

## 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.

### Fractional Flow Reserve from CTA Data in CAD

Driessen et al. from the VU Medical Center (Amsterdam, The Netherlands), the University of British Columbia (Vancouver, Canada), Turku University Hospital/University of Turku (Finland), the Royal Brompton Hospital (London, UK), and Stanford University (CA) reported in the January 22 issue of the *Journal of the American College of Cardiology* (2019;73:161–173) on an evaluation of the diagnostic performance of fractional flow reserve (FFR) calculated from coronary CT angiography (CTA) datasets and compared results with the diagnostic performances of CTA, SPECT, and PET in ischemia to assess the hemodynamic severity of coronary artery disease (CAD). The study included 208 patients with suspected stable CAD, each of whom underwent 256-slice coronary CTA,  $^{99m}\text{Tc}$ -tetrofosmin SPECT,  $^{15}\text{O}$ - $\text{H}_2\text{O}$  PET, and routine 3-vessel invasive FFR assessments. CTA-based FFR values were derived retrospectively. Interpretations of images from other modalities were compared using invasively measured  $\text{FFR} \leq 0.80$  as the reference standard. Of a total of 612 vessels assessed, 505 (83%) could

be evaluated with CTA-based FFR. CTA-based FFR had per-vessel diagnostic accuracy, sensitivity, and specificity of 87%, 90%, and 86%, respectively. Corresponding per-patient percentages were 78%, 96%, and 63%. The area under the receiver operating characteristic curve (AUC) for identification of ischemia-causing lesions was significantly greater for CTA-derived FFR than for coronary CTA and SPECT, on both per-vessel and per-patient analyses. CTA-derived FFR also outperformed PET on a per-vessel basis but not on per-patient assessment. PET showed the highest per-patient and per-vessel AUC on intention-to-diagnose analyses. The authors concluded that although CTA-derived FFR showed “higher diagnostic performance than standard coronary CTA, SPECT, and PET for vessel-specific ischemia,” this was dependent on whether standard coronary CTA images were evaluable by CTA-derived FFR (17% were not). Despite PET’s superior performance in per-patient and intention-to-diagnose analyses, they concluded that CTA-derived FFR “holds clinical potential to provide anatomic and hemodynamic significance of coronary lesions.”

*Journal of the American College of Cardiology*

### PET-Assessed Factors and Cognition in AD

In an article e-published ahead of print in the January 9 issue of *Neurology*, Ossenkopppele et al. from Lund University (Sweden), VU University (Amsterdam, The Netherlands), Skåne University Hospital (Malmö, Sweden), and the Veterans Affairs Medical Center (San Francisco, CA) reported on correlations among factors including regional tau,  $\beta$ -amyloid, and cortical thickness and related associations with neuropsychological function in both preclinical and clinical Alzheimer disease (AD). The study included 106 individuals from the Swedish Biomarkers for Identifying Neurodegenerative Disorders Early and Reliably (BioFINDER)

study, a larger investigation initiated to discover key pathologic mechanisms in AD and other neurodegenerative diseases such as parkinsonian disorders. Thirty-three of this study’s participants had preclinical AD (i.e., were  $\beta$ -amyloid-positive and cognitively normal), 25 had prodromal AD (i.e., were  $\beta$ -amyloid-positive with mild cognitive impairment), and 48 had probable AD dementia. All underwent  $^{18}\text{F}$ -flortaucipir PET imaging for tau and structural MR imaging for cortical thickness. In addition, 88 of the 106 participants underwent  $^{18}\text{F}$ -flutemetamol PET for  $\beta$ -amyloid. Results were analyzed for associations between 7 regions of interest and 7 neuropsychological tests for all 3 imaging modalities.

$^{18}\text{F}$ -flortaucipir uptake (but neither  $^{18}\text{F}$ -flutemetamol uptake nor cortical thickness) was associated with decreased global cognition, memory, and processing speed in preclinical AD. In both prodromal AD and AD dementia groups, increased  $^{18}\text{F}$ -flortaucipir uptake and reduced cortical thickness were associated with worse outcomes on neuropsychological tests. Increased  $^{18}\text{F}$ -flutemetamol uptake was specifically associated with lower scores on a delayed recall memory task assessment. The strongest relationships between both  $^{18}\text{F}$ -flortaucipir and cortical thickness and cognition were identified in the lateral and medial parietal cortices and lateral temporal cortex.  $^{18}\text{F}$ -flutemetamol associations with cognition were weaker and less region specific. The authors concluded that their findings suggest that “tau PET is more sensitive than  $\beta$ -amyloid PET and measures of cortical thickness for detecting early cognitive changes in preclinical AD” and that “both  $^{18}\text{F}$ -flortaucipir PET and cortical thickness show strong cognitive correlates at the clinical stages of AD.”

*Neurology*

### PET/CT + US and Primary Tumors in Malignant Ascites

Liu et al. from the Affiliated Hospital of Chengdu Medical College and

the Nanchong City Central Hospital (both in China) reported on December 26 ahead of print in *Cancer Biotherapy and Radiopharmaceuticals* on a study designed to determine the clinical value of PET/CT imaging combined with ultrasound in detection of primary tumors in patients with malignant ascites. The study included 122 patients with malignant tumors and ascites as an initial symptom and 48 patients with benign ascites. All participants underwent PET/CT and abdominal B-ultrasound imaging. The results were compared with pathology findings as the gold standard. PET alone detected primary disease foci in 79.5% of patients, with the detection rate highest in individuals with gastric cancer. The corresponding percentage for B-ultrasound was 62.5%, with the detection rate highest in individuals with ovarian cancer. B-ultrasound had the highest specificity for primary foci associated with malignant ascites at 73.2%, whereas PET/CT had the highest sensitivity in diagnosing primary foci of malignant ascites at 91.7%. PET/CT combined with abdominal B-ultrasound had the highest sensitivity and accuracy in diagnosing primary foci (98.1% and 89.1%, respectively). The diagnostic accuracy rate for B-ultrasound was highest in tumors >5 cm (77.0%), and PET/CT was highest in detecting 3–5-cm tumors (84.2%). The authors concluded that “PET/CT combined with ultrasound is conducive to improving the diagnostic efficiency for primary tumors in patients with malignant ascites.”

*Cancer Biotherapy and Radiopharmaceuticals*

### **<sup>18</sup>F-FCH PET/CT and 4D CT in Primary Hyperparathyroidism**

In an article e-published on January 18 ahead of print in the *World Journal of Surgery*, Amadou et al. from the Pitié-Salpêtrière Hospital/Sorbonne University (Paris, France) reported on a study evaluating <sup>18</sup>F-fluorocholine PET/CT and parathyroid 4D CT in guiding surgery in patients with primary hyperparathyroidism and previous neck surgery. The retrospective study included 29 patients referred for <sup>18</sup>F-fluorocholine

PET/CT with histories of neck surgery and indications for reoperation. All patients also underwent parathyroid ultrasound and <sup>99m</sup>Tc-sestamibi scintigraphy, with a subset of 20 also undergoing 4D CT. Results were compared against pathology findings and/or ultrasound-guided fine-needle aspiration products. <sup>18</sup>F-fluorocholine PET/CT identified 34 abnormal foci, including 19 ectopic localizations. In the 4D-CT subset 11 abnormal glands were initially detected, with 6 more identified under <sup>18</sup>F-fluorocholine PET/CT guidance. Ultrasound and scintigraphy identified concordant foci in 8 of the 29 patients. On a per-lesion basis, the sensitivity, specificity, and positive and negative predictive values were 96%, 13%, 77%, and 50%, respectively, for <sup>18</sup>F-fluorocholine PET/CT and 75%, 40%, 80% and 33% for 4D CT. On a per-patient analysis, sensitivity was 85% for <sup>18</sup>F-fluorocholine PET/CT and 63% for 4D CT. <sup>18</sup>F-fluorocholine PET/CT enabled successful removal of an abnormal gland in 21 patients, including 12 with negative or discordant ultrasound/scintigraphy findings, producing a global cure rate of 73%. The authors concluded that “<sup>18</sup>F-fluorocholine PET/CT is a promising tool in the challenging population of reoperative patients with primary hyperparathyroidism,” with parathyroid 4D CT appearing to serve as a confirmatory imaging modality.

*World Journal of Surgery*

### **<sup>18</sup>F-DOPA and <sup>18</sup>F-FET PET/CT in Recurrent High-Grade Glioma**

Evangelista et al. from the Veneto Institute of Oncology IOV-IRCCS (Padua, Italy) reported on January 15 ahead of print in *Current Radiopharmaceuticals* on a systematic analysis of the literature exploring the utility of L-3,4-dihydroxy-6-<sup>18</sup>F-fluorophenylalanine (<sup>18</sup>F-DOPA) and O-(2-<sup>18</sup>F-fluoroethyl)-L-tyrosine (<sup>18</sup>F-FET) PET/CT in patients with high-grade glioma, followed by experiential results with both tracers in a series of patients with recurrent disease. Although the literature search of keywords yielded 51 articles, only 2 were eligible for the comparison

analyses, and these data led to the conclusion that the 2 tracers have a similar accuracy in patients with high-grade glioma. The case series study from the researchers’ own institution included 29 patients who had undergone either <sup>18</sup>F-DOPA or <sup>18</sup>F-FET PET/CT for suspicion of recurrent disease, with a final confirmation/rule-out of recurrence made by MR imaging and/or clinical decision. Analysis of these data found that the sensitivity, specificity, and accuracy of <sup>18</sup>F-DOPA PET/CT in high-grade glioma were 100%, 63%, and 62%, respectively. Corresponding results for <sup>18</sup>F-FET PET/CT were all 100%. <sup>18</sup>F-FET PET/CT was true-positive in 4 and true-negative in 4 patients. The authors noted that <sup>18</sup>F-DOPA PET/CT imaging results may be affected by inflammation and that “large comparative trials are warranted in order to better understand the utility of <sup>18</sup>F-DOPA or <sup>18</sup>F-FET PET/CT in patients with high-grade glioma.”

*Current Radiopharmaceuticals*

### **PSMA PET/CT in PCa Salvage RT Planning**

In an article in the January 7 issue of *BMC Cancer* (2019;19[1]:18), Calais et al. from the University of California, Los Angeles, University Hospital Essen (Germany), and the Veterans Affairs Greater Los Angeles Healthcare System (CA) reported on initiation of a randomized prospective phase III trial designed to explore whether <sup>68</sup>Ga-PSMA-11 PET/CT-guided treatment planning can improve outcomes in salvage radiotherapy in prostate cancer patients with biochemical recurrence after prostatectomy. The rationale for the study is that salvage radiotherapy is routinely started in patients with prostate-specific antigen (PSA) levels <1 ng/mL, when conventional imaging is not likely to identify recurrence. The result is that salvage radiotherapy treatment planning volumes may be delineated without the guidance of visible disease on imaging. The purpose of this trial is to evaluate the success rate of salvage radiotherapy with and without <sup>68</sup>Ga-PSMA-11 PET/CT-guided planning for cancer recurrence after prostatectomy. The prospective study targets enrollment of 193 men

who will be randomized to standard-of-care planning (control arm, 90 patients) or  $^{68}\text{Ga}$ -PSMA-11 PET/CT before planning (investigational arm, 103 patients). Biochemical progression-free survival (with progression defined as PSA  $\geq$  0.2 ng/mL and rising) after initiation of salvage radiotherapy will be assessed as the primary endpoint. The treating radiation oncologist will choose whether the prostate bed alone or the prostate bed and pelvic lymph nodes are irradiated, with or without androgen deprivation therapy, and may choose to refine the radiation plan based on  $^{68}\text{Ga}$ -PSMA-11 PET/CT in the investigational arm. Patients will be followed for 5 y after randomization or until biochemical progression, diagnosis of metastatic disease, initiation of any additional salvage therapy, or death.

*BMC Cancer*

### Staging in Newly Diagnosed Lymphomatous Brain Lesions

Malani et al. from Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College (both in New York, NY) reported on January 10 ahead of print in *Leukemia and Lymphoma* on a study characterizing staging evaluations in patients with newly diagnosed brain lymphomas and focusing on the frequency of secondary central nervous system lymphoma and secondary malignancies. The study included 262 patients with lymphomatous central nervous system lesions. PET was used for staging in 180 (69%) patients, chest/abdomen/pelvis CT imaging in 195 (74%), and bone marrow biopsies in 177 (68%). Abnormal scans were reported in 34 of 180 (19%) patients undergoing PET, in 50 of 195 (26%) patients undergoing CT, and in 15 of 177 (8.5%) patients undergoing bone marrow biopsy. Staging with these modalities identified 24 (11.8%) non-central nervous system malignancies (19 systemic lymphomas, 5 secondary malignancies). The authors concluded that in “patients with new lymphomatous brain lesions, performing initial systemic staging procedures can identify systemic lymphoma and additional ma-

lignancies, highlighting the importance of staging evaluations, in particular PET and bone marrow biopsy.”

*Leukemia and Lymphoma*

### Incidental PET Findings in Psoriasis

In an article e-published on January 14 in the *Journal of the American Academy of Dermatology*, Wan et al. from the University of Pennsylvania/University of Pennsylvania Perelman School of Medicine (Philadelphia) and the National Heart, Lung, and Blood Institute (Bethesda, MD) reported on a study designed to assess the frequency of incidentalomas and malignancies identified by  $^{18}\text{F}$ -FDG PET/CT in clinical trial patients with moderate-to-severe psoriasis. The study included 259 healthy individuals with moderate-to-severe psoriasis, each of whom underwent  $^{18}\text{F}$ -FDG PET/CT imaging. Of these, 31 (11.97%) were found to have clinically significant incidentalomas on baseline imaging. Additional analysis showed that every 10-y increase in participant age was accompanied by an  $\sim$ 30% increased risk of incidentaloma identification on PET/CT. Findings suspicious for malignancy were identified in 28 patients on PET/CT; these were confirmed in 6 patients, for an overall 2.31% prevalence of malignancy and a positive predictive value for true cancer of 31.58% (range, 21%–54%). The authors concluded that incidentalomas on  $^{18}\text{F}$ -FDG PET/CT imaging “are common in otherwise healthy, asymptomatic clinical trial patients with moderate-to-severe psoriasis” and that these results “can help inform clinical trials safety data interpretation and emphasize the importance of compliance with cancer screening recommendations.”

*Journal of the American Academy of Dermatology*

### PET and Intraocular Sarcoidosis

Chauvelot and Skanjeti et al. from the Université Claude Bernard Lyon (France) reported on January 18 ahead of print in the *British Journal of Ophthalmology* on a study designed to determine the diagnostic and predic-

tive utility of  $^{18}\text{F}$ -FDG PET/CT for sarcoidosis in patients with uveitis and normal thoracic CT. The retrospective study included 67 patients with uveitis of unknown etiology or suspected intraocular sarcoidosis. Patients with normal thoracic CT underwent  $^{18}\text{F}$ -FDG PET/CT imaging. Nineteen of the 67 patients (28.4%) were found on PET/CT to have mediastinal hypermetabolic foci consistent with sarcoidosis. In addition, PET/CT identified a biopsy site in 2 cases, consistent with sarcoidosis. Overall, 6 patients (10%) had a proven sarcoidosis, 6 (9%) had a presumed sarcoidosis, and 18 (26.9%) had an indeterminate sarcoidosis. Results suggested that an older age at diagnosis and the presence of synechiae were significantly associated with positive  $^{18}\text{F}$ -FDG PET/CT imaging, with a trend toward significance for elevated serum angiotensin-converting enzyme (ACE). The authors included a nomogram to estimate the probability of positive findings on  $^{18}\text{F}$ -FDG PET/CT based on different predictive factors. They summarized their observations that “ $^{18}\text{F}$ -FDG PET/CT enabled the diagnosis of intraocular sarcoidosis even in patients with a normal CT scan” and that “older age at diagnosis, presence of synechiae, and elevated ACE are associated with positive findings on  $^{18}\text{F}$ -FDG PET/CT consistent with sarcoidosis.”

*British Journal of Ophthalmology*

### PET and Salvage Hysterectomy After CRT

In an article e-published on January 10 ahead of print in the *International Journal of Gynecological Cancer*, Rajasooriyar et al. from the Peter MacCallum Cancer Centre (Melbourne, Australia), the Jaffna Teaching Hospital (Sri Lanka), and the Royal Women's Hospital (Melbourne, Australia) reported on the role of  $^{18}\text{F}$ -FDG in patient selection for salvage hysterectomy. The retrospective study included 49 women with cervical cancer who were eligible for salvage hysterectomy after treatment. Patients were assigned to 1 of 3 groups: (1) those who underwent planned hysterectomy based on clinical, cytologic, or histologic suspicion ( $n = 15$ ); (2) those

who underwent posttreatment  $^{18}\text{F}$ -FDG PET/CT 3–6 mo after completion of chemoradiotherapy, either for suspicion of recurrence on examination or at high risk of recurrence at the primary site ( $n = 13$ ); and (3) those who showed isolated tracer uptake at the primary site on PET at 6 mo ( $n = 21$ ). In group 1, 3 (20%) patients were found to have residual disease on histology. Eight of the patients in group 2 underwent hysterectomy, and 4 showed positive histology for residual tumor. In group 3, an  $^{18}\text{F}$ -FDG PET/CT scan after 3 months showed disease progression in 7 and complete metabolic response in 14. Surgery was avoided in all group 3 patients. The authors concluded that  $^{18}\text{F}$ -FDG PET/CT at 6 mo after radiotherapy is “a good tool for assessing treatment response in patients with cervical cancer” and that in patients with “persistent uptake on 6 mo posttreatment  $^{18}\text{F}$ -FDG PET/CT, repeat imaging at a 3-mo interval helps in selecting patients for salvage hysterectomy.”

*International Journal of Gynecological Cancer*

### Prognostic Nodal PET Uptake Before Treatment

Jimenez-Jimenez et al. from the Complejo Hospitalario Universitario de Albacete (Spain), the Clinica IMQ Zorrotzaurre (Bilbao, Spain), and the Hospital Universitari Son Espases (Palma de Mallorca, Spain) reported on January 29 ahead of print in *Clinical and Translational Oncology* on a study assessing whether pretreatment lymph node uptake in patients with esophageal cancer is associated with survival and regional relapses or relapse patterns after radio/chemotherapy. The study included  $^{18}\text{F}$ -FDG PET/CT image datasets from patients who underwent imaging before definitive or neoadjuvant radio/chemotherapy. All patients suffering from persistent or recurrent local/regional-only disease after treatment were considered for salvage resection. Patients with adenocarcinoma without metastatic disease were considered for planned resection (usually within 3 mo after treatment). Patients with PET-positive lymph nodes before

treatment were found to have worse overall and shorter disease-free survival times than those without PET-positive nodes. These node-positive patients also had worse node and metastatic relapse-free survival. Patients staged as N2 had significantly worse outcomes than those staged at N1–N0 but better survival if the involved nodes were closer to the esophageal tumor. Involved node location on PET was also associated with global, nodal, and metastatic relapse. Increasing  $\text{SUV}_{\text{max}}$  values were correlated with increased relative risk of death and relative risk of node and metastatic relapses. The most frequent relapse was metastatic recurrence, followed by local recurrence. The majority represented “in-field” loco-regional recurrence. The number of PET-positive nodes was an independent and significant predictor for relapse. The authors concluded that their results “show that only FDG PET/CT can provide prognostic information in esophageal cancer” and that nodal PET/CT uptake is associated with outcome and relapse location among these patients.

*Clinical and Translational Oncology*

### PET/CT for Interstitial Lung Disease/Myositis in Dermatomyositis

In an article e-published on January 4 ahead of print in *The Journal of Dermatology*, Motegi et al. from the Gunma University Graduate School of Medicine (Maebashi, Japan) reported on a study evaluating the clinical utility of  $^{18}\text{F}$ -FDG PET/CT for detection of inflammatory lesions and disease activity associated with both myopathy and interstitial lung disease in patients with dermatomyositis. The study included 22 such patients who underwent  $^{18}\text{F}$ -FDG PET/CT, including assessment of  $\text{SUV}_{\text{max}}$  in muscle and lung. These measurements were compared with MR and high-resolution CT (HRCT) imaging results in the same muscle and lung regions and were also correlated with clinical findings. The location of increased  $^{18}\text{F}$ -FDG uptake was found to be nearly consistent with the regions of interstitial lung disease as detected by HRCT score and

myositis as detected by MR imaging. A significant positive correlation was noted between lung HRCT score and  $\text{SUV}_{\text{max}}$  in each lung. Serum Krebs von den Lungen-6 levels were also positively correlated with total  $\text{SUV}_{\text{max}}$  for both lungs. Total  $\text{SUV}_{\text{max}}$  in the muscles was significantly correlated with serum cytokeratin levels. The authors concluded that these results suggest that  $^{18}\text{F}$ -FDG uptake ( $\text{SUV}_{\text{max}}$ ) may be “useful for not only the detection of malignant tumors but also the evaluation of the location and activity of interstitial lung disease and myositis in dermatomyositis patients.”

*The Journal of Dermatology*

### PET/CT and Lymphoma in Sjögren Syndrome

Keraen et al. from the Hôpitaux Universitaires Paris-Sud (Le Kremlin Bicêtre, France), the Centre Chirurgicale Marie Lannelongue (Le Plessis-Robinson, France), the Université Paris Saclay/Université Paris Sud (Orsay, France), and Université Paris Descartes/Sorbonne Paris Cité (France) reported on January 7 ahead of print in *Arthritis and Rheumatology* on a study intended to compare abnormalities in  $^{18}\text{F}$ -FDG PET/CT imaging between patients with Sjögren syndrome with and without lymphoma to determine whether specific patterns are associated with lymphoma. The retrospective study included data from 45 patients, all of whom had undergone  $^{18}\text{F}$ -FDG PET/CT and 15 of whom had lymphoma. Mean size and  $\text{SUV}_{\text{max}}$  in the parotid glands were found to be higher in patients with lymphoma. Tracer lymph node uptake was seen in 53.3% of patients with lymphoma and 43.3% without, with no observed difference in number of nodes, repartition, or mean  $\text{SUV}_{\text{max}}$ . Focal pulmonary uptake was observed in 5 (33.3%) patients with lymphoma and 1 (3.3%) without. An  $\text{SUV}_{\text{max}} \geq 4.7$  in the parotid gland and/or identification of focal pulmonary lesions were highly suggestive of lymphoma, with a sensitivity of 80% and specificity 83.3%. The authors concluded that although pulmonary, lymphadenopathy, and salivary gland involvements can

be visualized by  $^{18}\text{F}$ -PET/CT in Sjögren syndrome, lymph nodes and parotid gland involvement is seen at similar rates in patients with and without lymphoma. An  $\text{SUV}_{\text{max}} \geq 4.7$  in the parotid glands and/or focal lung lesions, however, were associated with lymphoma diagnosis.

*Arthritis and Rheumatology*

### **$^{18}\text{F}$ -FCH PET in PCA**

#### **Biochemical Recurrence**

In an article e-published on January 17 ahead of print in *Medicina Clinica (Barcelona)*, Triviño-Ibáñez et al. from the Hospital Universitario Virgen de las Nieves and the Instituto de Investigación Biosanitaria de Granada (both in Granada, Spain) reported on a study evaluating the ability of  $^{18}\text{F}$ -fluorocholine ( $^{18}\text{F}$ -FCH) PET/CT to identify biochemical recurrence in patients with prostate cancer and investigating correlated prostate-specific antigen (PSA) kinetics and antiandrogen hormone therapy. The retrospective study included 203 men with prostate cancer who met European Association of Urology criteria for biochemical recurrence and/or resistance to chemical castration. Imaging results were classified as positive or negative, using pathology, other imaging, and/or clinical follow-up as comparative data.  $^{18}\text{F}$ -FCH detected recurrence in 43.3% of patients. Patients with positive  $^{18}\text{F}$ -FCH PET/CT results had more aggressive PSA kinetics. In the subgroup of patients with castration-resistant disease, the  $^{18}\text{F}$ -FCH PET/CT detection rate was 89.1%, significantly higher than the 29.9% in those with radical treatment. The authors concluded that  $^{18}\text{F}$ -FCH “is useful to detect biochemical recurrence of prostate cancer, especially in patients who receive hormone therapy or more aggressive PSA kinetics.”

*Medicina Clinica (Barcelona)*

#### **Predictive PET/CT in Endoscopic Resection**

Chung et al. from the Konkuk University Medical Center/Konkuk University School of Medicine and the Seoul Medical Center (both in Seoul,

South Korea) reported on January 2 ahead of print in the *Journal of Cancer Research and Clinical Oncology* on the value of  $^{18}\text{F}$ -FDG PET/CT as a complementary imaging modality for predicting successful outcomes after endoscopic submucosal dissection in early gastric cancer. The retrospective study included the records of 199 patients (mean age,  $67 \pm 10$  y; total of 210 tumors) with well or moderately differentiated adenocarcinoma who had undergone  $^{18}\text{F}$ -FDG PET/CT for initial routine staging of gastric cancer. PET/CT data were analyzed for primary tumor/background gastric uptake ratios, with each patient's case categorized as curable by endoscopic submucosal dissection (no discrete radioactivity) or not curable by this procedure (discrete radioactivity).  $^{18}\text{F}$ -FDG PET/CT showed an overall detection rate for early gastric cancer of 37.1% (identifying 78 lesions with discrete radioactivity out of 210). In the group identified on PET as not curable by endoscopic submucosal dissection, however, the sensitivity, specificity, positive and negative predictive values, and area under the receiver operating characteristic curve with 95% confidence intervals were 79%, 91%, 81%, 89%, and 0.85, respectively. The authors concluded that  $^{18}\text{F}$ -FDG PET/CT may be a “useful complementary imaging modality to endoscopy” to predict the success of endoscopic submucosal dissection in technical cures of early gastric cancer.

*Journal of Cancer Research and Clinical Oncology*

#### **Tau Accumulation in Aging and AD**

In an article e-published on December 31 ahead of print in *Annals of Neurology*, Harrison et al. from the University of California, Berkeley, the University of California, San Francisco, the German Center for Neurodegenerative Diseases (Magdeburg, Germany), and the Lawrence Berkeley National Laboratory (CA) reported on a study looking at the rate of tau accumulation in healthy older adults and patients with Alzheimer disease (AD)

and at correlations between tau accumulation and cortical atrophy. The study included 61 patients: 42 older adults (age,  $77.6 \pm 4.6$  y; 25 women, 17 men; 21 of whom had been found to be Pittsburgh compound B–positive [PiB+]) and 19 patients with AD (age,  $63.1 \pm 10.3$  y; 12 women, 7 men; all of whom were PiB+). Participants underwent 2  $^{18}\text{F}$ -flortaucipir PET and MR scans over a period of 1–3 y. Over the duration of the study voxelwise  $^{18}\text{F}$ -flortaucipir change in the group with AD showed the greatest increases in the lateral and medial frontal lobes. Atrophy during this time period was more widespread and included posteromedial cortical areas where tau accumulation rates were lower. In the older adult group  $^{18}\text{F}$ -flortaucipir binding increased in the bilateral temporal lobe and retrosplenial cortex, accompanied by atrophy in the same regions. No associations were identified between voxelwise change in  $^{18}\text{F}$ -flortaucipir and sex, PiB status, or apolipoprotein E. Regional  $^{18}\text{F}$ -flortaucipir uptake significantly increased at follow-up in both older adults and patients with AD, but additional analyses indicated greater  $^{18}\text{F}$ -flortaucipir increases in AD and no differences within older adults based on PiB status. The authors concluded that these findings indicate that “tau accumulates even in amyloid-negative healthy older adults” and that “this process can be measured with in vivo tau PET” and that “tau accumulation and atrophy share similar brain topographies in older adults, whereas tau increases more rapidly in AD and in frontal regions not yet undergoing significant atrophy.”

*Annals of Neurology*

#### **$^{99\text{m}}\text{Tc}$ -HDP SPECT $\text{SUV}_{\text{max}}$ in Accessory Navicular Bone**

Bae et al. from the Seoul National University Bundang Hospital and Seoul National University/Seoul National University College of Medicine (all in South Korea) reported in the January issue of *Medicine (Baltimore)* (2019;98:e14022) on a study designed

to provide quantitative assessment of  $^{99m}\text{Tc}$ -hydroxymethylene diphosphonate ( $^{99m}\text{Tc}$ -HDP) as a biomarker in accessory navicular bone (ANB). The retrospective study included 105 patients (median age, 32.0 y, range, 11–81 y; 61 female, 44 male). These included 31 controls without and 74 patients with ANB (7 unilateral and 67 bilateral). The researchers measured  $\text{SUV}_{\text{max}}$  in quantitative bone  $^{99m}\text{Tc}$ -HDP SPECT/CT studies of the foot. ANBs were classified into types I, II, III (Geist classification), and 0 (contralateral navicular or unilateral ANB). Type II ANBs were further subclassified into II-1 (with bony abnormality) or II-0 (without bony abnormality). All patients were assigned to observation, conservative treatment, or surgery. On  $^{99m}\text{Tc}$ -HDP SPECT/CT patients with type II-1 ANB had the highest  $\text{SUV}_{\text{max}}$ . Across all patients,  $\text{SUV}_{\text{max}}$  in symptomatic ANB was greater than that for asymptomatic ANB. The  $\text{SUV}_{\text{max}}$  for the surgically resected ANB group was also significantly higher than that for the observation-only or conservative treatment groups. Subtype II-1 had a significantly higher  $\text{SUV}_{\text{max}}$  than subtype II-0. Additional analyses in type II ANB showed that young age and higher  $\text{SUV}_{\text{max}}$  were significant predictors for proceeding to surgery. An  $\text{SUV}_{\text{max}}$  cutoff of 5.27 was found to be optimal for predicting final surgical treatment. The authors concluded that because “ $\text{SUV}_{\text{max}}$  derived from quantitative bone SPECT/CT was strongly associated with symptom, surgical treatment, and a known high-risk type of ANB,” that “risk stratification for final surgical treatment of ANB can be achieved using the  $\text{SUV}_{\text{max}}$  from quantitative bone SPECT/CT.”

*Medicine (Baltimore)*

### Whole-Body PET/CT After Sinonasal Cancer Therapy

In an article e-published on January 2 ahead of print in the *European Archives of Oto-Rhino-Laryngology*, Ozturk et al. from the University of Minnesota Medical Center (Minneapolis) reported on a study of whole-body  $^{18}\text{F}$ -FDG PET/CT for posttreatment surveillance of local tumor recurrence, regional lymph node metastasis, and distant metastasis in patients previously treated for sinonasal malignancies. The retrospective study included data from 80 patients (53 men, 27 women; mean age, 60 y, range, 28–92 y) who had undergone a total of 197 posttreatment whole-body  $^{18}\text{F}$ -FDG PET/CT scans. The researchers categorized the imaging findings as positive or negative separately for local tumor recurrence, regional lymph node metastasis, and distant metastasis and compared imaging results with final diagnoses from histologic data or clinical follow-up over a minimum of 12 mo. PET/CT identified 37 of 44 local recurrences, 21 of 23 regional lymph node metastases, and 30 of 37 distant metastases. The sensitivity, specificity, and positive and negative predictive values for local recurrence were 84%, 95%, 84%, and 95%, respectively. For regional lymph node metastases, the corresponding values were 91%, 99%, 91%, and 99%. For distant metastases, the corresponding values were 81%, 99%, 97%, and 96%. Whole-body  $^{18}\text{F}$ -FDG PET/CT was found to have affected changes in management for 85% of patients with recurrences. The authors concluded that “whole-body  $^{18}\text{F}$ -FDG PET/CT is a suitable surveillance tool for sinonasal malignancies in detecting locoregional and distant recurrences in asymptomatic patients without any evidence of recurrence on regular

follow-up and endoscopy during the posttreatment period.”

*European Archives of Oto-Rhino-Laryngology*

### 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 December and January. In an article in the December 5 issue of *The Journal of the Endocrine Society* (2018;3[1]:222–234) Martin et al. from the Universidad Nacional de Córdoba and the Consejo Nacional de Investigaciones Científicas y Técnicas (both in Córdoba, Argentina) provided insights into “Implications of  $\text{Na}^+/\text{I}^-$  symporter transport to the plasma membrane for thyroid hormonogenesis and radioiodide therapy.” Sgouros, from the Johns Hopkins University School of Medicine (Baltimore, MD), reviewed recent developments in “Radiopharmaceutical therapy” in the February issue of *Health Physics* (2019;116:175–178). In an overview e-published on January 11 ahead of print in *Molecular Psychiatry*, Leuzy et al. from the Karolinska Institutet, Stockholm University, and Karolinska University Hospital, all in Stockholm, Sweden, wrote about “Tau PET imaging in neurodegenerative tauopathies—still a challenge.” Reddy et al. from Texas A&M University/University Health Science Center (College Station/Bryan, TX) described “Neuroimaging biomarkers of experimental epileptogenesis and refractory epilepsy” in the January 8 issue of the *International Journal of Molecular Science* (2019;20[1]).