

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.

PET/CT and Pancreatic NET Recurrence

Sato et al. from Kyoto University and Shiga General Hospital (both in Japan) reported on March 20 ahead of print in the *Journal of Hepato-Biliary-Pancreatic Sciences* on a study on the utility of ^{18}F -FDG PET/CT in diagnosis and prediction of pancreatic neuroendocrine neoplasm recurrence. The retrospective study included 72 patients with ^{18}F -FDG-positive and -negative disease who were followed over a median of 65.6 mo. Among the variables assessed was whether PET/CT-positivity was related to earlier recurrence after curative treatment of nonfunctioning tumors. ^{18}F -FDG-positive tumors were found to be more pathologically advanced and significantly associated with metastasis. Four of 16 functional tumors and 1 of 12 of insulinomas were ^{18}F -FDG positive. Metastasis and World Health Organization (WHO) tumor grade were independently associated with tracer accumulation. In individuals with nonfunctioning tumors, ^{18}F -FDG positivity was significantly correlated with poorer recurrence-free but not overall survival. Factors associated with shorter recurrence-free survival on univariate analysis included male

sex, nodal metastases, WHO tumor grade $>G2$, and ^{18}F -FDG-positive disease; on multivariate analysis only ^{18}F -FDG-positive status was associated with shorter recurrence-free survival.

Journal of Hepato-Biliary-Pancreatic Sciences

Cost Effectiveness: SPECT/CT in Small Renal Masses

In an article e-published on February 27 ahead of print in *European Urology Focus*, Su et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) reported on a decision analysis model study of the cost effectiveness of $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT in management of small renal masses and the associated potential for avoiding biopsy in some benign tumors. The model estimated the costs and outcomes of 3 management strategies for a hypothetical healthy 65-y-old patient with an asymptomatic small renal mass: renal mass biopsy, $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT, and $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT followed by biopsy to confirm benign small renal masses. These were compared against 2 existing standard references: empiric surgery alone and empiric surgery with thermal ablation and active surveillance. Quality-adjusted life years and direct medical costs were calculated and compared for the 3 management options and the standard references. $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT followed by biopsy to confirm benign small renal masses was found to have a very low risk of leaving untreated malignant tumors (0.2%; with 2.1% for renal mass biopsy, 4.2% for $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT alone, and 0% for empiric surgery) and the highest probability of leaving benign tumors untreated (84.4%, with 53.9% for renal mass biopsy, 51.7% for $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT alone, and 0% for empiric surgery). $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT followed by biopsy was found to have the lowest project cost and highest quality-adjusted life years. Compared with the current practice reference of empiric surgery + thermal ablation + active

surveillance, all 3 management options were cost effective, but $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT followed by biopsy had the lowest cost and highest quality-adjusted life years. The authors concluded that " $^{99\text{m}}\text{Tc}$ -sestamibi SPECT/CT followed by confirmatory biopsy helps avoid surgery for benign small renal masses, minimizes untreated malignant small renal masses, and is cost effective compared with existing strategies."

European Urology Focus

PET/CT and Frozen Shoulder

Duchstein et al. from the Bispebjerg and Frederiksberg Hospital/Copenhagen University (Denmark) reported on March 13 ahead of print in *Knee Surgery, Sports Traumatology, Arthroscopy* on a study assessing the potential for ^{18}F -FDG PET/CT imaging in diagnosis of adhesive capsulitis and early differentiation from subacromial impingement. The study included 20 patients (11 with frozen shoulder and 9 with subacromial impingement) who underwent preoperative ^{18}F -FDG PET/CT imaging, with diagnoses confirmed at arthroscopy. Resulting images were assessed both visually (with good agreement) and by semiquantitative analyses and showed increased ^{18}F -FDG uptake in the frozen shoulders and no uptake in subacromial impingement. Sensitivity and specificity were 92% and 93%, respectively, for visual assessment and 77% and 93%, respectively, for semiquantitative analyses. When the 2 types of analyses were combined, sensitivity and specificity were 100% and 93%, respectively, for differentiating frozen shoulders from subacromial impingement and/or an unaffected shoulder. The authors concluded that " ^{18}F -FDG PET/CT seems to be a valid method to diagnose frozen shoulder," with specific utility in diagnostically challenging cases and in the early phase of frozen shoulder involvement.

Knee Surgery, Sports Traumatology, Arthroscopy

Tau vs. Amyloid in Depression

In an article e-published on March 2 ahead of print in the *Journal of Alzheimer's Disease*, Babulal et al. from the Washington University School of Medicine (St. Louis, MO) reported on the association of tau and amyloid PET imaging markers with depression diagnoses in cognitively normal adults and whether and how administration of antidepressants modified these associations. The study included 301 participants who underwent PET tau and amyloid imaging, with evaluation for depression made during an annual clinical examination and for antidepressant medication use. A series of logistic regression models assessed associations between PET tau and depression, between PET tau and antidepressant use, between PET amyloid and depression, and between PET amyloid and antidepressant use. The models were adjusted for age, sex, education, race, and apolipoprotein $\epsilon 4$. The researchers found that individuals with elevated tau were twice as likely to be depressed and that those with elevated tau who were taking antidepressants had even greater odds of being depressed. Elevated amyloid was not associated with depression in participants. The finding that "antidepressant use interacts with tau to increase the odds of depression among cognitively normal adults" was covered widely in the media.

Journal of Alzheimer's Disease

Adding PET/CT in Hepatocellular Carcinoma

John et al. from the Miami Veterans Affairs Medical Center (FL), Virginia Commonwealth University/Virginia Commonwealth School of Medicine (Richmond), McGuire Veterans Affairs Medical Center (Richmond, VA), and the University of Texas Southwestern Medical Center (Dallas) reported on March 3 ahead of print in *Liver Transplantation* on a study assessing the value of ^{18}F -FDG PET/CT in addition to cross-sectional imaging for staging and prediction in patients with hepatocellular carcinoma. The retrospective study included 148 patients who underwent PET/CT imaging after initial

staging with contrast-enhanced CT or MR imaging. Elements assessed were the benefit of PET in identification of new lesions and its potential detriment in false-positive findings. Associations between PET/CT results and risk of extrahepatic metastasis and progression-free and overall survival were also analyzed. The researchers found that PET/CT identified additional extrahepatic metastases in 11.9% of treatment-naïve and 13.8% of treated patients and changed Barcelona Clinic Liver Cancer (BCLC) staging in 5.9% of treatment-naïve and 18.8% of treated patients compared with CT/MR imaging alone. This resulted in changes in management for 9.9% of treatment-naïve and 21.3% of treated patients. Eight patients (5%) had false-positive PET/CT findings necessitating additional extrahepatic evaluation. A high tumor grade on PET/CT was independently associated with a higher likelihood of extrahepatic metastasis and worse overall survival. Patients who had been treated and had BCLC stages A or B were more likely to be upstaged with PET/CT. The authors summarized their findings: "PET/CT provides prognostic information and improves tumor staging beyond CT/MRI alone, with subsequent changes in management for patients with hepatocellular carcinoma."

Liver Transplantation

Reproducibility of Renal Allograft PET/CT

In an article e-published in the March 12 issue of *Scientific Reports*, Jadoul et al. from the University Hospital of Liège and the KU Leuven Campus Kulak Kortrijk (both in Belgium) reported on a study evaluating the repeatability and reproducibility of quantification of renal ^{18}F -FDG uptake on PET imaging in kidney transplant recipients under surveillance for allograft rejection. The study included 95 adult transplant recipients who underwent surveillance biopsy and PET/CT between 3 and 6 mo after transplantation. SUV_{mean} in the kidney cortex was independently assessed by 2 experienced observers in 4 volumes of interest distributed in the upper

and lower poles, with the first observer repeating SUV assessment in the uppermost volume of interest, unaware of the initial results. An intraclass correlation of 0.96 with 95% CI was calculated for the intraobserver measurements, and the intraclass correlations for interobserver reproducibility for each volume of interest were 0.87, 0.87, 0.85, and 0.83 for the upper to the lower renal poles. The authors concluded that "assessment of renal ^{18}F -FDG uptake in kidney transplant recipients is highly repeatable and reproducible if ^{18}F -FDG PET/CT images are evaluated by experienced observers with careful attention to the technique," a finding that makes this approach "transferrable to the clinical routine."

Scientific Reports

SPECT and ICA Test Balloon Occlusion

Sivakumaran et al. from the North Bristol Hospitals NHS Trust (UK) reported on March 10 ahead of print in *World Neurosurgery* on a study of the potential for SPECT-enhanced internal carotid artery test balloon occlusion in the management of complex cerebral aneurysms and skull base tumors. The records review included all test balloon procedures performed at the authors' institution over a 20-y period. Study data included semiquantitative cerebral blood flow analysis using $^{99\text{m}}\text{Tc}$ -HMPAO SPECT during internal carotid artery test balloon occlusion, supplemented with data from clinical assessment and angiographic collateral flow. Postocclusion collateral circulation, complications, and safety of permanent occlusions were recorded. A total of 83 patients in the study underwent test balloon occlusion without complication. Of the 45 patients with satisfactory occlusion, 28 then proceeded to permanent vessel occlusion. Thirty-eight patients had unsatisfactory test balloon occlusion, with 15 of these requiring permanent occlusion and a bypass procedure. This left a total of 40 patients who did not proceed to permanent occlusion. The authors concluded that "SPECT-enhanced test balloon occlusion is an important component of the management

of complex vascular pathology and skull base tumors, permitting safe permanent occlusion of the parent vessel and definitive treatment of the main pathology.”

World Neurosurgery

Neuroimaging in Chronic Traumatic Encephalopathy

In an article in the March supplement to the *Clinical Journal of Sport Medicine* (2020;30 suppl 1:S1–S10), Sparks et al. from the University of Bristol and the University of Oxford (UK) provided the results of a systematic review of the utility of neuroimaging in the diagnosis of chronic traumatic encephalopathy (CTE). The review is an update to a similar analysis of the literature published through 2014 (*Clin J Sport Med.* 2017 Oct 25). A total of 7 studies met the review criteria for the current study, with almost all study participants being professional athletes. All 7 studies compared individuals with CTE with normal controls. Assessment modalities included were categorized into structural MR imaging, diffusion MR imaging, and radionuclide studies. The authors found that in these studies the biomarkers that differed significantly between individuals with suspected CTE and controls were Evans index; cavum septum pellucidum rate, length, and ratio of cavum septum pellucidum length to septum length; regional differences in axial diffusivity and free/intracellular water fractions; SPECT perfusion abnormalities; and PET signals from tau-binding, glucose-binding, and GABA receptor-binding radionuclides. The authors noted that limitations in this literature included low specificity in identification of suspected cases of CTE across studies, the need for post-mortem validation, and a lack of generalizability to the population outside professional athletes. They concluded that “the most promising biomarker is tau-binding radionuclide PET signal because it is most specific to the underlying neuropathology” and because it “differentiated CTE from both controls and patients with Alzheimer disease.” They added that multimodal

imaging is likely to improve specificity in the future.

Clinical Journal of Sport Medicine

CCTA vs Functional Imaging Post-CABG

Small et al. from the University of Ottawa/University of Ottawa Heart Institute (Canada) reported on March 5 in the *International Journal of Cardiology. Heart and Vasculature* (2020;27:100494) on a study comparing rates of utilization and health care costs of coronary CT angiography (CCTA) and SPECT in patients with prior coronary artery bypass surgery (CABG). The analysis included 2,754 patients imaged by SPECT (2,163) or CCTA (591). Of these, 425 individuals (15.4%) underwent subsequent imaging, with CCTA being more common than SPECT (a comparison that persisted even when adjusted for baseline characteristic differences). When the highest risk patients (those who underwent repeat revascularization) were removed from the analysis, repeat testing with CCTA remained more common than SPECT. The costs of this “downstream” imaging per patient were more than twice as great for the CCTA group than the SPECT group ($\$366.79 \pm \29.59 and $\$167.35 \pm \10.12 , respectively). However, costs that included index imaging were lower in the CCTA group ($\$764.66 \pm \29.59) than in the SPECT group ($\$1,396.73 \pm \10.12). The authors summarized their findings that “index imaging with SPECT versus CCTA in CABG patients was associated with fewer downstream tests, less invasive coronary angiography, less repeat revascularization but greater expense.” They added that these findings “heighten the controversy regarding first test strategy in CABG patients by demonstrating that any potential cost saving of CCTA must be weighed against the increase in downstream testing associated with this modality.” They concluded that more extensive evaluation of costs and clinical outcome data “will be required before CCTA replaces functional imaging as the first-line investigation in CABG patients.”

International Journal of Cardiology. Heart and Vasculature

Metabolic Tumor Volume and DLBCL Outcomes

In an article published on March 24 in *Blood Advances* (2020;4[6]:1082–1092), Ceriani et al. from the Imaging Institute of Southern Switzerland (Bellinzona), the Università della Svizzera Italiana (Bellinzona), the Azienda Ospedaliera Papa Giovanni XXIII (Bergamo, Italy), the Swiss Institute of Bioinformatics (Lausanne), University Hospital/University of Zurich (Switzerland), the Swiss Group for Clinical Cancer Research Coordinating Center (Bern, Switzerland), University Hospital Basel/University of Basel (Switzerland), the University of Milan (Italy), the European Institute of Oncology (Milan, Italy), the Cantonal Hospital Aarau (Switzerland), and the University Hospital/University of Bern (Switzerland) reported on the ability of functional parameters from ^{18}F -FDG baseline PET/CT to predict outcomes in diffuse large B-cell lymphoma (DLBCL). Data were acquired as part of a large multicenter clinical trial. This study focused on 2 cohorts of DLBCL patients receiving conventional immunochemotherapy (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone [R-CHOP]) every 14 or 21 d. Baseline PET imaging was acquired in 141 patients treated with R-CHOP every 14 d as part of the larger clinical trial. Reproducibility was analyzed in a validation set of 113 patients treated with R-CHOP every 21 d. In the 14-d group, 5-y progression-free survival was 83% for individuals with low metabolic tumor volume on PET and 59% for those with high metabolic tumor volume. Corresponding overall survival percentages over the 5-y period were 91% and 64%, respectively. In the 21-d group, metabolic tumor volume remained the most significant predictor of outcome. In patients with elevated metabolic tumor volume, higher metabolic heterogeneity significantly predicted poorer outcomes. A validated model that integrated metabolic tumor volume and metabolic heterogeneity was able to identify high-risk patients

with shorter overall and progression-free survival times. The authors concluded that this approach “may allow early identification of refractory patients who might benefit from treatment intensification.”

Blood Advances

CSF Biomarkers and Differential AD Diagnosis

Barthélemy et al. from the Université de Montpellier (France), Washington University School of Medicine (St. Louis, MO), the Université Paris Saclay (France), and the Gui de Chauliac Hospital (Montpellier, France) reported in the March 17 issue of *Alzheimer's Research and Therapy* (2020;12[1]:26) on a study of the use of cerebrospinal fluid (CSF) biomarkers in differential diagnosis of Alzheimer disease (AD), with ¹¹C-Pittsburgh compound B (¹¹C-PiB) PET imaging as a comparative standard for study validation. The authors used a quantitative mass spectrometry technique that detects the CSF biomarkers of 2 phosphorylated tau isoforms, pT181 and pT217. The first cohort of subjects included 10 patients with probable AD, who were compared with 40 patients with non-AD diseases (Lewy body disease, progressive supranuclear palsy, corticobasal degeneration, adult chronic idiopathic hydrocephalus, mixed dementia, vascular dementia with possible AD, vascular dementia, brain metastasis) and 5 controls with normal neuropsychological profiles. The authors found that pT217 but not pT181 differentiated with high specificity and sensitivity between individuals with AD and those with other neurodegenerative diseases and control subjects. T217 phosphorylation was 6 times higher and T181 phosphorylation was 1.3 times higher in individuals with AD in comparison with controls. The validity of these results was checked in a second cohort that included 33 amyloid-positive and 51 amyloid-negative (as assessed by ¹¹C-PiB PET) participants who were cognitively normal or had mild cognitive impairment. In this cohort, pT217 CSF levels identified

amyloid-positive patients with sensitivity and specificity >90%. ¹¹C-PiB uptake levels were also highly correlated with pT217 CSF concentrations. The authors concluded that “increased CSF pT217 levels, more than those of pT181, are highly specific biomarkers for detecting both the preclinical and advanced forms of AD.” They added that not only should this finding improve AD diagnosis but that data from this study, in correlation with PET findings, suggest that “pT217 is a promising potential target for therapeutic applications and that a link exists between amyloid and tau pathology.”

Alzheimer's Research and Therapy

⁶⁸Ga-PSMA PET/CT and Distribution of Prostate Cancer Recurrence

In an article e-published on March 17 ahead of print in *BJU International*, Huits et al. from The Netherlands Cancer Institute (Amsterdam), Erasmus Medical Centre (Rotterdam, The Netherlands), St. Vincent's Hospital (Darlinghurst, Australia), and the Garvan Institute of Medical Research (Darlinghurst, Australia) reported on a study designed to assess the anatomic distribution of prostate cancer recurrence on ⁶⁸Ga-PSMA PET/CT in patients with biochemical recurrence after radical prostatectomy with pathologically confirmed lymph node metastasis at extended pelvic lymph node dissection. The retrospective study included data from 100 such patients who underwent ⁶⁸Ga-PSMA PET/CT to guide salvage therapy. Factors included in the analysis were clinical and pathologic features, anatomic location of recurrence on imaging, and effect on management. PET/CT findings were positive in 68 and negative in 32 patients. Among the PET/CT-positive patients 44 (65%) had abnormal uptake only in the pelvic area, 7 (10%) only outside the pelvic area, and 17 (25%) both inside and outside the pelvic area. Eighty-four percent of the PET/CT-positive pelvic lymph nodes were detected on the same side as the lymph node metastasis diagnosed at extended pelvic lymph node

dissection. ⁶⁸Ga-PSMA-PET/CT findings led to a change in management for 68% of patients. The authors added that “prospective studies are needed to support the long-term benefit of ⁶⁸Ga-PSMA PET/CT-dictated management changes.”

BJU International

PET/CT and MR Imaging in HNSCC Extracapsular Extension

Sheppard et al. from Bern University Hospital/University of Bern (Switzerland) reported on March 6 ahead of print in *Laryngoscope* on a study looking at the ability of features of PET/CT and MR imaging to contribute to identification of extracapsular extension in patients with head and neck squamous cell carcinoma (HNSCC). The retrospective study included 212 patients with advanced HNSCC who had undergone pretherapeutic PET/CT and/or MR imaging (PET/CT, 184 patients; MR, 186; both modalities, 158). Imaging reviewers performed blinded evaluations of PET/CT and MR features associated with the presence of extracapsular extension, with results compared to histopathology at neck dissection. The researchers found that clinical stage IV, ill-defined margins on both PET/CT and MR imaging, and SUV_{max} on PET were significant independent predictors of extracapsular extension. When these 4 features were combined and compared with histopathologic results, the cumulative score predicted extracapsular extension status with an accuracy of 91.43%. The authors concluded that these findings indicated that “specific features in PET/CT and MRI are potential predictors of extracapsular extension status and may help in pretherapeutic stratification in HNSCC.”

Laryngoscope

PET/CT Staging of Malignant Melanoma

In an article e-published on March 11 ahead of print in *Dermatologic Therapy*, Yilmaz et al. from Gaziantep University School of Medicine (Turkey) and BaŞkent University School of Medicine (Konya, Turkey) reported

on a study of the effectiveness of PET/CT imaging in staging malignant melanoma. The retrospective study included the records of 139 patients (79 women, 60 men) who underwent PET/CT imaging to identify metastasis before treatment. Variables assessed included Breslow thickness, Clark level, number of mitoses and ulceration reported in pathologic findings, and presence of lymph nodes and/or distant metastases on PET/CT. Patients with a Breslow thickness >3.4 mm and Clark level of 4–5 were found to have significantly more regional lymph node metastases after PET/CT imaging. Those with Breslow thickness >2.85 mm and Clark level of 4–5 had significantly more distant metastases after PET/CT. The authors concluded that these results “suggest that PET/CT imaging for metastasis scanning, starting with T2 patients, may be used in malignant melanoma staging to reduce the need for sentinel lymph node biopsy and lymph node dissection.”

Dermatologic Therapy

SPECT/CT After Total Ankle Replacement

Gurbani et al. from the University of California Los Angeles, the Hospital for Special Surgery (New York, NY), and Lenox Hill Hospital (New York, NY) reported on March 10 ahead of print in *Foot and Ankle International* on a study assessing the utility of SPECT/CT in evaluation of pain after total ankle replacement, including comparison with MR imaging in this setting. The retrospective study included 37 patients with painful total ankle replacement, all of whom underwent SPECT/CT imaging, 19 of whom underwent MR imaging, and 28 of whom underwent revision surgery. SPECT/CT results were consistent with the final documented diagnosis in 33 patients (89.2%). The most frequent final diagnoses were aseptic loosening (12 patients) and impingement (11 patients). SPECT/CT results in the 28 patients who underwent revision surgery were consistent with intraoperative findings in 26 (92.9%). For the 19 patients who underwent MR imaging, findings were consistent with clinical findings in only 3 patients

(36.8%). The authors concluded that SPECT/CT findings were highly consistent with documented clinical diagnoses and intraoperative findings and that “compared with MRI, SPECT/CT proved more useful in establishing a diagnosis of pain after total ankle replacement.”

Foot and Ankle International

Loading Protocols in ^{18}F -FDG PET Cardiac Viability Studies

In an article e-published on February 27 in the *World Journal of Nuclear Medicine*, Sarikaya et al. from Kuwait University (Kuwait City) and Trakya University (Edirne, Turkey) reported on research designed to assess whether oral glucose and intravenous loading protocols can affect ^{18}F -FDG uptake in the hibernating myocardium in PET cardiac viability studies. The retrospective analysis included 49 patients who underwent such studies. Variables assessed included fasting blood glucose, amount of glucose given, blood glucose level after glucose load, amount of insulin given, and blood glucose level at the time of ^{18}F -FDG injection. The authors compared these variables in PET-viable (31 patients) and PET-nonviable (18 patients) groups, as well as in subgroups to assess ^{18}F -FDG uptake in normal myocardium. In 22 patients (most in the PET-viable group), varying degrees of reduced ^{18}F -FDG uptake were noted in normal myocardium. No significant differences in the 2 groups were noted in the other variables assessed. Problems in oral glucose and intravenous insulin loading protocols included decisions on the amounts of glucose and insulin and the maximum amount of insulin to be given, managing diabetic patients, identifying optimal time to measure blood glucose after insulin administration, and interpretation of findings in patients with diffusely reduced ^{18}F -FDG uptake. The authors concluded that “further improvements in current guidelines are necessary to obtain images in optimal conditions for accurate results.”

World Journal of Nuclear Medicine

Detecting Early Amyloid in Cognitively Normal Adults

Guo et al. from the University of California (Berkeley) and the Lawrence Berkeley National Laboratory (CA) reported on March 18 ahead of print in *Neurology* on a study assessing the feasibility of cross-sectional ^{18}F -florbetapir PET to identify increased risk of early cognitive decline among β -amyloid ($\text{A}\beta$)-negative cognitively normal elderly adults. The study included 354 cognitively normal elderly adults from the Alzheimer’s Disease Neuroimaging Initiative who underwent ^{18}F -florbetapir PET imaging. The highest $\text{A}\beta$ -affected region was in the banks of the superior temporal sulcus, as determined by ranking baseline and accumulation rates of tracer regions. Subsequent analyses were used to categorize patients as stage 0 (191 patients), 1 (64 patients), or 2 (99 patients). Longitudinal cognitive change was assessed using linear mixed-effect models over more than 4 y, and ^{18}F -flortaucipir PET was repeated at 4.8 ± 1.6 y to track tau deposition. Over the follow-up, the linear mixed-effect models indicated that individuals in stages 1 and 2 experienced 2.5 and 4.8 times, respectively, the rate of memory decline than individuals in stage 0. Assignment to stages 1 and 2 also predicted higher tracer uptake in the entorhinal cortex on PET. The authors concluded that nominally $\text{A}\beta$ -negative/cognitively normal individuals with high $\text{A}\beta$ in the banks of the superior temporal sulcus are at “increased risk of cognitive decline, probably showing an earlier stage of $\text{A}\beta$ deposition” and that these findings “may help elucidate the association between brain $\text{A}\beta$ accumulation and cognition in $\text{A}\beta$ - cognitively normal cohorts.”

Neurology

“Ready-to-Use” ^{68}Ga -DOTATOC for Injection

In an article in the March issue of *ESMO Open*, Manoharan et al. from the ENETS Center of Excellence (Manchester and London, UK), the University of Manchester (UK), and

Advanced Accelerator Applications (New York, NY) reported on the safety, tolerability, and feasibility of clinical use of a ^{68}Ga -DOTATOC formulation for injection (SomaKIT TOC) for PET/CT imaging in patients with gastroenteropancreatic neuroendocrine tumors (GEP NETs). The study included a first-in-human phase I/II multicenter, open-label study of a single dose of the kit-prepared ^{68}Ga -DOTATOC in patients with biopsy-proven grade 1–2 GEP NETs. PET/CT imaging was performed after injection, and patients were followed for 4 weeks. Additional assessment of the new synthesis methodology in the clinical setting was performed over 11 mo. The study included 20 patients (14 men, 6 women; mean age, 58 y). Fourteen had grade 1 disease and 6 had grade 3 disease, with a total of 15 assessed as having stage IV disease. Although 12 patients experienced at least 1 adverse event during the study, no grade 3 or 4 toxicities were noted. Two adverse events were classified as possibly (headache, nausea) and 2 as probably (dysgeusia, paraesthesia) associated with the injection. Over the course of the 11-mo

clinical use of the kit, 113 vials of ^{68}Ga -DOTATOC were synthesized, and only 2 (1.77%) were rejected. The authors concluded that the SomaKIT TOC for injection was safe and well tolerated and noted that this finding has led to European Medicines Agency licensing for the use of this kit for PET imaging in patients with NETs.

ESMO Open

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in February and March. In an article published online on March 19 ahead of print in *Current Opinion in Oncology*, Hadavand et al. from the University of Maryland School of Medicine and Veterans Health Administration Research and Development Service (both in Baltimore, MD) reviewed the “Role of metabolic imaging in diagnosis of primary, metastatic, and recurrent prostate cancer.” Chen and Kantarci, from

the West China Hospital of Sichuan University (Chengdu) and the Mayo Clinic (Rochester, NY), respectively, detailed “Imaging biomarkers for neurodegeneration in presymptomatic familial frontotemporal lobar degeneration” on February 28 in *Frontiers in Neurology* (2020;11:80). Buffet et al. from the Sorbonne University (Paris, France), the Universidade Federal do Rio de Janeiro (Brazil), the Institut Gustave Roussy (Villejuif, France), and the Hôpital Cochin (Paris, France) summarized strategies for “Redifferentiation of radioiodine-refractory thyroid cancers” on March 1 ahead of print in *Endocrine Related Cancer*. In an article e-published on March 5 ahead of print in *Life Sciences*, Gu et al. from the Shengjiang Hospital of China Medical University looked at “Preclinical in vivo imaging for brown adipose tissue.” A review of “Nonprostatic diseases on PSMA PET imaging: A spectrum of benign and malignant findings,” was published by de Galiza Barbosa et al. from the Hospital Sirio-Libanês (Sao Paulo, Brazil) on March 14 in *Cancer Imaging* (2020;20[1]:23).