

# 2016 SNMMI Highlights Lecture: Oncology, Part 1

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*From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNMMI Annual Meeting, was originated and presented for more than 30 years by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided annually among 4 distinguished nuclear and molecular medicine subject matter experts. Each year Newsline publishes these lectures and selected images. The 2016 Highlights Lectures were delivered on June 15 at the SNMMI Annual Meeting in San Diego, CA. In this issue we feature part 1 of the lecture by Wolfgang A. Weber, MD, from the Memorial Sloan–Kettering Cancer Center (New York, NY), who spoke on highlights in oncology. The second part will be published in the February issue of Newsline. Note that in the following presentation summary, numerals in brackets represent abstract numbers as published in The Journal of Nuclear Medicine (2016;57[suppl 2]).*

It is a great pleasure to give this highlight lecture. At the 2016 SNMMI Annual Meeting 629 oncology-related abstracts were submitted from 39 countries and presented in 28 tracks. This number is slightly above the 620 presented last year. The distribution of oncology abstracts was about 60% clinical, 17% basic biology, 5% image-guided therapy, 10% radiopharmaceutical development, and 8% instrumentation. These percentages are similar to those from recent years. It is impossible to do justice to the broad range of presentations, so I must apologize in advance for all of the interesting abstracts that could not be covered in this brief highlights overview. I also want to thank those speakers who so graciously provided slides from their work for this lecture.

Two very important and recent highlights of oncologic imaging in nuclear medicine are the 2 approvals by the U.S. Food and Drug Administration (FDA) of new PET imaging agents.  $^{18}\text{F}$ -FACBC ( $^{18}\text{F}$ -fluciclovine; marketed as Axumin by Blue Earth Diagnostics, Ltd., Oxford, UK), an amino acid for imaging of suspected prostate cancer recurrence, was approved on May 27.  $^{68}\text{Ga}$ -DOTATATE injection (NETSPOT; marketed by Advanced Accelerator Applications USA, Inc.), an imaging agent for localization of somatostatin receptor (SSTR)-positive neuroendocrine tumors (NETs), was approved on June 1. These approvals are particularly remarkable when we look back at the history of FDA approval of new oncologic drugs since the turn of the century. Although 120 oncologic therapeutics were approved between 2000 and 2015, only 3 were oncologic molecular imaging agents (FDG, 2000; choline, 2012; and tilmanocept, 2014). (Three amyloid ligands were also approved for imaging of neurodegenerative disorders.) In the space of just a few weeks before this year's SNMMI meeting, then, we saw almost as many

new oncologic agents approved as in the last 15 years. This forward-looking energy was reflected in the presentations at this meeting.

## Neuroendocrine Tumors

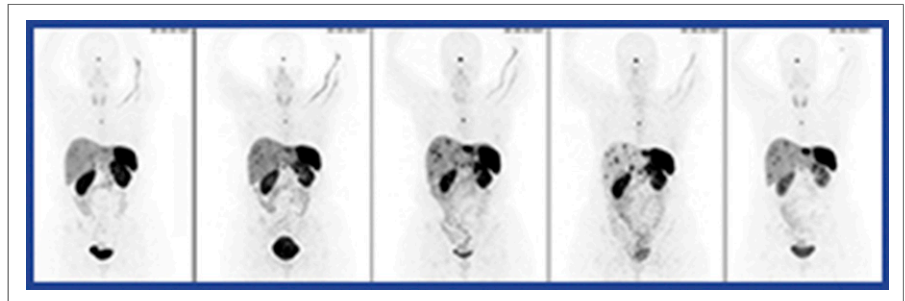
One very important international study, sponsored by Advanced Accelerator Applications (New York, NY), came from Strosberg and researchers from medical institutions in the United States, The Netherlands, France, the United Kingdom, Sweden, and Germany, who reported on “NETTER-1 phase III in patients with midgut NETs treated with  $^{177}\text{Lu}$ -DOTATATE: efficacy and safety results” [629]. This multicenter, randomized clinical trial focused on progression-free survival (PFS) and radiographic response in 229 patients, with surprisingly positive results. The researchers found a 79% reduction in the risk of disease progression/death in patients treated in the  $^{177}\text{Lu}$ -DOTATATE arm compared with patients in the standard arm receiving cold octreotide. Estimated median PFS in the  $^{177}\text{Lu}$ -DOTATATE arm was 40 months, compared with 8 months in the standard arm. The relevance of these results becomes clear when we look at published literature on the effectiveness of current medical treatments in pancreatic NETs, where the best PFS that can be expected is about 11.4 months with everolimus (compared with 5.4 months with placebo). The results with  $^{177}\text{Lu}$ -DOTATATE indicate that radiolabeled therapy can produce quantifiable improvements in outcomes in this disease setting in a multicenter controlled clinical trial. Interim data on overall survival (OS) from this study also suggested a positive trend, with only 14 deaths over the study period to date in the  $^{177}\text{Lu}$ -DOTATATE arm and 26 in the standard arm. Most other agents used in NETs have shown no improvement in OS. It is expected that data such as those shown at this meeting will lead to rapid approval of  $^{177}\text{Lu}$ -DOTATE in the United States for treatment of these NETs.

Looking at the NETTER-1 trial, which uses a fixed dosing of activity, suggests other possibilities for research. Can we further improve the effectiveness and safety of such agents by performing patient-specific dosimetry? In an educational session at this meeting, Madsen et al. from the University of Iowa (Iowa City) reported on “Personalized kidney dosimetry for  $^{90}\text{Y}$ -DOTATOC radionuclide therapy” [116A]. These authors quite nicely showed that doses can be adjusted by performing individual dosimetry. The idea is quite straightforward: the first treatment is performed with an activity known to be safe (in this case 120 mCi



Wolfgang A. Weber, MD

**FIGURE 1.**  $^{64}\text{Cu}$ -SARTATE PET/CT imaging and dosimetry estimation in NETs. PET/CT images acquired at (left to right) 30 minutes, 1 hour, 4 hours, and 24 hours after injection of  $^{64}\text{Cu}$ -SARTATE. Far right: Image acquired at 60 minutes after injection of  $^{68}\text{Ga}$ -DOTATATE.



$^{90}\text{Y}$ -DOTATOC), with subsequent patient-specific administrations calculated from kidney doses in the previous cycles (in this case, with 150 mCi as a maximum allowable activity per cycle). The result is the ability to treat some patients with higher doses and, presumably, higher efficacy.

Despite the fact that we now have level-1, evidence-based clinical data on SSTR targeting for imaging and therapy of NETs, a large number of questions remain and should be addressed. One simple question centers on identifying the mass of peptide that should be injected for imaging and therapy. It is generally assumed that the lowest mass of a receptor-binding radiopharmaceutical gives the best image and delivers the highest radiation dose to the tumor, but this is not necessarily true. Heidari et al. from the Massachusetts General Hospital (Boston and Charlestown, MA) reported on “Effects of  $^{68}\text{Ga}$ -DOTATOC specific activity on SSTR quantitation” [360]. This study looked at the relationship between the injected specific activity of  $^{68}\text{Ga}$ -DOTATOC and tumor uptake. These investigators neatly and systematically showed in an animal model that  $^{68}\text{Ga}$ -DOTATOC uptake was correlated to SSTR2 expression for a given specific activity and that uptake in SSTR-expressing tumors increased in a linear fashion with increasing specific activity—higher injected activities resulted in greater uptake. It will be important to repeat these studies in patients, not only for imaging but also for therapy in order to truly identify the optimal peptide mass.

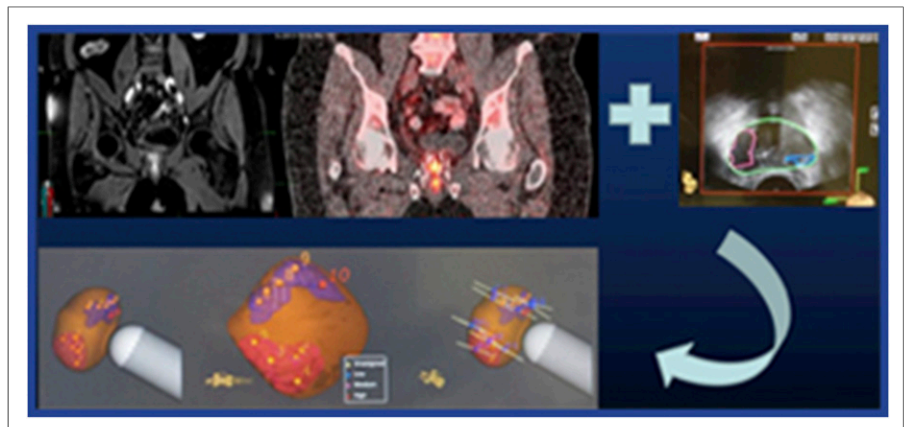
$^{68}\text{Ga}$ -DOTATATE is now approved for SSTR-positive NETs, but room remains for new tracers in this area. Hicks, from the University of Melbourne (Parkville, Australia) and

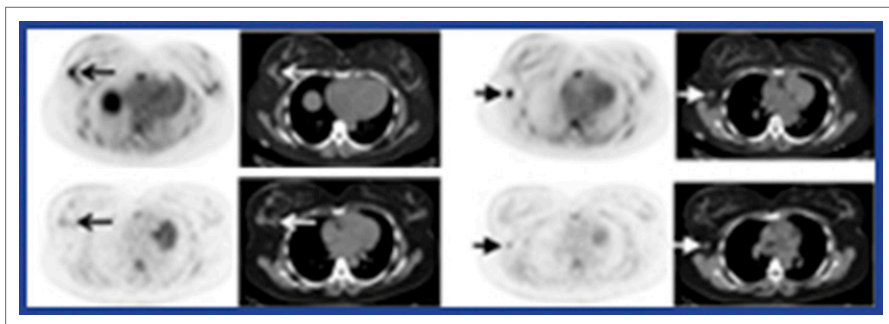
the Peter MacCallum Cancer Centre (East Melbourne, Australia), and colleagues from Australian industry and university centers reported on a “First-time-in-human trial of  $^{64}\text{Cu}$  MeCOSAR-octreotate (CuSARTATE) for imaging and dosimetry estimation in NETs” [26]. This SSTR-binding ligand uses a sarcophagine chelator which keeps the copper safely bound to the molecule over a period of days. The researchers showed that this leads to increasing image contrast, with resulting contrast higher than that of  $^{68}\text{Ga}$ -DOTATATE (Fig. 1). They concluded that progressively lower clearance enables visualization of small hepatic metastases at late time points. An interesting aspect of these results is that this PET tracer could be used not only for imaging these NETs but for estimating radiation dose that could be achieved with radiopeptide therapy. Specifically, combination of this same molecule with  $^{67}\text{Cu}$  might open new possibilities for imaging and therapy and for the use of PET to very precisely plan personalized treatments.

### Prostate Cancer

Goodman and Schuster from Emory University (Atlanta, GA) presented an educational session on  $^{18}\text{F}$ -FACBC, a non-natural amino acid analog that, as noted previously, has been approved for use in recurrent prostate cancer. The availability of this tracer opens numerous possibilities for research. Goodman and Schuster used  $^{18}\text{F}$ -FACBC PET to guide biopsies to confirm the meaning and relevance of lesion uptake of this radiotracer (Fig. 2.), with the hope that in the future  $^{18}\text{F}$ -FACBC PET imaging

**FIGURE 2.**  $^{18}\text{F}$ -fluciclovine PET/CT for prostate cancer biopsy.  $^{18}\text{F}$ -fluciclovine PET/CT images are fused with MR and transrectal ultrasound imaging to guide the biopsy.





**FIGURE 3.**  $^{18}\text{F}$ -fluciclovine and  $^{18}\text{F}$ -FDG imaging in a patient with invasive lobular carcinoma. SUVs for  $^{18}\text{F}$ -fluciclovine (top) were 4.9 in breast (left) and 5.8 in axillary node (right) lesions (arrows). Corresponding SUVs were 1.8 and 2.8 for  $^{18}\text{F}$ -FDG (bottom). Overall this study found a median  $\text{SUV}_{\text{max}}$  of 6.1 (range, 4.5–10.9) for  $^{18}\text{F}$ -fluciclovine and 3.7 (range, 1.8–6.0) for  $^{18}\text{F}$ -FDG.

might serve to reduce the numbers of nondiagnostic biopsies in prostate cancer patients.

$^{18}\text{F}$ -FACBC can also be used in other diseases, including breast cancer. Ulaner et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported on “Initial results of a prospective clinical trial of  $^{18}\text{F}$ -fluciclovine PET/CT in newly diagnosed invasive ductal and invasive lobular breast cancers” [581]. The researchers compared results with this amino acid analog with those from  $^{18}\text{F}$ -FDG and unexpectedly found that  $^{18}\text{F}$ -FACBC showed higher uptake in invasive lobular breast cancers (Fig. 3). It is well known that lobular cancers typically show low  $^{18}\text{F}$ -FDG uptake, so that  $^{18}\text{F}$ -FDG PET is limited for staging in this setting. The authors concluded that  $^{18}\text{F}$ -FACBC PET/CT demonstrated potential for imaging both invasive ductal and lobular carcinomas, including detection of unsuspected extraaxillary nodal metastases. They added that the low uptake concordance between  $^{18}\text{F}$ -fluciclovine and  $^{18}\text{F}$ -FDG suggests that these tracers measure different biologic phenomena within tumors.

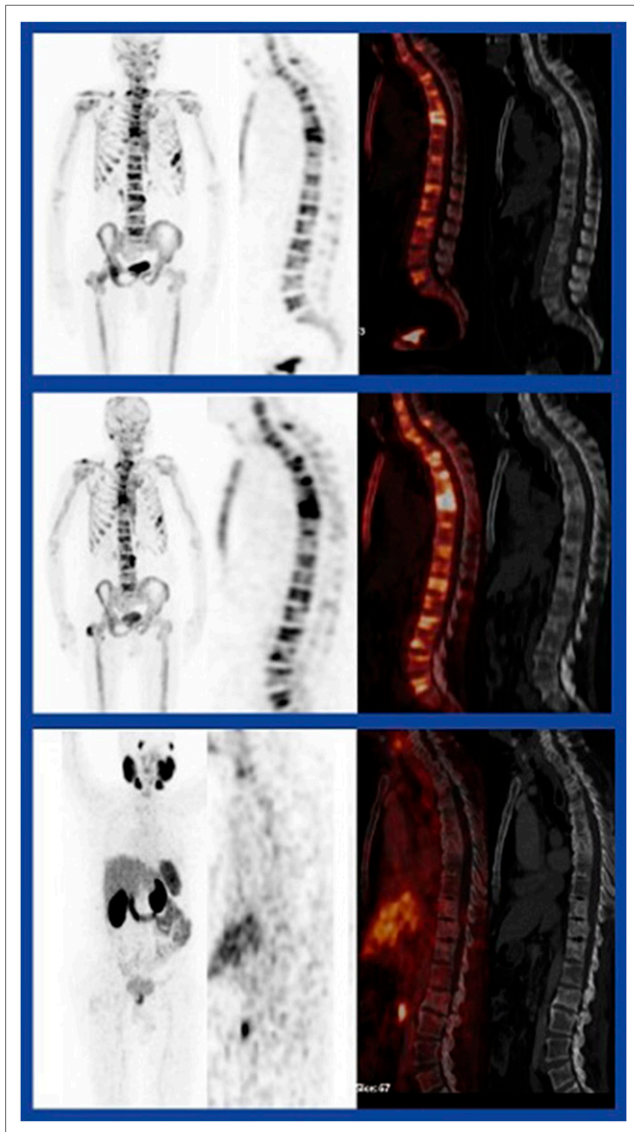
A clear focus in the oncologic sessions at SNMMI 2016 was on prostate-specific membrane antigen (PSMA) as an imaging target for prostate cancer. This was a major topic at last year’s meeting as well. Interest in PSMA imaging was indicated by the fact that some sessions were specifically “non-PSMA,” a clear indicator that this agent has a strong presence in shaping the way in which people are thinking about prostate cancer imaging. To review all of the PSMA abstracts would require a separate highlights session, so I will, instead, summarize some of the newer aspects of the studies presented. One welcome aspect is that we are seeing significantly larger patient series being evaluated and comparing PSMA imaging with other agents. Agrawal et al. from the Tata Memorial Hospital Mumbai (India) reported on “Evaluation of skeletal metastases of prostate cancer with  $^{68}\text{Ga}$ -PSMA PET/CT and  $^{18}\text{F}$ -NaF PET/CT and its comparison” [559]. These researchers found the sensitivities of both agents on the patient level to be quite similar. We know that  $^{18}\text{F}$ -NaF is extremely sensitive in prostate cancer metastases, but  $^{68}\text{Ga}$ -PSMA PET detected the overwhelming majority of bone metastases as well all bone metastases on a patient basis. In the posttreatment setting,  $^{18}\text{F}$ -NaF PET continued to show increased uptake in sclerotic lesions that were not positive on the PSMA scan, indicating that the PSMA ligand

could be useful not only for staging but also for response assessment and treatment monitoring of skeletal metastases (Fig. 4).

Other studies have been performed to assess PSMA imaging within the prostate. Fendler et al. from the Ludwig-Maximilians-University of Munich (Germany) reported that “ $^{68}\text{Ga}$ -PSMA-HBED-CC PET/CT detects location and extent of primary prostate cancer” [608]. This was a very systematic analysis of  $^{68}\text{Ga}$ -PSMA-HBED-CC uptake in which results showed a high tumor uptake, sensitivity of 67%, and specificity of 92% for affected segments of the prostate (Fig. 5). Interestingly, no correlation with Gleason scores was noted, and, although the majority of tumors were detected with high contrast, area under the curve/receiver operating characteristic analyses indicated that not all tumors were PSMA-positive.  $^{68}\text{Ga}$ -PSMA appears to be an excellent imaging agent for prostate cancer, but this and other evidence suggest that some prostate cancers produce little or no PSMA, indicating that more than one imaging probe may be needed for prostate cancer.

Another probe that has been available for a while but is now being studied more intensively is  $^{18}\text{F}$ -FDHT, an androgen receptor ligand that is not only of great interest for imaging prostate cancer but also for monitoring treatment with antiandrogens and, perhaps in the future, for selecting patients for such treatment. Kramer et al. from the VU University Medical Center (Amsterdam, The Netherlands) reported on “Assessment of simplified methods for quantification of  $^{18}\text{F}$ -FDHT uptake in patients with metastasized castrate-resistant prostate cancer” [464]. Whole-body imaging studies acquired by this group showed that patients with metastatic prostate cancer often have many lesions that are positive on  $^{18}\text{F}$ -FDHT PET (Fig. 6). SUVs present a possible method for assessing these lesions, assuming that these SUVs are correlated with the density of androgen receptors in these patients. Quantification, however, is needed to determine whether these static uptake measurements actually reflect the density of free androgen receptors. These researchers demonstrated a very close correlation between SUVs measured on whole-body studies and more sophisticated metrics of tracer uptake, such as the  $K_i$  influx constant from Patlak analysis. These results are quite encouraging and create the opportunity to estimate the density of free androgen receptors on whole-body scans. The authors also showed that the





**FIGURE 4.** Skeletal metastases in a 73-year-old patient with metastatic castration-resistant prostate cancer treated first with docetaxel then 1 year later with cabazitaxel. Top:  $^{18}\text{F}$ -NaF PET/CT acquired 1 month after initiation of cabazitaxel. Middle:  $^{18}\text{F}$ -NaF PET/CT acquired 17 months later. No new lesions were identified. Old lesions continued to show uptake. Bottom:  $^{68}\text{Ga}$ -PSMA PET/CT also acquired at 17 months showed no PSMA-avid sclerotic lesions. The authors concluded that a lack of PSMA avidity in healing lesions in the posttreatment setting opens new avenues for response assessment in skeletal metastases.

accuracy of these estimates can be improved by using an early dynamic scan to characterize the plasma input function.

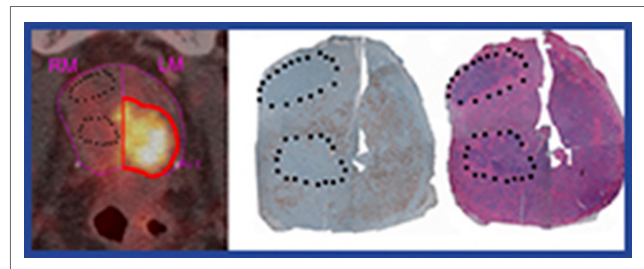
Another emerging class of imaging agents for prostate cancer includes ligands that bind to gastrin-releasing peptide receptors (GRPRs). Several ligands have already been developed for this probe and are in clinical trials. Nock, from INRASTES, NCSR Demokritos (Athens, Greece), and colleagues from Erasmus Medical Center (Rotterdam, The Netherlands) and the PET Center Bad Berka (Germany) reported on “ $^{68}\text{Ga}$ -NeoBomb1, a new

potent GRPR-antagonist for PET imaging: preclinical and first clinical evaluation in prostate cancer” [583]. This agent has shown very high affinity and high uptake in both primary prostate cancer and metastatic prostate cancer. It is also quite promising for imaging studies in patients with breast cancer (Fig. 7).

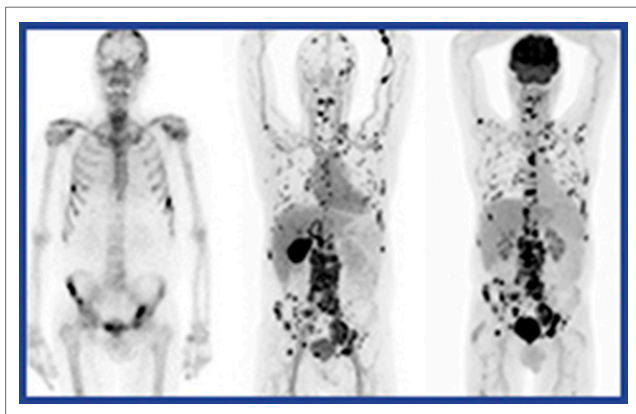
This proliferation of imaging agents leaves us with an interesting problem. Up until a few years ago we had only 1 or 2 imaging agents in prostate cancer: sodium fluoride and (with some limitations) FDG. Now we have a whole spectrum of available imaging agents—not only FDG and sodium fluoride but acetate, choline, various PSMA ligands, various GRPR ligands, and  $^{18}\text{F}$ -FDHT. The general response in the imaging research community has been to implement studies that compare 2 or more agents to determine which is the better tracer. However, this may not yield complete answers, because different tracers may provide complementary information.

This was nicely shown in the study from Iagaru and colleagues from Stanford University (CA) and Piramal Imaging GmbH (Berlin, Germany), who reported that “Biochemically recurrent prostate cancer:  $^{68}\text{Ga}$ -RM2 (formerly known as  $^{68}\text{Ga}$ -bombesin or BAY86-7548) PET/MRI is superior to conventional imaging” [466]. Figure 8 shows the results of different imaging agents in a single patient, with varying results in assessing disease. Although this might be interpreted to mean that the agent under investigation is more sensitive, it is more likely to mean that different imaging agents provide different information at varying times over the course of disease progression.

This was very nicely shown in a retrospective study by Regula et al. from the Akademiska Sjukhuset (Uppsala, Sweden), who reported that “ $^{11}\text{C}$ -acetate PET/CT accurately predicts prostate-cancer specific survival in patients with biochemical relapse after prostatectomy” [521]. For the 121 patients in the study, the mean prostate-specific antigen (PSA) level at the time of PET/CT was  $2.69 \pm 4.35$  ng/mL.  $^{11}\text{C}$ -acetate PET/CT identified at least 1 lesion in 55% of these patients (false-negative rate of 45%). Having looked at the very promising PSMA studies reported at this



**FIGURE 5.** Example of false-negative  $^{68}\text{Ga}$ -PSMA PET/CT for adenocarcinoma with partial neuroendocrine differentiation. Black dots in images indicate neuroendocrine differentiation (PSMA-negative). Left:  $^{68}\text{Ga}$ -PSMA PET/CT. Purple = segment borders. Red = tumor delineation based on PET/CT. Middle: PSMA immunohistochemistry. Right: Hematoxylin and eosin staining.



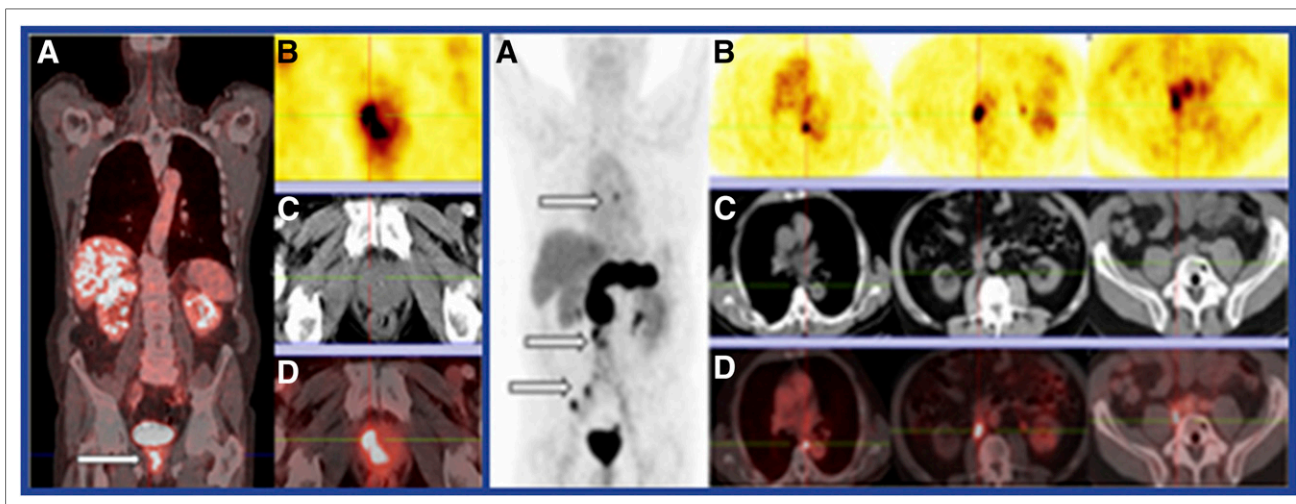
**FIGURE 6.** Patient with castration-resistant prostate cancer with multiple bone and lymph node metastases on bone scanning (left) and  $^{18}\text{F}$ -FDG PET/CT (right) imaging.  $^{18}\text{F}$ -FDHT uptake in these lesions (middle) suggests the presence of androgen receptors and the potential for  $^{18}\text{F}$ -FDHT PET/CT as an imaging biomarker in this patient population.

meeting, the conclusion might be that  $^{11}\text{C}$ -acetate PET is only moderately sensitive, so that the PSMA scan, where one might expect to identify 80%–90% of abnormalities, would be superior. However, when Regula et al. looked at follow-up in these patients imaged with  $^{11}\text{C}$ -acetate PET/CT, 5-year OS was 100% in the originally negative cases and only 80% in the originally positive cases. Although the test may not be exceptionally sensitive, it may provide very important information about specific patient outcomes. It may very well be that disease that is *not* detected by this tracer may require little or no treatment, and this information may be equally or even more important than mere identification of multiple lesions in an individual patient. This retrospective analysis needs future validation, but it illustrates the principle that just counting lesions and comparing sensitivities and specificities

may not be all we should consider in evaluating the range of new imaging agents in prostate cancer.

We have looked at presentations on agents that address staging and outcomes in prostate cancer. Other agents can also measure tumor response. Lee et al. from Queen's Medical Center (Honolulu, HI), Samsung Medical Center (Seoul, Republic of Korea), Sungkyunkwan University School of Medicine (Seoul, Republic of Korea), and the University of Hawaii (Honolulu) reported that “Whole-body tumor burden measurements on  $^{18}\text{F}$ -fluorocholine PET/CT may have predictive value following specific treatments for castrate-resistant prostate cancer” [463]. After treatment, 42 patients underwent  $^{18}\text{F}$ -fluorocholine PET/CT, with serial tumor burden indices then derived from metabolically active tumor volume segmentation. They showed a very strong correlation between tumor response based on whole-tumor burden volume, as well as striking differences in patient survival between those classified as responders and nonresponders based on metabolically active tumor volume response. This is highly relevant in prostate cancer, where, with the high prevalence of bone disease, no established imaging test is available to monitor tumor response. Current response assessment is driven to a large extent by PSA changes, and we know that these changes can be confounded by other factors. The possibility of having a reliable imaging test to assess response is quite appealing. If this methodology works well for  $^{18}\text{F}$ -fluorocholine, we will also want to explore the utility of PSMA and other imaging tests that might be used to monitor treatment response in metastatic prostate cancer.

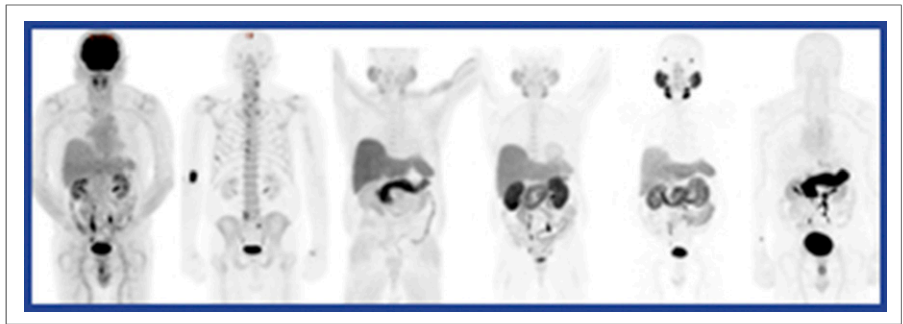
The interest in PSMA is high not only because it offers high sensitivity in tumor detection but also because the same or similar molecules can be used for treatment of prostate cancer. A series of studies have looked at the use of PSMA as a therapeutic target. Eiber and colleagues from the Technische Universität (Munich and Garching, Germany)



**FIGURE 7.** Left block: Strong uptake of  $^{68}\text{Ga}$ -NeoBomb1 in a patient with primary prostate adenocarcinoma (Gleason score 8 [4 + 4], PSA 6.33 ng/mL). Right block: High-contrast uptake of  $^{68}\text{Ga}$ -NeoBomb1 in multiple lymph node metastases in a patient with recurrent prostate cancer after prostatectomy and androgen deprivation therapy (PSA 21.77 ng/mL).



**FIGURE 8.** Eighty-three-year-old man who initially presented with a T2b nodule (PSA 5.4 ng/mL, Gleason score 9 [5 + 4]) confirmed to be prostate adenocarcinoma and treated with intensity-modulated pelvic radiation therapy and androgen blockade. After a PSA nadir of 0.11, biochemical recurrence occurred, with PSA of 1.83 and negative conventional imaging. Patient was followed for 40 months under “watch and wait” strategy because no sites of recurrent disease were identified despite PSA increasing to 18.7 ng/mL at the time of positive  $^{68}\text{Ga}$ -PSMA-11 and  $^{68}\text{Ga}$ -RM2 imaging.



Left to right, PET imaging acquired with:  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -NaF,  $^{11}\text{C}$ -acetate,  $^{11}\text{C}$ -choline,  $^{68}\text{Ga}$ -PSMA-11, and  $^{68}\text{Ga}$ -RM2. Note that these imaging studies were acquired over a period of several months and comparisons between individual modalities therefore need to be interpreted with caution.

reported on “Systemic radioligand therapy with  $^{177}\text{Lu}$ -PSMA I&T in patients with metastatic castration-resistant prostate cancer” [61]. This study, conducted in heavily pretreated patients, demonstrates how dramatic these therapeutic responses can be. The patient with diffuse bone marrow disease shown in Figure 9 was treated with 4 cycles of this  $^{177}\text{Lu}$ -labeled PSMA agent, and extraordinary changes in the amount of disease in the bone can be seen after 8 months. The patient’s tumor marker PSA went from 755 ng/mL to undetectable after treatment, and, in fact, continued to be undetectable at the time of the presentation at this meeting.

These striking responses have now been noted at multiple centers in Germany that have reported consistent and similar results. Kulkarni and colleagues from the Zentralklinik Bad Berka (Germany) reported on “PSMA radioligand therapy of metastatic castration-resistant prostate cancer: first results using the PSMA inhibitor 617” [139]. This study included a series of 53 heavily pretreated patients, with a complete response rate of 11.7% and partial response rate of 32.4%. Median OS and PFS had not been reached at the time the study was reported.

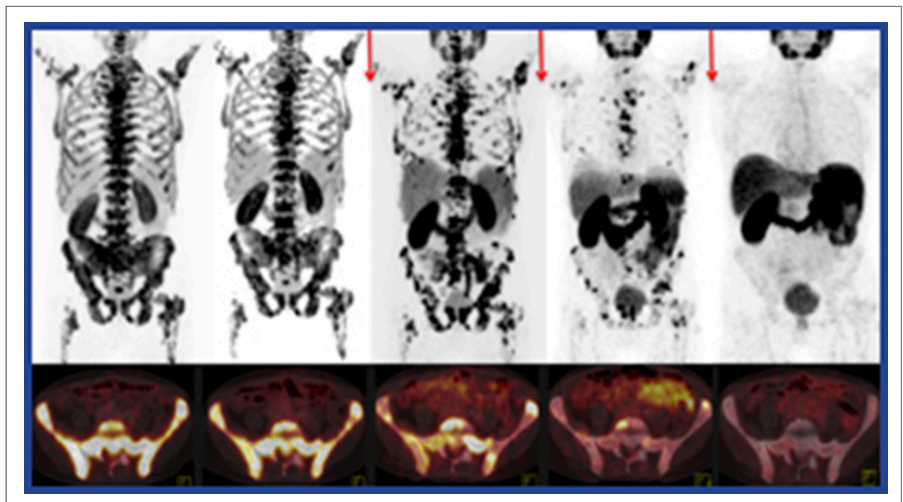
Rahbar and colleagues from University Hospital Münster, University Hospital Bonn, University Hospital

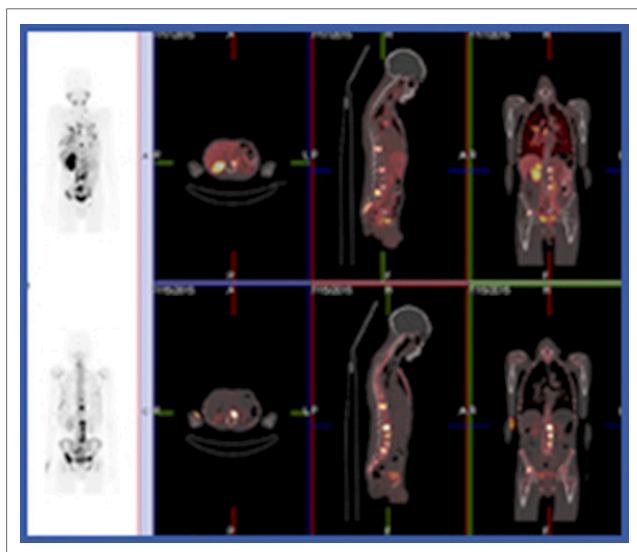
Aachen, and University Hospital Cologne (all in Germany) reported on “Response and tolerability after a single dose of  $^{177}\text{Lu}$ -PSMA-617 in patients with metastatic castration resistant prostate cancer: a multicenter study” [140]. This research included 80 patients who experienced marked declines in PSA levels and overall changes in tumor response.

Perhaps even more remarkable is evidence from these studies that this treatment is safe and well tolerated. In these patients with intense disease involvement in bone, one might expect to see significant hematologic side effects with radionuclide treatments. Amazingly, the studies summarized here reported consistently low hematologic toxicities, usually grade 1 or 2, with only exceptional grade 3 or 4 toxicities. Although exploration of treatment with these PSMA agents is still in its early stages, these results are quite encouraging. I hope that at the next SNMMI meeting we see additional systematic studies that evaluate well-defined patient populations that will help to identify those subgroups most likely to benefit from PSMA-targeted radioisotopes.

Progress was reported on other therapeutic radiopharmaceuticals. Pfannkuchen and colleagues from Johannes Gutenberg University (Mainz, Germany), Diagnostisch Therapeutisches Zentrum am Frankfurter Tor (Berlin,

**FIGURE 9.** Images acquired in heavily pretreated 71-year-old man with metastatic castrate-resistant prostate cancer serially treated with 4 cycles of  $^{177}\text{Lu}$ -PSMA I&T over (left to right) baseline and 1, 2, 4, and 7 months. At 1 year after treatment completion, patient had achieved a complete imaging response and PSA declined from 755 ng/mL to undetectable levels.





**FIGURE 10.** Comparison of  $^{68}\text{Ga}$ -PSMA-11 (top) and  $^{68}\text{Ga}$ -DOTA<sup>ZOL</sup> (bottom) imaging in a patient with bone metastases.  $\text{SUV}_{\text{max}}$  in bone lesions was higher for  $^{68}\text{Ga}$ -DOTA<sup>ZOL</sup> than for  $^{68}\text{Ga}$ -PSMA-11.

Germany), and the University of Pretoria & Steve Biko Academic Hospital (Pretoria, South Africa) reported on “DOTA<sup>ZOL</sup> as a novel bone seeking compound for  $^{68}\text{Ga}$  PET diagnosis and  $^{177}\text{Lu}$  endoradiotherapy of bone metastases: from preclinical to first human results” [472]. These investigators studied DOTA<sup>ZOL</sup>, a  $^{177}\text{Lu}$ - or  $^{68}\text{Ga}$ -labeled theranostic compound with chelated DOTA, in a preliminary imaging analysis of bone metastases in 10 patients and then treated 1 patient. Their first-in-human PET results showed excellent contrast and target-to-background ratio in bone metastases, superior to those of radiolabeled PSMA (for example,  $\text{SUV}_{\text{max}}$  for DOTA<sup>ZOL</sup> in L2 vertebra lesions was 68.9 compared to 8.8 for PSMA) (Fig. 10). Based on these encouraging data, they treated 1 patient with a single dose of 5.5 GBq of  $^{177}\text{Lu}$ -DOTA<sup>ZOL</sup>. The patient’s PSA decreased from 1,217.8 to 88.0 ng/mL over the 8-week period after treatment. This again shows that although PSMA is quite promising, we have other promising compounds that may be useful in this setting, and perhaps we can combine them to achieve even better responses in the treatment of prostate cancer.

## SNMMI, ASNC, IAC and Nuclear Cardiology Dose

**T**he American Society of Nuclear Cardiology (ASNC), the Intersocietal Accreditation Commission (IAC)’s Nuclear/PET accreditation division, and SNMMI in November reviewed recent efforts to encourage optimization of radiation doses used in nuclear cardiology studies. These efforts come in response to recently published research indicating that adherence to clinical nuclear imaging guidelines for reduced patient radiation exposure is variably implemented, resulting in administration of higher doses than necessary for some patients undergoing myocardial perfusion studies.

In February 2016, ASNC published guidelines for myocardial perfusion SPECT imaging, titled *ASNC Imaging Guidelines for SPECT Nuclear Cardiology Procedures: Stress Protocols and Tracers*, which included a chart on current SPECT myocardial perfusion imaging (MPI) protocols, with recommended radiopharmaceutical activities and corresponding radiation effective doses. The ASNC noted that dose reduction strategies based on weight-based radiotracer dosing, thoughtful selection of radiotracers, stress-only imaging when appropriate, software innovations, state-of-the-art SPECT systems, and utilization of PET for MPI are all recommended methods to achieve quality cardiac imaging at the lowest radiation exposure. “ASNC is committed to supporting nuclear cardiac imaging labs’ use of the lowest radiotracer dose that maintains diagnostic image quality, in conjunction with application of appropriate use criteria and the use of count

recovery software for general SPECT cameras, new solid-state SPECT cameras, and PET to provide the right test for the right patient,” said Brian G. Abbott, MD, ASNC president.

To ensure that facilities seeking nuclear cardiology accreditation focus their awareness on patient radiation doses, a September 2016 revision to the *IAC Standards and Guidelines for Nuclear/PET Accreditation* included required administered dose ranges as recommended by the 2016 ASNC guidelines. The IAC Nuclear/PET Board of Directors also mandated specific dose ranges for MPI studies to decrease radiation exposure while maintaining image quality. Scott D. Jerome, DO, IAC Nuclear/PET president, said, “Our ultimate goal is to ensure that nuclear cardiology facilities are guided to administer the lowest dose possible that provides optimal imaging results for patients referred for MPI studies.”

SNMMI President Sally W. Schwarz, MS, RPh, BCNP, said, “Working together, we can more effectively ensure that health care providers meet accreditation requirements and follow dose guidelines for nuclear cardiology. The goal is to keep radiation exposure as low as is reasonable.” Frederic H. Fahey, DSc, who serves on SNMMI’s Dose Optimization Task Force, added, “Accreditation requirements and dosing guidelines emphasize both patient safety and quality images. Our focus must always be on providing the highest quality care in the safest manner possible.”