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.

Early PET/CT in Head and Neck SCC with Erlotinib Tx

Porosnicu et al. from Atrium Health Wake Forest Baptist Medical Center/Wake Forest School of Medicine (Winston-Salem, NC) reported in the August 30 issue of *Frontiers in Oncology* (2022; 12:939118) on a study investigating targeted improvement in the relatively low documented treatment response to erlotinib in metastatic/recurrent head and neck squamous cell cancer (HSNCC) by patient smoking status–based erlotinib dose optimization and through early-in-treatment ^{18}F-FDG PET assessment to distinguish responders from nonresponders. The study included 19 patients (10 smokers, 9 nonsmokers) with operable HNSCC who received neoadjuvant erlotinib with doses determined by smoking status (150 and 300 mg for nonsmokers and active smokers, respectively). Patients underwent PET/CT before treatment, at 4–7 d of treatment, and before surgery. Response was defined by lesion measurement on diagnostic CT as a decrease in maximum tumor diameter of ≥20% (responders), 10%–19% (minimum responders), and <10% (nonresponders). Tumor response and assessed plasma erlotinib levels were similar between the treatment groups. Changes quantified on early and posttreatment PET/CT compared to pretreatment PET/CT were significantly correlated with response on posttreatment CT. The authors concluded that this pilot study suggested "that early-in-treatment PET/CT can predict response to erlotinib, and treatment with erlotinib dose adjusted according to smoking status is well-tolerated and may improve treatment response in HNSCC." They added that the study highlights the opportunity for improved patient selection for more individualized erlotinib treatment and cited this as an area for more study, particularly to support U.S. Food and Drug Administration decision-making in the use of erlotinib in HNSCC.

Frontiers in Oncology

^{11}C-Trimethoprim PET and Drug-Resistant Bacterial Infection

In an article published on September 15 in the *Journal of Clinical Investigation* (2022;132[18]:e156679), Lee et al. from the University of Pennsylvania/Hospital of the University of Pennsylvania (Philadelphia) and Children's Hospital of Philadelphia (PA) reported on a study exploring the question of whether antimicrobial resistance reduces specific accumulation of antibiotic-based PET tracers within bacteria, affecting the diagnostic utility of these promising imaging approaches in infection. The authors described a series of preclinical investigations, from in vitro studies to genomic surveys, and a first-in-human application with ^{11}C-labeled trimethoprim (^{11}C-TMP). Robust ^{11}C-TMP uptake was seen in both TMP-sensitive and -resistant bacteria. Genome database analyses indicated that most clinically relevant bacteria can be targeted with ^{11}C-TMP. A clinical protocol to assess the biodistribution of ^{11}C-TMP in humans included patients with a range of infectious lesions. ^{11}C-TMP PET showed focal radiotracer uptake in areas of infection. The authors concluded that these results highlight an approach to imaging bacterial infection in patients that "could affect our understanding of bacterial pathogenesis as well as our ability to better diagnose infections and monitor response to therapy."

Journal of Clinical Investigation

Cardiac, Vascular, and Pulmonary Pathobiology in Acute COVID-19

Alam et al. from Manchester University (UK), North Bristol Trust (UK), London School of Hygiene and Tropical Medicine (UK), Aga Khan University (Nairobi, Kenya), University of Bristol (UK), University of Washington (Seattle), University of Edinburgh (UK), and Emory University (Atlanta, GA) reported on September 14 ahead of print in the *Journal of the American Heart Association* on a study using multimodality imaging and biochemical sampling to characterize the pathobiology of acute COVID-19. The study included 33 patients (31 men, 2 women; median age, 51 y) testing positive for COVID 19, of whom 24 (73%) had respiratory symptoms and the rest had nonspecific viral symptoms. Patients underwent CT coronary angiography, cardiac ^{18}F-FDG PET/CT, and cardiac MR imaging, as well as biomarker sampling. On cardiac MR imaging, 9 patients had myocarditis; of these patients, 5 were found to have myocardial inflammatory cell infiltration. Two patients had elevated troponin levels, and, in general, cardiac troponin concentrations were not significantly higher in patients with or without myocarditis or myocardial cell infiltration. None of the patients were found to have obstructive coronary artery disease or vasculitis. Pulmonary inflammation and consolidation were 17% and 11%, respectively, and were not associated with the presence of myocarditis. The authors summarized that although myocarditis was present in a third of these patients with acute COVID-19 and the majority had inflammatory cell infiltration, pneumonitis inflammation was not directly associated with myocarditis. They concluded that "the mechanism of cardiac pathology is nonischemic

and not attributable to a vasculitic process" in COVID-19.

Journal of the American Heart Association

FAP-Specific Signaling in Adenoid Cystic Carcinoma Diagnosis

In an article published on August 31 in *Cancers (Basel)* (2022;14[17]:4253), Liew et al. from University Hospital Heidelberg/German Cancer Research Center (DKFZ), University Hospital Düsseldorf/German Center for Lung Research (DZL) (Heidelberg), and University Hospital Bonn (all in Germany) reported on an analysis characterizing the significance of ^{68}Ga-fibroblast-activation protein inhibitor (^{68}Ga-FAPI) uptake in adenoid cystic carcinomas by correlating ^{68}Ga-FAPI PET at serial time points with corresponding MR imaging assessments. The retrospective analysis included clinical PET/CT images acquired at 10, 60, and 180 min after injection in 12 patients with adenoid cystic carcinoma as well as corresponding T1- and T2-weighted MR imaging. PET/CT and MR images were coregistered and correlated for analysis. The ^{68}Ga-FAPI PET signals showed a very weak positive correlation with T1-weighted MR values and a weak negative correlation with T2-weighted values. The authors concluded that minimal correlation between the intensity of ^{68}Ga-FAPI PET signals and tumor appearance on MR scans "underlines that ^{68}Ga-FAPI PET signaling is not a surrogate marker of MRI sequences but an independent signal."

Cancers (Basel)

Ultra-Low-Dose Brain ^{18}F-FDG PET/MR Imaging

Soret et al. from the Hôpital Pitié-Salpêtrière (Paris), Sorbonne Université, CNRS, INSERM (Paris), and the Centre d'Acquisition et Traitement des Images (Saclay; all in France) reported on September 12 in *Scientific Reports* on a study simulating an ^{18}F-FDG PET/MR brain imaging ultra-low-dose protocol (0.2 MBq/Kg) and compared it to a reference protocol (2 MBq/Kg; from the group's previously published work) in 50 patients with cognitive impairment. They tested reproducibility between the 2 protocols' SUV ratio measurements and assessed the effect of the ultra-low-dose protocol on between-group comparisons and visual analyses by physicians. Agreement between visual assessments of PET with the 2 protocols in patients with severe anomalies was substantial to almost perfect. This agreement was only moderate in patients with normal metabolism or moderate hypometabolism. SUV ratios were strongly reproducible, and between-group comparisons were similar with the 2 protocols. The authors concluded that "these results suggest that a low-dose protocol (1 MBq/Kg) should be preferred in the context of neurodegenerative disease diagnosis."

Scientific Reports

PET/CT in Postop Follow-Up in NSCLC

In an article published on September 6 ahead of print in *Lung Cancer* (2022; 173:14–20), Kaumanns et al. from University Hospital Basel (Switzerland) reported on a study designed to determine the value of whole-body ^{18}F-FDG PET/CT as an optimal surveillance strategy in patients with resected non–small cell lung cancer (NSCLC). The retrospective study included data on 205 patients with resected stage I–III NSCLC and PET/CT surveillance data. All patients had preoperative ^{18}F-FDG PET-positive tumors and underwent additional PET/CT at 6, 12, and 24 mo after surgery and chest CT at 18 mo. Longer-term follow-up (median, 26.3 mo; range, 4.1–60.6 mo) included annual chest CT for patients initially diagnosed with stage I or II or annual PET/CT for stage III. Over the follow-up period, the rates for recurrence and secondary primary lung cancers were 22% and 8%, respectively, with associated symptoms present in 48% (recurrence) and 18% (secondary primary lung cancers) of patients. A total of 83% of recurrences and 65% of secondary primary lung cancers were detected on PET/CT, with 82% of recurrences detected in the first or second follow-up PET/CT scan. A second curative-intention treatment was possible in 37% of patients with recurrence and 100% with secondary primary lung cancers, with a 2-y recurrence-free survival rate after second treatment of 53%. ^{18}F-FDG PET/CT findings were positive in nonmalignant lesions (71% of these were possible infections) in 25% of patients. The authors concluded that additional studies are needed to identify patients who might "benefit from an even more intensive surveillance strategy."

Lung Cancer

^{11}C-MET and ^{18}F-FDG PET/CT in Multiple Myeloma

In an article published in the August 31 issue of the *International Journal of Molecular Sciences* (2022;23[17]:9895), Morales-Lozano et al. from the Clinica Universidad de Navarra and the Instituto de Investigación Sanitaria de Navarra (both in Pamplona, Spain) reported on the results of a study comparing the diagnostic accuracy and prognostic value of ^{18}F-FDG and ^{11}C-methionine (^{11}C-MET) PET in patients with multiple myeloma. The study included 52 such patients (median age, 61 y; range, 37–83 y; 28 men, 24 women; 8 smoldering, 18 newly diagnosed, and 26 relapsed), who underwent PET/CT with each of the tracers. Six patients negative for uptake on ^{18}F-FDG PET/CT were positive on ^{11}C-MET PET/CT. ^{11}C-MET PET/CT also identified a higher number of focal lesions in more than half of patients. Analysis of prognostic comparisons of the 2 tracers focused on the 26 relapsed participants. For ^{18}F-FDG, identification of >3 focal lesions and total metabolic tumor volume p50 or p75 were associated with adverse prognosis. For ^{11}C-MET, total metabolic tumor volume p50 or p75 and total lesion MET uptake p50 or p75 were associated with lower progression-free survival. The authors concluded that this study "confirmed the diagnostic and prognostic value of FDG in multiple myeloma" and also highlighted the higher sensitivity of ^{11}C-MET PET/CT

for detection of myeloma lesions, including focal lesions.

International Journal of Molecular Sciences

PET and Neoadjuvant Therapy Response in Pancreatic Adenocarcinoma

Abdelrahman et al. from the Mayo Clinic (Rochester, MN) reported in the September issue of the *Journal of the National Comprehensive Cancer Network* (2022;20[9]:1023–1032) on a retrospective study evaluating the utility of preoperative ^{18}F-FDG PET in predicting response to neoadjuvant therapy and survival in patients with borderline resectable/locally advanced pancreatic ductal adenocarcinoma. Neither anatomic imaging nor available biochemical markers have proven widely useful in this setting. The study included 202 patients who underwent neoadjuvant therapy within 60 d of resection, with pre- and posttherapy PET and biochemical responses assessed. After therapy, 58% of patients had optimization of CA 19-9 levels, with major metabolic responses seen on PET in 51% and pathologic responses in 38%. Median recurrence-free and overall survival times were 21 and 48.7 mo, respectively. Metabolic response on PET was superior to biochemical response in predicting pathologic response and was the only univariate preoperative predictor of overall survival. Metabolic response was the single largest independent preoperative predictor for pathologic response. The authors concluded that in patients with post-neoadjuvant therapy borderline resectable/locally advanced pancreatic ductal adenocarcinoma, ^{18}F-FDG PET is a preoperative metric of therapeutic efficacy, "thereby allowing potential therapeutic alterations and surgical treatment decisions." They suggested that ^{18}F-FDG PET should be an adjunct and recommended modality during the neoadjuvant therapy phase of care for these patients.

Journal of the National Comprehensive Cancer Network

^{99m}Tc-Sestamibi SPECT/CT and Oncocytic Renal Neoplasia

In an article published on September 5 ahead of print in the *Scandinavian Journal of Urology,* Tzortzakakis et al. from the Karolinska Institutet (Solna, Sweden), Karolinska University Hospital (Huddinge, Sweden), University of Birmingham (UK), Cheltenham General Hospital/Gloucestershire Hospitals NHS Foundation Trust (UK), and the Cumming School of Medicine/University of Calgary (Canada) reported on a study designed to determine whether ^{99m}Tc-sestamibi uptake in renal tumor and nontumor renal parenchyma on SPECT can provide information differentiating renal oncocytoma from renal cell carcinoma. The study included 52 patients with a total of 57 renal tumors. All patients underwent ^{99m}Tc-sestamibi SPECT/CT, with visual analysis and SUV_{max} metrics for uptake-based derivation of optimal cutoff values for detecting renal oncocytoma. Uptake was positive in a group of mostly indolent tumors with low malignant potential, including renal oncocytoma, low-grade oncocytic tumors, hybrid oncocytic tumors, and a subset of chromophobe renal cell carcinomas. Semiquantitative evaluation of uptake did not improve SPECT/CT performance in differentiating renal oncocytomas from other lesions. The authors concluded that "the imaging limitations for accurate differentiation of sestamibi-positive renal tumors mirror the recognized diagnostic complexities of the histopathologic evaluation of oncocytic neoplasia" and recommended that patients with sestamibi-positive renal tumors might be better suited for biopsy and follow-up, per current active surveillance protocols.

Scandinavian Journal of Urology

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 September. Kelly et al. from the Clinica Universitaria Colombia (Bogotá), Clinica Reina Sofia (Bogotá, Colombia), Fundacion Universitaria Sanitas (Bogotá, Colombia), and the "Sapienza" University (Rome, Italy) summarized "Sjögren syndrome: New insights in the pathogenesis and role of nuclear medicine" on September 4 in the *Journal of Clinical Medicine* (2022;11[17]:5227). In an article published on September 7 ahead of print in *Future Oncology*, de Vries et al. from University Medical Center Utrecht (The Netherlands) reviewed "Sentinel lymph node detection in thyroid carcinoma using ^{68}Ga-tilmanocept PET/CT: A proof of concept study protocol." Wei et al. from West China Hospital of Sichuan University (Chengdu, China) presented an overview of "Peritoneal carcinomatosis with intraperitoneal immunotherapy: Current treatment options and perspectives" on September 15 ahead of print in *Expert Review of Gastroenterology and Hepatology*.