

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 DCE MR in ACL Reconstruction

Garika et al. from the All India Institute of Medical Sciences (New Delhi) reported on November 27 ahead of print in the *American Journal of Sports Medicine* on a comparison of ^{18}F -FDG PET/CT and dynamic contrast-enhanced (DCE) MR imaging to assess ligamentization within anterior cruciate ligament (ACL) grafts. The study included 26 patients (3 women, 23 men) who completed 2 follow-ups at a mean of 125 ± 22 and 259 ± 38 d after arthroscopic ACL reconstruction. At each follow-up, patients underwent clinical assessments (anterior drawer test, Lachman test, and Lysholm scoring) and MR and PET/CT imaging (including SUV_{max} , SUV_{max} ratio to the contralateral side, and normalized enhancement in 3 zones: femoral, intraarticular, and tibial). Median Lysholm scores improved from 78.5 (range, 62–90) at the first follow-up to 94.5 (range, 84–100) at the second. PET/CT found all grafts to be viable and MR imaging found all grafts to be vascularized. All grafts were judged to be continuous on MR, except for 1 at the second follow-up. DCE MR imaging identified a single-vessel supply to all grafts at first follow-up and multiple-

vessel supply in 10 patients at second follow-up. Reductions in the median SUV_{max} and SUV_{max} ratio to the contralateral side were seen at second follow-up, as well as normalized enhancement in all 3 zones. Only SUV_{max} ratio to the contralateral side in the intraarticular zone showed a significant reduction, and patients with excellent Lysholm scores at second follow-up had significantly higher reductions than those with simply good Lysholm scores. SUV_{max} ratio to the contralateral side and SUV_{max} in the intraarticular zone correlated negatively with Lysholm scores at second follow-up only. The authors concluded that “glucose metabolism and vascularity in the graft tissue can be used to assess ligamentization of ACL graft.” They noted that PET/CT determination of viability and MR assessment of vascularity at first follow-up were associated with good-to-excellent final outcomes. However, because no correlation was observed between PET/CT and MR imaging parameters, these imaging techniques may be assessing different domains of the same process. Higher normalized enhancement in the intraarticular zone at the first follow-up and lower SUV_{max} on the contralateral side in the same region at second follow-up were associated with better outcomes.

American Journal of Sports Medicine

^{18}F -Flortaucipir PET and Postmortem AD Tau Pathology

On December 3 ahead of print in *JAMA Neurology*, Smith et al. from Skåne University Hospital (Lund and Malmö), Lund University, and Ängelholm Hospital (all in Sweden) reported on a study designed to determine the association of regional in vivo retention of ^{18}F -flortaucipir on PET imaging with tau neuropathology in corresponding brain regions in a patient with Alzheimer disease (AD). The patient had premature AD associated with a PSEN1 mutation. He underwent imaging twice with ^{18}F -flortaucipir PET at a 20-mo interval for regional SUV ratios of the tracer. After

his death 12 mo later, AD tau pathology results were obtained from postmortem analyses (phosphorylated tau immunohistochemistry, Gallyas silver staining, regional total tau pathology burden, density of tau-positive neurites and intrasomal tau tangles, and β -amyloid-containing plaques). Tau PET retention of 20%–40% in many cortical regions corresponded to the patient’s rapid decline and increased clinical symptoms over the 20-mo in vivo analysis. In vivo uptake of ^{18}F -flortaucipir was correlated with the postmortem density of tau-positive neurites, intrasomal tau tangles, and total tau burden. ^{18}F -flortaucipir in vivo uptake was not correlated with β -amyloid pathology. The authors concluded that their results “indicate that ^{18}F -flortaucipir PET retention is a robust in vivo measure of the total AD tau burden.”

JAMA Neurology

European Perspective on 2015 ATA Guidelines

Luster, from the University Hospital Marburg (Germany), and 21 members of a diverse European Association of Nuclear Medicine task force reported on November 28 ahead of print in *Thyroid* on the European perspective on the 2015 American Thyroid Association (ATA) Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer (DTC). This position paper, contrasting the European perspective with that of the ATA, was generated after an invited symposium that included 17 European thyroid specialists, 4 ATA Guidelines Taskforce members, and an audience of 200 international experts. Topics discussed included preoperative assessment of thyroid nodules, surgery and the role of pathology, radioiodine therapy (RAIT), assessment of initial therapy and dynamic risk stratification, treatment of persistent disease, recurrences, and advanced thyroid cancer. The group suggested modifications to approximately one-third of the ATA recommendations. Among the areas of

discrepant opinions were issues relating to: (1) the ATA allowance for lobectomy for primary tumors ≤ 4 cm. Here the symposium participants cited questions about preclusion of RAIT, the potential need for completion thyroidectomy, frequent inability to avoid chronic thyroid hormone replacement, and limitations of supporting evidence as arguments against applying lobectomy so widely; (2) ATA limitations on postoperative RAIT. Panelists at the symposium endorsed wider use of postoperative RAIT, citing favorable patient outcomes, generally limited toxicity, and lack of high-quality evidence supporting withholding RAIT; (3) ATA limitations on recombinant human thyrotropin in some settings. The panelists cited avoidance of hypothyroid morbidity and quality-of-life impairment without apparent sacrifice in oncologic outcomes as evidence to support use in a wider range of settings. In addition, the experts advocated dosimetric rather than fixed-activity RAIT in advanced DTC, citing the difficulties of implementing the ATA risk stratification system when requisite information may not be available in everyday practice, and noted that the ATA recommendations for radioiodine-refractory DTC should consider the potential palliative benefits of RAIT in patients who also have radioiodine-susceptible lesions. The task force members concluded by noting that identification of “varying European and ATA 2015 perspectives can stimulate analysis and discussion of literature and performance of primary research to resolve discrepant recommendations and potentially improve patient outcomes.”

Thyroid

Lung Cancer, Ultra-Low-Dose PET, and Machine Learning

In an article e-published in the December issue of *Lung Cancer* (2018;126:170–173), Schwyzer et al. from the University Hospital Zurich/University of Zurich (Switzerland) reported on initial results from a study evaluating whether machine learning may be helpful in increasing the clinical feasibility of automated ultra-low-dose

^{18}F -FDG PET detection of lung cancer. The image analysis study looked at the ability of an artificial neural network to differentiate 50 patients with lung cancer from 50 controls without pulmonary malignancies. The study included 3,936 PET slices representing imaging in which the patients' tumors were visible as well as images from the controls. The artificial neural network “read” the PET images at the clinical standard dose as well as with simulations of 10-fold and 30-fold (PET_{3.3%}) reductions in radiation doses. The resulting areas under the curve of the deep learning algorithm for lung cancer detection were 0.989, 0.983, and 0.970 for the standard dose images and the 10- and 30-fold reduced dose reconstructions, respectively. The artificial neural network showed sensitivities of 95.9% and 91.5% and specificities of 98.1% and 94.2% for the standard dose imaging and ultra-low dose (PET_{3.3%}) reconstruction, respectively. The authors concluded that these results suggest that “machine learning algorithms may aid fully automated lung cancer detection even at very low effective radiation doses of 0.11 mSv” and that additional development of this technology “might improve the specificity of lung cancer screening efforts and could lead to new applications of ^{18}F -FDG PET.”

Lung Cancer

Deauville Score and Early PET/CT After Allogeneic Transplant in Lymphoma

Bouard et al. from the Centre Hospitalier Universitaire (Nantes), the University of Nantes, and the Institut de Cancérologie René Gauducheau (Saint-Herblain; all in France) reported on November 24 ahead of print in *Biology of Blood and Marrow Transplantation* on a retrospective study examining the relationship between lymphoma-free survival and ^{18}F -FDG PET/CT results early after allogeneic transplantation. The study included 103 adults (69 men, 34 women; median age, 51.6 y; range, 22–67 y) with Hodgkin (HL) or non-Hodgkin (NHL) lymphoma (NHL, 47; low-grade NHL, 6; T-cell lymphoma, 34; HL, 16). These patients

had undergone PET/CT imaging within 1 mo before and/or early after (>3 and <6 mo) allogeneic stem cell transplantation and remained without documented progression or relapse at the time of subsequent PET/CT imaging (median 49.5 mo; range 6–140.5 mo). These PET/CTs were reviewed and restaged according to the Deauville scale as positive when uptake was higher than liver background (Deauville score ≥ 4). At follow-up, the median 3-y overall and lymphoma-free survivals were 81% (range, 71%–87%) and 65% (range, 54%–74%), respectively. A positive PET/CT at 3 mo was the strongest independent factor associated with poorer lymphoma-free survival. The authors concluded that ^{18}F -FDG PET/CT positivity at 3 mo appears to be highly predictive of poor lymphoma-free survival in patients after allogeneic transplantation and “may help to guide strategies to prevent relapse.”

Biology of Blood and Marrow Transplantation

^{89}Zr -Atezolizumab and Response to PD-L1 Blockade

In an article in the December issue of *Nature Medicine* (2018;24[12]:1852–1858) Bensch et al. from the University Medical Center Groningen/University of Groningen (The Netherlands), University Medical Center Utrecht/Utrecht University (The Netherlands), and Genentech (San Francisco, CA, and Basel, Switzerland) reported initial results from a first-in-human clinical trial assessing the feasibility of PET imaging with ^{89}Zr -atezolizumab (anti-programmed cell death protein ligand-1 [anti-PD-L1]) and the potential of this imaging technique to predict response to PD-L1 blockade. Twenty-two patients with locally advanced or metastatic non-small cell lung cancer, bladder cancer, or triple-negative breast cancer underwent ^{89}Zr -atezolizumab imaging before the start of atezolizumab therapy. The resulting PET signal was high in lymphoid tissues and at sites of inflammation, with heterogeneous but generally high uptake in tumors. This uptake varied among patients, tumor types, and within and among lesions.

Clinical responses were found to be better correlated with pretreatment PET imaging than with immunohistochemistry- or RNA sequencing-based predictive biomarkers. The authors concluded that these results encourage “further development of molecular PET imaging for assessment of PD-L1 status and clinical response prediction.” Completion of this study may provide additional supporting data for this conclusion.

Nature Medicine

Radioiodine Ablation and Disease Recurrence after HiLo Trial

Dehbi et al. from Cancer Research UK and University College London Cancer Institute/University College London, Freeman Hospital (Newcastle upon Tyne), Weston Park Hospital (Sheffield), Royal Marsden Hospital (Sutton), and the Independent Doctors Federation (London; all in the UK) reported on November 27 ahead of print in *The Lancet. Diabetes & Endocrinology* on a study looking at long-term recurrence rates in patients after high- and low-dose radioiodine ablation with or without recombinant human thyroid-stimulating hormone (rhTSH) for differentiated thyroid cancer (DTC). The 29-site HiLo trial included 438 patients with histologic confirmation of disease who were randomly assigned to 1.1- or to 3.7-GBq ablations, following either rhTSH or thyroid hormone withdrawal. Median follow-up was 6.5 y in 434 evaluable patients (217 in each of the low- and high-dose groups). Recurrences were seen in 21 patients: 11 who had undergone low-dose ablation and 10 who had undergone high-dose ablation. Four recurrences (2 in each group) were evaluated as persistent disease. Cumulative recurrence rates were not significantly different between the low- and high-dose groups, nor was a difference in risk seen for T3 or N1 disease with the 2 doses. Recurrence rates were also similar in patients who received rhTSH and those who underwent thyroid hormone withdrawal before ablation. The authors concluded that “these findings provide further evidence in favor of using low-dose

radioactive iodine for treatment of patients with low-risk DTC” and that recurrence risk was not affected by use of rhTSH.

The Lancet. Diabetes & Endocrinology

PRRT in GEP NEN G3

In an article in the February 1 issue of *Endocrine-Related Cancer* (2019; 26[2]:227–239), Carlsen et al. from the Rigshospitalet/University of Copenhagen (Denmark) and collaborating researchers from Italy, Sweden, Israel, Germany, The Netherlands, Poland, Switzerland, the UK, Norway, and Denmark reported on a study assessing the benefits and side effects of peptide-receptor radionuclide therapy (PRRT) in patients with high-grade gastroenteropancreatic (GEP) neuroendocrine neoplasms (NEN G3). The retrospective study performed at 12 centers assessed the efficacy and toxicity of PRRT in patients with GEP NEN G3, including data on response rate, disease control rate, progression-free survival, overall survival, and toxicity. A total of 149 patients with 89 pancreatic primary tumors, 34 gastrointestinal primary tumors, and 46 unknown loci of primary tumors were included. PRRT was administered as first-line treatment in 30 patients, second-line in 62, or later-line treatment in 57. Of the 114 evaluable patients 1% had complete response, 41% partial response, 38% stable disease, and 20% progressive disease after treatment. Of the 104 patients with documented progressive disease before PRRT, the disease control rate after treatment was 69%. Over all patients, the median progression-free survival was 14 mo and overall survival was 29 mo. Grade 3–4 hematologic or renal toxicity occurred in 17% of patients. The authors concluded that this study demonstrated “promising response rates, disease control rates, progression-free and overall toxicity, as well as toxicity in patients with mainly progressive disease.” They added that these results support consideration of PRRT for patients with GEP NEN G3.

Endocrine-Related Cancer

Single Calculated ¹³¹I Dose in Graves Hyperthyroidism

Wong et al. from the University of Michigan (Ann Arbor), St. Jude Children’s Research Hospital (Memphis, TN), and the Department of Veterans Affairs Health System (Ann Arbor, MI) reported online on November 28 in *Clinical Diabetes and Endocrinology* (2018;4:20) on a study evaluating the success rate of therapeutic administration of a single calculated ¹³¹I activity for eliminating hyperthyroidism resulting from Graves disease. The study enrolled 316 hyperthyroid patients with Graves disease (248 women, 78 men; mean age 42.1 ± 16 y, range 4–94 y). Six patients had undergone previous surgery, 131 had been treated with antithyroid medication, and 179 were treatment naïve. All participants underwent pinhole thyroid imaging, 24-h radioactive iodine uptake (RAIU) measurements, and clinical assessment in association with receipt of calculated ¹³¹I activity of 0.2 mCi per estimated gram of thyroid tissue, adjusted for 24-h RAIU. Response to therapy was assessed at 7-wk and 3-mo follow-ups. Successful treatment of hyperthyroidism was noted after a single therapeutic ¹³¹I activity administration in 295 of 316 (93.3%) patients. The mean response time after successful therapy was 110.2 d, with cumulative responses of 25% at 61 d, 50% at 84 d, and 75% at 118 d after treatment. Failure of radioiodine therapy was associated with previous propylthiouracil administration. The mean time to respond for those with such prior medication was 297 d compared to 116 d for those on methimazole and 109 d for those not previously treated with antithyroid medications. In those patients with persistent hyperthyroidism, failure of radioiodine therapy was documented in 16 patients (76.2%) ≤1 y after ¹³¹I administration and in 5 patients (23.8%) >1 y after initial therapy. The authors concluded that “successful ¹³¹I therapy for Graves hyperthyroidism with a single calculated dose can be achieved in the majority (>90%) of patients, adjusting for

the thyroid size and 24-h uptake measurement.”

Clinical Diabetes and Endocrinology

PET/CT in Benign Tissue and Response to Immunotherapy

In an article e-published on November 26 ahead of print in *Cancer Immunology, Immunotherapy*, Sachpekidis et al. from the German Cancer Research Center (DKFZ) (Heidelberg), University Medical Center Mannheim/Ruprecht-Karl University of Heidelberg (Mannheim), and University Hospital Heidelberg (all in Germany) reported on ^{18}F -FDG PET/CT evaluation of lymphoid tissue changes in the mediastinal/hilar lymph nodes and the spleen in response to ipilimumab administration in patients with metastatic melanoma. The study included 41 patients with unresectable disease who underwent PET/CT imaging before the start of ipilimumab therapy, after 2 cycles, and at the end of treatment. Imaging analyses focused on the mediastinal/hilar lymph nodes and the spleen. Using each patient's basic clinical response as a reference, 31 patients showed disease control and 10 showed progressive disease over the course of the study. Assessment of interim and late PET/CT in mediastinal/hilar lymph nodes showed 4 patients with a “sarcoid-like lymphadenopathy” as a response to treatment, classified as lymph-node positive. These patients responded to ipilimumab with disease control. PET/CT imaging results did not correlate with either baseline spleen-related parameters or response to treatment. The authors concluded that the fact that the patients who showed sarcoid-like lymphadenopathy on interim or late PET/CT achieved disease control implies “a relation between the appearance of sarcoid-like lymphadenopathy and the clinical benefit of anti-cytotoxic T-lymphocyte-associated protein 4 therapy.”

Cancer Immunology, Immunotherapy

^{18}F -FDG PET Hypometabolism vs MR Atrophy in PD

Albrecht et al. from the Max Planck Institute for Human Cognitive and Brain

Sciences (Leipzig), Leipzig University Medical Center, the University of Applied Science (Jena; all in Germany), and the German Consortium on Frontotemporal Lobar Degeneration reported on November 15 ahead of print in *NeuroImage. Clinical* on the results of a systematic metaanalysis designed to identify Parkinson disease (PD)-specific markers in whole-brain structural MR, ^{18}F -FDG PET, and diffusion tensor imaging (DTI) studies. Seventy-four published studies (MR, 50; PET, 14; and DTI, 10) met the inclusion criteria, with 2,323 patients and 1,767 healthy controls. Imaging groups were divided into subcohorts based on clinical phenotypes. Using a range of meta-analytic approaches, the researchers found that glucose hypometabolism on PET was seen extensively in the bilateral inferior parietal cortex and left caudate nucleus. On further analysis, this hypometabolism pattern was found to be associated with cognitive deficits in the inferior parietal cortex and motor symptoms in the caudate nucleus. Structural MR imaging showed small focal gray matter atrophies in the middle occipital gyrus, but these were not confirmed in additional analyses. DTI showed fractional anisotropy reductions in the cingulate bundle near the orbital and anterior cingulate gyri in patients with PD. The authors concluded that the results of this metaanalysis “suggest that ^{18}F -FDG PET reliably identifies consistent functional brain abnormalities in PD, whereas structural MRI and DTI show only focal alterations and rather inconsistent results.” They added, however, that neither PET assessment of hypometabolism nor structural MR appear to offer disease-specific imaging biomarkers for PD.

NeuroImage. Clinical

PET/MR and Lytic Lesions in Multiple Myeloma

In an article e-published on December 11 ahead of print in *Annals of Hematology* Zambello et al. from the Padua University School of Medicine, Ca' Foscari University (Venice), and Camposampiero Hospital (Padua; all

in Italy) reported on differences in density and ^{18}F -FDG PET/MR imaging features in lytic bone lesions (LBLs) identified by whole-body low-dose CT in patients with newly diagnosed multiple myeloma. The study included 18 such patients in whom 135 unequivocal LBLs were identified by CT. Lesions were characterized for inner density (negative or positive Hounsfield units [HUs]), with negative density ($\text{HU} < 0$) characterizing normal yellow marrow and positive HU correlating with a tissue-like infiltrative pattern. These lesions were analyzed by ^{18}F -FDG PET/diffusion-weighted MR imaging, coregistering the diffusion-weighted signals with apparent diffusion coefficients (ADCs) and SUV_{max} values. Thirty-five lesions were found to have a negative density (-56.94 ± 31.87 HU), 100 lesions were found to have a positive density (44.87 ± 23.89 HU). Only positive HU LBLs were found in 8 patients, and in 7 patients both positive and negative HU LBLs were detected. Three patients (16%) demonstrated only negative HU LBLs. Analysis of the hybrid imaging showed that negative HU LBLs had low ADC values and low SUV_{max} values (1.69 ± 0.56), consistent with fatty marrow. Positive HU LBLs showed an infiltrative pattern with higher ADC and SUV_{max} (mean, 5.04 ± 1.94) values. At histologic analysis, negative HU LBLs showed infiltration by neoplastic plasma cells scattered among adipocytes. The authors concluded that whole-body low-dose CT detected 2 different patterns of LBLs in patients with multiple myeloma. They added that although both types of lesions were indicative of active disease, “only positive HU LBLs were captured by ^{18}F -FDG PET/diffusion-weighted MR imaging, indicating that whole-body low-dose CT adds specific information.”

Annals of Hematology

OAR Dosimetry in ^{177}Lu -PRRT

Marin et al. from the Institut Jules Bordet-Université Libre de Bruxelles and Ghent University (both in Belgium) reported in the December issue of *Physica Medica* (2018;56:41-49) on development of an organ-at-risk dosimetry

procedure for ^{177}Lu -labeled peptide-receptor radionuclide therapy (PRRT) in patients with neuroendocrine tumors. The study included 47 such patients undergoing ^{177}Lu -DOTATATE therapy. SPECT/CT imaging was performed at 4, 24 and 144–192 h after injection along with blood draws at each scan. Two additional blood samples were drawn 30 min and 1 h after injection. OLINDA/EXM software was used to calculate organ-at-risk absorbed doses, and median values for all patients were computed for absorbed dose coefficient D/A_0 and for late effective half-life for kidneys, spleen, and red marrow. For kidneys, spleen, and marrow, dosimetry resulted in medians of 0.78, 1.07, and 0.028 Gy/GBq, respectively, for absorbed dose coefficient and of 55, 71, and 52 h, respectively, for late effective half-life. The authors concluded that “a dosimetry procedure for organs at risk in ^{177}Lu -DOTATATE therapy based on serial SPECT/CT images and blood samples can be implemented routinely in a clinical context with limited patient burden.”

Physica Medica

^{18}F -FCH PET/CT in Primary Hyperparathyroidism and Inconclusive Imaging

In an article published on November 28 in *Physiological Research* (2018; 67[suppl 3]:S551–S557) Zajířková et al. from the Institute of Endocrinology (Prague, Czech Republic) reported on parathyroid imaging with ^{18}F -fluorocholine PET/CT in patients with primary hyperparathyroidism and inconclusive conventional imaging (neck ultrasound and $^{99\text{m}}\text{Tc}$ -sestamibi SPECT scintigraphy). The study included 13 patients (mean age, 64.3 y; preoperative calcium 2.74 mmol/L; parathyroid hormone, 114.6 ng/L) who underwent ^{18}F -fluorocholine PET/CT to localize abnormal parathyroid glands before surgery, with results compared to postoperative histopathologic findings. ^{18}F -fluorocholine PET/CT was able to localize hyperfunctioning parathyroid glands in 12 patients (per-patient sensitivity, 92%; positive predictive value, 100%). A total of 14 parathyroid lesions

(11 adenomas, 3 hyperplastic glands) were resected with a mean size of 11.9 mm (per-lesion sensitivity 93%; positive predictive value, 81%). At histopathology, 4 adenomas and 1 hyperplastic gland had only chief cells, and 5 lesions contained both chief and oxyphil cells. One exclusively oxyphil adenoma was found in each of 3 patients; these lesions had been negative on $^{99\text{m}}\text{Tc}$ -sestamibi scintigraphy despite the high mitochondria content in oxyphil parathyroid cells. Twelve of the 13 patients were confirmed to have thyroid disease. The authors concluded that, in this limited study sample, ^{18}F -fluorocholine PET “correctly identified parathyroid adenomas and/or hyperplastic glands in 92% of patients with previously inconclusive conventional imaging,” adding that unlike $^{99\text{m}}\text{Tc}$ -sestamibi, “ ^{18}F -fluorocholine successfully localized small, hyperplastic, and multiple hyperfunctioning parathyroid glands” regardless of their histopathologic composition.

Physiological Research

PET and Secondary Stabilization After THA

Ullmark et al. from Gävle Hospital and Uppsala University/Uppsala University Hospital; both in Sweden) reported on December 6 ahead of print in *Hip International* on a clinical trial of the utility of ^{18}F -FDG PET/CT in assessing new bone mineralization in periprosthetic bone adjacent to femoral stems after total hip arthroplasty. The study included 26 patients with hip osteoarthritis who were assigned to receive either a hydroxyapatite-coated femoral stem or a cemented one at total hip arthroplasty. All patients underwent PET/CT and radiography before surgery and at 6 wk and 6 mo thereafter, with concurrent clinical scoring and assessment. Polar mapping was used to analyze and present PET findings in 13 regions of interest adjacent to the whole stem. All patients experienced good clinical results with no major complications, and all stems were stable on conventional radiography. PET imaging after 6 wk indicated that bone mineralizing activity was significantly higher around uncemented stems than in cemented

stems or in contralateral healthy reference femurs. Moreover, mineralizing activity in the uncemented group as observed with PET/CT decreased at a slower rate than in the cemented group. The authors concluded that PET/CT “is a useful new tool for analyzing secondary stabilization of femoral stems after total hip arthroplasty.”

Hip International

PET/CT–Guided Targeted Bone Marrow Biopsy in Lymphoma

In an article published in the November 29 issue of *BMC Cancer* (2018;18:1192), Hao et al. from the Xiamen Cancer Hospital and the First Affiliated Hospital of Xiamen University (Fujian, China) reported on a study designed to determine whether ^{18}F -FDG PET/CT–guided bone marrow biopsy adds additional or complementary information to conventional evaluation of bone marrow involvement in patients with newly diagnosed lymphoma. The retrospective study included 299 such patients who had undergone both ^{18}F -FDG PET/CT imaging and bone marrow biopsy (either PET/CT-guided or routine unilateral crest biopsy). Thirty of 34 patients with focal lesions on PET/CT underwent both PET/CT-guided targeted biopsy and iliac crest biopsy; 4 patients underwent PET/CT-targeted biopsy without iliac crest biopsy. PET/CT results led to classification of bone lesions as isolated (16/5.4%), multifocal (≥ 2 lesions, 67/22.4%), diffuse (homogeneous uptake for the entire axial skeleton; 52/17.4%), or negative (64/54.8%). ^{18}F -FDG PET/CT identified focal and diffuse bone marrow involvement with a sensitivity of 48% and 56%, respectively, when only positive iliac crest biopsy was used as the reference standard. Corresponding specificities were 70% and 83%. Lesions in 3 of 30 patients (10.0%) with focal lesions on PET/CT were found to be false-positive by targeted bone marrow biopsy, and lesions in 25 of 30 patients (83.3%) with focal lesions on PET/CT were found to be false-negative by iliac crest biopsy. The authors concluded that it would be “insufficient” to evaluate bone marrow

involvement in newly diagnosed lymphomas using both ^{18}F -FDG PET/CT and routine iliac crest biopsy and that ^{18}F -FDG PET/CT imaging should be performed before bone marrow biopsy. They added that “in focal bone lesions, PET/CT-guided targeted bone marrow biopsy may complement the results of possible false-positive PET/CT and false-negative iliac crest biopsy findings” but that “in diffuse and negative lesions, iliac crest biopsy cannot be safely omitted.”

BMC Cancer

PET and MTV in Hypopharyngeal Cancer

Okazaki et al. from Saiseikai Nakatsu Hospital and Osaka City University Graduate School of Medicine (both in Osaka, Japan) reported on December 7 ahead of print in *Head & Neck* on a retrospective study designed to assess the utility of pretreatment PET and the metabolic volumes of the primary tumor and lymph nodes in advanced hypopharyngeal cancer. The retrospective study included 61 individuals with advanced disease who underwent ^{18}F -FDG PET imaging before treatment with definitive radiation therapy. Analysis of results indicated that the metabolic tumor volumes of primary tumors were significantly related to local control rates and overall survival. In individuals with lower primary tumor metabolic volumes, the metabolic volumes of metastatic lymph nodes were significantly related to disease-specific and overall survival.

Head & Neck

PET/CT in Nodal Staging of Breast Cancer

In an article in the December issue of *Anticancer Research* (2018;38:6639–6652) Orsaria et al. from Tor Vergata University Hospital (Rome, Italy) reported on the use of ^{18}F -FDG PET/CT for axillary nodal staging of breast cancer. The study included 50 women with early primary unilateral, locally advanced, or recurrent invasive operable disease. After preoperative PET/CT imaging, results were compared with histopathologic and immunohistochemical

analyses of both primary and recurrent resected axillary lymph nodes. The sensitivity, specificity, overall accuracy, and positive and negative predictive values of PET/CT for axillary lymph node staging were 87%, 90%, 88%, 93%, and 82%, respectively. Pathology analyses showed strong relationships between primary tumor SUV and nuclear grade, progesterone receptor expression, Ki-67 index, and local relapse. High SUVs in axillary lymph nodes correlated significantly with higher nuclear grade score, estrogen receptor negativity, progesterone receptor negativity, high Ki-67 index, lymph node metastasis, basal tumors, and locoregional recurrence. The authors concluded that “PET/CT is a reproducible, noninvasive imaging modality that is useful for evaluating a primary breast cancer mass and its relationship with metastatic axillary lymph nodes, thereby predicting tumor behavior and guiding clinical practice.”

Anticancer Research

FDG PET/CT and Advanced Renal Cell Carcinoma

Pankowska et al. from the Oncology Centre and the Collegium Medicum of Nicolaus Copernicus University (both in Bydgoszcz, Poland) reported on November 28 ahead of print in *Clinical and Experimental Medicine* on an evaluation of ^{18}F -FDG PET/CT as a prognostic marker for survival in patients with advanced renal cell carcinoma. The study included 121 patients with stage IV disease and multifocal metastases. The assessment metric was the highest SUV measurement (SUV_{max}) in each patient in a single examination. SUV_{max} values across all patients had a median of 6.9 (range, 1.3–30.0). SUV_{max} was then compared with several clinical risk factors routinely used in prognosis. Patients were followed up at a median of 19 mo (range, 3–61 mo), at which point higher SUV_{max} was found to be correlated with poorer prognosis. Additional analyses showed that SUV_{max} was an independent factor for overall survival: for $\text{SUV}_{\text{max}} < 7.0$, the median was 32 mo, and for $\text{SUV}_{\text{max}} \geq 7.0$ but

< 12.0 , the median was 12.5 mo. For $\text{SUV}_{\text{max}} \geq 12.0$, median overall survival was 10 mo. The authors concluded that “a preliminary SUV_{max} assessment conducted using FDG PET/CT can provide information useful in the prediction of survival of patients with advanced renal cell carcinoma.”

Clinical and Experimental Medicine

Imaging ^{223}Ra Response in mCRPC

In an article published in a supplement to the November issue of *Asia-Pacific Journal of Clinical Oncology* (2018;14[suppl 5]:16–23), Iizuka from Tokyo Women’s Medical University (Japan) provided preliminary reporting on interim assessment of response to ^{223}Ra using bone scintigraphy and ^{18}F -FDG PET/CT to explore possibilities for targeted α therapy monitoring and response evaluation in metastatic castration-resistant prostate cancer (mCRPC). The author noted that in the Alpharadin in Symptomatic Prostate Cancer Patients trial (now complete with >900 patients enrolled, bone scintigraphy was used to detect lesions (osteoblastic bone metastases) and CT was used to exclude visceral metastases, with no interim imaging until ^{223}Ra treatment completion unless clinically indicated. In this case, the author looked at interim evaluations using PET/CT and found that earlier response showed discrepancies between bone scintigraphy and PET/CT in patterns of bone lesions observed, with more lesions detected by PET/CT. These early results suggested that the additional lesions detected by PET/CT could represent bone marrow metastases not effectively targeted by ^{223}Ra , with a conclusion that “although the clinical significance of the discordance requires further clarification, it makes sense to consider ^{223}Ra early on in the course of mCRPC, when marrow involvement is minimal, so as to optimize treatment outcomes.”

Asia-Pacific Journal of Clinical 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 November and December. In an article in *Lancet Oncology* (2018;19[12]:e696–e708) Fanti, from the University of Bologna (Italy), and coauthors from a large consortium of university and clinical centers in Italy, the UK, Spain, Germany, France, Switzerland, Australia, Belgium, and The Netherlands reported on a

“Consensus on molecular imaging and theranostics in prostate cancer.” Dos Santos and colleagues from the Universidade Federal do Rio de Janeiro and the D’Or Institute for Research and Education (both in Rio de Janeiro, Brazil) summarized “The contribution of endogenous modulatory systems to TMS- and tDCS-induced analgesia: Evidence from PET studies” in the November 13 issue of *Pain Research and Management* (2018: 2368386). In an article e-published on November 22 ahead of print in the *International Journal of Molecular Sciences*, Femminella and colleagues from Imperial College London

(UK), the University of Molise (Campobasso, Italy), Federico II University of Naples (Italy), and the Istituti Clinici Scientifici Maugeri SPA–Società Benefit (Telese Terme, Italy) presented “Imaging and molecular mechanisms of Alzheimer’s disease: A review.” Press and colleagues from Emory University and the Georgia Institute of Technology (both in Atlanta, GA) reviewed “The role of standard and advanced imaging for the management of brain malignancies from a radiation oncology standpoint,” which was e-published on December 11 ahead of print in *Neurosurgery*.

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expertise in quantitative imaging to measure radionuclide uptake, retention, and clearance for dosimetry and treatment planning does not exist or may not be functional at an expert level at many medical institutions.” To support development of this expertise, SNMMI and the Intersocietal Accreditation Commission (IAC) are discussing strengthening the IAC nuclear medicine/PET accreditation program for radionuclide therapy by increasing clinical expertise on the existing IAC Nuclear Medicine/PET Board and by delineating standards for nuclear therapy. The groups’ overall goal is to increase

positive outcomes by standardizing therapy approaches across medical centers. SNMMI is also exploring collaborations with other organizations on quality and standards for therapy practice. All these efforts will ensure the highest quality and value of nuclear medicine therapy for patients who suffer from cancer and related medical conditions.

At the 2019 Annual Meeting, SNMMI will for the first time recognize the “Therapy of the Year.” SNMMI will continue to widen its efforts to support nuclear medicine therapy and theranostics in upcoming years.