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 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 increasingly blurred, as radiolabels are used as adjuncts to treatment 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.

**Preclinical Biomarkers of Alzheimer Disease**

Long et al. from the Washington University School of Medicine in St. Louis (MO) reported on July 22 ahead of print in *Brain* on a study designed to determine whether amyloid PET imaging and/or cerebrospinal fluid (CSF) biomarkers accurately predict cognitive outcomes in Alzheimer disease (AD) and neuropathologic findings at autopsy. The study included 720 individuals (age range, 42–91 y) who were cognitively normal at baseline, underwent amyloid PET imaging and/or CSF collection within 1 y of initial clinical assessment, and had subsequent clinical follow-ups. Cognitive status was assessed serially over follow-up, and biomarkers were defined by uptake cutoffs for amyloid PET imaging and CSF p-tau181/amyloid-β42 levels. Over the course of the study, 57 participants died, with subsequent post-mortem neuropathologic examination for AD-related changes. Among normal participants with PET or CSF biomarkers defined as positive, 34.4% developed cognitive impairment, compared to only 8.4% with negative biomarkers. Preclinical AD biomarker status, APOE ε4 carrier status, polygenic risk score, and age were identified as significant factors influencing risk of developing cognitive impairment. Among individuals with autopsy results, 90.9% of those who were biomarker-positive and 8.6% of those who were biomarker-negative had AD neuropathologic changes. The combination of the preclinical biomarkers yielded a sensitivity of 87.0%, specificity of 94.1%, and positive- and negative-predictive values of 90.9% and 91.4%, respectively, for subsequent detection of AD neuropathology. As individual predictors, CSF and amyloid PET at baseline were also predictive of AD neuropathologic changes, as well as Thal phase and Braak stage of pathology at autopsy. Of note, participants who were biomarker-negative and went on to develop cognitive impairment were more likely than other participants to exhibit non-AD pathology at autopsy. The authors concluded that “detection of preclinical AD biomarkers is strongly predictive of future cognitive impairment and accurately predicts presence of AD neuropathology at autopsy.”

*Brain*

**18F-Florzolotau PET in Multiple System Atrophy Parkinsonian Subtype**

In an article published on July 21 ahead of print in *Movement Disorders*, Lin et al. from Huashan Hospital/Fudan University (Shanghai) and APRINOIA Therapeutics Co., Ltd. (Suzhou; both in China) and representing the Progressive Supranuclear Palsy Neuroimage Initiative reported on a study investigating localization and uptake volume of 18F-florzolotau (previously known as 18F-APN-1607) on PET in patients with the parkinsonian subtype of multiple system atrophy. The study included 31 such patients, 24 with Parkinson disease, and 20 age-matched healthy controls. Uptake in the striatum was visually assessed as positive or negative, and regional binding was evaluated as SUV ratios. In both assessments, patients with the parkinsonian subtype of multiple system atrophy showed elevated tracer uptake in the putamen, globus pallidus, and dentate compared with patients with Parkinson disease. This increased signal was significantly associated with the core clinical symptoms of the parkinsonian subtype of multiple system atrophy. In those patients with the subtype cerebellar ataxia, tracer uptake was elevated in the cerebellar dentate. The authors concluded that “18F-florzolotau tau PET imaging findings may reflect the clinical severity of parkinsonian subtype of multiple system atrophy and can potentially discriminate between this condition and Parkinson disease.”

*Movement Disorders*

**PET/CT of Cranial Arteries in Giant Cell Arteritis**

Thibault et al. from Dijon University Hospital, the Centre Georges François Leclerc, and the Université Bourgogne Franche-Comté, INSERM (all in Dijon, France) reported on July 22 ahead of print in *Rheumatology (Oxford)* on a study of the performance of cranial PET/CT in the sometimes challenging diagnosis of giant cell arteritis (GCA). The investigation was part of a clinical trial designed to evaluate the sensitivity and specificity of PET of the cephalic arteries for diagnosis of GCA and compare these with results from echo Doppler and MR imaging of the temporal arteries. A total of 70 adults with suspected GCA were enrolled in the study and underwent baseline cranial artery evaluation with PET/CT before or immediately (within 72 h) after starting glucocorticoid treatment. Cranial PET/CT was considered positive if at least 1 arterial segment showed hypermetabolism similar to or greater than liver uptake. The diagnosis of GCA was retained after ≥6 mo of follow-up when no other diagnosis was considered and the patient had gone into remission after ≥6 consecutive mo of treatment. Cranial PET/CT sensitivity, specificity, and positive- and negative-predictive values were 73.3%, 97.2%, 91.7%, and 89.7%, respectively. Corresponding values for extracranial PET/CT diagnostic performance were 66.7%, 80.6%,
neuronal damage may manifest as a decrease in central benzodiazepine receptors in patients with cerebral infarction and internal carotid artery or middle cerebral artery disease, which may be associated with frontal lobe dysfunction.”

Stroke

68Ga-FAPI vs 18F-FDG in Newly Diagnosed NSCLC

Wu et al. from the Affiliated Hospital of Southwest Medical University, the Nuclear Medicine and Molecular Imaging Key Laboratory of Sichuan Province, and Academician (Expert) Workstation of Sichuan Province (all in Luzhou, China) reported on July 4 ahead of print in Frontiers in Oncology on a study comparing 68Ga-fibroblast-activation protein inhibitor (68Ga-FAPI) and 18F-FDG PET/CT in evaluation of newly diagnosed non–small cell lung cancer (NSCLC). The prospective study included 28 patients (15 women, 13 men; median age, 60.5 y; age range, 35–78 y) with new and histopathologically confirmed NSCLC. All participants underwent both 68Ga-FAPI and 18F-FDG PET/CT imaging, and the performance of the tracers was compared by visual assessment, rates of cancer detection, and semiquantitative parameters for both primary tumors and metastases. The 2 tracers were found to have similar detection performance in primary tumors. 68Ga-FAPI PET/CT was more effective than 18F-FDG PET/CT in evaluation of most metastases, including those in lymph nodes (53 vs 49), pleura (8 vs 7), liver (4 vs 1), and bone (41 vs 35). SUV\(_{\text{max}}\) and tumor-to-background ratio values for 68Ga-FAPI were significantly superior to those with 18F-FDG in lymph node, pleural, and bone metastases. SUV\(_{\text{max}}\) assessments for the tracers were comparable in hepatic metastases, but 68Ga-FAPI produced a significantly higher tumor-to-background ratio than 18F-FDG. 68Ga-FAPI PET/CT showed excellent staging accuracy (80% of N and 92.9% of M stage disease). The authors concluded that 68Ga-FAPI PET/CT is excellent for evaluation of newly diagnosed NSCLC and “improves the detection rates of most metastases, facilitating the superior staging of patients with newly diagnosed NSCLC, relative to that achieved by 18F-FDG PET/CT.”

Frontiers in Oncology

68Ga-FAPI vs 18F-FDG in Staging/Restaging Gastric Cancer

In an article from some of the same researchers, in the July 1 issue of Frontiers in Oncology (202,12:925100), Zhang et al. from the Affiliated Hospital of Southwest Medical University (Luzhou), Nuclear Medicine and Molecular Imaging Key Laboratory of Sichuan Province (Luzhou), Southwest Medical University (Luzhou), the Fourth People’s Hospital of Chengdu, and the Clinical Hospital of Chengdu Brain Science Institute/University of Electronic Science and Technology of China (Chengdu; all in China) reported on a study comparing the diagnostic efficacy of 68Ga-fibroblast-activated protein inhibitor (68Ga-FAPI-04) and that of 18F-FDG PET/CT for primary tumors, lymph nodes, and distant metastatic lesions in gastric cancer and assessing respective results in tumor staging and restaging. The study included 25 patients (mean age, 56 ± 12 y) with pathologically confirmed gastric cancer. Patients underwent imaging with both tracers within a 1-wk period. 68Ga-FAPI-04 showed higher sensitivity than 18F-FDG PET/CT for detecting primary tumors (94.74% vs 68.42%), lymph node metastases (97.40% vs 41.56%), and distant metastases (97.17% vs 43.11%), with significantly higher uptake in tumors (median SUV\(_{\text{max}}\) 10.28 vs 3.20), lymph node metastases (9.20 vs 3.15), and distant metastases (8.00 vs 4.20). 68Ga-FAPI-04 PET/CT resulted in new oncolgic findings in 14 of the 25 patients and corrected tumor staging or restaging in 7 patients. The authors concluded that these results highlight the potential of 68Ga-FAPI-04 PET/CT tumor staging in increasing the accuracy of gastric cancer diagnosis, “which may facilitate treatment decision making.”

Frontiers in Oncology
Early Revascularization, Inducible Ischemia, and Outcomes

Rozanski et al. from Mount Sinai Morningside Hospital and Mount Sinai Heart (New York, NY), the University of Calgary (Alberta, Canada), Cedars-Sinai Medical Center (Los Angeles, CA), and the David Geffen School of Medicine at the University of California, Los Angeles reported in the July 19 issue of the Journal of the American College of Cardiology (2022;80[3]202–215) on a study using stress/rest SPECT myocardial perfusion imaging (MPI) to assess the relationships between stress-induced myocardial ischemia, revascularization, and all-cause mortality in patients with normal or low left ventricular ejection fractions (LVEFs). The retrospective study included data from 43,443 patients who underwent stress/rest SPECT MPI from 1998 to 2017, with a median follow-up of 11.4 y. Myocardial ischemia was evaluated for its relationship to early revascularization and mortality. The researchers found that the frequency of myocardial ischemia varied widely depending on LVEF and angina, ranging from 6.7% in patients with LVEF ≥55% and no typical angina to 64.0% in patients with LVEF <45% and typical angina. Of the 39,883 patients with LVEF ≥45%, early revascularization was associated with increased mortality in those without ischemia and lower mortality among patients with severe (≥15%) ischemia. Of the 3,560 patients with LVEF <45%, revascularization was not associated with mortality benefits in those with no or mild ischemia but was associated with decreased mortality in those with moderate (10%–14%) and severe (≥15%) ischemia. The authors summarized their findings that in this very large cohort “early myocardial revascularization was associated with a significant reduction in mortality among both patients with normal LVEF and severe inducible myocardial ischemia and patients with low LVEF and moderate or severe inducible myocardial ischemia.”

Journal of the American College of Cardiology

Optimizing Prostate Cancer Lymph Node Staging

In an article published on July 21 ahead of print in Prostate, Wang et al. from Xiangya Hospital/Central South University (Changsha City, China) reported on a study developed to explore approaches to improving the utility of 68Ga–prostate-specific membrane antigen (68Ga-PSMA) PET/CT imaging for diagnosing lymph node metastasis in prostate cancer patients through combined evaluation of inflammatory hematologic markers. The retrospective study included pretreatment data on a group of patients, including initial total prostate-specific antigen levels, hematologic findings, biopsy and surgical pathology results, and 68Ga-PSMA PET/CT findings. The researchers identified SUVmax, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, initial prostate-specific antigen levels, and clinical T stage as independent predictors of lymph node metastasis. A nomogram combining optimal cutoff values for these variables was constructed and found to be associated with good predictability. The authors concluded that “SUVmax, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, initial prostate-specific antigen levels, and clinical T stage represent valuable independent predictors of lymph node metastasis in prostate cancer patients, offering an opportunity to further optimize lymph node staging.”

Prostate

Metabolic Abnormality Patterns in Lewy Body Dementia

Lu et al. from Huashan Hospital/Fudan University (Shanghai), Zhongnan Hospital of Wuhan University, and Shanghai Jiao Tong University Affiliated Sixth People’s Hospital (Shanghai; all in China) reported on July 20 ahead of print in Movement Disorders on a study designed to identify disease-specific metabolic patterns that can illuminate the question of whether dementia with Lewy bodies (DLB) and Parkinson disease (PD) dementia represent the same disease, distinct entities, or conditions within the same spectrum. Sixty-seven patients with DLB, 50 with PD dementia, and 15 healthy controls were enrolled and assigned to 2 cohorts, 1 for pattern identification and 1 for validation. The study also included 30 patients with PD without dementia for pattern discrimination and differentiation. All participants underwent 18F-FDG PET/CT, with 21 undergoing 2 serial scans. DLB-related and PD dementia–related patterns shared similarities: comparative hypometabolism in the middle temporal gyrus, middle occipital gyrus, lingual gyrus, precuneus, cuneus, angular gyrus, superior and inferior parietal gyr, cingulate, and caudate, as well as comparative hypermetabolism in the cerebellum, putamen, thalamus, precentral/postcentral gyrus, and paracentral lobule. These metabolic characteristics differed from PD-related patterns. Patients with DLB and PD dementia, however, could not be distinguished from one another successfully by any pattern, but patients with PD could be recognized easily. DLB-related and PD dementia–related pattern expression showed similar efficacies in cross-sectional disease severity assessment and, in the subset of twice-imaged patients, longitudinal progression monitoring. The authors concluded that “consistent abnormalities in metabolic patterns of DLB and PD dementia might underlie the potential continuum across the clinical spectrum from PD to DLB.”

Movement Disorders

18F-PI-2620 Tau PET Imaging in Alzheimer Disease

In an article published on July 17 ahead of print in Neuropsychopharmacology Reports, Bun et al. from Keio University School of Medicine (Tokyo), Eisai Co., Ltd. (Tokyo), and the National Institute of Radiological Sciences/National Institutes for Quantum and Radiological Science and Technology (Chiba; all in Japan) reported on a pilot study of the second-generation tau tracer 18F-PI-2620 in Alzheimer disease (AD). The study included 7 individuals with probable AD and 7 healthy
controls. Imaging variables compared between the 2 groups included SUV ratios in regions of interest in the medial temporal region and neocortex. Correlations between these uptake ratios and plasma p-tau181 and cognitive test scores were also assessed. Tracer uptake was significantly increased in AD individuals across all regions of interest. SUV ratios in these regions were significantly correlated with plasma p-tau181 levels and with cognitive scores. The authors concluded that these results “add to accumulating evidence suggesting that $^{18}$F-PI-2620 is a promising tau PET tracer that allows patients with AD to be distinguished from healthy controls.” They emphasized the importance of early identification of abnormal tau in the brain for development of new therapeutic interventions and called for larger studies.

Neuropsychopharmacology Reports

$^{124}$I PET/CT and $^{124}$I PET/MR in Resected DTC

Grafe et al. from University Hospital Essen/University Duisburg-Essen and University Hospital Düsseldorf (both in Germany) reported on June 21 in Cancers (Basel) (2022;14[13]:3040) on the results of a study of quantitative differences between $^{124}$I PET/CT and $^{124}$I-PET/MR findings in a group of patients after thyroidectomy for differentiated thyroid carcinoma (DTC). Thirty-five patients (23 female, 12 male; median age, 52 y; range, 16–85 y) with a total of 43 imaging studies were included. All patients underwent whole-body (skull base to mid thigh) PET/CT and a dedicated head–neck (skull base to upper lung) PET/MR examination on the same day, allowing for intra-individual comparisons of the same anatomic areas. CT-based attenuation correction in PET/CT and MR-based attenuation correction in PET/MR with bone atlas were compared. In all, 111 $^{124}$I-avid lesions were detected on PET/CT and 132 on PET/MR. The median SUV$\text{mean}$ for 98 congruent lesions measured on PET/CT was 12.3. For PET/MR, the median SUV$\text{mean}$ was 16.6 with MR-based AC. The authors concluded that although these 2 hybrid imaging approaches in patients with resected DTC provided overall comparable quantitative results in a clinical setting (despite different patient positioning and attenuation correction methods), the number of detected lesions and average SUV$\text{mean}$ values for congruent lesions was higher for PET/MR.

Cancers (Basel)

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 June and July. Parpinel et al. from the Sant’Anna Hospital/University of Turin and the Ospedale degli Infermi (Ponderano; both in Italy) published “Use of positron emission tomography for pregnancy-associated cancer assessment: A review” in the July 1 issue of the Journal of Clinical Medicine (2022;11[13]:3820). In an overview in the July 20 issue of Expert Review of Molecular Diagnostics, Faldu and Shah from Nirma University (Ahmedabad, India) provided “Alzheimer’s disease: A scoping review of biomarker research and development for effective disease diagnosis.” Manafi-Farid et al. from Shariati Hospital/Tehran University of Medical Sciences (Iran), Massachusetts General Hospital and Harvard Medical School (Boston, MA), University Hospital Salzburg/Paracelsus Medical University (Austria), and Iran University of Medical Sciences (Tehran) reported in the June 28 issue of Frontiers in Medicine (Lausanne) on “ImmunoPET: Antibody-based PET imaging in solid tumors.” An overview of “Immune checkpoint molecules in neuroblastoma: A clinical perspective” was published by Pathania et al. from the University of Nebraska Medical Center (Omaha), the National Institutes of Biomedical Innovation, Health, and Nutrition (Osaka, Japan), Sri Rajiv Gandhi College of Dental Sciences & Hospital (Bengaluru, India), Sree Sai Dental College & Research Institute (Srikakulam, India), and Bannaras Hindu University (Varanasi, India) in the July 3 issue of Seminars in Cancer Biology. Omorphous et al. from Heartlands Hospital/University Hospitals Birmingham, St. Bartholomew’s Hospital (London), Mount Vernon Cancer Centre (London), Lister Hospital (Stevenage), University of Hertfordshire (Northwood), King’s College London, Guy’s Hospital (London), and Brunel University (London; all in the UK), and Apollo Hospitals Educational and Research Foundation (Chennai, India) surveyed “The increasing indications of FDG-PET/CT in the staging and management of invasive bladder cancer” on July 5 ahead of print in Urologic Oncology.