

a part of a fusion or hybrid modality imaging study. SNMMI worked with the American Registry of Radiologic Technologists (ARRT), American Society of Radiologic Technologists, and the Nuclear Medicine Technology Certification Board (NMTCB) to formulate and propose new language that establishes and clarifies the qualifications needed for nuclear medicine technologists who perform standalone diagnostic CT exams. The comments letter, signed by April Mann, MBA, CNMT, NCT, RT(N), president of the SNMMI Technologist Section, included 3 recommended alternative standards for individuals who perform these exams. These include certification and registration in CT by the ARRT or active certification in CT by the NMTCB. A third alternative “grandfathering provision” would apply to those individuals with “no eligibility pathway to earning CT certification due to not having graduated from an accredited educational program in radiography, nuclear medicine technology, or radiation therapy” and would require specific doc-

umentation and standards to be supplied by the employing hospital. The letter also contained suggested steps for clarifying language on technologist certification. The complete text of the letter is available at: http://www.snmmi.org/files/FileDownloads/SNMMI%20Letter%20to%20The%20Joint%20Commission%20-%202013-9-2015_FINAL.pdf.

SNMMI

Varmus Steps Down at NCI

The National Institutes of Health (NIH) announced on March 4 that Harold Varmus, MD, who had led the National Cancer Institute (NCI) for almost 5 would step down from his post as director, effective March 31. “It has been our great fortune to have Harold at the helm of the NCI,” said NIH Director Francis S. Collins, MD, PhD. “His breadth and depth of expertise in biomedical research is unparalleled, and he’s been a tremendous colleague to me and invaluable to the agency.” Douglas Lowy, MD, who previously served as NCI deputy director, became acting director on April 1. He is

a long-time NCI intramural researcher and received the National Medal of Technology and Innovation in 2014 for his research leading to development of the human papillomavirus vaccine.

As NCI director, Varmus instituted the Provocative Questions initiative, created NCI’s new Center for Global Health, revitalized the cooperative clinical trials system, launched an initiative to identify drugs that target the cell signaling pathway controlled by the RAS oncogene, led the cancer component of the Precision Medicine Initiative, and continued to make contributions to biomedical research. Varmus has maintained a long-standing association with NIH, dating back to 1968, when, as a young Public Health Service officer, he studied bacterial gene expression with Ira Pastan, MD, currently chief of NCI’s Laboratory of Molecular Biology.

For more information, including Varmus’s letter to NCI staff, see: <http://www.cancer.gov/aboutnci/director/messages/harold-varmus-resignation>.

National Institutes of Health

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 in Multiple Myeloma Treatment

In an article e-published on March 6 ahead of print in *Biology of Blood and Marrow Transplantation*, Patriarca et al. from the University of Udine (Italy) and a consortium of researchers from 6 other Italian research centers reported on the ability of ¹⁸F-FDG PET/CT to provide prognostic information and monitor treatment in patients with multiple myeloma undergoing allogeneic stem cell transplantation. The study included 54 patients after upfront autologous stem cell transplantation who underwent PET/CT before and/or 6 mo after allogeneic transplantation, either as consolidation or salvage treatment. Twenty-two patients (41%) had negative imaging

results at transplantation, 11 (20%) had 1–3 focal lesions, and 21 (39%) had either diffuse bone marrow involvement or >3 focal lesions. Extramedullary disease was seen in 6 patients (11%) and maximum standardized uptake value (SUV) was >4.2 in 21 (39%). Analysis of results showed that persistence of extramedullary disease at allogeneic transplantation was an independent predictor of poor progression-free survival and that SUV > 4.2 and unrelated donor status were factors that negatively affected overall survival. For posttransplant imaging, persistence of extramedullary disease and failure to reach a complete or very good partial response were associated with shorter progression-free and overall survival. Forty-six patients

had both pre- and posttransplantation PET/CT scans. Of these the 23 who maintained or attained complete remission on imaging showed significantly longer 2-y progression-free survival than those who did not (51% and 25%, respectively; 81% and 47%, respectively, for overall survival). The authors concluded that these results suggest that “PET/CT imaging before and after allogeneic stem cell transplantation is significantly associated with the outcome, suggesting the utility of this technique for multiple myeloma staging before allogeneic stem cell transplantation and for response monitoring after the transplantation.”

Biology of Blood and Marrow Transplantation

Octreoscan vs ^{18}F -FDG PET in NET Staging

Squires et al. from Emory University (Atlanta) reported ahead of print in the March 19 issue of the *Annals of Surgical Oncology* on a study comparing the sensitivity of ^{111}In -DTPA-octreotide (OctreoScan) scintigraphy with that of ^{18}F -FDG PET imaging in patients with neuroendocrine tumors (NETs), with pathologic correlation to identify the optimal approach to NET staging after conventional cross-sectional imaging. The study included 153 patients with NETs of gastrointestinal or pancreatic origin, of whom 131 underwent scintigraphy, 43 underwent PET, and 21 underwent imaging with both modalities. For all NETs, the sensitivity of Octreoscan and PET for NET detection was not significantly different (77% and 72%, respectively). When pathology results were included in the analysis, the modalities showed significant differences. Octreoscan had better sensitivity (80%) than PET (60%) in well-differentiated NETs, whereas PET had better sensitivity (100%) than Octreoscan (57%) in patients with poorly differentiated NETs. These comparative sensitivities were constant when results were analyzed using World Health Organization tumor grading. The authors concluded that these results suggest that pathology can be beneficially used to

inform imaging choices in this setting, noting that “tumor differentiation can be used to guide selection of nuclear imaging modalities for staging gastrointestinal and pancreatic NETs.”

Annals of Surgical Oncology

Octreotide, ^{123}I -MIBG, and Genetics in Paragangliomas

In an article e-published on March 13 ahead of print in *Neuroendocrinology*, Michalowska et al. from the Institute of Cardiology (Warsaw, Poland) reported on a study investigating the varying sensitivities of somatostatin receptor scintigraphy (SRS) using $^{99\text{m}}\text{Tc}$ -[HYNIC, Tyr3]-octreotide and of ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) imaging in patients and relatives with SDHx-related syndromes in whom paragangliomas had been detected by CT. The study included 46 individuals who were SDHx gene mutation carriers, all of whom underwent both SRS and ^{123}I -MIBG imaging. A total of 102 benign tumors were identified in 39 patients, and 7 patients were diagnosed with malignant disease (sensitivity for benign tumors: SRS = 77%, ^{123}I -MIBG = 22%). The sensitivity of the 2 imaging approaches was highly dependent on area and type of lesion. SRS was most sensitive in the head and neck (91.4%) and least sensitive in abdominal paragangliomas and pheochromocytomas (40% and 42.9%, respectively). ^{123}I -MIBG was most sensitive in pheochromocytomas (100%) and least sensitive in the head and neck (3.7%). For metastatic disease, the sensitivity of SRS was significantly greater than that of ^{123}I -MIBG (95.2% and 23.8%, respectively).

Neuroendocrinology

^{18}F -FLT PET/CT in Brain Mets from Breast Cancer

Bates et al. from the National Institutes of Health (Bethesda, MD) reported in a March supplement to the *Annals of Oncology* (2015;26 suppl 2: ii20) on a study evaluating the utility of ^{18}F -3'-fluoro-3'-deoxythymidine (^{18}F -FLT) PET/CT in assessing the

effectiveness of a novel paclitaxel-containing agent designed to cross the blood-brain barrier in treatment of taxane-sensitive brain metastases. The study include 8 patients with 18 measurable brain lesions metastasized from breast cancer who underwent ^{18}F -FLT PET/CT before and after 1 cycle of therapy. Gadolinium-based MR imaging assessed clinical response. Maximum standardized uptake value (SUV_{max}) ranged from 0.8 to 4.0 at baseline, with a mean of 1.8. Tumor-to-normal tissue ratios ranged from 2.9 to 3.3, with a mean of 7.7. Of the 18 lesions, 12 showed >20% decreases in SUV_{max} after therapy (the level deemed to constitute significant change), with an overall average decrease in SUV_{max} of 24.8% and an overall decrease in tumor-to-normal tissue ratios of 7.7%. Response assessments on ^{18}F -FLT PET and MR were in frequent disagreement. Two patients experienced partial responses with durations of response of 6 and 13 cycles, and one had an unconfirmed partial response, with progression after 6 cycles. Two patients had stable disease after undergoing 6 and 8 treatment cycles. The authors concluded that ^{18}F -FLT PET is a promising tool for detection and measurement of central nervous system disease, particularly in the challenging setting of metastases from breast cancer.

Annals of Oncology

Myocardial ^{123}I -MIBG, DLB, and AD

In an article published in the March 20 issue of *PLoS One* (2015;10: e0120540), Yoshita, from the Kanazawa University Graduate School of Medical Science (Japan), and a large consortium of researchers from other Japanese research centers reported on a study of the diagnostic accuracy of ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) myocardial scintigraphy in differentiation of dementia with Lewy bodies (DLB) from Alzheimer disease (AD). The study included 133 patients with clinical diagnoses of probable ($n = 61$) or possible ($n = 26$) DLB or probable AD ($n = 46$), all of whom

underwent ^{123}I -MIBG myocardial scintigraphy. Images were categorized by imaging specialists as normal or abnormal, and heart-to-mediastinum ratios of tracer uptake were calculated using an automated system. Use of heart-to-mediastinum ratio cutoffs resulted in sensitivity and specificity of 68.9% and 89.1%, respectively, in differentiating probable DLB from probable AD. Expert assessment of images resulted in similar sensitivity and specificity of 68.9% and 87.0%, respectively. Use of the delayed heart-to-mediastinum ratio resulted in sensitivity and specificity of 77.4% and 93.8%, respectively, in a subpopulation of individuals with mild dementia. These results confirmed the association of abnormal cardiac sympathetic activity and DLB and the ability of ^{123}I -MIBG myocardial scintigraphy to differentiate between DLB and AD. The authors concluded that “the diagnostic accuracy is sufficiently high for this technique to be clinically useful in distinguishing DLB from AD, especially in patients with mild dementia.”

PLoS One

Serial Imaging During HNSCC Treatment

Subesunghe et al. from St. James' University Hospital (Leeds, UK) reported in March in *BMC Cancer* (2015;15:1154) on a pilot study designed to assess the treatment implications of serial changes in ^{18}F -FDG PET/CT and MR imaging during therapy for head and neck squamous cell carcinoma (HNSCC). The study included 8 patients with locally advanced HNSCC who underwent CT, PET/CT, and diffusion-weighted and dynamic contrast-enhanced MR imaging at baseline and twice during radiation therapy (after fractions 11 and 21). Parameters assessed included gross tumor volume, maximum standardized uptake value (SUV_{max}), and mean apparent diffusion coefficient and other MR values, with changes at serial time points analyzed. Significant decreases in gross tumor volume as assessed by CT, MR, and diffusion-weighted MR were seen

from baseline to final imaging, with corresponding changes on PET not reaching the level of statistical significance. The researchers noted significant changes in SUV_{max} and mean apparent diffusion coefficient value and other MR values between baseline imaging and imaging after fraction 11. The significance of these changes persisted to the fraction 21 timepoint only in SUV_{max} . Across the range of imaging modalities, numerous anatomic and functional correlations were observed over the 3 timepoints, with the most significant occurring between baseline and fraction 11 and between baseline and fraction 21, with fewer between fractions 11 and 21. The authors concluded that “all functional imaging modalities are potentially complementary and should be considered in combination to provide multiparametric tumor assessment, to guide potential treatment adaptation strategies.”

BMC Cancer

^{177}Lu -mAb Radioimmunotherapy in Prostate Cancer

In an article e-published on March 13 ahead of print in *Current Radiopharmaceuticals*, Vallabhajosula et al. from Weill Cornell Medical College (New York, NY) reviewed the methodology and results of 5 phase I and II studies using ^{177}Lu -DOTA-huJ591, an anti-prostate-specific membrane antigen monoclonal antibody, as radioimmunotherapy in men with metastatic castrate-resistant prostate cancer. The methodology and the results of these clinical studies were briefly reviewed. Across these studies, the maximum tolerated single dose was 70 mCi/m^2 , with maximum tolerated fractionated dose of 90 mCi/m^2 ($2 \times 45 \text{ mCi}/\text{m}^2$ at a 2-wk interval). In the phase II study, a dose of 65–70 mCi/m^2 resulted in significant decreases in prostate-specific antigen in 60% of patients. Dose fractionation (either with ^{177}Lu -DOTA-huJ591 alone or in combination with docetaxel) resulted in significant prostate-specific antigen decreases with markedly lower toxic-

ity rates. Imaging with ^{177}Lu verified accurate targeting of metastatic sites in >90% of patients and correlated well with declines in prostate-specific antigen. The authors concluded that “these clinical studies clearly documented the potential therapeutic value of radioimmunotherapy in metastatic prostate cancer.”

Current Radiopharmaceuticals

PET/CT Prognosis in Liver Transplantation

Detry et al. from the Centre Hospitalier Universitaire Liège (Belgium) reported on March 14 in the *World Journal of Gastroenterology* (2015;21:3049–3054) on a study assessing the prognostic utility of preoperative ^{18}F -FDG PET/CT in patients with hepatocarcinoma treated with liver transplantation. The retrospective study included the records of 27 patients who underwent routine ^{18}F -FDG PET/CT before transplantation. Maximum and mean standardized uptake values (SUV_{max} and SUV_{mean} , respectively) in tumor and normal liver and tumor-to-liver activity ratios were assessed as prognostic factors. These were compared against several currently applied standard sets of prognostic criteria in liver transplantation as well as against a number of clinical and pathologic factors in each patient. In this small patient group, overall survival was 80.7% at 3 y and recurrence-free survival was 67.4% at 3 y. Corresponding percentages at 5 y were 70.6% and 67.4%. Out of the numerous variables assessed only PET/CT tumor/liver SUV_{max} with a cutoff value of 1.15 accurately predicted recurrence-free survival. On the basis of this finding, the authors noted that “further prospective studies should test whether this metabolic index should be systematically included in the preoperative assessment.”

World Journal of Gastroenterology

^{111}In -Amatuximab in Mesothelin-Expressing Cancers

In an article in the February 28 issue of *Oncotarget* (2015;6:4496–4504)

Lindenberg et al. from the National Cancer Institute (Bethesda and Frederick, MD), Johns Hopkins University (Baltimore, MD), the National Institutes of Health Clinical Center (Bethesda, MD), and Morphotek (Exton, PA) reported on studies characterizing the biodistribution and dosimetry of ^{111}In -amatuximab, a chimeric high-affinity monoclonal IgG1/k antibody targeting mesothelin. The study included 6 patients, 4 with malignant mesothelioma and 2 with pancreatic adenocarcinoma, all of whom underwent SPECT/CT imaging at 3 time points (2–4, 24–48, and 96–168 h) after ^{111}In -amatuximab injection. Results from all patients showed that tumor-to-background ratios met or exceeded targeted uptake values, with ratios significantly higher in tumors in patients with mesothelioma than in those with pancreatic adenocarcinoma. Uptake was visualized in primary tumors and in metastatic sites. Administration of the tracer was generally well tolerated, with physiologic uptake in heart, liver, kidneys, and spleen. The authors described this as the “first study to show tumor localization of an anti-mesothelin antibody in humans,” with results that supported additional investigations.

Oncotarget

Management of Incidental Colon Uptake on PET/CT

Na et al. from the Jeju National University Hospital (Korea) reported on March 11 ahead of print in the *Scandinavian Journal of Gastroenterology* on a study designed to provide data guiding selection of patients for colonoscopy after incidental colon uptake on PET/CT. The study included the records of 306 patients, all of whom underwent

colonoscopy within 3 mo of undergoing PET/CT. The resulting per-patient and per-lesion PET/CT sensitivities for detection of malignancies were 93.3% and 93.5%, respectively, with a 90.0% sensitivity for both assessments in high-grade dysplasia. A maximum standardized uptake value ($\text{SUV}_{\text{max}} \geq 2.5$) yielded a 92.3% per-lesion sensitivity and a 42.9% per-lesion positive predictive value (PPV). In additional analyses, a cut-off value of $\text{SUV}_{\text{max}} = 5.8$ was established, at which the sensitivity, PPV, and positive likelihood ratio for diagnosing malignancy and high-grade dysplasia were 71.8%, 84.8%, and 6.9, respectively. The authors concluded that in patients in whom incidental colon uptake was noted on PET/CT, although optimal cutoff values were identified at $\text{SUV}_{\text{max}} = 5.8$, “to avoid missing a malignancy or high-grade dysplasia, a colonoscopy should be performed above a $\text{SUV}_{\text{max}} = 2.5$.”

Scandinavian Journal of Gastroenterology

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches by offering valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in March 2015. In an article e-published on March 11 ahead of print in *Progress in Cardiovascular Diseases*, Taqueti and DiCarli from the Brigham and Women’s Hospital/Harvard Medical School (Boston, MA) provided an overview of “Radionuclide myocardial perfusion imaging for the evaluation of patients with known or suspected coronary artery disease in the era of multimodality cardiovascular imaging.”

Fasano, from Toronto Western Hospital (Ontario, Canada) and colleagues from Tel Aviv Sourasky Medical Center (Israel), Second University of Naples (Italy), and the University of Michigan (Ann Arbor) described the current status of “Neuroimaging of freezing of gait” on March 10 ahead of print in the *Journal of Parkinson’s Disease*. In an article e-published on March 13 ahead of print in *Current Radiopharmaceuticals*, Das and Banerjee from the Bhabha Atomic Research Centre (Mumbai, India) reviewed “Theranostic applications of lutetium-177 in radionuclide therapy.” Rudroff et al. from Colorado State University (Fort Collins) and the University of Turku (Finland) looked at “ ^{18}F -FDG positron emission tomography: an established clinical tool opening a new window into exercise physiology” as an introduction to articles appearing on March 12 ahead of print in the *Journal of Applied Physiology*. In an article published in the May issue of *Current Urology Reports*, Hughes and Nix from the University of Alabama at Birmingham described the “Role of sodium fluoride PET imaging for identification of bony metastases in prostate cancer patients.” Barthel et al. from Leipzig University (Germany) summarized “The role of positron emission tomography imaging in understanding Alzheimer’s disease” on March 9 ahead of print in *Expert Review of Neurotherapeutics*. In the March 12 issue of *Cardiology* (2015;130:211–220) Kundu et al. from the University of Virginia (Charlottesville) published “Remodeling of glucose metabolism precedes pressure overload-induced left ventricular hypertrophy: review of a hypothesis.”