

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 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 include a small section on noteworthy reviews of the literature.

⁶⁸Ga-DOTATATE PET/CT in Sarcoidosis

Lee et al. from the Hospital of the University of Pennsylvania (Philadelphia) and the Brigham and Women's Hospital/Harvard Medical School (Boston, MA) reported on October 20 ahead of print in the *Journal of Nuclear Cardiology* on the potential clinical utility of ⁶⁸Ga-DOTATATE PET/CT compared with that of ¹⁸F-FDG PET/CT for diagnosis and response assessment in cardiac sarcoidosis. The study included 11 patients who underwent imaging with both tracers, and the 2 studies were interpreted independently before comparison. The researchers found that patient-level concordance between studies with the 2 tracers was 91%, with 10 patients having multifocal DOTATATE uptake indicating active cardiac sarcoidosis and 1 with diffuse DOTATATE uptake. Segment-level agreement between the 2 types of studies was 77.1%. The SUV_{max}-to-blood pool ratio was lower with ⁶⁸Ga-DOTATATE PET/CT (3.2 ± 0.6) than with ¹⁸F-FDG (4.9 ± 1.5). Eight patients also underwent follow-up ⁶⁸Ga-DOTATATE PET/CT, which showed 1 case of complete response and 1 of partial response, compared with 3 complete and 1 partial response on follow-up ¹⁸F-FDG PET/CT. The authors summarized

their findings that “compared to ¹⁸F-FDG PET/CT, ⁶⁸Ga-DOTATATE PET/CT can identify active cardiac sarcoidosis with high patient-level concordance but with moderate segment-level concordance, low signal-to-background ratio, and underestimation of treatment response.”

Journal of Nuclear Cardiology

Predictive and Prognostic Imaging Biomarkers in the TheraP Trial

The TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group published on October 14 ahead of print in *Lancet Oncology* an analysis from their landmark trial, focusing on ⁶⁸Ga-prostate-specific membrane antigen (PSMA)-11 PET and ¹⁸F-FDG PET parameters as predictive and prognostic biomarkers in patients receiving ¹⁷⁷Lu-PSMA-617 or cabazitaxel for metastatic castration-resistant prostate cancer. After reviewing the overall protocol and criteria for the TheraP study, a multicenter, open-label, randomized phase 2 trial with 200 participants (99 treated with the PSMA agent and 101 with cabazitaxel), the authors evaluated an SUV_{mean} of ≥10 on ⁶⁸Ga-PSMA-11 PET as a predictive biomarker of response. A metabolic tumor volume of ≥200 mL on ¹⁸F-FDG PET was tested as a prognostic biomarker. Over a median follow-up of 18.4 mo, 35 of the men assigned to ¹⁷⁷Lu-PSMA-617 and 30 assigned to cabazitaxel therapy had high PSMA uptake (SUV_{mean} ≥ 10). The odds of prostate-specific antigen (PSA) response to the PSMA agent were significantly higher for those with SUV_{mean} ≥ 10 than those with SUV_{mean} < 10. The PSA response rate in patients with SUV_{mean} ≥ 10 was 91% for ¹⁷⁷Lu-PSMA-617 and 47% for cabazitaxel treatment. Corresponding response rates in patients with SUV_{mean} < 10 were 52% and 32%. High metabolic tumor volumes (≥200 mL) on ¹⁸F-FDG PET were seen in 30% of patients assigned to

¹⁷⁷Lu-PSMA-617 treatment and 30% of those assigned to cabazitaxel. The authors concluded that “in men with metastatic castration-resistant prostate cancer, PSMA PET SUV_{mean} was predictive of higher likelihood of favorable response to ¹⁷⁷Lu-PSMA-617 than cabazitaxel, which provided guidance for optimal ¹⁷⁷Lu-PSMA-617 use.” High ¹⁸F-FDG PET metabolic tumor volumes were associated with lower responses, regardless of randomly assigned treatment, an indication that additional research may define the need for treatment intensification.

Lancet Oncology

PET/CT and Prognosis in RT of Rhabdomyosarcoma

Cheriyalinal Parambil et al. from Tata Memorial Hospital/Homi Bhabha National Institute (Mumbai, India) reported on October 14 ahead of print in the *Journal of Pediatric Hematology/Oncology* on a study of the prognostic significance of persistent ¹⁸F-FDG avidity on PET in residual masses after definitive radiation treatment in pediatric rhabdomyosarcoma. The retrospective study included 63 children with group III ($n = 55$) and group IV ($n = 8$) rhabdomyosarcoma who underwent PET/CT imaging at 3 mo after radiation for local control. Residual masses were visualized in 10 patients (15.9%), and anatomic residual disease was visualized in 24 (38.1%), with no ¹⁸F-FDG-avid areas in 29 (46.0%). Over a median follow-up of 38 mo, 3-y event-free survival for children with ¹⁸F-FDG-avid residual masses was 40.0% compared with 71.9% for those who had no such masses. Three-year overall survival of patients with ¹⁸F-FDG-avid residual masses was 50.8% compared with 77.0% for the remaining patients. These results were sustained on multivariate analysis. The authors concluded that “persistent metabolic activity in residual disease postchemoradiotherapy in rhabdomyosarcoma may portend a poorer prognosis with an increased risk of relapse.” They added that “this subset of high-risk patients needs to be identified, and further trials are warranted

to develop strategies to improve their outcomes.”

Journal of Pediatric Hematology/Oncology

¹¹C-Choline PET/CT in Primary Hyperparathyroidism

In a study published on October 10 ahead of print in *Surgery*, Saha et al. from the Mayo Clinic (Rochester, MN) reported on ¹¹C-choline PET/CT in evaluation of primary hyperparathyroidism, with a focus on utility when conventional imaging techniques fail to provide accurate preoperative localization. The study included 43 patients in whom multiple standard imaging modalities had failed to localize disease and who underwent limited-coverage neck-and-chest ¹¹C-choline PET/CT. Thirty-three patients had positive findings on ¹¹C-choline PET/CT. Of the 25 patients who proceeded to surgery, 18 were reoperations. Twenty of the 25 patients achieved an operative cure. ¹¹C-choline PET/CT was found to have a sensitivity of 64% and positive predictive value of 72%, with 5 false-positive findings (lymph nodes, normal parathyroid, and a recurrent laryngeal nerve neuroma). These results were compared with those from standard imaging modalities, including ultrasound, ¹²³I-sestamibi, and 4D CT. The authors concluded that ¹¹C-choline PET/CT “is a useful adjunct for parathyroid localization in a complex population of patients who have failed standard localization techniques, including ultrasound, ¹²³I-sestamibi, 4D CT, and/or prior operations.” They added that although ¹¹C-choline PET/CT may not be needed routinely, “it may aid in preoperative localization in the reoperative setting.”

Surgery

Clinical Experience with Implementation of 2015 ATA Guidelines

Wu et al. from the University of Calgary/University of Calgary Cumming School of Medicine (Canada) reported on October 13 ahead of print in *Thyroid* on the clinical outcomes of the implementation of the 2015 American Thyroid

Association (ATA) guidelines for management of thyroid nodules and differentiated thyroid cancer (DTC) using the modified ATA recurrence risk (RR) stratification system. A total of 479 patients with DTC were assigned a modified ATA RR (253 [53%] low-, 129 [27%] intermediate-, and 97 [20%] high-RR) and American Joint Committee on Cancer 8th-edition stage. These and the ATA recommendations guided surgical management, radioiodine treatment, and adjuvant therapies. Responses to treatment were evaluated at 2 y after surgery, which included 227 (47%) total thyroidectomies plus radioiodine, 178 (37%) total thyroidectomies only, and 74 (16%) lobectomies. The 2-y responses to treatment were excellent for 66 (89%) patients undergoing lobectomy, 149 (84%) with total thyroidectomy only, and 121 (53%) with total thyroidectomy plus radioiodine treatment. Of patients stratified at low-RR, 216 (85%) had excellent responses to treatment, 32 (13%) had indeterminate treatment responses, 4 (2%) had biochemical incomplete responses, and 1 had a structural incomplete response to treatment. Of patients stratified at intermediate-RR, 83 (64%) saw excellent, 30 (23%) saw indeterminate, 7 (6%) saw biochemical incomplete, and 9 (7%) saw structural incomplete treatment responses. With the worst study outcomes, patients in the high-RR saw 37 (38%) excellent responses, 18 (19%) indeterminate, 10 (10%) biochemical incomplete, and 32 (33%) structural incomplete responses to treatments. The authors concluded that the “2015 ATA RR stratification system is useful for predicting disease status at 2-y posttreatment in patients with DTC” and “may reduce thyroid cancer overtreatment by including lobectomy as a definitive treatment option for low-risk thyroid cancers and selective use of radioiodine for intermediate- and high-risk patients.”

Thyroid

Cardiovascular Complications and Long COVID

In an article published on September 23 in *Frontiers in Cardiovascular Medicine* (2022;9:968584), Murata et al. from

Nihon University School of Medicine (Tokyo, Japan) reported on a study using multimodality imaging to investigate the prevalence of cardiovascular disorders, particularly in patients with cardiovascular “long COVID.” The study drew patients from a total of 584 individuals admitted to the hospital with COVID-19 between January 2020 and September 2021. At clinical assessment over a median follow-up of 163 d, 52 (9%) patients with complaints of chest pain, dyspnea, or palpitations were suspected to have cardiovascular long COVID and were enrolled in the study. Patients underwent electrocardiography, chest X-ray imaging, and echocardiography, as well as cardiac MR and SPECT/CT imaging depending on initial findings. Cardiovascular disorders were present in 27%; of these, 15% had myocardial injury, 8% had pulmonary embolisms, and 4% both. Patients with cardiovascular disorders had significantly higher incidences of severe COVID conditions (36% vs 8%) and in-hospital cardiac events (71% vs. 24%) than those who did not. A severe COVID condition and in-hospital severe condition proved to be independent risk factors for cardiovascular disorders in cardiovascular long COVID patients. No patients died during the study period, and no adverse events were reported. The authors cited other investigators’ observations that long COVID itself is unlikely to result in organic cardiovascular disease, and, when it does, is likely to be quite mild. Despite the fact that patients with long COVID and cardiovascular complications tended to have longer-lasting symptoms of long COVID, the prognosis did not seem to be worse. They concluded that “early detection of cardiovascular problems in cardiology for symptomatic long COVID patients may inform patients of the duration of symptoms and allow symptoms to be shortened through appropriate therapeutic intervention.”

Frontiers in Cardiovascular Medicine

PSMA PET/CT and Dose-Escalated Salvage RT in PCa

Tamihardja et al. from the University of Würzburg (Germany) reported on

October 10 in *Cancers (Basel)* (2022; 14[19]:4956) on a study of oncologic outcomes with prostate-specific membrane antigen (PSMA) PET/CT-guided salvage radiotherapy for localized macroscopic prostate cancer recurrence. The study included 367 men who received such radiation treatment after radical prostatectomy. Of these, 111 patients were staged by either ^{68}Ga -PSMA-I&T or ^{18}F -PSMA-1007 before radiation. A total of 59 (53.2%) of these patients were treated for PSMA PET-positive macroscopic prostatic fossa recurrence. Over a median follow-up of 38.2 mo, the 3-y biochemical progression-free survival rate was 89.1% and the 3-y metastasis-free survival rate reached 96.2%. The cumulative 3-y late grade 3 genitourinary toxicity rate was 3.4%, with no late grade 3 toxicities reported. The authors concluded that “PSMA PET/CT-guided dose-escalated salvage radiotherapy with a simultaneous integrated boost to the local recurrence achieved encouragingly high rates of 3-y biochemical progression-free survival, metastasis-free survival, and overall survival,” with effective disease control and low toxicity rates.

Cancers (Basel)

Choroid Plexus Imaging in Presymptomatic MS

In an article published on October 13 in *Neurology, Neuroimmunology, and Neuroinflammation* (2022;9[6]:e200026), Ricigliano et al. from the Sorbonne Université; Paris Brain Institute, ICM, CNRS, Inserm; St Antoine Hospital; Pitié-Salpêtrière Hospital; Hôpital Fondation Adolphe de Rothschild; Université Paris-Saclay, CEA, CNRS, Inserm; and Service Hospitalier Frédéric Joliot, Orsay (all in Paris, France) reported on a study assessing whether imaging characteristics of the choroid plexus are detectable at the earliest stages of multiple sclerosis (MS), before clinical symptom onset. The retrospective study included 27 individuals with presymptomatic MS, 97 with clinically definite MS (CDMS), and 53

healthy controls, all of whom underwent cross-sectional 3T-MR imaging. A subset of 22 CDMS individuals, 19 healthy controls, and 1 individual with presymptomatic MS (imaged 8 mo before conversion to CDMS) also underwent translocator protein (TSPO) ^{18}F -DPA-714 PET imaging. Choroid plexus ^{18}F -DPA-714 uptake was calculated as the average SUV. Compared with healthy controls, individuals with presymptomatic MS had 32% larger choroid plexuses, similar to those with MS. Baseline PET imaging in the presymptomatic case who later developed MS showed 33% greater choroid plexus inflammation than in healthy controls. Postmortem studies in the choroid plexus of this individual identified a population of CD163⁺ mononuclear phagocytes expressing TSPO in MS, possibly contributing to the increased ^{18}F -DPA-714 uptake. The authors concluded that “by identifying an imaging signature in choroid plexuses already in presymptomatic MS, our work supports their role from the early phases of disease development and encourages further investigations on the involvement of choroid plexus immune infiltration and blood-cerebrospinal fluid barrier dysfunction in disease onset.”

Neurology, Neuroimmunology, and Neuroinflammation

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 and October. Linguanti et al. from the University of Florence and the IRCCS-Humanitas Research Hospital (Rozzano; both in Italy) reported in the September 27 issue of *Cancers (Basel)* (2022;14[19]:4700) on “Metabolic imaging in B-cell lymphoma during CAR-T cell therapy.” In the October 17 issue of the *Medical Journal of Australia* (2022;217[8]:424–433), Williams et al. from the Royal Melbourne Hospital,

Peter MacCallum Center Centre, Monash University, Cabrini Institute/Cabrini Health (all in Melbourne, Australia), Singapore General Hospital, and University College London (UK) presented “Modern paradigms for prostate cancer detection and management.” An overview of “Positron emission tomography in autoimmune encephalitis: Clinical implications and future directions” was provided by Li et al. from Beijing Tiantan Hospital/Capital Medical University and the China National Clinical Research Center for Neurological Diseases (both in Beijing, China) on October 19 ahead of print in *Acta Neurologica Scandinavica*. Hawkey et al. from Duke University School of Medicine (Durham, NC) and Tulane Cancer Center (New Orleans, LA) published an assessment of “The value of phenotypic precision medicine in prostate cancer” on October 6 ahead of print in the *Oncologist*. “Novel tracers for molecular imaging of interstitial lung disease: A state of the art review” was offered online ahead of print in the September 21 issue of *Autoimmunity Reviews* by Broens et al. from the Vrije Universiteit Amsterdam (The Netherlands). The October issue of *Surgical Oncology Clinics of North America* published several reviews of state-of-the-art imaging techniques, including Szidonya et al. from the Oregon Health and Science University (Portland), Semmelweis University (Budapest, Hungary), University of Iowa Hospitals and Clinics (Iowa City), and University of Colorado School of Medicine (Aurora) with “Molecular and anatomic imaging of neuroendocrine tumors (2022;31[4]:649–671); Graves et al. from the University of California Davis (Sacramento), the University of California, San Francisco, and New York University Langone Health (NY) with “Innovations in parathyroid localization imaging (2022;31[4]:631–647); and Goodman et al. from the University of California, San Francisco, with “Molecular imaging for estrogen receptor-positive breast cancer: Clinical applications of whole body and dedicated breast positron emission tomography” (2022;31[4]: 569–579).