C-Suite Watch List: Hospital Technology Issues for 2013," the report covers a range of technologies, with electronic health records topping the list of areas for concern. Imaging and image procedure–related concerns account for more than half of the items on the list. These include: (1) imaging and surgery, with a focus on placement of full-scale angiography, CT, MR, and other imaging systems in operating rooms (ORs) as adjuncts to interventional radiology and minimally invasive procedures; (2) minimally invasive cardiac surgery, specifically transcatheter aortic valve implantation, requiring hybrid OR imaging environments; (3) PET MR, with a focus on when a hospital should decide to acquire this technology and considerations in this decision; (4) added supply expenses associated with MR-compatible pacemakers; (5) issues associated with CT radiation dose safety; and (6) questions about lung cancer screening, particularly about the inherent costs of false-positive results. The report is available for free download at: https://www.ecri.org/Forms/Pages/2013-C-Suite-Watch-List.aspx.

ECRI

AAAS Honors Nuclear Medicine Researcher

Nasima Akhter, PhD, was recognized by the American Association for the Advancement of Science (AAAS) for early-career excellence on February 16 at the AAAS Minority and Women Scientists and Engineers Networking Breakfast at the society's 2013 Annual Meeting in Boston, MA. Akhter is a senior medical officer at the Center for Nuclear Medicine and Ultrasound, Dhaka Medical College Hospital, Bangladesh. Her work has spanned a broad range of radionuclide applications, including bone scintigraphy in breast cancer, imaging in Alzheimer disease, and cardiac imaging. She is currently conducting clinical research on nuchal translucency–based fetal screening for congenital anomalies during the first trimester of pregnancy. She is also investigating the usefulness of nonradioactive iodine adjunct medication with radioiodine therapy in Graves disease. Her work, recognized with the Society of Nuclear Medicine, Bangladesh, 2011 Young Scientist Award gold medal, was praised by the AAAS for its focus on the specific needs of developing countries.

American Association for the Advancement of Science

Demographic Patterns of PET Use

In a study published online on February 15 in *Radiology*, Dinan et al. from the Duke University School of Medicine (Durham, NC) reported on an exploration of demographic and regional factors associated with changing patterns of use of PET in patients with non–small cell lung cancer (NSCLC). The authors used Surveillance Epidemiology and End Results Medicare data on individuals who received a diagnosis of NSCLC between 1998 and 2007. They looked at changes in the number of PET studies in the period from 2 mo before to 4 mo after diagnosis. The final study group included 46,544 patients with 46,935 cases of NSCLC. By 2005, more than half of these patients had undergone at least 1 PET study, regardless of demographic subgroup. The authors found that patients who underwent PET were more likely to be married, nonblack, younger than 80 y, and to live in census tracts with higher education levels and/or in the northeast United States. Although living in relative proximity (within 40 miles) was a factor associated with higher use in the earliest years of the study, this association was no longer significant in 2007. Over the total study period, imaging rates increased more rapidly in patients who were nonblack, younger than 81 y, and/or who lived in the northeast or southern United States.

Radiology

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.

Selumetinib and ^{131}I Uptake

In an article in the February 14 issue of the *New England Journal of Medicine* (2013;368:623–632), Ho et al. from the Memorial Sloan–Kettering Cancer Center and Weill Cornell Medical College (New York, NY) reported on a study designed to determine whether the MAPK kinase (MEK) 1 and MEK2 inhibitor selumetinib could reverse radioiodine refractory status in patients with metastatic thyroid cancer. The study included 20 evaluable patients (11 men, 9 women; median age, 61 y, range, 44–77 y). Tumors in 9 patients showed BRAF mutations and in 5 patients showed NRAS mutations. All patients underwent thyrotropin-α stimulation as well as ^{124}I PET dosimetry, performed before and 4 wk after treatment with selumetinib (75 mg BID). When the second dosimetric results indicated that a dose ≥2,000 cGy ^{131}I could be administered to a metastatic lesion, the dose was administered along with selumetinib.

The administration of selumetinib was found to increase ^{124}I uptake in 12 patients (4 patients with BRAF and 5 with NRAS mutations). Of these patients, 8 reached the dosimetry threshold for ^{131}I therapy, including all 5 patients with NRAS mutations. After ^{131}I therapy, 5 of the 8 patients had confirmed partial responses and 3 had stable disease, with all 8 showing significant decreases in serum thyroglobulin levels. No toxic effects of grade 3 or higher were noted, although a single patient received a late (51 wk posttherapy) diagnosis of myelodysplastic syndrome with progression to acute leukemia. The authors concluded that "selumetinib produces clinically meaningful increases in iodine uptake and retention in a subgroup of patients with thyroid cancer that is refractory to radioiodine" and that "the effectiveness may be greater in patients with RAS-mutant disease."

New England Journal of Medicine

PET and PTSD Biomarkers

Sullivan et al. from Columbia University College of Physicians and Surgeons and the New York State Psychiatric Institute (New York, NY) reported on February 13 ahead of print in *Depression and Anxiety* on a quantitative PET study comparing regional brain serotonin-1A receptor (5-HT$_{1A}$) binding in medication-free participants with posttraumatic stress disorder (PTSD) and in healthy volunteers. The study included 20 patients with DSM-IV PTSD (including 13 with comorbid major depressive disorder) and 49 healthy volunteers. All participants underwent ^{11}C-WAY100635 PET imaging. Other data collected included arterial blood sampling for a metabolite-corrected input function and concentration of free ligand in plasma for estimation of regional binding potential. Regional binding potential was compared between groups across regions of interest (ROIs). The PTSD group was found to have higher 5-HT$_{1A}$ binding potential across brain ROIs, including all cortical ROIs (26%–33% higher), amygdala (34%), and brainstem raphe nuclei (43%), but not in the hippocampus. The subgroup of 7 PTSD patients without comorbid major depressive disorder also had higher binding potentials than healthy volunteers. The authors pointed to this as the first report of higher brainstem and forebrain 5-HT$_{1A}$ binding in vivo in PTSD, a finding independent of major depressive disorder. The authors observed that PTSD and major depressive disorder have in common "an upregulation of 5-HT$_{1A}$ binding including midbrain autoreceptors that would favor less firing and serotonin release," and concluded that "this abnormality may represent a common biomarker of these stress-associated brain disorders."

Depression and Anxiety

PET and SPECT in ^{90}Y Microsphere Distribution

In an article e-published on February 6 in *PLoS One* (2013;8:e55742), Elschot et al. from University Medical Center Utrecht (The Netherlands) conducted phantom studies to compare Bremsstrahlung SPECT, as used for evaluation of extrahepatic activity and liver dosimetry in ^{90}Y microsphere radioembolization, and ^{90}Y PET, particularly for the ability to detect small accumulations of ^{90}Y and to assess liver dosimetry accuracy. The authors described phantom studies with both SPECT/CT and PET/CT, including time-of-flight PET. They found PET to be superior to SPECT in detecting smaller "hot" spheres simulating extra- and intrahepatic metastases. Time-of-flight PET estimates of dose in the spheres were superior to those estimates based on SPECT, with underestimates of 11%–45% (for 37- to10-mm spheres) for PET and 58%–78% (for 37- to 10-mm spheres) for SPECT. These findings were illustrated in a small clinical study of comparative SPECT- and PET-based estimated liver dose distributions in 5 radioembolization patients. PET was found to have higher contrast recovery coefficients than SPECT, with the highest obtained with time-of-flight PET reconstruction including resolution recovery. The authors concluded that these results suggest that "the image quality of state-of-the-art PET is superior over Bremsstrahlung SPECT for the assessment of the ^{90}Y microsphere distribution after radioembolization."

PLoS One

Aging Brain and Vascular Injury

Marchant and a consortium of California neuroresearchers reported on February 11, ahead of print in the *Journal of the American Medical Association. Neurology*, on a study designed to determine the relationship between neuroimaging measures of vascular brain injury and brain β-amyloid (Aβ) deposition and related effects on cognition. Study participants included 30 clinically normal individuals (mean age, 77.1 y) and, from a vascular at-risk clinic, 24 cognitively impaired individuals (mean age, 78.0 y) and 7 mildly demented individuals (mean age, 79.8 y). All participants underwent MR imaging for presence and location of infarct and to quantify white matter lesion volume, Pittsburgh compound B (PiB) PET imaging for uptake across regions vulnerable to early Aβ deposition, and cognitive testing, including executive function and verbal/nonverbal memory assessments. MR identified 34 infarct-positive and 27 infarct-negative participants. PET was assessed as PiB positive in 29 and PiB negative in 32 participants. Results indicated that vascular brain injury and Aβ deposition were independent in all participant groups. Infarction (particularly in cortical and subcortical gray matter) was associated with lower cognitive performance. PiB positivity was not a predictor of cognition or significantly associated with vascular brain injury. The authors concluded that no evidence suggested that vascular brain injury increases the likelihood of Aβ deposition. They added that "this finding highlights the importance of vascular brain injury in mild cognitive impairment and suggests that the impact of cerebrovascular disease should be considered with respect to defining the etiology of mild cognitive impairment."

Journal of the American Medical Association. Neurology

PET/CT and Breast Ca Therapy Response

In an article e-published on February 12 ahead of print in *Breast*, Koolen et al. from The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (Amsterdam) reported on the relevance of breast cancer subtypes in ^{18}F-FDG PET/CT monitoring of neoadjuvant chemotherapy response. The study included 98 women with stage II or III breast cancer. All participants underwent ^{18}F-FDG PET/CT before and after 6 or 8 wk of neoadjuvant chemotherapy. PET was quantified by maximum standardized uptake value (SUV_{max}) calculation. Tumors were classified into 3 subtypes: HER2-positive (25 patients), ER-positive/HER2-negative (45 patients), and triple negative (28 patients). Tumor response at surgery was assessed by evidence of residual disease and by breast response index. Nearly complete pathologic responses were seen in 19 (76%) HER2-positive, 7 (16%) ER-positive/HER2-negative, and 20 (71%) triple negative tumors. PET tracer uptake was found to be significantly related to breast cancer subtype, with average areas under the receiver operating characteristic curve at 0.35 for HER2-positive, 0.90 for ER-positive/HER2-negative, and 0.96 for triple negative tumors. No association was identified between age, stage, histology, or baseline SUV_{max} and pathologic response. The authors concluded that although "response monitoring with PET/CT during neoadjuvant chemotherapy in breast cancer seems feasible" it is dependent on breast cancer subtype. They added that "PET/CT may predict response in ER-positive/HER2-negative and triple negative tumors, but seems less accurate in HER2-positive tumors."

Breast

Rituximab and False-Positive PET

Avivi et al. from the Rambam Health Care Campus and the Israel Institute of Technology (both in Haifa) reported on February 20 ahead of print in the *American Journal of Hematology* on a study comparing the prognostic utility of surveillance ^{18}F-FDG PET in patients with diffuse large B-cell lymphoma treated with either chemotherapy with rituximab or chemotherapy alone. The retrospective study included 119 patients, 35 of whom underwent cyclophosphamide, hydroxydaunorubicin hydrochloride, vincristine, and prednisone (CHOP) therapy alone and 84 of whom underwent CHOP with rituximab. Achievement of complete remission and surveillance PET imaging were requirements for inclusion. At a median follow-up of 3.4 y, 31 patients had relapsed (17 CHOP and 14 CHOP + rituximab). Although PET accurately detected all relapses, with no false-negative results, a high rate of false-positives was seen. Specificity and positive predictive values were lower for patients receiving CHOP with rituximab than CHOP alone (84% and 87%, and 23% vs 74%, respectively). In the CHOP + rituximab group, the false-positive rate remained high up to 3 y after therapy. The authors concluded that routine surveillance with ^{18}F-FDG PET is "not recommended in diffuse large B-cell lymphoma treated with rituximab; strict criteria identifying patients in whom follow-up PET is beneficial are required."

American Journal of Hematology

PET, Recurrent Colorectal CA, and CEA

In an article e-published on February 14 ahead of print in the *International Journal of Colorectal Disease*, Lu et al. from the Taichung Veterans General Hospital (Taiwan) reported on the results of a systematic review and metaanalysis of literature on the diagnostic performance of ^{18}F-FDG PET and PET/CT in detection of recurrent colorectal cancer in patients with elevated carcinoembryonic antigen (CEA). The initial search yielded 11 studies that met inclusion criteria, with a total of 510 patients. Of these, 106 (20.8%) had true-negative PET or PET/CT results in detection of recurrent colorectal cancer in the presence of elevated CEA. The pooled estimates of sensitivity, specificity, and positive and negative likelihood ratios for PET detection of disease in these patients were 90.3%, 80.0%, 2.88, and 0.12, respectively. The corresponding values for PET/CT were 94.1%, 77.2%, 4.70, and 0.06. The authors concluded that "whole-body FDG-PET and PET/CT are valuable imaging tools for the assessment of patients with suspected colorectal cancer tumor recurrence based on the increase of CEA."

International Journal of Colorectal Disease

PET/CT and Preop Chemotherapy in Breast Cancer

Zucchini et al. from the S. Orsola-Malpighi University Hospital Bologna (Italy) reported on January 28 ahead of print in the *European Journal of Cancer* on the ability of ^{18}F-FDG PET/CT to assess early metabolic response to preoperative chemotherapy in patients with early or locally advanced breast cancer. The study included 60 such patients who received 6–8 cycles of preoperative chemotherapy. Patients underwent PET/CT imaging at baseline and after 2 cycles of therapy. An optimal pathologic response was defined as an absence of cancer cells in breast and axillary lymph nodes at surgery; all other conditions were defined as pathologic nonresponses. Metabolic response was defined as >50% change in standardized maximum uptake values (SUV_{max}) on PET, and these results were compared with histopathology. Histopathology indicated that 13 (22%) patients achieved an optimal pathologic response, representing 16% of ER-positive/HER2-negative, 29% of HER2-positive, and 27% of triple-negative patients. PET/CT results had the highest specificity (38%) and negative predictive value (100%) in ER-positive/HER2-negative patients. In this subgroup, median disease-free survival had not been reached at 36 mo by metabolic responders. Early metabolic nonresponse was always associated with histochemical evidence of nonresponse and poor prognosis in ER-positive/HER2-negative patients. The authors concluded that "in this subgroup, ^{18}F-FDG PET/CT might

be useful to select patients who will probably benefit from early therapeutic strategy modifications."

European Journal of Cancer

^{11}C-MET PET and Craniopharyngioma

In an article e-published on 13 February ahead of print in *Neuro-Oncology*, Laser et al. from the University of Maryland School of Medicine (Baltimore), St. Jude Children's Research Hospital (Memphis, TN), and the University of Florida Proton Therapy Institute (Jacksonville) reported on ^{11}C-methionine (^{11}C-MET) and ^{18}F-FDG PET evaluation of children with craniopharyngioma before proton therapy. The study included 10 newly diagnosed patients (median age, 9 y; range, 5–19 y) who underwent PET imaging with ^{11}C-MET and ^{18}F-FDG. PET images were coregistered with those from MR to assess tumor volumes. Tumor standardized maximum uptake values (SUV_{max}) were compared with noninvolved left frontal background white matter, and uptake was graded using a 4-point scale. The median ^{18}F-FDG SUV_{max} for tumor and background were 2.65 and 3.2, respectively. The corresponding values for ^{11}C-MET were 2.2 and 1.0. The difference between MET tumor and MET background SUV_{max} was significant; whereas that for ^{18}F-FDG was not. The authors concluded that ^{11}C-MET PET uptake is significantly greater within the tumor compared with noninvolved background white matter, making it more useful than FDG PET in identifying active tumor in patients with craniopharyngioma." They added that future work will focus on the ability of ^{11}C-MET PET to discriminate between active and inactive tumor after irradiation.

Neuro-Oncology

Imaging, Proton Therapy, and Meningiomas

Combs et al. from the University Hospital of Heidelberg (Germany) reported on February 12 ahead of print in *Acta Oncologica* on evaluation of early treatment outcomes in patients with meningiomas treated with particle therapy based on target volume definition with MR and ^{68}Ga-DOTATOC PET imaging. The study included 70 patients (median age, 55 y; 24 males, 46 females) treated with proton (38) or carbon ion radiotherapy (26). Histology indicated benign meningiomas in 26 (37%) and was atypical in 23 (33%) and anaplastic in 4 patients (6%). The remaining patients had skull-based meningiomas. For benign meningiomas, total doses of 52.2–57.6 GyE were applied with protons. For high-grade lesions, the boost volume was 18 GyE carbon ions, with a median dose of 50 GyE applied as highly conformal radiation therapy. Very low rates of side effects, mild or severe, were noted. No severe treatment-related toxicities were observed. Treatment achieved local control of 100% in benign meningiomas. Actuarial local control after re-irradiation of high-risk meningiomas was 67% at 6 and 12 mos. In patients treated with primary radiotherapy, only 1 of 13 patients (8%) developed tumor recurrence 17 mo after radiation therapy (photon and carbon ion boost). The authors concluded that "when proton therapy is available, meningioma patients can be offered a treatment at least comparable to high-end photon therapy." They added that "continuous prospective follow-up and development of novel study concepts are required to fully exploit the long-term clinical data after particle therapy for meningiomas."

Acta Oncologica

^{18}F-FLT PET and PI3-Kinase Inhibition

In an article e-published on February 20 ahead of print in *Molecular Cancer Therapeutics*, Cawthorne et al. from the University of Manchester (UK) reported on a study designed to determine whether ^{18}F-fluorothymidine (^{18}F-FLT) can be used for PET imaging of the effects of a novel phosphatidylinositide 3-kinase (PI3-K) inhibitor (GDC-0941), which is now in phase II clinical trials. The study was conducted in mice bearing U87 glioma and HCT116 colorectal xenografts. Mice were imaged with ^{18}F-FLT PET at baseline, at 18 h, and at multiple timepoints after either twice-daily administration of GDC-0941 or of vehicle alone (controls). Tumor uptake was calculated, and tissues were analyzed. GDC-0941 treatment was found to induce tumor stasis in U87 xenografts; inhibition of HCT116 tumors was more variable. Tracer uptake in tumors was significantly reduced after GDC-0941 administration in responsive tumors at 18-h imaging and was correlated with pharmacodynamic markers of PI3-K signaling inhibition and significant reduction in TK1 expression in U87 but not HCT116 tumors. The authors concluded that these results "indicate that ^{18}F-FLT is a strong candidate for the noninvasive measurement of GDC-0941 action."

Molecular Cancer Therapeutics

In-Room PET and Proton Therapy

Min et al. from the Massachusetts General Hospital and Harvard Medical School (Boston, MA) reported on February 4 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on the utility of in-room PET for treatment verification and monitoring in proton therapy. The study included 9 patients who underwent passive scattering proton therapy and immediately thereafter underwent PET imaging with a unit positioned next to the treatment head. CT-based Monte Carlo calculations were used to reproduce PET activities for each patient, and a novel technique assessed proton beam range uncertainty. Repositioning for PET imaging required an average of 2 min. PET images were subsequently reconstructed to simulate varying scan times to determine the scan time dependency of the method. For 8 patients treated with a single field, the average range difference between PET measurements and Monte Carlo results was <5 mm (<3 mm for 6 of these patients), with PET–CT image coregistration errors of ~ 2 mm. These results indicated that a PET scan of 5 min can yield results similar to those of a 20-min PET scan. The authors concluded that these initial studies of in-room PET showed its potential for in

vivo treatment monitoring in proton therapy.

International Journal of Radiation Oncology, Biology, Physics

"Virtual" Skin Biopsy

In an article e-published on February 20 ahead of print in *Annals of the Rheumatic Diseases*, Abignano et al. from the University of Leeds (UK) reported on the use of optical coherence tomography (OCT) for "virtual skin biopsy," a process pointing toward what the group called "the first quantitative imaging biomarker for scleroderma." The study focused on the ability of OCT to detect and quantify skin fibrosis in systemic sclerosis. The study included 21 patients with systemic sclerosis and 22 healthy volunteers. More than 450 OCT images were acquired and compared with histology from clinical assessments and from 3 skin biopsies per patient. These comparisons indicated a progressive loss of visualization of the dermal–epidermal junction associated with dermal fibrosis. Systemic sclerosis–affected skin showed a consistent decrease of optical density in the papillary dermis, which became progressively worse in patients with worsening modified Rodnan skin scores. Clinically unaffected skin was distinguishable from healthy skin by its specific pattern of optical density decrease in the reticular dermis. The OCT technique showed excellent intraobserver and interobserver reliability. The authors concluded that "OCT of the skin could offer a feasible and reliable quantitative outcome measure in systemic sclerosis." They added that "studies determining OCT sensitivity to change over time and its role in defining skin vasculopathy may pave the way to defining OCT as a valuable imaging biomarker in systemic sclerosis."

Annals of the Rheumatic Diseases

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 and March. In an article published on March 15 in *Current Cardiology Reports* (2013;14:344), Valenta, from University Hospitals of Geneva (Switzerland), and an international team of colleagues described "Quantitative PET/CT measures of myocardial flow reserve and atherosclerosis for cardiac risk assessment and predicting adverse patient outcomes." Morrison et al. from the University of Wisconsin (Madison) reported on February 15 ahead of print in *Current Opinion in Urology* on "Imaging of castration-resistant prostate cancer: development of imaging response biomarkers." In the February 20 issue of *ACS Chemical Neuroscience* (2013;4:225–237), Syvänen and Eriksson from Uppsala University (Sweden) reviewed "Advances in PET imaging of P-glycoprotein function at the blood–brain barrier." Shah et al. from the University of Miami (FL), in an article released on January 24 ahead of print in the *Journal of Neuro-Oncology*, asked "Discriminating radiation necrosis from tumor progression in gliomas: a systematic review. What is the best imaging modality?" In the February issue of *Magma* (2013;26:1–4), Beyer and Moser from CMI-Experts GmbH (Zurich, Switzerland) discussed "MR/PR or PET/MRI: does it matter?" Ehling et al. from the Universitätklinikum Aachen (Germany) reviewed "Noninvasive imaging for studying antiangiogenic therapy effects" in the February 14 issue of *Thrombosis and Haemostasis* (2013;109:375–390). In an article e-published on February 15 ahead of print in *Molecular Imaging and Biology*, Blomberg et al. from the University Medical Center Utrecht (The Netherlands) described "Beta cell imaging: call for evidence-based and scientific approach."