SNMMI COVID-19 Resource Center

n March 27, SNMMI President Vasken Dilsizian, MD, announced the launch of the society's online COVID-19 Resource Center in response to the global pandemic. He noted a confluence of factors that were changing the nature of day-to-day nuclear medicine practice across the country. Among these were:

- Nuclear medicine physicians and technologists were being called on to step outside their areas of practice to help with issues related to COVID-19, sometimes with inadequate protection.
- Nuclear medicine researchers were facing mandatory closure of labs and discontinuation or delay of important research studies.
- Nuclear medicine pharmacists were challenged to ensure the availability of all needed clinical drugs, with growing concern about isotope supply pipelines.
- Educators were transitioning rapidly to virtual learning, with little preparation and limited resources.
- Residents and other trainees were confronting questions about ways to continue their educational paths in uncertain times.
- In some cases, nuclear medicine professionals were facing furloughs or layoffs as a result of decreases in or elimination of elective, outpatient, and other procedures.

As of this writing, these challenges not only persist but have been magnified by the impact of the virus spread. The SNMMI COVID-19 Resource Center continues to consolidate information and resources to address these issues. Special features include:

- Information specific to nuclear medicine, including advice on ventilation/perfusion studies and updates on radioisotope supply, as well as useful articles from The Journal of Nuclear Medicine;
- Government agency resources on COVID-19;
- Other resources, such as American Medical Association and COVID-19 data websites;
- Training and certification resources, with advice from nuclear medicine-related boards and associations; and
- Current status of SNMMI activities, including the SNMMI Annual Meeting in June.

Information on the center is frequently updated and expanded with new resources. Individuals with special concerns and questions are urged to send these to covidhelp@snmmi. org. The SNMMI COVID-19 Resource Center is available at http://www.snmmi.org/COVID-19.

SNMMI

Newsline is Looking for First-Hand Accounts

The COVID-19 pandemic is affecting the nuclear medicine community in multiple ways—some that we all share but also with many highly personal or practice-site specific repercussions. The Newsline editor is seeking first-hand reports from nuclear medicine physicians, technologists, physicists, and others about their experiences in dealing with, working through, and meeting the challenges of this difficult time. A special Newsline issue will be dedicated to these reports and to overall effects on nuclear medicine practice and research. Contributions can be short anecdotes or longer reports and can be sent to Nancy Knight, PhD, the consulting Newsline editor, at nknight@umm.edu.

DOE Accepting Isotope Production R&D Applications

he U.S. Department of Energy (DOE) announced on March 24 the availability of up to \$16 million in new funding to advance research and development (R&D) for isotope production. In a press release, the DOE said that this effort is aimed at sustaining longstanding U.S. leadership in isotope production, research, and development. "Isotopes are commodities of strategic importance for the nation," said Under Secretary for Science Paul Dabbar. "This R&D is essential to developing innovative production and processing techniques for scarce isotopes, which will lead to advancements in science, medicine, and industry as well as strengthen our economic and national security."

The DOE's National Laboratories, universities, and non-profits are eligible to submit applications for the 2-year award, which will be selected in a peer-reviewed process. The DOE Isotope Program is managed by the Office of Nuclear Physics in the Office of Science, which is funding the effort. The application process is open to both single investigators and small multi-institutional collaborations.

The funding announcement calls for "novel methods to produce or improve production of radioactive or enriched stable isotopes needed for a wide variety of research and applications....The proposed R&D should generate data relevant to isotope production or lead to new and innovative technologies, or improvements to existing technologies to foster enhanced production of isotopes. Successful applications will clearly describe how the outcome of the proposed work would support and enhance the production of isotopes used for research and applications in medicine, homeland security, the physical sciences, biological and geological sciences, energy, industry, etc." The announcement also strongly encourages applications that incorporate effective ways to train personnel.

Total funding of up to \$8 million is anticipated for Fiscal Year (FY) 2021, with an additional \$8 million in funding anticipated in FY 2022, for a total of \$16 million over the 2-year grant period. Funding is contingent on congressional appropriations. Individual awards will be funded at a maximum of \$750,000 per year.

Final applications for this funding opportunity are due on June 15 by 5 PM Eastern time. Letters of intent are not required. The full text of the Funding Opportunity Announcement for universities and nonprofits, along with a parallel, companion announcement for DOE National Laboratories, is available at https://science.osti.gov/-/media/grants/pdf/foas/2020/SC_FOA_0002301.pdf.

Monitoring Radioisotope Production and Transport

he COVID-19 pandemic has resulted in delays and interruptions in medical supplies across the world. Early concerns about radioisotope production and delivery have proved to be well founded. Severely curtailed commercial and cargo flights, staffing changes and interruptions across the supply chain, and radically altered demand for routine nuclear medicine tests have challenged efforts to monitor radioisotope availability for near- and long-term planning. On March 30, the Security of Supply Working Group of the Nuclear Medicine Europe Emergency Response Team (ERT) held a teleconference to discuss the effects of the COVID-19 pandemic on ⁹⁹Mo and other radioisotope production.

NTP Radioisotopes SOC Ltd. (Pretoria, South Africa) informed the ERT that cancellation of most scheduled international flights had interrupted bulk ⁹⁹Mo shipments from South Africa during the previous week and that options were under investigation to resume these shipments. The Australian Nuclear Science and Technology Organisation (ANSTO) reported that it had received regulatory approval from the Australian nuclear regulator Australian

Radiation Protection and Nuclear Safety Agency to resume ⁹⁹Mo export production. However, ANSTO noted that a gradual transition from its current 2 production runs per week will be required, in addition to putting in place measures to protect staff and to ensure production during the COVID-19 pandemic. User research programs in association with ANSTO had been canceled or put on hold for the duration of the international emergency. Other radioisotope producers participating in the teleconference reported that they have been able to maintain operations with suitable personnel protection measures for COVID-19.

Nuclear Medicine Europe also advised teleconference participants that ^{99m}Tc generator shortages may be foreseen in various regions because of transportation challenges for both bulk ⁹⁹Mo and ^{99m}Tc generators and urged medical institutions to contact their ^{99m}Tc generator suppliers or radiopharmacies for updates.

Information associated with radioisotope supply and demand is changing on a daily basis. SNMMI has developed a Coronavirus-19 Response Center at http://www.snmmi.org/covid-19 and will post updates as these become available.

ABNM: Helping Diplomates and Trainees During the COVID-19 Pandemic

Leonie Gordon, MD, Associate Executive Director, American Board of Nuclear Medicine

he American Board of Nuclear Medicine (ABNM) recognizes the strains under which diplomates are currently practicing and wants them to prioritize their time to serve the immediate needs of their practice, their families, and themselves. We realize that many medical professionals and trainees are working tirelessly to treat and monitor those exposed to or diagnosed with coronavirus disease 2019 (COVID-19), and we recognize the associated enhanced health risks and potential for training disruptions. We have taken the actions outlined here after careful consideration of options available for our diplomates, candidates, staff, and the public.

The ABNM understands that physicians may not have time for nonurgent professional activities during the COVID-19 public health emergency and so extended the end of the first quarter of CertLink from March 31 to June 30, 2020, to give diplomates more time to answer the questions released in January 2020. Diplomates will not receive additional questions during this time (even those who have already completed their assignment), and no one will receive extra questions when new questions become available on July 1. The net effect will be a reduction in the total number of questions in 2020 by one-fourth. This action will have no impact on diplomates' CertLink performance as shown on their dashboards.

The ABNM also recognizes that COVID-19 has affected trainees and training programs. The ABNM leave policy was modified to allow an additional 2 weeks of leave (10 working days) in 2020 for all COVID-19-related reasons, including home quarantine. We also understand that cancellation/deferral of nonurgent medical procedures will reduce the number of diagnostic nuclear medicine studies performed in adults and children and will also likely reduce the number of oral radioiodine therapies for hyperthyroidism when thyroid scans are deferred and/or patients are maintained on antithyroid medication. The impact of COVID-19 on radioiodine treatment for thyroid cancer and parenteral therapies for other cancers is likely to be somewhat less but may still be significant. Because it may be impossible for residents who complete training this year to obtain experience with the required number of studies, the ABNM has made a 1-time modification of the case experience requirements in 2020 for all COVID-19related reasons. The changed requirements include:

- Cardiovascular stress test supervision (exercise or pharmacologic): 75 studies (normally 100 studies).
- Pediatric nuclear medicine: 75 studies (normally 100 studies).
- Radiotherapy with 131 I: 20 cases (at least 10 benign plus 10 malignant, including $3 \le 33$ mCi and 3 > 33 mCi) (normally 30 cases).



Leonie Gordon,

 Parenteral therapies requiring a written directive: 3 cases (normally 5 cases).

Candidates for the ABNM certification examination are also required to be certified in advanced cardiac life support (ACLS). The American Heart Association is allowing a 60-day extension of ACLS instructor cards beyond the renewal date and recommends that employers and regulatory bodies extend provider cards 60 days beyond renewal date. The ABNM is adopting this recommendation:

• ACLS certification: 60-day extension beyond renewal date of current provider cards.

If trainees do not meet these modified requirements, program directors will be required to provide the ABNM with an educational plan and request for exemption that will be considered on a case-by-case basis.

The ABNM is still planning to give the Certification and Maintenance of Certification Examination during the first week of October 2020, with applications accepted April 1 through May 31. We are monitoring the situation very closely and will make adjustments if necessary.

The ABNM office staff is working remotely, but diplomates, program directors, and the public should notice no difference and receive the same level of excellent service that we always try to provide.

The ABNM recognizes the importance of the broad community of nuclear medicine professionals and all the work they are doing during the COVID-19 pandemic. We appreciate the patience of our diplomates and trainees during this chaotic time. We will continue to thoughtfully evaluate the situation as it evolves and notify our diplomates of any changes.

SNMMI Announces "Ones to Watch 2020" Selections

NMMI announced on March 6 its annual list of 30 early-career professionals selected as "Ones to Watch" in 2020. Launched in 2018, this effort recognizes those with "the potential to shape the future of precision medicine across all spectrums of the field." SNMMI members nominate themselves or someone they know whose actions, work, or studies set them apart as future thought leaders in nuclear medicine and molecular imaging. Recipients are selected with the help of the SNMMI Committee on Councils and Centers, the SNMMI Early Career Professionals Committee, and the SNMMI-TS Professional Development Committee.

This year's Ones to Watch are currently in-training or have completed training within the past 5 years. An SNMMI press release stated that "We are proud to showcase rising talent in the field, offering a platform to increase recognition for early career professionals within our specialty." The honorees were Oladunni Akin-Akintayo, MD, MPH (Emory University); Jeremie Calais, MD, MSc (University of California at Los Angeles); Lukas M. Carter, PhD (Memorial Sloan Kettering Cancer Center); Elizabeth Dibble, MD (Rhode Island Medical Imaging); Shana Elman, MA, MD (University of New Mexico); Saeed Elojeimy, MD, PhD (University of New Mexico); Shadi Esfahani, MD, MPH (Massachusetts General Hospital); Robert R. Flavell, MD, PhD (University of California, San Francisco); Matthew David Gott, PhD (Argonne National Laboratory); Kristina Elizabeth Hawk, MD, PhD (Stanford University and Radiology Partners); Pedram Heidari, MD (Massachusetts General Hospital); Reinier Hernandez, PhD (University of Wisconsin-Madison); Jana Ivanidze, MD, PhD (New York Presbyterian Hospital/Weill Cornell Medical College); Joseph Lau, PhD (National Institutes of Health); Nadine Mallak, MD (Oregon Health & Science University);



Carmela Nappi, MD, PhD (Federico II University); Lorenzo Nardo, MD, PhD (University of California, Davis); Dalong Ni, PhD (University of Wisconsin–Madison); Ashwin Singh Parihar, MBBS, MD (Postgraduate Institute of Medical Education Research); Justin Peacock, MD, PhD (San Antonio Uniformed Services Health Education Consortium, US Air Force); James Louis Reynolds, MHA, CNMT, PET (Banner Health); Patricia Manuela Ribeiro Pereira, PhD (Memorial Sloan Kettering Cancer Center); Sheryl Roberts, PhD (Memorial Sloan Kettering Cancer Center); Rodney Y. Rodriguez, CNMT, PET, NCT, RT (CT)(ARRT) NMTCB(RS) (VA Palo Alto Health Care System); Sara Sheikhbahaei, MD, MPH (Johns Hopkins Hospital); Sixiang Shi, PhD (University of Texas MD Anderson Cancer Center); Jakub Toczek, PhD (Yale Cardiovascular Molecular Imaging Laboratory); Duy Tran, RT(N), CNMT, NMTCB (CT) (Thomas Jefferson University Hospital); Angela Weiler, BS, CNMT, RT(N) (Mayo Clinic-Rochester); and Navid Zeraatkar, PhD (University of Massachusetts Medical School).

SNMMI

SNMMI Strong: Advancing the Profession through Advocacy, Collaboration, and Awareness

Vasken Dilsizian, MD, SNMMI President

Ithough the past few months have been extremely challenging for SNMMI and its members, this has been a productive year with strong forward momentum for the society and the profession. Here are some highlights of what we have been able to accomplish.

Regulatory and Legislative Success. SNMMI has achieved notable progress on the regulatory front this year. The year started with publication by the U.S. Pharmacopeia (USP) of a new chapter for nuclear medicine that, for the first time, recognizes compounded sterile radiopharmaceuticals and provides standards for their preparation, which will help ensure the best possible care for patients.

SNMMI, working with the Centers for Medicare & Medicaid Services (CMS) and in collaboration with peer societies, achieved a major save: instead of making technical component cuts of as much as 80% to myocardial PET reimbursement, CMS will continue to pay the technical component according to contractor pricing in 2020. In addition, instead of a significant (as much as 157%) decrease in reimbursement for SPECT studies, SNMMI members saw a 3.5% increase for 2020. More recently, SNMMI identified coding errors that would have led to incorrect reimbursement for nuclear medicine procedures, and CMS has taken steps to correct the situation.

The society's productive relationship with the U.S. Food and Drug Administration (FDA) continued this year with FDA approval of a New Drug Application for ⁶⁸Ga-DOTATOC injection for PET imaging in localization of somatostatin receptor–positive neuroendocrine tumors (NETs) in adult and pediatric patients. Also notable: the agency added arginine and lysine to its bulk drug substances list, which will help patients with gastroenteropancreatic NETs undergoing ¹⁷⁷Lu-DOTATATE therapy.

SNMMI has been working persistently to educate the U.S. Nuclear Regulatory Commission (NRC) on the training and experience necessary to administer radiopharmaceuticals. Most recently, SNMMI participated in a briefing at NRC headquarters during which we highlighted the importance of appropriate training and experience requirements for authorized users, addressed concerns about patient safety and patient release materials, and spoke about the future of the field. We expect a ruling within the next few months.

On the legislative front, SNMMI collaborated with clinicians, patients, and industry representatives to advance H.R. 3772, the Medicare Diagnostic Radiopharmaceutical Payment Equity Act of 2019. The society coordinated introduction

of the bill, cohosted a Capitol Hill briefing, and conducted a vigorous grassroots letter-writing and lobbying campaign in support of the bill, which calls for all diagnostic radiopharmaceuticals that reach a cost of more than \$500 per day to be paid separately in the Hospital Outpatient Prospective Payment System. Successful enactment would be significant for hospitals and for patients.



Vasken Dilsizian, MD, SNMMI President

Taking the Lead on Therapeutics. From October 25 to 27, SNMMI held its inaugural Therapeutics Conference—Therapies, Theranostics, and Building Your Radionuclide Clinical Practice—in Las Vegas, NV. The conference explored the latest innovations in therapy, including information on acquiring knowledge and resources to effectively deliver theranostic agents and the fundamental steps necessary to establish an institutional nuclear medicine therapy program. The meeting welcomed referring physicians and others seeking to learn more about the profession. SNMMI will be repeating the conference in the coming year.

In December, SNMMI's Therapy Center of Excellence and Clinical Trials Network collaborated with the National Cancer Institute (NCI) on the fifth Theranostic Consensus Conference. The symposium focused on the question, "What is the goal with radionuclide therapies: palliative, curative, or adjuvant treatment?" and covered dose optimization, treatment efficacy, clinical trial design, and strategies. This meeting continues to be highly attended. Proceedings from the meeting will be published in 2020.

Collaborating with Peer Societies and the International Community. Collaboration with peer societies, both domestic and international, has been another focus this past year. Referring physicians—cardiologists, oncologists, endocrinologists, neurologists, and others—are vital partners in ensuring positive outcomes for patients. Working with these clinical colleagues is key to advancing patient care.

SNMMI is collaborating with the American Society of Nuclear Cardiology to develop an 80-hour course to ensure members have adequate training and are up to date on NRC requirements. SNMMI and the American Society for Radiation Oncology have developed a Care Pathway Working Group that drafted a report entitled "Patient-Centered Path

of Care for Targeted Radiopharmaceutical Therapies," which will soon be published.

The society is working on projects with both the International Atomic Energy Agency and the U.S. Department of Energy to make the benefits of nuclear and molecular imaging more available worldwide, particularly in resource-challenged countries.

SNMMI continues to participate in the Nuclear Medicine Global Initiative (NMGI), which has begun work on training requirements/education/recommendations for the practice of theranostics. The project, led by Jean-Luc Urbain, MD, PhD, aims to define the global availability of theranostics and impediments to training and education in the specialty. Another NMGI group, led by Andrew Scott, MD, is drafting a summary of its project on the availability of radiopharmaceuticals around the world.

Reaching Out Early to Medical Students. The use of nuclear medicine imaging and therapy will expand over the coming decades, so SNMMI is working on a number of initiatives to enhance the pipeline of medical students pursuing a career in the field. The society's bylaws now include a membership category for medical students. SNMMI is exhibiting at medical conferences to introduce students in person to the field. In addition, we have established new

research grants to introduce high-achieving students to nuclear medicine, molecular imaging, and targeted radiotherapy as a potential career path by supporting their participation in a related research project.

Responding to the COVID-19 Pandemic. In March, as COVID-19 escalated across the world, SNMMI launched a COVID-19 Resource Center to consolidate information and resources to support members. The center includes information specific to nuclear medicine, such as advice on ventilation/perfusion studies and updates on radioisotope supply, as well as useful articles from *The Journal of Nuclear Medicine*, government agency resources on COVID-19, resources from other societies and organizations, and training and certification resources from nuclear medicine—related boards and associations. SNMMI has also launched a forum where members can raise issues and share solutions to COVID-related problems.

In coming months SNMMI will be working to engage the media in telling the story of nuclear medicine through a series of articles to raise awareness of this extraordinary medical discipline and, in particular, therapeutics. Our profession is taking enormous strides toward curing cancer. The public needs to know what nuclear medicine is, what it is doing, and where it will take us in the coming decade.

IAEA Launches Curie Fellowships for Women

n March 9 at its headquarters in Vienna, Austria, the International Atomic Energy Agency (IAEA) launched a fellowship program to provide incentives for young women considering a career in nuclear science and technology. The Marie Skłodowska-Curie Fellowship Program is intended to increase the number of women studying in nuclear science and technology and nonproliferation studies through scholarships and work experience opportunities.

The IAEA will provide scholarships at an accredited university for up to 2 years for women pursuing a graduate degree in nuclear sciences and technologies or nonproliferation studies. Selected recipients will also have the opportunity to pursue 6–12-mo internships at the IAEA related to their fields of study. The program is open for students from IAEA Member States who meet the following criteria: female candidates; above average academic credentials; fluency in Arabic, English, Chinese, French, Russian, or Spanish; and acceptance by an accredited university for a relevant Master's course. Up to 100 women per year will be selected, subject to availability of funding. The scholarship will cover university tuition fees up to a maximum of €10,000 per year and a lump sum payment for living expenses based on the cost of living for the university's location, up to a maximum of €10,000 per year. Geographical

balance will be part of internal selection criteria. Fellowships will be awarded once per year. The first round of fellowships will be awarded for the academic year starting in 2021.

An outreach toolbox is under development to support universities and partners to encourage applications from qualified candidates. A dedicated webpage and, eventually, an alumni portal will be created, highlighting partners as well as students.

Countries expressing support included: Belgium, Canada, China, France, Japan, Kuwait, Morocco, The Netherlands, Pakistan, Paraguay, Poland, the United Kingdom, the United States, and Uruguay. The G77 group of countries, the Association of Southeast Asian Nations, the European Union, the Texas A&M system, the Australian Nuclear Science and Technology Organisation, and the Ban Ki-moon Centre for Global Citizens also expressed their support for the fellowship program.

Introductory information on the program is available at: https://www.iaea.org/sites/default/files/20/03/marie-curie-fellowship-programme.pdf. A related video and updated information are available at: https://www.iaea.org/newscenter/multimedia/videos/marie-sklodowska-curie-fellowship-programme-launches.

International Atomic Energy Agency

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

PET/CT and Pancreatic NET Recurrence

Sato et al. from Kyoto University and Shiga General Hospital (both in Japan) reported on March 20 ahead of print in the Journal of Hepato-Biliary-Pancreatic Sciences on a study on the utility of ¹⁸F-FDG PET/CT in diagnosis and prediction of pancreatic neuroendocrine neoplasm recurrence. The retrospective study included 72 patients with ¹⁸F-FDG-positive and -negative disease who were followed over a median of 65.6 mo. Among the variables assessed was whether PET/CT-positivity was related to earlier recurrence after curative treatment of nonfunctioning tumors. ¹⁸F-FDG-positive tumors were found to be more pathologically advanced and significantly associated with metastasis. Four of 16 functional tumors and 1 of 12 of insulinomas were ¹⁸F-FDG positive. Metastasis and World Health Organization (WHO) tumor grade were independently associated with tracer accumulation. In individuals with nonfunctioning tumors, ¹⁸F-FDG positivity was significantly correlated with poorer recurrence-free but not overall survival. Factors associated with shorter recurrence-free survival on univariate analysis included male

sex, nodal metastases, WHO tumor grade >G2, and ¹⁸F-FDG-positive disease; on multivariate analysis only ¹⁸F-FDG-positive status was associated with shorter recurrence-free survival.

Journal of Hepato-Biliary-Pancreatic Sciences

Cost Effectiveness: SPECT/ CT in Small Renal Masses

In an article e-published on February 27 ahead of print in European Urology Focus, Su et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) reported on a decision analysis model study of the cost effectiveness of 99mTc-sestamibi SPECT/CT in management of small renal masses and the associated potential for avoiding biopsy in some benign tumors. The model estimated the costs and outcomes of 3 management strategies for a hypothetical healthy 65-y-old patient with an asymptomatic small renal mass: renal mass biopsy, ^{99m}Tc-sestamibi SPECT/CT, and 99mTc-sestamibi SPECT/ CT followed by biopsy to confirm benign small renal masses. These were compared against 2 existing standard references: empiric surgery alone and empiric surgery with thermal ablation and active surveillance. Quality-adjusted life years and direct medical costs were calculated and compared for the 3 management options and the standard references. 99mTc-sestamibi SPECT/CT followed by biopsy to confirm benign small renal masses was found to have a very low risk of leaving untreated malignant tumors (0.2%; with 2.1% for renal mass biopsy, 4.2% for 99mTc-sestamibi SPECT/CT alone, and 0% for empiric surgery) and the highest probability of leaving benign tumors untreated (84.4%, with 53.9% for renal mass biopsy, 51.7% for 99mTc-sestamibi SPECT/CT alone, and 0% for empiric surgery). 99mTc-sestamibi SPECT/CT followed by biopsy was found to have the lowest project cost and highest quality-adjusted life years. Compared with the current practice reference of empiric surgery + thermal ablation + active surveillance, all 3 management options were cost effective, but ^{99m}Tc-sestamibi SPECT/CT followed by biopsy had the lowest cost and highest quality-adjusted life years. The authors concluded that "^{99m}Tc-sestamibi SPECT/CT followed by confirmatory biopsy helps avoid surgery for benign small renal masses, minimizes untreated malignant small renal masses, and is cost effective compared with existing strategies."

European Urology Focus

PET/CT and Frozen Shoulder

Duchstein et al. from the Bispebjerg and Frederiksberg Hospital/Copenhagen University (Denmark) reported on March 13 ahead of print in Knee Surgery, Sports Traumatology, Arthroscopy on a study assessing the potential for ¹⁸F-FDG PET/CT imaging in diagnosis of adhesive capsulitis and early differentiation from subacromial impingement. The study included 20 patients (11 with frozen shoulder and 9 with subacromial impingement) who underwent preoperative ¹⁸F-FDG PET/CT imaging, with diagnoses confirmed at arthroscopy. Resulting images were assessed both visually (with good agreement) and by semiquantitative analyses and showed increased ¹⁸F-FDG uptake in the frozen shoulders and no uptake in subacromial impingement. Sensitivity and specificity were 92% and 93%, respectively, for visual assessment and 77% and 93%, respectively, for semiquantitative analyses. When the 2 types of analyses were combined, sensitivity and specificity were 100% and 93%, respectively, for differentiating frozen shoulders from subacromial impingement and/ or an unaffected shoulder. The authors concluded that "18F-FDG PET/CT seems to be a valid method to diagnose frozen shoulder," with specific utility in diagnostically challenging cases and in the early phase of frozen shoulder involvement.

Knee Surgery, Sports Traumatology, Arthroscopy

Tau vs. Amyloid in Depression

In an article e-published on March 2 ahead of print in the Journal of Alzheimer's Disease, Babulal et al. from the Washington University School of Medicine (St. Louis, MO) reported on the association of tau and amyloid PET imaging markers with depression diagnoses in cognitively normal adults and whether and how administration of antidepressants modified these associations. The study included 301 participants who underwent PET tau and amyloid imaging, with evaluation for depression made during an annual clinical examination and for antidepression medication use. A series of logistic regression models assessed associations between PET tau and depression, between PET tau and antidepressant use, between PET amyloid and depression, and between PET amyloid and antidepressant use. The models were adjusted for age, sex, education, race, and apolipoprotein $\epsilon 4$. The researchers found that individuals with elevated tau were twice as likely to be depressed and that those with elevated tau who were taking antidepressants had even greater odds of being depressed. Elevated amvloid was not associated with depression in participants. The finding that "antidepressant use interacts with tau to increase the odds of depression among cognitively normal adults" was covered widely in the media.

Journal of Alzheimer's Disease

Adding PET/CT in Hepatocellular Carcinoma

John et al. from the Miami Veterans Affairs Medical Center (FL), Virginia Commonwealth University/ Virginia Commonwealth School of Medicine (Richmond), McGuire Veterans Affairs Medical Center (Richmond, VA), and the University of Texas Southwestern Medical Center (Dallas) reported on March 3 ahead of print in Liver Transplantation on a study assessing the value of 18F-FDG PET/CT in addition to cross-sectional imaging for staging and prediction in patients with hepatocellular carcinoma. The retrospective study included 148 patients who underwent PET/CT imaging after initial

staging with contrast-enhanced CT or MR imaging. Elements assessed were the benefit of PET in identification of new lesions and its potential detriment in false-positive findings. Associations between PET/CT results and risk of extrahepatic metastasis and progression-free and overall survival were also analyzed. The researchers found that PET/CT identified additional extrahepatic metastases in 11.9% of treatment-naïve and 13.8% of treated patients and changed Barcelona Clinic Liver Cancer (BCLC) staging in 5.9% of treatment-naïve and 18.8% of treated patients compared with CT/MR imaging alone. This resulted in changes in management for 9.9% of treatmentnaïve and 21.3% of treated patients. Eight patients (5%) had false-positive PET/CT findings necessitating additional extrahepatic evaluation. A high tumor grade on PET/CT was independently associated with a higher likelihood of extrahepatic metastasis and worse overall survival. Patients who had been treated and had BCLC stages A or B were more likely to be upstaged with PET/CT. The authors summarized their findings: "PET/CT provides prognostic information and improves tumor staging beyond CT/MRI alone, with subsequent changes in management for patients with hepatocellular carcinoma."

Liver Transplantation

Reproducibility of Renal Allograft PET/CT

In an article e-published in the March 12 issue of Scientific Reports, Jadoul et al. from the University Hospital of Liège and the KU Leuven Campus Kulak Kortrijk (both in Belgium) reported on a study evaluating the repeatability and reproducibility of quantification of renal 18F-FDG uptake on PET imaging in kidney transplant recipients under surveillance for allograft rejection. The study included 95 adult transplant recipients who underwent surveillance biopsy and PET/ CT between 3 and 6 mo after transplantation. SUV_{mean} in the kidney cortex was independently assessed by 2 experienced observers in 4 volumes of interest distributed in the upper

and lower poles, with the first observer repeating SUV assessment in the uppermost volume of interest, unaware of the initial results. An intraclass correlation of 0.96 with 95% CI was calculated for the intraobserver measurements, and the intraclass correlations for interobserver reproducibility for each volume of interest were 0.87, 0.87, 0.85, and 0.83 for the upper to the lower renal poles. The authors concluded that "assessment of renal ¹⁸F-FDG uptake in kidney transplant recipients is highly repeatable and reproducible if ¹⁸F-FDG PET/CT images are evaluated by experienced observers with careful attention to the technique," a finding that makes this approach "transferrable to the clinical routine."

Scientific Reports

SPECT and ICA Test Balloon Occlusion

Sivakumaran et al. from the North Bristol Hospitals NHS Trust (UK) reported on March 10 ahead of print in World Neurosurgery on a study of the potential for SPECT-enhanced internal carotid artery test balloon occlusion in the management of complex cerebral aneurysms and skull base tumors. The records review included all test balloon procedures performed at the authors' institution over a 20-y period. Study data included semiquantitative cerebral blood flow analysis using 99mTc-HMPAO SPECT during internal carotid artery test balloon occlusion, supplemented with data from clinical assessment and angiographic collateral flow. Postocclusion collateral circulation, complications, and safety of permanent occlusions were recorded. A total of 83 patients in the study underwent test balloon occlusion without complication. Of the 45 patients with satisfactory occlusion, 28 then proceeded to permanent vessel occlusion. Thirty-eight patients had unsatisfactory test balloon occlusion, with 15 of these requiring permanent occlusion and a bypass procedure. This left a total of 40 patients who did not proceed to permanent occlusion. The authors concluded that "SPECT-enhanced test balloon occlusion is an important component of the management of complex vascular pathology and skull base tumors, permitting safe permanent occlusion of the parent vessel and definitive treatment of the main pathology."

World Neurosurgery

Neuroimaging in Chronic Traumatic Encephalopathy

In an article in the March supplement to the Clinical Journal of Sport Medicine (2020;30 suppl 1:S1-S10), Sparks et al. from the University of Bristol and the University of Oxford (UK) provided the results of a systematic review of the utility of neuroimaging in the diagnosis of chronic traumatic encephalopathy (CTE). The review is an update to a similar analysis of the literature published through 2014 (Clin J Sport Med. 2017 Oct 25). A total of 7 studies met the review criteria for the current study, with almost all study participants being professional athletes. All 7 studies compared individuals with CTE with normal controls. Assessment modalities included were categorized into structural MR imaging, diffusion MR imaging, and radionuclide studies. The authors found that in these studies the biomarkers that differed significantly between individuals with suspected CTE and controls were Evans index; cavum septum pellucidum rate, length, and ratio of cavum septum pellucidum length to septum length; regional differences in axial diffusivity and free/intracellular water fractions; SPECT perfusion abnormalities; and PET signals from taubinding, glucose-binding, and GABA receptor-binding radionuclides. The authors noted that limitations in this literature included low specificity in identification of suspected cases of CTE across studies, the need for postmortem validation, and a lack of generalizability to the population outside professional athletes. They concluded that "the most promising biomarker is tau-binding radionuclide PET signal because it is most specific to the underlying neuropathology" and because it "differentiated CTE from both controls and patients with Alzheimer disease." They added that multimodal

imaging is likely to improve specificity in the future.

Clinical Journal of Sport Medicine

CCTA vs Functional Imaging Post-CABG

Small et al. from the University of Ottawa/University of Ottawa Heart Institute (Canada) reported on March 5 in the International Journal of Cardiology. Heart and Vasculature (2020;27:100494) on a study comparing rates of utilization and health care costs of coronary CT angiography (CCTA) and SPECT in patients with prior coronary artery bypass surgery (CABG). The analysis included 2,754 patients imaged by SPECT (2.163) or CCTA (591). Of these, 425 individuals (15.4%) underwent subsequent imaging, with CCTA being more common than SPECT (a comparison that persisted even when adjusted for baseline characteristic differences). When the highest risk patients (those who underwent repeat revascularization) were removed from the analysis, repeat testing with CCTA remained more common than SPECT. The costs of this "downstream" imaging per patient were more than twice as great for the CCTA group than the SPECT group ($\$366.79 \pm \29.59 and 167.35 ± 10.12 , respectively). However, costs that included index imaging costs were lower in the CCTA group $(\$764.66 \pm \$29.59)$ than in the SPECT group ($\$1,396.73 \pm \10.12). The authors summarized their findings that "index imaging with SPECT versus CCTA in CABG patients was associated with fewer downstream tests, less invasive coronary angiography, less repeat revascularization but greater expense." They added that these findings "heighten the controversy regarding first test strategy in CABG patients by demonstrating that any potential cost saving of CCTA must be weighed against the increase in downstream testing associated with this modality." They concluded that more extensive evaluation of costs and clinical outcome data "will be required before CCTA replaces functional imaging as the first-line investigation in CABG patients."

International Journal of Cardiology.

Heart and Vasculature

Metabolic Tumor Volume and DLBCL Outcomes

In an article published on March 24 in Blood Advances (2020;4[6]:1082-1092), Ceriani et al. from the Imaging Institute of Southern Switzerland (Bellinzona), the Università della Svizzera Italiana (Bellinzona), the Azienda Ospedaliera Papa Giovanni XXIII (Bergamo, Italy), the Swiss Institute of Bioinformatics (Lausanne), University Hospital/University of Zurich (Switzerland), the Swiss Group for Clinical Cancer Research Coordinating Center (Bern, Switzerland), University Hospital Basel/University of Basel (Switzerland), the University of Milan (Italy), the European Institute of Oncology (Milan, Italy), the Cantonal Hospital Aarau (Switzerland), and the University Hospital/ University of Bern (Switzerland) reported on the ability of functional parameters from ¹⁸F-FDG baseline PET/CT to predict outcomes in diffuse large B-cell lymphoma (DLBCL). Data were acquired as part of a large multicenter clinical trial. This study focused on 2 cohorts of DLBCL patients receiving conventional immunochemotherapy (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone [R-CHOP]) every 14 or 21 d. Baseline PET imaging was acquired in 141 patients treated with R-CHOP every 14 d as part of the larger clinical trial. Reproducibility was analyzed in a validation set of 113 patients treated with R-CHOP every 21 d. In the 14-d group, 5-y progression-free survival was 83% for individuals with low metabolic tumor volume on PET and 59% for those with high metabolic tumor volume. Corresponding overall survival percentages over the 5-y period were 91% and 64%, respectively. In the 21-d group, metabolic tumor volume remained the most significant predictor of outcome. In patients with elevated metabolic tumor volume, higher metabolic heterogeneity significantly predicted poorer outcomes. A validated model that integrated metabolic tumor volume and metabolic heterogeneity was able to identify high-risk patients with shorter overall and progressionfree survival times. The authors concluded that this approach "may allow early identification of refractory patients who might benefit from treatment intensification."

Blood Advances

CSF Biomarkers and Differential AD Diagnosis

Barthélemy et al. from the Université de Montpellier (France), Washington University School of Medicine (St. Louis, MO), the Université Paris Saclay (France), and the Gui de Chauliac Hospital (Montpellier, France) reported in the March 17 issue of Alzheimer's Research and Therapy (2020;12[1]:26) on a study of the use of cerebrospinal fluid (CSF) biomarkers in differential diagnosis of Alzheimer disease (AD), with ¹¹C-Pittsburgh compound B (11C-PiB) PET imaging as a comparative standard for study validation. The authors used a quantitative mass spectrometry technique that detects the CSF biomarkers of 2 phosphorylated tau isoforms, pT181 and pT217. The first cohort of subjects included 10 patients with probable AD, who were compared with 40 patients with non-AD diseases (Lewy body disease, progressive supranuclear palsy, corticobasal degeneration, adult chronic idiopathic hydrocephalus, mixed dementia, vascular dementia with possible AD, vascular dementia, brain metastasis) and 5 controls with normal neuropsychological profiles. The authors found that pT217 but not pT181 differentiated with high specificity and sensitivity between individuals with AD and those with other neurodegenerative diseases and control subjects. T217 phosphorylation was 6 times higher and T181 phosphorylation was 1.3 times higher in individuals with AD in comparison with controls. The validity of these results was checked in a second cohort that included 33 amyloid-positive and 51 amyloid-negative (as assessed by ¹¹C-PiB PET) participants who were cognitively normal or had mild cognitive impairment. In this cohort, pT217 CSF levels identified

amyloid-positive patients with sensitivity and specificity >90%. ¹¹C-PiB uptake levels were also highly correlated with pT217 CSF concentrations. The authors concluded that "increased CSF pT217 levels, more than those of pT181, are highly specific biomarkers for detecting both the preclinical and advanced forms of AD." They added that not only should this finding improve AD diagnosis but that data from this study, in correlation with PET findings, suggest that "pT217 is a promising potential target for therapeutic applications and that a link exists between amyloid and tau pathology."

Alzheimer's Research and Therapy

⁶⁸Ga-PSMA PET/CT and Distribution of Prostate Cancer Recurrence

In an article e-published on March 17 ahead of print in BJU International, Huits et al. from The Netherlands Cancer Institute (Amsterdam), Erasmus Medical Centre (Rotterdam, The Netherlands), St. Vincent's Hospital (Darlinghurst, Australia), and the Garvan Institute of Medical Research (Darlinghurst, Australia) reported on a study designed to assess the anatomic distribution of prostate cancer recurrence on ⁶⁸Ga-PSMA PET/CT in patients with biochemical recurrence after radical prostatectomy with pathologically confirmed lymph node metastasis at extended pelvic lymph node dissection. The retrospective study included data from 100 such patients who underwent ⁶⁸Ga-PSMA PET/CT to guide salvage therapy. Factors included in the analysis were clinical and pathologic features, anatomic location of recurrence on imaging, and effect on management. PET/CT findings were positive in 68 and negative in 32 patients. Among the PET/CTpositive patients 44 (65%) had abnormal uptake only in the pelvic area, 7 (10%) only outside the pelvic area, and 17 (25%) both inside and outside the pelvic area. Eighty-four percent of the PET/CT-positive pelvic lymph nodes were detected on the same side as the lymph node metastasis diagnosed at extended pelvic lymph node

dissection. ⁶⁸Ga-PSMA-PET/CT findings led to a change in management for 68% of patients. The authors added that "prospective studies are needed to support the long-term benefit of ⁶⁸ Ga-PSMA PET/CT-dictated management changes."

BJU International

PET/CT and MR Imaging in HNSCC Extracapsular Extension

Sheppard et al. from Bern University Hospital/University of Bern (Switzerland) reported on March 6 ahead of print in Laryngoscope on a study looking at the ability of features of PET/ CT and MR imaging to contribute to identification of extracapsular extension in patients with head and neck squamous cell carcinoma (HNSCC). The retrospective study included 212 patients with advanced HNSCC who had undergone pretherapeutic PET/ CT and/or MR imaging (PET/CT, 184 patients; MR, 186; both modalities, 158). Imaging reviewers performed blinded evaluations of PET/ CT and MR features associated with the presence of extracapsular extension, with results compared to histopathology at neck dissection. The researchers found that clinical stage IV, ill-defined margins on both PET/CT and MR imaging, and SUV_{max} on PET were significant independent predictors of extracapsular extension. When these 4 features were combined and compared with histopathologic results, the cumulative score predicted extracapsular extension status with an accuracy of 91.43%. The authors concluded that these findings indicated that "specific features in PET/CT and MRI are potential predictors of extracapsular extension status and may help in pretherapeutic stratification in HNSCC."

Laryngoscope

PET/CT Staging of Malignant Melanoma

In an article e-published on March 11 ahead of print in *Dermatologic Therapy*, Yilmaz et al. from Gaziantep University School of Medicine (Turkey) and BaŞkent University School of Medicine (Konya, Turkey) reported on a study of the effectiveness of PET/ CT imaging in staging malignant melanoma. The retrospective study included the records of 139 patients (79 women, 60 men) who underwent PET/CT imaging to identify metastasis before treatment. Variables assessed included Breslow thickness, Clark level, number of mitoses and ulceration reported in pathologic findings, and presence of lymph nodes and/or distant metastases on PET/CT. Patients with a Breslow thickness >3.4 mm and Clark level of 4-5 were found to have significantly more regional lymph node metastases after PET/CT imaging. Those with Breslow thickness >2.85 mm and Clark level of 4-5 had significantly more distant metastases after PET/CT. The authors concluded that these results "suggest that PET/CT imaging for metastasis scanning, starting with T2 patients, may be used in malignant melanoma staging to reduce the need for sentinel lymph node biopsy and lymph node dissection."

Dermatologic Therapy

SPECT/CT After Total Ankle Replacement

Gurbani et al. from the University of California Los Angeles, the Hospital for Special Surgery (New York, NY), and Lenox Hill Hospital (New York, NY) reported on March 10 ahead of print in Foot and Ankle International on a study assessing the utility of SPECT/CT in evaluation of pain after total ankle replacement, including comparison with MR imaging in this setting. The retrospective study included 37 patients with painful total ankle replacement, all of whom underwent SPECT/CT imaging, 19 of whom underwent MR imaging, and 28 of whom underwent revision surgery. SPECT/CT results were consistent with the final documented diagnosis in 33 patients (89.2%). The most frequent final diagnoses were aseptic loosening (12 patients) and impingement (11 patients). SPECT/CT results in the 28 patients who underwent revision surgery were consistent with intraoperative findings in 26 (92.9%). For the 19 patients who underwent MR imaging, findings were consistent with clinical findings in only 3 patients

(36.8%). The authors concluded that SPECT/CT findings were highly consistent with documented clinical diagnoses and intraoperative findings and that "compared with MRI, SPECT/CT proved more useful in establishing a diagnosis of pain after total ankle replacement."

Foot and Ankle International

Loading Protocols in ¹⁸F-FDG PET Cardiac Viability Studies

In an article e-published on February 27 in the World Journal of Nuclear Medicine, Sarikaya et al. from Kuwait University (Kuwait City) and Trakya University (Edirne, Turkey) reported on research designed to assess whether oral glucose and intravenous loading protocols can affect ¹⁸F-FDG uptake in the hibernating myocardium in PET cardiac viability studies. The retrospective analysis included 49 patients who underwent such studies. Variables assessed included fasting blood glucose, amount of glucose given, blood glucose level after glucose load, amount of insulin given, and blood glucose level at the time of ¹⁸F-FDG injection. The authors compared these variables in PET-viable (31 patients) and PET-nonviable (18 patients) groups, as well as in subgroups to assess 18F-FDG uptake in normal myocardium. In 22 patients (most in the PET-viable group), varying degrees of reduced ¹⁸F-FDG uptake were noted in normal myocardium. No significant differences in the 2 groups were noted in the other variables assessed. Problems in oral glucose and intravenous insulin loading protocols included decisions on the amounts of glucose and insulin and the maximum amount of insulin to be given, managing diabetic patients, identifying optimal time to measure blood glucose after insulin administration, and interpretation of findings in patients with diffusely reduced ¹⁸F-FDG uptake. The authors concluded that "further improvements in current guidelines are necessary to obtain images in optimal conditions for accurate results."

World Journal of Nuclear Medicine

Detecting Early Amyloid in Cognitively Normal Adults

Guo et al. from the University of California (Berkeley) and the Lawrence Berkeley National Laboratory (CA) reported on March 18 ahead of print in Neurology on a study assessing the feasibility of cross-sectional ¹⁸F-florbetapir PET to identify increased risk of early cognitive decline among β-amyloid (Aβ)-negative cognitively normal elderly adults. The study included 354 cognitively normal elderly adults from the Alzheimer's Disease Neuroimaging Initiative who underwent ¹⁸F-florbetapir PET imaging. The highest AB-affected region was in the banks of the superior temporal sulcus, as determined by ranking baseline and accumulation rates of tracer regions. Subsequent analyses were used to categorize patients as stage 0 (191 patients), 1 (64 patients), or 2 (99 patients). Longitudinal cognitive change was assessed using linear mixed-effect models over more than 4 y, and ¹⁸F-flortaucipir PET was repeated at 4.8 ± 1.6 y to track tau deposition. Over the follow-up, the linear mixed-effect models indicated that individuals in stages 1 and 2 experienced 2.5 and 4.8 times, respectively, the rate of memory decline than individuals in stage 0. Assignment to stages 1 and 2 also predicted higher tracer uptake in the entorhinal cortex on PET. The authors concluded that nominally ABnegative/cognitively normal individuals with high AB in the banks of the superior temporal sulcus are at "increased risk of cognitive decline, probably showing an earlier stage of AB deposition" and that these findings "may help elucidate the association between brain AB accumulation and cognition in AB- cognitively normal cohorts."

Neurology

"Ready-to-Use" ⁶⁸Ga-DOTATOC for Injection

In an article in the March issue of *ESMO Open*, Manoharan et al. from the ENETS Center of Excellence (Manchester and London, UK), the University of Manchester (UK), and

Advanced Accelerator Applications (New York, NY) reported on the safety, tolerability, and feasibility of clinical use of a 68Ga-DOTATOC formulation for injection (SomaKIT TOC) for PET/CT imaging in patients with gastroenteropancreatic neuroendocrine tumors (GEP NETs). The study included a first-in-human phase I/II multicenter, open-label study of a single dose of the kit-prepared ⁶⁸Ga-DOTATOC in patients with biopsy-proven grade 1-2 GEP NETs. PET/CT imaging was performed after injection, and patients were followed for 4 weeks. Additional assessment of the new synthesis methodology in the clinical setting was performed over 11 mo. The study included 20 patients (14 men, 6 women; mean age, 58 y). Fourteen had grade 1 disease and 6 had grade 3 disease, with a total of 15 assessed as having stage IV disease. Although 12 patients experienced at least 1 adverse event during the study, no grade 3 or 4 toxicities were noted. Two adverse events were classified as possibly (headache, nausea) and 2 as probably (dysgeusia, paraesthesia) associated with the injection. Over the course of the 11-mo

clinical use of the kit, 113 vials of ⁶⁸Ga-DOTATOC were synthesized, and only 2 (1.77%) were rejected. The authors concluded that the SomaKIT TOC for injection was safe and well tolerated and noted that this finding has led to European Medicines Agency licensing for the use of this kit for PET imaging in patients with NETs.

ESMO Open

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 February and March. In an article published online on March 19 ahead of print in Current Opinion in Oncology, Hadavand et al. from the University of Maryland School of Medicine and Veterans Health Administration Research and Development Service (both in Baltimore, MD) reviewed the "Role of metabolic imaging in diagnosis of primary, metastatic, and recurrent prostate cancer." Chen and Kantarci, from

the West China Hospital of Sichuan University (Chengdu) and the Mayo Clinic (Rochester, NY), respectively, detailed "Imaging biomarkers for neurodegeneration in presymptomatic familial frontotemporal lobar degeneration" on February 28 in Frontiers in Neurology (2020;11:80). Buffet et al. from the Sorbonne University (Paris, France), the Universidade Federal do Rio de Janeiro (Brazil), the Institut Gustave Roussy (Villejuif, France), and the Hôpital Cochin (Paris, France) summarized strategies for "Redifferentiation of radioiodine-refractory thyroid cancers" on March 1 ahead of print in Endocrine Related Cancer. In an article e-published on March 5 ahead of print in Life Sciences, Gu et al. from the Shengjiang Hospital of China Medical University looked at "Preclinical in vivo imaging for brown adipose tissue." A review of "Nonprostatic diseases on PSMA PET imaging: A spectrum of benign and malignant findings," was published by de Galiza Barbosa et al. from the Hospital Sirio-Libanes (Sao Paulo, Brazil) on March 14 in Cancer Imaging (2020;20[1]:23).