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.

Short-Term Memory and Tau and Amyloid Burden Assessment

In an article e-published on August 21 ahead of print in *Alzheimer's Research and Therapy*, Norton et al. from Massachusetts General Hospital/Harvard Medical School (Boston, MA), Gordon College (Wenham, MA), the University of Strathclyde (Glasgow, UK), the Autonomous University of the Caribbean (Barranquilla, Colombia), Brigham and Women's Hospital (Boston, MA), Universidad de Antioquia (Medellin, Colombia), and the Banner Alzheimer's Institute (Phoenix, AZ) reported on a comparison of Visual Short-Term Memory (VSTM) binding tests with direct in vivo PET measurements of amyloid and tau levels with ^{11}C-Pittsburgh compound B and ^{18}F-flortaucipir, respectively. This comparison of behavioral and neurochemical markers was conducted in individuals with the presenilin-1 E280A mutation predisposing to Alzheimer disease (AD), including 21 clinically unimpaired subjects and 7 with early mild cognitive impairment, as well as 30 family members without the mutation. The authors found that VSTM performance correlated strongly with tau PET findings in the entorhinal cortex and inferior temporal lobe and, in asymptomatic carriers, with amyloid burden. They identified interesting questions raised by the relationship between PET data results and aspects of the VTSM test in early AD and concluded that "it will be necessary to continue exploring the precise stimulus conditions that are optimal for serving as a proxy for biochemical pathology in AD or for discriminating between individuals with and without preclinical AD."

Alzheimer's Research and Therapy

Chemotherapy, Liver Injuries, and SPECT

Truant et al. from the University of Lille/CHRU Lille, INSERM Lille, and Biopredic Laboratory (Rennes; all in France) reported on August 24 ahead of print in the *Annals of Surgical Oncology* on a study designed to assess the ability of ^{99m}Tc-mebrofenin SPECT hepatobiliary scintigraphy to predict the likelihood of liver dysfunction from chemotherapy and/or chemotherapeutic-associated liver injuries, such as sinusoidal obstruction syndrome and nonalcoholic steatohepatitis. The study included 115 patients scheduled for major hepatectomy (defined as ≥3 segments) who underwent presurgical SPECT hepatobiliary scintigraphy to measure segmental liver function. Imaging results were compared between patients with and without (1) preoperative chemotherapy and (2) chemotherapy-associated liver injuries. Other factors were included in the analysis. A total of 55 (47.8%) patients received chemotherapy, 16 of whom developed sinusoidal obstruction syndrome and 35 experienced nonalcoholic steatohepatitis, with worse postoperative outcomes. However, chemotherapy had no impact on liver function, except when >12 cycles were administered. In patients with chemotherapeutic-associated liver injuries, steatosis ≥30% significantly compromised function, as did nonalcoholic steatohepatitis. Other factors impairing function were diabetes, overweight/obesity, and fibrosis. The authors concluded that ^{99m}Tc-mebrofenin SPECT hepatobiliary scintigraphy appeared to be "a valuable tool to select heavily treated patients at risk of liver dysfunction through steatosis or nonalcoholic steatohepatitis."

Annals of Surgical Oncology

^{68}Ga-PMSA PET Before Radical Prostatectomy

In an article e-published on August 21 ahead of print in *Prostate Cancer and Prostatic Diseases,* Koseoglu et al. from the Koç University School of Medicine/Koç University Hospital and the VKF American Hospital (both in Istanbul, Turkey) reported on a study investigating the incremental contribution of ^{68}Ga–prostate-specific membrane antigen (^{68}Ga-PMSA) PET as a primary staging tool in patients with prostate cancer in single Prostate Imaging Reporting & Data System (PI-RADS) 4 or 5 index lesions. The study included 81 biopsy-naïve patients (49 with PI-RADS 4 and 32 with PI-RADS 5 index lesions) who underwent multiparametric MR and ^{68}Ga-PMSA PET imaging before radical prostatectomy. Characteristics of dominant and nondominant tumors as assessed postoperatively were compared with index lesion imaging findings. ^{68}Ga-PMSA PET identified dominant tumors in 100% of patients, including 13 in whom MR was negative. ^{68}Ga-PMSA PET accurately identified nondominant tumors in 24 of 45 (53.3%) patients. Six patients (12.2%) in the PI-RADS 4 group were upgraded; ^{68}Ga-PMSA PET localized the dominant tumor in each of these patients, and MR missed the location in 2. Eight patients (25%) in the PI-RADS 5 group were upgraded; both imaging modalities accurately located the dominant tumor in each of these patients. Detection rates for extracapsular extension and seminal vesicle invasion were 51.1% and 53.8%, respectively, with MR imaging and 27.9% and 30.7%, respectively, with PET. When the 2 modalities were combined, detection rates for extracapsular extension and seminal vesicle invasion

increased to 65.1% and 61.5%, respectively. In addition, ^{68}Ga-PMSA PET identified 6 of 10 patients with positive lymph nodes, whereas multiparametric MR imaging identified none. The authors concluded that ^{68}Ga-PMSA PET has a better diagnostic accuracy in detecting dominant and nondominant tumors, in upgrading, and in adverse pathology in patients with PI-RADS 4 index lesions and that multiparametric MR imaging has a different set of predictive advantages in this setting.

Prostate Cancer and Prostatic Diseases

PET/CT and Smoldering Multiple Myeloma

Zhou et al. from the University Hospital of Würzburg and the University of Augsburg (both in Germany) reported on August 18 ahead of print in *Cancers (Basel)* (2020;12[8]:E2333) on a study exploring correlations between imaging patterns and clinical features in patients with smoldering multiple myeloma who underwent simultaneous PET/CT imaging with ^{18}F-FDG, ^{11}C-methionine, and ^{68}Ga-pentixafor. The study included 10 patients who also underwent bone marrow biopsy at the time of imaging. The authors found a significant correlation between bone marrow plasma cell infiltration and SUV_{mean} for lumbar vertebrae L2–L4 on ^{11}C-methionine PET/CT and ^{68}Ga-pentixafor PET/CT but no significant correlation between bone marrow involvement in these lumbar vertebrae and ^{18}F-FDG uptake. Mean target-to-background ratios for these lumbar vertebrae on ^{11}C-methionine PET/CT and ^{68}Ga-pentixafor PET/CT also correlated with bone marrow plasma cell infiltration, with no similar correlation with ^{18}F-FDG uptake. ^{11}C-methionine PET/CT also showed a significant correlation between bone marrow plasma cell infiltration and maximum target-to-background ratios in the target lumbar vertebrae. The authors summarized their findings that "^{11}C-methionine and ^{68}Ga-pentixafor PET/CT demonstrate higher sensitivity than ^{18}F-FDG PET/CT in detecting bone marrow involvement in smoldering multiple myeloma."

Cancers (Basel)

^{225}Ac-PSMA-617 Targeted Therapy in MCRPC

In a study published on July 23 in *Theranostics* (2020;10[20]:9364–9377) Yadav et al. from the All India Institute of Medical Sciences (New Delhi) reported on the safety and therapeutic efficacy of ^{225}Ac–prostate-specific membrane antigen-617 (^{225}Ac-PSMA-617) targeted α therapy in metastatic castration-resistant prostate cancer. The study included 28 men (mean age, 69.7 y; range, 46–87 y), 15 of whom who were refractory to previous ^{225}Ac-PSMA-617 treatment and 13 of whom were ^{225}Ac-PSMA-617 treatment naïve. Twenty-seven of the patients had extensive skeletal metastases on baseline ^{68}Ga-PSMA-11 PET/CT imaging, and 1 had lymph node–dominant disease and an advanced primary prostatic tumor. Patients were treated with a fixed dose of 100 KBq/kg body weight of ^{225}Ac-PSMA-617 at intervals of 8 wk up to a cumulative dose of 62.9 MBq (range, 25–62.9 MBq; median of 3 cycles; range, 1–7 cycles). In assessments performed at 8 wk after the first cycle and at end-of-treatment follow-up, a >50% decrease in serum prostate-specific antigen was seen in 25% and 39% of participants at the respective time points. Median progression-free and overall survival times were 12 and >17 mo after initial treatment, respectively. PET Response Criteria in Solid Tumors 1 assessment of molecular response could be performed in 22 (78.6%) patients and indicated complete response in 2 (9%), partial response in 10 (45.4%), stable disease in 2 (9%), and progressive disease in 8 (36%) patients. Disease control rates as calculated first from biochemical and then molecular tumor response criteria were 82% and 63.6%, respectively. Multivariate analyses indicated that increasing prostate-specific antigen progression was adversely prognostic for overall survival, whereas any prostate-specific antigen reduction was a positive prognostic indicator of progression-free survival. No grade III/IV toxicities were noted, with the most common reported side effects being transient fatigue (50%) and grade I/II xerostomia (29%). The authors concluded that "^{225}Ac-PSMA-617 targeted α therapy showed promising disease control rates, even when all other therapeutic options were exhausted, with low treatment-related toxicities."

Theranostics

DTC Persistent Disease Tumor Burden and Treatment

Ciappuccini et al. from the François Baclesse Cancer Centre (Caen), Caen University/Caen University Hospital, and Rouen University (all in France) reported on August 13 ahead of print in *BMC Cancer* (2020;20[1]:765) on a study correlating tumor burden of persistent disease in differentiated thyroid cancer with American Thyroid Association (ATA) risk stratification and effect on response to initial therapy and outcomes. The retrospective study included 618 patients with differentiated thyroid cancer referred for ^{131}I treatment. Postoperative data were used to risk stratify patients per the ATA criteria prior to treatment. Posttreatment tumor burden was classified by volume as very small (presence of abnormal foci on postradioiodine scintigraphy with SPECT/CT or ^{18}F-FDG PET/CT without identifiable lesions on anatomic imaging), small (largest legion <10 mm), or large (largest legion ≥10 mm) persistent disease. Persistent disease was seen in 107 patients over a mean follow-up of 7 ± 3 y. Increases in large-volume persistent disease were significantly correlated with ATA-stratified risk, with a significant trend for a decrease in excellent response rate from the very small-, small-, to large-volume groups at 9–12 mo after initial therapy and at last follow-up. Additional analyses indicated that age ≥45 y, distant and/or thyroid bed disease, small- or large-volume tumor burden, and ^{18}F-FDG–positive persistent disease were independent risk factors for indeterminate or incomplete response at last follow-up. The authors summarized their findings that "the tumor burden of persistent disease correlates with the ATA risk

stratification, affects the response to initial therapy, and is an independent predictor of residual disease after a mean 7-y follow-up." They added that this variable may be useful in addition to postoperative ATA risk stratification in refining outcome prognostication after initial treatment.

BMC Cancer

PET/CT vs Bone Scan in Pediatric Sarcoma

In an article e-published on August 18 ahead of print in the *Journal of Pediatric Hematology/Oncology*, Tal et al. from Albert Einstein College of Medicine (New York, NY) and the Montefiore Medical Center (Bronx, NY) compared identification of osseous metastases using bone scanning with that using ^{18}F-FDG PET/CT at diagnosis and relapse in a pediatric sarcoma population. The retrospective study included chart reviews of paired bone scan and PET/CT imaging in 16 patients with osseous sarcoma and 15 with Ewing sarcoma. Fifteen patients had distant osseous metastases. The report also included a review of the pertinent literature. In the patients with osseous sarcoma, 8 of 16 had osseous metastases, with 100% detected on PET/CT and 75% on bone scan. A total of 31 bony lesions were identified on imaging in this patient group: 100% on PET/CT and only 29% on bone scan. Six of the 15 patients with Ewing sarcoma had osseous metastases, with 100% detected on PET/CT and 50% on bone scan. A total of 18 bony lesions were seen on imaging in this patient group: 94% on PET/CT but only 28% on bone scan. The authors concluded that these findings suggest that for pediatric patients with osseous sarcoma or Ewing sarcoma, osseous metastases are more likely to be detected using ^{18}F-FDG PET/CT.

Journal of Pediatric Hematology/Oncology

^{18}F-FDG and ^{18}F-NaF PET in Carotid Atherosclerosis and Stroke

Kim et al. from Chung-Ang University Hospital/Chung-Ang University College of Medicine, Korea University Medical Center/Korea University College of Medicine, and Seoul National University (all in Seoul, Korea) reported in the September issue of the *Journal of Lipid and Atherosclerosis* (2020;8[2]:232-241) on a study looking at tracer uptake patterns in ^{18}F-FDG and ^{18}F-sodium fluoride (^{18}F-NaF) PET in carotid atheroma patients after acute stroke or transient ischemic attacks. The study included 18 patients with ≥50% proximal internal carotid artery stenosis on brain CT angiography, with 36 involved carotid arteries, and 10 patients diagnosed as having experienced acute cerebral infarction. All patients underwent ^{18}F-FDG and ^{18}F-NaF PET imaging after clinical stabilization. Tracer uptakes were compared by target-to-blood ratios according to calcification burden, atheroma volume, and presence or absence of a necrotic core of carotid atheroma. The authors found that ^{18}F-FDG uptake in symptomatic carotid arteries was significantly more increased than that in asymptomatic arteries, whereas ^{18}F-NaF uptake showed no such differentiation. ^{18}F-NaF uptake increases were correlated with calcification burden increases. The authors concluded that "carotid evaluation by ^{18}F-FDG is superior to ^{18}F-NaF PET in the detection of symptomatic carotid atherosclerosis among stroke patients," but that ^{18}F-NaF uptake on PET reflects overall calcification burden.

Journal of Lipid and Atherosclerosis

Molecular Pathology and Neurodegeneration in AD

In an article e-published on August 18 ahead of print in *Cerebral Cortex*, Iaccarino et al. from the University of California San Francisco, the University of California Berkeley, the Lawrence Berkeley National Laboratory (CA), and the VU University Medical Center (Amsterdam, The Netherlands) reported on a study designed to explore the spatial relationships of β-amyloid (Aβ), tau, and neurodegeneration in Alzheimer disease (AD). The study included 81 amyloid-positive patients (median age, 64.4 ± 9.5 y) diagnosed with AD dementia or AD-related mild cognitive impairment who had undergone ^{11}C-PiB, ^{18}F-flortaucipir, and ^{18}F-FDG PET and 3T MR imaging. The study also included 31 amyloid-positive, cognitively normal participants (median age, 77.3 ± 6.5 y). Using comparative data from amyloid-negative cognitively normal adults, neurodegeneration (ND) voxel maps were created for study participants. Aβ-associated pathology showed the greatest proportion of cortical gray matter suprathreshold voxels (spatial extent) for both symptomatic (median, 94%) and asymptomatic participants (median, 55%), followed by tau (79% and 11%, respectively), and ND (41% and 3%, respectively). For both groups, the most frequent hierarchy was amyloid > tau > ND, followed by tau > amyloid > ND and amyloid > ND > tau. For the symptomatic group, most abnormal voxels were ^{11}C-PiB– and ^{18}F-flortaucipir–positive and ND-negative. The majority (91%) of ND-positive voxels were correlated with molecular pathology. Amyloid spatially exceeded tau and ND, with individual heterogeneities. These findings led the authors to conclude that "molecular pathology and neurodegeneration showed a progressive overlap along AD course, indicating shared vulnerabilities or synergistic toxic mechanisms."

Cerebral Cortex

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 July and August. In an article published on August 6 in the *Journal of Clinical Medicine* (2020;9[8]:E2548) Romanò et al. from the University of Milan (Italy), the National Institute for Infective Diseases "La Spallanzani" (Rome, Italy), AOU Sant'Andrea (Rome, Italy), the IRCCS Istituto Ortopedico Galeazzi (Milan, Italy), Ente Ospedaliero Cantonale (Bellinzona, Switzerland), Lausanne University Hospital/University of Lausanne (Switzerland), the Hospital of the University of Pennsylvania (Philadelphia),

the University of Groningen (The Netherlands), Cliniques Universitaires Saint-Luc (Brussels, Belgium), AZ Groeninge/KU Leuven (Kortrijk, Belgium), "Sapienza" University of Rome (Italy), and the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell (Hempstead, NY) summarized "The role of imaging techniques to define a periprosthetic hip and knee joint infection: Multidisciplinary consensus statement." Raji et al. from the David Geffen School of Medicine at the University of California, Los Angeles and the Mallinckrodt Institute of Radiology at Washington University in St. Louis (MO) offered an overview of "Optimizing use of neuroimaging tools in evaluation of prodromal Alzheimer's disease and related disorders" online ahead of print in the *Journal of Alzheimers Disease.* "Current applications for nuclear medicine imaging in pulmonary disease" were reviewed by Kusmirek et al. from the University of Wisconsin (Madison) on July 22 ahead of print in *Current Pulmonology Reports.* Bauckneht et al. from the IRCCS Ospedale Policlinico San Martino (Genoa), the University of Brescia/Spedali Civili Brescia, IRCSS Regina Elena National Cancer Institute (Rome), the University of Bari Aldo Moro, AO Brotzu (Cagliari), Sapienza University of Rome, the University of Messina, the University of Padova, and the Fondazione Istituto G. Giglio (Cefalù; all in Italy) published on August 16 in *Diagnostics (Basel)* (2020;10[8]:E598) on "Somatostatin receptor PET/CT imaging for the detection and staging of pancreatic NET: A systematic review and meta-analysis." In an overview released online on July 27 ahead of print in *Current Medical Chemistry*, Mengshu and colleagues from the University of Iowa (Iowa City), Viewpoint Molecular Targeting, Inc. (Coralville, IA), Eichrom Technologies, LLC (Lisle, IL), Lantheus Medical Imaging (Billerica, MA), the U.S. Department of Energy (Oak Ridge, TN), the National Institute of Standards and Technology (Gaithersburg, MD), and Sciencons AS (Oslo, Norway) looked at "$^{203/212}$Pb theranostic radiopharmaceuticals for image-guided radionuclide therapy for cancer." Fur et al. from the Massachusetts General Hospital/Harvard Medical College (Boston) published "Toward molecular imaging of intestinal pathology" on August 14 online ahead of print in *Inflammatory Bowel Diseases.*