

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.

¹⁸F-Fluorocholine PET/CT and Parathyroid Imaging

Jacquet-Francillon et al. from the Saint-Étienne University Hospital/University of Saint-Étienne, Hospices Civils de Lyon, Université Jean Monnet (Saint-Étienne), and the Université de Lyon (Saint-Étienne; all in France) reported in the August 2 issue of *Frontiers in Medicine (Lausanne)* (2022;9:956580) on a study evaluating the performance of quantitative criteria in ¹⁸F-fluorocholine PET/CT for localization of hyperfunctioning parathyroid glands, as well as correlations between detection rates of ¹⁸F-fluorocholine PET/CT and serum parathyroid hormone levels. The retrospective study included 120 patients (135 lesions) with biologic hyperparathyroidism who had undergone imaging with ¹⁸F-fluorocholine PET/CT. Images were assessed first with visual analysis and then with a blinded reading of standardized measurements of SUV_{max} and liver, thyroid, and size ratios. Results were compared with histology, with a special emphasis on differentiation between adenomas and hyperplasias. The researchers found that areas under the receiver operating characteristic curve representing SUV_{max} and liver ratio were significantly increased in the study group; optimal cutoff values for these variables were >4.12 and >27.4, respectively.

Beyond threshold values of SUV_{max} >4.12 and/or liver ratio >38.1, all lesions were confirmed to be adenomas on histology. ¹⁸F-fluorocholine PET/CT was correlated with serum parathyroid hormone levels. The authors concluded that semi-quantitative measurements (specifically, SUV_{max} and liver ratio) should be considered as additional tools in interpretation of ¹⁸F-fluorocholine PET/CT. Although these quantitative parameters have lower overall performance than visual analysis, they have higher specificity in identifying adenomas, so that above certain PET/CT threshold values, all lesions are adenomas. PET/CT in this setting is also useful for detection of hyperfunctional parathyroids.

Frontiers in Medicine (Lausanne)

Discordant Understanding of the Freeform PET/CT Report in Head and Neck SCC

In an article published on August 18 ahead of print in *JAMA Otolaryngology: Head and Neck Surgery*, Patel et al. from the Wake Forest School of Medicine (Winston-Salem, NC) reported on a study focusing on clinicians' perceptions of PET/CT freeform reports and the incidence of discordance between clinician understanding and the intention of the nuclear medicine physicians generating the reports. The retrospective study included 171 patients (45 women, 126 men; median age, 61 y, range, 54–65 y) with head and neck squamous cell carcinoma (HNSCC; 149 with stage III–IV disease) in routine oncologic management who underwent ¹⁸F-FDG PET/CT for assessment of response to radiation treatment with or without concurrent chemotherapy. Four clinicians independently reviewed the freeform PET/CT reports and assigned perceived modified Deauville scores (MDS). These results were then compared with the criterion standard nuclear medicine MDSs derived from image review. Clinical outcomes assessed included locoregional control, progression-free survival, and overall survival. The researchers found that although reliability/agreement between oncology clinicians was moderate

(κ = 0.68), consensus was minimal (κ = 0.36) between clinicians and nuclear medicine physicians. Exact agreement between clinician consensus and nuclear medicine physicians was 64%. The authors concluded that “the results of this cohort study suggest that considerable variation in perceived meaning exists among oncology clinicians reading freeform HNSCC postradiation therapy PET/CT reports, with only minimal agreement between MDS derived from clinician perception and nuclear medicine image interpretation.” These data suggest that nuclear medicine use of “a standardized reporting system, such as MDS, may improve clinician–nuclear medicine communication and increase the value of HNSCC postradiation treatment PET/CT reports.”

JAMA Otolaryngology: Head and Neck Surgery

Improving Transthoracic Lung Mass Biopsy with Intraoperative CT and Prior PET/CT Fusion

Lin et al. from the China-Japan Friendship Hospital (Beijing, China) and the Hospital Seberang Jaya (Penang, Malaysia) reported on August 13 in *BMC Pulmonary Medicine* (2022;22[1]:311) on a study evaluating the utility of intraoperative CT and prior PET/CT fusion imaging in improving the diagnostic yield of CT-guided transthoracic core-needle biopsy in lung masses. The study included 145 individuals with lung masses suspicious for malignancy scheduled to undergo image-guided transthoracic core-needle biopsy. Seventy-six patients had undergone PET/CT imaging ≤14 d before biopsy, and their imaging data were integrated with intraoperative CT images. The resulting fused images were used to plan puncture sites. The remaining 69 patients underwent routine CT-guided biopsy procedures. Clinical characteristics, diagnostic yield of the biopsies, diagnostic accuracy, procedure-related complications, and procedure duration were compared between the 2 patient groups. Final clinical diagnosis

was determined by histopathology and/or at ≥ 6 -mo follow-up. The overall diagnostic yield and accuracy rate were 80.3% and 82.9%, respectively, for the fusion imaging group, with corresponding percentages of 70.7% and 75.4% for the group under routine procedures. The diagnostic yield for malignancy in the fusion imaging group was higher than that in the routine group (98.1% and 81.3%, respectively). No serious procedure-related adverse events were noted in either of the groups. The authors concluded that “core-needle biopsy with prior PET/CT fusion imaging is particularly helpful in improving diagnostic yield and accurate rate of biopsy in lung masses, especially in heterogeneous ones, thus providing greater potential benefit for patients.”

BMC Pulmonary Medicine

Fibroblast-Activation Protein Expression in Interstitial Lung Disease

In an article published on August 19 ahead of print in the *American Journal of Respiratory and Critical Care Medicine*, Yang et al. from the State Key Laboratory of Respiratory Disease (Guangzhou), the First Affiliated Hospital of Guangzhou Medical University, Southern Medical University (Guangzhou), Wuxi People's Hospital of Nanjing Medical University, General Hospital of Southern Theatre Command of PLA (Guangzhou), and the Shenzhen International Institute for Biomedical Research (all in China) reported on a study investigating whether the expression intensity of fibroblast-activation protein (FAP), a recognized surface biomarker of activated fibroblasts, can be used to estimate/measure the amounts of activated fibroblasts in interstitial lung disease (ILD). The researchers detailed multiple in vitro studies characterizing FAP expression in human primary lung fibroblasts and clinical lung specimens, including qPCR, Western blot, immunofluorescence staining, deep-learning measurement of whole-slide immunohistochemistry, and single-cell sequencing. They also analyzed FAP-targeted PET/CT imaging in patients with various ILDs

to determine correlations between FAP tracer uptake and pulmonary function parameters. They found that FAP expression was significantly upregulated in the early phase of lung fibroblast activation in response to a low dose of profibrotic cytokine. Single-cell sequencing data indicated that almost all FAP-positive cells in ILD lungs were collagen-producing fibroblasts. Immunohistochemistry confirmed that FAP expression levels were closely correlated with fibroblastic foci on human lung biopsy sections from patients with ILDs. The total SUV for the FAP-inhibitor PET tracer was significantly related to lung function decline in these patients. The authors concluded that these results “strongly support that in vitro and in vivo detection of FAP can assess the profibrotic activity of ILDs, which may aid in early diagnosis and selection of an appropriate therapeutic window.”

American Journal of Respiratory and Critical Care Medicine

Preoperative PET/CT in Advanced Serous Ovarian Cancer

Wang et al. from the First Affiliated Hospital of Chongqing Medical University, the People's Hospital of Yubei District of Chongqing City, and Chongqing General Hospital/University of Chinese Academy of Sciences (all in China) reported on August 18 ahead of print in *Acta Obstetrica et Gynecologica Scandinavica* on a study analyzing and comparing the predictive values of preoperative PET/CT score, CT score, metabolic parameters, tumor markers, and hematologic markers for incomplete resection after debulking surgery for advanced serous ovarian cancer. The retrospective study included data from 62 such patients who had undergone ^{18}F -FDG PET/CT imaging before primary or secondary debulking surgery. Variables assessed included PET/CT and CT predictive scores (based on the Suidan model), SUV_{max} , metabolic tumor volume, human epididymis protein 4, cancer antigen 125, lymphocyte-to-monocyte ratio, platelet-to-lymphocyte ratio, and neutrophil-to-lymphocyte ratio. Preoperative PET/CT was found to have the

highest predictive value for incomplete resection in the primary debulking surgery group (sensitivity, 65.0%; specificity, 88.9%). In the secondary debulking surgery group, preoperative PET/CT and CT scores were the same but remained higher than the other tumor and hematologic variables (sensitivity, 80.0%; specificity, 94.7%). A preoperative PET/CT score ≥ 3 predicted a high risk of incomplete resection after primary debulking, and a preoperative PET/CT score ≥ 2 was highly predictive of incomplete resection after secondary debulking. The authors concluded that “the preoperative PET/CT score may be a feasible and quantitative model for predicting incomplete resection after debulking surgery for advanced serous ovarian cancer.”

Acta Obstetrica et Gynecologica Scandinavica

Multiparametric Model for PET in Thymic Lesion Diagnosis

In an article published on August 16 in *BMC Cancer* (2022;22[1]:895), Wang et al. from the Beijing Friendship Hospital/Capital Medical University and the First Medical Center/Chinese PLA General Hospital (both in Beijing, China) reported on a study investigating the diagnostic performance of multiparametric ^{18}F -FDG PET combined with clinical characteristics in differentiating thymic epithelial tumors from thymic lymphomas. The study included 173 patients (80 with thymic epithelial tumors and 93 with thymic lymphomas) who underwent ^{18}F -FDG PET/CT before treatment. PET/CT parameters included in the evaluation were lesion size, SUV_{max} , SUV_{mean} , total lesion glycolysis, metabolic tumor volume, and tumor-to-normal liver SUV ratio. Clinical data were also included in assessing differential diagnostic and comparative efficacy. Age, clinical symptoms, and PET metabolic parameters were found to differ significantly between patients with thymic epithelial tumors and those with thymic lymphomas. The calculated SUV ratio showed the highest individual differentiating diagnostic value (sensitivity, 76.3%; specificity, 88.8%). A combined model of age, clinical symptoms,

and SUV ratio resulted in the highest differentiating diagnostic value (sensitivity, 88.2%; specificity, 96.3%). The clinical efficacy of the model was confirmed by further analysis. The authors concluded that this “multiparameter diagnosis model based on ^{18}F -FDG PET and clinical characteristics had excellent value in the differential diagnosis of thymic epithelial tumors and thymic lymphomas.” They added that use of this model has the potential to avoid unnecessary treatment and surgery.

BMC Cancer

Tau Distribution in Early-Onset AD

Frontzkowski et al. from University Hospital/LMU Munich (Germany), the German Center for Neurodegenerative Diseases (DZNE) (Munich, Germany), the Munich Cluster for Systems Neurology (SyNergy) (Germany), Lund University (Sweden), the Vrije Universiteit Amsterdam/Amsterdam UMC (The Netherlands), and Skåne University (Lund, Sweden) reported on August 20 in *Nature Communications* (2022;13[1]: 4899) on a study combining resting-state functional MR and longitudinal ^{18}F -flortaucipir PET imaging to investigate tau distribution and accumulation in individuals with early-onset AD. The study drew data from almost 300 participants in 2 independent clinical trials, each cohort including patients with biomarker-confirmed and symptomatic Alzheimer disease (AD), cognitively normal but amyloid-positive individuals, and cognitively normal controls with no AD-associated pathologies. High-resolution resting-state functional MR imaging data from 1,000 healthy participants was used to map the topology of globally connected “hubs” across the brain. ^{18}F -flortaucipir PET patterns in AD patients and others in the study were mapped to the topology of these globally connected hubs to determine the degree to which individual tau patterns are expressed in globally connected hub regions in the frontoparietal association cortex compared to weakly connected nonhub regions. Detailed

imaging analyses indicated: (1) that individual tau deposition patterns on PET are stronger in globally connected hub regions in younger patients with symptomatic AD and that these patterns are associated with earlier symptom onset; (2) that this hub-like pattern of tau deposition at baseline PET is associated with subsequent accelerated tau accumulation on annual assessment; and (3) that this hub-like pattern contributes to the acceleration of cognitive decline. The authors concluded that “this suggests that earlier symptom manifestation is not driven by specific pathophysiological characteristics but rather by a tau distribution pattern that preferentially targets brain hubs important for cognitive function.” They added that “knowledge about drivers of tau onset, heterogeneous tau spreading patterns, and clinical trajectories may become important to facilitate precision medicine prediction of cognitive and pathological progression, as well as for patient stratification in clinical trials.”

Nature Communications

Articular ^{18}F -FDG Uptake in RA

In an article published online ahead of print in the *Journal of Rheumatology*, Ferraz-Amaro et al. from the Hospital Universitario de Canarias (Tenerife, Spain), Kettering Health (Dayton, OH), and Columbia University College of Physicians and Surgeons (New York, NY) reported on a study using ^{18}F -FDG PET/CT to quantify joint inflammation in rheumatoid arthritis (RA) and explore correlations between PET-derived uptake parameters and RA disease activity measures. The authors studied 34 patients with RA who were part of the Rheumatoid Arthritis Study of the Myocardium. Associations between disease activity scores and articular ^{18}F -FDG SUVs were calculated. Weighted joint volume SUVs representing 25%, 50%, 75% and maximal (100%) uptake were calculated as global parameters of the total volume of joint inflammation in each patient. The 25%, 50%, and 75% weight joint volume

SUVs were found to be significantly correlated with the number of swollen joints. No associations were found between articular FDG uptake and nonarticular RA-related variables, such as disease duration, seropositivity, or RA treatments. The authors concluded that although articular FDG uptake was significantly correlated with the number of swollen joints in RA, it was not associated with biochemical measures of inflammation and disease activity.

Journal of Rheumatology

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 August. Sparano et al. from the University of Florence (Italy) and the Institut Gustave Roussy/Université Paris-Saclay (Villejuif, France) provided an overview of “Strategies for radioiodine treatment: What’s new?” in the August 4 issue of *Cancers (Basel)* (2022;14[15]: 3800). In the August 3 issue of the *Journal of Clinical Medicine* (2022;11[15]: 4514), Dondi et al. from the ASST Spedali Civili di Brescia (Italy), the Università degli Studi di Brescia (Italy), Ente Ospedaliero Cantonale (Bellinzona, Switzerland), Lausanne University Hospital/University of Lausanne (Switzerland), and the Università della Svizzera Italiana (Lugano, Switzerland) surveyed the “Emerging role of FAPI PET imaging for the assessment of benign bone and joint disease.” Albano and experts from the same universities reported in the August 5 issue of *Cancers (Basel)* (2022; 14[15]:3814) on “The role of [^{68}Ga]Gantaxin PET/CT or PET/MRI in lymphoma: A systematic review.” In the same issue of *Cancers (Basel)* (2022;14[15]: 3768), Rasul and Haug from the Medical University of Vienna (Austria) summarized “Clinical applications of PSMA PET examination in patients with prostate cancer.”