

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.

⁶⁸Ga-PSMA-11 PET, PCa Recurrence, and Salvage Radiotherapy

Boreta et al. from the University of California San Francisco and the San Francisco Veterans Affairs Medical Center (CA) reported on March 27 ahead of print in *Urology* on a study using ⁶⁸Ga-prostate-specific membrane antigen (⁶⁸Ga-PSMA)-11 PET imaging to visualize locations of prostate cancer recurrence after radical prostatectomy in men with prostate-specific antigen (PSA) levels <2 ng/mL and to assess the coverage of standard radiation treatment fields in such recurrences. The retrospective study included 125 patients imaged for biochemical recurrence after radical prostatectomy with a median PSA at imaging of 0.40 ng/mL. PET showed PSMA-avid disease in 66 (53%) men. Twenty-five (38%) of these patients were found to have PSMA-avid disease outside of the pelvis, 33 (50%) had tracer uptake confined to the pelvic lymph nodes and prostate bed, and 8 (12%) had PSMA-avid recurrence only in the prostate bed. In a comparison of these locations with standard radiation therapy fields, salvage radiation (including standard intensity-modulated radiation therapy) pelvic nodal volumes would not have covered PSMA-avid nodal disease in 38 (30%)

patients. Higher PSA levels at the time of imaging were statistically associated with having PSMA-avid disease outside of standard nodal fields. The authors concluded that not only does ⁶⁸Ga-PSMA-11 PET imaging detect disease in a majority of patients after radical prostatectomy with PSA levels <2 ng/mL, but nearly a third of the patients in this study had PSMA-avid disease that would not be covered by standard radiation fields. They added that “this imaging modality may dramatically impact the design and use of post-radical prostatectomy salvage radiotherapy.”

Urology

In Vivo PET and CTE

In an article e-published on April 10 ahead of print in the *New England Journal of Medicine* and covered extensively in the media, Stern et al. from the Boston University School of Medicine (MA), the Boston University School of Public Health (MA), Brigham and Women’s Hospital (Boston, MA), Harvard Medical School (Boston, MA), the Veterans Affairs Boston Healthcare System (MA), the Mayo Clinic Arizona (Scottsdale), Banner Alzheimer’s Institute (Phoenix, AZ), Arizona State University (Tempe), and Avid Radiopharmaceuticals (Philadelphia, PA) reported on a study using ¹⁸F-flortaucipir (¹⁸F-AV-1451) and ¹⁸F-florbetapir for in vivo detection of patterns of tau and amyloid- β deposition, respectively, in individuals at risk for chronic traumatic encephalopathy (CTE). The study included 26 former National Football League (NFL) players (ages, 40–69 y) with cognitive and neuropsychiatric symptoms and 31 asymptomatic controls. Regional tau SUV ratios (SUVRs) in the 2 groups were compared, and the relationship between SUVRs and symptom severity and years of football play in the former players was analyzed. The researchers found that the mean flortaucipir SUVR was higher among former players than controls in the bilateral superior frontal, bilateral medial temporal, and left parietal regions. Correlation coefficients in these 3 regions between

SUVRs and years of play were 0.58, 0.45, and 0.50, respectively. No association was identified between tau deposition and scores on cognitive and neuropsychiatric tests. A single former player showed levels of amyloid- β deposition similar to those in individuals with Alzheimer disease. The authors concluded that these innovative in vivo studies showed that this group of NFL players with cognitive and neuropsychiatric symptoms had higher PET-assessed tau levels in brain regions affected by CTE but did not show elevated amyloid- β levels. They noted that additional studies are needed to determine whether elevated CTE-associated tau can be routinely detected. This method for assessing tau deposition in living brains opens the door for potential early (as opposed to post-mortem) identification of degeneration associated with traumatic brain injury.

New England Journal of Medicine

Somatostatin Receptor PET/CT in Metastatic NETs

De Dosso et al. from the Oncology Institute of Southern Switzerland, the Imaging Institute of Southern Switzerland, and the Ente Ospedaliero Cantonale (all in Bellinzona, Switzerland), Lausanne University Hospital/University of Lausanne (Switzerland), Ente Ospedaliero Cantonale (Lugano, Switzerland), Johns Hopkins University School of Medicine (Baltimore, MD), and Medical University Innsbruck (Austria) reported on April 19 ahead of print in *Endocrine* on a metaanalysis of reports on somatostatin receptor-targeted PET/CT in patients with metastatic neuroendocrine tumors and unknown primary tumors. The authors conducted a comprehensive search of the literature using major databases, looking at reports of detection rates and resulting changes in management. A total of 12 studies met the metaanalysis criteria and included 383 patients with metastatic neuroendocrine tumors and unknown primaries who underwent PET/CT imaging. Per-patient analysis showed a

primary tumor detection rate of 56%, with the most common locations being the bowel and pancreas. Imaging resulted in a change in management in 20% of patients in the study. The authors concluded that somatostatin receptor PET/CT is quite useful in detecting unknown primaries in patients with metastatic neuroendocrine tumor disease. They called for additional studies on imaging factors affecting changes in management in this setting.

Endocrine

Renal Cell Carcinoma, Nivolumab Treatment, and ^{18}F -FDG PET/CT

In an article e-published on April 2 ahead of print in *BMC Cancer*, Tabei et al. from the Yokohama City University Graduate School of Medicine, the Yokosuka Kyosai Hospital, and the Yokohama Minami Kyosai Hospital (all in Yokohama, Japan) reported on a study of the utility of ^{18}F -FDG PET/CT before and after initiation of nivolumab therapy in patients with renal cell carcinoma. The work builds on previous reports by the group on ^{18}F -FDG PET/CT in prediction in renal cell carcinoma treated with molecular-targeting agents. The current study included 9 patients with metastatic disease (total of 30 lesions) who underwent PET/CT imaging at baseline and at 1 mo after treatment initiation and CT imaging at 4 mo. The 3 imaging points were used to assess and evaluate potential imaging predictors. Lesions with diameters decreased $\geq 30\%$ at 4-mo CT were defined as responding, and those that did not decrease $\geq 30\%$ were defined as nonresponding. Eighteen lesions were classified as responding and 12 as nonresponding. All lesions with decreased diameter and elevated SUV_{max} at 1-mo PET/CT were classified as responding at 4-mo CT imaging, whereas most lesions with increased diameter and decreased SUV_{max} at 1-mo PET/CT were nonresponders at 4-mo CT. Multivariate analyses showed elevation of SUV_{max} at 1 mo to be the sole independent predictor among a variety of factors. The authors concluded that “our findings suggest that the early assessment using FDG PET/CT can be

effective to predict the response of renal cell carcinoma to nivolumab,” but called for larger studies to validate these results.

BMC Cancer

Correlation in PET/MR and PET/CT Pediatric Imaging

Uslu-Besli et al. from the Istanbul University–Cerrahpaşa, Gazi University Medical Faculty (Ankara), and the Istanbul Sultan Abdülhamid Han Training and Research Hospital (all in Turkey) reported on March 29 ahead of print in the *Journal of Pediatric Hematology/Oncology* on a comparison of ^{18}F -FDG PET/MR and ^{18}F -FDG PET/CT imaging in pediatric oncology patients. The group looked specifically at anatomic correlation of tracer-positive lesions with the 2 modalities and also compared diffusion-weighted MR imaging (DWI) with PET to assess correlations between apparent diffusion coefficients and SUVs. The retrospective study included sequential PET/CT and PET/MR images and/or whole-body DWI and apparent diffusion coefficient mapping in 34 pediatric patients. ^{18}F -FDG–positive lesions were assessed visually on the CT, T1-weighted, T2-weighted, and DWI images for the 2 modalities for anatomic correlation. Additional correlation analyses were performed for SUV parameters and apparent diffusion coefficient values. Of the 47 ^{18}F -FDG–positive lesions identified on both PET/CT and PET/MR imaging, 37 were positive on CT and 46 were positive on at least 1 MR sequence. In the 32 ^{18}F -FDG–positive lesions for which DWI data were available, 31 could be clearly visualized on DWI, resulting in a significant difference compared with CT alone in detection of ^{18}F -FDG–positive lesions. No correlations were identified between apparent diffusion coefficients and SUVs. Because ^{18}F -FDG PET/MR imaging showed better performance than PET/CT in terms of anatomic correlation of ^{18}F -FDG–avid lesions, the authors concluded that “PET/MRI may be more advantageous than PET/CT, not only due to reduced ionizing radiation dose but also for a better depiction of FDG-avid lesions in pediatric PET imaging.”

Journal of Pediatric Hematology/Oncology

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 April. In an article e-published on April 14 ahead of print in *Clinical Gastroenterology and Hepatology*, Allocca et al. from Humanitas Clinical and Research Center (Milan, Italy) and the University Hospital of Nancy/Lorraine University (Nancy, France) provided an overview of “Non-invasive multi-modal methods to differentiate inflamed vs. fibrotic strictures in patients with Crohn’s disease.” Kim et al. from the Sungkyunkwan University School of Medicine (Seoul, Korea) reported on “Diffusely increased ^{18}F -FDG uptake in the thyroid gland and risk of thyroid dysfunction: A cohort study” on April 2 ahead of print in the *Journal of Clinical Medicine*. In an article e-published on April 19 ahead of print in *Head & Neck*, Zafareo et al., representing a multiinstitutional committee of subject-matter experts, presented an “American Head and Neck Society Endocrine Surgery Section update on parathyroid imaging for surgical candidates with primary hyperthyroidism.” Hanssen et al. from the Centre Hospitalier Universitaire de Liège and the Université de Liège (Belgium) reviewed ^{18}F -FDG positron emission tomography in non-oncological renal pathology: Current indications and perspectives” (in French) on April 11 ahead of print in *Nephrologie & Therapeutique*. In an article e-published on April 15 ahead of print in *Hormones (Athens, Greece)* Bertagna et al. from the University of Brescia/Spedali Civili di Brescia (Italy), the Oncology Institute of Southern Switzerland (Bellinzona), Lausanne University Hospital (Switzerland) and the Ente Ospedaliero Cantonale (Bellinzona, Switzerland) presented a systematic review on “ ^{68}Ga -PSMA PET thyroid incidentalomas.”