SNMMI 2020 Annual Meeting—Virtual Edition

SNMMI will venture into new territory with its 2020 Annual Meeting, which will be an innovative virtual experience offered from July 11 through 14. The online meeting will feature an exceptional program of topics in nuclear medicine and molecular imaging, including a science pavilion highlighting the latest scientific research, an interactive virtual exhibit hall, networking events, and additional "surprise" elements. The easy-to-use virtual platform has been designed to mimic the dynamics of a physical meeting. "This promises to be an enriching experience for us all," said SNMMI President Vasken Dilsizian, MD. "We wanted to do the planning and lay the groundwork to ensure that we could offer online the same vibrant, diverse, and scientifically cutting-edge content to which we have become accustomed at SNMMI Annual Meetings. Through the efforts of the entire SNMMI community—leadership, members, industry, presenters, and staff—we are confident that this will be both a success and a forward-looking bright spot as we emerge from challenging times."

The 2020 SNMMI Annual Meeting—Virtual Edition will feature scientific and poster presentations in a variety of formats. State-of-the-art, interactive continuing education (CE) sessions will be offered on each of the 4 days. These will be 1-hour sessions with live chat functionalities for questions and discussion. Participants can earn approximately 25 CE credits over the course of the meeting. The Virtual Science Pavilion will be the destination for viewing abstract presentations and posters, including recorded oral presentations. Viewers will be able to ask authors questions by e-mail. As always, the meeting will conclude with the Highlights Symposium, at which expert presenters review the scientific highlights of the meeting and the SNMMI Image of the Year is announced.

Many of the online events and offerings will be familiar to attendees at past SNMMI Annual Meetings. At 2:30 on July 11, the meeting will begin with the traditional Opening Ceremony and Welcome Session. Each day's schedule will include plenary sessions with noted speakers and a range of annual awards and named lectures. The plenary session on July 12 will feature additional welcome remarks and the annual Henry N. Wagner, Jr., MD, Lectureship, this year delivered by Jagat Narula, MD, PhD, who will speak on "Molecular Imaging in Cardiovascular Medicine: Setting Tiny Targets for Greater Goals."

Between special events and educational/scientific sessions, participants can visit the Virtual Exhibit Hall, with customized virtual booths from top industry suppliers in nuclear medicine and molecular imaging, including videos and downloadable presentations. Participants will also be able to schedule direct interactions with exhibit personnel while visiting their booths. The value of networking at SNMMI Annual Meetings will be replicated for participants with offerings such as Molecular Hub Meet-Ups for first-time attendees, a movie viewing party, the annual President's Town Hall and Reception, facilitated group chats, and 1-on-1 attendee messaging. Even the annual Hot Trot 5K Run/Walk will be held, with participants running or walking at their own locations and posting the results. Proceeds will benefit the SNMMI-Technologist Society Professional Development and Education Fund.

Special scientific sessions will address topics of current interest, including a session on Nuclear Medicine in the Time of COVID-19, organized by the SNMMI COVID-19 Taskforce; on Theranostics: How to Do Radiation Safety Right, organized by the Quality and Evidence Committee; New Imaging Boot Camp: FES, ^{18}F-DOPA, New Net Imaging Agents, FAPI, organized by the Clinical Trials Network; On the Horizon: Developing Techniques, New Isotopes and Production Chemistry, organized by the Center for Molecular Imaging Innovation and Translation; and Prostate Cancer Theranostics: Applications of Molecular Targeted Radiotherapy, organized by the Therapy Center of Excellence.

Registration and Attendance

The 2020 SNMMI Annual Meeting—Virtual Edition will be free for SNMMI members. Nonmembers may either join SNMMI to attend at no cost or pay a modest registration fee. Registration for the meeting is available at: www.snmmi.org/AMregister. Answers to frequently asked questions are available at: http://www.snmmi.org/AM2020FAQ.

Time for a Next-Generation Nuclear Medicine Gamma Camera?

I. George Zubal, PhD, Program Director for Nuclear Medicine, CT, and X-Ray, National Institute of Biomedical Imaging and Bioengineering, Bethesda, MD

Hal Anger invented the gamma camera in 1957, and it is fair to say that the basic geometry and components of his camera design have remained substantially the same, while its use in general clinical applications has been optimized for imaging 140-keV gamma rays. The past 60 years have seen some improvements in NaI scintillators, readout electronics, collimators, reconstruction algorithms, and image analysis. During a short period in the late 1990s and early 2000s, opposing Anger cameras were used for clinically acquiring positron-emitting isotopes, and some camera components were reengineered for imaging 511-keV coincident photons. Not surprisingly, dedicated PET cameras proved to be the better choice for imaging PET radiotracers.

One clinical application, however, generated substantial camera variations. The highly successful use of cardiac imaging in the United States has spurred interesting new camera designs and novel radiopharmaceuticals. Nuclear cardiology currently represents more than 50% of all U.S. nuclear medicine scans. Dedicated cardiac cameras have implemented 7-, 9-, and 19-pinhole collimators, early use of new detectors (CsI and CZT), L-shaped camera configurations, and chair-based imaging. Given this important and well-recognized clinical application, camera designs morphed into a variety of geometries, detector materials, and associated reconstruction methods. Whole-body (bone scans) and brain-imaging cameras have evolved over these same years, but current whole-body scanners employ a standard Anger camera translated along the patient bed. Dedicated brain cameras have not yet achieved broad acceptance and, perhaps, are awaiting new breakthroughs in theranostic applications for brain imaging.

Recent developments in unsealed source therapies using electron- and α-emitting radiopharmaceuticals would benefit from improvements in patient-specific dosimetry estimates. ^{177}Lu, ^{90}Y, and ^{223}Ra are the most common isotopes currently used to deliver high doses to the targeted cancer and to spare healthy tissue. Because of the high radiation doses delivered locally by these radiotherapeutic agents, it is important to know the patient-specific uptake distribution of these ligands. Analogs of these ligands have been developed to assess uptakes. By imaging the analog (labeled with ^{68}Ga, for example), one assumes that the analog has the same pharmacodynamics and pharmacokinetics as the ^{90}Y- or ^{177}Lu-labeled therapy ligand. Such an assumption becomes complicated with ^{223}Ra, where such a process would be ignoring the doses to healthy tissues delivered by ^{223}Ra daughters.

Imaging of these radiotherapy ligands has been investigated. Two of the 6 photopeaks (113 and 208 keV) of ^{177}Lu were imaged with additional energy windows set to subtract scatter from higher energy emissions (*1*). An array of bremsstrahlung emissions, together with internal pair-production annihilation radiation, was used to produce ^{90}Y images (*2*). Images of ^{223}Ra (and its daughter ^{219}Rn) were acquired using 3 photopeaks (85, 154, and 270 keV) with 3 additional windows to deal with scattered events (*3*). Imaging protocols become more complicated for other α emitters, including ^{225}Ac, ^{211}At, ^{212}Pb, and others yet to be considered for therapy. These isotopes pose a challenge to nuclear medicine camera systems because the radiations lie outside current clinical imaging protocols. New camera designs could lead to improved image quantitation.

Is it time to reconsider the instrumentation we use for theranostic methods for these α-emitting unsealed sources? If nuclear cardiology could develop an array of specialized camera designs and acquisition methods to specifically image the heart, can we consider new instrumentation and image analysis methods that would give us improved insights into targeted cancer therapy? The next phases of therapy outcomes that use these new ligands will speak to this question. A dedicated therapy camera could help to maximize dose to the cancer and minimize dose to healthy tissues. It seems axiomatic that by improving methods for imaging these new ligands, we would improve the success of the clinical therapy outcomes. This tandem step forward appears reasonable.

To which ideas can we turn for meeting this imaging challenge? The gamma emissions of these new therapy isotopes are often low yield. Can previous work on high-sensitivity coded apertures or Compton cameras be reinvestigated for some of the higher energy emissions? Can gas electron multiplication detectors be used to measure gamma rays and their incident angles without the use of collimators (*4,5*)? New detector systems have been and are being developed by PET instrumentation investigators, with some promising coincidence timing approaching 1 picosecond. Can any of these detectors be reapplied for single-photon imaging? Because some of the α emitters (despite the low yield of individual gamma emissions) emit many 10s of gammas at various energies (e.g., ^{225}Ac), could very high-energy resolution detectors be used to acquire the various gammas by picking out these photopeaks (and rejecting most other scattered photons) to assemble an image of unscattered multienergy gammas? Can recent advances in deep learning play an important role in imaging and estimating patient dose?

(Continued on page 17N)

NCRP Issues Radiation Research Risk Guidance

The National Council on Radiation Protection and Measurements (NCRP) in May issued a new report on *Evaluating and Communicating Radiation Risks for Studies Involving Human Subjects: Guidance for Researchers and Institutional Review Boards* (Report No. 185). The report was developed by an NCRP scientific committee chaired by Julie Timins, MD, an experienced diagnostic radiologist board certified in general radiology and nuclear medicine, who is also chair of the New Jersey Commission on Radiation Protection. In an executive summary, the report's authors noted that the extent of knowledge about ionizing radiation in medical procedures and potential adverse effects varies substantially among members of the public and within the medical community. This variation is also seen in guidelines used across academic and other institutions for the conduct of human research involving radiation. The report is intended to address the need for "comprehensive, consistent, and accurate guidance on radiation risks of research protocols that involve the use of ionizing radiation to those who develop protocols and conduct research involving human subjects and to institutional review boards (IRBs) that review these protocols." In a release accompanying the publication, NCRP said that the report seeks to fill existing guidance gaps by: (1) providing basic information about ionizing radiation and radiation biology, including medical imaging and treatments that involve radiation; (2) identifying the governmental agencies that oversee research and radiation; (3) citing the relevant regulatory requirements; (4) providing guidance regarding the estimation of radiation dose and risk in research protocols; (5) discussing ethical considerations involved in human studies research; and (6) presenting in detail the requirements for ensuring and obtaining truly informed consent.

The comprehensive document has specific value for research staff, IRBs, and other research review entities that involve personnel who may have limited backgrounds in radiation science. For these individuals, the report is intended "to help researchers optimize radiation use in research protocols, IRBs to perform due diligence in review of those protocols, and to promote understanding of the potential short- and long-term health effects" by providing historical and regulatory background, definitions, descriptions of medical imaging studies and procedures, and more than 500 reference sources. The report covers information needed for research protocol development and evaluation, including basic information on radiobiology, radiation protection, and metrics pertinent to radiation; regulatory requirements for the conduct and supervision of research; in-depth discussions on estimation of radiation dose and risk and the appropriate use of effective and absorbed dose; ethical principles relevant to human studies research involving radiation exposure, including those unique to vulnerable populations, including children; and the informed consent process and examples of language to assist in developing informed consent documents. These examples include "plain language" suggestions to simplify and clarify protocols for participants.

The report is available for purchase from NCRP at https://ncrponline.org/shop/reports/report-no-185-evaluating-and-communicating-radiation-risks-for-studies-involving-human-subjects-guidance-for-researchers-and-institutional-review-boards-2020/. Members of the American Association of Physicists in Medicine may download the document at no charge at https://www.aapm.org/pubs/ncrp/detail.asp?docid=185.

(Continued from page 16N)

These and other questions will be considered and discussed at a National Institute of Biomedical Imaging and Bioengineering (NIBIB) workshop on "Engineering New Instrumentation for Imaging Unsealed Source Radiotherapy Agents," to be held August 17 and 18 at the Natcher Center on the main National Institutes of Health (NIH) campus in Bethesda, MD. We believe that such discussions are timely for moving hand-in-hand into the testing and use of α-emitting therapy trials.The mission of NIH's NIBIB is to improve health by leading the development and accelerating the application of biomedical technologies. Among the many technologies supported, NIBIB researchers believe the challenge of considering cameras that would deliver improved dosimetry measurements for optimizing the outcome of α-emitting radiotherapy ligands is one that merits a serious look. For more information on the workshop, see https://www.imagingtherapy.nibib.nih.gov/.

REFERENCES

1. Sanders JC, Kuwert T, Hornegger J, Ritt P. Quantitative SPECT/CT imaging of Lu-177 with in vivo validation in patients undergoing peptide receptor radionuclide therapy. *Mol Imaging Biol.* 2015;17(4):585–593.
2. Wright CL, Zhang J, Tweedle MF, Knopp MV, Hall NC. Theranostic imaging of yttrium-90. *Biomed Res Int.* 2015;2015:481279.
3. Benabdallah N, Bernardini M, Bianciardi M, de Labriolle-Vaylet C, Franck D, Desbrée A. ^{223}Ra-dichloride therapy of bone metastasis: Optimization of SPECT images for quantification. *EJNMMI Res.* 2019;9(1):20.
4. Sauli F. The gas electron multiplier (GEM): Operating principles and applications. *Nucl Instrum Methods Phys Res A.* 2016;805(1):2–24.
5. Brunbauer FM, Lupberger M, Oliveri et al. Radiation imaging with optically read out GEM-based detectors. *J Instrum.* 2018;13:T02006. Available at: https://iopscience.iop.org/article/10.1088/1748-0221/13/02/T02006/pdf.

SNMMI Honors New Fellows for 2020

On July 13, as part of its 2020 Annual Meeting: Virtual Edition, 10 new SNMMI Fellows will be recognized at the SNMMI Business Meeting. The SNMMI Fellowship was established in 2016 to recognize distinguished service to the society as well as exceptional achievement in the field of nuclear medicine and molecular imaging. It is among the most prestigious formal recognitions available to longtime SNMMI members. Vasken Dilsizian, MD (University of Maryland School of Medicine, Baltimore), the 2019–2020 SNMMI president, will join the new fellowship ranks. Also recognized as new fellows will be Xiaoyuan Chen, PhD (National Institute of Biomedical Imaging and Bioengineering, Bethesda, MD), Paul E. Kinahan, PhD (University of Washington, Seattle), Michael A. King, PhD (University of Massachusetts Medical School, Worcester), Suzanne Lapi, PhD (University of Alabama at Birmingham), J. Anthony Parker, MD, PhD (Beth Israel Deaconess Medical Center, Boston, MA), Todd Peterson, PhD (Vanderbilt University Medical Center, Nashville, TN), Terrence Ruddy, MD (University of Ottawa Heart Institute, Canada), Heinrich Schelbert, MD, PhD (University of California at Los Angeles School of Medicine), and Arnold Strashun, MD (State University of New York Downstate Health Sciences University; Brooklyn, NY).

2020 Henkin Fellows Named

SNMMI and the Education and Research Foundation for Nuclear Medicine and Molecular Imaging announced on May 18 the selection of Domnique Newallo, MD, RT(R)(CT), and Justin Peacock, MD, PhD, as the 2020 Robert E. Henkin Government Relations Fellows. Each year, fellowship recipients travel to Washington, DC, and spend a week with SNMMI staff, visiting Congress, federal agencies, and other medical societies. Throughout the visit, fellows learn about ways in which federal legislative and regulatory processes affect nuclear medicine and molecular imaging. The program is designed for young professionals, defined as residents or fellows (physicians, scientists, or technologists) who have completed training within the last 10 years. Contributions from Robert E. Henkin, MD, made possible the creation and continuation of this fellowship opportunity. "This year we are very happy to award the Henkin Fellowship to not 1 but 2 very qualified recipients," said Munir Ghesani, MD, chair of the SNMMI Government Relations Committee. "The society is busier than ever during COVID-19, and we are certain that both Justin and Domnique will have very enriching experiences."

Newallo is currently completing her nuclear medicine residency at Emory University (Atlanta, GA). She earned her medical degree from the Medical University of South Carolina (Charleston) in 2017 and completed her surgery internship at Grand Strand Medical Center (Myrtle Beach, SC). Before becoming a physician, she served in the U.S. Army, where she worked as an x-ray and CT technologist until 2004. As a nuclear medicine resident, Newallo was awarded the Academic Council Board of Directors SNMMI internship for 2019–2021 and is an elected officer of the American College of Nuclear Medicine (ACNM) Nuclear Medicine Residents Organization (NMRO). She is also a recent graduate of the 2020 SNMMI Future Leaders Academy. As part of the Henkin fellowship, she expressed an interest in exploring "the relationship between economic and regulatory models of health care policy to hopefully advance a more holistic perspective on why policies are put in place and the effects they have on patient care."

Domnique Newallo, MD, RT(R)(CT)

Peacock is a nuclear medicine fellow at the San Antonio Uniformed Services Health Education Consortium (TX). He received his doctorate in molecular biophysics and biochemistry from Yale University (New Haven, CT) and his MD from the Mayo Clinic School of Medicine (Rochester, MN). His internship and residency in radiology were completed at Brooke Army Medical Center (Fort Sam Houston, TX). He has served as vice president and president of the ACNM NMRO and vice chair of the SNMMI In-Training Committee. He was a 2019 graduate of the SNMMI Future Leaders Academy and also recently contributed to an SNMMI/ACNM ad hoc workgroup addressing the Nuclear Regulatory Commission's "Draft Regulatory Guide DG-8057, Release of Patients Administered Radioactive Material." His interest in health policy is directly related to his interest in improving care. On being named a Henkin fellow, he said, "When the evidence is seen and advocates push for change, I believe that health policy can change to ensure that all patients receive the care that they deserve."

Justin Peacock, MD, PhD

Notes from the Top

Alan B. Packard, PhD, 2020–2021 SNMMI President

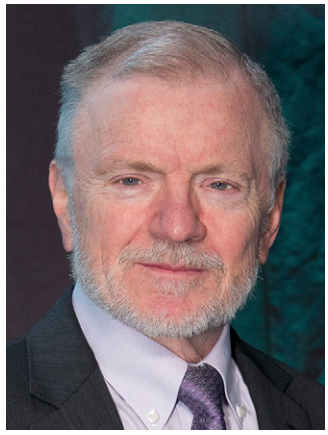
Greetings, fellow SNMMI members. Since March, COVID-19 has disrupted pretty much every part of our lives, making previous plans largely irrelevant. That said, the central premise of my campaign for president—enhancing the value of SNMMI membership—is now even more important. Although the paths we will take to accomplish this goal have changed dramatically, they still involve "building bridges" to improve our connections both within and outside the SNMMI community.

One important way to enhance the value of SNMMI membership is to make the SNMMI Annual Meeting an essential experience for today's physicians, scientists, and technologists. This is more critical than ever this year as, for the first time in the 66-year history of the society, we were forced to cancel the face-to-face Annual Meeting. The SNMMI Scientific Program Committee, Board of Directors, and staff have worked closely together to plan an exciting virtual meeting that will be the best possible alternative to a face-to-face meeting—achieving our goals of offering continuing education, presenting the latest research, and providing networking opportunities, all while ensuring the safety of our attendees. Best of all, this year registration is *free* for SNMMI members! I wholeheartedly encourage everyone to join us online July 11–14 for the 2020 SNMMI Meeting—Virtual Edition.

Applying what we learn from this year's virtual meeting, we are already thinking about how SNMMI meetings will look in the future and, more generally, what scientific conferences will look like in the face of the challenges of travel and of gathering in large groups. We are, above all, social animals, and one of the primary reasons we go to conferences is to get together with friends and to meet new people. We now have the opportunity to redefine how we do this in the future.

Continuing education is a core service that SNMMI provides to its members. In response to COVID-19, the society is expanding its virtual curriculum and increasing the number and scope of continuing education webinars and other virtual options. In addition to webinars geared to physicians and technologists, the society is also presenting webinars focused on the needs of our scientist members, including addressing the challenge of reopening our laboratories in a new and very different environment.

Another core element of SNMMI membership is *JNM*, which has supported both clinical practice and basic science for 60 years as the leading journal in the world for nuclear medicine and molecular imaging. The journal is an extraordinarily valuable tool for advancing important, peer-reviewed research and promoting active discussion within the community. It is, therefore, essential that the society continue to support this resource both for our members and for the broader nuclear medicine community.



Alan B. Packard, PhD

The society can serve our younger members by providing pathways for advancement within the society that will help in their careers. This year we are revising the committee appointment process to provide more opportunities for early-career physicians and scientists to serve on SNMMI committees and to develop within SNMMI's councils and centers.

My predecessor, Vasken Dilsizian, MD, led the society in its development of strong communications and outreach efforts, and we need to build upon and expand these efforts to build bridges to those outside our community. Perhaps the greatest strength of SNMMI is the diversity of its membership, with physicians, scientists, and technologists working together in one society dedicated to advancing the field of nuclear medicine. All of us, as members of SNMMI, need to continue to reach out to referring physicians, regulators, patients, and the general public to share with them the value of nuclear medicine.

The society has been very fortunate in receiving strong support from our Value Initiative Partners, who continue to recognize the strategic role of SNMMI in demonstrating the essential value of nuclear medicine and molecular imaging to the medical community, regulators, patients, and the general public. This remarkable partnership will continue to enhance the value of society membership and the success of the nuclear medicine and molecular imaging profession.

As a member of SNMMI leadership, I intend to be accessible to all society members and to ensure that your voices are heard. I am very much looking forward to an exciting and innovative year, and I thank you all in advance for your help in accomplishing our shared goals.

Estrogen Receptor Agent Approved

PETNET Solutions, Inc. (a part of Siemens Medical Solutions USA, Inc.; Malvern, PA), and Zionexa USA (New York, NY) announced on May 27 U.S. Food and Drug Administration (FDA) approval of the Cerianna (fluoroestradiol F 18) injection for intravenous use. Cerianna is a molecular imaging agent indicated for use in PET imaging for detection of estrogen receptor–positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer. It is the first ^{18}F-labeled PET agent specifically indicated for use in patients with recurrent or metastatic breast cancer. Cerianna will be commercially available beginning in late 2020/early 2021 through PETNET Solutions, Inc., Zionexa USA's manufacturer and exclusive commercial distributor in the United States. Additional manufacturing sites will be added as each receives regulatory approval to begin manufacturing. "Cerianna (fluoroestradiol F 18) will provide clinicians with additional, previously unavailable data on the estrogen receptor status of tumors across the patient's entire body, providing additional data to enhance therapeutic decision making," said Peter Webner, chief executive officer of Zionexa USA. The 2 companies announced on December 5, 2019, that they had entered into an exclusive agreement for the manufacture and distribution of the agent, pending FDA approval.

PETNET Solutions, Inc.
Zionexa USA

Hospital Reporting of Radionuclide Infiltrations

On May 18, David Townsend, PhD, a co-inventor of PET/CT and a pioneer in 3D reconstruction algorithms for hybrid imaging, wrote on the *STAT* news site about appropriate hospital reporting of radioisotope injection infiltration. In addition to explaining for nonmedical readers how infiltrations occur and the potential effects, both in incorrect image assessment and unintentional tissue dose, Townsend reviewed the history of associated reporting requirements. The Nuclear Regulatory Commission (NRC) first required hospitals to report isotope "misadministration" in 1980, changing that term to "medical event" in 2002 and establishing risk-based reporting limits of 500-mSv tissue exposure. However, the NRC specifically exempts hospitals from reporting infiltrations, even when these exceed the designated threshold of 500-mSv exposure. Townsend pointed to this "loophole" as contributing to a situation in which reporting requirements are inconsistent—radioactive isotopes spilled and exposing tissue to >500 mSv trigger the reporting requirement, whereas internal infiltration of the same or higher amounts does not. The result, he stated, "is that the NRC—along with patients and physicians—have no idea of the true impact of infiltrations." He cited the increasingly important role of radioisotope-based theranostics as a compelling reason for readdressing this inconsistency. He noted that the NRC is now re-evaluating the reporting requirement. He concluded by stating that "as with all other medical events, if an infiltration exceeds the reporting threshold, it should be reported. This will drive quality improvements and improve patient care and safety." The complete perspective article is available at: https://www.statnews.com/2020/05/18/hospitals-shouldnt-be-exempt-from-reporting-radioisotope-infiltrations/.

STAT

Retevmo Approved in Lung and Thyroid Cancers

On May 8, the U.S. Food and Drug Administration (FDA) announced the approval of Retevmo (selpercatinib) capsules to treat 3 types of tumors: non–small cell lung cancer (NSCLC), medullary thyroid cancer (MTC), and other types of thyroid cancers in patients whose tumors have an alteration (mutation or fusion) in a specific gene (RET or "rearranged during transfection"). Retevmo, from Loxo Oncology (Stamford, CT; a subsidiary of Eli Lilly), is the first therapy approved specifically for cancer patients with RET gene alterations. "Innovations in gene-specific therapies continue to advance the practice of medicine at a rapid pace and offer options to patients who previously had few," said Richard Pazdur, MD, director of the FDA Oncology Center of Excellence and acting director of the Office of Oncologic Diseases in the FDA Center for Drug Evaluation and Research. "The FDA is committed to reviewing treatments like Retevmo that are targeted to specific subsets of patients with cancer."

The specific settings in which Retevmo was approved include: NSCLC that has spread in adults; advanced MTC or MTC that has spread in patients 12 y and older who require systemic therapy; and advanced RET fusion-positive thyroid cancer in those age 12 y and older that requires systemic therapy and has stopped responding to radioactive iodine or is not appropriate for radioactive iodine therapy. Retevmo is a kinase inhibitor, and administration of the agent requires laboratory testing to select for the RET gene alteration. For the radioactive iodine–refractory or –inappropriate group, efficacy studies were conducted in 19 radioactive iodine–refractory patients with RET fusion-positive thyroid cancer who had received another prior systemic treatment and 8 who had not received any additional therapy other than radioiodine treatment. The overall response rate for the 19 previously treated patients was 79%. For 87% of these patients who saw a response to the treatment, this response lasted at least 6 mo. Overall response for the remaining 8 patients was 100%, with 6 patients seeing a response to the treatment and responses lasting at least 6 mo. Retevmo was approved under the Accelerated Approval pathway, which addresses drugs that treat serious or life-threatening diseases and generally provide a meaningful advantage over existing treatments. In addition, Retevmo received Orphan Drug

designation, which provides incentives to assist and encourage the development of drugs for rare diseases.

U.S. Food and Drug Administration

NRC and Regulatory Relief During COVID-19

In a teleconference held on April 30, the Nuclear Regulatory Commission (NRC) Advisory Committee on the Medical Uses of Isotopes (ACMUI) met with NRC staff to review and discuss the ACMUI COVID-19 Subcommittee's draft recommendations for regulatory relief measures for medical licensees during the COVID-19 public health emergency. In its report, the subcommittee provided several recommendations in specific areas in which licensees may be unable to meet regulatory requirements in a timely manner because of the public health emergency. The full ACMUI endorsed the draft, which covered the following general areas: (1) training and education; (2) regulatory reporting; (3) medical event reporting; (4) radiation protection activities; (5) physical presence; (6) inspections; and (7) regulatory fees. As part of the discussion, ACMUI members cited hypothetical scenarios in which a facility's authorized user (AU) or authorized medical physicist (AMP) could not be physically present for treatment because of suspected or confirmed COVID-19 infection. The ACMUI concluded that there should be no change to the physical presence requirements for high-dose-rate brachytherapy or gamma knife stereotactic radiosurgery because these are high-risk procedures that require the physical presence of the AU and AMP. In addition, the ACMUI discussed and considered concerns about the possibility of regulatory relief for patient release criteria after radionuclide therapy during the pandemic. The ACMUI agreed that for exceptional situations related to patient release during COVID-19, medical licensees should contact the NRC or their regional regulatory office to seek temporary exemptions on a case-by-case basis. NRC staff will consider the ACMUI recommendations when developing guidance for medical licensees that request temporary exemptions during the pandemic. Full transcripts and handouts from the ACMUI meeting are available at: https://www.nrc.gov/reading-rm/doc-collections/acmui/meetings/2020.html. The ACMUI COVID-19 Subcommittee report is available under ACMUI Subcommittee Reports at: https://www.nrc.gov/reading-rm/doc-collections/acmui/reports/.

Nuclear Regulatory Commission

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. We have also added a small section on noteworthy reviews of the literature.

PET/CT as a Predictor in Primary Gastric Adenocarcinoma

Harada et al. from the University of Texas MD Anderson Cancer Center (Houston, TX) and Kumamoto University (Japan) reported on May 14 ahead of print in *Surgery Today* on the potential of pretreatment SUV_{max} and total lesion glycolysis as assessed on PET/CT as predictors of response to chemoradiation therapy (CRT) in patients with localized gastric adenocarcinoma. The study included data from 59 such patients who underwent preoperative CRT. Relationships between PET/CT metrics and pathologic complete response and overall survival were analyzed. Of the 59 patients, 29 (49%) had Siewert type III adenocarcinoma and 30 (51%) had tumors in the lower stomach. Disease was poorly differentiated in 41 patients, and 26 had signet ring cells. Over all, the median SUV_{max} was 7.3 (range, 0–28.2), and the median total lesion glycolysis was 56.6 (0–1,881.5). Patients with signet ring cells were found to have low pathologic complete response rates, SUV_{max}, and total lesion glycolysis. On additional analysis, high SUV_{max} was found to be a predictor of pathologic complete response, but neither SUV_{max} nor total lesion glycolysis was associated with overall survival. The authors concluded that "a high SUV_{max} was associated with sensitivity to chemoradiation and pathologic response in gastric adenocarcinoma, and signet ring cells seemed to confer resistance."

Surgery Today

^{18}F-FMISO vs ^{64}Cu-ATSM PET in Focal Cerebral Ischemia

In an article e-published on May 19 ahead of print in the *Journal of Cerebral Blood Flow and Metabolism*, Little et al. from the Karolinska Institutet/Karolinska University Hospital (Stockholm, Sweden) and the Technical University of Denmark (Roskilde) reported on a study comparing ^{18}F-FMISO and ^{64}Cu-ATSM PET as hypoxia tracers in focal cerebral ischemia in a murine M2 occlusion model with preserved collateral blood flow. Rats underwent the occlusion procedure and imaging with either ^{18}F-FMISO or ^{64}Cu-ATSM, with the latter group also undergoing MR imaging. Levels of hypoxia in neurons and astrocytes were assessed by immunofluorescence analysis, with pimonidazole as a surrogate for ^{18}F-FMISO. An increase in ^{18}F-FMISO uptake but not ^{64}Cu-ATSM uptake was found in the occluded cortex. Pimonidazole intensity in neurons and astrocytes was increased in hypoxic regions, an intensity that was higher in neurons than astrocytes. In most rats, immunofluorescence showed a loss of astrocytes in regions with increased pimonidazole uptake. The authors concluded that ^{18}F-FMISO is superior to ^{64}Cu-ATSM in detecting hypoxia in acute ischemic stroke. In addition, "^{18}F-FMISO may provide efficient diagnostic imaging beyond the hyperacute phase." They added that "results do not provide encouragement for the use of ^{64}Cu-ATSM in experimental acute ischemic stroke."

Journal of Cerebral Blood Flow and Metabolism

Understanding ^{18}F-Fluciclovine PET/CT Reports

Lowentritt, from Chesapeake Urology (Towson, MD), and Kipper, from Genesis Healthcare (San Diego, CA), provided on April 26 ahead of print in *Prostate Cancer* a helpful primer for referring physicians on understanding and interpreting results from ^{18}F-fluciclovine PET/CT in men with biochemical recurrence of prostate cancer. The authors noted that in the absence of a standardized grading system for such imaging assessment, interpretation may be challenging. They listed 6 key features of which referring physicians should be aware: (1) The attributes of the tracer as a radiolabeled synthetic amino acid targeting the amino acid transporters ASCT2 and LAT1, overexpressed in prostate cancer. (2) The fact that ^{18}F-fluciclovine PET/CT image interpretation is mainly visual and qualitative, with radiotracer uptake in suspicious lesions compared against uptake in bone marrow or blood pool. (3) ^{18}F-fluciclovine PET/CT detection rates increase as prostate-specific antigen (PSA) levels rise. (4) Detection rates may vary among centers, possibly as a result of different equipment and variations in reader experience. (5) ^{18}F-fluciclovine PET/CT data (like any imaging results) should not be used in isolation. (6) ^{18}F-fluciclovine PET/CT results have frequently led to changes in disease management plans. The authors added that communication is key to improving results: physicians and imaging physicians should collaborate to improve the quality and utility of reports. Referrers should clearly convey critical information, including prescan PSA levels, and raise pertinent clinical questions. Imaging specialists should provide complete consultative reports, including thoughts on next diagnostic steps. The article provides valuable information for distribution to referring physicians of patients with prostate cancer.

Prostate Cancer

FDG PET/MRI in Renal Transplant

In an article e-published on May 19 ahead of print in *Scientific Reports*, Pajenda et al. from the Medical University of Vienna (Austria) reported on the use of ^{18}F-FDG PET/MR imaging for functional graft assessment in patients after solid organ kidney transplantation with acute kidney injury. The study included 13 such patients and 24 healthy volunteers who served as controls. SUVs and time/activity curves were used to assess general kidney performance, initial flow, and renal response function. General kidney performance for the total kidney and medulla was significantly higher for the volunteers than the patients, with no difference found in the general kidney performance of the cortex. Initial flow in the patient group was found to correlate with renal recovery, defined as change in serum creatinine 10 d after PET/MR imaging. A negative correlation between renal response function and tubular damage was identified in the patient group. The authors noted several implications of their results, including the suggestion that the repair mechanism at the proximal tubules requires glucose as an energy supply, so that "higher FDG uptake might translate into higher energy turnover and cellular repair mechanisms indicating regain of kidney function." These observations, they noted, require additional investigation. The authors concluded that "parameters obtained from FDG PET/MRI showed a possible predictive feature for renal recovery in solid organ kidney transplantation patients undergoing acute kidney injury."

Scientific Reports

Hypoxia PET in HNSCC

Zschaeck et al. from the the Technische Universität Dresden (Germany), the German Cancer Research Center (DKFZ) (Heidelberg, Germany); the Charité–Universitätsmedizin Berlin (Germany), the German Cancer Consortium (DKTK) (Dresden, Germany), Eberhard Karls University Tübingen (Germany), Aarhus University Hospital (Denmark), Odense University Hospital (Denmark), and St. Luc University Hospital (Brussels, Belgium) reported on May 14 ahead of print in *Radiotherapy and Oncology* on an analysis of original hypoxia PET imaging in a large cohort of patients with head and neck squamous cell carcinoma treated at 5 institutions on 4 prospective imaging trials. The study included 102 patients who underwent ^{18}F-FMISO hypoxia imaging and 51 who underwent ^{18}F-FAZA hypoxia imaging for localized disease and who were treated with curative radiochemotherapy. Despite baseline patient characteristics that varied widely among participating centers, maximal tumor-to-muscle ratio and hypoxic volume with a 1.6 threshold on PET were found to have strong and consistent associations with locoregional control and overall survival. Not only were these findings consistent across the 2 tracers but the same cutoff values could be used. These findings and additional analyses led the authors to conclude that PET-measured hypoxia is robust and strongly associated with locoregional control and overall survival in head and neck squamous cell cancer and that "the most commonly investigated tracers, FMISO and FAZA, can probably be used equivalently in multicenter trials." Hypoxia-directed treatment, however, did not show improved outcomes in centrally categorized hypoxic tumors, leading the authors to note that "optimal strategies to improve the dismal outcome of hypoxic tumors remain elusive."

Radiotherapy and Oncology

PET/CT in Suspected PCNSL

In an article e-published on May 13 ahead of print in the *Journal of Neuro-Oncology*, Bertaux et al. from the Hôpital Pitié-Salpêtrière (Paris), the Sorbonne Université (Paris), Institut Curie (Saint-Cloud), and the Université Paris (all in France) reported on a study assessing the potential utility of pre-chemotherapy whole-body ^{18}FDG-PET/CT in suspected primary central nervous system lymphoma (PCNSL). The retrospective study included initial PET/CT and contrast-enhanced CT imaging, bone marrow biopsy, and pathology results in 130 immunocompetent patients. Pathology analysis of central nervous system lesions determined that 95% of patients had large B-cell lymphoma, including 11 with primary vitroretinal lymphoma. Ten of the 130 patients (8%) went on to be diagnosed with systemic lymphoma involvement, including 5 confirmed on pathology, all of which were detected by PET/CT. PET/CT also showed incidental systemic findings unrelated to lymphoma in 14% of patients. The authors reported that an SUV_{max} threshold of 9 was sufficient for discrimination between systemic lymphoma and other lesions, with a sensitivity of 92% and specificity of 89%. Contrast-enhanced CT and bone marrow biopsy were inferior in detecting systemic disease. They summarized their findings: "All of our patients ultimately diagnosed with concomitant systemic involvement had positive ^{18}FDG-PET/CT. We believe it constitutes a safe one-stop shop evaluation for the systemic pretreatment imaging of suspected PCNSL."

Journal of Neuro-Oncology

PET/CT in Inflammatory Breast Cancer Staging

van Uden et al. from the Rijnstate Hospital (Arnhem), the University of Twente (Enschede), and Radboud University Medical Center Nijmegen (all in The Netherlands) reported on May 7 online ahead of print in *Critical Reviews in Oncology/Hematology* on a systematic review of the utility of ^{18}F-FDG PET/CT for initial staging in patients with inflammatory breast cancer. Their results from a broad survey of available literature showed that in 10.3% of patients PET/CT detected additional locoregional lymph node metastases and distant metastases not identified on standard staging imaging. They concluded that ^{18}F-FDG PET/CT should be used as part of the standard diagnostic work-up in inflammatory breast cancer, particularly because as many as 78% of such patients present with axillary lymph node involvement and as many as 40% with distant metastases.

Critical Reviews in Oncology/Hematology

Measuring Amyloid in Down Syndrome

In an article e-published on April 16 ahead of print in *Alzheimer's & Dementia*, Zammit et al. from the University of Wisconsin–Madison, the University of Pittsburgh (PA), the Cleveland Clinic Nevada (Las Vegas), and the University of Cambridge (UK) reported on the application of a new PET index of amyloid load, developed as an alternative to SUV ratios to quantify amyloid burden, in individuals with Down syndrome. The study included 169 such individuals (mean age, 39.6 ± 8.7 y) who underwent ^{11}C-Pittsburgh compound B PET imaging and in whom amyloid load was calculated using syndrome-specific templates for the tracer created for amyloid-carrying capacity and nonspecific binding. Longitudinal changes in the amyloid load index were less variable than SUV ratios, with the highest values of amyloid load identified in the striatum and precuneus. Rates of amyloid accumulation in Down syndrome were similar to those seen in late-onset Alzheimer disease, which suggested to the authors that Alzheimer disease progression in Down syndrome "is of earlier onset but not accelerated." They noted the utility of the PET amyloid load index for characterizing and monitoring amyloid in Down syndrome.

Alzheimer's & Dementia

^{123}I-FP-CIT SPECT in PD

Nicastro et al. from the University of Cambridge (UK) and the University of Geneva/Geneva University Hospitals (Switzerland) reported on May 16 ahead of print in *BMC Neurology* on a case-controlled analysis of ^{123}I-FP-CIT SPECT images in Parkinson disease (PD) to measure extrastriatal serotonergic transporters. Patient and control data were drawn from the Parkinson's Progression Markers Initiative cohort, a multinational observational study to identify biomarkers of disease progression. This analysis included 154 patients with PD (mean age, 61.6 y; 62% men, 38% women; average disease duration, 26 mo) and 62 control subjects who had undergone both ^{123}I-FP-CIT SPECT imaging and coregistered high-resolution T1-weighted MR imaging, as well as multiple other assessments. PD patients showed reduced uptake in the bilateral caudate nucleus, putamen, insula, amygdala, and right pallidum compared with controls. After advanced image analysis, the researchers identified a trend associating higher geriatric depression scale and lower pallidum uptake in PD, as well as associating higher Scales for Outcomes in Parkinson's Disease–Autonomic Dysfunction (SCOPA-AUT) gastrointestinal subscores with lower uptake in mean putamen and caudate nucleus. Urologic SCOPA-AUT subscores were inversely correlated with mean caudate nucleus, putamen, and pallidum uptake in PD. Other findings correlated changes on PET with reported sleep behavior. The authors concluded that "in addition to the well-established striatal deficit, this study provides evidence of a major extrastriatal ^{123}I-FP-CIT impairment, and therefore of an altered serotonergic transmission in early PD."

BMC Neurology

MTV as Local Recurrence Predictor in NSCLC

In a study e-published on May 19 ahead of print in *Radiation Oncology*, Binkley et al. from the Stanford University School of Medicine/Stanford Cancer Institute (CA) and the Indiana University School of Medicine (Indianapolis) reported on a study assessing ^{18}F-FDG PET/CT pre- and midtreatment metabolic tumor volume (MTV) prediction of per-lesion local recurrence in patients treated with definitive radiation therapy for locally advanced non–small cell lung cancer (NSCLC). The retrospective study included the records of 111 patients (median age, 68 y; 69% men, 31% women) with stage III NSCLC (387 lesions; 112 lung tumors and 275 lymph nodes; 46.8% of patients with adenocarcinoma and 39.6% with squamous cell carcinoma) who had undergone PET/CT imaging before and during radiation therapy. MTVs were measured and compared on sequential PET images, including a per-lesion analysis of local recurrence. Over a median follow-up of 38.7 mo, 3-y overall survival was 42.3% and the 3-y cumulative incidence of local recurrence was 26.8% per patient and 11.9% per lesion. MTVs at both timepoints were found to be predictive of local recurrence, and the results led the authors to conclude that midtreatment MTV "may hold higher predictive utility, particularly in the setting of small lesions." They suggested that "this may be the basis for designing adaptive dose painting strategies to maximize therapeutic index" and called for additional studies.

Radiation Oncology

Repeated PSMA PET-Directed Radiotherapy

Henkenberens et al. from the Hannover Medical School and the University of Lübeck (both in Germany) reported on May 12 ahead of print in *Strahlentherapie und Onkologie* on a study assessing outcomes in hormonenaïve patients with oligorecurrent prostate cancer after curative therapy treated with a first and second ^{68}Ga-prostate-specific membrane antigen (^{68}Ga-PSMA) PET–directed course of radiation therapy (RT). The retrospective study included 32 patients who received their first PSMA PET-directed RT of all identified metastases after relapse and their second after biochemical progression. Over a median follow-up of 39.5 mo (range, 18–60 mo), biochemical progression-free survival and androgen deprivation therapy–free survival were analyzed in relation to changes in prostate-specific antigen (PSA) levels over the survival and treatment intervals. All patients showed biochemical responses after the first PSMA PET-directed RT, and the median PSA level decreased significantly (from 1.70 ng/mL before RT to 0.39 ng/mL after). The median PSA level at biochemical progression after the first PSMA PET-directed RT was 2.9 ng/mL and at last follow-up after the second PSMA PET-directed therapy was not significantly different from the median PSMA before the first PSMA PET-directed RT. Median biochemical progression-free survival was 16.0 mo after the first PSMA PET-directed RT and was significantly shorter (8 mo) after the second. Median androgen deprivation therapy–free survival was 31.0 mo, and patients with bone metastases at

first PSMA PET-directed RT had significantly higher chances of requiring androgen deprivation therapy by the last follow-up visit. The authors concluded that "if patients are followed up closely, including PSMA PET scans, a second PSMA PET-directed RT represents a viable treatment option for well-informed and well-selected patients."

Strahlentherapie und Onkologie

^{123}I-FP-CIT SPECT in Progressive Apraxia

Seckin et al. from the Mayo Clinic/Mayo Clinic College of Medicine and Science (Rochester, MN) reported on May 9 ahead of print in the *Journal of Neurology* on a study describing ^{123}I-FP-CIT (DAT scan) SPECT findings in patients with progressive apraxia of speech and comparing these findings with those from patients with progressive supranuclear palsy and corticobasal syndrome. The study included 17 patients with apraxia of speech who underwent ^{123}I-FP-CIT SPECT, with quantitative analyses of uptake in the left and right caudate and anterior/posterior putamen, including striatum-to-background ratios. The results were compared with those from previous imaging in 15 patients with progressive supranuclear palsy and 8 with corticobasal syndrome. Five (29%) patients with progressive apraxia were found to have abnormalities in at least 1 striatal region. These 5 patients' images showed lower uptake in the posterior putamen than did patients with progressive supranuclear palsy or corticobasal syndrome. No other differences were observed. The authors concluded that an "abnormal DAT scan is observed early in the disease course in approximately 30% of progressive apraxia of speech patients, with striatal abnormalities similar to those in progressive supranuclear palsy and corticobasal syndrome."

Journal of Neurology

PET/CT and Regional LN Metastases in ESCC

In an article e-published on May 19 ahead of print in *Strahlentherapie und Onkologie*, Münch et al. from the Technical University Munich, the German Cancer Consortium (DKTK) (Munich), the Helmholtz Zentrum München (Oberschleißheim), and the Universitätsklinikum Jena (all in Germany) reported on the use of ^{18}F-FDG PET imaging to analyze patterns of regional lymph node metastasis in esophageal squamous cell carcinoma (ESCC) and their correlation with the primary tumor. The goal of the study was to evaluate the potential utility of PET/CT in guiding elective nodal irradiation. The retrospective study included 102 patients with ESCC who had undergone pretreatment PET/CT. A total of 76 patients with PET-positive lymph node metastases were included in the final analysis. All lymph node metastases were assigned to 16 predefined anatomic regions and classified according to their position relative to the primary tumor. The longitudinal distance to the primary tumor was measured for each metastasis above or below the primary tumor. The length of the primary tumor was measured using PET data and separately using all other available clinical and imaging data. Significantly more lymph node metastases were identified with PET/CT than CT alone (177 and 131, respectively). The most common lymph node metastasis sites were paraesophageal (63% of patients, 37% of metastases) and paratracheal (33% of patients, 20% of metastases), and $<$5% of patients were found to have supraclavicular, subaortic, diaphragmatic, or hilar lymph node metastases. Fifty-one percent of these metastases were at the same height as, 25% were above, and 24% were below the primary tumor. For 33 (19%) of these metastases, the distance to the primary tumor was $>$4 cm. The authors concluded that "^{18}F-FDG PET can help to identify subclinical lymph node metastases which are located outside of recommended radiation fields" and that "PET-based involved-field irradiation might be the ideal compromise between small treatment volumes and decreasing the risk of undertreatment of subclinical metastatic lymph nodes and should be further evaluated."

Strahlentherapie und Onkologie

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in May. Gallegos and Miller from the Yale University School of Medicine (New Haven, CT) summarized "Advances in PET-based cardiac amyloid radiotracers" on May 19 ahead of print in *Current Cardiology Reports*. On May 17 ahead of print in the *Journal of Clinical Medicine*, Lauri et al. from the Sapienza University of Rome (Italy), the University of Groningen (The Netherlands), the Università Cattolica del Sacro Cuore (Rome, Italy), and the University of Pisa (Italy) published "Imaging modalities for the diagnosis of vascular graft infections: A consensus paper amongst different specialists." Evans et al. from Macquarie University (Sydney), the Royal Prince Alfred Hospital (Camperdown), and the Australian Nuclear Science and Technology Organisation (Lucas Heights, all in Australia) reviewed "Methods to enhance the metabolic stability of peptide-based PET radiopharmaceuticals" on May 14 ahead of print in *Molecules*. On the same day in *Molecules*, Becker et al. from the University of Liège (Belgium) described "The rise of synaptic density PET imaging." On May 20 ahead of print in *Molecular Pharmaceutics*, Allott and Aboagye from Imperial College (London, UK) detailed "Chemistry considerations for the clinical translation of oncology PET radiopharmaceuticals."