SNMMI Hosts FDA Workshop

On February 21, SNMMI and the U.S. Food and Drug Administration (FDA), Medical Imaging Technology Alliance, and World Molecular Imaging Society hosted "PET Drugs: A Workshop on Inspections Management and Regulatory Issues," at the FDA White Oak Conference Center in Silver Spring, MD. The purpose of the workshop was to provide a forum for exchange of information and perspectives on the regulatory and compliance framework for PET drug manufacturing and thereby improve global understanding of PET drug manufacturing. The workshop organizers included Sue Bunning, MA (MITA), Dalton Clark (SNMMI), Steve Mattmuller, MS, RPh (Kettering Medical Center), Sally Schwarz, MS (Washington University), Henry VanBrocklin, PhD (University of California San Francisco), and Steve Zigler, PhD (PETNET Solutions). The workshop was attended by approximately 150 members of the PET community and the FDA.

Among the specific goals and objectives of the 1-day meeting were to: discuss regulatory compliance for development and manufacturing of PET drugs and pathways for drug applications, application maintenance, and inspections based on Code of Federal Regulations Part 212 (Current Good Manufacturing Practice [cGMP] for Positron Emission Tomography Drugs); share perspectives from industry, academia, investigators, and regulators on inspection findings and trends; and provide information on the management of Part 212 inspections and maintenance of PET New Drug Applications (NDAs) and Abbreviated New Drug Applications (ANDAs). The workshop included 4 sessions, each co-moderated by an FDA staff member and a member of the PET community. The speakers included representatives of PET drug manufacturers from academia, industry, as well as the FDA.

The first session looked at considerations and trends in inspections and compliance, including manufacturing process assessment and preapproval inspections, and recent experience with PET surveillance cGMP inspections of PET manufacturers; and current trends and observations on inspections and PET surveillance inspections through the FDA pilot program for tablet-based inspections for PET drugs. A panel discussion and questions followed. The second session focused on lifecycle management of PET drug applications, including management of PET drug applications (NDA or ANDA), and PET community perspectives on PET drug application, with a follow-up discussion and question period. After lunch, the third session looked at chemistry and product quality assurance, including the microbiological regulatory perspective; product quality and sterility assurance; and chemistry and product quality assurance. The final session covered the changing landscape of PET drugs, labeling requirements for NDAs, and requirements for electronic filing of regulatory applications.

At the Workshop on PET Drug Manufacturing: Sue Bunning, MS, Steve Zigler, PhD, Sally Shwarz, MS, Steve Mattmuller, MS, RPh.

Themes stressed throughout the workshop included: the need for uniformity in FDA inspections of PET drug establishments, a consensus on a science-based risk profile for PET drugs, improvements to training for FDA investigators and the regulated community, and the need for continued dialog between the FDA and PET drug stakeholders. The organizers plan to make slides from the workshop available to the public and are also planning a follow-up session at the upcoming SNMMI annual meeting in New Orleans, LA.

SNMMI

SNMMI at NRC Commissioners' Meeting

On January 28 at a Commissioners' Meeting of the Nuclear Regulatory Commission (NRC) in Rockville, MD, SNMMI President Vasken Dilsizian, MD, and patient advocate Josh Mailman provided their perspectives on recent NRC staff initiatives related to medical uses of radioactive materials. The meeting was organized into 2 panels: 1 featuring NRC staff and 1 with stakeholders from the medical community who use or have patient perspectives on radioactive materials. Five presenters in each panel gave 8-minute presentations. For the NRC staff, these included an overview of the NRC program for medical uses of radioactive materials, the status of recent NRC staff activities, innovation opportunities and initiatives, efforts to prepare for review of emerging medical technologies, and regional perspectives on licensing and oversight of medical licensees. The external stakeholder panel addressed emerging issues in the national program for regulation of medical uses of radioactive materials, medical community suggestions about transformation/innovation opportunities, perspectives on recent NRC staff initiatives related to medical uses of radioactive materials, and patient suggestions for transformation/innovation and opportunities for the NRC to explore. These presentations were followed by an extended period in which NRC commissioners asked questions and followed up on the panelists' comments.

In his remarks, Dilsizian highlighted the importance of appropriate training and experience requirements for authorized users, addressed concerns about patient safety and patient release materials and guidelines after treatment with radioactive materials, and described potential barriers to patient access.

At the January 28 NRC Commissioners' Meeting, from left: Commissioner Jeff Baran; Commissioner Annie Caputo; American Society for Radiation Oncology President Thomas Eichler, MD; patient advocate Josh Mailman; NRC Chair Kristine L. Svinicki; SNMMI President Vasken Dilsizian, MD; and Commissioner David A. Wright.

Mailman was the only patient to sit on a panel. In his presentation, he offered views as an "end user" of medical radioactive materials. His focus was on treatment of neuroendocrine tumors, and he echoed Dilsizian's concerns about training and education requirements. A complete transcript of the meeting and panelists' slides are available at: https://www.nrc.gov/reading-rm/doc-collections/commission/tr/2020/.

Nuclear Regulatory Commission
SNMMI

Congressional Briefing: Diagnostic Imaging and Alzheimer Disease

SNMMI, the Council on Radionuclides and Radiopharmaceuticals, and the Medical Imaging Technology Alliance cohosted on January 29 a Capitol Hill congressional briefing on "A New Hope: Advancements in Diagnostic Imaging and Alzheimer's." The briefing was an opportunity for physicians, patients, and industry representatives to talk with congressional representatives and staff about the growing importance of access to diagnostic radiopharmaceuticals—in particular, those for amyloid PET imaging for diagnosis, research, and treatment in Alzheimer disease (AD). Event speakers also addressed the need for fair payment for radiopharmaceuticals and passage of the Medicare Diagnostic Radiopharmaceutical Payment Equity Act of 2019 (HR 3772).

Speakers included AD patient and caregiver team Geri and Jim Taylor; William Klunk, MD, PhD, codirector of the University of Pittsburgh (PA) Alzheimer's Disease Research Center; and Gersham Dent, PhD, MBA, senior director of clinical imaging at Biogen (Cambridge, MA). Congressman Bobby Rush (D-IL), one of the original cosponsors of HR 3772, attended to voice his support for the bill.

Klunk, coinventor of the first amyloid imaging radiotracer, Pittsburgh compound-B, discussed the history of amyloid PET scans and their role in diagnosis and development of treatment plans. "Relative to past diagnostic approaches, amyloid PET scans allow us to track disease progression in a way that is clear and striking," he said. "Put in simpler terms, these tools are shining a light on important dimensions of the disease that were previously unclear."

Dent spoke about the importance of amyloid PET imaging in AD drug development. "Amyloid imaging is used to select the right patients for clinical trials," he said. "It may be critical for patient identification when therapies enter the market, and patients can benefit from new therapies only if infrastructure issues are addressed and appropriate reimbursement is in place."

Members of the nuclear medicine community who would like to express their support for ensuring patient access to lifesaving diagnostic radiopharmaceutical can go to: https://snmmi.quorum.us/campaign/23260/ to write to their Congressional representatives.

SNMMI

Future Leaders of SNMMI and SNMMI-TS

During the SNMMI 2020 Mid-Winter Meeting in Tampa, FL, in January, SNMMI and SNMMI-Technologist Section (SNMMI-TS) held leadership academies. These academies are open to physicians, scientists, and technologists with strong leadership abilities who are interested in taking more active roles in the societies, as well as within the nuclear medicine and molecular imaging community.

SNMMI Future Leaders Academy

On January 25, during the House of Delegates meeting, SNMMI recognized the graduates of its 5th Future Leaders Academy. The academy was facilitated by Jon Burroughs, MD, MBA, with the American Association for Physician Leadership, and included the opportunity to engage with current and past SNMMI leaders. The academy leadership development workshop focused on ways to guide successful efforts in health care transformation, conflict resolution, and strategic planning and on the future of the field and SNMMI's role in this evolution. Participants were then invited to various SNMMI governance events throughout the Mid-Winter Meeting to see first-hand the organizational structure of the society.

The 12 graduates of the Future Leaders Academy Class of 2020 were Yoram Baum, MD; Sarah Cheal, PhD; Shadi Esfahani, MD, MPH; Pedram Heidari, MD, MPH; Mary Ellen Koran, MD, PhD; Courtney Lawhn-Heath, MD; Maria Menendez, DVM, PhD; Domnique Newallo, MD, RT (R)(CT); Thomas Ng, MD, PhD; Daniella Pinho, MD; Ali Salavati, MD, MPH; and Vanessa Sanders, PhD.

SNMMI-TS Leadership Academy

SNMMI-TS graduated its 13th class of its Leadership Academy during the National Council of Representatives meeting on January 24. Long-time facilitator Shawn Dunning from Adventure Associates and SNMMI-TS leadership, including President Mark Crosthwaite, CNMT, led a day of lessons, team-building activities, and networking sessions to build personal skills while promoting SNMMI-TS leadership opportunities. Participants included practicing nuclear medicine technologists, student attendees, and staff representatives. SNMMI-TS President Elect Tina Buehner, MS, CNMT, NMTCB(CT)(RS), RT(N)(CT), noted that she looks forward to seeing these graduates on future SNMMI-TS committees to continue their involvement with the society.

The 14 graduates of the SNMMI-TS Leadership Academy Class of 2020 were Roberta Alvarez, MS, ARRT(N)(MR); Garrett Anderson; Dalton Clark; Rebecca Gallagher; Jane Kamm; Nicole LaBrecque; Jose Meza, CNMT, PET, NCT, RT(N); Samantha Miller, RT(N); Keexia Osborne; Christopher Owens, CNMT, PET, RT(R)(CT)(MR)(N); Kait Solomon, MPS; Taylor Steenburgen; Laura Wotta, CNMT; and Thalia Zolis.

2020 SNMMI Future Leaders Academy graduates and society leadership at the SNMMI Mid-Winter Meeting.

2020 SNMMI-TS Leadership Academy graduates and society leadership at the SNMMI Mid-Winter Meeting.

To the SNMMI-TS: Congratulations on 50 Years of Dedicated Service to SNMMI and Your Patients

Vasken Dilsizian, MD, SNMMI President

On behalf of the senior leadership of the Society, I would like to express our heartfelt congratulations to the nuclear medicine technologists for their historic 50th anniversary celebrations as dedicated members of the Society of Nuclear Medicine and Molecular Imaging–Technologist Section (SNMMI-TS). We are grateful for your passionate commitment to and enthusiasm for the field of nuclear medicine. To improve the human condition through imaging and image-guided therapy is the heart of SNMMI's mission. The honorable profession that you have chosen, partnering with nuclear medicine physicians to deliver the highest quality of images and care to our patients, is perhaps the highest calling of all. Your compassionate care changes the lives of patients every day, and we are grateful for all of your efforts.

On this festive occasion, I would like to recognize the seminal contributions of nuclear medicine technologists to the advancement of science and direct care of patients. When reviewing historical discoveries, it becomes clear that many of the remarkable achievements in the field were the result of close collaboration between nuclear medicine physicians and technologists. For example, the imaging parameters for the rectilinear scanner, the technical details of tracer injection, and the imaging of stress myocardial perfusion with ^{43}K were developed through close collaboration between chief nuclear medicine technologists and nuclear medicine physicians.

The SNMMI-Technologist Section is celebrating its 50th year in 2020.

Vasken Dilsizian, MD

The strength and merit of our scientific publications are laudable, but we must recognize and give credit to the other pivotal components of our professions that may significantly influence health care delivery. We must pay attention to our patients' perspectives, education, and fears in the context of understanding their concerns about longevity and health. With this in mind, our nuclear medicine technologists have played a pivotal role as the "face" of our profession, having direct access to our patients during the busy clinic day.

Through 50 years of collaboration we have charted new paths, reached across disciplines, built consensus, and overcome roadblocks to deliver the best of care to our patients. We have appreciated the importance of exploiting the radiotracer principles for understanding human physiology and biochemistry and, thereby, improving the diagnosis and treatment of disease. Recent advances in molecular-targeted radiopharmaceutical therapy will undoubtedly further transform our field by extending healthy lives, an achievement of which we can all be proud.

Congratulations to the SNMMI-TS for achieving this major milestone! Together, we have come far. But, as in most of our endeavors, we have a long way to go. I am confident that our journey will become more noble and altruistic in the years to come.

Ngai named Director of NIH BRAIN Initiative

National Institutes of Health (NIH) Director Francis S. Collins, MD, PhD, announced on January 29 the selection of John J. Ngai, PhD, as director of the NIH Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Until joining NIH in March, Ngai was the Coates Family Professor of Neuroscience at the University of California, Berkeley.

The NIH BRAIN Initiative is a large-scale effort to accelerate neuroscience. Since its launch in 2013, the initiative has funded hundreds of research projects that have led to breakthroughs, including creation of a self-tuning brain implant that could help treat Parkinson disease, development of a computer program that can mimic natural speech from brain signals, and construction of a brain cell inventory. BRAIN-funded researchers have also shown the ability to make high-speed, high-resolution, 3D films of functional nervous system activity.

"Recent technological and scientific advances are transforming our understanding of the brain," said Ngai. "I am deeply inspired by these advances and look forward to my new role in enabling BRAIN Initiative investigators to unlock the secrets of the brain and lay new foundations for treating human brain disorders." He will oversee the long-term strategy and day-to-day operations of the initiative as it takes on the challenges of the next 5-year plan, announced in fall 2019. Congress has consistently supported BRAIN through the appropriations process and the 21st Century Cures Act.

"Dr. Ngai's appointment marks a new chapter in the BRAIN Initiative," said Walter J. Koroshetz, MD, director of NIH's National Institute of Neurological Disorders and Stroke. "He will provide the initiative and the clear vision the project needs to navigate through this critical period."

National Institutes of Health

IAEA and Dose Projection for Radiologic Emergencies

In a press release issued on February 13, the International Atomic Energy Agency (IAEA) reviewed presentations and discussions for its first research coordination meeting on using dose projection tools in nuclear or radiologic emergencies. Participants in the meeting, held at the IAEA in Vienna, Austria, from January 20 to 24, came from 21 countries and 25 institutes to share their experience and knowledge about using dose projection tools when preparing for and responding to such emergencies. "The goal of this coordinated research project [CRP] is to outline the plans and details, which will be implemented over the next 3 years, to help improve the performance of dose projection tools in the preparedness and response to nuclear or radiological emergencies," said Phillip Vilar Welter, IAEA Emergency Preparedness Officer.

Researchers, technical experts, and observers attended the course organized by the IAEA Incident and Emergency Centre and IAEA Division of Radiation, Transport, and Waste Safety. Attendees represented a broad range of organizations, including national laboratories, public health organizations, and nuclear safety institutions.

IAEA noted the importance of dose projection tools in ensuring effective emergency preparedness and response. In the preparedness phase, tools such as the Real-time On-line Decision Support system (RODOS) or the MELCOR Accident Consequence Code System (MACCS) are used to assess the potential radiologic consequences of an event. These projections can help authorities develop emergency plans that specifically address the expected consequences. For example, these tools can be used to determine the size of emergency planning zones needed for protective actions, prioritize locations for radiation monitoring, estimate the location and type of contamination on the ground, or project the dose received by the public, among many other projections.

The CRP will use findings from these discussions to help IAEA Member States better understand the advantages and limitations of using dose projection tools, including uncertainties associated with modeling and variations in implementation of different models by different sites. At the meeting, experts considered reported experience from the use of dose projection tools and approaches in improving them. Their analysis will inform CRP recommendations to improve the tools' effectiveness in supporting emergency preparedness and response.

International Atomic Energy Agency

WHO Reports on Global Cancer Burden

The World Health Organization (WHO) on February 4 released its International Agency for Research on Cancer *World Cancer Report: Cancer Research for Cancer Prevention.* In addition to a separate report issued on the same day on current statistics and findings on cancer, this report emphasized the need to enhance cancer services in low- and middle-income countries. WHO warned that, if current trends continue, the world will see a 60% increase in cancer cases over the next 2 decades, with the global cancer burden expected to reach 29 million new cancer cases per year by 2040. The greatest increase (an estimated 81%) in new cases will occur in low- and middle-income countries, where survival rates are currently lowest, with severely limited resources focused on urgent needs in combating infectious diseases and improving maternal and child health. In 2019, more than 90% of high-income countries reported that comprehensive treatment services for cancer were available in the public health system compared to less than 15% of low-income countries.

"This is a wake-up call to all of us to tackle the unacceptable inequalities between cancer services in rich and

poor countries," said Ren Minghui, MD, PhD, Assistant Director General, Universal Health Coverage/Communicable and Noncommunicable Diseases, WHO. "If people have access to primary care and referral systems then cancer can be detected early, treated effectively, and cured. Cancer should not be a death sentence for anyone, anywhere."

"At least 7 million lives could be saved over the next decade by identifying the most appropriate science for each country situation, by basing strong cancer responses on universal health coverage, and by mobilizing different stakeholders to work together," said Tedros Adhanom Ghebreyesus, PhD, MSc, Director General, WHO.

The WHO report highlighted a wide range of proven interventions to prevent new cancer cases. These include controlling tobacco use (responsible for 25% of cancer deaths), vaccinating against hepatitis B to prevent liver cancer, eliminating cervical cancer by vaccinating against human papilloma virus, enhancing screening and treatment, implementing high-impact cancer management interventions that bring value for money, and ensuring access to palliative care, including pain relief.

The complete report is available for download at https://shop.iarc.fr/products/world-cancer-report-cancer-research-for-cancer-prevention-pdf.

World Health Organization

Database Documents Loss of Radioactive Material

The International Atomic Energy Agency (IAEA; Vienna, Austria) in 2019 received notifications of nearly 190 incidents of nuclear and other radioactive material being out of regulatory control, including some cases of trafficking and other criminal activities. The data, submitted to the IAEA Incident and Trafficking Database (ITDB) by countries on a voluntary basis, was highlighted in an annual fact sheet published during the February IAEA ministerial conference on strengthening nuclear security and countering the threat of nuclear terrorism. With 140 participating States, the database fosters international cooperation and information sharing among countries. The data are shared with the IAEA, other Member States, and relevant international organizations supporting the retrieval of lost or stolen material and the prosecution of suspected criminals.

"As a unique asset in the IAEA's work to strengthen nuclear security, the ITDB allows us to identify threats and trends so that we can support our Member States in improving the implementation of their nuclear security commitments," said Raja Raja Adnan, Director of the IAEA Division of Nuclear Security.

In 2019, 189 incidents were reported by 36 States, indicating that unauthorized activities and events involving nuclear and other radioactive material, including incidents of trafficking and malicious use, continue to occur. Six of the incidents were related to trafficking or malicious use, continuing a slight downward trend since a peak of 20 such incidents around 2005. For the other 183 incidents, either insufficient information was available to determine any connection with trafficking or malicious use or sufficient information was available to rule out criminal activity.

Since 1993, 3,686 incidents have been reported to the ITDB, of which 290 involved a confirmed or likely act of trafficking or malicious use. Twelve of those incidents included high-enriched uranium and 2 included plutonium. Radioactive sources continue to be reported as stolen or missing, underscoring the need to improve security measures for such sources, especially during transport.

Attendees at the IAEA conference adopted a declaration to enhance global nuclear security, including a specific commitment "to combatting illicit trafficking of nuclear and other radioactive material and to ensure that the material cannot be used by non-State actors for malicious purposes." The related fact sheet is available at: https://www.iaea.org/sites/default/files/20/02/itdb-factsheet-2020.pdf

International Atomic Energy Agency

FDA Electronic Formats for Pharmaceutical Submissions

On February 24 the U.S. Food and Drug Administration (FDA) issued specifications for electronic formats for submissions to the agency. The document, titled *Providing Regulatory Submissions in Electronic Format: Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications. Guidance for Industry*, describes how sponsors and applicants must organize electronic content submitted to FDA for all submission types under section 745A(a) of the Food, Drug, and Cosmetic Act. The guidance also references several technical specification documents and the *Electronic Common Technical Document Conformance (eCTD) Guide*, which provide additional details about organization of content. The final document is available at https://www.fda.gov/media/135373/download.

FROM THE LITERATURE

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.

Guidelines for Publishing PET Brain Data

In an article published online on February 16 ahead of print in the *Journal of Cerebral Blood Flow and Metabolism*, experts from more than 25 PET centers around the world detailed the results of a consensus effort to standardize the organization and sharing of PET neuroimaging data. The authors recommended publishing standards for tracer characteristics, image acquisition, image preprocessing, and outcomes estimation for PET studies. Reporting information was classified as mandatory, recommended, or optional. They also presented a framework for data archiving and sharing within and across centers and institutions. Special note was made that "because of the high cost of PET neuroimaging studies, sample sizes tend to be small and relatively few sites worldwide have the required multidisciplinary expertise to properly conduct and analyze PET studies." Encouragement of data sharing and agreed-upon methods to standardize such data will enable the aggregation of multiple datasets to create large sample sizes with stronger statistical power than is currently possible across disparate sites.

Journal of Cerebral Blood Flow and Metabolism

^{18}F-Fluciclovine PET in Recurrent Prostate Cancer

Scarsbrook et al. from the Leeds Teaching Hospitals NHS Trust/University of Leeds, Oxford University Hospitals NHS Foundation Trust, University College London Hospitals, NHS Foundation Trust, the Royal Marsden NHS Foundation Trust (London), Mount Vernon Cancer Centre (London), King's College London and Guy's & St. Thomas' Hospital (London), Gartnavel General Hospital (Glasgow), the University of Glasgow, and Blue Earth Diagnostics (Oxford; all in the UK), representing the FALCON study group, reported on February 14 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on the effect of ^{18}F-fluciclovine PET on management in patients with biochemical recurrent prostate cancer. The study included 104 men at multiple institutions with a first episode of biochemical recurrence after curative-intent primary therapy. Patients underwent ^{18}F-fluciclovine PET/CT, with management plans documented before and after imaging. Changes to the planned treatment modality were classified as major and those within treatment modality as minor. Additional data included identification of optimal prostate-specific antigen (PSA) thresholds for disease detection, salvage treatment outcomes as assessed by PET, and overall safety. When lesions were identified on PET (56 lesions; 56% of patients), about 33% were positive at PSA levels $\leq$1 ng/mL and 93% were positive at PSA levels $>$2.0 ng mL. After imaging, 66 patients (64%) were assigned changes in management, with 43 of these defined as major: 16 (24%) from salvage or systemic therapy to watchful waiting (16/66; 24%); 16 from salvage therapy to systemic therapy (24%); and 11 (17%) to changes in treatment modality. The remaining 23 patients with management changes saw their preimaging plans modified, 22 by adjustments to planned brachytherapy/radiotherapy to include a ^{18}F-fluciclovine–guided boost. Where ^{18}F-fluciclovine guided salvage therapy, the PSA response rate was higher. The authors concluded that "incorporating ^{18}F-fluciclovine PET/CT into treatment planning may optimize targeting of recurrence sites and avoid futile salvage therapy."

International Journal of Radiation Oncology, Biology, Physics

Quality Improvement for PET/CT Radiotracer Infiltrations

In an article e-published on February 11 in *JCO Oncology Practice*, Kiser et al. from the Carilion Clinic (Roanoke, VA), the University of North Carolina (Chapel Hill), and Lucerno Dynamics (Cary, NC) reported on a study describing a quality improvement initiative aimed at assessing and reducing PET/CT radiotracer infiltration. The multicenter initiative used the Define, Measure, Analyze, Improve, and Control methodology. For the Measure and Improve phases, 5 technologists monitored quality in 263 injections with a 13.3% infiltration rate. In the Improve phase, after implementation of a quality improvement plan, the same technologists monitored 278 injections with a 2.9% infiltration rate. In the Control phase, 7 new technologists were added and the resulting group of 12 monitored 1,240 injections with a 3.1% infiltration rate. The 7 added technologists had significantly higher infiltration rates. The authors concluded that a quality improvement plan "can significantly improve and sustain injection quality; however, ongoing monitoring is needed as new technologists join the team."

JCO Oncology Practice

Postadjuvant Therapy PET/CT in Oral SCC

Qian et al. from the Winship Cancer Institute of Emory University and Emory University School of Medicine (Atlanta, GA) reported on February 14 in *Laryngoscope* on a study of the outcomes and predictive value of 3-mo postadjuvant therapy PET/CT in patients with locally advanced oral squamous cell carcinoma. The study included 220 patients with stage III, IVA, or IVB disease who had undergone resection and adjuvant radiation or chemoradiation therapy. PET/CT images were classified as suspicious (primary or neck category $\geq$3 or distant lesion present) or nonsuspicious. Factors compared between the 2 groups were locoregional and distant progression, overall survival, positive and negative predictive values of imaging, sensitivity and specificity of imaging, and success rates of salvage. Of the 220 patients, 67 (30%) were found to have lesions suspicious on imaging, and this was significantly associated with local and distant failure as well as poorer overall survival. Positive predictive value, locoregional predictive value, negative predictive value, sensitivity, and specificity of imaging were 85%, 79%, 73%, 58%, and 92%, respectively. Thirty-seven patients (65% of those with biopsy-confirmed progression) underwent salvage therapy, and 4 (11%)

showed no evidence of disease at last follow-up. The authors concluded that "for locally advanced oral squamous cell carcinoma, a PET/CT scan 3 months after adjuvant therapy is strongly predictive of disease recurrence and survival, demonstrating improved performance over postoperative imaging in previous studies."

Laryngoscope

Perfusion PET Cardiac Outcomes Predictors

In an article e-published on February 13 in *PloS One* (2020;15(2):e0228931), Guerraty et al. from the University of Pennsylvania (Philadelphia) and Prairie Cardiovascular (Belleville, IL) compared data from ^{82}Rb PET cardiac imaging–assessed quantitative myocardial blood flow and flow reserve with traditional cardiac risk factors as prognostic biomarkers of adverse outcomes. The study included 1,283 participants (a diverse population, with 60% African American and 35.3% Caucasian) who underwent rest–dypyridamole stress ^{82}Rb PET. Over a mean follow-up of 2.3 y, major adverse cardiovascular events (unstable angina, non-ST and ST-elevation myocardial infarction, stroke, and death) were documented. Resting myocardial blood flow (1.1 ± 0.4 mL/min/g) was found to be associated with adverse cardiovascular outcomes. Myocardial blood flow reserve (2.1 ± 0.8) was found to be more independently and inversely associated with major adverse coronary events than were either traditional cardiovascular risk factors or perfusion defects in regression analysis. Flow reserve was also more strongly associated with major adverse events than traditional cardiovascular risk factors and perfusion defects in regression analysis. A decision tree analysis confirmed myocardial blood flow reserve as superior to established cardiovascular risk factors in predicting outcomes. The authors concluded that "incorporating resting myocardial blood flow and myocardial blood flow reserve in coronary artery disease assessment may improve clinical decision making."

PloS One

SPECT/CT in Critical Limb Ischemia

Chou et al. from Nationwide Children's Hospital and The Ohio State University College of Medicine (both in Columbus, OH) reported on March 1 in *Advances in Wound Care* (2020;9 [3]:103–111) on a single-patient study intended to evaluate the feasibility of serial radiotracer-based imaging for quantifying volumetric changes in microvascular perfusion within angiosomes of the foot after lower extremity revascularization in the setting of critical limb ischemia (CLI). The researchers reported on their experience with a 63-y-old man with CLI, type 2 diabetes mellitus, and nonhealing foot ulcers of the first and second digits of the right foot. The patient underwent ^{99m}Tc-tetrofosmin SPECT/CT perfusion imaging before and after clinically indicated revascularization (balloon angioplasty of the superficial femoral and popliteal arteries) of the lower extremity. The authors found that quantitative improvements in stenosis of the superficial femoral artery after surgery were associated with angiosome-dependent SPECT-assessed improvements in microvascular foot perfusion. Serial changes in angiosome perfusion as assessed by SPECT/CT were compared with quantitative changes in peripheral vascular anatomy and hemodynamics, as assessed by standard clinical tools. The authors concluded that "SPECT/CT imaging allows for quantification of serial perfusion changes within angiosomes containing nonhealing ulcers and provides physiological assessment that is complementary to conventional anatomical and hemodynamic measures in the evaluation of lower extremity revascularization."

Advances in Wound Care

SPECT/CT, Hypermetabolic Facet ID, and Pain

In an article e-published on February 11 in *World Neurosurgery*, Perez-Roman et al. from the University of Miami Miller School of Medicine (FL) reported on a study investigating the incidence of hypermetabolic facets on SPECT/CT imaging in patients with axial neck or back pain to explore the value of SPECT/CT in identifying pain generators. The retrospective study included 190 (age, 58 ± 13 y; 51% men, 49% women) patients who had undergone high-resolution ^{99}Tc-methyl diphosphonate SPECT/CT for axial neck or back pain assessment. Facet joints with increased tracer uptake were classified as hypermetabolic, and other study imaging data included number, level, and laterality of hypermetabolic facets. Eighty-five patients (48%) showed zygopophyseal joint hypermetabolism (ZJH) on SPECT, with 202 hypermetabolic facets identified (average number of facets with ZJH, 2.38 ± 1.91). In patients with a positive scan, lumbar facets were most commonly affected (69% with ZJH), followed by the cervical (24%) and thoracic regions (6%). C1-2 and C2-3 (22% each with cervical ZJH) and L4-5 (32% with lumbar ZJH) were most often affected in the cervical and lumbar regions, respectively. The authors concluded that the finding that almost half of all patients with axial neck or back pain showed ZJH on SPECT/CT supported ZJH sites as potential pain generators and targets for treatment. They added that "our results support the role for SPECT/CT in the work-up of patients with axial neck or back pain, which may reduce invasive diagnostic procedures and aid in treatment planning."

World Neurosurgery

PET/CT Volumetric Parameter Predictions in Pancreatic Cancer

Mohamed et al. from the Royal Liverpool University Hospital, the Liverpool Cancer Research Centre, and the Mount Vernon Hospital (Middlesex; all in the UK) reported on February 7 ahead of print in the *European Journal of Surgical Oncology* on a study intended to determine the prognostic value of ^{18}F-FDG PET/CT volumetric parameters in survival prediction in pancreatic cancer. The retrospective study included 89 patients with pancreatic cancer who had undergone ^{18}F-FDG PET/CT imaging. Imaging data collected included tumor SUV_{max} and

SUV_{mean}, metabolic tumor volume, and total lesion glycolysis. The prognostic value of ^{18}F-FDG PET/CT for overall survival was compared with that of clinical and pathology parameters. Median survival times for patients with high and low total lesion glycolysis ($\geq$55 and $<$55) were 18 and 5 mo, respectively. The respective high and low SUV_{mean}, metabolic tumor volume, and SUV_{max} survival times were 18 and 6 mo, 16 and 6 mo, and 18 and 6 months. On subsequent multivariate and subgroup analysis, total lesion glycolysis was identified as the only significant PET metric, after adjusting for the presence of distant metastases. The authors concluded that ^{18}F-FDG PET/CT "is a useful tool in the preoperative evaluation of patients with pancreatic cancer," with tumor total lesion glycolysis offering an independent prognostic value in both potentially operable and metastatic disease.

European Journal of Surgical Oncology

Imaging-Guided Diagnostic Algorithm for Joint Replacement Complications

In an article e-published on February 11 in *Diagnostics (Basel)*, Khalid et al. from Aalborg University/Aalborg University Hospital (Denmark) reported on a multidisciplinary diagnostic algorithm for evaluation of patients presenting with prosthetic hip or knee complications. The algorithm included multimodal radionuclide imaging and microbiologic analyses. A total of 156 patients with 163 arthroplasties were included in the study. When surgeons suspected prosthetic joint infection or aseptic failure, patients proceeded to surgery. When the cause of pain was not evident, imaging was scheduled with ^{99}Tc-HDP SPECT/CT, ^{111}In-labeled white blood cells combined with ^{99}Tc-nanocolloid bone marrow SPECT/CT, and ^{18}F-FDG PET/CT. A total of 118 revision surgeries were performed in 112 patients (71 for aseptic failure and 41 for revision of prosthetic joint infection). Fifty-five patients underwent radionuclide imaging. Thirty-four patients were determined to have chronic pain, with no revision surgery scheduled. The structured diagnostic approach facilitated by the algorithm was determined to be useful by clinicians in the study in patient management in failing arthroplasties. The authors concluded that the algorithm served as an effective tool, allowing up to 20% of patients to avoid revision surgery.

Diagnostics (Basel)

^{99m}Tc-HDP SPECT/CT in Cervicogenic Headache

Cho et al. from Ajou University College of Medicine (Suwon-si), Yonsei University College of Medicine (Seoul), Cham Teun Research Institute (Seoul), and Hwalgichan Hospital (Ilsan-si, all in Korea) reported on February 2 ahead of print in the *Journal of Clinical Medicine* on a study assessing the utility of ^{99m}Tc-HDP SPECT/CT in diagnosing and guiding treatment in cervicogenic headache. The retrospective study included 23 patients diagnosed with cervicogenic headache who were divided into 2 groups: those who had undergone SPECT/CT (n = 11) and controls (n = 12). The SPECT/CT group was subdivided into SPECT/CT-positive and –negative finding groups. Individuals in the SPECT/CT group received an intraarticular injection at SPECT/CT–verified lesion sites, and those in the control group received third occipital nerve blocks. Patients were evaluated with a range of assessments at 1, 3, and 6 mo after this intervention. At 6 mo, individuals in the SPECT/CT group scored lower on the visual analog scale, the neck disability index, and the global perceived effect scale. More successful responders were in the SPECT/CT-positive group at 6 mo than in the control group (75% and 0%, respectively). The authors concluded that "SPECT/CT can identify arthritic changes and accurately define therapeutic targets" in this disease setting.

Journal of Clinical Medicine

^{18}F-NaF PET and Bone Histomorphometry in Dialysis

In an article e-published on February 10 in *Bone*, Aaltonen et al. from the Turku University Hospital/University of Turku and the University of Eastern Finland (Kuopio; all in Finland) reported on a study investigating correlations between ^{18}F-sodium fluoride PET and bone histomorphometry in the diagnosis of renal osteodystrophy. The study included 26 patients on dialysis with biochemical abnormalities indicating mineral and bone disorder. All patients underwent ^{18}F-NaF PET imaging and a bone biopsy. Activity on PET was measured in the lumbar spine and at the anterior iliac crest. Dynamic and static parameters from the bone biopsy were assessed, using bone formation rate per bone surface and activation frequency per year as histomorphometric markers. They identified a statistically significant correlation between fluoride activity on PET and multiple histomorphometric parameters. ^{18}F-NaF PET sensitivity and specificity in differentiating low turnover from non–low turnover were 76% and 78%, respectively. The authors concluded that, on the basis of this strong correlation, "^{18}F-NaF PET may possibly be a noninvasive diagnostic tool in dialysis patients with low-turnover bone disease, but further research is needed."

Bone

PET and/or PET/CT in Posttransplant Lymphoproliferative Disorder

Ballova et al. from the Cantonal Hospital Baden (Switzerland), the Ente Ospedaliero Cantonale (Bellinzona, Switzerland), the University of Brescia and Spedali Civili Brescia (Italy), Niguarda Hospital (Milan, Italy), the Università della Svizzera Italiana (Lugano, Switzerland), and the University of Lausanne/Lausanne University Hospital (Switzerland) reported on February 12 in *Diagnostics (Basel)* on a systematic review and metaanalysis of the published literature on the diagnostic performance of ^{18}F-FDG PET and/or ^{18}F-FDG PET/CT in detection of posttransplant lymphoproliferative disorder. Five published articles met the review criteria, with a total of 336 transplant recipients. Analysis showed that the pooled sensitivity and specificity for ^{18}F-FDG PET and/or ^{18}F-FDG PET/CT detection of posttransplant lymphoproliferative disorder were 89.7%

and 90.9%, respectively. Pooled positive and negative likelihood ratios and the diagnostic odds ratio were 8.9, 0.13, and 70.4, respectively. The authors concluded that "^{18}F-FDG PET or PET/CT demonstrated good diagnostic performance for the detection of posttransplant lymphoproliferative disorder, but large prospective studies are needed to strengthen these findings."

Diagnostics (Basel)

Cost-Effectiveness of ^{68}Ga-PSMA PET/MR in Biochemical Recurrence of Prostate Cancer

In an article e-published on February 17 ahead of print in *Clinical and Experimental Metastasis*, Gordon et al. from the QIMR Berghofer Medical Research Institute, the University of Queensland, Queensland University of Technology (all in Brisbane, Australia), and Princess Alexandra Hospital (Woolloongabba, Australia) reported on a study exploring the cost-effectiveness of ^{68}Ga-prostate-specific membrane antigen (^{68}Ga-PSMA) PET/MR imaging for staging in men with biochemical recurrence of prostate cancer. The methodology used a decision-analytic model with Markov chains, in which ^{68}Ga-PSMA PET/MR imaging was compared with conventional clinical approaches in staging patients with suspected prostate cancer recurrence. Men with biochemical recurrence from a study in Brisbane ($n = 30$) provided key estimates for the model. The authors found that, on average, integration of ^{68}Ga-PSMA into the care strategy was expected to cost US$39,426 and produce 7.48 life years, whereas the usual clinical approach was expected to cost US$44,667 and yield 7.41 life years. ^{68}Ga-PSMA was potentially cost saving (US$5,258) and somewhat more effective (by 0.07 life years). The likelihood that the ^{68}Ga-PSMA strategy was cost-effective at acceptable thresholds was 87%. These findings took into consideration the lesion detection rate of the ^{68}Ga-PSMA strategy and the cost of follow-up in conventional care. The authors concluded that "In this exploratory economic evaluation, using ^{68}Ga-PSMA PET/MRI to detect prostate cancer recurrence appears to be cost-effective relative to usual care."

Clinical and Experimental Metastasis

Advanced Imaging Advantages in Nonlocalizing Primary Hyperparathyroidism

Frank et al. from Loma Linda University Medical Center/Loma Linda University School of Medicine (CA) reported on February 17 ahead of print in *Laryngoscope* on a study intended to determine whether different types of advanced imaging are more cost-effective than primary bilateral neck exploration in the management of nonlocalizing primary hyperparathyroidism. The study used a decision tree model and financial data from Medicare patients. A total of 347 patients were included and were scheduled to have a parathyroidectomy for primary hyperparathyroidism with either positive, concordant ultrasound and sestamibi imaging or negative sestamibi and negative ultrasound. Modeling indicated the following costs and success rates for each of the following: bilateral neck exploration, $9,578 and 97.3%; SPECT + minimally invasive parathyroidectomy, $8,197, 98.6%; SPECT/CT + minimally invasive parathyroidectomy, $8,271 and 98.9%; and 4D-CT + minimally invasive parathyroidectomy, $8,146, 99%. The authors summarized their findings by saying that "in patients with nonlocalizing primary hyperparathyroidism, advanced imaging is associated with cost-savings compared to routine bilateral neck exploration." The greater the accuracy of the imaging approach, the higher the predicted cost savings and the lower the imaging costs.

Laryngoscope

^{68}Ga-PSMA vs ^{11}C-Choline PET/CT in Salvage Lymph Node Dissection

In an article e-published on February 18 ahead of print in the *Journal of Urology*, Fossati et al. from research sites in Italy, the United States, Germany, Belgium, and Austria reported on a large study comparing ^{11}C-choline and ^{68}Ga-prostate-specific membrane antigen (^{68}Ga-PSMA) PET/CT in men undergoing salvage lymph node dissection for nodal recurrent prostate cancer. The study included 641 men in whom prostate-specific antigen (PSA) levels were rising with nodal recurrence after radical prostatectomy. All underwent salvage lymph node dissection. A total of 407 patients underwent ^{11}C-choline PET/CT imaging and 234 underwent ^{68}Ga-PSMA imaging. The focus was on underestimation of tumor burden, defined as the difference between the number of positive nodes on final pathology and number of positive sites on PET/CT with each of the tracers. The authors found that the extent of underestimation of tumor burden was significantly higher with ^{11}C-choline. Including PSA in the analysis, the underestimation of tumor burden was lower with ^{68}Ga-PSMA when the PSA was $\leq$1.5 ng/mL and the underestimation of the 2 tracers was similar when PSA was $>$1.5 ng/mL. In addition, the higher the number of positive spots, the higher the underestimation of tumor burden with either tracer. The authors concluded that PET/CT scanning "significantly underestimates the burden of prostate cancer recurrence, regardless of the tracer used. Although ^{68}Ga-PSMA was associated with a lower rate of underestimation in patients with a PSA $<$1.5 ng/mL and limited nodal tumor load, for "all other men, there was no benefit from ^{68}Ga-PSMA over ^{11}C-choline in assessing the extent of nodal recurrence."

Journal of Urology