2019 SNMMI Highlights Lecture: Oncology and Therapy, Part 2

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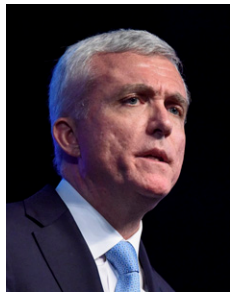
From the Newsline Editor: The Highlights Lecture, presented at the closing session of each SNMMI Annual Meeting, was originated and presented for more than 30 years by Henry N. Wagner, Jr., MD. Beginning in 2010, the duties of summarizing selected significant presentations at the meeting were divided 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.

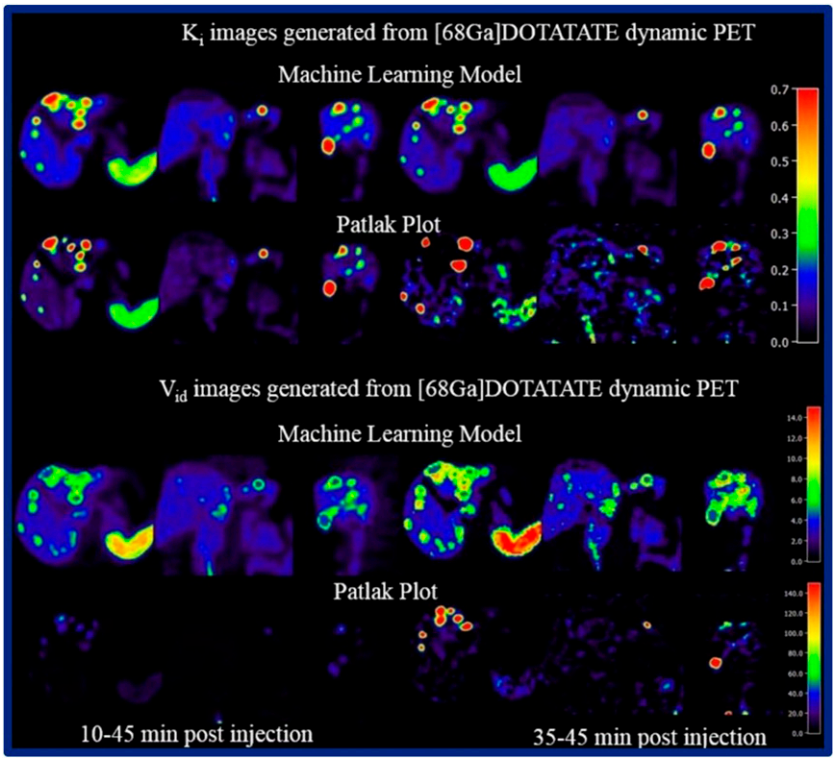


FIGURE 1. A machine learning–based parametric imaging algorithm for noninvasive quantification of dynamic ^{68}Ga-DOTATATE PET/CT. Top block: K_i images generated from ^{68}Ga-DOTATATE dynamic PET using: (top row) a machine learning model and (bottom row) Patlak plots. Bottom block: V_{id} images generated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

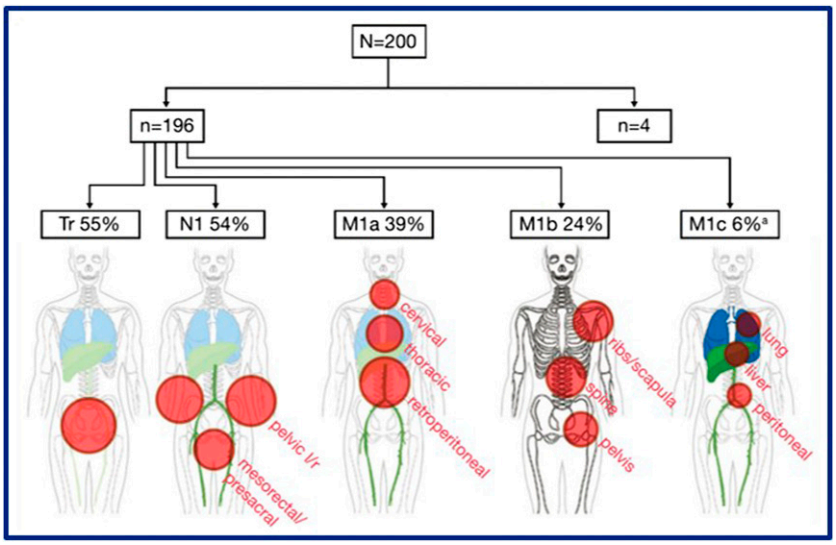


FIGURE 2. Prostate-specific membrane antigen (PSMA) PET detected M1 disease in more than half of nonmetastatic castration-resistant prostate cancer patients. Image shows results from a predefined protocol for retrospective analysis of PSMA PET databases at 6 centers. PSMA PET detected metastatic disease 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,

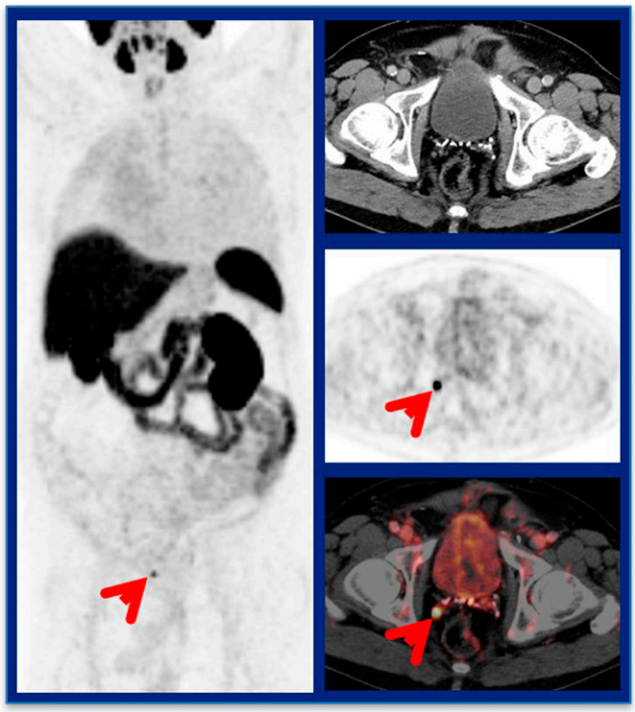


FIGURE 3. ^{18}F-rhPSMA-7 PET for detection of biochemical recurrence of prostate cancer following radical prostatectomy. The study included 532 patients with noncastrate biochemical recurrence after initial prostatectomy, with an initial prostate-specific antigen (PSA) average of 0.97 ng/mL (range, 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.

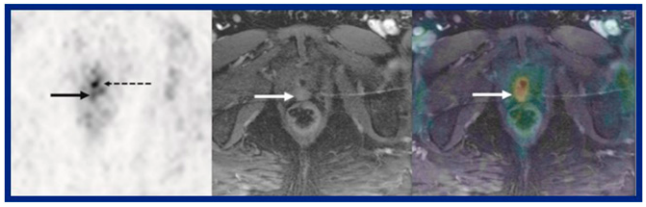


FIGURE 4. Contribution of multiparametric pelvic and whole-body MR to interpretation of ^{18}F-fluoromethylcholine or ^{68}Ga-HBED-CC PSMA-11 PET/CT in detection of pelvic recurrence or distant metastases in patients with biochemical failure following radical prostatectomy. Interpretation of PET with 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

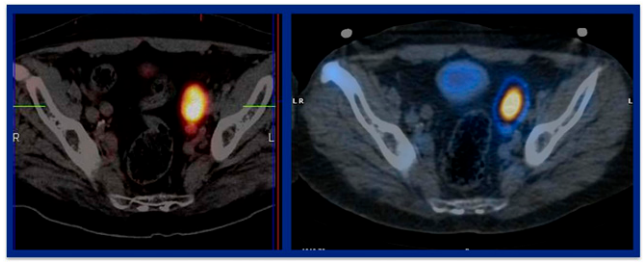


FIGURE 5. Prostate-specific membrane antigen (PSMA) imaging with technetium. ^{99m}Tc-PSMA/CT (right) and ^{68}Ga-PSMA/CT (left) images were compared in individuals with PSA levels ranging from 0.13 to 270 ng/mL. Agreement between ^{68}Ga-PSMA and ^{99m}Tc-PSMA imaging was moderate. In institutions without 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

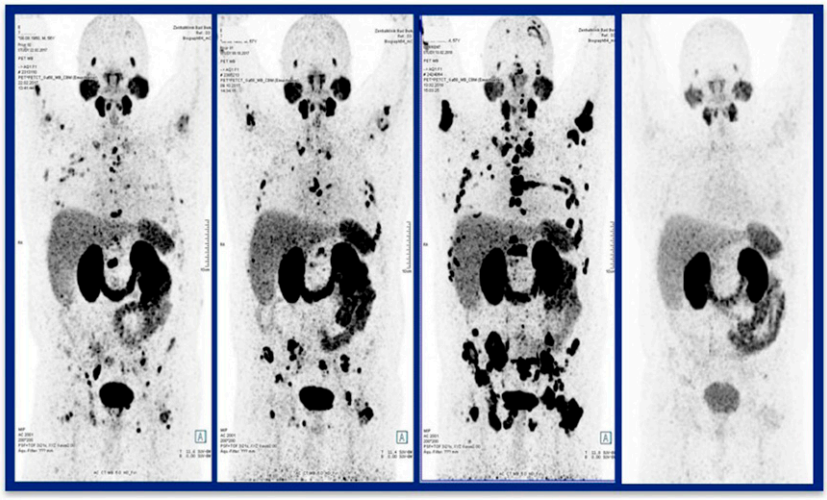


FIGURE 6. ^{225}Ac- and ^{177}Lu-labeled prostate-specific membrane antigen (PSMA) ligands for treatment of progressive end-stage metastatic prostate cancer. The researchers combined the 2 agents (referred to as tandem αβ–PSMA-targeted radioligand therapy [PRLT]) in 24 patients. ^{68}Ga-PSMA images are 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

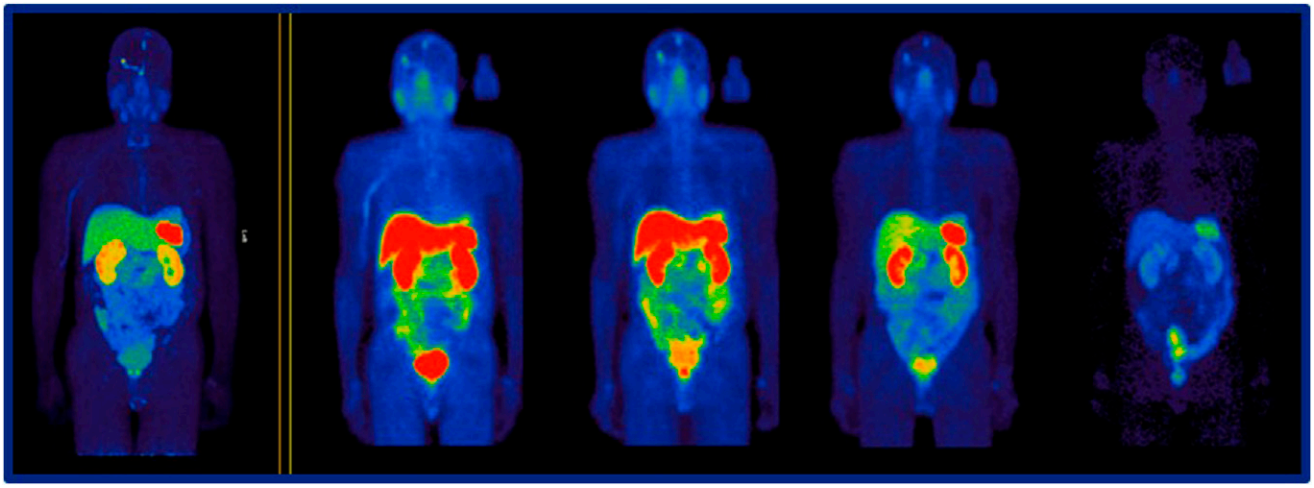


FIGURE 7. Theranostic ^{64}Cu/^{67}Cu with 3D pretreatment dosimetry. Subjects with somatostatin receptor–positive meningiomas received ^{64}Cu-MeCOSar-octreotate followed by 5–6 GBq of ^{67}Cu-MeCOSar-octreotate. Left to right: [^{64}Cu]Cu-SARTATE PET planning at 4 hours after injection; [^{67}Cu]Cu-SARTATE 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

ABNM Certification Trends, 1977–2019

George M. Segall, MD, Executive Director, American Board of Nuclear Medicine

The American Board of Nuclear Medicine (ABNM) was incorporated in 1971, a time when no Accreditation Council for Graduate Medical Education (ACGME)–accredited nuclear medicine training programs existed. The first certification examination was given in 1972. For the first 5 years, physicians could take the examination if they were certified by 1 of the founding specialty boards (radiology, internal medicine, or pathology) and met other requirements. Training in an ACGME-certified nuclear medicine program became a requirement in 1977. The length of nuclear medicine residency training was initially 2 years. The average number of candidates taking the ABNM examination each year from 1977 to 2007 was 105, and the average number of candidates who passed the examination was 74 (Fig. 1).

In 2007, the length of training was increased to 3 years, and the number of candidates taking and passing the examination declined to 88 and 70, respectively, for the years 2008–2015. During the same period, the number of accredited nuclear medicine residency programs declined from 56 to 43, and the number of residents in training declined from 149 to 93. The increase in the length of training had an unanticipated adverse impact on the number of physicians entering nuclear medicine residency programs. This decline continued in recent years as a result of changes in health care and the poor job market for nuclear medicine physicians who were not also certified in radiology.

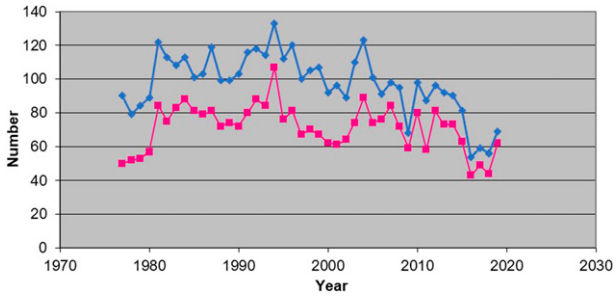


FIGURE 1. Numbers of candidates who took (blue) and who passed (pink) the ABNM examination from 1977 to 2019.

George M. Segall, MD

The nadir was reached in 2016. Since that time, the numbers of physicians in nuclear medicine training programs has increased, as has the number of physicians certified by the ABNM. This positive trend is partly the result of new integrated training pathways in nuclear medicine and radiology that allow physicians to complete training required for both specialties in 4–5 years. The increase is also due to development of new radiopharmaceuticals for diagnosis and treatment, which has made nuclear medicine training more appealing to young professionals. This year, 69 candidates took the certification examination and 62 passed, compared to 54 and 43, respectively, in 2016.

The same forces responsible for these trends are responsible for changes in the number of ABNM-certified physicians who are also certified by another member board of the American Board of Medical Specialties (ABMS). From 2001 to 2016, 49% of ABNM physicians were also certified by the American Board of Radiology (ABR), and 24% were also certified by another ABMS member board. Since 2016, the percentage of ABNM physicians also certified by the ABR has remained steady, whereas the percentage of ABNM physicians also certified in internal medicine or other specialties has fallen to $<10\%$. In the future, the ABNM expects the percentage of physicians who are also certified by the ABR to increase. It remains to be seen how recent developments in targeted radionuclide therapy and the increasing number of therapies being performed will affect these trends.

The ABNM sees a bright future for nuclear medicine and is encouraged by the recent number of young professionals interested in the specialty. The ABNM is committed to ensuring that nuclear medicine continues to be strong.

Conrad Nagle, MD, 1946–2019

Conrad Ernest Nagle, MD, a nuclear medicine physician influential in medical school and graduate medical education and active in SNMMI, died suddenly at his farm in Sperryville, VA, on November 25. He was born and grew up in Baltimore County, MD, attending the University of Maryland College Park for his undergraduate degree. He graduated from the University of Maryland School of Medicine in 1972 and completed his residency in internal medicine and nuclear medicine fellowship training at the University of Maryland Medical Center in 1977. He was recruited in 1980 as the chief of nuclear medicine at Troy Beaumont Hospital (MI) and spent the rest of his career in practice and leadership positions in the Beaumont Health System in southeast Michigan. He retired in 2011.

Conrad was a compassionate physician who enjoyed providing direct patient care while educating young physicians in Beaumont's radiology and nuclear medicine training programs. He had a wide variety of interests in nuclear medicine applications, including but not limited to sports medicine, chronic pain, and simplifying diagnostic workups by incorporating appropriate imaging procedures earlier in the evaluation process. Working with Conrad was always a pleasure. His colleagues admired his integrity, honesty, and commitment to making the right decisions. He developed a keen interest in health care economics and made administrative changes in anticipation of health care market trends. His administrative skills were recognized by his designation as Corporate Chief of Diagnostic Imaging by the Beaumont System in January 2004, leading to significant streamlining of health care delivery across 4 separate radiology and nuclear medicine departments during his 5-year tenure. After stepping down from this position, Conrad devoted his last 2 years of practice to designing the first- and second-year course curriculum (called "The Art and Practice of Medicine") for the new Oakland University William Beaumont Medical School that opened in 2011. This innovative curriculum emphasizes the importance of mastery of clinical and diagnostic skills while developing communication skills that foster the best patient–physician interactions. The curriculum has served as the template for several new medical schools and has provided the impetus for revising other established medical school curricula for the first 2 years of study.

Throughout his medical career, Conrad was an active leader in both regional and national nuclear medicine arenas, serving as vice-president and then president of the Central Chapter of the Society of Nuclear Medicine (1992 and 1993). On the national level, he brought new ideas and a fresh approach to *The Journal of Nuclear Medicine* (*JNM*) as its Newsline editor (1999–2012). His advice and solid judgment significantly enhanced the information disseminated to the nuclear medicine community. Heinrich R. Schelbert, MD, PhD, immediate past editor of *JNM*, noted that "The news of Conrad's passing filled me with deep sadness. I had the privilege of working closely with him for 8 years, when, as associate editor of *JNM,* he managed the journal's Newsline section. During this time, I came to know him as a highly dedicated colleague and reliable friend. I admired his integrity and dedication to serve our nuclear medicine community and fully trusted his advice and solid judgment. He will be missed."

Conrad's expertise in health care delivery made him a valued member (2003–2012) of the SNM Publications Committee (chair, 2005–2010) and SNM Board of Trustees (2005–2010). His steady hand and thoughtful approach to problem resolution also made him a sought-after member of many other SNM committees, including Practice Management, Education, Awards, and Quality Assurance. He also served on the society's Commission on Health Care Policy and Practice, the Maintenance of Certification Part IV Task Force, the Molecular Imaging Communications Task Force, and the Accreditation Council.

Following his retirement in 2011, Conrad maintained his interest in the practice of medicine and completed an internal medicine review course at the University of Virginia shortly before his death. He derived much pleasure from his country life, caring for the family dogs and horses. Conrad is survived by Kim, his wife of 49 years; 3 children, Chris, Drew, and Kerry; and 3 grandchildren, Arella, Leo, and Kepler.

John E. Freitas, MD
Emeritus Clinical Professor of Radiology
University of Michigan Medical School

Paving the Way for Research and Discovery

Virginia Pappas, CAE, SNMMI CEO

SNMMI's strategic plan includes a strong focus on research and discovery, with an overarching goal of advancing the development and approval of nuclear medicine and molecular imaging technologies. SNMMI has made significant progress in this area within the past few years.

The SNMMI Clinical Trials Network (CTN)—which celebrates its 10th anniversary this year—has been particularly successful in fulfilling its mission to optimize the use of radiopharmaceuticals in clinical trials and, ultimately, advance them into clinical practice. As a result, the field has seen an increase in the availability and performance of molecular imaging radiopharmaceuticals in the clinic.

A key component of the CTN is its scanner validation program, which uses a proprietary anthropomorphic oncology phantom. The current version of this clinical simulator has 13 lesions of variable size that mimic the National Electrical Manufacturers Association (NEMA) IQ phantom, which is the standard in Europe. Scanner Validation Committee members are working with their European and Australian counterparts to develop international acceptance criteria.

As PET/CT imaging becomes more common in the management of many types of cancer patients, accreditation programs increasingly require phantom-based scanner measurements to ensure imaging accuracy. To meet this growing demand, the Scanner Validation Committee released a new cloud-based, automated Phantom Analysis Toolkit. The toolkit is designed to produce rapid, reliable, reproducible, and fully automated phantom analysis for the 4 most common PET phantoms currently in use in clinical trials and clinical practice: the American College of Radiology PET Phantom, CTN Oncology Phantom, NEMA Image Quality Phantom, and the Uniform Phantom. SNMMI members receive access to the toolkit free of charge.

Educating our members on research-related topics and the latest imaging agents also is a core function of the CTN. Our last 2 webinar series—designed for technologists, fellows, residents, and supervising physicians—focused on anatomy and radiopharmaceuticals and were very well attended; both series are available on-demand on the SNMMI website. In January, a new continuing medical education course, "Gallium-68-Labeled Somatostatin Receptor PET/CT Imaging Reader Training," went live in the SNMMI Learning Center. For the second year in a row, a CTN-submitted session will be presented at the American Society of Clinical Oncology; this year's topic is "Recent Advances in Nuclear Medicine Theranostics for Cancer," with planned lectures from Jonathan McConathy, MD, PhD, and Michael Hofman, MBBS. The SNMMI Nuclear Medicine Clinical Trial Group, LLC (NMCTG), offers reader training in-person at SNMMI meetings as well as online and has been highly utilized.

The NMCTG has assisted nearly a dozen companies and entities with incorporating molecular imaging in multicenter trials and has made great strides in enhancing the quality of data collected. Trial activities have included scanner validation and harmonization of study scanners, image quality control, study personnel training, and trial design consultation. Once agents are approved, reader training modules are developed and made available at no charge on the NMCTG web page. Modules are currently available for ^{18}F-fluciclovine, ^{68}Ga-DOTATATE, and ^{68}Ga-DOTATOC—all with embedded case reads. Training is also offered via live webinar, at the SNMMI Annual Meeting, and at other meetings.

Progress has also been made in promoting development of targeted radionuclide therapies. In 2018, SNMMI sponsored a Theranostics Consensus Conference that served as a springboard for several intersocietal initiatives to encourage development of the professional practice of theranostics. SNMMI hosted a categorical session on theranostics at its 2019 Annual Meeting to discuss regulatory perspectives on products that combine an imaging modality with therapeutic radiopharmaceuticals. Based on the success of these 2 initiatives, major stakeholders in theranostics gathered for a productive day of in-depth discussions at the third Targeted Radionuclide Therapy Conference in December 2019.

In addition to theranostics, artificial intelligence (AI) has become a promising topic of interest in the nuclear medicine and molecular imaging field. The Research and Discovery domain and the Physics, Instrumentation, and Data Sciences Council have created an Artificial Intelligence Taskforce that will identify areas where AI can benefit the field.

I am happy to announce that SNMMI has introduced several new research grants and plans for fellowships to promote research in the field. These include 5 grants to introduce high-achieving students to molecular imaging and targeted radiotherapy as a potential career path, a grant to study the value of nuclear medicine tests, and fellowships in targeted radionuclide therapy.

I would like to express my appreciation to those who have led the society's efforts in research and discovery. Bonnie Clarke, BS, SNMMI's director of research and discovery, has managed the CTN and the NMCTG from their inception. Over its 10 years, the CTN has been chaired by several dedicated members, including Sandy McEwan, MD, PhD, Peter Conti, MD, PhD, Michael Graham, PhD, MD, and John Hoffman, MD, as well as John Sunderland, PhD, and Jonathan McConathy, MD, PhD, the current co-chairs. Thanks to these individuals, as well as many others, we can look forward to an exciting future for nuclear medicine and molecular imaging.

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

PET/CT and Kidney Allograft Subclinical Rejection

Hanssen et al. from the University of Liège Hospital (Belgium) and the Necker Hospital/Assistance Publique-Hôpitaux de Paris (France) reported on December 16 ahead of print in the *American Journal of Transplantation* on a study to investigate the potential of ^{18}F-FDG PET/CT as a noninvasive alternative to biopsy in assessing subclinical kidney allograft acute rejection, defined as "the unexpected histological evidence of acute rejection in a stable patient." The study included 92 adult patients who underwent ^{18}F-FDG PET/CT at the time of surveillance biopsy at ~3 mo after transplantation, with the mean SUV ratio (mSUVR) between kidney cortex and psoas muscle calculated. Urinary levels of chemokine (C-X-C motif) ligand 9 (CXCL9) were also quantified. The Banff 2017 classification was used to categorize participants as normal (70), borderline (16), and subclinical rejection (6). No clinical or biologic differences were seen between these groups. The mSUVRs were 1.87 ± 0.55, 1.94 ± 0.35, and 2.41 ± 0.54 in the normal, borderline, and subclinical rejection groups, respectively. mSUVR was significantly higher in the subclinical rejection group than in the normal group. The area under the receiver operating characteristics curve (area under the curve [AUC]) was 0.79, with 83% sensitivity using an mSUVR threshold of 2.4. The AUC of urinary CXCL-9/creatinine ratios reached 0.79. mSUVR positively correlated with tubulointerstitial damage and acute composite Banff scores. The authors concluded that "^{18}F-FDG-PET/CT helps noninvasively exclude subclinical kidney allograft acute rejection, with a negative predictive value of 98%."

American Journal of Transplantation

^{18}F-PSMA-1007 PET/CT in Biochemically Relapsed PCa

In an article e-published on November 28 ahead of print in *Prostate Cancer and Prostatic Diseases*, Witkowska-Patena et al. from the Military Institute of Medicine (Warsaw), the Affidea Mazovian PET/CT Medical Centre (Warsaw), and Synektik Pharma (Kielce, all in Poland) reported on a study prospectively evaluating the diagnostic performance of ^{18}F-PSMA-1007 PET/CT in patients with prostate cancer after radical treatment and low but rising prostate-specific antigen (PSA) levels. The study included 40 patients after radical treatment (32 after radical prostatectomy, 8 after radiation therapy) with low (0.008–≤2.0 ng/mL) and rising PSA levels. Each underwent skull-to-midthigh ^{18}F-PSMA-1007 PET/CT imaging, and results were compared with PSA levels, Gleason scores, and tumor stage. The sensitivity, specificity, and negative and positive predictive values of imaging were assessed at 10.3 (± 4.7)–mo follow-up. ^{18}F-PSMA-1007 PET/CT was positive in 24 (60%) patients. Detection rates were 39%, 55%, and 100% for PSA levels <0.5, 0.5–<1.0, and 1.0–≤2.0 ng/mL, respectively. PET/CT identified metastases in locoregional lymph nodes in 55% of patients, in bones in 36% of patients, and local recurrence in 9% of patients. PET/CT positivity was independent of Gleason score and tumor stage. Follow-up assessment in 40 lesions yielded sensitivity, specificity, and positive and negative predictive values of 100%, 94.4%, 66.7%, and 100%, respectively. The authors summarized their results: "^{18}F-PSMA-1007 PET/CT shows relatively high detection rate in patients with prostate cancer after radical treatment and low, rising PSA levels...." as well as "excellent sensitivity, specificity, and negative predictive values."

Prostate Cancer and Prostatic Diseases

Multinational PET/CT Study of Extrapulmonary TB Presentation

Bomanji et al. from the University College London Hospitals NHS Foundation Trust (UK) and research centers in India, Pakistan, Bangladesh, Austria, South Africa, Serbia, Thailand, and other UK institutions representing the International Atomic Energy Agency Extrapulmonary Tuberculosis Consortium reported on December 12 in the *European Respiratory Journal* on the potential for ^{18}F-FDG PET/CT for localizing sites and extent of disease in extrapulmonary tuberculosis (EPTB). The study included 358 EPTB patients (189 women; 169 men; age range, 18–83 y) from centers in India, Pakistan, Thailand, South Africa, Serbia, and Bangladesh who underwent imaging within 2 wk of presentation to assess extent of disease and common sites of involvement. A total of 118 (33.7%) had a single extrapulmonary site and 232 (66.3%) had more than 1 site (organ) affected. Lymph nodes, bone, pleura, and brain were common sites. A total of 100 (28%) had ^{18}F-FDG PET/CT–positive sites in the lung, and 110 patients were ^{18}F-FDG PET/CT–positive in more body sites than noted clinically at first presentation. The authors concluded that ^{18}F-FDG PET/CT scanning "has potential for further elucidating the spectrum of disease, pathogenesis of EPTB, and monitoring the effects of treatment on active lesions over time, and requires longitudinal cohort studies, twinned with biopsy and molecular studies."

European Respiratory Journal

PD-L1 Inhibitor-Induced Thyroiditis and Survival

In a study e-published on December 6 ahead of print in *Thyroid*, Kotwal et al. from the Mayo Clinic (Rochester, MN) reported on a study investigating the association of programmed cell death protein-ligand 1 (PD-L1) inhibitor-induced thyroiditis with overall survival in patients with cancer. The retrospective study characterized thyroid immune-related adverse events in patients treated with PD-L1 inhibitors and evaluated treatment impact on overall survival. A total of 91 patients' records were included. All had been treated with atezolizumab and avelumab and were followed for a median of 10.1 mo. Thyroid immune-related adverse events included new onset hypothyroidism, thyrotoxicosis, and worsening of preexisting hypothyroidism. Nineteen patients (21%) developed new onset thyroid dysfunction (14 presenting with hypothyroidism, 5 with thyrotoxicosis), of whom 3 progressed to hypothyroidism and 2 returned to euthyroidism. Four patients (4%) had worsening of preexisting hypothyroidism. Thyroid immune-related adverse events occurred after a median of 2 doses (6 wk), and although 48% of these patients required thyroid hormone replacement, none required steroids or discontinuation of immunotherapy. Two of the 4 patients with thyroid peroxidase antibody >9 IU/mL at baseline developed thyroid immune-related adverse events. The median thyroid peroxidase antibody titer was not higher in patients with adverse events but was higher in those with overt (as compared to subclinical) hypothyroidism and those prescribed thyroid hormone replacement. Diffusely increased ^{18}F-FDG thyroid uptake was seen on PET in 71% with thyroid immune-related adverse events compared to 6% without. Of note, patients who developed adverse events had longer overall survival and lower mortality after adjusting for potential confounders. The authors summarized their findings that, in most cases, management of thyroid immune-related adverse events in PD-L1 treatment can be managed supportively, without steroids or discontinuation of immunotherapy. Diffuse ^{18}F-FDG thyroid uptake on PET may predict the occurrence of thyroiditis, and thyroid peroxidase antibodies may help to assess its severity. They concluded that "thyroiditis may be a biomarker for antitumor immune response, highlighting the need to further characterize its underlying mechanism."

Thyroid

PET/CT and Postoperative Surveillance in Malignant Pleural Mesothelioma

Kitajima et al from the Hyogo College of Medicine (Japan) reported in the November 26 issue of *Oncotarget* (2019; 10[63]:6816–6828) on a study of the clinical utility of ^{18}F-FDG PET/CT for postsurgical surveillance in malignant pleural mesothelioma and the comparable utility of contrast-enhanced CT, including their respective impacts on clinical management. The study included 50 patients who had undergone radical surgery for malignant pleural mesothelioma, with lesion status determined on the basis of histopathology, radiologic imaging, and clinical follow-up for >6 mo. All had undergone ^{18}F-FDG PET/CT and contrast-enhanced CT, for which the respective sensitivities were 90.8% and 75.0%, specificities were 80.0% and 90.0%, and accuracies were 88.0% and 78.0%. The areas under the curve (AUC) (0.915 and 0.805, respectively) and sensitivity were significantly different between PET/CT and contrast-enhanced CT. Patient-based AUC values for diagnosis of locoregional recurrence (ipsilateral hemithoracic) and distant metastases (peritoneal dissemination and lung, bone, muscle, and liver metastases) were also significantly different. ^{18}F-FDG PET/CT findings resulted in management changes for 14 patients (28%). Contrast-enhanced CT did not identify a recurrence in 6 patients who were found to have recurrence on PET/CT. Management was changed in 4 of these patients. The authors concluded that "^{18}F-FDG PET CT findings were shown to be more accurate for assessing malignant pleural mesothelioma recurrence and more often led to therapy change than contrast-enhanced CT."

Oncotarget

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in late November and December. Langen et al. from the Forschungszentrum Jülich (Germany), the University of Aachen (Germany), the Jülich–Aachen Research Alliance (Germany), Maastricht University Medical Center (The Netherlands), and the University of Cologne/University Hospital of Cologne (Germany) summarized the "Advantages and limitations of amino acid PET for tracking therapy response in glioma patients," e-published on December 12 ahead of print in *Expert Review of Neurotherapeutics*. In an article published on December 15 ahead of print in *Expert Review of Anticancer Therapy*, Galldiks et al. from the University of Cologne/University Hospital of Cologne, the Research Center Jülich, and University Hospital RWTH Aachen (all in Germany) reviewed "Molecular imaging and advanced MRI findings following immunotherapy in patients with brain tumors." Signore et al. from the Sapienza University of Rome (Italy), the University of Brescia/Spedali Civili of Brescia (Italy), and the Imaging Institute of Southern Switzerland (Lugano)/Ente Ospedaliero Cantonale (Bellinzona, Italy) presented "Evidence-based data about prevalence and risk of malignancy of thyroid incidentalomas detected by different PET radiopharmaceuticals" on December 11 ahead of print in *Current Radiopharmaceuticals.* In an article in the November 28 issue of the *International Journal of Molecular Sciences* (2019;20(23):E5984), Ruiz-Bedoya et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) and the Johns Hopkins All Children's Hospital (St. Petersburg, FL) reviewed new research in "Molecular imaging of diabetic foot infections: New tools for old questions."