

Mammography Quality Program. OIR combines pre- and postmarket responsibilities into a single multidisciplinary office and also administers the Clinical Laboratory Improvement Amendments.

The OIR includes 6 divisions: Chemistry and Toxicology Devices, Immunology and Hematology Devices, Microbiology Devices, Radiological Health, Mammography and Quality Standards, and Program Operations and Management. Additional information is available at: www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHOffices/ucm115904.htm.

U.S. Food and Drug Administration

New Molecular Imaging Journal

On December 10 Springer (part of Springer Science + Business Media) announced the 2013 launch of a new bimonthly journal, *Clinical and Translational Imaging: Reviews in Nuclear Medicine and Molecular Imaging*, which will be the official publication of the Italian Association of Nuclear Medicine and Molecular Imaging (AIMN) as of 2013. Giovanni Lucignani, MD, editor-in-chief of the new journal and president of AIMN, said, "AIMN has long been committed to consistently raising the standard and impact of its scientific publications, and we now feel that the time has come to launch our own official journal."

Targeting nuclear medicine practitioners and other professionals involved in molecular imaging and therapy, this international peer-reviewed journal will publish timely and updated reviews, collected in single-themed issues, on clinical practice and translational research. It will also present clinical applications of approved and experimental radiopharmaceuticals for diagnostic and therapeutic purposes. Advanced preclinical evidence in the fields of physics, dosimetry, radiation biology, and radiopharmacy with relevance to clinical applications will also be included.

Springer Science + Business Media

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.

CHOP and RIT in Follicular NHL

Members of the Southwest Oncology Group (SWOG) and the Cancer and Leukemia Group B, both National Cancer Institute–sponsored clinical research networks, reported on December 10 ahead of print in the *Journal of Clinical Oncology* on results of a phase III randomized intergroup trial of

cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy plus rituximab compared with CHOP chemotherapy plus ¹³¹I-tositumomab for previously untreated follicular non-Hodgkin lymphoma. The lead author was Oliver W. Press, MD, PhD, from the University of Washington Medical Center (Seattle). The study (SWOG S0016) included 554 patients with previously untreated, advanced-stage (bulky stage II, III, or IV) follicular lymphoma of any grade. One group of patients received 6 CHOP cycles at 3-wk intervals, with 6 doses of rituximab (CHOP-R). Another group received the 6 cycles of CHOP followed by consolidation therapy with tositumomab/¹³¹I-tositumomab radioimmunotherapy (CHOP-RIT). Over a median follow-up of 4.9 y, 2-y estimates of progression-free survival rates were similar for the CHOP-R and CHOP-RIT groups (76% and 80%, respectively), with 2-y estimates of overall survival also similar (97% and 93%, respectively). The authors concluded that the study had found "no evidence of a significant improvement in progression-free survival comparing CHOP-RIT with CHOP-R," but

that both progression-free and overall survival were "outstanding on both arms of the study." They called for future studies to determine the potential benefits of combining CHOP-R induction chemotherapy with RIT consolidation and/or extended rituximab maintenance therapy.

Journal of Clinical Oncology

PET/CT in Recurrent Sarcoma

In an article e-published on December 11 ahead of print in *Cancer*, Al-Ibraheem et al. from the Technische Universität München (Germany) and the King Hussein Cancer Center (Amman, Jordan) reported on the results of a clinical study of the diagnostic accuracy and incremental value of ¹⁸F-FDG PET/CT in patients with a history of sarcoma and clinically suspected disease recurrence. The study included 43 patients with histories of bone or soft tissue sarcoma and complete remission. All underwent ¹⁸F-FDG PET/CT imaging. The 43 ¹⁸F-FDG PET images; 30 contrast-enhanced spiral CT images; and 43 combined PET/CT images were separately analyzed, with imaging findings rated

on a 5-point scale and reported as malignant, benign, or equivocal. Imaging findings were compared with histopathology in 24 patients and clinical follow-up in the remaining 19. PET/CT was found to have greater sensitivity and specificity (94% and 92%, respectively) than contrast-enhanced CT alone (78% and 67%, respectively), resulting in significantly greater accuracy (93% for PET/CT and 73% for CT alone). PET/CT was especially useful in detection of local recurrence, soft tissue lesions, and bone metastases. The authors summarized their findings that ^{18}F -FDG PET/CT was superior to contrast-enhanced CT in detection of recurrent bone or soft tissue sarcoma, with the most evident advantage being detection of local recurrence.

Cancer

Radiation-Induced Perfusion Changes

Lawrence et al. from the University of North Carolina (Chapel Hill) reported in the December issue of *Medical Physics* (2012;39:7644–7649) on a study designed to assess the impact of radiation-induced changes in soft tissue density/thickness on the study of radiation-induced perfusion changes in the lung and heart. Radiation therapy (RT) may increase soft tissue density surrounding the lung and heart, leading to apparent SPECT diffusion defects. The authors quantitatively assessed the degree of density changes and effective depth in soft tissues after radiation in phantom models and in patients. The study included 23 patients (4 with breast cancer, 19 with lung cancer) who underwent pre- and serial post-RT thoracic CT imaging. Changes in tissue density and effective depth (in Hounsfield units and tissue thickness/cm, respectively) were calculated. The potential effects of these changes on SPECT results were simulated using a SPECT thorax phantom with varying tissue densities. Data were generated from soft tissue regions receiving doses of 20–50 Gy. The average increase in density of the chest pre- and post-RT was 5 HU (range, 46 to –69). Average

change in breast tissue density was –1 HU (range, 13 to –13). The average increase in tissue effective depth was 0.2 cm (range, –1.9 to 2.2 cm), with changes in HU representing a <2% average change in tissue density, which the authors noted was unlikely to yield meaningful changes in either SPECT lung or heart perfusion. They summarized the findings by stating that “RT doses of 20–50 Gy can cause up to a 46 HU increase in soft tissue density 6 mo post-RT,” when soft tissue effective depth may increase by 2.0 cm. They concluded that these “modest increases in soft tissue density and effective depth are unlikely to be responsible for the perfusion changes seen on post-RT SPECT lung or heart scans” and that “there was no clear dose response of the soft tissue density changes.” These findings suggest that “prior perfusion reports do reflect changes in the physiology of the lungs and heart.”

Medical Physics

PET and MR in Temporal Lobe Epilepsy

In an article e-published on December 8 ahead of print in *Neuroradiology*, Gok et al. from Drexel University (Philadelphia, PA) reported on a study evaluating the utility of ^{18}F -FDG PET imaging for localization of epileptogenic foci in patients with MR-positive and -negative temporal lobe epilepsy. The study included 98 patients who underwent surgical treatment for drug-resistant temporal lobe epilepsy after neuropsychological evaluation, scalp video electroencephalography (EEG) monitoring, ^{18}F -FDG PET imaging, and MR imaging and/or long-term intracranial EEG and >12 mo clinical follow-up. Findings from PET imaging were compared with those from MR imaging histopathology, scalp video EEG, and long-term intracranial EEG monitoring. PET successfully lateralized the seizure focus in 95% of MR-positive, 69% of MR-equivocal, and 84% of MR-negative patients. No statistically significant difference was seen in surgical outcomes among these groups. Patients with positive unilateral PET findings, however, showed

excellent postsurgical outcomes, with 96% Engel class I and II results. Histopathology showed focal lesions in 75% of MR-equivocal, 84% of MR-positive, and 23% of MR-negative temporal lobe epilepsy cases. The authors concluded that ^{18}F -FDG PET is “an accurate noninvasive method in lateralizing the epileptogenic focus in temporal lobe epilepsy, especially in patients with normal or equivocal MRIs, or nonlateralized EEG monitoring.” They added that very subtle findings in MR imaging are often associated with histopathologic lesions and should be described in imaging reports.

Neuroradiology

β -Amyloid in LBD and AD

Shimada et al. from the National Institute of Radiological Sciences and Chiba University (both in Chiba Japan) reported on December 5 ahead of print in *Movement Disorders* on a study designed to investigate whether amyloid deposition is associated with Alzheimer disease (AD)-like cortical atrophy in Lewy body disease (LBD). The study included 45 participants (15 with LBD and dementia [8 with LBD dementia and 7 with Parkinson disease [PD] with dementia], 13 with AD, and 17 healthy controls). Groups were matched for age, sex, and mental state examination scores. All participants underwent PET imaging with ^{11}C -Pittsburgh Compound B and 3-dimensional T1-weighted MR imaging. Gray matter volumes were estimated, and volume-of-interest analyses were performed. PET results indicated that all of the AD patients, 40% of patients with LBD and PD dementias, and none of the healthy participants were amyloid positive. Amyloid-positive patients with either LBD/PD dementia or AD showed similar patterns of cortical atrophy in the parahippocampal area and lateral temporal and parietal cortices, with 95.2% of cortical atrophy distribution overlapped in the 2 groups. Amyloid-negative patients with LBD/PD dementia showed no significant cortical atrophy. On MR, parahippocampal gray matter volumes were reduced by 26% in the amyloid-

positive patients with LBD/PD dementia and AD groups and by 10% in the amyloid-negative patients with LBD/PD dementia. The authors concluded that these results suggest “that amyloid deposition is associated with AD-like atrophy” in patients with LBD/PD dementia and that early intervention against amyloid may prevent or delay AD-like atrophy in these patients.

Movement Disorders

PET, SPECT, and Aerosol Deposition

Two articles in the December supplement to the *Journal of Aerosol Medicine and Pulmonary Drug Delivery* focused on techniques for PET and SPECT in assessment of aerosol deposition of inhaled therapeutics. Fleming et al. from University Hospital Southampton (UK) described standardization of techniques for using SPECT for aerosol deposition assessment of orally inhaled products (2012;25 suppl 1:S29–S51). The review covered the use of SPECT to measure the 3-dimensional (3D) distribution of inhaled aerosol deposition in the lungs as a method for evaluating and optimizing drug delivery by inhalation. The article described a standardized protocol and key recommendations to ensure consistency. With use of this protocol, the authors noted, “results of 3D imaging of the deposition of orally inhaled aerosols using SPECT should be more comparable, which should enhance collaborations between centers and ensure that this form of imaging becomes acceptable to the regulatory authorities.” In the same issue of the journal (2012;25 suppl 1:S52–S71), Dolovich and Baily from McMaster University (Hamilton, Ontario) described the use of PET to provide quantitatively accurate localization of the amount and distribution of an inhaled or injected radiotracer in the lung. The article described procedures for administering ^{18}F -FDG aerosol to human subjects for the purpose of determining dose and distribution after inhalation from an aerosol drug delivery device. The authors discussed

the advantages of using direct-labeled PET drugs; methods for designing the inhalation system; proper radiation shielding, calibration, and validation of administered radioactivity; scanner set up; and data handling procedures. As a whole, the authors said, “This article should provide guidance for those interested in using PET to determine quantity and distribution of inhaled therapeutics.”

Journal of Aerosol Medicine and Pulmonary Drug Delivery

Bone Scan vs PET/CT in Prostate Cancer

Takesh et al. from Heidelberg University Hospital (Germany) reported on November 28 ahead of print in *ISRN Oncology* on a study designed to determine the efficacy of PET/CT with ^{18}F -ethylcholine (^{18}F -FECH) in assessing bone status in prostate cancer and to compare results with those from conventional bone scan findings. The study included 37 men (mean age, 69 ± 7 y) who had been referred for restaging as a result of biochemical recurrence of disease. All participants underwent both ^{18}F -FECH PET/CT and bone scanning. ^{18}F -FECH PET/CT accurately identified bone involvement in 15 of 18 patients (sensitivity, 83.3%). Bone scans correctly identified 17 of these 18 patients (sensitivity, 94.4%). Lesion-related results varied by anatomic region with each approach. The authors concluded that “no significant gain in sensitivity was achieved using bone scan compared with ^{18}F -FECH-PET/CT.”

ISRN Oncology

Smoking, Alcohol, and μ -Opioid Receptors

In an article e-published on December 18 ahead of print in *Addiction Biology*, Weerts et al. from The Johns Hopkins University School of Medicine (Baltimore, MD) reported on a study investigating whether individual differences in μ -opioid receptor availability are correlated with tobacco use, nicotine dependence, and level of nicotine craving. The study included 25 alcohol-dependent subjects who completed an inpatient pro-

tol, including medically supervised alcohol withdrawal, monitored alcohol abstinence, transdermal nicotine maintenance, and ^{11}C -carfentanil PET imaging before (baseline scan) and during (treatment scan) treatment with naltrexone.

Participants who had higher scores on the Fagerström Nicotine Dependence Test were found to have significantly lower baseline binding potential across mesolimbic regions, including the amygdala, cingulate, globus pallidus, thalamus, and insula. The number of cigarettes previously smoked per day was negatively associated with baseline binding potential in mesolimbic regions. Higher nicotine craving was significantly associated with lower baseline binding potential in amygdala, globus pallidus, putamen, thalamus, and ventral striatum. Although somewhat ameliorated during naltrexone treatment, this negative association persisted for nicotine dependence and cigarettes per day but not for nicotine craving. The authors concluded that these findings “suggest that intensity of cigarette smoking and severity of nicotine dependence symptoms are systematically related to reduced binding potential across multiple brain regions in alcohol-dependent subjects.”

Addiction Biology

Amyloid and Cognition in PD

Gomperts et al. from Massachusetts General Hospital (Boston) and the Autonomous University of Barcelona (Spain) reported on December 12 ahead of print in *Neurology* on a study designed to determine whether amyloid burden, as indexed by Pittsburgh Compound B (PiB) retention on PET, successfully identifies and differentiates patients with Parkinson disease (PD) with mild cognitive impairment (MCI) from those PD patients with normal cognition. They also sought to determine whether amyloid burden can predict cognitive decline in a cohort of subjects with PD without dementia. The study included 46 participants with PD without dementia (35 with normal cognition and 11 meeting cri-

teria for PD with MCI at the outset of the study). All participants underwent neurologic and neuropsychological examinations and PiB PET imaging at baseline, as well as annual clinical examinations for up to 5 y. PET at baseline did not distinguish PD with MCI from PD with normal cognition. Participants with PD with MCI experienced more rapid declines on tests of memory, executive function, and activation retrieval. Of the 35 participants with normal cognition at baseline, 8 progressed to PD with MCI and 1 to dementia over the follow-up period. For the 11 individuals with PD and MCI at baseline, 5 converted to dementia. Higher tracer retention on PET and an original diagnosis of PD with MCI were independent predictors of greater risk of conversion to MCI or dementia. The APOE ϵ 4 allele was also found to be associated with decline in executive function, visuospatial function, activation retrieval, and performance on the Mini-Mental State Examination. PiB retention on PET did not predict progression of motor impairment. The authors summarized their findings: “At baseline measurements, amyloid burden does not distinguish between cognitively impaired and unimpaired subjects with PD without dementia, but our data suggest that amyloid contributes to cognitive, but not motor, decline over time.”

Neurology

Gastroesophageal Cancer and Surgery Decisions

In an article e-published on December 17 ahead of print in *Annals of Oncology*, Cheedella et al. from the University of Texas M.D. Anderson Cancer Center (Houston) reported on a study of the association between clinical complete response and pathologic complete response after preoperative chemoradiation in patients with gastroesophageal cancer. Clinical complete response is defined as a negative post-chemoradiation (preoperative) endoscopic biopsy with PET showing physiologic uptake. The concern is that with a determination of clinical complete response some patients may be

reluctant to proceed to surgery or may delay surgery. The study included 284 patients with gastroesophageal cancer who underwent chemoradiation and esophagectomy. Of these, 218 (77%) achieved a clinical complete response but only 67 (31%) of these 218 achieved pathologic complete response. The sensitivity of clinical complete response for pathologic complete response was 97.1% (67 of 69), but the specificity was low (29.8%; 64 of 215 patients). Of the 66 patients who had less than a clinical complete response, only 2 (3%) had a pathologic complete response. The authors concluded that clinical complete response is not highly associated with pathologic complete response and that the specificity of clinical complete response is “too low to be used for clinical decision making on delaying/avoiding surgery.” They added that “surgery-eligible gastroesophageal cancer patients should be encouraged to undergo surgery following chemoradiation despite achieving a clinical complete response rate.”

Annals of Oncology

PET/CT and Soft Tissue Sarcoma Staging

Roberge et al. from McGill University Health Centre and Notre-Dame Hospital (both in Montreal, Quebec) reported on December 2 ahead of print in *Sarcoma* on the use of ^{18}F -FDG PET/CT in initial staging of adult soft tissue sarcoma. The study group included 109 adults with limb and body wall soft tissue sarcoma and chest CTs, who also underwent ^{18}F -FDG PET/CT (patients with Ewing’s sarcoma, rhabdomyosarcoma, gastrointestinal stromal tumors, desmoid tumors, visceral tumors, bone tumors, and retroperitoneal sarcomas were excluded, as were patients imaged for follow-up, response assessment, or recurrence). In the study group, 87% had intermediate- or high-grade tumors. The most common pathologic diagnoses were leiomyosarcoma (17%), liposarcoma (17%), and undifferentiated or pleomorphic sarcoma (16%). Almost all (98%) of previously unresected primary tumors were ^{18}F -FDG avid.

PET results were negative for distant disease in 91 patients (negative predictive value of 89%). PET results were positive in 14 patients. Of these, 6 were already known to have metastases, 3 were false-positives, and 5 were new findings of metastasis (positive predictive value of 79%; 4.5% of patients upstaged by PET imaging). The authors concluded that “although PET scans may be of use in specific circumstances, routine use of FDG PET imaging as part of the initial staging of soft-tissue sarcomas was unlikely to alter management in our series.”

Sarcoma

PET in ESCC

In an article e-published on December 13 ahead of print in *Annals of Surgical Oncology*, Kita et al. from Kagoshima University (Japan) reported on a study designed to assess the clinical utility of ^{18}F -FDG PET in diagnosing superficial esophageal squamous cell carcinoma (ESCC). The study included 80 patients with superficial ESCC who had not undergone neoadjuvant treatment. All underwent ^{18}F -FDG PET imaging. Of the 80 patients, 57 proceeded to radical esophagectomy and 23 patients to endoscopic resection. Preoperative imaging results were compared with clinicopathologic findings and with immunohistochemical examination of glucose transporter 1 (Glut-1) expression in primary tumors. FDG uptake in primary tumors was found to correlate with histology, depth of tumor invasion, lymph node metastasis, lymphatic invasion, vascular invasion, and Glut-1 expression. All patients with maximum standardized uptake values >4.4 showed deeper invasion of submucosa. Tracer uptake, depth of tumor invasion, lymph node metastasis, and histology were found to be significant prognostic factors, and histology was an independent prognostic factor. In ^{18}F -FDG uptake-positive patients, the depth of tumor invasion and histology were prognostic factors. The authors concluded that ^{18}F -FDG PET is “useful for diagnosing tumors with deeper invasion of submucosa and is helpful in making decisions regarding endoscopic

treatment for superficial ESCC.” They advised that patients with ^{18}F -FDG uptake-positive disease, deeper invasion of submucosa, poorly differentiated tumor, and poor prognoses should receive multimodal treatment.

Annals of Surgical Oncology

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 December and January. In an article e-published on December 19 ahead of print in *Cancer Biology & Therapy*, Ganapathy-Kanniappan et al. from Johns Hopkins University School of Medicine (Baltimore, MD) reviewed recent reports that “Statins impair glu-

cose uptake in tumor cells.” Kalles et al. from the University of Athens (Greece) reviewed “The current status of positron emission mammography in breast cancer diagnosis” on December 13 ahead of print in *Breast Cancer*. In an article e-published on December 19 in *Pediatric Blood & Cancer*, Kelly, from Columbia University Medical Center (New York, NY) and members of the COG Hodgkin Lymphoma Committee described the content of the “Children’s Oncology Group’s 2013 blueprint for research: Hodgkin Lymphoma.” Rose et al. from Emory University School of Medicine (Atlanta, GA) presented “A systematic literature review and meta-analysis of radioimmunotherapy consolidation for patients with untreated follicular lymphoma” in the December issue of *Clinical Lymphoma, Myeloma, & Leukemia* (2012;12:393–399). In the December is-

sue of *JACC Cardiovascular Imaging* (2012;5:1269–1284), Dilsizian, from the University of Maryland School of Medicine (Baltimore), and Taillefer, from the Hôpital du Haut-Richelieu (Saint-Jean-Sur-Richelieu, Quebec), provided an overview of the history of nuclear cardiology titled “Journey in evolution of nuclear cardiology: will there be another quantum leap with the F-18-labeled myocardial perfusion tracers?” Koba et al. from the Albert Einstein College of Medicine (Bronx, NY) discussed “MicroPET/SPECT/CT imaging of small animal models of disease” on December 5 ahead of print in the *American Journal of Pathology*. In the January issue of *Current Cardiology Reports* (2013;15:320), Dweck et al. from the University of Edinburgh (UK), reviewed “Imaging of inflammation and calcification in aortic stenosis.”