A physician's experience: Theranostics offers personalized care for prostate cancer

Professor Joseph R. Osborne, MD, PhD, chief of Molecular Imaging and Therapeutics, and professor of radiology at a leading academic institution's hospital in New York City, NY, USA, discusses theranostics and its rapidly expanding role in prostate cancer care.

By Sameh Fahmy | Photography by James Farrell | Data courtesy on file

Osborne's colleague, a professor of urology, led the team that developed the first monoclonal antibodies to prostate-specific membrane antigen (PSMA) that effectively bind prostate cancer cells. The team later showed that after an antibody binds to PSMA, the antibody-PSMA complex is rapidly internalized into the cancer cell. In the early 2000s, they applied this knowledge to pioneer the application of PSMA-targeted agents to treat patients.

Advances like these laid the foundation for the March 2022 FDA approval of a PSMA-targeted radioligand therapeutic agent for the treatment of advanced prostate cancer. This milestone allowed Osborne and his colleagues to transition from exploring the potential of PSMA targeting in a research setting to applying the theranostic approach in routine patient care.

"As soon as it became available clinically and was approved, we jumped all over it," says Osborne, who is also chief of Molecular Imaging and Therapeutics at his institution. "The thing that we were working on became something that was of immediate impact to patients."

What is theranostics?

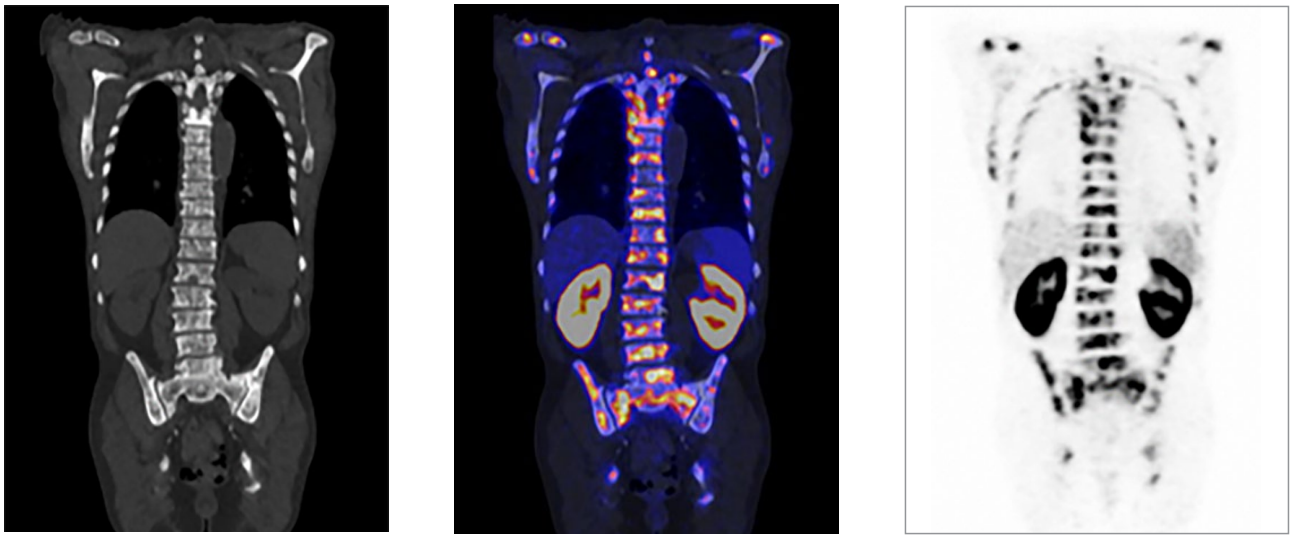
Theranostics is an innovative form of personalized therapy that focuses on both the accurate selection of patients and providing them with targeted radioligand therapy to improve their prognosis.[1] Theranostics refers to a process involving structurally similar diagnostic and therapeutic agents that share a molecular-specific target. Molecular targets are proteins on the surface of cancer cells and where the radioligand will bind. Throughout the theranostics process, molecular imaging techniques are used to identify, personalize, and monitor therapy response. Pharmaceuticals, such as radioligands, can be used to target and treat specific areas.[2] A radioligand is made up of a radioisotope that damages cancer cells and a target ligand that binds to specific markers on cancer cells.

Establishing a theranostics program

Osborne says patients are increasingly seeking treatment at his institution after learning it offers theranostic treatment, and he is open to sharing his experience establishing the program at his institution. He also wants to ensure all eligible patients—including those who have historically been underserved by the healthcare system—have access to such a promising development in prostate cancer care. "Of course, quality is really important. It's not like hanging a bag of saline or even administering chemotherapy. One has to go into this intentionally and with the right equipment, people, and instruments."

Besides diagnostic imaging that includes PET/CT and SPECT/CT, the theranostics care pathway also requires a clinical team trained to work safely with radiation. A floor plan that enables the sequestration of patients in rooms where they can access designated bathrooms without posing a risk to other patients is essential. Osborne notes that nurses, physicists, and technicians at his institution are well-versed in the treatment protocols, and newly recruited radiologists come in with the expectation that they will work closely with patients.

Theranostics for prostate cancer can involve medical oncologists, radiation therapists, and urologists. Osborne says. "It really is a team



^{68}Ga-PSMA PET/CT coronal images of patient John. From left to right: coronal CT only, coronal fused PET/CT, and coronal PET only. Data courtesy on file.

Diagnosis and patient selection: John's PET/CT scans provided data showing he was a strong candidate for theranostics to treat his advanced-stage prostate cancer.

Personalized treatment: Osborne and his nuclear medicine team collaborated to provide personalized treatment for John.

approach, and it has to be a team approach if you're going to get the right patients into the program. No one single modality or one among us is going to do it."

Theranostics care pathway

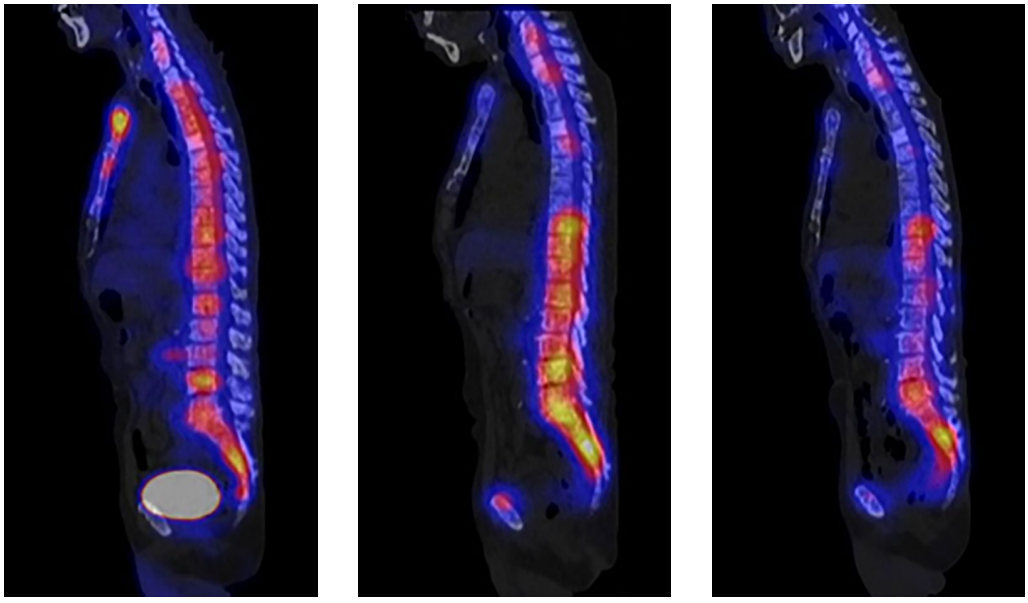
The theranostics care pathway involves a series of steps and a range of laboratory diagnostic and imaging modalities. Beginning with patient selection, the additional steps include personalized treatment, therapy response monitoring, and follow-up and survivorship monitoring.

Diagnosis and patient selection

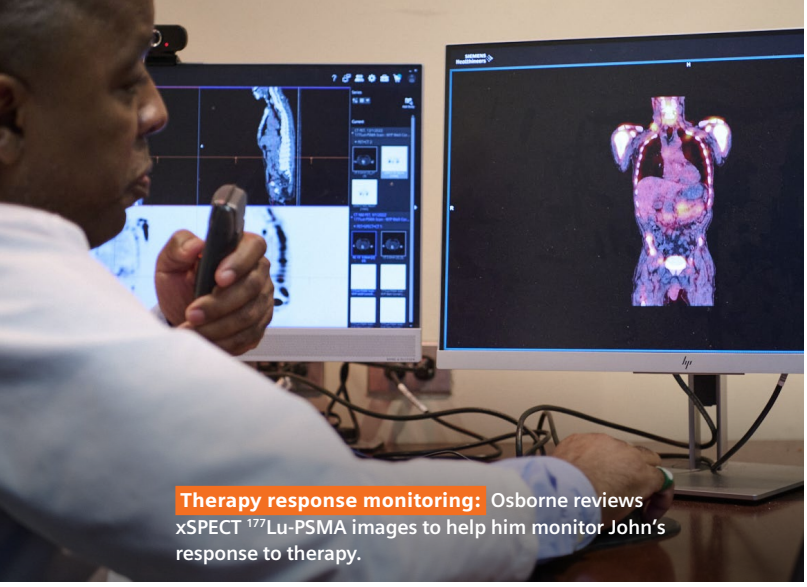
A patient is selected based on the review of multiple tests. In metastatic prostate cancer, treatment response is typically evaluated using CT or bone scans. In addition to detecting disease extent in patients with metastatic castration resistant prostate cancer, PSMA-ligand PET/CT is used to confirm eligibility for theranostic treatment, since documentation of PSMA expression in metastatic sites is required prior to initiation.

Osborne says that advances in PET/CT, such as the use of long axial field of view scanners equipped with time-of-flight technology, are accelerating patient care. "With the long axial field of view scanners, the scan times are getting into the range where they're almost as fast as CT, so the workflow depends on how fast the techs can get patients on and off the table," Osborne says. "If you're going to do a lot of patients, you have to be able to evaluate them in a reasonable way, which means quickly."

Osborne notes that although results from clinical trials have provided clearly defined PET/CT imaging



^{177}Lu-PSMA-fused SPECT/CT post treatment images acquired throughout John's personalized treatment to assess therapy response. From left to right: sagittal fused SPECT/CT cycle 1, sagittal fused SPECT/CT cycle 3, and sagittal fused SPECT/CT cycle 6. Data courtesy on file.



Therapy response monitoring: Osborne reviews xSPECT ^{177}Lu-PSMA images to help him monitor John's response to therapy.

Follow-up and survivorship monitoring: Osborne continues meeting regularly to monitor John's positive response and level of survivorship.

criteria for treatment eligibility, he and his colleagues are now working to translate those criteria into the routine care they deliver to the wider population of patients.

"We're trying to figure out who is going to benefit the most and where can we jump in and really find benefit," he says. "That is what all of us in the field, especially the subset of the field who have really tried to push things forward, are trying to figure out."

One of his early patients, a 78-year-old man named John with advanced prostate cancer, highlights the potential that the theranostic approach provides. Osborne emphasizes that patients such as John can gain not just longevity from applying theranostics, but also dramatically improved overall health. "It can bring back functional longevity, where someone gets back to doing the things they love for the people they love," he says. "And that's really what we're all in this for."

Personalized treatment

Another key step in the theranostic care pathway is personalized treatment. Because the theranostic approach uses the same ligand to monitor and treat patients, treatment is inherently personalized to the patient's specific disease state.

Osborne notes that total-body standard uptake value (SUV) mean is emerging as a key indicator of patient response to therapy. Using the xSPECT Quant™ tool in conjunction with Symbia™ SPECT/CT for SUV evaluation allows Osborne and his colleagues to assess response to treatment over time using a standardized, automated approach that produces accurate and reproducible quantitative values. *syngo*.via® for Molecular Imaging facilitates the reading, interpretation, reporting, and sharing of results while enabling physicians to efficiently compare results over time to accurately track response to treatment.

"Reporting total-body SUV_{mean} is not what most physicians are used to doing, but it's something that is available to us if we just push a little bit harder with the output of imaging and the programs that we use," he says. "If we want to get towards doing total body SUV_{mean}, we'll be able to do that with *syngo*.via and xSPECT Quant."[3]

Therapy response monitoring

During the therapy response monitoring step in the theranostic care pathway, SPECT/CT is an essential tool used for visualizing PSMA-positive prostate lesions and metastases to help monitor the response to therapy. The PSMA-targeted radioligand therapeutic agent used for John is administered by injection into a vein over approximately five minutes, typically in six doses six weeks apart. The drug can cause severe and life-threatening myelosuppression, so physicians review complete blood counts before each infusion. Post-therapy quantitative SPECT/CT imaging examines the biodistribution of the radionuclide within the body so that physicians can guide further treatment.

"There are some instances where the SPECT/CT imaging that we do may say stop after two cycles because the patient is doing exceptionally well—or because it's not working," Osborne says. "Maybe if the patient is doing well, we stop and then maybe six months down the line we start again. The plasma markers, as well as the imaging, are going to tell us what to do."

Follow-up and survivorship monitoring

To follow up on a patient and monitor survivorship, Osborne and his colleagues rely on a combination of laboratory diagnostics and imaging modalities after treatment has concluded, including CTs, bone scans, and PSMA PET/CT. Depending on different theranostic programs, SPECT/CT can be utilized during this step.

Osborne discusses John's positive response with theranostics with John and his partner Mary.

He notes that the theranostic approach is evolving rapidly, and post-therapy follow-up and monitoring vary among practices. "Every place I talk to handles it differently," Osborne says, "and we're all trying to figure out the best way."

Ongoing development of theranostics therapies

Osborne noted that the results of clinical trials that are currently examining the use of theranostic treatment using different radioisotopes and in patients who have not undergone chemotherapy have the potential to dramatically expand the number of patients eligible for treatment. He and his colleagues provide theranostic PSMA therapy to between five and 10 patients each week, but he is already thinking about the increased need for infusion rooms and scanners that can handle an increase in patient volume.

"We have everything we need for the volume that we have right now, but I know we're going to need to do between 10 and 15 per week in a year, and then maybe 15 to 20 per week the year after, so I have to think about not letting what we have right now be our ceiling for growth, because I would like to grow as the indications grow."

Osborne believes advances in molecular imaging and the ongoing development of new theranostic therapies are creating a new era of personalized care. "We can't continue just throwing doses at patients," Osborne says. "The best theranostics is going to figure out which patients benefit, how, when, and with what kind of dose. And it's going to be different in different people."

He points out that the current guidelines for the use of PSMA theranostics specify that patients are

"For medical centers that are starting to put together a program, I would say 'the water is good, come on in.'"

Joseph Osborne, MD, chief of Molecular Imaging and Therapeutics, New York City, USA

eligible for treatment after unsuccessful treatment with chemotherapy, but several clinical trials are underway that could expand patient eligibility to include patients who have not received or are currently undergoing chemotherapy.

"If we find out that there are positive results in these trials, then all of a sudden we're looking at many more patients," Osborne says. "If they don't have to fail chemo, they're pre-chemo, they're less sick and more numerous, so I see the number of indications for the therapy potentially becoming more plentiful on a six-month basis. Every six months, we're going to learn something that's going to say, expand, or stay the same. And I haven't seen yet anything that says stay the same."

When asked about what he thinks about the future of theranostics, "The more places that do it, the better," Osborne says. "For medical centers that are starting to put together a program, I would say 'the water is good, come on in.'" ●

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For More Information

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