very helpful in the diagnosis of dementia.

Gore    What is that like? Can you tell me anything about that?

Saperstein    Well, basically, the clinical diagnosis of dementia is difficult in exact. So, there are agents we use - one of them is the glucose analog that we talked about before that show typical patterns with Alzheimer's disease and there are other agents that bind to a protein called amyloid in the brain and those can be very helpful in diagnosing Alzheimer's disease. So, nuclear medicine really runs the gamut of medicine, with cancer, heart disease, those were done by the cardiologists, neurologic disease and all physiologic processes in the body.

Gore    Interesting. And you mentioned that Yale has a cyclotron. What is that used for?
Saperstein: Well, Yale has a dedicated PET research center and they are doing amazing things down there -- discovering and developing novel tracers that can bind disease. They work with humans and animals, so it is really a remarkable facility. I am more involved with the clinical arena in the Smilow Cancer Hospital, but you know, I only have wonderful things to say about the PET center, it is truly amazing.

Gore: And they are in your same department?

Saperstein: They are in the department of radiology and biomedical.

Gore: But it is more of a??

Saperstein: A research center.

Gore: Yeah, but you are research as well, but it is more about developmental research. Yeah, I have driven by it, but I never knew what it was really so...thanks for enlightening me about this.

Saperstein: Yeah. I feel really fortunate to be involved in the treatment of these patients and these exciting technologies. It is really a thrill.

Gore: So, when you have given treatment like the Lutathera or any of these things, do patients come back for follow-up with you or they are followed by their oncologists?
Saperstein  It is a multi-disciplinary follow-up. They are seen by their medical oncologists, GI oncologists specifically, we see them when they return for their therapy, but most of their medical care is done by the medical oncologists and the follow-up.

Gore  So, at the end of the day, you really do not know necessarily how much of your work is reaping benefit right?

Saperstein  Well, actually that is a good point. We do have regular meetings with the multi-disciplinary tumor board and we discuss these patients to see exactly how they are doing.