2019 SNMMI Highlights Lecture: Oncology and Therapy, Part 2

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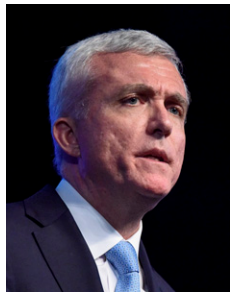
From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNMMI Annual Meeting, was originated and presented for more than 30 years by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided annually among 4 distinguished nuclear and molecular medicine subject matter experts. Each year Newsline publishes these lectures and selected images. The 2019 Highlights Lectures were delivered on June 25 at the SNMMI Annual Meeting in Philadelphia, PA. In this issue we feature the second part of the lecture by Andrew Scott, MD, Director, Department of Molecular Imaging and Therapy, and Head, Tumour Targeting Laboratory, Olivia Newton-John Cancer Research Institute, Austin Health (Melbourne, Australia), who spoke on oncology highlights from the meeting. Note that in the following presentation summary, numerals in brackets represent abstract numbers as published in The Journal of Nuclear Medicine *(2019;60[suppl 1]).*

Part 1 of this Highlights Lecture appeared in the January 2020 issue of Newsline and covered topics in novel molecular imaging probes and immunooncology.

Molecular Imaging in Treatment Response Assessment

When looking at different cancer treatments it is very important that we understand the underlying tumor biology, as well as the different therapeutic approaches used that may have varying response characteristics. Tumor types may differ in pathologic and metabolic features, which can affect treatment response and have effects on molecular imaging studies. Patient populations must be defined carefully for prognostic and predictive imaging biomarker studies.

Bailey et al. from the Royal North Shore Hospital (Sydney, Australia) reported on "The prognostic impact of dual FDG/somatostatin receptor PET in metastatic neuroendocrine tumours: Updated overall survival from the NETPET study" [505]. The group previously reported on the creation of an assessment score that looks at both ^{18}F-FDG and somatostatin receptor uptake, deriving ^{18}F-FDG and somatostatin scores to produce a "NETPET" score from 1 to 5 (*Theranostics.* 2017;7[3]:1149–1158). In their presentation at this meeting, they looked at an updated overall survival analysis and found that the NETPET score was statistically significant on multivariate analysis in predicting improved outcomes. The NETPET score correlated not only with histologic grade but with overall survival independent of histologic grade. We know that comparison of ^{18}F-FDG uptake and somatostatin receptor expression is important in identifying patients for potential treatment and also in stratification of predicted outcomes. These authors concluded that "dual FDG/DOTATATE PET is a promising tool for 'whole body molecular biopsy' of NET" and should be tested prospectively.



Andrew Scott, MD

In a large-scale study, Georgi et al. from the University of Leipzig (Germany), King's College London and Guy's & St. Thomas' PET Centre (London, UK), and the University of Manchester and Christie National Health Service Foundation Trust (Manchester, UK) reported on "Quantitative assessment of interim PET in Hodgkin lymphoma: An evaluation of the qPET method in adult patients in the RAPID [Randomized phase III trial to determine the role of FDG PET imaging in clinical stages IA/IIA Hodgkin's lymphoma] trial" [140]. Working with 450 PET scans from European patients with lymphoma after 3 cycles of adriamycin, bleomycin, vinblastine, and dacarbazine, the researchers used SUV_{peak} tumor uptake in a small number of voxels in the tumor divided by SUV_{mean} in the liver. This approach had been previously validated in a pediatric population. The researchers were able to generate a stratification of Deauville scores through visual assessment and qPET. By looking at thresholds from 0.95, 1.30, and 2.00, they were able to quite accurately differentiate Deauville scores of 2, 3, 4, and 5, a determination that is critically important in treatment decision making in patients with Hodgkin lymphoma. This is a potentially quantifiable method—apart from visual Deauville scoring only—for assessing treatment response in patients with lymphoma.

We saw a great deal at this conference and have read much in the recent literature about the ability of applied quantitation combined with artificial intelligence to improve our diagnostic capabilities. Zhou et al. from the Mallinckrodt Institute of Radiology/Washington University in St. Louis School of Medicine (MO) and the Peking University First Hospital/Peking University School of Oncology (Beijing, China) reported on "A machine learning-based parametric imaging algorithm for noninvasive quantification of dynamic ^{68}Ga-DOTATATE PET-CT" [1186]. They used a random forest regression model and found that, compared to the standard Patlak plot, both computer simulation and neuroendocrine tumor patient data showed that machine learning with this approach was

robust and could generate parametric images of tracer net uptake rate constant K_i and initial distribution volume V_{id} (Fig. 1). This has the potential for use in clinical ^{68}Ga-DOTATATE PET scans as short as 10 minutes. Determining and refining biologically relevant end points for the use of artificial intelligence will be increasingly important as we move forward.

Prostate Cancer: Imaging and Theranostics

Prostate cancer has emerged in the last 5 years, diagnostically and therapeutically, as one of the most important areas of progress in nuclear medicine oncology. Multiple PET probes are being used clinically and are in development, with numerous diagnostic and therapeutic trials ongoing or planned. More than 90 abstracts in this area were presented at the SNMMI 2019 Annual Meeting, and I am able to highlight only a few. Among the key takeaway points were the broad range of PET probes (^{11}C, ^{68}Ga, ^{18}F) now being evaluated for multiple targets; the rising number of multicenter trials underway for initial staging in high-risk disease, staging following biochemical relapse, prognosis, management impact, and as part of therapeutic (theranostic) evaluation of patients; the importance of considering the status of competing modalities (e.g., multiparametric MR and whole-body MR imaging) for staging investigations; and the need to explore remaining questions about specific use in oligometastatic disease, appropriate management (and outcomes) based on results, and interpretation of equivocal results.

Fendler et al. from the University of Essen (Germany), the University of Munich (Germany), the Peter MacCallum Cancer Centre (Melbourne, Australia), the Technische Universität München (Germany), the University of California Los Angeles, and the University of California San Francisco reported that "PSMA-PET localizes M1 disease in more than half of 'non-metastatic' castration-resistant prostate cancer patients" [591]. They used a predefined protocol and retrospectively screened 8,825 patient files from the prostate-specific membrane antigen (PSMA) PET databases of 6 centers. They identified and recruited 200 patients with nonmetastatic castrate-resistant prostate cancer. Inclusion criteria included histologically confirmed disease, prostate-specific antigen (PSA) $>$ 2 ng/mL, PSA doubling time of $\leq$10 months or Gleason score $\geq$8; no pelvic nodes $\geq$2 cm; and no known extrapelvic metastases before the PSMA scan. Blinded experts performed centralized reads. PSMA PET detected prostate cancer in 196 of 200 (98%) patients. Of these, 44% had pelvic disease only (24% local recurrence only, 20% pelvic nodal involvement), and 55% had M1 disease despite negative conventional imaging (including 24% bone and 6% visceral). In 75 (38%) patients, 116 regions were validated, including 30 regions with histopathology. The PSMA PET positive predictive value was 96% on a regional basis (97% for histopathology validation only). Interobserver agreement for PET interpretation was almost perfect. The important takeaway point here is that PSMA PET detected metastatic disease in more than half of patients who, prior to that scan, were thought to have no metastatic disease (Fig. 2). This emphasizes the importance of PSMA PET in being able to accurately stage patients and, thereby, assign the most appropriate therapy.

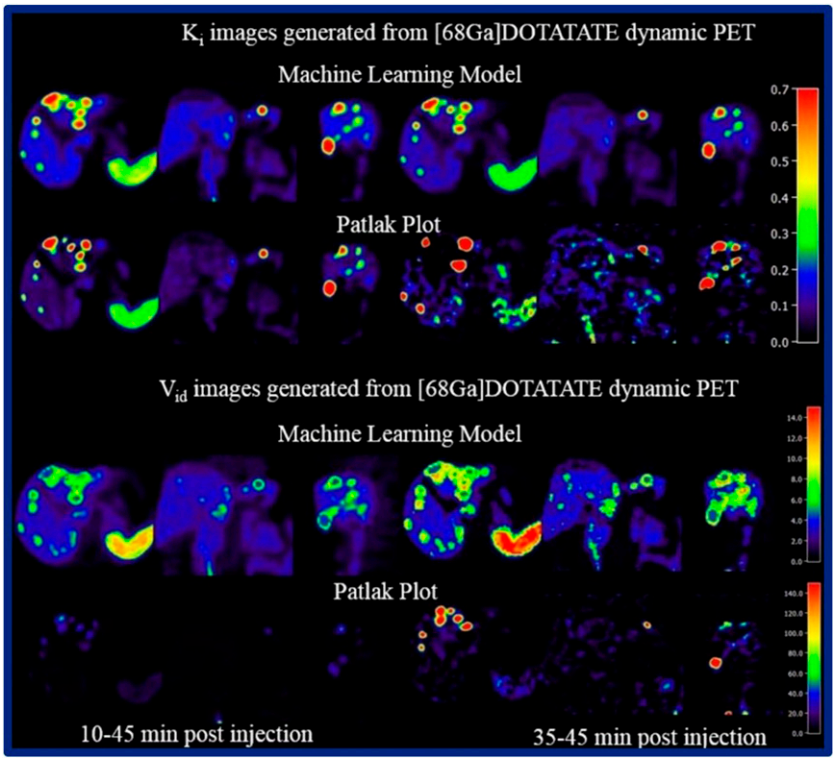


FIGURE 1. A machine learning–based parametric imaging algorithm for noninvasive quantification of dynamic ^{68}Ga-DOTATATE PET/CT. Top block: K_i images generated from ^{68}Ga-DOTATATE dynamic PET using: (top row) a machine learning model and (bottom row) Patlak plots. Bottom block: V_{id} images generated from ^{68}Ga-DOTATATE dynamic PET using: (top row) a machine learning model and (bottom row) Patlak plots.

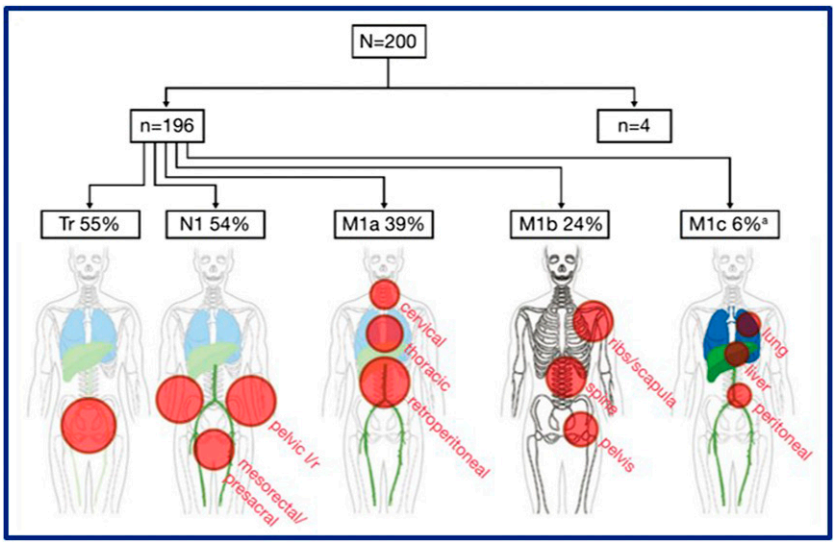


FIGURE 2. Prostate-specific membrane antigen (PSMA) PET detected M1 disease in more than half of nonmetastatic castration-resistant prostate cancer patients. Image shows results from a predefined protocol for retrospective analysis of PSMA PET databases at 6 centers. PSMA PET detected metastatic disease in more than half of patients who, prior to that scan, were thought to have no metastatic disease.

A number of abstracts compared different PET tracers for identifying prostate cancer. Calais et al. from the University of California Los Angeles, Loyola University Medical Center (Maywood, IL), Oslo University Hospital (Norway), Ospedale S. Orsola-Malpighi (Bologna, Italy), the Peter MacCallum Cancer Institute (Melbourne, Australia), and the Technische Universität München (Germany) reported that "^{68}Ga-PSMA-11 PET/CT detects prostate cancer at early biochemical recurrence with superior detection rate and reader agreement when compared to ^{18}F-fluciclovine PET/CT in a prospective head-to-head comparative phase 3 study" [587]. They looked at 50 paired fluciclovine and PSMA PET/CT scans in patients with biochemical recurrence and PSA levels ranging from ≥0.2 to ≤2.0 ng/mL with no prior salvage therapy. The median time interval was 6 days between scans, with primary endpoints of detection rates per patient and per region. The researchers identified a significant advantage of the ^{68}Ga-PSMA-11 over ^{18}F-fluciclovine for overall PET scans and for nodal and metastatic disease. Although this was a single-site study, it was well controlled and suggests the potential advantage of ^{68}Ga-PSMA in patients with early biochemical recurrence.

Kroenke et al. from the Technische Universität München (Germany) and the Memorial Sloan Kettering Cancer Center (New York, NY) reported on "PSMA-ligand PET/CT in patients with biochemical recurrent prostate cancer after radical prostatectomy: Matched-pair comparison of ^{68}Ga-PSMA-11 and ^{18}F-PSMA-1007" [588]. A total of 204 patients underwent imaging with either of the tracers, with matched selection based on Gleason scores, TNM, and PSA levels. PET-positive lesions were noted and categorized, and suspicious lesions were differentiated from probably benign lesions based on known pitfalls/information from CT imaging. The researchers found that the detection rate for biochemical recurrence was similar for the 2 tracers, with a slightly higher percentage of suspicious lesions identified by ^{68}Ga-PSMA-11. They made the important observation that ^{18}F-PSMA-1007 had a higher incidence of visually detectable benign lesions with increased PSMA-ligand uptake. The caveat with this study is that this imaging was not performed and compared in the same patients, which should be a goal of a future study. There is great interest in the development of fluorinated PSMA probes for ease of use and to extend availability of these imaging techniques to sites without ^{68}Ga generators.

Another form of PSMA that is being labeled with fluorine is radiohybrid (rh)-PSMA-7. The rhPSMA-targeted agents are monozygotic chemical twins and allow efficient labeling with ^{18}F and radiometals. rhPSMA-7 is the lead compound selected for development by Blue Earth Diagnostics (Oxford, UK; Burlington, MA). At this meeting, Eiber et al. from the Technische Universität München (Munich and Garching, Germany), Scintomics GmbH (Fürstenfeldbruck, Germany), and the Memorial Sloan Kettering Cancer Center (New York, NY) reported on "^{18}F-rhPSMA-7 PET for the detection of biochemical recurrence of prostate cancer following radical prostatectomy" [649]. The study included 532 patients with noncastrate biochemical recurrence after initial prostatectomy, with an initial PSA average of 0.97 ng/mL (range, 0.01–372 ng/mL). The ability to detect lesions was found to be highly dependent on PSA range, and very high-quality imaging studies were obtained (Fig. 3). ^{18}F-rhPSMA-7 PET identified 423 (79.5%) patients with pathologic findings. Suspicious lesions were seen in 38.5% (15/39) of patients with a PSA <0.2 ng/mL. Detection rates were 63.8% (81/127), 86.5% (90/104), 85.3% (87/102), and 93.8% (150/160) at PSA levels of 0.2–<0.5, 0.5–<1, 1–<2, and ≥2 ng/mL, respectively. ^{18}F-rhPSMA-7 PET showed local recurrence in 42.1% (224) of patients. Lymph node metastases were present in the pelvis in 41.4% (220), in the retroperitoneum in 16.6% (88), and supradiaphragmatic location in 6.8% (36) patients.

Metser et al. from the Garvan Institute of Medical Research (Sydney, Australia), the University of Toronto (Canada), Austin Health (Melbourne, Australia), the London Health Sciences Centre (London, Canada), McMaster University (Hamilton,

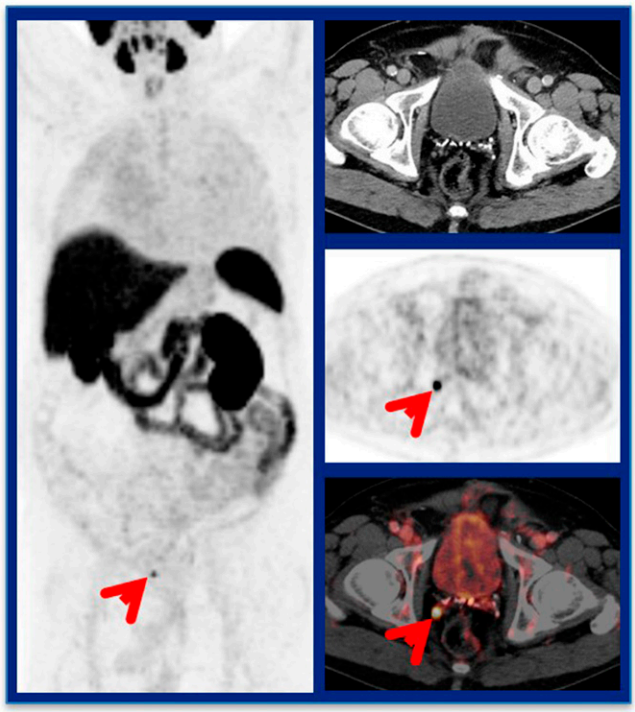


FIGURE 3. ^{18}F-rhPSMA-7 PET for detection of biochemical recurrence of prostate cancer following radical prostatectomy. The study included 532 patients with noncastrate biochemical recurrence after initial prostatectomy, with an initial prostate-specific antigen (PSA) average of 0.97 ng/mL (range, 0.01–372 ng/mL). Image shows a 78-year-old man (pT3a, pNO, Gleason score 8, and PSA = 0.35 ng/mL) who had pelvic disease identified on PSMA PET (arrow), not detected on pre-study CT scan. The ability to detect lesions was found to be highly dependent on PSA range.

Canada), Monash University Eastern Health Clinical School (Melbourne, Australia), Peter MacCallum Cancer Institute (Melbourne, Australia), the Royal Marsden Hospital (London, UK), Université Laval (Quebec, Canada), and University College London (UK) reported on "The contribution of multiparametric pelvic and whole-body MR to the interpretation of ^{18}F-fluoromethylcholine or ^{68}Ga-HBED-CC PSMA-11 PET/CT in the detection of pelvic recurrence or distant metastases in patients with biochemical failure following radical prostatectomy" [593]. They compared not only fluorinated and gallium-labeled imaging agents but also included comparisons with multiparametric MR imaging. Interpretation of PET with multiparametric MR results showed a higher detection rate for local tumor recurrence in the prostate bed in men with biochemical failure after radical prostatectomy. However, the addition of whole-body MR to ^{18}F-fluoromethylcholine/^{68}Ga-HBED-CC PSMA-11 did not improve detection of regional or distant metastases (Fig. 4). Large prospective studies are currently underway looking at MR in this context, but this multicenter trial suggests that whole-body MR is not superior to our PET imaging approaches. These results could aid in refining PET/MR imaging protocols for this patient population.

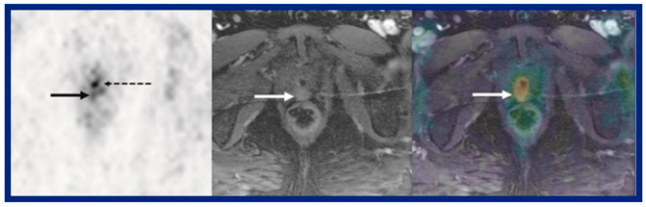


FIGURE 4. Contribution of multiparametric pelvic and whole-body MR to interpretation of ^{18}F-fluoromethylcholine or ^{68}Ga-HBED-CC PSMA-11 PET/CT in detection of pelvic recurrence or distant metastases in patients with biochemical failure following radical prostatectomy. Interpretation of PET with multiparametric MR results showed a higher detection rate for local tumor recurrence in the prostate bed. However, the addition of whole-body MR to ^{18}F-fluoromethylcholine/^{68}Ga-HBED-CC PSMA-11 did not improve detection of regional or distant metastases. Images of axial PSMA PET/multiparametric MR, with left image (PSMA PET) showing intense radiotracer activity in urethra at level of surgical anastomosis (dotted arrow) and ill-defined moderate uptake posterior to the urethra, not interpreted prospectively as tumor on PET. Fused PET/MR image (right) shows the radiotracer uptake corresponds to a focus of abnormal enhancement on dynamic contrast-enhanced MR (arrow, middle and right), suggestive of local tumor recurrence.

Vangu and Kasapato from the University of the Witwatersrand (Johannesburg, South Africa) asked the question "Imaging with PSMA: Which approach when only Tech rather than Galli is available?" [1559]. This research was prompted, in part, by a search for alternatives when there are radioisotope shortages. The study included 18 participants (PSA range, 0.13–270 ng/mL) who underwent ^{99m}Tc-PSMA and ^{68}Ga-PSMA scans. A total of 26 sites of abnormal uptake were seen with ^{68}Ga-PSMA and 17 with ^{99m}Tc-PSMA. Additional analyses showed abnormal uptake in only 4 participants on ^{99m}Tc-PSMA planar imaging compared with 12 on SPECT and SPECT/CT. Agreement between ^{68}Ga-PSMA and ^{99m}Tc-PSMA imaging was moderate, and ^{99m}Tc-PSMA provided very good images (Fig. 5). In institutions without a PET/CT facility or ^{68}Ga generator, ^{99m}Tc-PSMA appears to be

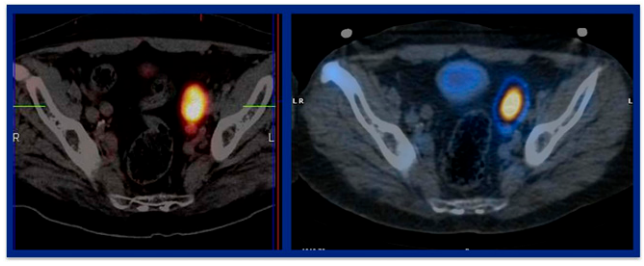


FIGURE 5. Prostate-specific membrane antigen (PSMA) imaging with technetium. ^{99m}Tc-PSMA/CT (right) and ^{68}Ga-PSMA/CT (left) images were compared in individuals with PSA levels ranging from 0.13 to 270 ng/mL. Agreement between ^{68}Ga-PSMA and ^{99m}Tc-PSMA imaging was moderate. In institutions without a PET/CT facility or ^{68}Ga generator, ^{99m}Tc-PSMA appears to be feasible provided that SPECT (preferably SPECT/CT) is available.

well worth considering, provided (as the authors noted) that SPECT or preferably SPECT/CT is available. The use of ^{99m}Tc-PSMA may also have utility in staging prior to surgery for oligometastatic disease.

Novel Therapeutic Approaches

We have seen remarkable progress in radionuclide therapy in the last 12 months, much of it focusing on prostate cancer treatment with β or α particle molecules. We are seeing an increase in the number of multicenter studies examining these types of treatments, for example, with ^{177}Lu-PSMA trials. New and innovative approaches are being reported in treatment regimens, dosing, scheduling, rechallenge treatment, and combination therapies. Advances in α-particle peptide-receptor radionuclide therapy (PRRT)/PSMA-targeted radioligand therapy (PRLT) are making news in our field and in the wider media. We are also confronting ongoing challenges in these novel areas, including standardization of protocols, providing compelling evidence of outcome improvement, and creation of robust economic models.

Saidi et al. from Orano Med SAS (Courbevoie, France), Nordic Nanovector ASA (Oslo, Norway), the University of Oslo (Norway), and Orano Med LLC (Plano, TX) reported on "Targeted α therapy with ^{212}Pb-NNV003 for the treatment of CD37 positive B-cell chronic lymphocytic leukemia (CLL) and non-Hodgkin lymphoma (NHL)" [354]. CD37 is highly and selectively expressed on the surface of mature B lymphocytes and B-cell malignancies. These authors have developed and reported previously on a targeted α therapy in which the CD37-specific antibody NNV003 is coupled to the α-particle-emitting radioisotope ^{212}Pb. The resulting compound is highly effective in animal models of Burkitt lymphoma and CLL (*Blood.* 2018;132:4422). In the study reported at this meeting, the authors looked at the therapeutic effect of a range of specific activities in a preclinical model of CLL. The results showed that labeling this molecule with ^{212}Pb led to improved responsiveness and suggested that ^{212}Pb-NNV003 is a safe and effective method for treatment of CD37-positive CLL and NHL in mouse models, with clinical testing warranted. An increase in the number of different α particle approaches and the promise of their transition to the clinical space is something that I look forward to in the coming years.

Dizdarevic et al. from Bayer AG (Wuppertal, Germany), Bayer Consumer Care AG (Basel Switzerland), Brighton & Sussex University Hospitals NHS Trust (UK), the Dana-Farber Cancer Institute (Boston, MA), Weill Cornell Medicine (New York, NY), the University of Messina (Italy), St. James's University Hospital (Leeds, UK), the Christie NHS Foundation Trust (Manchester, UK), Tulane University School of Medicine (New Orleans, LA), the University of Montreal Hospital Center (Canada), and Wichita Urology (KS) reported on "Co-treatment with ^{223}Ra and enzalutamide: Outcomes in patients with metastatic castration-resistant prostate cancer from a prospective multicenter observational study" [467]. This analysis was a part of the REASSURE (Evaluation of long-term safety of ^{223}Ra used for the treatment of metastatic castration resistant prostate cancer) study, including more than 1,400 patients who were treated with ^{223}Ra, some of whom also received enzalutamide. REASSURE is a prospective, non-interventional, multicenter study designed to assess the short- and long-term safety (over a 7-year follow-up) of patients treated with ^{223}Ra in real-world clinical practice. The authors at this meeting presented an exploratory analysis evaluating clinical outcomes of the combined use (concurrent or layered) of ^{223}Ra and enzalutamide. Of particular interest was the question of the effects of this combined treatment on symptomatic skeletal events. Their data indicated that in routine clinical practice the combined treatment did not appear to increase the rate of such events. The rate of reported fractures was also generally low and was slightly lower in patients with concomitant use of bone health agents. These findings are encouraging as part of postmarketing assessment and also illustrate the fact that this approach has significant utility in the population with metastatic castrate-resistant prostate cancer.

Strosberg et al. from Advanced Accelerator Applications (New York, NY), Boston Medical Center (MA), Cedars-Sinai Medical Center (Santa Monica, CA), Mayo Clinic (Rochester, MN), Memorial Sloan Kettering Cancer Center (New York, NY), Moffitt Cancer Center (Tampa, FL), Stanford Cancer Center (CA), the University of Iowa (Iowa City), and the University of Texas MD Anderson Cancer Center (Houston) presented "Does liver tumor burden affect the therapeutic effect of ^{177}Lu-DOTATATE treatment? Analysis of progression-free survival, safety, and quality of life in NETTER-1 study" [623]. The study included patients who had well-differentiated, metastatic midgut neuroendocrine tumors who received either ^{177}Lu-DOTATATE or octreotide LAR (long-acting release) alone. ^{177}Lu-DOTATATE treatment showed significant improvement in progression-free survival, regardless of the extent of baseline liver tumor burden. In addition, clinically significant liver function test abnormalities were rare and were not associated with high liver tumor burden. The researchers observed that ^{177}Lu-DOTATATE treatment was also associated with quality of life benefit regardless of baseline liver tumor burden. In short, ^{177}Lu-DOTATATE appeared to be safe and effective, even when patients were affected by high liver burden.

Combination treatments will become increasingly important as we move forward with developing new radionuclide therapy approaches. Emmett et al. from Monash University (Melbourne), the Peter MacCallum Cancer Centre (Melbourne), and St. Vincent's Hospital (Sydney, all in Australia) reported on "Interim results of a phase I/II prospective dose escalation trial evaluating safety and efficacy of combination ^{177}Lu PSMA-617 and NOX66 in men with metastatic castrate-resistant prostate cancer post androgen-signaling inhibition and 2 lines of taxane chemotherapy (LuPIN trial)" [465]. This prospective, open-label, single-arm, nonrandomized phase I dose escalation/phase II dose expansion study included 8 men treated with 6 doses of ^{177}Lu PSMA-617 and 400 mg of the radiosensitizer NOX66 and

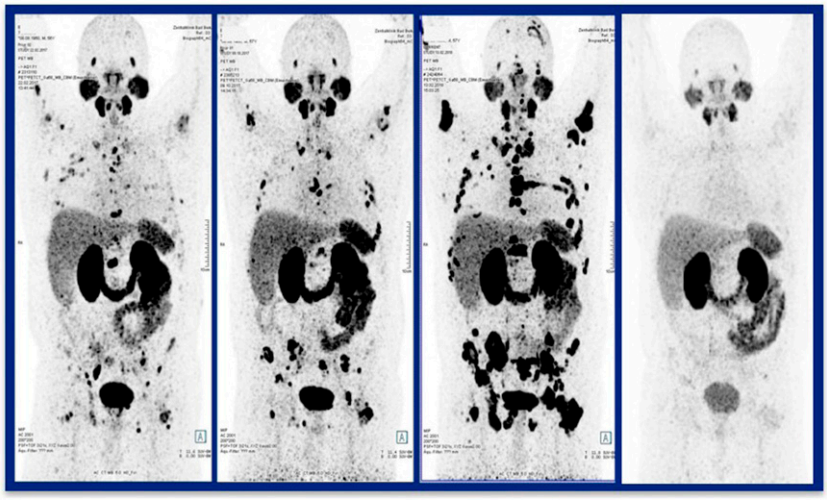


FIGURE 6. ^{225}Ac- and ^{177}Lu-labeled prostate-specific membrane antigen (PSMA) ligands for treatment of progressive end-stage metastatic prostate cancer. The researchers combined the 2 agents (referred to as tandem αβ–PSMA-targeted radioligand therapy [PRLT]) in 24 patients. ^{68}Ga-PSMA images are shown in a patient who experienced disease progression through 3 cycles of ^{177}Lu-PRLT (left 3 images: pre-PRLT1, PSA = 0.93; post-PRLT2, PSA = 11.2; post-PRLT3, PSA = 137). After tandem αβ-PRLT (right image), marked response was observed, and the PSA was 0.9.

8 men treated with 6 doses of ^{177}Lu PSMA-617 and 800 mg of NOX66. At both dosages, the combination appeared to be safe and well tolerated, with early signs of efficacy. The trial is being expanded to include 24 men scheduled to receive ^{177}Lu PSMA-617 and 1,200 mg of NOX66. Further studies will be required to demonstrate whether the radiosensitizer will convey longer term advantages over PSMA alone. We will be seeing more of these types of studies as improvements in PSMA treatments in prostate cancer populations are explored.

Zang et al. from the National Institute of Biomedical Imaging and Bioengineering (Bethesda, MD), the Peking Union Medical College/Hospital (Beijing, China), and the Chinese Academy of Medical Science (Beijing, China) reported on "Safety and response to ^{177}Lu-EB-PSMA-617 in patients with metastatic castration-resistant prostate cancer" [536]. The study included 46 patients who received up to 3 cycles of ^{177}Lu-EB-PSMA-617 at 1.9 or 3.7 GBq. The researchers observed frequent responses and acceptable toxicity. Additional investigations are warranted to increase the number of patients and the frequency of administration.

We await with great interest the results of the study of ^{177}Lu-PSMA-617 in metastatic castrate-resistant prostate cancer (VISION study) and the trial of ^{177}Lu-PSMA-617 versus cabazitaxel in progressive metastatic castration-resistant prostate cancer (TheraP study). Other multicenter studies are commencing in earlier disease stages, and combination approaches, as mentioned, are becoming more prevalent.

Kulkarni et al. from the Zentralklinik Bad Berka (Germany) reported on "Radioligand therapy using a combination of ^{225}Ac- and ^{177}Lu-labeled PSMA ligands for progressive end-stage metastatic prostate cancer: Effective trade-off between response and toxicity" [464]. The researchers combined the 2 agents (referred to as "tandem αβ-PRLT) in 24 patients. Even in some patients who had shown progression after previous

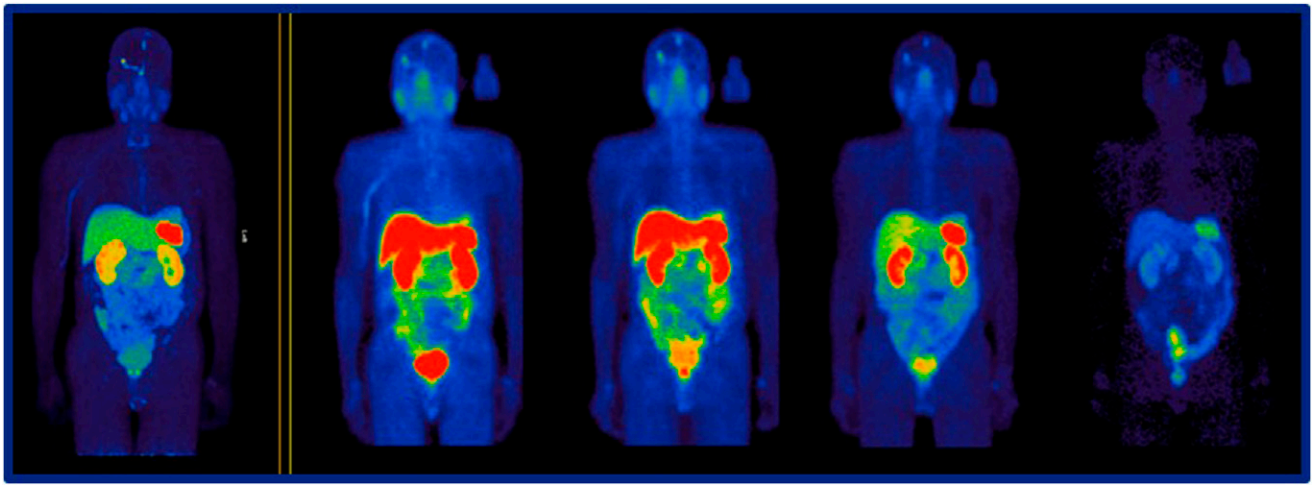


FIGURE 7. Theranostic ^{64}Cu/^{67}Cu with 3D pretreatment dosimetry. Subjects with somatostatin receptor–positive meningiomas received ^{64}Cu-MeCOSar-octreotate followed by 5–6 GBq of ^{67}Cu-MeCOSar-octreotate. Left to right: [^{64}Cu]Cu-SARTATE PET planning at 4 hours after injection; [^{67}Cu]Cu-SARTATE SPECT at 1, 4, 24, and 96 hours after initiation of therapy. ^{64}Cu/^{67}Cu-MeCOSar-octreotate appears to be a potential alternative theranostic combination for subjects with somatostatin-expressing tumors.

^{177}Lu-PRLT, the combination of the 2 agents resulted in an excellent response (Fig. 6), with no severe xerostomia or renal/hepatic toxicity and no worsening of preexisting anemia/pancytopenia. These preliminary results highlight the opportunity and potential for combining these and other agents to enhance and refine treatment.

Lutetium is not the sole focus of exploratory methods in combining treatments. Bailey et al. from Royal North Shore Hospital (Sydney and St. Leonards, Australia) and Clarity Pharmaceuticals (Eveleigh and Sydney, Australia) reported on "A novel theranostic trial design using ^{64}Cu/^{67}Cu with fully 3D pretreatment dosimetry" [204]. Individuals with somatostatin receptor–positive meningiomas received ^{64}Cu-MeCOSar-octreotate followed by 5–6 GBq of ^{67}Cu-MeCOSar-octreotate. No significant adverse events were observed, and estimated doses projected from ^{64}Cu PET to ^{67}Cu SPECT were predictive for liver and red marrow (blood-derived for ^{67}Cu). The researchers showed excellent comparability of biodistribution between the SARTATE-conjugated agents (Fig. 7). They concluded that ^{67}Cu-octreotate appears to be a safe alternative theranostic agent for individuals with somatostatin-expressing tumors, adding that "the long half-life of the companion diagnostic imaging radionuclide (^{64}Cu) permits pretherapeutic estimates of dosimetry in a number of organs. . . ." They noted the potential utility in pediatric patients, for whom no reliable dose scaling for age and size is available.

Summary

This has been a terrific meeting, with many exciting presentations and posters. Nuclear medicine is becoming much more prominent and gaining more recognition for diagnostic and therapeutic progress in the global oncology community. We have a growing number of multicenter and multinational trials providing the type of evidence that will support and accelerate future research and clinical acceptance. This progress will rely on our continued engagement with oncologists and surgeons, as well as patient advocacy groups. I encourage you all to continue with your research and to particularly think about health care outcomes, including economic analyses. The pivotal role of nuclear medicine in exploring cancer biology and developing more effective therapies is clear, and we should all be encouraged as we see the associated innovations applied to the benefit of patients worldwide.

NEWSBRIEFS

NCRP Reports Medical Radiation Doses Decreasing

The National Council on Radiation Protection and Measurements (NCRP) issued on November 18 a new report showing a 15%–20% reduction in diagnostic and interventional medical radiation doses to the U.S. population from 2006 to 2016. Except for CT scans, most medical imaging doses are stable or decreasing. This finding is a contrast to the dramatic rise documented in a 2009 NCRP report that showed a 6-fold increase from the early 1980s to 2006. NCRP Report No. 184, entitled "Medical Radiation Exposure of Patients in the United States," is a 10-year update to the 2009 NCRP report.

"Our report demonstrates that medical radiation doses in the United States are on the decline, which is a positive shift from a decade ago when doses were increasing significantly," said Fred Mettler, MD, MPH, chair of the NCRP report and professor emeritus and clinical professor in the Department of Radiology and Nuclear Medicine at the University of New Mexico School of Medicine (Albuquerque). "In the report, we pay particular attention to medical procedures that contribute the largest share of dose and provide information on average doses that patients may experience from a specific examination." NCRP Report No. 184 indicates that CT scans made up 63% of collective dose from medical imaging procedures in 2016, compared to 50% in 2006. Although the number of CT scans increased by 20% over that decade, the overall dose per person for CT procedures was essentially unchanged. For a number of other modalities, the report shows the average radiation dose per person has decreased. The report discusses technology advances that have yielded hardware improvements and protocols leading to higher quality images at lower doses. Efforts by imaging and other organizations have also increased awareness and understanding of medical radiation doses, dose optimization, and reduction in dose.

National Council on Radiation Protection and Measurements