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 Cost/Outcomes in Suspected CAD

Hlatky, from Stanford University School of Medicine (CA), and investigators on the Study of Myocardial Perfusion and Coronary Anatomy Imaging Roles in Coronary Artery Disease (SPARC) study reported in the March 18 issue of the *Journal of the American College of Cardiology* (2014;63:1002–1008) on a comparison of economic outcomes in patients undergoing various noninvasive tests for evaluation of suspected coronary artery disease (CAD). The study included 1,703 individuals at 41 centers from the SPARC registry who underwent coronary CT angiography (CTA; $n = 590$), PET ($n = 548$), or SPECT ($n = 565$) assessment for suspected CAD. Average 2-y after-imaging costs were, in descending order: $6,647 after PET, $4,909 after CTA, and $3,965 after SPECT. After adjusting for a number of baseline and treatment variables, CTA costs averaged 15% higher than SPECT, and PET costs averaged 22% higher than SPECT. Two-year mortality rates were 0.7%, 1.6%, and 5.5% after CTA, SPECT, and PET, respectively. After all analyses, the authors concluded

that "SPECT was economically attractive compared with PET, whereas CTA was associated with higher costs and no significant difference in mortality compared with SPECT."

Journal of the American College of Cardiology

LV Dyssynchrony and MP-Gated SPECT

In an article e-published on March 13 in the *Journal of Nuclear Cardiology*, Zafrir et al. from the Rabin Medical Center (Petah Tikva, Israel) reported on a study of the routine use of phase analysis with myocardial perfusion–gated SPECT imaging for predicting cardiac outcomes in patients with left ventricular dysfunction. The study included 787 such individuals (81% men, 19% women; age, 66.5 ± 11 y) who underwent gated SPECT imaging and phase analysis and who were followed for a mean of 18.3 ± 6.2 mo. Over this follow-up period, 45 individuals (6%) experienced cardiac events defined as composite endpoints (cardiac death in 26 and new-onset or worsening heart failure and life-threatening arrhythmias in 19). New York Heart Association (NYHA) functional classification, diabetes mellitus status, and left ventricular ejection fraction <50% were independent predictors for inclusion in this composite endpoint group. Independent predictors for cardiac mortality were NYHA class and incremental standard deviation in SPECT phase analysis. The authors concluded that "gated SPECT with phase analysis for the assessment of left ventricular dyssynchrony can successfully predict cardiac death together with NYHA class in patients with left ventricular dysfunction."

Journal of Nuclear Cardiology

PET/MR vs PET/CT in Oncologic Indications

Tian et al. from the General Hospital of the Chinese People's Liberation Army (Beijing, China) reported on March 6 in *PLoS One*

(2014;9:390844) on a study comparing the capabilities of PET/MR with PET/CT imaging in lesion detection and quantitative measurement. The study included 285 patients referred for oncologic indications who underwent same-day imaging with both hybrid modalities. Imaging was positive in 228 patients (368 lesions: 278 malignant, 68 benign, and 22 undetermined) and negative in 57 patients. When hybrid imaging results were broken out by single modalities, PET identified 31 lesions missed by CT and 12 missed by MR imaging. CT and MR imaging identified 38 and 61 lesions, respectively, missed by PET. MR detected 40 lesions missed by CT but missed 8 identified by CT. PET/CT correctly detected 6 lesions missed by PET/MR imaging but provided false-negative findings in 30 patients in whom PET/MR was accurate. Over the entire study, PET/MR performed comparatively to PET/CT in lesion detection and quantitative measurements. PET results from each of the hybrid modalities provided almost the same information despite significant differences in hardware and configuration.

PLoS One

Trends in PET Literature

In an article e-published on March 12 ahead of print in *Annals of Nuclear Medicine*, Baek et al. from the Hallym University College of Medicine (Seoul, Korea) reported on the results of a "bibliometric" analysis of scientific publications focused on PET imaging over a decade in which PET use grew rapidly around the world. Large English-language scientific databases were searched for the years 2002, 2007, and 2012 to assess trends and changing foci. PET publications for these years totaled 547, 986, and 1,838, respectively. The United States led with 948 articles (28.1%), with Japan second at 345 (10.2%) and Germany third at 335 (9.9%). Among other reported data points were: the use

of ^{18}F-FDG as a tracer in 1,698 (50.4%) studies; the dominance of clinical (2,378; 70.5%) over basic science and translational (993; 29.5%) articles; and large number of studies (1,337; 39.7%) supported by government funding. The authors identified several trends, including growing use of PET/MR and expanded average sample sizes.

Annals of Nuclear Medicine

SPECT and MACE Prognosis

Bom et al. from Deventer Hospital (The Netherlands) reported in the April issue of the *Netherlands Heart Journal* (2014;22:151–157) on the utility of SPECT in predicting major adverse cardiac events (MACE), particularly in patients with comorbidities, including diabetes, renal impairment, left bundle branch block, and atrial fibrillation. The study included 762 patients with no history of prior coronary artery disease who underwent SPECT with no perfusion defects. Data points for the study included clinical information, electrocardiography (ECG) results, and SPECT results. Participants were followed for 2 y for MACE. SPECT was found to have a 2-y negative predictive value of 95.8% for MACE and, along with a positive baseline stress ECG and low left ventricular ejection fraction, to be a significant predictor of MACE occurrence. None of the comorbidities assessed was found to have a significant effect on prognosis after normal SPECT imaging. MACE-free survival, however, was found to be lower in men.

Netherlands Heart Journal

Dose Rates for Fukushima Residents

In an article in the March 11 issue of the *Proceedings of the National Academy of Sciences of the United States of America* (2014;111:E914–E923), Harada et al. from the Kyoto Graduate School of Medicine (Japan) reported on radiation dose rates to individuals living in 3 areas adjacent to the restricted areas now surrounding the Fukushima Daiichi nuclear power plant. These rates were assessed in

August and September of 2012 and then projected for the years 2022 and 2062. Study participants in the 3 areas wore personal dosimeters for external dose equivalents. For the village of Kawauchi, the Tamano area, and the Haramachi area, these external dose rate equivalents (almost entirely from ground-deposited radionuclides attributed to the nuclear plant event) averaged 1.03, 2.75, and 1.66 mSv/y, respectively. Internal dose rates, estimated from dietary intake of radiocesium, averaged 0.0058, 0.019, and 0.0088 mSv/y, respectively, for the 3 areas. Average dose rates for inhalation of resuspended radiocesium averaged <0.001 mSv/y. Average annual doses from radiocesium in 2012 in the 3 areas were close to the average background radiation exposure (2 mSv/y) in all of Japan and were deemed "unlikely to exceed the ordinary permissible dose rate for the majority of the Fukushima population." However, data gathered in the study indicated that post-2012 annual doses in the Tamano area will increase lifetime solid cancer, leukemia, and breast cancer incidences by 1.06%, 0.03% and 0.28% respectively. The authors cautioned that these assessments and predictions did NOT evaluate first-year (event) dose or subsequent radioiodine exposure.

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

[124]I PET/CT in Pretherapy RAIU Assessment

Westphal et al. from Friedrich Schiller University of Jena (Germany) reported on February 25 ahead of print in the *Journal of Clinical Endocrinology and Metabolism* on a study designed to compare the utility of [124]I PET/CT and standard ^{131}I probe measurements in pretherapy assessment of radioactive iodine uptake (RAIU) in benign thyroid disease. The study included 24 patients who received a standard ^{131}I scintillation probe uptake test 30 h after administration of 3 MBq [131]I. Seven days later all patients underwent [124]I PET/CT imaging 30 h

after administration of 1 MBq [124]I. Uptake values were compared for the 2 techniques, and 3 volume-of-interest (VOI)–based approaches were assessed for PET/CT: whole neck, automatic iso-contouring, and manual contouring. [124]I PET/CT and ^{131}I probe measurement provided similar mean RAIUs (31.7% ± 8.9% and 30.7% ± 10.3%, respectively). Of the 3 contouring VOI approaches in PET, manual contouring resulted in the lowest uptake values. The authors concluded that these data suggest that [124]I-PET/CT "is a suitable alternative for pretherapy RAIU evaluations" and may offer additional benefits in areas such as PET/ultrasound fusion and CT volumetry.

Journal of Clinical Endocrinology and Metabolism

SPECT in TBI

In an article e-published on March 19 in *PLoS One* (2014;9:e91088), Raji, from the University of California Los Angeles, and a consortium of U.S. and Canadian researchers provided a systematic review of published data on the clinical utility of SPECT in traumatic brain injury (TBI). After analysis of a larger database of English-language articles, a subset of 71 articles met review criteria of foci on SPECT in mild, moderate, or severe TBI with cerebral lobar SPECT finding specificity and the existence of comparison modalities. The final studies selected for analysis included 19 longitudinal and 52 cross-sectional investigations. Both types of studies provided evidence of SPECT lesion localization not detected by CT or MR imaging, with the most common abnormal regions on SPECT in cross-sectional studies being in the frontal (94%) and temporal (77%) lobes. Longitudinal studies showed positive predictive value increasing from 59% at initial SPECT shortly after trauma to 95% at 1-y post-trauma. SPECT was determined to be more informative than CT or MR in both acute and chronic TBI imaging, with marked advantages in mild TBI, and was found to have a near 100% negative predictive value. The authors concluded that given these demonstrated advantages of

SPECT over CT and MR imaging in detection of mild TBI and "given its excellent negative predictive value, it may be an important second test in settings where CT or MRI are negative after a closed head injury with postinjury neurological or psychiatric symptoms."

PLoS One

PET and Response to Carboplatin Treatment

Witney et al. from Imperial College London (UK) reported online on March 11 in *PLoS One* (2014;9:e91694) on a preclinical study assessing the potential utility of ^{18}F-ICMT-11 PET as a noninvasive imaging technique for monitoring carboplatin treatment in non–small cell lung cancer (NSCLC). Uptake of ^{18}F-ICMT-11, which detects caspase-3/7 activation, was compared with biochemical measures of cell death in PC9 and A549 NSCLC cells after treatment with carboplatin in vitro and in mouse models. In the in vitro studies, carboplatin-induced apoptosis in ERCC1 low/mutant EGFR PC9 cells showed time- and dose-related increases in caspase-3/7 activation, poly-ADP-ribose polymerase cleavage, and annexin V staining. ^{18}F-ICMT-11 uptake was increased up to 14-fold at 200 μM carboplatin when compared with vehicle-treated cells. Necrosis rather than carboplatin-induced cell death was the main apoptotic mechanism in ERCC1 high/wt EGFR A549 cells, with no accompanying elevation in ^{18}F-ICMT-11 uptake. In mouse studies, average ^{18}F-ICMT-11 uptake on PET in PC9 tumor xenografts was not sensitive to changes in cell death, particularly in areas with substantial pre-existing necrosis. However, PET-based voxel intensity sorting distinguished specific intratumoral regions of high tracer uptake "enabling accurate assessment of apoptosis and therefore therapy response."

PLoS One

PET/CT in Large-Vessel Vasculitis

Muto et al. from the National Center for Global Health and Medicine (Tokyo, Japan) reported on March 19 ahead of print in *Rheumatology International* on a retrospective study evaluating the utility of ^{18}F-FDG PET and contrast-enhanced CT in early diagnosis of large-vessel vasculitis and treatment follow-up in elderly patients with new-onset inflammation of unknown origin (IUO). The study included 88 elderly patients admitted to the hospital for IUO and 11 age-matched control individuals, all of whom underwent both ^{18}F-FDG PET and contrast-enhanced CT imaging. Variables included maximum standardized uptake (SUV$_{max}$) and aortic wall PET score on PET/CT and aortic wall thickness and its ratio against the radius (W/R) on contrast-enhanced CT. Overall, 78 patients had abnormal imaging results, and findings indicated large-vessel vasculitis in 13 (10.5%) of these. Patients with large-vessel vasculitis were found to have significantly higher aortic wall SUV$_{max}$ on PET and aortic wall thickening on contrast-enhanced CT than control individuals. In follow-up, these elevations were reduced in patients receiving steroid therapy. The authors concluded that "imaging examination comprising contrast-enhanced CT and FDG PET/CT is useful for early diagnosis and early treatment evaluation of large-vessel vasculitis, allowing for amelioration of reversible aortic wall thickening."

Rheumatology International

PET and Prognosis in Esophageal Cancer

In an article e-published on March 18 ahead of print in the *Journal of Gastrointestinal Surgery*, Schollaert et al. from the Université Catholique de Louvain (Yvoir, Belgium) reported on a meta-analysis of published literature on the ability of ^{18}F-FDG PET to predict disease-free and overall survival in patients with esophageal and esophagogastric junction cancer. Inclusion criteria included studies with >10 patients with locally advanced esophageal cancer with ^{18}F-FDG PET imaging results (sequential scans or at least 1 postadjuvant treatment scan) and >6-mo follow-up. The final analysis included 26 studies with a total of 1,544 patients (average age, 62 y; 82% males, 18% females). Patients in these studies had TNM stages at inclusion of I (7%), II (24%), II (53%), and IV (15%). Pooled hazard ratios for complete metabolic response versus no response were 0.51 for overall survival and 0.47 for disease-free survival. After several stratified subanalyses, the authors found no individual study aspects that might affect these predictive capabilities. They concluded that "despite methodological and clinical heterogeneity, metabolic response on ^{18}FDG-PET is a significant predictor of long-term survival data."

Journal of Gastrointestinal Surgery

Sorafenib in ^{131}I-Refractory DTC

Shen et al. from the Shanghai Jiao Tong University Affiliated Sixth People's Hospital (People's Republic of China) reported in the February issue of *Endocrine-Related Cancer* (2014; 21:253–261) on a meta-analysis of the literature on the efficacy and safety of sorafenib administered to patients with radioiodine-refractory differentiated thyroid cancer. A total of 7 eligible studies were included. A partial response was seen in 22% of patients in these studies, with hand–foot syndrome (80%), diarrhea (68%), fatigue (67%), rash (66%) weight loss (52%), and hypertension (31%) noted as the most frequent adverse effects of sorafenib administration. Sorafenib toxicity resulted in dose reductions in 62% of patients. The authors concluded that the results of this meta-analysis suggest that sorafenib "has a modest effect in patients with radioiodine-refractory differentiated thyroid cancer, and the high incidence of adverse effects associated with this agent may affect the quality of patients' lives." They added that despite the fact that some clinicians consider sorafenib promising in this setting, "more effective agents with less toxicity and cost are still needed."

Endocrine-Related Cancer

PET and Malignancy in Focal Thyroid Lesions

In an article e-published on March 13 ahead of print in *Tumour Biology*,

Qu et al. from Fudan University (Shanghai, China) reported on a meta-analysis of literature on the ability of maximum standardized uptake value (SUV_{max}) on ^{18}F-FDG PET or PET/CT to discriminate between benign and malignant tissues in focal thyroid lesions. A total of 29 studies were identified to meet analytical criteria for review. Ultrasound was not reliably able to differentiate between benign and cancerous lesions, whereas a significantly higher focal SUV_{max} (especially at a threshold ≥ 3.3) on PET was associated with malignancy.

Tumour Biology

PET and Colon Cancer Staging

Lee and Lee from the Chonbuk National University Medical School (Jeonju, Korea) reported in the February issue of *Annals of Coloproctology* (2014;30:23–27) on a study comparing PET/CT and conventional assessments in staging of colon cancer. The study included 266 patients diagnosed with colon cancer who underwent both PET/CT and conventional studies. Intraoperative and pathology reports, along with follow-up imaging, were used to resolve discordance between PET/CT and conventional assessments. Multidetector CT and PET/CT imaging were similar in ability to identify metastases in patients with clinical stage III and IV disease. PET/CT led to changes in clinical management associated with disease stage (stage I, 2.5%; stage II, 0%; stage III, 6.5%; and stage IV, 12.7%). The authors concluded that these findings "suggest that PET/CT may be considered as a routine staging tool for clinical stage III and IV colon cancers."

Annals of Coloproctology

Other noteworthy articles published during this period include:

- Wang Y, Zhang H, Cui X, Fang N, Zeng L, Zhang C. [Clinical value of ^{18}F-FDG PET/CT in differentiation between benign lesions and lung cancer for large shadows in patients with pneumoconiosis.] In Chinese. *Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi.* 2014;32:186–189.

- Guo J, Hong H, Chen G, et al. Theranostic unimolecular micelles based on brush-shaped amphi-

philic block copolymers for tumor-targeted drug delivery and positron emission tomography imaging. *ACS Appl Mater Interfaces.* E-published on March 14 ahead of print.

- Raemekers JM, Andre MP, Federico M, et al. Omitting radiotherapy in early positron emission tomography-negative stage I/II Hodgkin lymphoma is associated with an increased risk of early relapse: clinical results of the preplaned interim analysis of the randomized EORTC/LYSA/FIL H10 trial. *J Clin Oncol.* E-published on March 17 ahead of print.

- Castillo R, Pham N, Ansari S, et al. Pre-radiotherapy FDG PET predicts radiation pneumonitis in lung cancer. *Radiat Oncol.* 2014;9:74.

- Owen DR, Gui Q, Kalk NJ, et al. Determination of ^{11}C-PBR28 binding potential in vivo: a first human TSPO blocking study. *J Cereb Blood Flow Metab.* E-published on March 19 ahead of print.

- Falchi L, Keating MJ, Marom EM, et al. Correlation between FDG/PET findings, histologic features, clinical characteristics and survival in 332 patients with chronic lymphocytic leukemia. *Blood.* E-published on March 10 ahead of print.

- Shin S, Kim HK, Choi YS, Kim K, Shim YM. Clinical stage T1-T2N0M0 oesophageal cancer: accuracy of clinical staging and predictive factors for lymph node metastasis. *Eur J Cardiothoracic Surg.* E-published on March 14 ahead of print.

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 from February through May. In an article e-published on February 27 ahead of print in *Frontiers in Oncology*, Pasciak et al. from the University of Tennessee Medical Center and Graduate School of Medicine (Knoxville) and the Mayo Clinic (Jacksonville, FL) summarized "Radioembolization and the dynamic role of ^{90}Y PET/CT." Gallamini and Borra from the A. Lacassagne Cancer Center (Nice, France) reported on March 12 ahead of print in *Current Treatment Options in Oncology* on the "Role of PET in lymphoma." In the March 15 issue of *Translational Neurodegeneration* (2014;3:6), Zimmer et al. from McGill University (Montreal, Canada) described "In vivo tracking of tau pathology using positron emission tomography (PET) mo-

lecular imaging in small animals." Vorster et al. from the University of Pretoria and Steve Biko Academic Hospital (Pretoria, South Africa) and University College London Hospitals NHS Trust (UK) detailed "Advances in imaging of tuberculosis: the role of ^{18}F-FDG PET and PET/CT" on March 7 ahead of print in *Current Opinion in Pulmonary Medicine.* In an article in the March 5 issue of the *Yale Journal of Biology and Medicine* (2014;87:33–54), Morris et al. from Yale University (New Haven, CT) described "How to design PET experiments to study neurochemistry: application to alcoholism." Nakazato et al. from the St. Luke's International Hospital (Tokyo, Japan) reported in the May issue of *Current Cardiology Reports* (2014;16:484) on "CFR and FFR assessment with PET and CTA: strengths and limitations." On March 6 ahead of print in the *Journal of Alzheimer's Disease*, Congdon et al. from the New York University School of Medicine (NY) reviewed prospects for "Harnessing the immune system for treatment and detection of tau pathology."

Other noteworthy reviews published during this period include:

- Terán MD, Brock MV. Staging lymph node metastases from lung cancer in the mediastinum. *J Thorac Dis.* 2014;6:230–236.

- Demetriades AK, Almeida AC, Bhangoo RS, Barrington SF. Applications of positron emission tomography in neuro-oncology: a clinical approach. *Surgeon.* E-published on March 10 ahead of print.

- Chen X, Li M, Wang S, Zhu H, Xiong Y, Liu X. Pittsburgh compound B retention and progression of cognitive status: a meta-analysis. *Eur J Neurol.* E-published on February 24 ahead of print.

- Kunkler IH, Audisio R, Belkacemi Y, et al. on behalf of the SIOG Radiotherapy Task Force. Review of current best practice and priorities for research in radiation oncology for elderly patients with cancer: the International Society of Geriatric Oncology (SIOG) task force. *Ann Oncol.* E-published on March 13 ahead of print.

- Niccolini F, Su P, Politis M. Dopamine receptor mapping with PET imaging in Parkinson disease. *J Neurol.* E-published on March 15 ahead of print.

- Wang SC, Xie Q, Lv WF. Positron emission tomography/computed tomography imaging and rheumatoid arthritis. *Int J Rheum Dis.* E-published on March 10 ahead of print.