a comment letter to Mostashari expressing concern about the absence of specific reference to access to medical images and reports through the electronic record. On February 24, SNM applauded the Office of the National Coordinator for HIT for recognizing the important role access to imaging plays in coordination of care.

Centers for Medicare & Medicaid Services

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.

Imaging Crohn Disease

In an article e-published on February 22 ahead of print in *Inflammatory Bowel Diseases*, Lenze et al. from the University of Muenster (Germany) reported on a study designed to determine the optimal noninvasive imaging method for detection of and differentiation between inflammatory and fibromatous stenoses in Crohn disease and to compare the results with those of endoscopic and histologic evaluation. The study included 37 patients with 37 strictures (22 inflamed, 12 mixed, and 3 fibromatous as classified by endoscopy and histology). Each patient underwent ^{18}F-FDG PET/CT, MR enteroclysis, and transabdominal ultrasound imaging. PET/CT and MR enteroclysis each detected 81% of strictures, and ultrasound detected 68%. MR enteroclysis was able to differentiate between inflammatory and fibromatous stenoses in 57% of strictures, with figures for PET/CT and ultrasound of 53% and 40%, respectively. Ultrasound, combined with either of the 2 other imaging techniques, was able to detect all strictures that required invasive treatment by surgery or endoscopic dilation therapy. The authors concluded that these results suggest a combination of these imaging approaches "as an alternative to endoscopy at least in the group of patients not able to perform an adequate bowel preparation."

Inflammatory Bowel Diseases

PET/CT and Tonsil SCC Therapy

Moon et al. from Sungkyunkwan University School of Medicine (Seoul, Republic of Korea) reported on February 6 ahead of print in *Head & Neck* on a study detailing the prognostic value of volume-based metabolic parameters as assessed by ^{18}F-FDG PET/CT in patients with squamous cell carcinoma of the tonsil. The study included 69 such patients who underwent PET/CT imaging before initiation of treatment. Parameters assessed were maximum standardized uptake value, metabolic tumor volume, total lesion glycolysis, and asymmetry indices of these 3 metrics. After adjusting for age, sex, and cancer stage, statistical analysis indicated that only total lesion glycolysis was an independent predictive factor in decreased overall survival.

Head & Neck

^{11}C-Mephobarbital PET at the BBB

In an article e-published on February 16 ahead of print in *Epilepsy Research*, Mairinger et al. from the Austrian Institute of Technology (Seibersdorf), the University of Vienna (Austria), and the Medical University of Vienna (Austria) reported on a study designed to determine whether the antiepileptic drug ^{11}C-mephobarbital is a substrate of P-glycoprotein (Pgp) and can be used with PET imaging to assess Pgp function at the blood–brain barrier (BBB). The study first assessed brain distribution of ^{11}C-mephobarbital in paired rats and mice before and after intravenous administration of the Pgp inhibitor tariquidar. The before and after scans were similar, suggesting that in vivo brain distribution of ^{11}C-mephobarbital is not influenced by Pgp efflux. This was confirmed in in vitro studies. Additional PET experiments in mice with and without pretreatment with multidrug resistance protein (MRP) inhibitor MK571 suggested that ^{11}C-mephobarbital is also not transported by MRPs at the murine BBB. This was also confirmed by in vitro transport experiments. The authors found these results to be surprising because "phenobarbital, the *N*-desmethyl derivative of mephobarbital, has been shown to be a substrate of Pgp, which suggests that *N*-methylation abolishes the Pgp affinity of barbiturates."

Epilepsy Research

PET Prediction in Soft Tissue Sarcomas

Herrmann et al. from the University of California Los Angeles reported on February 14 ahead of print in *Clinical Cancer Research* on a study designed to determine whether ^{18}F-FDG PET/CT after an initial cycle of neoadjuvant therapy can serve as an early intermediate endpoint biomarker of overall survival in patients with primary high-grade soft tissue sarcomas. The group had previously reported that PET identified treatment responders at the end of and after a single cycle of neoadjuvant therapy. The current study group included 57 patients who

underwent therapy followed by surgery. All patients underwent a baseline scan before initiation of therapy, and 39 patients underwent a second scan after the initial chemotherapy cycle and before surgery. Fifty-six patients underwent end-of-treatment (late follow-up) scanning. Results in overall survival and other factors were correlated with changes in peak standardized uptake values (SUV_{peak}) and histopathology. Over all participants, 1, 2, and 5-y survival rates were 95% ± 3.0%, 86% ± 4.6%, and 68% ± 6.6%, respectively, with a median time to death of 30.9 mo (mean, 27.7 mo; range, 6.9–50.1 mo). Of the 15 early PET nonresponders (based on optimal cut-offs for early and late decreases in SUV_{peak}), 7 died during the follow-up period, whereas only 4 of the 24 PET responders died during the same period. Surgical margin positivity was the only other factor identified as a significant survival predictor. The authors concluded that because ^{18}F-FDG PET in this study predicted survival after an initial cycle of neoadjuvant chemotherapy in patients with soft tissue sarcomas, that such imaging "can potentially serve as an intermediate endpoint biomarker in clinical research and patient care."

Clinical Cancer Research

Early PET and RT in HNSCC

In an article e-published on February 11 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics*, Huang et al. from the William Beaumont Hospital (Royal Oak, MI) reported on a small animal study investigating the metabolic information provided by ^{18}F-FDG PET imaging on early response of head and neck squamous cell carcinoma (HNSCC) xenografts to radiation therapy. The study was conducted in mice with xenografted low-passage HNSCC cell tumors grown to 400–500 mm^3 and then treated with radiation or a sham radiation procedure. Animals underwent 2-h dynamic PET at set time points, with direct histologic correlation for each imaging session. Among the factors correlated in subsequent analysis were kinetic index, standardized uptake value (SUV), sensitivity factor, retention index, and tumor specific growth rate. Radiation successfully arrested tumor growth for the first 20 d after radiation. Tumor growth resumed thereafter. On histology, radiation changes were observed in tumor peripheral regions between d 7 and 23. Radiation necrosis was seen in tumor central regions between d 7 and 40. The kinetic index correlated best with specific growth rate, and SUV was the strongest predictor of late radiation necrosis. The retention index and the sensitivity factor were accurate in predicting radiation change. The authors concluded that dynamic ^{18}F-FDG PET analyses "may provide informative assessment of early radiation necrosis or radiation changes of HNSCC xenografts after radiation therapy."

International Journal of Radiation Oncology, Biology, Physics

PET and Tumor Metabolic Heterogeneity

Vriens et al. from Radboud University Nijmegen Medical Centre (The Netherlands) reported on February 11 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on a study proposing a technique for segmentation (as an alternative to using whole-tumor volumes of interest) for quantitative ^{18}F-FDG PET assessment of heterogeneity in tumor metabolism. The study included 41 previously untreated patients who underwent dynamic PET imaging of 104 lesions of various types. On resulting images, tumors were segmented in quartiles of varying background-subtracted metabolic rate of glucose percentages. Additional pharmacokinetic studies were performed to determine the rate constants of FDG metabolism. From the high to low quartiles, results showed significant and directly corresponding decreases of uptake, washout, and phosphorylation rate constants with significant increases in tissue blood volume fraction. The authors concluded that these results "support the hypothesis that regional tumor glucose phosphorylation rate is not dependent on the transport of nutrients (i.e., FDG) to the tumor." They added that the technique may be useful for dose painting in radiation therapy and in exploring the mechanisms of FDG uptake.

International Journal of Radiation Oncology, Biology, Physics

PET/CT and Esophageal Ca Survival

In an article appearing in the February issue of the *British Journal of Surgery* (2012;99:239–245), Gillies et al. from the Oxford Cancer and Haematology Centre (UK) reported on the prognostic value of PET/CT performed before neoadjuvant chemotherapy and surgery in patients with esophageal cancer. The study included 121 patients (mean age, 63 y; 97 men, 24 women) with esophageal adenocarcinoma who underwent ^{18}F-FDG PET/CT before neoadjuvant chemotherapy and (in 103 patients) surgical resection. Factors assessed included maximum standardized uptake value (SUV_{max}), tracer-avid tumor length, and the presence of tracer-avid local lymph nodes. Results indicated that FDG avidity in local lymph nodes was a significant and independent predictor of poor overall survival. Neither SUV_{max} nor tracer-avid tumor length was a significant predictor.

British Journal of Surgery

Stress ECG Changes and Normal MPI

Uthamalingam et al. from the Massachusetts General Hospital and Harvard Medical School (Boston, MA) reported on February 8 ahead of print in *Angiology* on a study describing the prevalence and prognostic significance of ischemic electrocardiographic (ECG) changes during regadenoson vasodilator stress testing in patients with normal SPECT myocardial perfusion imaging (MPI) results. The initial study pool included 2,473 patients and resulted in a focus on 43 patients (mean age, 73 ± 9 y; 33 women, 10 men) who underwent re-

gadenoson SPECT MPI with normal results but with ischemic ECG changes. Baseline characteristics were recorded, as were various hemodynamic parameters. During a mean follow-up of 14 ± 7 mo, none of the patients experienced myocardial infarction (1 died from pneumonia and respiratory failure). Of the 5 patients who underwent coronary revascularization, 4 had percutaneous coronary interventions and 1 had coronary artery bypass surgery. The annual rates of cardiac death and coronary revascularization were 1.9% and 9.9%, respectively. The authors concluded that the results of this small-group study suggest that the finding of ischemic ECG changes with normal SPECT MPI during regadenoson vasodilator stress testing is uncommon, may occur primarily in older women, and may be associated with a moderately higher subsequent cardiac event rate.

Angiology

β-Amyloid in Healthy Aging

In an article in the February 7 issue of *Neurology* (2012;78:387–395), Rodrigue et al. from the University of Texas at Dallas reported on a study indicating that increased β-amyloid (Aβ) burden is present even in healthy aging individuals and that this increase is accompanied by subtle cognitive changes. The study was widely covered in the public media. The goal of the study was to map the cortical distribution of β-amyloid in a healthy adult lifespan sample and to assess the relationship between elevated amyloid and cognitive performance. The study included 137 well screened, highly educated, cognitively healthy adults (ages 30–89 y) who underwent ^{18}F-florbetapir PET imaging. All participants were genotyped for apolipoprotein E (APOE) and underwent tests for processing speed, working memory, fluid reasoning, episodic memory, and verbal ability. Aβ burden was estimated from 8 cortical regions and was found to be positively correlated with poorer cognitive performance on processing speed, working memory, and reasoning. Aβ burden appeared to progress at varying rates with age across different cortical brain regions. A subset of cognitively healthy adults ≥60 y old with markedly elevated Aβ deposition also had higher rates of APOE ε4 than nonelevated adults (38% and 19%, respectively). Many of the study's findings suggest a steady, linear increase in amyloid burden with aging. "A key question for future research is whether some adults with high levels of Aβ will maintain good mental function for a long period of time, and whether higher Aβ deposits in healthy adults always predetermines cognitive decline," said senior investigator Denise Park, PhD, in a news release accompanying the publication.

Neurology

PET and MR as AD Biomarkers

Thurfjell et al. from GE Healthcare (Uppsala, Sweden) reported on February 1 ahead of print in *Neurodegenerative Diseases* on a study designed to determine the separate and combined utility of hippocampus volumes from MR imaging and neocortical standard uptake value ratios from ^{18}F-flutemetamol PET as biomarkers for Alzheimer disease (AD) and for categorizing and predicting the course of the disease. The study included 27 patients previously diagnosed with AD, 20 with amnestic mild cognitive impairment (MCI), and 25 healthy volunteers. All patients underwent MR and PET imaging, and clinical follow-up was performed 2 y after initial assessment. Results indicated that hippocampus volumes did not differ significantly between AD patients and volunteers, whereas PET neocortical standard uptake value ratios clearly differentiated between the 2 groups. When PET and MR measures were combined, PET-positive MCI participants showed large variability in hippocampus volumes, suggesting that these individuals were in different stages of neurodegeneration. At 2-y follow-up, 8 of 9 MCI-to-AD converters came from the group who had positive PET scans. The authors concluded that combining ^{18}F-flutemetamol PET with structural MR imaging "provides additional information for categorizing disease and potentially predicting shorter time to progression from MCI to AD," a finding that should be validated in larger longitudinal studies.

Neurodegenerative Diseases

Autofluorescence and GI Motion

In an article e-published on February 6 ahead of print in *Neurogastroenterology and Motility*, Kown et al. from the University of Texas Health Science Center (Houston) reported on noninvasive autofluorescent imaging of intestinal motion using red chlorophyll and without an exogenous imaging agent. The study was conducted in mice that were illuminated with 660-nm light from a fluorescent laser. Fluorescent imaging data were acquired dynamically and used to generate a 3D spatiotemporal map that quantitated peristaltic and segmental motions in vivo. The technique has promise in monitoring intestinal motility disorders and response to therapeutic agents.

Neurogastroenterology and Motility

Preoperative PET/CT and Breast Ca

Bernsdorf and colleagues from the Rigshospitalet and Copenhagen University Hospital (Denmark) reported on February 21 ahead of print in the *Annals of Oncology* on a study designed to assess the diagnostic and therapeutic impact of preoperative PET/CT in initial staging of patients with early-stage breast cancer. The study included 103 women with newly diagnosed and operable breast cancer (tumors ≥2 cm) who underwent independent preoperative PET/CT imaging and conventional evaluation (mammography, breast/axillary ultrasound, chest radiography, and hematology). PET/CT alone identified the primary tumor in 100 patients (97%), detected distant metastases (ovary, bones, and lung) in 6 patients, and identified new primary cancers (ovary, lung) in

another 2 patients, in addition to detecting 12 cases of extraaxillary lymph node involvement. PET/CT alone detected extraaxillary malignancy in 15 patients (15%), with a change in initial staging in 14% (14/103) and modification of planned treatment in 8% (8/103). The authors concluded that "PET/CT is a valuable tool to provide information on extraaxillary lymph node involvement, distant metastases, and other occult primary cancers" and that preoperative ^{18}F-FDG PET/CT has a "substantial impact on initial staging and on clinical management in patients with early-stage breast cancer with tumors ≥2 cm."

Annals of Oncology

PET/CT in Recurrent Laryngeal Cancer

In a study that appeared online on February 16 ahead of print in *Laryngoscope*, Gilbert et al. from the University of Pittsburgh School of Medicine (PA) reported on a study designed to determine whether preoperative PET/CT can predict the pathologic status of the neck in patients with locally recurrent laryngeal cancer and clinically N0 necks. The retrospective study included 15 such patients who had undergone PET/CT before neck dissection. Negative PET/CT proved to be 100% specific in the 5 patients with pathologically negative surgical results. PET/CT determined to be positive for cervical disease in 7 patients was correlated pathologically with positive nodes. Negative PET/CT results were discordant in 3 patients with clinically N0 neck and positive nodal pathology, resulting in a sensitivity of 70% and negative predictive value of only 62.5%. The authors concluded that "this false negative rate is too high to warrant deferring neck dissection based on PET/CT" and recommended that patients who are clinically N0 for recurrent laryngeal cancer be offered neck dissection along with salvage laryngectomy.

Laryngoscope

MR and BAT

Chen et al. from the Massachusetts General Hospital and Harvard University (Boston, MA) reported on February 20 ahead of print in *Obesity (Silver Spring)* on MR anatomic and functional assessment of brown adipose tissue (BAT). The study was conducted with a 9.4-T MR scanner in rats and was designed to demonstrate the feasibility of mapping and estimating BAT volume and metabolic function using sequences available on current clinical MR scanners. Among the studies successfully completed were MR measurement of volume distribution of BAT, assessment of BAT volume using spin-echo MR sequences, correlation of findings with direct histopathologic assessment of BAT at dissection, mapping of hemodynamic responses to changes in BAT metabolism resulting from administration of a β3-adrenergic receptor agonist, and comparison of MR results with those from ^{18}F-FDG PET imaging. The authors concluded that this approach is sound and that the "measurement of BAT volume is consistent with quantitative measurement of the tissue ex vivo."

Obesity (Silver Spring)

SUV and Incidental Thyroid Nodules

In an article e-published on February 3 ahead of print in *Otolaryngology–Head and Neck Surgery*, Boeckmann et al. from the University of Arkansas Medical Sciences (Little Rock) reported on an investigation to determine whether standardized uptake values (SUVs) on PET can predict thyroid pathology and whether serial SUV assessments over time have clinical utility in this setting. The study population was drawn from more than 23,000 PET or PET/CT scans at the authors' institution over a 10-y period. Among the variables included in the study were incidental thyroid uptake, maximum SUV (SUV_{max}), age, sex, size of thyroid lesion, original indication for PET scan, and cytology/pathology results. Incidental thyroid uptake was identified in 5.60% of the total scans, focal uptake in 2.95%, and diffuse uptake in 2.65%. Data on all variables were available for 103 patients (359 PET scans). Twenty-eight (27%) of these patients were determined to have malignant lesions, and, of these, 25 (89%) were primary thyroid malignancies. SUV_{max} was found to be a significant differentiator between malignant and benign lesions. Additional analysis on patients with PET data within 3 mo of diagnosis suggested that an SUV_{max} of 4.2 was the most accurate cut-off for such differentiation. Assessment of serial SUV uptake provided no additional useful information, and the size of the primary nodule was not related to SUV_{max}. The authors concluded that "all thyroid nodules with focal uptake on ^{18}F-FDG PET/CT should be considered at higher risk of malignancy than those discovered incidentally by other imaging modalities" and recommended that all lesions be evaluated with ultrasonography ± fine-needle aspiration in the absence of clinical contraindications.

Otolaryngology–Head and Neck Surgery

^{11}C-PiB and Cortical Atrophy

Chételat and researchers from the Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing group reported in the February 14 issue of *Neurology* (2012;78:477–484) on a focused assessment of data gathered in their prospective, longitudinal study of cognition in more than 1,000 individuals ≥60 y of age, including participants with Alzheimer disease (AD) and with mild cognitive impairment and healthy volunteers. The aim of the current study was to assess whether brain β-amyloid (Aβ) influences the rate of neuronal and synaptic loss in cognitively normal individuals. The study group included 74 healthy elderly individuals who underwent both MR and ^{11}C-Pittsburgh compound B (^{11}C-PiB) PET scanning, followed 18 mo later by a second MR scan. The rate of atrophy over the

study period was found to be significantly higher in those participants with high ^{11}C-PiB uptake and was significantly correlated with baseline neocortical tracer uptake, with the highest significance in the temporal neocortex and the posterior cingulate cortex. The authors concluded that these findings indicate that "the presence of Aβ in the brain, known to occur in about one-third of asymptomatic elderly individuals, is actually a pathologic state associated with accelerated atrophy." They added that therapy "aimed to reduce the neurodegenerative process" should be initiated in presymptomatic individuals with high ^{11}C-PiB uptake on PET.

Neurology

PET and NETs Metaanalysis

In an article e-published on February 20 ahead of print in *Endocrine*, Treglia et al. from the Catholic University of the Sacred Heart (Rome, Italy) described the results of a metaanalysis of reports on the diagnostic accuracy of ^{68}Ga-somatostatin receptor PET and PET/CT in patients with neuroendocrine tumors (NETs). Surveying published literature through 2011, the authors selected studies in which somatostatin receptor PET or PET/CT was performed in patients with thoracic and/or gastroenteropancreatic NETs (medullary thyroid and neural crest derived tumors were excluded). The resulting metaanalysis database included a total of 16 studies with 567 patients. The pooled sensitivity of PET or PET/CT in detecting NETs was 93%, with 91% sensitivity on a per patient-based analysis. The authors concluded that ^{68}Ga-somatostatin receptor PET and PET/CT "should be considered as first-line diagnostic imaging methods in patients with suspicious thoracic and/or gastroenteropancreatic NETs."

Endocrine

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 February. In an article e-published on February 12 ahead of print in *Current Cardiology Reports*, Slomka et al. from Cedars–Sinai Medical Center (Los Angeles, CA) reported on "Advances in nuclear cardiac instrumentation with a view towards reduced radiation exposure." On February 7 ahead of print in the *Journal of Clinical Neuroscience*, Caroline and Rosenthal from the Royal Melbourne Hospital and the University of Melbourne (Australia) reviewed literature on "Imaging modalities in high-grade gliomas: pseudoprogression, recurrence, or necrosis?" In an article e-published on February 21 ahead of print in *Radiation Research*, Robbins et al. from the Wake Forest University School of Medicine (Winston-Salem, NC) provided an overview of technologies and techniques for "Imaging radiation-induced normal tissue injury." Brogan et al. from Duke University Medical Center (Durham, NC) reported in the same online issue of *Radiation Research* on "Novel optical imaging approaches for noninvasive study of tumor biology in vivo based on bioluminescence and fluorescent proteins." Reviews of novel approaches are especially useful as introductions to fields that may soon play vital roles in research and clinical practice. Bednar and Ntziachristos from the Technische Universität München (Germany) described on February 15 ahead of print in *Current Pharmaceutical Biotechnology* the potential of "Opto-acoustic imaging of drug discovery biomarkers." On February 4 ahead of print in *Advanced Drug Delivery Reviews*, Shim and Kwon from the University of California (Irvine) looked at a broad range of "Stimuli-responsive polymers and nanomaterials for gene delivery and imaging applications." Keyaerts et al. from the Vrije Universiteit Brussel and UZ Brussel (Belgium) in the February 7 online edition of *Trends in Molecular Medicine* provided a review of "Bioluminescence imaging: looking beyond the light."