Ezster Boros, PhD (New England Chapter); Delphine Chen, MD (Missouri Valley Chapter); Saurabh Malhotra, MD, MPH (Eastern Great Lakes Chapter), and Devaki Surasi, MD (Southeastern Chapter).

SNMMI

NIH Plans for Precision Medicine Initiative Network

The National Institutes of Health (NIH) announced on March 31 the creation of a team of experts in precision medicine and large clinical research studies that will seek public input from the larger stakeholder community interested in the development of President Obama's Precision Medicine Initiative. This team will articulate a vision for building the initiative's national cohort of >1 million participants and help define what can be learned from this study, what issues should be addressed and considered as part of the study design, and what will define success 5 and 10 y after start-up. Formed as a Working Group of the Advisory Committee to the NIH Director, the team of experts will deliver a preliminary report in September 2015 that will inform efforts to accelerate the understanding of individual differences that play a role in health, with the goal of informing better prevention and treatment strategies tailored for each individual.

President Obama launched the new initiative on January 30 and called for initial funding of $215 million in the federal year 2016 budget. Of this total, $130 million would be dedicated to beginning the process of building the group of research participants who will volunteer to share their biologic, environmental, lifestyle, and behavioral information and tissue samples with qualified researchers. Participant input through representation on the working group, workshops, and other feedback mechanisms will be central to the design and implementation of the study. For more information about the Precision Medicine Initiative, see http://www.nih.gov/precisionmedicine/.

National Institutes of Health

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.

^{68}Ga-DOTATATE PET/CT in SDHB-Associated Metastases

In an article e-published on April 14 ahead of print in *Clinical Cancer Research*, Janssen, from the National Institute of Child Health and Human Development (Bethesda, MD), and colleagues from the National Institutes of Health, the Bichat-Claude-Bernard Hospital (Paris, France), and the University of Lübeck (Germany) reported on a study on the relative merits of ^{68}Ga-DOTATATE PET/CT in accurate localization of succinate dehydrogenase subunit-B (SDHB) mutation–associated metastatic pheochromocytoma and paraganglioma (PHEO/PGL). ^{68}Ga-DOTATATE PET/CT in this disease setting was compared with ^{18}F-fluorodopamine (^{18}F-FDA), ^{18}F- fluorodihydroxyphenylalanine (^{18}F-FDOPA), and ^{18}F-FDG tracers in PET/CT as well as with CT/MR imaging. The study included 17 patients with SDHB-related metastatic PHEO/PGL, all of whom underwent ^{68}Ga-DOTATATE and ^{18}F-FDG PET/CT and CT/MR imaging. All except 1 patient also underwent ^{18}F-FDA and ^{18}F-DOPA PET imaging. The numbers of metastatic lesions detected by each modality were compared against a composite synthesis of findings from all modalities. Detection rates of ^{68}Ga-DOTATATE, ^{18}F-FDG, ^{18}F-FDOPA, and ^{18}F-FDA PET/CT and MR/CT were 98.6%, 85.8%, 61.4%, 51.9%, and 84.8%, respectively. The authors concluded that because of its superior detection rate in comparison with these other more commonly used imaging approaches, ^{68}Ga-DOTATATE PET/CT "may represent the preferred future imaging modality in the evaluation of SDHB-related metastatic PHEO/PGL."

Clinical Cancer Research

PET and Large-Vessel Vasculitis

Soussan et al. from the Sorbonne Paris Cité, Avicenne Hospital, and the Saint-Antoine Hospital (all in Paris, France) reported in the April issue of *Medicine (Baltimore)* (2015;94:e622) on a systematic literature review and meta-analysis designed to clarify the role of ^{18}F-FDG PET in the management of large-vessel vasculitis. The authors specifically targeted articles that addressed ^{18}F-FDG PET-based criteria for diagnosis of vascular inflammation, ^{18}F-FDG PET performance in diagnosis of large-vessel inflammation in giant cell arteritis, and ^{18}F-FDG PET performance in evaluating inflammatory activity associated with Takayasu arteritis. Twenty-one studies with a total of 413 patients and 299 controls met criteria for inclusion in the analysis. Vascular

uptake on ^{18}F-FDG PET was seen in 70% of patients and 7% of controls, with only vascular uptake ≥ liver uptake found to be significantly different between patients and controls. ^{18}F-FDG PET had high sensitivity (90%) and specificity (98%) for diagnosis of large-vessel inflammation in patients with giant cell arteritis. These figures were 87% and 73% (up to 84% using National Institutes of Health criteria) in assessing disease activity in patients with Takayasu arteritis. The authors concluded that "although a vascular uptake equal to or higher than the liver uptake appears to be a good criterion for the diagnosis of vascular inflammation, further studies are needed to define the threshold of significance as well as the clinical significance of the vascular uptake."

Medicine (Baltimore)

^{18}F-Florbetaben PET and β-Amyloid Plaque

In an article e-published on March 28 ahead of print in *Alzheimer's & Dementia*, Sabri, from the University of Leipzig (Germany), and researchers from Germany, the United States, Japan, Australia, and Scotland reported on the result of a phase 3, open-label, nonrandomized multicenter study to evaluate the ^{18}F-labeled β-amyloid tracer florbetaben (^{18}F-florbetaben) by comparing in vivo PET β-amyloid plaque imaging results with those from postmortem histopathology. The study included PET images and tissue from 74 individuals (57 with clinical diagnoses of Alzheimer disease, 3 with dementia with Lewy bodies, 6 with other dementias, and 8 without dementia). The mean time elapsed from PET imaging to death was 329 ± 272 d. Of 47 subjects whose tissues were β-amyloid–positive at autopsy, 46 had positive PET images. Of 27 subjects whose tissues were β-amyloid–negative at autopsy, 24 had negative PET findings (sensitivity, 97.9%; specificity, 88.9%). The authors concluded that ^{18}F-florbetaben PET "shows high sensitivity and specificity for the detection of histopathology-confirmed neuritic β-amyloid plaques and may thus be a valuable adjunct to clinical diagnosis, particularly for the exclusion of Alzheimer disease."

Alzheimer's & Dementia

^{11}C-Choline PET vs T2W/DW MR in IPL Delineation

Chang, from the University of Melbourne and Austin Health (Australia), and a consortium of Australian researchers reported on April 8 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on a study comparing the accuracy of ^{11}C-choline PET with that of combined T2-weighted (T2W) and diffusion-weighted (DW) MR imaging in assessing malignant intraprostatic lesions. The study included 21 patients, each of whom underwent ^{11}C-choline PET and T2W/DW MR imaging before radical prostatectomy. Automatic and manually generated contours for each scan were compared with prostatectomy specimens and against reference standard contours. The authors found that results from the optimal automatic contouring method for PET and manual PET contouring were similarly correlated with histopathology results and were each more accurate than manual MR imaging contours. Respective sensitivity and specificity were 72% and 71% for automatic contouring (at 60% of the maximum standardized uptake value), 53% and 86% for PET manual contouring, and 28% and 92% for MR manual contouring. The tumor volume and a transition zone pattern were found to independently predict the accuracy of ^{11}C-choline PET. The authors concluded that although ^{11}C-choline PET is superior to combined T2W/DW MR imaging for delineating intraprostatic lesions, its accuracy is "insufficient for gland-sparing focal therapies but may be accurate enough for focal boost therapies." The transition zone pattern identified in this study may be useful in predicting how well ^{11}C-choline PET may delineate intraprostatic lesions in specific cases.

International Journal of Radiation Oncology, Biology, Physics

PD, β-Amyloid, and Cognitive Impairment

In an article e-published on April 16 ahead of print in *Movement Disorders*, Petrou et al. from the University of Michigan (Ann Arbor) and the Johns Hopkins University School of Medicine (Baltimore, MD) reported on a systematic review designed to estimate the prevalence of Alzheimer disease (AD)–range cortical amyloid deposition among patients with Parkinson disease with dementia (PDD), Parkinson disease with mild cognitive impairment (PD-MCI), and dementia with Lewy bodies (DLB) as assessed by ^{11}C-Pittsburgh compound B (^{11}C-PiB) PET. Eleven articles were identified meeting inclusion criteria, with a total of 233 participants (74 diagnosed with PDD, 99 with DLB, and 60 with PD-MCI) Point prevalence estimates were calculated for patients showing cortical β-amyloid deposition considered to be in typical ranges for AD. The prevalence of these "^{11}C-PiB–positive" studies was 0.68 in the DLB group, 0.34 in the PDD group, and 0.05 in the PD-MCI group. The authors discussed potential explanations for the substantial variability in the prevalence of ^{11}C-PiB–positive studies in individuals with PD and cognitive impairment and called for "prospective, systematic, larger studies employing uniform recruitment, clinical, and imaging characterization protocols and concurrent evaluation of vulnerable neuronal populations in synucleinopathies to clarify the roles of amyloidopathy in synucleinopathy-related cognitive impairments."

Movement Disorders

IAEA PET/CT Recommendations on Curative RT in NSCLC

Konert, from The Netherlands Cancer Institute (Amsterdam), and a consortium of experts from The Netherlands, Australia, Germany, Belgium, Austria, Italy, and Ireland representing the International Atomic Energy Agency (IAEA) published a consensus report on best-practice and

evidence-based recommendations for PET/CT imaging for target volume delineation in curative intent radiotherapy of non–small cell lung cancer (NSCLC) on April 10 ahead of print in *Radiotherapy and Oncology.* The recommendations were created as part of a coordinated IAEA research project designed to improve PET-based radiation treatment planning in low- and middle-income countries. The recommendations are intended to be relevant to routine clinical practice of radiotherapy for NSCLC patients treated with concurrent chemoradiation or radiotherapy alone, where ^{18}F-FDG is used and a calibrated PET system equipped for radiation treatment planning patient positioning is available. Recommendations are also provided for PET and CT image visualization and interpretation and for tumor delineation with planning CT, both with and without breathing motion compensation. The recommendations concluded with the statement that "it remains the recommendation of an IAEA expert panel that an appropriately timed and technically adequate PET/CT imaging is an essential component in the radiotherapy treatment planning process for lung cancer," adding that "it is also recognized that further research is needed in the fields of 4D PET/CT imaging and automated treatment volume delineation techniques."

Radiotherapy and Oncology.

SPECT/CT Classifies Postthyroidectomy Remnant ^{131}I Foci

In an article e-published on April 17 in *The Laryngoscope*, Zeuren et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported on a novel SPECT/CT anatomic classification system for radioactive iodine thyroid bed uptake and preservation of adjacent neural structures after total thyroidectomy. The retrospective study included the records of 141 patients with differentiated thyroid cancer undergoing total thyroidectomy in whom radioactive iodine–uptake foci were localized by SPECT/CT in the thyroid bed at the time of ^{131}I remnant ablation. Diagnostic planar whole-body imaging and posttherapy SPECT/CT imaging detected residual ^{131}I uptake in 93% and 99% of patients, respectively. SPECT/CT imaging identified discrete uptake foci at Berry's ligament, the superior thyroid poles, paratracheal–lobar regions, the isthmus region, and in the pyramidal lobe in 87%, 79%, 67%, 54%, and 46% of patients, respectively. However, nonstimulated thyroglobulin levels before remnant ablation were < 0.6 ng/mL in 53% and < 1 ng/mL in 73% of patients. The authors classified ^{131}I-avid foci detected after extracapsular total thyroidectomy as neural related and capsule related and noted the importance of distinguishing between such foci. The findings suggest that most "common residual foci have no relationship to postoperative nonstimulated thyroglobulin, suggesting that attempts at radical removal of thyroid tissue in these locations may not be warranted."

The Laryngoscope

^{18}F-FES and ^{18}F-FDG in Metastatic Breast Cancer

Koleva-Kolarova et al. from the University of Groningen (The Netherlands) reported on April 16 ahead of print in the *British Journal of Cancer* on a computer simulation study of the value of PET/CT with 16α-[^{18}F] fluoro-17β-oestradiol (^{18}F-FES) or ^{18}F-FDG as a first-line imaging approach for diagnosis of metastatic breast cancer in estrogen receptor–positive women with symptoms. After establishing a simulated cohort, 3 strategic models were explored: (1) a standard workup based on Dutch clinical guidelines, including radiography, bone scintigraphy, CT, ultrasound, MR imaging, and biopsies; (2) upfront, whole-body ^{18}F-FES PET/CT alone, with biopsy/no biopsy and follow-up based on imaging results and persistence of symptoms; and (3) upfront, whole-body ^{18}F-FDG PET/CT alone, with biopsy/no biopsy and follow-up based on imaging results and persistence of symptoms. With the ^{18}F-FES PET/CT strategy, the projected number of biopsies decreased by 39% ± 9% when compared with the standard workup, whereas these numbers increased by 38% ± 15% with the ^{18}F-FDG PET/CT model. Both PET/CT models reduced the number of imaging tests and false-positives, but the number of false-negative results decreased only with ^{18}F-FES PET/CT. Avoidance of biopsies in the ^{18}F-FES PET/CT model resulted in significant savings, whereas the ^{18}F-FDG strategy was more expensive. The authors validated these models with data from a study of records of a cohort of 108 patients diagnosed and treated with estrogen receptor–positive breast cancer.

British Journal of Cancer

^{18}F-Choline PET/CT in Recurrence After Prostatectomy

In a study e-published on April 1 ahead of print in the *World Journal of Urology*, Kjölhede et al. from Lund University (Växjö, Sweden) reported on a study investigating the utility of ^{18}F-choline PET/CT for early detection of metastases in biochemical recurrence following radical prostatectomy. The study included 58 patients with untreated biochemical recurrence after radical prostatectomy, prostate-specific antigen (PSA) levels <2 ng/mL, and Gleason scores ≥ 7 or PSA doubling time ≤ 6 mo. Each participant underwent ^{18}F-choline PET/CT, with focal tracer uptake in lymph nodes or skeletal sites noted. PET/CT identified metastases in 16 (28%) patients, in whom imaging indicated bone metastases in 5 (9%) and regional lymph node metastases alone in 11 (19%). PET identified metastatic recurrence in 25% of those patients with PSA levels <1.0 ng/mL. The authors concluded that "^{18}F-choline PET/CT may be valuable for selecting patients with biochemical recurrence following radical prostatectomy for salvage radiation therapy or experimental treatment of oligometastases, even at low PSA values."

World Journal of Urology

PET and CTE in Football Players

Barrio and colleagues from the University of California Los Angeles,

the University of California Davis (Sacramento), and the University of Chicago Pritzker School of Medicine (IL) reported in the April 21 issue of the *Proceedings of the National Academy of Sciences of the USA* (2015;112: E2039–E2047) on the potential for in vivo characterization of chronic traumatic encephalopathy using ^{18}F-FDDNP PET brain imaging. The study group included 14 retired professional football players with suspected chronic traumatic encephalopathy, 24 patients with Alzheimer disease (AD), and 28 non–cognitively impaired control individuals. The authors found distinctly different neuropathologic patterns in the 3 groups. In the retired players, imaging indicated patterns consistent with concussion, in which brainstem white matter tracts undergo early axonal damage and later cumulative axonal injuries along subcortical, limbic, and cortical brain circuitries affecting mood, emotions, and behavior. In individuals with AD, paired helical filament–tau and β-amyloid deposition most often begins in the medial temporal lobe and progress along the cortical default mode network with little subcortical structure involvement. The authors noted that the observed ^{18}F-FDDNP PET patterns in suspected chronic traumatic encephalopathy are consistent with paired helical filament–tau distributions seen at autopsy in individuals with a history of mild traumatic injury and autopsy-confirmed diagnosis of chronic traumatic encephalopathy.

Proceedings of the National Academy of Sciences of the USA

PET and Posterior Cortical Atrophy

In an article e-published on April 11 ahead of print in the *Journal of Neurology*, Singh et al. from the Mayo Clinic (Rochester, MN) reported on clinical, ^{18}F-FDG PET, and ^{11}C-Pittsburgh compound B (^{11}C-PiB) findings in patients with posterior cortical atrophy (PCA). The study included 25 patients with PCA, each of whom underwent a set of standardized clinical tests and ^{11}C-PiB PET imaging. Of these, 17 (68 %) also underwent ^{18}F-FDG PET scanning. Thirteen individuals at the median disease duration of 4 y formed a subcohort for investigation of clinical and ^{18}F-FDG PET correlates of early PCA. Over all patients in the study, the most common clinical features were simultanagnosia (92%), dysgraphia (68%), polyminimyoclonus (64%), and oculomotor apraxia (56.5%). Associated ^{18}F-FDG PET findings were hypometabolism in the right occipital lobe and posterior cingulum with simultanagnosia, hypometabolism in the left occipital lobe in optic ataxia, and hypometabolism in the left parietal lobe and posterior cingulate gyrus in oculomotor apraxia. All 25 patients were β-amyloid positive on ^{11}C-PiB PET imaging. Simultanagnosia was the only clinical feature present in 85% of early PCA patients. The authors noted that although many of the classic clinical features of PCA show associated imaging foci in the posterior hemispheric regions, these are "not widespread." They concluded that "simultanagnosia appears to be the most common and hence sensitive feature of early PCA."

Journal of Neurology

^{99m}Tc-HDP SPECT, PET, and MR in Bone Metastases

Jambor et al. from the University of Turku (Finland) reported on April 2 ahead of print in *Acta Oncologica* on a study comparing ^{99m}Tc-hydroxymethane diphosphonate (^{99m}Tc-HDP) planar bone scintigraphy, ^{99m}Tc-HDP SPECT, ^{99m}Tc-HDP SPECT/CT, ^{18}F-NaF PET/CT, and whole-body 1.5-T MR imaging, including diffusion-weighted imaging, in detection of bone metastases in high-risk breast and prostate cancer patients. The study included 26 women with breast cancer and 27 men with prostate cancer at high risk of bone metastases, each of whom underwent all of the imaging procedures under investigation. The individual imaging results were reviewed and compared against consensus reading reviews and clinical and imaging follow-up (range, 6–32 mo). Bone findings were compared at lesion, regional, and patient levels. For the region-based analyses, the sensitivities of ^{99m}Tc-HDP bone scintigraphy, ^{99m}Tc-HDP SPECT, ^{99m}Tc-HDP SPECT/CT, ^{18}F-NaF PET/CT, and MR imaging were 62%, 74%, 85%, 93%, and 91%, respectively. The respective numbers of equivocal findings were 50, 44, 5, 6, and 4. The authors summarized their results with the conclusion that MR with diffusion-weighted imaging showed diagnostic accuracy similar to that of ^{18}F-NaF PET/CT and superior to ^{99m}Tc-HDP SPECT, ^{99m}Tc-HDP SPECT/CT, and ^{99m}Tc-HDP bone scintigraphy.

Acta Oncologica

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches by offering valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in spring 2015. In an article e-published on March 31 ahead of print in *Trends in Pharmacological Sciences*, Blennow, from the University of Gothenburg (Mölndal, Sweden), and colleagues from Sweden, the United States, and the United Kingdom provided an overview of "Amyloid biomarkers in Alzheimer's disease." Zhu et al. from the Zhejiang University (Hangzhou, China) reviewed "Molecular and functional imaging of Internet addiction" on March 24 ahead of print in *BioMed Research International*. In an article in the March 31 issue of *Frontiers in Pharmacology*, Kraeber-Bodéré, from University of Nantes (France) and researchers from France and the United States described achievement and progress toward "A pretargeting system for tumor PET imaging and radioimmunotherapy." Rischpler et al. from the Technische Universitat München (Germany) offered perspectives on "Cardiac PET for translational imaging in the May issue of *Current Cardiology Reports* (2015;17:581).