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.

PET/CT and Kidney Allograft Subclinical Rejection

Hanssen et al. from the University of Liège Hospital (Belgium) and the Necker Hospital/Assistance Publique-Hôpitaux de Paris (France) reported on December 16 ahead of print in the *American Journal of Transplantation* on a study to investigate the potential of ^{18}F-FDG PET/CT as a noninvasive alternative to biopsy in assessing subclinical kidney allograft acute rejection, defined as "the unexpected histological evidence of acute rejection in a stable patient." The study included 92 adult patients who underwent ^{18}F-FDG PET/CT at the time of surveillance biopsy at ~3 mo after transplantation, with the mean SUV ratio (mSUVR) between kidney cortex and psoas muscle calculated. Urinary levels of chemokine (C-X-C motif) ligand 9 (CXCL9) were also quantified. The Banff 2017 classification was used to categorize participants as normal (70), borderline (16), and subclinical rejection (6). No clinical or biologic differences were seen between these groups. The mSUVRs were 1.87 ± 0.55, 1.94 ± 0.35, and 2.41 ± 0.54 in the normal, borderline, and subclinical rejection groups, respectively. mSUVR was significantly higher in the subclinical rejection group than in the normal group. The area under the receiver operating characteristics curve (area under the curve [AUC]) was 0.79, with 83% sensitivity using an mSUVR threshold of 2.4. The AUC of urinary CXCL-9/creatinine ratios reached 0.79. mSUVR positively correlated with tubulointerstitial damage and acute composite Banff scores. The authors concluded that "^{18}F-FDG-PET/CT helps noninvasively exclude subclinical kidney allograft acute rejection, with a negative predictive value of 98%."

American Journal of Transplantation

^{18}F-PSMA-1007 PET/CT in Biochemically Relapsed PCa

In an article e-published on November 28 ahead of print in *Prostate Cancer and Prostatic Diseases*, Witkowska-Patena et al. from the Military Institute of Medicine (Warsaw), the Affidea Mazovian PET/CT Medical Centre (Warsaw), and Synektik Pharma (Kielce, all in Poland) reported on a study prospectively evaluating the diagnostic performance of ^{18}F-PSMA-1007 PET/CT in patients with prostate cancer after radical treatment and low but rising prostate-specific antigen (PSA) levels. The study included 40 patients after radical treatment (32 after radical prostatectomy, 8 after radiation therapy) with low (0.008–≤2.0 ng/mL) and rising PSA levels. Each underwent skull-to-midthigh ^{18}F-PSMA-1007 PET/CT imaging, and results were compared with PSA levels, Gleason scores, and tumor stage. The sensitivity, specificity, and negative and positive predictive values of imaging were assessed at 10.3 (± 4.7)–mo follow-up. ^{18}F-PSMA-1007 PET/CT was positive in 24 (60%) patients. Detection rates were 39%, 55%, and 100% for PSA levels <0.5, 0.5–<1.0, and 1.0–≤2.0 ng/mL, respectively. PET/CT identified metastases in locoregional lymph nodes in 55% of patients, in bones in 36% of patients, and local recurrence in 9% of patients. PET/CT positivity was independent of Gleason score and tumor stage. Follow-up assessment in 40 lesions yielded sensitivity, specificity, and positive and negative predictive values of 100%, 94.4%, 66.7%, and 100%, respectively. The authors summarized their results: "^{18}F-PSMA-1007 PET/CT shows relatively high detection rate in patients with prostate cancer after radical treatment and low, rising PSA levels...." as well as "excellent sensitivity, specificity, and negative predictive values."

Prostate Cancer and Prostatic Diseases

Multinational PET/CT Study of Extrapulmonary TB Presentation

Bomanji et al. from the University College London Hospitals NHS Foundation Trust (UK) and research centers in India, Pakistan, Bangladesh, Austria, South Africa, Serbia, Thailand, and other UK institutions representing the International Atomic Energy Agency Extrapulmonary Tuberculosis Consortium reported on December 12 in the *European Respiratory Journal* on the potential for ^{18}F-FDG PET/CT for localizing sites and extent of disease in extrapulmonary tuberculosis (EPTB). The study included 358 EPTB patients (189 women; 169 men; age range, 18–83 y) from centers in India, Pakistan, Thailand, South Africa, Serbia, and Bangladesh who underwent imaging within 2 wk of presentation to assess extent of disease and common sites of involvement. A total of 118 (33.7%) had a single extrapulmonary site and 232 (66.3%) had more than 1 site (organ) affected. Lymph nodes, bone, pleura, and brain were common sites. A total of 100 (28%) had ^{18}F-FDG PET/CT–positive sites in the lung, and 110 patients were ^{18}F-FDG PET/CT–positive in more body sites than noted clinically at first presentation. The authors concluded that ^{18}F-FDG PET/CT scanning "has potential for further elucidating the spectrum of disease, pathogenesis of EPTB, and monitoring the effects of treatment on active lesions over time, and requires longitudinal cohort studies, twinned with biopsy and molecular studies."

European Respiratory Journal

PD-L1 Inhibitor-Induced Thyroiditis and Survival

In a study e-published on December 6 ahead of print in *Thyroid*, Kotwal et al. from the Mayo Clinic (Rochester, MN) reported on a study investigating the association of programmed cell death protein-ligand 1 (PD-L1) inhibitor-induced thyroiditis with overall survival in patients with cancer. The retrospective study characterized thyroid immune-related adverse events in patients treated with PD-L1 inhibitors and evaluated treatment impact on overall survival. A total of 91 patients' records were included. All had been treated with atezolizumab and avelumab and were followed for a median of 10.1 mo. Thyroid immune-related adverse events included new onset hypothyroidism, thyrotoxicosis, and worsening of preexisting hypothyroidism. Nineteen patients (21%) developed new onset thyroid dysfunction (14 presenting with hypothyroidism, 5 with thyrotoxicosis), of whom 3 progressed to hypothyroidism and 2 returned to euthyroidism. Four patients (4%) had worsening of preexisting hypothyroidism. Thyroid immune-related adverse events occurred after a median of 2 doses (6 wk), and although 48% of these patients required thyroid hormone replacement, none required steroids or discontinuation of immunotherapy. Two of the 4 patients with thyroid peroxidase antibody >9 IU/mL at baseline developed thyroid immune-related adverse events. The median thyroid peroxidase antibody titer was not higher in patients with adverse events but was higher in those with overt (as compared to subclinical) hypothyroidism and those prescribed thyroid hormone replacement. Diffusely increased ^{18}F-FDG thyroid uptake was seen on PET in 71% with thyroid immune-related adverse events compared to 6% without. Of note, patients who developed adverse events had longer overall survival and lower mortality after adjusting for potential confounders. The authors summarized their findings that, in most cases, management of thyroid immune-related adverse events in PD-L1 treatment can be managed supportively, without steroids or discontinuation of immunotherapy. Diffuse ^{18}F-FDG thyroid uptake on PET may predict the occurrence of thyroiditis, and thyroid peroxidase antibodies may help to assess its severity. They concluded that "thyroiditis may be a biomarker for antitumor immune response, highlighting the need to further characterize its underlying mechanism."

Thyroid

PET/CT and Postoperative Surveillance in Malignant Pleural Mesothelioma

Kitajima et al from the Hyogo College of Medicine (Japan) reported in the November 26 issue of *Oncotarget* (2019; 10[63]:6816–6828) on a study of the clinical utility of ^{18}F-FDG PET/CT for postsurgical surveillance in malignant pleural mesothelioma and the comparable utility of contrast-enhanced CT, including their respective impacts on clinical management. The study included 50 patients who had undergone radical surgery for malignant pleural mesothelioma, with lesion status determined on the basis of histopathology, radiologic imaging, and clinical follow-up for >6 mo. All had undergone ^{18}F-FDG PET/CT and contrast-enhanced CT, for which the respective sensitivities were 90.8% and 75.0%, specificities were 80.0% and 90.0%, and accuracies were 88.0% and 78.0%. The areas under the curve (AUC) (0.915 and 0.805, respectively) and sensitivity were significantly different between PET/CT and contrast-enhanced CT. Patient-based AUC values for diagnosis of locoregional recurrence (ipsilateral hemithoracic) and distant metastases (peritoneal dissemination and lung, bone, muscle, and liver metastases) were also significantly different. ^{18}F-FDG PET/CT findings resulted in management changes for 14 patients (28%). Contrast-enhanced CT did not identify a recurrence in 6 patients who were found to have recurrence on PET/CT. Management was changed in 4 of these patients. The authors concluded that "^{18}F-FDG PET CT findings were shown to be more accurate for assessing malignant pleural mesothelioma recurrence and more often led to therapy change than contrast-enhanced CT."

Oncotarget

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 late November and December. Langen et al. from the Forschungszentrum Jülich (Germany), the University of Aachen (Germany), the Jülich–Aachen Research Alliance (Germany), Maastricht University Medical Center (The Netherlands), and the University of Cologne/University Hospital of Cologne (Germany) summarized the "Advantages and limitations of amino acid PET for tracking therapy response in glioma patients," e-published on December 12 ahead of print in *Expert Review of Neurotherapeutics*. In an article published on December 15 ahead of print in *Expert Review of Anticancer Therapy*, Galldiks et al. from the University of Cologne/University Hospital of Cologne, the Research Center Jülich, and University Hospital RWTH Aachen (all in Germany) reviewed "Molecular imaging and advanced MRI findings following immunotherapy in patients with brain tumors." Signore et al. from the Sapienza University of Rome (Italy), the University of Brescia/Spedali Civili of Brescia (Italy), and the Imaging Institute of Southern Switzerland (Lugano)/Ente Ospedaliero Cantonale (Bellinzona, Italy) presented "Evidence-based data about prevalence and risk of malignancy of thyroid incidentalomas detected by different PET radiopharmaceuticals" on December 11 ahead of print in *Current Radiopharmaceuticals.* In an article in the November 28 issue of the *International Journal of Molecular Sciences* (2019;20(23):E5984), Ruiz-Bedoya et al. from the Johns Hopkins University School of Medicine (Baltimore, MD) and the Johns Hopkins All Children's Hospital (St. Petersburg, FL) reviewed new research in "Molecular imaging of diabetic foot infections: New tools for old questions."