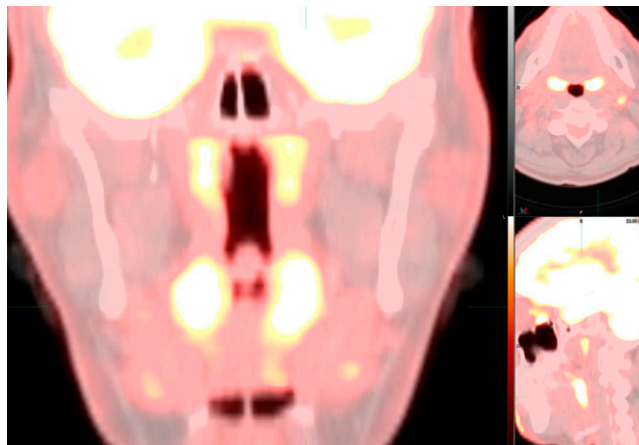


SNMMI Statement: Possible Effect of Omicron Infection on ^{18}F -FDG–Based Imaging

On January 14 the SNMMI COVID-19 Task Force released a statement on reports of an unusual imaging pattern seen in ^{18}F -FDG PET/CT and ^{18}F -FDG PET/MR imaging that could be the result of COVID-19 Omicron infection. Unlike ^{18}F -FDG PET/CT patterns seen with infections from previous strains of COVID-19 with principal involvement of the lungs, the new array of findings associated with Omicron are primarily centered in the upper aerodigestive tract and cervical lymph nodes. This includes prominent, symmetric ^{18}F -FDG uptake throughout the nasopharynx, oropharynx, and tonsils, with or without associated ^{18}F -FDG–avid cervical lymphadenopathy, particularly in the suprahyoid neck. The Task Group reported that “based on what we know about the Omicron variant, it is conceivable that this pattern, whenever correlated with COVID-19 infection, is a result of the presently dominant Omicron strain.”

The Task Force recommended that this pattern be taken into consideration at the time of ^{18}F -FDG PET/CT interpretation and that the possibility of infection with the Omicron variant of COVID-19 should be entertained in differential diagnosis. Because this pattern can by no means be diagnostic of COVID-19 infection, the Task Force made the following recommendations:

1. Check the patient records to see if there is a recent positive COVID-19 test.
2. Determine if the patient is at higher risk of COVID-19 infection based on current symptoms or due to recent exposure or travel. If so, a recommendation can be made to test for COVID-19 in the appropriate setting.
3. Compare with prior ^{18}F -FDG PET/CT examinations and the patient’s history to determine if this represents a chronic inflammatory/reactive process or stable malignancy, such as lymphoma.
4. Various differential diagnostic possibilities should be considered if this pattern is new or if there is interval



SNMMI COVID-19 Task Force members have observed an unusual imaging pattern on ^{18}F -FDG PET/CT and ^{18}F -FDG PET/MR imaging, including symmetric ^{18}F -FDG uptake throughout the nasopharynx, oropharynx, and tonsils, with or without associated ^{18}F -FDG–avid cervical lymphadenopathy, particularly in the suprahyoid neck. They reported that this pattern is a possible result of COVID-19 infection with the Omicron variant.

progression, including, but not limited to, infection with COVID-19, other viruses such as Epstein-Barr virus, malignancy, and bacterial infections.

5. This pattern may also be seen in children and younger adults but should be interpreted cautiously in view of normal increased activity that can be physiologic. Correlation with history and symptoms and comparison to prior examinations are recommended.

Over the past 18 months, the SNMMI COVID-19 Task Force has met regularly to monitor, support, educate, and provide guidance to the nuclear medicine and molecular imaging communities. The Task Force is led by Munir Ghesani, MD (Mount Sinai Health System; New York, NY).

SNMMI

CMS Proposes Medicare Coverage Policy for Monoclonal Antibody–Based Alzheimer Treatment

On January 11 the U.S. Centers for Medicare & Medicaid Services (CMS) released a proposed National Coverage Determination (NCD) decision memorandum that would cover U.S. Food and Drug Administration (FDA)–approved monoclonal antibodies that target β -amyloid for the treatment of Alzheimer disease (AD) through coverage with evidence development (CED). This means that FDA-approved drugs in this class would be covered for people with Medicare only if they are enrolled in qualifying clinical trials.

Aducanumab (Aduhelm; Biogen, Inc. [Cambridge, MA] and Eisai, Co., Ltd. [Tokyo, Japan]) is currently the only monoclonal antibody directed against β -amyloid approved by the FDA for treatment of AD. The FDA issued conditional approval of the drug on June 7, 2021. At that time, Biogen announced that the cost of the drug would be \$56,000 per year (\$4,300/monthly infusion). Widespread public and scientific media coverage focused on the high cost, as well as on efficacy data and potential side effects. In November 2021, CMS announced that Medicare Part B premiums would be increased by almost 15% in 2022, citing the potential impact of coverage for aducanumab as 1 of 5 factors in projected costs. On December 20, Biogen announced a 50% reduction in the price for aducanumab, to \$28,000/year.

The January 11 announcement of the proposed NCD and limited coverage of the drug included a 30-day period for public comment. After reviewing all comments received on the proposed determination, CMS will announce its final decision by April 11, 2022. If the proposed NCD is finalized, CMS will review each submitted clinical trial to determine whether specific criteria are met. All CMS-approved clinical trials would be posted on the CMS Coverage website. In addition to CMS-approved trials, National Institutes of Health (NIH)–sponsored clinical trials would be covered. Medicare patients participating in these trials would be eligible to receive coverage of the drug, related services, and other routine costs, which may include 1 β -amyloid PET scan if required by a clinical trial protocol.

“We believe that any appropriate assessment of patient health outcomes must weigh both harm and benefit before arriving at a final decision,” said Lee Fleisher, MD, CMS Chief Medical Officer and Director of the Center for Clinical Standards and Quality. “Therefore, based on the public comments submitted previously and evidence CMS reviewed, the potential for harm, and important questions that remain, we have determined that coverage with evidence development through clinical trials is the right decision for Medicare patients, clinicians, and caregivers, and we look forward to receiving feedback on the proposal.”

SNMMI Reacts to CMS Coverage Decision

On January 12 SNMMI released the following statement on the CMS proposed NCD, including the decision to cover only 1 β -amyloid PET scan per patient in the approved trials:

In our first round of comments to CMS, we stressed the greater benefits of β -amyloid PET scans for early and accurate diagnosis of AD (compared to cerebrospinal fluid and blood biomarkers). Currently, PET is the only FDA-approved biomarker for identifying β -amyloid plaque.

Beta-amyloid PET is critical in the process of selecting patients who can benefit from therapy with aducanumab. Patients who are clinically thought to have AD but who show no evidence of brain amyloid in a PET scan do not have AD; they very likely would not be helped by the drug, and they could be negatively affected by drug-related toxicities. Although amyloid PET was not required by recent FDA prescribing information, the trials that led to approval of aducanumab required PET biomarker confirmation of positive amyloid status before therapy.

National coverage of β -amyloid PET will increase patient access to this therapy and will also more clearly identify patients who are amyloid negative and would not be eligible for most trials. Currently, 3 FDA-approved radiopharmaceuticals are approved for use with PET to identify β -amyloid plaque: ^{18}F -florbetapir, ^{18}F -flutemetamol, and ^{18}F -florbetaben. Their very limited use currently is covered under CED through the New IDEAS Study, a successor to the IDEAS Study that is focused on minority populations. Outside of this trial, however, these tracers are not covered by CMS.

We are concerned that CMS did not significantly change their CED requirement for β -amyloid PET scans. This may continue to limit access of patients to clinical trials of the drug. Removing the CED requirement would have been timely—given the approval of aducanumab and the coverage of tau PET diagnostics as of January 1—and would also have helped ensure equitable access to the new therapy. In addition, the current limited CMS coverage pays the provider far less than the cost of the imaging agent, a situation that limits access to the scans for our most vulnerable populations.

SNMMI is continuing to review the proposed NCD and will be submitting comments to CMS. Our preliminary thoughts are that CMS’s decision to cover AD therapy under CED is an incomplete solution rather than a productive resolution that would allow widespread and equitable patient access to monoclonal antibody therapy or clinical trials of that treatment. We hope CMS will change its position in its final decision, due in April 2022. The Society seeks broad national coverage of the scans either by a positive NCD or at Medicare Administrative Contractor (MAC) discretion.

HFR Outage and Isotope Supply

The Nuclear Medicine Europe (NMEu) Emergency Response Team alerted its stakeholders on January 24 to a delay in the restart of the High-Flux Reactor (HFR) (Petten, The Netherlands) that was expected to affect the supply of ^{99}Mo and ^{177}Lu for medical uses. The reactor supplies 60% of the European demand for these isotopes and 30% of the worldwide need. According to the accompanying release, the NMEu was informed by the Nuclear Research and Consultancy Group (NRG), which operates the reactor, that the delay was the result of discovery of a water leak in the reactor beam tube cooling system. Neither workers nor the general public was said to be at risk, and the reactor remained in safe standby status pending investigation of the cause of the leak. Inspections of difficult-to-access piping were performed but were not informative. Additional inspections were planned, and the NRG project

team was in place to identify remedial actions and enable the reactor to return to service after regulatory review and approval. Targets had been scheduled to be irradiated in the HFR reactor during the week of January 24 for both ^{99}Mo and ^{177}Lu production, and the delay affected the supply of these radioisotopes. Medical institutions were advised to contact their radioisotope suppliers to determine specific impacts on orders. On January 31, NRG provided an update and noted that investigators had listed options for restoring functionality and intended to select an approach in early February. A target date for HFR restart, however, could not be provided. Some shortages of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ were termed inevitable, with additional reports of effects on supplies of ^{177}Lu and ^{131}I .

Nuclear Research and Consultancy Group

FDA Guidance on Patient Engagement in Medical Device Clinical Studies

On January 25 the U.S. Food and Drug Administration (FDA) issued 2 final guidance documents containing recommendations for including patient perspectives in medical device clinical studies. Drafts issued in 2019 were modified by public comment and expert input to create the final documents. “Patient Engagement in the Design and Conduct of Medical Device Clinical Studies” describes how device developers, sponsors, and industry can voluntarily use patient engagement to improve clinical study design and conduct; provides examples of approaches to consider when device developers, sponsors, and industry wish to incorporate patient advisor input in clinical studies; describes which patient engagement activities are generally not considered by the FDA to constitute an activity subject to FDA regulations regarding institutional review boards; and clarifies how sponsors can receive feedback from the FDA on plans to voluntarily include patient advisors’ input on their clinical studies. The FDA encouraged patient engagement in medical device clinical studies in appropriate circumstances, but the recommendations are nonbinding. The document provides an overview of the potential value, challenges, and potential solutions related to involving patient advisors in the design and conduct of clinical studies. Entities considering incorporating such input in medical device clinical studies were encouraged to engage in early interactions with FDA and to obtain feedback from the relevant FDA office/division on appropriate design and any applicable regulatory requirements. The guidance states “FDA believes appropriate patient engagement may lead to improved efficiency

and quality in the design and conduct of medical device clinical studies and greater uptake of results by patients and providers when making treatment decisions about a legally marketed medical device, ultimately leading to earlier U.S. patient access to beneficial medical devices.”

The second guidance, “Principles for Selecting, Developing, Modifying, and Adapting Patient-Reported Outcome Instruments for Use in Medical Device Evaluation,” describes principles that may be considered for instruments that capture and measure patient-reported outcomes; provides recommendations about the importance of ensuring that these instruments are suited to the purposes to which they are applied; and outlines best practices for selecting, developing, modifying, or adapting a patient-reported outcome instrument for use in medical device evaluation. In the document summary, FDA noted that “to further integrate patient voices throughout the total product life cycle of medical devices, it is important to consider concepts important to patients in the regulatory evaluation and surveillance of medical devices. Well-designed patient-reported outcome instruments facilitate incorporating patient perspectives as scientific evidence to support regulatory and health care decision-making.” The guidance is intended to help ensure that patient-reported outcome instruments are developed, modified, adapted, and used in evaluation of medical devices in ways that generate “relevant, reliable, and sufficiently robust data to assess outcomes of importance to patients, regulators, and health care providers.”

U.S. Food and Drug Administration

SNMMI Launches Radiopharmaceutical Therapy Centers of Excellence Program

SNMMI announced in February the launch of a program offering nuclear medicine facilities the opportunity to qualify as designated and certified Centers of Excellence in Radiopharmaceutical Therapy. The centers will meet strict regulatory, training, qualification, experience, and performance criteria to help assure patients, their families, referring physicians, and payers that rigorous procedures are in place and followed, leading to appropriate patient selection and outcomes from radiopharmaceutical therapy. “Our goal with this program is to ensure that patients have reliable access to high-quality radiopharmaceutical therapy that is well integrated into their pathways of care and delivered by highly qualified therapy teams at technically qualified sites,” said Richard Wahl, MD, SNMMI President. “These teams will be led by physicians appropriately trained in nuclear medicine who will act as ‘nuclear oncologists’, working across disciplines to provide the right treatment with the most advanced and evidence-based approaches tailored to the needs of each patient.”

Designation as an SNMMI-recognized Radiopharmaceutical Therapy Center of Excellence will be a visible and prestigious sign that each site: carefully evaluates patients for suitability for radiopharmaceutical therapy, including in-person assessments in a clinical setting; that treatment providers are suitably qualified by training, experience, appropriate board certification, and continuing medical education to deliver the relevant radiopharmaceutical therapy and to use relevant imaging methods and equipment to assess patients before, during, and after treatment; that patients will receive follow-up care with deep engagement by the treating physicians and/or the broader therapy team; and that total patient care will be supported by a team of experts in nuclear medicine and molecular imaging, pathology, endocrinology, urology, social work, physics, and other relevant care domains. Three levels of designation will be awarded to qualifying sites.

Registered Therapy Site designation is intended mainly for those sites that administer only 1 type of radiopharma-

ceutical therapy. This designation does not require a registration fee.

Clinical Radiopharmaceutical Therapy Center of Excellence designation will be awarded to sites with experience administering multiple radiopharmaceutical therapies and at which procedure frequency is sufficiently high in relevant imaging methods and therapy procedures to assure continued excellence as evidenced by experience. Care teams at these sites will include physicians certified to read nuclear medicine studies and certified nuclear medicine technologists. Detailed site requirements include specifications for board and professional certifications for team members and modality/technology access.

Comprehensive Radiopharmaceutical Therapy Center of Excellence designation will indicate sites that are leading growth in the field. These centers will have experience administering multiple radiopharmaceutical therapies, supported by established care teams in at least 2 specific disease areas. These sites will also be actively involved in radiopharmaceutical therapy research, patient education, and provision of quality improvement and continuing medical education. Detailed requirements for the members of care teams and their appropriate certification and training are also included.

All 3 designated site types will be listed on the SNMMI Therapy Centers of Excellence portal, accessible to patients seeking treatment. Designations are valid for 2 years. Sites meeting the Center of Excellence criteria will receive certificates and door/window stickers with the designation. “It is our hope that this effort establishes a widely respected ‘gold standard’ by which prospective patients, colleagues in other disciplines, and the wider community can recognize quality and continued excellence in the rapidly advancing field of radiopharmaceutical therapy,” said Dr. Wahl.

Additional information and detailed requirements for each type of designation are available at: <https://www.snmmi.org/RPTCoE>.

SNMMI

Call the Nuclear Oncologist

Richard L. Wahl, MD, SNMMI President

The field of nuclear medicine began with a focus on therapy. Early applications of radiopharmaceutical therapy included the pioneering efforts of the sometimes forgotten Anastas Kocarev, a Macedonian physician who worked with Marie Curie on radium therapies in the 1920s. In 1941, ^{131}I was used for the therapy of thyroid disease by Dr. Saul Hertz and colleagues. Early nuclear medicine physicians included endocrinologists, with a focus on thyroid disease, and internists, among others. The inventions of the rectilinear scanner, gamma camera, PET, and PET/CT imaging, as well as development of innovative radiopharmaceuticals utilizing radioisotopes such as $^{99\text{m}}\text{Tc}$ and ^{18}F , changed the trajectory of nuclear medicine to a more diagnostic path. Now, with the continuing growth and evolution of radiopharmaceutical therapies—such as those developed for non-Hodgkin lymphoma, paragangliomas, neuroendocrine tumors, and bone metastases in castration-resistant prostate cancer—and the promise of new prostate-specific membrane antigen targeting agents in prostate cancer, as well as the growth in α -emitter treatments, we see nuclear medicine moving at accelerating speed back toward its therapeutic roots.

Our Practices Will Change and Evolve

Patients undergoing the broad range of cancer therapies are often under the care of a multidisciplinary team of specialists that frequently includes medical, surgical, interventional, and radiation oncologists. In addition, pathologists and nuclear medicine practitioners play important roles. As the new radiopharmaceutical therapies become more and more commonplace, the makeup of teams will expand, and roles will take shape and crystallize. Nuclear medicine must be a key and integral part of these treatment teams.

Nuclear medicine professionals have been the innovators and are currently most often the experts leading radiopharmaceutical therapy globally, but this may not always be the case. With so many professionals experienced and trained in closely related disciplines, there is ample opportunity for others to assume a growing role in radiopharmaceutical therapy. In the future, our role could grow further, but it could also be a more modest role—it all depends on the path we take and how we plan for that future.

We Need To Move Now To Define Our Path

If we are to stay critically involved in leadership in this new, fast-moving area of medicine, nuclear medicine physicians need to maintain a clearer and more distinct profile for the public and within health care. We need to be recognized as the specialists to whom cancer patients are sent for

evaluation for radiopharmaceutical therapy and, if appropriate, treatment. We must clearly be expert and recognized for our competence in radiopharmaceutical therapy of cancer. We need to take definitive action.

In May 2020, the SNMMI board of directors approved the term “nuclear oncologist” to define a nuclear medicine physician who works with radioisotope therapies. One cannot be a nuclear oncologist without being a nuclear medicine physician, because the nuclear medicine body of knowledge is essential to the role. To transition from nuclear medicine specialists to nuclear oncologists, however, several steps must be taken.



Richard L. Wahl, MD

First: Understand the Overall Cancer Management Paradigm

First, nuclear medicine professionals need to understand the bigger picture. We need to know how to better manage patients with cancer—not only with nuclear therapies but also with non-nuclear therapies. We need to take on a bigger role in the management and oversight of cancer patients; we need to take increased ownership of patients’ well-being while they are under our care. We need to understand all the care options and how they fit together: which options are best under which circumstances? Where does radiopharmaceutical therapy fit into that landscape, given the remarkable evolution of nonradioactive cancer therapies of a variety of types in the “precision medicine” revolution?

Next: New Knowledge, Experience and Training

To achieve that new level of understanding, nuclear oncologists will need wider exposure, an expanded body of knowledge, and additional/refined training. For example, we will need to gain more in-depth knowledge about the specific diseases that utilize both radiopharmaceutical and non-radioactive therapies. We will need increased involvement in medical, surgical, interventional, and radiation oncology to understand how information from nuclear medicine and molecular imaging impacts and interacts with other therapies. Increased involvement in multidisciplinary conferences can help to achieve this goal to understand new elements of research and care.

To have full command of this information, changes will likely be needed in nuclear medicine training programs, which must continue to evolve. There has been a push to

(Continued on page 17N)

Brookhaven National Lab 75th Anniversary

The U.S. Department of Energy (DOE) Brookhaven National Laboratory (BNL; Upton, NY) on January 27 held a live-streamed seminar as a launch event in celebration of its 75th y. The virtual event featured a panel discussion, including Haiyan Gao, PhD, Associate Lab Director, Nuclear and Particle Physics; John Hill, PhD, Director, National Synchrotron Light Source II; and Allison McComiskey, PhD, Chair, Environmental and Climate Sciences, who shared their visions for the future of particle physics, climate science, quantum information science, and more. The panel answered questions from a virtual audience through YouTube, Facebook, and Twitter.

Primarily supported by the DOE Office of Science, BNL is a multidisciplinary laboratory with 7 Nobel Prize-winning discoveries, 37 R&D 100 Awards, and 75 y of pioneering research. The lab was founded in 1947 with a post-World War II goal to explore peaceful applications of atomic energy. BNL today applies its expertise and world-class facilities to a wide range of scientific questions, from the fundamental forces of physics to complex interactions of ecosystems and the environment. The laboratory's almost 3,000 scientists, engineers, and support staff are joined each year by more than 5,000 visiting researchers from around the world. ^{99m}Tc was first developed at BNL in the 1950s, and in 1976 the lab synthesized and developed ^{18}F -FDG for initial medical imaging. The Brookhaven Linac Isotope Producer today produces many medical isotopes for both imaging and therapy research and continues to develop new ones. Learn more about BNL research initiatives at <https://www.bnl.gov/science/>.

Brookhaven National Laboratory

CMS Funding 1,000 New Residency Slots

The Centers for Medicare & Medicaid Services (CMS) on December 17 issued a final rule that includes funding for additional medical residency positions in hospitals

servicing rural and underserved communities. The Fiscal Year (FY) 2022 Inpatient Prospective Payment System final rule established policies to distribute 1,000 new Medicare-funded physician residency slots to qualifying hospitals, phasing in 200 slots per year over 5 y. CMS estimates that funding for the additional residency slots, once fully phased in, will total approximately \$1.8 billion over the next 10 y. As part of implementation of the Consolidated Appropriations Act (CAA, 2021), this is the largest increase in Medicare-funded residency slots in more than 25 y. Additional sections of the CAA being implemented promote increased training in rural areas and graduate medical education payments to hospitals meeting certain criteria. In allocating these new residency slots, CMS will prioritize hospitals with training programs in areas demonstrating the greatest need for providers, as determined by Health Resources and Services Administration data. The first round of 200 residency slots was announced at the end of January and will begin with the start of the academic year on July 1, 2023.

“Doctors are most likely to practice in the areas where they do their residencies. Having additional residents train in the very areas that need the most support can not only bolster the numbers of providers in these underserved areas but also train them with a unique understanding of the specific needs of these communities,” said Meena Seshamani, MD, PhD, Director of the CMS Center for Medicare.

For the relevant CMS fact sheet, see <https://www.cms.gov/newsroom/factsheets/fiscal-year-fy-2022-medicare-hospital-inpatient-prospective-payment-system-ipps-final-rule-comment>.

Centers for Medicare & Medicaid Services

FDA CDRH Health of Women Strategic Plan

On January 18, Terri Cornelison, MD, PhD, Chief Medical Officer and Director of the Health of Women Program at the Center for Devices and Radiological Health (CDRH) of the U.S. Food and Drug Administration (FDA) shared the

CDRH Health of Women Program Strategic Plan. Originally proposed for public feedback in 2019, the plan lays out the framework to advance the FDA mission by protecting and promoting the health of women, strengthening regulatory science, and identifying and addressing current and emerging issues in medical device research and regulation for the health of all women.

“Now, more than ever, we need to understand the implications sex and gender present for the performance of medical devices in all individuals,” said Cornelison. “The CDRH Health of Women program is a comprehensive, collaborative, landmark program built on the premise that both sex and gender have a considerable impact on a woman's overall health, not just their reproductive or sexual health. With patients at the heart of this initiative, and with the strategic plan as a blueprint for the center's priorities, Health of Women intends to ensure all women have access to innovative, safe, and effective medical devices.”

The CDRH Health of Women program was created in 2016 to address the steadily growing importance of sex- and gender-specific issues arising from medical technology design and development, clinical trial design, and other medical device-related matters. The new plan prioritizes the patient experience and leverages partnerships across CDRH to establish a portfolio of women-specific device efforts and strategize around gap areas to inform research. Cornelison outlined 3 main priorities: sex- and gender-specific analysis and reporting, an integrated approach for current and emerging issues related to the health of women, and creation of a research roadmap.

FDA Center for Devices and Radiological Health

DOE Isotope R&D Training

The U.S. Department of Energy (DOE) announced in December \$2 million in funding to establish a first-of-its-kind traineeship program in isotope research and development, production, and processing. The effort will be led by Texas A&M University (College Station) serving as the

Isotope Traineeship Coordination (ITC) site in collaboration with a team of 17 institutions—14 institutions of higher education (8 of which are Minority Serving Institutions) and 3 DOE/National Nuclear Security Administration national laboratories (Argonne National Laboratory, Lemont, IL; Lawrence Livermore National Laboratory, CA; and Los Alamos National Laboratory, NM). This investment is intended to boost exposure to the field of isotope science and accelerate the time usually required for a junior scientist to enter the workforce.

The workforce bolstered through this investment makes contributions daily by supporting the activities of the DOE Isotope Program, a key federal program that

produces critical isotopes in short supply. The isotopes produced have applications in medicine, national security, domestic and global industry, and discovery research.

“The DOE Isotope Program supports novel isotope production and processing activities at a suite of world-class facilities throughout the federal complex and at universities,” said Jehanne Gillo, PhD, Director of the DOE Isotope Program. “To ensure a strong and innovative program in the future, it is critical to nurture a broad and diverse workforce.”

The ITC collaboration aims to promote innovative and transformative approaches to isotope production and

processing through leveraging advances in manufacturing, artificial intelligence, machine learning, and robotics. The team will recruit a diverse population of ~20 undergraduate and 10 graduate students from the 14 degree-granting sites, develop a collaborative network and variety of in-person and virtual training mechanisms, establish peer-support groups and peer-to-peer mentoring, provide training for mentors, and assist in trainee career advancement. The program will train participants in isotope science through coursework as well as research and isotope production experiences within the DOE Isotope Program.

U.S. Department of Energy

(Continued from page 15N)

shortened curricula to increase the size of the workforce. Such training may have limitations if it is not cancer focused. Our colleagues in interventional radiology have recently evolved into an independent specialty, and those who do more oncology-focused practice identify themselves as “interventional oncologists.” We could take the same approach with a self-designated “nuclear oncologist” moniker for those nuclear medicine physicians who function in the radiopharmaceutical therapy/oncologic imaging domain. But for a comprehensive understanding of nuclear oncology, a cancer-focused training curriculum—which could include an additional year of training in the form of a nuclear oncology fellowship—may be necessary. A specific certification could also help set nuclear oncologists apart, recognizing them for their excellence.

Should we take these steps to ensure our place in the future of radiopharmaceutical therapy? If we do not, our role in radiopharmaceutical therapies may become limited and possibly entail only a brief interaction with a patient. If we do take these steps, we can feel confident that the nuclear oncologist’s body of knowledge is sufficient to deliver the best care to patients with cancer. As well-qualified nuclear oncologists, we can ensure our continued seat at the cancer therapy table—in many instances sitting at the head of that table. Nuclear medicine physicians have long been and will, with appropriate action, remain the innovators in radiopharmaceutical therapies, defining therapy into the future and advancing the relevance of our field. If we evolve as nuclear oncologists, we will drive this important field forward for our profession and, most important, for our patients.

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.

⁶⁸Ga-PSMA-11 vs ¹³¹I in Thyroid Cancer

Pitalua-Cortes et al. from the National Cancer Institute (Mexico City, Mexico) and the Universidad Autónoma de Bucaramanga (Colombia) reported in the December 22 issue of *Frontiers in Endocrinology (Lausanne)* (2021;12:794759) on a comparison of ⁶⁸Ga-prostate-specific membrane antigen (PSMA)-11 and ¹³¹I in the follow-up of well-differentiated metastatic thyroid cancer. The retrospective study included 10 patients (8 women, 2 men; mean age, 58 ± 11.6 y) who underwent posttherapeutic ¹³¹I whole-body scanning and SPECT/CT, as well as ⁶⁸Ga-PSMA-11 PET/CT imaging. A total of 64 metastatic lesions were analyzed (67% papillary, 33% follicular), with 58% of metastatic lesions in bone, 17% in lung, 8% in lymph nodes, 5% in the postoperative thyroid bed, 5% in brain, and 7% in other sites. ⁶⁸Ga PSMA-11 PET/CT identified all 64 lesions, whereas ¹³¹I SPECT/CT identified only 55. Lesions not detected by ¹³¹I SPECT/CT were in the lung (44.4%), brain (22.2%), postoperative thyroid bed (11.1%), lymph nodes (11.1%), and bone (11.1%). Although observer agreement was high for both tracers, it was almost 100% for ⁶⁸Ga

PSMA-11 PET/CT. The authors concluded that the superior performance of ⁶⁸Ga-PSMA PET/CT for metastatic lesion detection when compared with ¹³¹I SPECT/CT suggests that PSMA-based imaging could possibly be used for early identification of radioiodine refractory disease. They added that, in addition to avoiding some of the challenges of ¹³¹I-based follow-up, PSMA uptake values may both expedite diagnoses and provide a rationale for development of theranostic applications.

Frontiers in Endocrinology (Lausanne)

Integrating PSMA PET in NCTN Trials

In an article published on January 11 ahead of print in the *Journal of Clinical Oncology*, Schöder and members of the National Cancer Institute (NCI) Clinical Imaging Steering Committee (CISC) Prostate-Specific Membrane Antigen (PSMA) PET Working Group reported on the results of an expert review and survey of challenges to clinical use of PSMA. The working group was tasked with identification of these challenges across various clinical scenarios and development of consensus recommendations on most effectively integrating PSMA PET into National Clinical Trials Network (NCTN) studies. In this article, the group identified challenges in stage migration, response assessment, trial logistics, and statistical analysis and offered proposed solutions. The report was also informed by the results of an anonymous, open-ended survey about these challenges, as well as serial overviews of related clinical trials. The authors discussed implications for patient selection and definition of study end points and provided guidance and potential solutions for different clinical scenarios, particularly with regard to best practices in defining eligibility criteria and outcome measures.

Journal of Clinical Oncology

PET + MRI in Symptomatic Carotid Stenosis

Gianotti, from University College Dublin, and colleagues from Mater Misericordiae University Hospital, St. Vincent's University Hospital, Connolly Hospital, St. James Hospital, Trinity College Dublin, and Beaumont Hospital and Royal College Surgeons Ireland (all in Dublin, Ireland) reported on December 23 in *Frontiers in Neurology* (2021; 12:731744) on a study investigating the association of selected imaging characteristics of plaque vulnerability measured with ¹⁸F-FDG PET and MRI in patients with symptomatic carotid stenosis. The study included 25 patients (≥50 y old, mean age, 65 y; 72% men, 28% women) from a larger clinical trial who had experienced an ischemic stroke or motor/speech/vision transient ischemic attack within the last 30 d, had ipsilateral internal carotid artery stenosis (≥5.0% lumen narrowing); and had undergone carotid PET/CT angiography and MRI. MRI imaging quantified morphologic features of plaque instability. In addition to inflammation-related metabolism as represented by SUV_{max} on PET, data from CT- and MRI-assessed plaque volume were compared. Plaque volume was greater in men (1,708–1,286 mm³), patients who had experienced strokes (1,856–1,440 mm³), and non-statin users (1,325–1,797 mm³). PET SUV_{max} values were directly associated with MRI-measured plaque lipid-rich necrotic cores in the corresponding axial slices and inversely associated with whole-plaque fibrous cap thickness and calcium volume. The authors concluded that these novel correlations of noninvasive imaging biomarkers of inflammation-related plaque metabolism and morphologic MRI markers of plaque instability “may support the application of combined MRI and PET to detect vulnerable plaque in future clinical practice and randomized trials.”

Frontiers in Neurology

COVID-19, Myocardial Injury, and PET + MRI

In an article in the January 12 issue of *JAMA Cardiology*, Hanneman et al. from the University of Toronto (Canada) and the University of Cologne (Germany) reported on a study investigating myocardial metabolic changes early after recovery from COVID-19 using ^{18}F -FDG PET and correlating these changes with abnormalities in cardiac MRI-based function and tissue characterization measures and with inflammatory blood markers. The study, which took place between November 2020 and June 2021, included 47 patients (24 women, 23 men; mean age 43 y), who were an average of 67 d (± 16 d) post-COVID 19 diagnoses at the time of combined PET/MRI imaging and blood marker evaluation. Most patients (85%) had not been hospitalized during acute stages of infection. Eight patients (17%) were found to have focal ^{18}F -FDG uptake on PET consistent with myocardial inflammation and were asked to return for repeat assessment 2 mo later. Patients with focal ^{18}F -FDG uptake were found on combined imaging to have higher regional T2, T1, and extracellular volume, higher prevalence of late gadolinium enhancement, lower left ventricular ejection fraction, worse global longitudinal and circumferential strain, and higher systemic inflammatory blood markers, including interleukin 6, interleukin 8, and high-sensitivity C-reactive protein. In these patients, PET/MRI findings and inflammatory blood markers resolved or improved at 2-mo follow-up assessment. The authors concluded that these “imaging findings are generally consistent with an imaging phenotype with good prognosis; however, it does emphasize the importance of studies examining the longer-term effects of COVID-19 on the heart.”

JAMA Cardiology

^{11}C -PABA PET in Bacterial Infection

Ordonez et al. from the Johns Hopkins University School of Medicine

(Baltimore, MD) and the University of California San Francisco reported on January 11 in *JCI Insight* (2022;7[1]:e154117) on the use of ^{11}C -para-aminobenzoic acid (^{11}C -PABA) PET imaging for detection and monitoring of pyogenic bacterial infections in a range of clinically relevant animal models and healthy human participants. In a rabbit model of experimentally induced myositis with *E. coli* or *S. aureus*, ^{11}C -PABA PET was able to selectively localize sites of infection and differentiate these from sterile inflammation. In a prosthetic joint model in rabbits, ^{11}C -PABA PET successfully detected prosthetic-related methicillin-resistant *S. aureus* infection. ^{11}C -PABA PET also correctly detected involved sites in bone in rats infected with *S. aureus*. No adverse or clinically detectable pharmacologic effects were noted in biodistribution and radiation dosimetry studies in 5 healthy human volunteers, and the tracer was rapidly cleared from most organs. The authors concluded that “ ^{11}C -PABA has the potential for clinical translation to detect and localize a broad range of bacteria” and called for additional clinical studies in patients with confirmed infections to evaluate the role of ^{11}C -PABA PET imaging in diagnosing and monitoring bacterial infections.”

JCI Insight

PET MTV and Rhabdomyosarcoma Prognosis

In an article published on January 14 in *PLoS One* (2022;17[1]:e0261565), Fayolle et al. from Toulouse Purpan University Hospital, Curie Institute/PSL Research University (Paris), the Léon Bérard Cancer Centre (Lyon), and the Toulouse Paul Sabatier University-INSERM (all in France) reported on a multicenter study of the utility of pretreatment ^{18}F -FDG PET-derived metabolic tumor volumes (MTVs) in providing prognostic information in pediatric patients with rhabdomyosarcoma. MTV in the study was defined as the sum of the primary tumor and the largest metastasis (where relevant) with a 40% threshold of the primary

tumor SUV_{max} . The prognostic values of SUV_{max} , SUV_{peak} , and bone lysis were also evaluated. The study included 101 patients (62 boys, 39 girls; median age, 7.4 y) with localized disease ($n = 35$), regional nodal spread ($n = 43$), or distant metastases ($n = 23$). A total of 44 patients had alveolar subtypes. The researchers found that an MTV $> 200 \text{ cm}^3$ was associated with a 2.5-factor increased risk of death or disease progression. SUV_{max} , SUV_{peak} , and bone lysis also were correlated with both overall and progression-free survival. The authors concluded that “given the therapeutic challenges in a pediatric population, with the risk of developing secondary toxicities, our study brings an additional argument to include metabolic PET parameters in the decision-making trees for the management of rhabdomyosarcoma. And it could help to adapt patients’ therapeutic management.”

PLoS One

Consensus Statement: Postoperative ^{131}I in DTC

Pacini et al. from the University of Siena (Italy), University Hospital Essen/University Duisburg-Essen (Germany), University of Pisa (Italy), Maria Skłodowska-Curie National Research Institute of Oncology (Gliwice, Poland), Gustave Roussy Cancer Campus and University Paris-Saclay (Villejuif, France), University Hospital Marburg (Germany), and Radboud University Medical Center (Nijmegen, The Netherlands) provided on January 1 in the *European Thyroid Journal* (2022;11[1]:e210046) a European Thyroid Association Consensus Statement intended to deliver rational recommendations for indications for postoperative radioiodine therapy in differentiated thyroid cancer tailored to the specific goals of these indications and the needs of each patient. The 8 recommendations addressed the questions of which patients are candidates for which form of radioiodine therapy, appropriate activities of radioiodine for specific scenarios, and optimal preparation methods. The authors recommended individual risk-based assessment of candidates for postoperative ^{131}I treatment.

They added that because this consensus statement was based largely on retrospective studies in which biases could not be excluded, “the only way to scientifically compare 2 treatment modalities and to exclude biases is to perform randomized prospective studies,” which they termed “clearly feasible.”

European Thyroid Journal

PET and Immunotherapy Discontinuation in Melanoma

In an article published online on January 9 ahead of print in the *International Journal of Cancer*, Ellebaek et al. from Copenhagen University Hospital (Herlev, Denmark) reported on a study of the clinical value of routine ¹⁸F-FDG PET imaging as a decision-assisting tool for early immunotherapy discontinuation in advanced melanoma. The retrospective study included data from 140 patients in the Danish Metastatic Melanoma Database. Patients treated with an anti-PD-1–based regimen for <18 mo and who had experienced ≥4 mo without disease progression after stopping treatment were included. Serial ¹⁸F-FDG PET/CT had evaluated these patients as having partial or complete responses. Patients were divided into “elective” and “toxicity” groups, depending on the reasons for which their treatment had been discontinued. Over a median 29.3-mo follow-up, a higher percentage of patients remained alive in the elective group (93%) than in the toxicity group (75%), with improved melanoma-specific survival. Patients without ¹⁸F-FDG–avid lesions when treatment was discontinued showed improved melanoma-specific survival. In multivariate analysis, the absence of lesions was the only independent predictive feature of improved melanoma-specific survival. The authors concluded that patients with metastatic melanoma who obtain an early response and discontinue immunotherapy early “have an excellent prognosis, especially in the absence of ¹⁸F-FDG PET–avid lesions when discontinuing treatment.” They added that “these data support the option of early

discontinuation, limiting possible over-treatment and thereby toxicity, health, and economic expenses and improving logistics.”

International Journal of Cancer

PET/CT in Untreated Multiple Myeloma

Li et al. from the Second Hospital of Anhui Medical University (Hefei, People’s Republic of China) reported on January 9 ahead of print in *Clinical and Experimental Medicine* on a systematic review and metaanalysis of the prognostic value of ¹⁸F-FDG PET/CT at diagnosis and before treatment in patients with multiple myeloma. The researchers systematically reviewed the major medical literature databases for relevant articles, with a resulting study set of 16 qualifying articles including 2,589 patients. Statistical analyses indicated that PET/CT has an excellent prognostic role in multiple myeloma and that higher SUV_{max}, more focal lesions, and extramedullary disease at the time of diagnosis were associated with poor overall and progression-free survival. Similar results were seen in most subgroup analyses. The authors concluded that “pretreatment ¹⁸F-FDG PET/CT examination has prognostic value for myeloma patients and has guiding significance for clinical treatment.”

Clinical and Experimental Medicine

Predicting Chemoimmunotherapy Outcomes in NSCLC

In an article in the January 9 issue of *Therapeutic Advances in Medical Oncology* (2022;14:17588359211068732), Kim et al. from Yonsei University College of Medicine (Seoul and other sites in the Republic of Korea) evaluated whether imaging biomarkers of ¹⁸F-FDG PET/CT and routinely assessed clinical and laboratory values were associated with clinical outcomes in patients with advanced non–small cell lung cancer (NSCLC) receiving pembrolizumab plus platinum-doublet chemotherapy as first-line treatment.

The retrospective study included 52 patients with advanced disease who underwent ¹⁸F-FDG PET/CT before beginning treatment. Over a median follow-up period of 16.7 mo (range, 15.7–17.7 mo), 43 (82.7%) patients experienced disease progression and 31 (59.6%) died. An objective response to treatment was seen in 23 (44.2%). After analysis, SUV_{max}, metabolic tumor volume, total lesion glycolysis, and bone marrow-to-liver uptake ratio on PET/CT, as well as neutrophil-to-lymphocyte ratio in laboratory analyses, were independently and significantly predictive of treatment response, progression-free survival, and overall survival. The authors concluded that these results suggest the potential of these variables as “effective markers for combined PD-1 blockade and chemotherapy” in patients with NSCLC.

Therapeutic Advances in Medical Oncology

SSTR Expression and PET/CT in Pancreatic NENs

Majala et al. from Turku University Hospital/University of Turku and Helsinki University Hospital/University of Helsinki (both in Finland) reported in the December 29 issue of *Cancers (Basel)* (2021;14[1]:162) on a study designed to correlate immunohistochemical tissue levels of somatostatin receptors 1–5 with receptor density as seen in ⁶⁸Ga-DOTA-NOC uptake on PET/CT in a prospective series of patients with nonfunctional pancreatic neuroendocrine neoplasms (PNENs). The study included 21 patients with a total of 35 such lesions and with 21 lymph node metastases on histologic analysis who underwent both ⁶⁸Ga-DOTANOC and ¹⁸F-FDG PET/CT imaging. Twenty patients proceeded to surgery, and 1 underwent endoscopic ultrasonography and core-needle biopsy. Histology and PET/CT findings were correlated. Expression of SSTR1 was detected in 74% of lesions, SSTR2 in 91%, SSTR3 in 80%, SSTR4 in 14%, and SSTR5 in 77%. SSTR2 immunohistochemistry significantly correlated with

^{68}Ga -DOTANOC PET/CT findings. All ^{68}Ga -DOTANOC-avid tumors expressed SSTR2, SSTR3, or SSTR5. SSTR5 expression was associated with low Ki-67 proliferation, possibly associated with better prognoses. The authors noted that “further prospective studies, in larger tumor series, are needed to study the correlation of SSTR expression profile with ^{68}Ga -labeled SST and ^{18}F -FDG PET/CT for the personalized management of PNEN patients.”

Cancers (Basel)

Interim Report on the GastroPET Study

In an article in the January 5 issue of *Therapeutic Advances in Medical Oncology* (2022;13:17588359211065153), Obermannova et al. from Masaryk Memorial Cancer Institute (Brno), Charles University and General University Hospital (Prague), University Hospital Olomouc, and University Hospital Brno (all in the Czech Republic) reported on the methodology, study design, and initial patient safety data for GastroPET, a large multicenter phase II trial assessing an ^{18}F -FDG PET/CT preoperative treatment strategy for localized esophagogastric junction adenocarcinoma, with the R0 resection rate as a primary endpoint. The report included data on the first 63 patients enrolled. Patients with locally advanced esophagogastric junction adenocarcinoma (Siewert I–III) stages Ib–IIIc underwent baseline PET/CT scanning and repeat imaging after 14 d of oxaliplatin-5FU (docetaxel) chemotherapy. Response was defined as a $\geq 35\%$ decrease in $\text{SUV}_{\text{average}}$ from baseline. Responders ($n = 35$) were then continued on the same chemotherapy for 2–3 mo before surgery. Management for nonresponders ($n = 28$) was changed to preoperative chemoradiotherapy (weekly carboplatin and paclitaxel with concurrent radiotherapy [45 Gy in 25 fractions]). In addition to initial reporting on feasibility, the study group compared local and centralized reading of imaging results. At the time of this report, 47 patients (28 responders,

19 nonresponders) had completed surgery. Grade 3 or higher postoperative complications were reported in 5 responders and 2 nonresponders (no statistical difference). Two patients died after surgery, 1 in each arm of the study. Centralized and local image interpretations of changes in SUV were 100% concordant. The authors noted that these results confirm “the accuracy of a PET response-guided treatment algorithm for locally advanced esophagogastric junction cancer in a multicenter setting” and that preoperative treatment adaption based on PET/CT appeared to be feasible and safe.

Therapeutic Advances in Medical Oncology

^{68}Ga -PSMA-11 PET/CT and Glial Tumors

Kunikowska et al. from the Medical University of Warsaw, Poznan University of Medical Sciences, National Centre for Nuclear Research (Otwock), and the Maria Skłodowska-Curie National Research Institute of Oncology (Warsaw; all in Poland) reported on January 13 in *Science Reports* (2022;12[1]:652) on a study using ^{68}Ga -prostate-specific membrane antigen-11 (^{68}Ga -PSMA-11) PET/CT to study PSMA expression in recurrent glial tumors. The study included 34 patients (ages, 44.5 ± 10.3 y) with suspected recurrence of histologically confirmed grade III ($n = 6$) and grade IV ($n = 28$) gliomas. All patients underwent both contrast-enhanced MR and ^{68}Ga -PSMA-11 PET/CT imaging. PET/CT was positive in all areas indicated as suspicious for recurrence on MR, and recurrence was confirmed by histopathology and/or follow-up imaging. Median SUV_{max} for tumors was 6.5 (range, 0.9–15.6) and SUV_{mean} was 3.5 (range, 0.9–7.5). The median target-to-background ratio was 152 (range, 15–1,400), and median target-to-liver background ratio was 1.3 (range, 0.2–2.6). No significant differences were found in PET/CT parameters between grades III and IV. The authors concluded that because treatment options in recurrent glioma are limited,

this observation may point to therapeutic innovations using radiolabeled agents targeting PSMA.

Science Reports

PET/CT in Neurofibromatosis Type 1

In an article published online on January 13 ahead of print in the *Journal of NeuroOncology*, Geitenbeek et al. from University Medical Center Utrecht, Erasmus Medical Center Cancer Institute (Rotterdam), and Maastricht University Medical Center (all in The Netherlands) reported on the diagnostic accuracy and value of ^{18}F -FDG PET/CT in detecting malignant peripheral nerve sheath tumors (MPNSTs) in adult and pediatric patients with neurofibromatosis type 1. The retrospective study included 60 patients, all of whom underwent PET/CT and in whom 70 tumors were identified (10 MPNSTs and 60 benign peripheral nerve sheath tumors [BPNSTs]; 40 in females, 30 in males; 15 in children, 55 in adults). Over a mean follow-up of 3.5 ± 1.6 y at the time of the report, 7 MPNST patients and 4 BPNST patients had died. The authors developed a diagnostic algorithm for PET/CT findings. They identified ideal threshold values of 5.8 for SUV_{max} (sensitivity 70%, specificity 92%), 5.0 for SUV_{peak} (sensitivity 70%, specificity 97%), 1.7 for maximum tumor-to-liver ratio (TL_{max}) (sensitivity 90%, specificity 86%), and 2.3 for TL_{mean} (sensitivity 90%, specificity 79%). A standard TL_{mean} threshold value of 2.0 yielded a sensitivity of 90% and specificity of 74%, and the standard SUV_{max} threshold value of 3.5 yielded a sensitivity of 80% and specificity of 63%. SUV_{max} and adjusted SUV for lean body mass were somewhat lower in children, but TL ratios were similar in the 2 groups. Using thresholds of $\text{TL}_{\text{mean}} > 2.0$ or $\text{TL}_{\text{mean}} < 2.0 + \text{SUV}_{\text{max}} > 3.5$, the authors' algorithm achieved sensitivity of 100% and specificity of 63%. They concluded that these semiquantitative PET markers “offer acceptable diagnostic accuracy for detecting malignant

transformation of peripheral nerve sheath tumors in neurofibromatosis type 1,” adding that the potential differences between uptake values of adults and children did not impact the diagnostic algorithm.

Journal of NeuroOncology

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 Newslines editor recommends several general reviews accessioned into the PubMed database in December and January. In an article e-published on January 10 in *Geburtshilfe und Frauenheilkunde* (2022;82[1]:50–58), Unger et al. from Universitätsklinikum Freiburg and the St. Vincentius Kliniken (Karlsruhe, both in

Germany) provided a structured overview of “Expression of prostate specific membrane antigen (PSMA) in breast cancer.” Taralli et al. from the Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Rome), S. Orsola-Malpighi University Hospital (Bologna), Azienda Ospedaliera San Camillo Forlanini (Rome), and the Università Cattolica del Sacro Cuore (Rome, all in Italy) summarized data on “The prognostic value of ¹⁸F-FDG PET imaging in staging in patients with malignant pleural mesothelioma: A literature review” on December 22 in the *Journal of Clinical Medicine* (2021;11[1]:33). In an article published on January 17 ahead of print in the *British Journal of Haematology*, El-Galaly et al. from Aalborg University (Denmark), the BC Cancer Centre for Lymphoid Cancer/University of Brit-

ish Columbia (Vancouver, Canada), Sir Charles Gairdner Hospital (Perth, Australia), and the University of Western Australia asked “Pretreatment total metabolic tumour volumes in lymphoma: Does quantity matter?” Bidakhvidi et al. from University Hospitals Leuven (Belgium) reviewed on December 28 in *Cancers (Basel)* (2021;14[1]:129) “Peptide receptor radionuclide therapy targeting the somatostatin receptor: Basic principles, clinical applications, and optimization strategies.” In the December 31 issue of the *International Journal of Molecular Sciences* (2021;23[1]:474), Ben-Shalom et al. from Tel Aviv Sourasky Medical Center, Weizmann Institute of Science (Rehovot), and Tel Aviv University (all in Israel) reported on “The role of molecular imaging as a marker of remyelination and repair in multiple sclerosis.”