agency and the nation," said Jaczko. "They bring exceptional backgrounds and talents to the NRC. Their insights and experience will strengthen our decision making and help us to continue to meet our critical mission to protect public health, safety, and the environment."

Nuclear Regulatory Commission

Joint Workshop on Imaging Standardization

The U.S. Food and Drug Administration (FDA), SNM, and the Radiological Society of North America (RSNA) hosted a joint 2-topic workshop on April 13 and 14 at the Natcher Conference Center of the National Institutes of Health (Bethesda, MD). The goal of the meeting was to generate discussion on the use of imaging for assessing endpoints in clinical trials. Participants came from academia, industry, and regulatory groups. The first day of the workshop focused on general issues of standardization to control variability and inconsistency in methods of acquisition, interpretation, and analysis of images in clinical trials. The second day included an interactive tutorial on ways to address FDA regulatory expectations for PET drugs, particularly with respect to recently issued regulations establishing Current Good Manufacturing Practice (CGMP).

"This workshop offers a unique opportunity to work with the imaging community to help optimize the role of imaging in public health," said Dwaine Rieves, MD, director of the Division of Medical Imaging Products in the FDA's Center for Drug Evaluation and Research.

"We are delighted to partner with the FDA and RSNA to bring the molecular imaging community together on the important transition to the new regulations," said Michael M. Graham, PhD, MD, president of SNM. "The PET community remains very focused on preparing to comply with these regulations and is committed to working together to ensure a smooth transition."

The FDA published a final regulation on CGMP for the production of PET drugs in December 2009. The new regulations (21 CFR Part 212) take effect on December 12, 2011. All PET drug manufacturers will be required to submit a new or abbreviated drug application for PET drugs in commercial/clinical use by that date. In the interim, U.S. facilities must continue to comply with USP General Chapter <823>, which sets standards for the production of PET drugs.

The agenda, supporting documentation, and many of the workshop PowerPoint presentations are available at: www.rsna.org/snm/index.htm.

Society of Nuclear Medicine
Radiological Society of North America

PET/CT H&N Cancer Staging Trial

The American College of Radiology Imaging Network (ACRIN) recently activated "A Multicenter Trial of FDG-PET/CT Staging of Head and Neck Cancer and its Impact on the N0 Neck Surgical Treatment in Head and Neck Cancer Patient" (ACRIN 6685). Led by Val Lowe, MD, professor of radiology, Division of Nuclear Medicine, at Mayo Clinic (Rochester, MN), the trial's primary aims are to determine the predictive value of PET/CT for staging the clinically defined negative neck based on pathologic sampling of the neck lymph nodes and to determine the potential of PET/CT to change patient management in this setting.

Participants with newly diagnosed head and neck squamous cell carcinoma will undergo a PET/CT scan before surgical resection. The surgeon will have access to the PET/CT results before the surgical procedure. Resulting data will demonstrate the effect of PET/CT on determination of extent of disease, disease characterization and prognosis, and changes in surgical plan from plans originally devised from clinical nodal assessment and CT or MR imaging. Quality of life assessments and cost effectiveness analyses will be included in the study to determine the impact of PET/CT in treatment of the N0 neck.

The study is expected to confirm that ^{18}F-FDG PET/CT imaging improves characterization of the N0 neck by accurately diagnosing disease, better defining extent of primary disease, discovering unappreciated distant metastases, reducing morbidity, and representing value to society. Up to 15 participating sites are expected to accrue 292 study participants in approximately 2 y. Additional details are available at: http://clinicaltrials.gov/ct2/show/NCT00983697 and by contacting the project manager at imahon@acr-arrs.org.

American College of Radiology Imaging Network

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. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. The lines between di-

agnosis 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.

DIAGNOSIS

Intraoperative PET/CT Image Fusion

Feichtinger et al. from the Medical University of Graz (Austria) reported on April 6 ahead of print in the *Journal of Cranio-maxillo-facial Surgery* on a new method of assessing head and neck cancer resection margins intraoperatively using 3D image-guided surgery based on PET/CT image fusion. The study included 6 patients with head and neck stage T4a and/or T4b carcinomas who were scheduled for surgery. Each patient underwent PET/CT imaging, and intraoperative image-guided navigation based on this information was performed to identify remnant tumor immediately after initial resection. An unsafe resection margin was noted in 4 patients. In 3 of these patients additional image-guided resection was possible and resulted in local control of the target tumor. Additional resection was not possible in the fourth patient. Histopathology in these "corrected" resections confirmed positive or close resection margins. The authors concluded that these results suggest "that intraoperative control of the surgical margins using a 3D-navigation system based on PET/CT image fusion can be a useful tool to assess and improve local control in advanced cancer of the head and neck."

Journal of Cranio-maxillo-facial Surgery

D_2 Receptors and Bariatric Surgery

In an article e-published on March 31 ahead of print in *Brain Research*, Dunn, from Vanderbilt University School of Medicine (Nashville, TN), and a consortium of other researchers reported on findings of decreased dopamine type 2 (D_2) receptor availability after bariatric surgery. The authors hypothesized that dopaminergic neurotransmission would be enhanced after Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) procedures and that this enhancement was likely to contribute to positive outcomes after bariatric surgery. The study included 5 obese women who underwent PET with a D_2 receptor radioligand that was sensitive to competition with endogenous dopamine. Patients were imaged preoperatively and at ~7 wk after RYGB or VSG surgery. Regions of interest previously found to be relevant to eating behaviors were delineated, and fasting enteroendocrine hormones were quantified at each imaging procedure. The authors found that body weight decreased at a normal rate after the bariatric procedures, and that D_2 receptor availability decreased in parallel. Regional decreases in D_2 receptor availability (expressed as mean ± standard error of the mean) included: caudate, 10% ± 3%; putamen, 9% ± 4%; ventral striatum, 8% ± 4%; hypothalamus, 9% ± 3%; substantia nigra, 10% ± 2%; medial thalamus, 8% ± 2%; and amygdale, 9% ± 3%. Significant decreases in plasma insulin (62%) and leptin (41%) were also noted. The authors concluded that decreases in D_2 receptor availability after RYGB and VSG "most likely reflect increases in extracellular dopamine levels" and that "enhanced dopaminergic neurotransmission may contribute to improved eating behavior (e.g., reduced hunger and improved satiety) following these bariatric procedures."

Brain Research

BP and Chest Pain in Stress Tests

Ditto et al. from McGill University (Montreal, Canada) reported on April 9 ahead of print in *Pain* on a study evaluating the relationship between resting blood pressure and pain/angina in patients undergoing exercise stress testing for coronary artery disease. The study included stress testing results in 904 individuals, and the presence or absence of ischemia was documented by SPECT imaging. Participants with ischemia were found to have higher scores on the McGill Pain Questionnaire after exercise, although these scores were found to moderate significantly with higher diastolic blood pressure readings, especially in women. Individuals with higher pre-exercise resting diastolic blood pressures in whom SPECT diagnosed ischemia were found to have pain questionnaire scores comparable to individuals with no ischemia, a finding that was independent of age, exercise duration, medication, and/or cardiac history. The authors concluded that "awareness of the potential association between blood pressure and angina may provide patients with coronary artery disease and their physicians important guidance."

Pain

BNP Levels and SPECT

In an article e-published on April 12 ahead of print in *Cardiology Research and Practice*, Sir et al. from Inje University College of Medicine (Busan, South Korea) reported on a study designed to evaluate whether B-type natriuretic peptide (BNP) levels add value to SPECT findings in patients with normal left ventricular (LV) systolic function. The study included data from 224 patients who underwent rest ^{201}Tl-dipyridamole stress/^{99m}Tc-sestamibi-gated SPECT and coronary angiography because of chest pain. Patients with true-positive SPECT findings had significantly higher BNP levels than those with false-positive defects. Patients with true-negative SPECT also showed significantly lower BNP levels than those with false-negative SPECT. An elevated BNP level (cutoff value of 23.0 pg/mL) was found to be both an independent and the strongest predictor of coronary artery disease over all

patients and in those with positive SPECT. The authors concluded that these results suggest "that BNP level has additive diagnostic value to SPECT findings in predicting coronary artery disease in patients with normal LV systolic function."

Cardiology Research and Practice

^{18}F-FDG Imaging of the Coronary Arteries

Rogers et al. from the Massachusetts General Hospital and Harvard Medical School (Boston, MA) reported in the April issue of *JACC. Cardiovascular Imaging* (2010;3:388–397) on a study testing the hypothesis that ^{18}F-FDG uptake on PET in the ascending aorta and left main coronary artery (LM) would be greater in patients with recent acute coronary syndrome (ACS) than in those with stable angina. The study included 25 patients (18 men, 7 women; mean age, 57.9 ± 9.8 y; 10 with ACS and 15 with stable angina) who underwent cardiac CT angiography and ^{18}F-FDG PET imaging after conventional angiography. PET and CT images were coregistered, and tracer uptake was measured at locations of interest to calculate target-to-background ratios (TBRs). Uptake was also measured at the site of the lesion identified as clinically responsible for the presenting syndrome (culprit) and at which the stent was deployed to treat the syndrome. ^{18}F-FDG uptake was found to be higher in the ascending aorta and the LM in patients with ACS than in those with stable angina. TBRs were greater for culprit lesions associated with ACS than for lesions stented for stable coronary syndromes. TBRs in stented lesions (in both ACS and stable angina) were found to be correlated with C-reactive protein levels. The authors concluded that the observation that ^{18}F-FDG accumulation is increased both within the culprit lesion and the ascending aorta and LM in patients with recent ACS suggests "inflammatory activity within atherosclerotic plaques in acute coronary syndromes and supports intensification of efforts to refine PET methods for molecular imaging of coronary plaques."

JACC. Cardiovascular Imaging

Brown Fat and Age

In an article e-published on March 31 ahead of print in *Diabetes*, Pfannenberg et al. from the University of Tübingen (Germany) investigated the hypothesis that because brown adipose tissue (BAT) mass and activity decrease with age in humans, that the effect of BAT in regulating energy homeostasis and fat mass may decline as well. As part of the study they also evaluated whether such changes are different in men and women. The study included data from 260 individuals (98 with BAT; 162 controls) who underwent ^{18}F-FDG PET/CT under thermoneutral conditions to determine BAT activity and mass in the upper body. BAT activity and mass were found to be higher in females than in males, and body mass index (BMI) was found to be independently associated with BAT activity. Only in males, however, were BMI and age together significantly related to BAT activity and mass. BMI decreased with increasing BAT activity and mass in the lowest but not in the higher male age groups. BAT activity and mass differed between females and males only in the upper 2 age groups. The authors concluded that these data "corroborate that, in general, BAT activity and BAT mass are elevated in females and in younger people" and provide "novel evidence that only in males the impact of BAT activity and BAT mass on adiposity appears to decline with aging" and that "with increasing age BAT activity and BAT mass merely moderately decline in females, a much stronger effect is found in males."

Diabetes

PET and Nanoparticles

In an article e-published on April 7 ahead of print in *Inhalation Toxicology*, Palko et al. from the University of California–Davis reported on a novel PET technique for investigating the biodistribution and transport of nanoparticles in a mouse model. The focus of the group's research is on the effects of particulate matter (PM) both in the lungs and in subsequent biodistribution outside the pulmonary system. Previous PM studies have tracked biodistribution of nanoparticles into animal models or humans using γ counting, γ cameras, and inductively coupled plasma mass spectrometry. The authors described the development of ^{64}Cu-labeled polystyrene nanoparticles bound with *p*-SCN-Bn-DOTA. PET imaging was used to track initial deposition and biodistribution of nanoparticles after intratracheal delivery into C57BL/6 mice. It was determined that particle deposition and clearance could be clearly tracked with PET and that the same animals could be imaged repeatedly. In addition to static imaging, dynamic imaging was performed in a Sprague-Dawley rat model to verify that PET could capture particle movement in "time lapse" video sequences. Based on these results, the authors concluded that "PET has the potential to require many fewer animals than traditional methods while still providing quantitative results" and that because initial deposition patterns can be determined and the same animal monitored over time "data interpretation is not clouded by variations in initial deposition profiles."

Inhalation Toxicology

Automatic Dispensing and Injection During PET

In an article e-published on April 11 ahead of print in *Radiation Protection Dosimetry*, Covens et al. from Vrije Universiteit Brussel and UZ Brussel (Belgium) reported on the effects of implementation of an automated ^{18}F-FDG dispensing and injection system on whole-body and extremity doses to nuclear medicine staff members. The authors described dosimetric studies using thermoluminescent and direction storage dosimetry conducted before and after the introduction of the system. The results

indicated that extremity doses to staff could be reduced by more than 95%, up to a mean level of 10 μSv per handled GBq. Whole-body doses could be halved during tracer injection. The cumulative dose reduction over the entire process of injection, escorting, and positioning could be 20% with automated dispensing and injection, which the authors term "a considerable staff dose reduction."

Radiation Protection Dosimetry

THERAPY

Protective Nanoparticles for Radiation Therapy

Schweitzer and researchers from the Albert Einstein College of Medicine (Bronx, NY), the Howard Hughes Medical Institute (Chevy Chase, MD), and the Mount Sinai School of Medicine (New York, NY) reported on April 24 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on the development of novel melanin-covered nanoparticles for protection of bone marrow against radiotoxicity during radiation therapy for cancer. The authors hypothesized that melanin, which is naturally occurring, radioprotective, and insoluble, could be delivered to the bone marrow by intravenously administered melanin-covered nanoparticles, using the human body's "self-sieving" ability. The development and synthesis of the nanoparticles, with 15-nm-thick melanin layers, was described. Initial biodistribution studies indicated that nanoparticle uptake in bone marrow was 0.3% and 0.2% of injected dose per gram at 3 and 24 h, respectively, and that preinjection with pluronic acid increased these respective uptakes to 6% and 3% of injected dose per gram. The nanoparticles were then injected intravenously into both healthy and melanoma tumor–bearing mice 3 h before either whole-body exposure to 125 cGy or treatment with 1 mCi of ^{188}Re-labeled 6D2 melanin-binding antibody. Systemic administration of the nanomolecules was found to reduce hematologic toxicity in mice treated with external radiation or with radioimmunotherapy, and no inhibition of radiation effect on tumors was noted. The authors concluded that melanin-covered nanoparticles or similar structures "provide a novel approach to protection of bone marrow from ionizing radiation based on prevention of free radical formation by melanin."

International Journal of Radiation Oncology, Biology, Physics

MOLECULAR IMAGING/ THERAPY

Evaluating Prion Deposits and Microglial Activation

Song et al. from INSERM (Tours, France) reported on April 8 ahead of print in *Molecular Imaging and Biology* on in vitro and ex vivo autoradiography studies in evaluation of microglial activation related to PrP amyloid fibril desposition in prion disease. The study was conducted first in frozen cerebral sections from scrapie-infected mice and controls, where accumulation of prion deposits was confirmed by histoblot staining with a prion protein–specific monoclonal antibody. These studies indicated that PrP deposits were colocalized with active microglia as early as 60 d after inoculation. Progressive levels of PrP and translocator protein staining were observed in the hippocampus, cortex, and left thalamus of infected mouse brain sections over the course of the disease and correlated with signals obtained by histoblot staining. Mice at the terminal stage of infection were killed, and ex vivo autoradiographic studies were conducted using ^{125}I-CLINDE and ^{125}I-IMPY. Significant translocator labeling was also observed ex vivo in the cortex, hippocampus, and thalamus of scrapie-infected mice. The authors concluded that these findings "indicate the ability of ^{125}I-CLINDE and ^{125}I-IMPY to evaluate prion deposits and microglial activation in vitro and ex vivo in scrapie-infected mice at different stages of the disease."

Molecular Imaging and Biology

Bombesin-Functionalized Gold Nanoparticles

Chanda et al. from the Harry S. Truman Veterans Affairs Medical Center and the University of Missouri (Columbia) reported on April 21 ahead of print in the *Proceedings of the National Academy of Sciences of the United States of America* on results of investigations synthesizing a library of gastrin-releasing peptide (GRP) receptor–avid nanoplatforms assembled by conjugating gold nanoparticles with bombesin peptides. Bombesin peptides have demonstrated high affinity in vivo toward GRP receptors that are overexpressed in prostate, breast, and small-cell lung carcinoma. The authors detailed studies verifying the cellular interactions and binding affinities of their conjugates toward GRP receptors on human prostate cancer cells. In vivo studies using radiolabeled bombesin-functionalized gold nanoparticles indicated that the conjugates were GRP receptor–specific and accumulated with high selectivity in GRP receptor–rich tumors in mice. Preclinical studies demonstrated "realistic clinical potential in molecular imaging via x-ray CT techniques." The authors observed that "Development of cancer receptor–specific gold nanoparticles will allow efficient targeting/optimum retention of engineered gold nanoparticles within tumors and thus provide synergistic advantages in oncology as it relates to molecular imaging and therapy."

Proceedings of the National Academy of Sciences of the United States of America

Imaging of Meningioma Progression

Agar et al. from the Brigham and Women's Hospital and Harvard Medical School (Boston, MA) reported in the April 1 issue of *Analytical Chem-*

istry (2010;82:2621–2625) on an approach to tissue characterization based on matrix-assisted laser desorption ionization time-of-flight mass spectrometry imaging (MSI), introduced in an attempt to develop a reference database for predictive classification and differentiation of meningiomas. The pilot study was conducted on 5 recurrent and progressive meningiomas for which surgical specimens were available from original and progressed grades. These were tested with the MSI technique and compared with results from nonprogressive high-grade meningiomas, high-grade gliomas, and nontumor brain specimens. The common profiling approach of data acquisition was compared with MSI results, which showed significant benefits in yielding spatially resolved acquisition for improved spectral definition. A preliminary classifier showed the ability to distinguish meningioma image spectra from nontumor brain and from gliomas and to enable class imaging of surgical tissue. The authors concluded that "although the development of classifiers was shown to be sensitive to data preparation parameters such as recalibration and peak picking criteria," these results also "suggested the potential for maturing into a predictive algorithm if provided with a larger series of well-defined cases."

Analytical Chemistry

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in late March and April. An entire issue of *Current Topics in Medicinal Chemistry*, which appeared online on April 13 before publication, focused on reviews of nuclear medicine topics, including "PET designated fluoride 18 production and chemistry," "C-11 radiochemistry in cancer imaging applications," "PET with nonstandard nuclides," "The medicinal chemistry of theragnostics, multimodality imaging, and applications of nanotechnology in cancer," and "Noninvasive cell tracking in cancer and cancer therapy." Other reviews of note included: "Nuclear imaging of autoimmunity: focus on IBD and RA" by McBride from Amgen, Inc. (Thousand Oaks, CA) published on April 14 ahead of print in *Autoimmunity*; "Imaging ovarian cancer and peritoneal metastases—current and emerging techniques," by Kyriazi et al. from the Institute of Cancer Research and Royal Marsden National Health Service Foundation Trust (Sutton, UK) published on April 14 ahead of print in *Nature Reviews. Clinical Oncology*; "Neuropathic pain and neuroplasticity in functional imaging studies" [in German] by Maihöfner et al. from the Neurologische Klinik der Universität Erlangen-Nürnberg (Germany) in the April issue of *Schmerz* (2010;24:137–145); "Studies on cerebral processing of pain using functional imaging : Somatosensory, emotional, cognitive, autonomic and motor aspects" [in German] by Valet et al. from the Technische Universität München (Germany) on pages 114–121 of the same issue of *Schmerz*; and "Emerging roles for multimodal optical imaging in early cancer detection: a global challenge," by Bedard et al. from Rice University (Houston, TX) in the April issue of *Technology in Cancer Research and Treatment* (2010;9: 211–217).

(Continued from page 13N)

the International Atomic Energy Agency (*7*); developed a Web-based interactive tool for calculation of doses from released patients (www.doseinfo-radar.com/ExposureCalculator.html), supported by several guidance and training documents; and completed research on a comparison of point, line, and realistic voxel-phantom representation of patients. The work has been submitted for publication.

(3) RADAR has developed a review manuscript on renal dosimetry for peptide receptor radionuclide therapy (PRRT), reviewing results and methods of several authors and recommending that the research community continue to gather data and proceed with more critical evaluation of different dosimetric quantities in the management of nephrotoxicity in PRRT.

(4) RADAR will present 2 continuing education sessions at the SNM Annual Meeting this month: "Dose Estimation and Reduction in PET/CT Imaging" and "New Internal Dose Models–Evaluation and Impact."

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