Regulatory and Legislative Issues: SNMMI at Work

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Over the past 2 decades, nuclear medicine has seen the introduction and clinical implementation of multiple new modalities, techniques, and radiopharmaceutical agents for diagnosis and therapy. Compounding the challenges that come with rapid technologic change has been the accelerated growth of regulatory and legislative oversight affecting all aspects of the field. Our continued success—and the welfare of our patients—depends on our ability to meet changing regulatory demands while proactively influencing those demands. This process involves not only maintaining open and goal-directed communication with regulatory and legislative bodies but also gathering and delivering the most relevant scientific information for evidence-based regulatory decisions. SNMMI leaders work closely with society members and those of affiliated professional societies to track proposed actions affecting the field, to anticipate and be prepared for changes, to collaborate with federal and other agencies on regulatory actions that can positively impact the field, and to serve as an expert resource on the economic and social impact of nuclear medicine. I have personally been involved in a number of these activities and know first-hand the degree of dedicated and highly specialized effort required from SNMMI staff, leadership, and member volunteers in these activities. A few highlights of our recent collaborative projects provide insight into the complexities of these efforts.

SNMMI has worked successfully to advance nuclear medicine at the national level, with a goal of increasing the availability of the field's most promising innovations. On August 21, the U.S. Food and Drug Administration (FDA) approved a New Drug Application (NDA) for ^{68}Ga-DOTATOC injection for PET imaging in localization of somatostatin receptor–positive neuroendocrine tumors (NETs) in adult and pediatric patients. The University of Iowa PET Imaging Center is the holder of the approved NDA. SNMMI coordinated closely with the FDA in the effort to secure orphan drug designation for the agent. The University of Iowa plans to relinquish exclusivity of its ^{68}Ga-DOTATOC NDA so that other institutions can pursue Abbreviated NDAs with the FDA.

In 2018, SNMMI, with input from members, petitioned the FDA to add arginine and lysine to its 503B bulks list or move them to the 503B Category 1 list. The FDA responded on March 4 this year by adding these to the categories of bulk drug substances under its interim policy under section 503B of the Federal Food, Drug, and Cosmetic Act. This will ultimately make it easier for manufacturers to compound and make available an arginine/lysine–only solution, which will help patients with gastroenteropancreatic NETs to better tolerate and thereby benefit from ^{177}Lu-DOTATATE therapy.

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The SNMMI leadership, staff, and volunteer team is at its most impressive when pooling expertise to advance nuclear medicine initiatives with legislators at the national level. On July 17, SNMMI cohosted a briefing on Capitol Hill with clinicians, patients, and industry representatives to discuss the importance of nuclear medicine and diagnostic radiopharmaceuticals and to highlight H.R. 3772 (Medicare Diagnostic Radiopharmaceutical Payment Equity Act of 2019). The bill was introduced on the previous day by Reps. Scott Peters (CA-52), Bobby Rush (IL-01), and George Holding (NC-02). The bill calls for all diagnostic radiopharmaceuticals that reach a cost of more than $500 per day to be paid separately in the Hospital Outpatient Prospective Payment System. The change in reimbursement would correct the current flawed payment policy, under which many hospitals cannot afford to offer these procedures. Successful enactment of the bill would be significant for patients, helping ensure the most appropriate care possible. SNMMI representatives met with more than 40 Congressional offices and have launched a vigorous grassroots letter-writing and lobbying campaign to support the bill as it advances toward potential passage.

Many achievements in support of nuclear medicine are the result of years of coordination, fact finding, collaboration, and evidence gathering. In 2016 SNMMI developed a white paper with recommendations on public standards for compounded sterile radiopharmaceuticals that recommended that that the U.S. Pharmacopeia (USP) create a separate general chapter for radiopharmaceutical preparation, compounding, and dispensing. Using elements of the white paper as a basis for discussion, the USP held a stakeholders workshop on radiopharmaceutical compounding, resulting in USP agreement to create the new General Chapter <825> dedicated to radiopharmaceuticals. The chapter, published on June 1, provides uniform minimum standards to provide, in the words of the USP, "a reasonable and rational basis for the protection of patients from unsafe practices."

Multiple similar efforts to represent nuclear medicine are underway right now at SNMMI, with the pace of new regulatory and legislative challenges and opportunities matching those of innovations in the field. The resulting achievements do not happen in a vacuum or outside the reach of individual participation—they require the widest representation from the entire spectrum of the nuclear medicine and molecular imaging community. SNMMI members can be involved by joining an SNMMI council; by staying up to date through the SNMMI website (http://www.snmmi.org/GRNews); and by working directly with the society on emerging issues that call for grassroots or volunteer response. Some of the most wide-reaching efforts with which SNMMI has been involved have begun with anecdotal reports of local regulatory, legal, or guidance challenges. Members are urged to let the society know about relevant activities in their communities as SNMMI continues to speak out on decision making that will affect the field for years to come.

LETTER TO THE EDITOR

^{68}Ga-PSMA Ligand as Potential ^{99m}Tc-DMSA Alternative

To the Newsline Editor: I read with great interest the paper by Lim et al. (*1*) that was published in the August issue of *JNM* Newsline. The article highlighted the importance of ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA) scans in pyelonephritis and other renal cortical diseases and the implications of current shortages of ^{99m}Tc DMSA in the United States. We have recently published ^{68}Ga–prostate-specific membrane antigen (^{68}Ga-PSMA) ligand PET/CT images of the kidneys that show a high degree of uptake and excellent distribution of this radiotracer in the renal cortex and demonstrate renal parenchymal defects caused by various sizes of renal cysts (*2,3*). ^{68}Ga-PSMA ligand renal images appear to be superior to those acquired with ^{99m}Tc-DMSA (*2,3*).

The main limitations of DMSA scanning include the relatively long waiting time after radiotracer injection, long acquisition time, high radiation dose (particularly important in repeated studies in children), and limited spatial resolution with gamma cameras. ^{68}Ga has a shorter half-life (68 min) than ^{99m}Tc (6 h). Effective and kidney radiation doses with the ^{68}Ga-PSMA ligand appear to be comparable to those with ^{99m}Tc-DMSA, but this should be further studied (*4–6*). The CT component of PET/CT imaging further increases radiation dose, but CT images may not be needed because non–attenuation-corrected PET also provides good quality images of the kidneys as a result of high renal cortical uptake. This is particularly important when used in pediatric patients (*2,3*). Waiting time after radiotracer injection and image acquisition time is less with ^{68}Ga-PSMA ligand PET (30–60 min and 2–6 min, respectively) than for the DMSA scan (2–3 h and 15–30 min, respectively). PET scanners offer higher efficiency for detecting gamma photons and higher spatial resolution than gamma cameras (*7*).

Although the ^{68}Ga-PSMA ligand is more expensive than ^{99m}Tc-DMSA and not available at every institute, it would be worthwhile to directly compare PSMA PET to DMSA scanning in renal diseases to better understand whether this PET radiotracer could be used to image the renal cortex and serve as an alternative to DMSA scanning, particularly in countries with shortages of ^{99m}Tc-DMSA. We have recently received institutional approval for a prospective research project for such a comparison in adult patients with pyelonephritis, and the study will begin soon.

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Trends in Imaging Usage

Smith-Bindman, from the University of California San Francisco, and authors from across the United States and Canada published an article in the September issue of *JAMA* (2019;322 [9]:843–856) on "Trends in use of medical imaging in U.S. health care systems and in Ontario, Canada, 2000–2016." The authors assessed annual and relative imaging rates for CT, MR, ultrasound, and nuclear imaging by country, health system, and patient demographic factors. A total of 135,774,532 imaging studies were included. As expected, imaging rates were significantly higher in 2016 than in 2000 for CT, MR, and ultrasound but with a slower pace of growth in the most recent years. Nuclear imaging, however, was the 1 modality that experienced a downward trend in usage over the study period, showing the greatest decline in adults ≤65 y of age and in children.

As an example of usage increases cited in the article, CT imaging rose from 56 per 1,000 person-years in 2000 to 141 in 2016; MRI from 16 to 64 per 1,000 person-years, and ultrasound from 177 to 347 per 1,000 person-years. During the same period, nuclear medicine usage decreased from 33 to 25 per 1,000 person-years. Figures were similar in Ottawa. For older adults (>65 y old), nuclear medicine usage fell from 94 to 64 per 1,000 person-years in the United States, with a comparable decline from 87 to 74 in Ottawa. The study made no assessments of whether the observed imaging utilization was appropriate or associated with improved outcomes, and the authors did not suggest reasons for the decline in nuclear medicine use. The article contains a wealth of data and analyses that merit further exploration by the nuclear medicine community.

JAMA

NIH-Sponsored Trials and Clinical Cancer Care

In an article published on September 4 in *JAMA Network Open*, Unger and colleagues from the SWOG Cancer Research Network Statistics and Data Management Center (Seattle, WA), the Fred Hutchinson Cancer Research Center (Seattle, WA), Columbia University Medical Center (New York, NY), and the Oregon Health and Science University (Portland) offered data indicating that 82 of 182 phase 3 clinical trials led by SWOG or by other National Cancer Institute Clinical Trial Network (NCTN) groups with SWOG participation were "practice influential." To be considered as practice influential, the trials must have been completed with published results and have been associated with guideline care through effects on National Comprehensive Cancer Network (NCCN) clinical guidelines or U.S. Food and Drug Administration (FDA) approvals in favor of a recommended treatment.

According to a press release about the article released on September 18 by the National Cancer Institute (NCI), the study results suggested that NCTN trials add value regardless of whether findings were positive or negative. In addition, the authors also found that the cost of a U.S. FDA approval from an NCTN trial was much less than the costs incurred in a trial run by pharmaceutical companies. "We found that the NCTN program contributes clinically meaningful, cost-effective evidence to guide care of cancer patients," said Joseph Unger, PhD, a health services researcher and biostatistician for SWOG at the Fred Hutchinson Cancer Research Center. "These trials are largely funded by the public, which is getting good value for their investment."

The data included the records of 148,028 patients treated on phase 3 cancer trials at multiple institutions between 1980 and 2017 led by SWOG or other NCTN groups with SWOG participation. Of the 82 practice-influential trials, 70 influenced NCCN guidelines, 6 influenced new FDA drug approvals, and 6 influenced both.

Of note, the number of practice-influential trials was 47 of 65 (72.3%) among those with positive findings and 35 of 117 (29.9%) among those with negative findings. A surprising 42.7% of practice-influential results were based on studies with negative findings, with nearly half of these studies (17 of 35; 48.6%) reaffirming standard of care over experimental therapy. The total federal investment spent in conducting the trials was $1.36 billion, a rate of $7.5 million per study or $16.6 million per practice-influential trial.

The authors also estimated that total federal investment supporting the trials in the study was $1.36 billion. This suggests that for 182 trials, average costs were $7.5 million per completed phase 3 trial (all trials), $16.6 million per practice-influential trial, and $123.6 million per new drug approval. In a review of 10 studies of the cost of new drug approvals by industry, the researchers found that the mean inflation-adjusted cost for a single new drug approval was $1.73 billion.

Despite some limitations in variables assessed, Unger noted that "The take-home message from the study is that NCTN studies provide a lot of clinically meaningful evidence for patients that influences their care routinely and does so at a relatively cost-effective level. It's important that people appreciate just how valuable these trials are in terms of benefit to patients with cancer."

JAMA Network Open
National Cancer Institute

DOE Awards 4th Cooperative Agreement for U.S. ^{99}Mo Production

The Department of Energy (DOE) National Nuclear Security Administration (NNSA) announced on August 28 that it had issued its fourth and final cooperative agreement award in fiscal year (FY) 2019 to Northwest Medical Isotopes, LLC (Corvallis, OR) for the production of ^{99}Mo without the use of highly enriched uranium. Three other cooperative agreement awards were announced in July to Niowave, Inc. (Lansing, MI), NorthStar Medical Radioisotopes,

LLC (Beloit, WI), and SHINE Medical Technologies (Janesville, WI). The NNSA entered into these agreements with a goal of establishing and maintaining a reliable domestic supply of ^{99}Mo without the use of highly enriched uranium. To achieve this, the United States is supporting companies that will have the capacity to supply approximately 3,000 6-d curies of ^{99}Mo per week. The American Medical Isotopes Production Act of 2012 directed DOE to implement a technology-neutral program, in cooperation with nonfederal entities. Congress appropriated $40 million for these awards in FY 2018 and $20 million in FY 2019 and directed DOE to issue a funding opportunity announcement to competitively award cooperative agreements. NNSA will fund each agreement at $15 million and require each awardee to provide $15 million of matching funds. More information on the DOE/NNSA program is available at https://www.energy.gov/nnsa/nnsa-s-molybdenum-99-program-establishing-reliable-supply-mo-99-produced-without-highly.

U.S. Department of Energy

^{99}Mo Shortage in Australia

On September 12, the Australian Nuclear Science and Technology Organisation (ANSTO) announced that it had stopped production of ^{99}Mo because of detection of a valve fault that exposed 2 workers to unsafe levels of radiation. With an uncertain repair timeline, ANSTO immediately began working on alternative supplies. ANSTO operates the Open-Pool Australian Lightwater reactor. In the first days after the shutdown, an ANSTO spokesperson said that "ANSTO has 4 teams working in parallel to progress options to rectify the issue. We thank the nuclear medicine community, and in particular the Nuclear Medicine Working Group, who are helping ensure that the reduced amount of nuclear medicine gets to areas needed most."

Compounding the impact of the shutdown was the prospect of a scheduled 3-week maintenance shutdown of the SAFARI-1 reactor at NTP Radioisotopes SOC Ltd. near Praetoria, South Africa. The ability of ANSTO to bridge supply gaps from already challenged global sources would be constrained. In a September 26 release to its customers, ANSTO indicated that bulk ^{99}Mo shipments would arrive from NTP on September 27 and 28, with ^{99m}Tc generators manufactured on September 28 and 29, and generators delivered to all sites by September 30. A similar supply was expected for the weeks of October 7 and 14. Because of NTP's scheduled maintenance shutdown, ANSTO was seeking alternative suppliers for the weeks of October 21, October 28, and November 4. At Newsline press time, no date had been targeted for resumption of domestic production of ^{99}Mo by ANSTO.

ANSTO
SNMMI

Proposed Myocardial PET Cuts

On September 3 SNMMI, along with the American College of Cardiology, the American College of Nuclear Medicine, the American Society of Nuclear Cardiology, and the Cardiology Advocacy Alliance, responded to proposed cuts for myocardial PET imaging in the Centers for Medicare & Medicaid Services (CMS) Medicare Physician Fee Schedule (MPFS) for 2020. These cuts could lead to technical component payment reductions as high as 80% for some services. These revisions resulted from updates to the Current Procedural Terminology codes used to report these services and review of the direct practice expense inputs that inform the calculation for the technical component payment.

One driver of the cuts is a decision by CMS to assume a 90% utilization rate for PET cameras, an assumption that the 5 organizations indicated should be changed. Pricing information for other equipment also may need to be further refined. Although the organizations indicated that they "support the valuation process used to develop input recommendations administered by the American Medical Association's Relative Value Scale Update Committee, payment cuts of this magnitude and on such short notice are not sustainable and could lead to practice disruptions and impact patient access to PET services." In a joint statement, the organizations indicated that if aggressive work to correct the inputs and calculations for the payment formula through the public comment process and communication with policymakers was not successful within the constraints of the rulemaking timeline, they would seek alternative approaches, such as a delay period, to allow further analysis and other efforts to continue.

On September 9 the groups held a webinar on this topic and requested technology cost information from the nuclear medicine community. Public comment to CMS was solicited, although the comment period was short and is no longer open.

The societies on September 23 called for community action and Congressional sign-on to a letter to CMS addressing the cuts and potential patient impacts. The first Congressional signees were Reps. Mike Kelly, (R-PA), Ron Estes (R-KS), and Ron Kind, (D-WI). Members of all 5 societies were urged to write, call, or email their representatives and senators and ask them to sign the letter and voice concerns directly with CMS. The specific goal of this effort was to persuade members of Congress to ask CMS to defer the proposed PET pricing and continue current payment levels while working with stakeholders to ensure that costs are accurately accounted for when setting payment rates for cardiac PET. After the announcement of the proposed cuts, the foci of these groups have been on correcting inputs and calculations for the payment formula through the public comment process and communication with policymakers, and on educating CMS staff and more than 50 Congressional offices, including professional staff from relevant committees.

SNMMI

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.

^{124}I PET/CT vs. Conventional ^{131}I Imaging in DTC

Wu et al. from MedStar Health Research Institute and the MedStar Washington Hospital Center (both in Washington, DC) reported on August 27 ahead of print in *Thyroid* on a review of the literature intended to assess ^{124}I PET/CT sensitivity and specificity in detection of differentiated thyroid cancer (DTC) lesions in different patient populations, including comparison data with conventional ^{131}I imaging. The literature search included multiple databases covering the time period 1996 through 2018. The final review included 4 retrospective and 10 prospective studies with a total of 495 patients with DTC undergoing ^{124}I and ^{131}I imaging. In reports that compared the 2 tracers in diagnostic imaging, a total of 72 patients had 120 lesions detected with ^{124}I PET, whereas only 52 of these lesions were detected on ^{131}I imaging. When comparing the 2 methods after therapy in 266 patients, the review found that 410 lesions were detected on ^{124}I PET/CT but only 390 on ^{131}I scanning. The authors reviewed ^{124}I PET/CT staging in 6 studies and found that it resulted in TNM stage revisions in 15%–21% of patients and that disease management was changed in 5%–29% of patients. Other information gathered in the review led the authors to conclude that ^{124}I PET "may have better detection compared to posttherapy ^{131}I scan in patients who are ^{131}I therapy naïve, have less aggressive pathology, or do not have disseminated lung metastases" and that "additional metastatic lesion detection by ^{124}I PET has significant clinical impact in the management of patients prior to ^{131}I therapy in some patients."

Thyroid

^{18}F-AV-1451 Tau PET in AD

In an article e-published on September 18 ahead of print in the *Journal of Neurology*, Lagarde et al. from the Université Paris Descartes, Sorbonne Paris Cité, and Centre Hospitalier (Paris, France); the Hospitalier Frédéric Joliot, CEA, Inserm, Université Paris Sud, and Université Paris-Saclay (Orsay, France); and UNIACT, Neurospin, CEA (Gif-sur-Yvette, France) reported on studies testing the hypothesis that ^{18}F-AV-1451 tau PET imaging with later-than-usual acquisition times would allow detection of cortical tau pathology in some behavioral-variant frontotemporal dementia patients and in patients with nonfluent primary progressive aphasia (most often seen in conjunction with tau pathology). The hypothesis rested on previous data in Alzheimer disease (AD) suggesting that the tracer, which has a lower affinity for the straight tau filaments seen in non-AD tauopathies, could allow better cortical tau detection. The study included 16 patients with AD, 11 control patients, 7 patients with behavioral-variant frontotemporal dementia, and 2 patients with nonfluent primary progressive aphasia. The authors compared uptake obtained at the usual early time window (80–100 min after tracer injection) to those at a later acquisition window (190–210 min after injection). They found that in individuals with AD, ^{18}F-AV-1451 late acquisition uptake was significantly higher in the temporoparietal cortex and lower in subcortical regions. The late acquisition window allowed detection of significantly increased tau binding in the frontal or temporal cortex that was not detectable at early acquisition in 3 of the behavioral-variant frontotemporal dementia patients and in the 2 nonfluent primary progressive aphasia patients. The authors concluded that the "^{18}F-AV-1451 late acquisition window could allow cortical binding to abnormal tau deposits to be revealed in a subset of behavioral-variant frontotemporal dementia patients, which may distinguish them from the TDP-43 subtype."

Journal of Neurology

PSMA PET in Nonmetastatic Castrate-Resistant PCa

In an article e-published on September 11 ahead of print in *Clinical Cancer Research*, Fendler, from the University of Duisburg–Essen and German Cancer Consortium/University Hospital Essen (Germany), and a group of researchers from academia and industry in Australia, the United States, Canada, and other sites in Germany reported on the results of a study using ^{68}Ga- or ^{18}F-DCFPyL–prostate-specific membrane antigen (PSMA) PET to characterize cancer burden in patients with high-risk nonmetastatic castration-resistant prostate cancer (nmCRPC) without detectable metastases on conventional imaging. The study, performed at 6 high-volume PET centers, included 200 patients with nmCRPC and prostate-specific antigen (PSA) >2 ng/mL, who were at high risk for metastatic disease (prostate-specific antigen [PSA] doubling time ≤10 mo and/or Gleason score ≥8). The PSMA PET detection rates were reviewed for pelvic disease and distant metastases. A subset of men enrolled in a phase 3 study of nmCRPC was also stratified by risk factors for PSMA PET–detected distant metastatic disease. The researchers found that PSMA PET was positive in 196 of 200 patients. Forty-four percent had pelvic disease, including 24% with local prostate bed recurrence. Fifty-five percent had distant metastases with previous negative conventional

imaging. Interobserver agreement on PSMA PET was quite high. A PSA ≥5.5 ng/mL, locoregional nodal involvement at pathology, prior primary radiation, and prior salvage radiation therapy were independent predictors of distant metastases. The authors concluded that "future indication statements for systemic treatment may be adapted to accurately describe the respective trial populations (eg, nonmetastatic by conventional imaging)" and that "patients who meet indication criteria should receive such treatment even if they have metastases detected by PSMA PET." They added that "clinical trials correlating PSMA PET staging and data on outcomes such as metastasis-free and overall survival are clearly needed."

Clinical Cancer Research

^{68}Ga-PSMA PET/CT in PCa Staging

Van Kalmthout et al. from the University Medical Center (Utrecht), St. Antonius Hospital (Nieuwegein and Utrecht), and Meander Medical Center (Amesfoort, all in The Netherlands) reported on September 5 ahead of print in the *Journal of Urology* on a prospective study assessing the diagnostic accuracy of ^{68}Ga–prostate-specific membrane antigen (^{68}Ga-PSMA) PET/CT in detection of lymph node metastases in patients with intermediate-to-high risk prostate cancer. The study included 103 patients with newly diagnosed prostate cancer, negative bone scans, and >10% Memorial Sloan Kettering Cancer Center (MSKCC) nomogram-determined risk of lymph node metastases. ^{68}Ga-PSMA PET/CT imaging was acquired prior to planned surgery in candidates for extended pelvic lymph node dissection. Scans were assessed to determine potential changes in management. Sensitivity, specificity, and positive and negative predictive values for detection of lymph node metastases were calculated on a per patient and per resection basis, with histopathology results as the reference. A total of 97 extended pelvic lymph node dissections were performed, and 41 patients (42.3%) had a total of 85 lymph node metastases. Seventeen patients were positive on PET, for a patient-based sensitivity of 41.5% for detection of lymph node metastases. Patient-based specificity was 90.9%, and positive and negative predictive values were 77.3% and 67.6%, respectively. Management was changed on the basis of PET findings in 13 (12.6%) patients. The authors concluded that "in newly diagnosed prostate cancer patients with >10% MSKCC risk of lymph node involvement, ^{68}Ga-PSMA PET/CT detects lymph node metastases with high specificity and moderate sensitivity."

Journal of Urology

PSMA PET/CT–Guided SABR for Oligometastatic Prostate Cancer

In an article e-published on September 11 ahead of print in *BJU International*, Ong et al. from Austin Health (Heidelberg), Monash University (Melbourne and Clayton), the University of Melbourne, and Epworth Healthcare (Melbourne; all in Australia) and the University of Cambridge (UK) and the Royal Marsden National Health Service Foundation Trust (London, UK) provided a single-institution report and review of the literature on outcomes of stereotactic ablative body radiotherapy (SABR) in men with oligometastatic prostate cancer (PCa) diagnosed using prostate-specific membrane antigen (PSMA) PET/CT. The retrospective institutional study included 20 men with oligometastatic PCa with biochemical recurrence after previous curative treatment (surgery/radiotherapy), who had no evidence of local recurrence, were not on palliative androgen deprivation therapy (ADT), and whose disease was confirmed by PSMA PET/CT (≤3 lesions). These individuals were treated with SABR (30 Gy in 3 fractions for bone metastases; 35–40 Gy in 5 fractions for nodal metastases). Factors assessed in record reviews included prostate-specific antigen (PSA) response, local progression-free survival, distant progression-free survival, and ADT-free survival. After SABR, 12 of the 20 men showed a decline in PSA levels. One individual experienced local progression 6 mo after SABR, for an overall 12-mo local progression-free survival rate of 93%. Two men experienced distant progression outside the SABR treatment fields, as confirmed on PSMA PET/CT. The overall 12-mo distant progression-free survival rate was 62%, with 4 men treated with palliative ADT, 2 with prostate bed radiotherapy for local progression, and 4 with an additional course of SABR. At the most recent follow-up, 6 men (1 with local and 5 with distant progression) had received palliative ADT. The 12-mo ADT-free survival rate was 70%. The researchers observed that men with longer time periods between local curative treatment and SABR had better distant progression-free survival and ADT-free survival. A search of the literature identified 4 additional studies reporting on PSMA PET/CT–guided SABR, with results added to the institutional findings to yield a total of 346 patients. Overall, PSA decline was seen in 60%–70% of men after SABR. Two-year local progression-free survival, distant progression-free survival, and ADT-free survival rate ranges were 76%–100%, 27%–52%, and 58%–62%, respectively. The authors concluded that PSMA PET/CT "could have an important role in identifying men with true oligometastatic prostate cancer who would benefit the most from metastases-directed therapy with SABR."

BJU International

^{18}F-DOPA PET/CT in Localization of Persistent/Recurrent MTC

Terroir et al. from the Institut Gustave Roussy (Villejuif, France), the University Hospital of Lausanne (Switzerland), and the University Hospital City of Science and Health Turin/San Vito Hospital (Torino, Italy) reported on September 18 ahead of print in *Thyroid* on a study of the comparative disease detection rates of ^{18}F-DOPA PET/CT, whole-body MR imaging, ^{18}F-FDG PET/CT, whole-body CT scanning, neck ultrasonography, and bone scintigraphy in medullary thyroid carcinoma patients with increased postoperative serum calcitonin levels and unknown localization of the source. The study included 35 such patients (21 women, 14 men; mean

age, 57 y) with median serum calcitonin levels of 760 pg/mL. Twenty-six of the patients were classified as having sporadic MTC. Overall, localized disease was seen in 24 (64%) patients, with lesions detected in: the thyroid bed (8), neck lymph nodes (15), mediastinal lymph nodes (6), lung (1), liver (2), bones (3), and 1 other site. Detection rates at the patient level were 64% for ^{18}F-DOPA PET/CT with early acquisitions, 40% for ^{18}F-FDG PET/CT, 40% for whole-body MR imaging, and 48% for whole-body CT. The authors concluded that in medullary thyroid carcinoma patients "with increased serum calcitonin levels and no known distant metastases, ^{18}F-DOPA PET CT is more sensitive to detect structural disease than any other imaging modality, including whole-body MRI."

Thyroid

Plasmon-Activated Water and Amyloid Burden

In an article published in *Scientific Reports* on September 13 (2019;9[1]: 13252) Cheng et al. from Taipei Medical University (Taiwan), Linkou Chang Gung Memorial Hospital/Chang Gung University (Taoyuan City, Taiwan), and McGill University (Montreal, Canada) reported on an innovative strategy to retard the progression of Alzheimer disease (AD) by daily consumption of negatively charged plasmon-activated water (PAW). PAW is generated through the use of resonantly illuminated gold nanoparticles, which reduce the hydrogen-bonded structure of water. The study was conducted in transgenic mice that were given either PAW or normal deionized water from the age of 5–14 mo. At the end of the study period, mice on PAW were found to have better memory performance on an object recognition test than the mice fed normal deionized water. The PAW group was also found to have a significantly lower amyloid burden on ^{18}F-florbetapir amyloid PET and a lower phosphorylated-tau burden on Western blot and immunohistochemistry assessments. No obvious side effects of the PAW regimen were observed. The authors noted, however, that the protein levels of molecules involved in amyloid metabolism and oligomeric amyloid did not change between the 2 groups of mice. They suggested that the effects of PAW in reducing amyloid burden and improving memory function could not be attributed to synthesis or degradation of amyloid-β protein, but, instead, probably acted by "preventing aggregation of amyloid-β proteins or other mechanisms, including antiinflammation."

Scientific Reports

Pretreatment ^{18}F-FDG PET/CT Staging in Gynecologic Cancers

Sponholz et al. from the University of Southern Denmark/Odense University Hospital and Aarhus University/Aarhus University Hospital (Denmark) reported on September 10 ahead of print in *Acta Obstetricia et Gynecologica Scandinavica* on a study assessing the clinical impact of pretreatment ^{18}F-FDG PET/CT on the staging of primary ovarian, fallopian tube, and peritoneal cancer in women. The study focused specifically on the effects of PET/CT findings on additional examinations and delays or changes in treatment plans. The study included 44 women (21.1% of a total of 209) who had additional findings on PET/CT. Additional studies/examinations were performed in 35 (79.5%) of these women. Malignancy was identified in 15/35 (42.9%; 11 with metastases from ovarian, fallopian tube, or peritoneal cancer; 3 with a synchronous primary cancer; and 1 with a recurrence of a previous cancer. The ovarian, fallopian tube, or peritoneal metastases were localized in the lungs, uterus, colon, vagina, and breasts. Findings in the remaining 20 patients showed 2 benign lesions and 1 premalignant lesion, with no abnormality identified in 17 patients. The addition of studies/examinations as a result of PET/CT findings produced a median time delay to treatment start of 4 d (range, 1–83 d). The authors concluded that the clinical implications of this time delay "must be balanced against the gain of detecting unrecognized malignancy in 15 of 209 women (7.2%)."

Acta Obstetricia et Gynecologica Scandinavica

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 September. In an article e-published on September 14 ahead of print in *Human Brain Mapping*, Chandra et al. from the King's College London (UK) and the Alzheimer's Disease Neuroimaging Initiative provided an overview of "Applications of amyloid, tau, and neuroinflammation PET imaging to Alzheimer's disease and mild cognitive impairment." Iglesias et al. from the Hospital Universitario Puerta de Hierro Majadahonda and the Universidad Autónoma de Madrid (both in Madrid, Spain) reported on September 10 ahead of print in the *European Journal of Nuclear Medicine* on "The pituitary in nuclear medicine imaging." On September 13 ahead of print in the *British Journal of Pharmacology*, Srirajan et al. from the University of Cambridge Addenbrooke's Centre for Cardiovascular Investigation (Cambridge, UK) reviewed the current state of "Atherosclerosis imaging using positron emission tomography (PET): Insights and applications." Verhoeven et al. from Erasmus MC (Rotterdam, The Netherlands) surveyed "Therapeutic applications of pretargeting" in the September 1 issue of *Pharmaceutics* (2019;11[9]:E434). In an article in the September issue of *Current Opinions in Cardiology* (2019;34[5]:473–483), Malhotra et al. from Cook County Health and Rush University Medical Center (both in Chicago, IL) offered an overview of "Assessment of myocardial viability using single-photon emission computed tomography myocardial perfusion imaging." Aashiq et al. from the University of Texas MD Anderson Cancer Center (Houston, TX) and the Israel Institute of Technology (Haifa) surveyed "Radioiodine-refractory thyroid cancer: Molecular basis of redifferentiation therapies, management, and novel therapies" in the September 17 issue of *Cancers (Basel)* (2019;11[9]:E1382).

Notification of Proposed SNMMI Bylaws Changes

The current version of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) Bylaws is included below in its entirety; unaffected sections are not included. Proposed deletions are struck through. Proposed additions are underlined. The proposed amendments include some housekeeping changes that have accrued since the last amendments in 2015 and several more substantive changes as described below.

The substantive amendments are as follows:

1. Mission statement: Updated to reflect the core purpose of the organization.
2. Members in training: Medical students are added to this membership category. The SNMMI has initiated activities for medical students through the Workforce Pipeline Domain. We are advertising and marketing to medical students and need a formal process and opportunity for these individuals to join SNMMI. The existing in-training category in the SNMMI Bylaws is for residents, scientists, and technologists, who will not be affected by the amendment.
3. Lifetime membership category: This membership category is deleted from the Bylaws in this revision. Although SNMMI will continue to recognize the existing Lifetime Members, no new Lifetime Members have been accepted for many years.
4. General Program Chair: This position is removed as a nonvoting position on the SNMMI Board of Directors. The General Program Chair currently serves on the Scientific Program Committee and works with staff to visit potential sites for the SNMMI Annual Meeting. With the recent direction from the Board to restrict site consideration to a few cities, there is no longer a need for this position on the Board.
5. Center and Council Renewal: The Society recognizes the need for subspecialty interests and expertise within the field of nuclear medicine and molecular imaging. Both Councils and Centers provide expertise, professional networking, and educational programs for nuclear medicine and molecular imaging professionals in their respective areas and serve as resources for development and implementation of Society policy. Center status is reserved for those nuclear medicine and molecular imaging subspecialty or subdisciplinary areas of interest that have been so designated by the Board of Directors. As the profession changes and subspecialty and subdisciplinary interests evolve and change, there is a need for the Councils and Centers to evaluate their relevance and continued contributions to the Society. A recurring 5-year review enables Councils and Centers to evaluate their roles in SNMMI. If they feel they still have valuable contributions and work to do in their subspecialty areas of interest, they will ask the House of Delegates (Councils) or Board of Directors (Centers) to renew their approvals for an additional 5 years.
6. Technologist Section Immediate Past President: This position is added to the SNMMI Board of Directors. The SNMMI Immediate Past President is a member of the Board, but the SNMMI-TS Immediate Past President currently is not. The addition will enhance continuity on the Board.

James M. Woolfenden, MD
Chair, SNMMI Committee on Bylaws

Society of Nuclear Medicine and Molecular Imaging Bylaws

ARTICLE II MISSION AND OBJECTIVES

Section 1: MISSION

The Society is a multidisciplinary professional medical organization dedicated to <u>improving human health by advancing nuclear medicine, molecular imaging and radionuclide therapy.</u> ~~the advancement of excellence in the education, research, and clinical practice of nuclear medicine.~~

ARTICLE III MEMBERSHIP

Section 1: CLASSIFICATIONS

A. Full Membership

Physicians, scientists or pharmacists possessing an advanced degree who have presented credentials indicating their professional activity, either medical, paramedical, investigational or educational in the scientific or clinical disciplines of molecular imaging or nuclear medicine, may join the Society as Full Members. This includes the diagnostic, therapeutic or investigational use of radionuclides or other molecular imaging technologies. These individuals have the right to vote

and to be elected an Officer of the Society. The Board of Directors by majority vote may extend Full Membership to individuals who have made exceptional contributions to molecular imaging or nuclear medicine, but who do not otherwise qualify for Full Membership.

B. Associate Membership

1. Scientists or other health professionals with a master or baccalaureate degree (or the equivalent qualification as determined by the Committee on Membership) who have presented credentials indicating their professional activity, either paramedical, investigational, or educational, in the scientific or clinical disciplines of molecular imaging or nuclear medicine may join as Associate Members. This includes the diagnostic, therapeutic or investigational use of radionuclides or other molecular imaging technologies. These individuals have the right to vote but may not be elected an Officer of the Society.
2. Nuclear medicine and molecular imaging technologists, with a master or baccalaureate degree (or the equivalent qualification as determined by the Committee on Membership) who have presented credentials indicating their professional activity, either paramedical, investigational, or educational, in the scientific or clinical disciplines of molecular imaging or nuclear medicine may join as Associate Members. This includes the diagnostic, therapeutic or investigational use of radionuclides or other molecular imaging technologies. These individuals have the right to vote but may not be elected an Officer of the Society.
3. Scientific Laboratory Professionals with a masters or baccalaureate degree (or equivalent qualification as determined by the Committee on Membership) who have presented credentials indicating their professional activity in molecular imaging research at the pre-clinical or translational level in fields including utilization of optical imaging, radiopharmaceuticals, MRI, MR spectroscopy, ultrasound, stem cell research and cell trafficking, may join as Associate Members. These individuals have the right to vote but may not be elected an Officer of the Society.

C. Technologist Membership

Technologists who have presented credentials indicating professional activity in molecular imaging or nuclear medicine technology or other related fields may join the Society as Technologist members without the rights to vote or to be elected an Officer of the Society. This membership does include membership in the Technologist Section with the right to vote and to be elected an Officer in the Technologist Section.

Scientific Laboratory Professionals who lack a master or baccalaureate degree or equivalent qualification, and who have presented credentials indicating their professional activity in molecular imaging research at the pre-clinical or translational level in fields including utilization of optical imaging, radiopharmaceuticals, MRI, MR spectroscopy, ultrasound, stem cell research and cell trafficking, may join the Society without the right to vote or to be elected an Officer of the Society. This membership includes membership in the Technologist Section with the right to vote and to be elected an Officer in the Technologist Section.

D. Members-in-Training (Student, Resident, Fellow)

Physicians, scientists, ~~and~~ technologists and medical students who are enrolled in accredited training programs, medical schools or postdoctoral fellowships may join the Society as Members-in-Training with all rights and privileges of membership, except the rights to vote and to be elected an Officer of the Society.

E. Affiliate Membership

Individuals committed to the advancement of molecular imaging or nuclear medicine, but not qualifying for membership in other categories, may join the Society as Affiliate Members with all rights and privileges of membership, except the rights to vote and to be elected an Officer of the Society.

F. Honorary Membership

Individuals who have rendered outstanding service in an area of nuclear medicine may be granted Honorary Membership in the Society with all rights and privileges of membership, except the rights to vote and to be elected an Officer of the Society.

G. Emeritus Membership

Individuals upon their retirement after at least ten (10) years of consecutive membership in the Society may be granted Emeritus Membership. Emeritus members have the full privileges of the membership category from which they entered the emeritus status except the right to be elected an Officer of the Society.

~~**Section 2: LIFE MEMBERSHIP**~~

~~Members of the Society in any membership classification who have made special contributions and commitments to the Society may be designated by the Board of Directors as Life Members. Criteria for eligibility and selection procedures shall be determined by the Board. Life Members shall retain all rights, privileges and responsibilities of their membership classification and shall have such additional privileges and recognition as are granted by the Board, consistent with the Bylaws.~~

Section ~~3~~2: RESPONSIBILITIES OF MEMBERSHIP

A. General Responsibility: Each member has the responsibility to support the Mission and Objectives of the Society and to adhere to the Bylaws.
B. Good Standing: A member must be in good standing to vote, hold office, or receive the benefits and services otherwise reserved for members of the Society.

Section 43: DISCIPLINE

A. Members may be subject to discipline, including deprivation of membership, if they are guilty of unprofessional conduct or if they have been convicted of a felony in a court of law.
B. The Committee on Ethics shall review, either on its own initiative or on written and signed complaint, any case in which the circumstances in Sections 3:A or 4:A may lead to potential discipline and shall forward to the House of Delegates any recommendation on possible action. Such review shall afford the accused member an opportunity for a hearing.
C. Members who have been convicted of a felony in a court of law may not hold a voting position in the House of Delegates or the Board of Directors and may not be appointed ~~General Program Chair,~~ Scientific Program Chair, Editor of the *Journal of Nuclear Medicine*, Editor of the *Journal of Nuclear Medicine Technology*, or chair of a standing committee. This prohibition is lifelong unless overridden by a two-thirds (2/3) vote of the House of Delegates.
D. Recommendations for discipline of a member shall be referred to the House of Delegates, which will take final action by a two-thirds (2/3) majority vote.

ARTICLE V ORGANIZATIONAL CATEGORIES

Section 3: COUNCILS

A. Description: The Society recognizes the need for sub-specialty interests/expertise within the field of nuclear medicine and molecular imaging. Councils provide the expertise, professional networking, and educational programs for nuclear medicine and molecular imaging professionals in respective areas and serve as a resource for development and implementation of Society policy.
B. Mission: The mission of councils shall be to:
   1. Serve as a forum for members with like interests,
   2. Provide expertise in the field to the membership-at-large,
   3. Foster research and education in their areas of interest,
   4. Serve as a resource to Society leadership, and
   5. Provide outreach to other professionals and organizations.
C. Membership: Council membership is voluntary. Society members are eligible for council membership.
D. Organization:
   1. Each council shall adhere to Society Bylaws and policies, while operating under its own Operating Procedures, as approved by the House of Delegates, and its own business plan and budget, as approved by the Board of Directors.
   2. Each council shall have a Board of Directors, at least one member of which shall be a member of the Society's Board of Directors.
E. Renewal: Every five (5) years each Council shall review its relevance and contributions to the Society and decide whether to continue operations. Each continuing Council shall request renewed approval from the House of Delegates.

Section 4. CENTERS

A. Mission: Center status is reserved for nuclear medicine and molecular imaging subspecialty or sub-disciplinary areas of interest, each approved by the Board of Directors. Centers provide professional networking and educational programs for nuclear medicine and molecular imaging professionals in respective areas, while simultaneously serving as a resource for development and implementation of Society policy. Leadership of centers is composed of elected members of the center and appointed members from the Board of Directors. Centers will manage Society programs and activities related to their subspecialty or sub-disciplinary areas of interest.
B. Membership: Center membership is voluntary. Society members are eligible for center membership.
C. Organization: Centers adhere to Society bylaws and policies, while operating under their own Operating Procedures and budget process, approved by the Board of Directors.
D. Renewal: Every five (5) years each Center shall review its relevance and contributions to the Society and decide whether to continue operations. Each continuing Center shall request renewed approval from the Board of Directors.

ARTICLE VI OFFICERS

Section 3: TERM OF OFFICE

A. The President, Vice President, and Vice President-Elect serve for a one (1)-year term.
B. The Secretary/Treasurer serves for a single term of three (3) years except that the Secretary/Treasurer may serve out a vacancy of the office plus a full term, if elected.
C. Except for the Secretary/Treasurer who shall serve for three (3) consecutive years, and except for an Officer who assumes office due to a vacancy as described in these Bylaws, the term of office for each Officer shall commence with the conclusion of the Annual Meeting of the Society and shall terminate at the conclusion of the subsequent Annual Meeting.
D. At the conclusion of the ~~term~~s of office of the President, the Vice President shall automatically succeed to the office of President, and the Vice President-Elect shall automatically succeed to the office of Vice President.

ARTICLE VII HOUSE OF DELEGATES

Section 2: RESPONSIBILITIES

A. To develop and recommend to the Board of Directors, Society policies and programs regarding professional issues affecting nuclear medicine and molecular imaging.
B. To elect the seven (7) Directors-at-Large, the majority of the voting members of the Board of Directors.
C. To approve amendments to the Bylaws in accordance with the Bylaws and Procedures.
D. To approve establishment, suspension, renewal and dissolution of chapters and councils.
E. To review the strategic plan annually.
F. To oversee and monitor the work of the committees of the House of Delegates.
G. To elect the ~~Speaker of the House, the~~ Vice-Speaker of the House (who ascends to speaker), and the Historian.
H. To elect the members-at-large of the Committee on Nominations.
I. To elect the members of the Audit Committee.
J. To approve the selection of the Editor of *The Journal of Nuclear Medicine.*

Section 4: MEETINGS

A. Regular and Annual Meetings
   1. The House of Delegates shall have at least two regular meetings each year. One of the regular meetings shall be designated as the Annual Meeting and shall be held in conjunction with the Annual Meeting of the Society.
   2. Formal notice of regular and Annual Meetings of the House of Delegates shall be ~~published~~ distributed in the manner specified in Procedures.

B. Special Meetings: Special Meetings of the House of Delegates shall be summoned by the Board of Directors or the Speaker of the House, as circumstances warrant.
C. Notification: Delegates shall be given at least sixty (60) days advance notice of the two regularly scheduled meetings of the House of Delegates and five (5) working-days' notice of a special meeting of the House of Delegates.
D. Quorum: A quorum for all meetings of the House of Delegates is a majority of the total voting Delegates.

ARTICLE X BOARD OF DIRECTORS

Section 3: COMPOSITION

The Board of Directors shall be composed of ~~fourteen~~ fifteen (15~~4~~) voting members and ~~seven~~ six (~~7~~6) non-voting members.

A. Voting Members
   1. Society Officers: ~~the~~ President, Vice President, Vice President-Elect, and the Secretary/Treasurer. The President shall serve as Chair of the Board of Directors.
   2. Immediate Past President
   3. President of the Technologist Section
   4. Immediate Past President of the Technologist Section
   5. Speaker of the House of Delegates
   6. Seven (7) Directors-at-Large
      a) Directors-at-Large shall serve for a three (3)-year term, which shall commence at the conclusion of the Annual Meeting at which they are elected and which shall terminate at the conclusion of the third subsequent Annual Meeting following the election. A Director-at-Large chosen by the Technologist Section may serve for a term of less than three years at the discretion of the Technologist Section. Directors-at-Large may serve no more than two (2) consecutive terms, following which at least three years must elapse before service as a Director-at-Large is again permitted.

b) Candidates for Director-at-Large must have been a member of the Society for at least three (3) years to be eligible to serve on the Board of Directors.
c) Four (4) Directors-at-Large shall be elected by the House of Delegates from the voting Delegates of the House. Three (3) Directors-at-Large shall be elected by the Technologist Section from the eight (8) Technologist Section delegates in accordance with procedures established by the Technologist Section.

B. Non-Voting Members: there shall be six ~~seven~~ (~~7~~6) non-voting members on the Board of Directors:
1. Chair, Committee on Finance
2. Chair, Committee on Government Relations
3. ~~General Program Chair~~
~~4.~~3. Chair, Committee on Publications
~~5.~~4. Chair, Scientific Program Committee
~~6.~~5. Education and Research Foundation (ERF) President
~~7.~~6. Chief Executive Officer

Section 6: VACANCIES

Vacancies of a voting member of the Board of Directors shall be handled in accord with Bylaws and Procedures. Vacancies of Officer positions shall be handled as described in Article VI. In the event of a vacancy in a Director-at-Large position, the Speaker of the House shall appoint an interim Director to serve until the next annual election. Vacancies in Director-at-Large positions from the technologist section shall be filled in the manner prescribed in the technologist section procedures.

ARTICLE XII COMMITTEES

Section 1: DESCRIPTION

A. The House of Delegates shall have the following standing committees, as well as such additional committees or subcommittees as may be required by the House:
1. Committee on Chapters
2. Committee on Councils and Centers
3. Committee on Ethics
4. Committee on Nominations
5. Committee on Bylaws

B. The Board of Directors shall have the following standing committees, as well as such additional committees or subcommittees as may be required by the Board:
1. Committee on Awards
2. Committee on Audit
3. Committee on Finance
4. Committee on Government Relations
5. Committee on Membership
6. Committee on Publications
7. Committee on Education
8. Committee on Radiopharmaceuticals
9. Committee on ~~Young Professionals~~ Early Career Professionals