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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/MR and GTVs in Cervical Cancer

In an article e-published on February 18 ahead of print in the *International Journal of Gynecological Cancer*, Zhang et al. from the Shengjing Hospital of China Medical University (Shenyang) reported on a study comparing gross tumor volumes (GTVs) as assessed by the PET and MR components of hybrid PET/MR in patients with cervical cancer. The study included 27 women who underwent PET/MR before scheduled radiotherapy for cervical cancer. GTVs were outlined manually on T2-weighted images and autocontoured using a 40% maximum standardized uptake value threshold on PET. Despite significant correlation between GTVs on PET and MR imaging, PET GTVs were smaller than MR GTVs in 23 of 27 tumors. For analysis, results were assigned to groups according to MR GTVs: (a) $<$14 mL (n = 6); (b) 14–62 mL (n = 12); and (c) $\geq$62 mL (n = 9). For group a, the mean MR GTV, PET GTV, ratio, and overlap between MR and PET GTVs were 9.6 mL, 16.7 mL, 0.77, and 0.47, respectively. PET overestimated MR GTV in 4 of the 6 lesions by a mean of 11.1 mL. For group b, the mean MR GTV, PET GTV, ratio, and overlap between MR and PET GTVs were 38.6 mL, 24.9 mL, 1.54, and 0.87, respectively. PET underestimated MR GTV for 12 tumors by a mean of 13.7 mL. For group b, the mean MR GTV, PET GTV, ratio, and overlap between MR and PET GTVs were 85.9 mL, 54.3 mL, 1.61, and 0.87, respectively. PET underestimated MR GTV in 9 tumors by a mean of 31.6 mL. The authors summarized their findings that GTVs were assessed differently by MR and PET in PET/MR imaging of cervical cancer and noted that a higher degree of overlap was seen in larger tumors.

International Journal of Gynecological Cancer

Incidental Prostate ^{18}F-FDG Uptake

Seino et al. from Hirosaki University Graduate School of Medicine (Japan) reported on February 4 ahead of print in *Oncology Reports* on a study designed to determine whether maximum standardized uptake values (SUV_{max}) provide indications of malignancy or benign states in incidental prostate uptake on ^{18}F-FDG PET imaging. The study included the records of 3,236 men who underwent ^{18}F-FDG PET/CT imaging at a single academic medical center over a 4-y period. Final diagnoses were based on serum prostate-specific antigen levels, biopsy, imaging studies, and clinical follow-up. These were correlated with PET findings. Incidental ^{18}F-FDG uptake in the prostate was observed in 53 (2%) individuals, with 4 excluded for insufficient clinical and follow-up data. Of the 49 remaining cases included as the study population, 8 (16%) had prostate cancer and 41 (84%) had benign findings. PET in all 8 of the patients with malignancies showed high uptake in all prostate zones but with no coexistence of calcification and tracer uptake. In the 41 benign cases, tracer location varied, with 19 individuals having high uptake in the inner zone, 17 in the peripheral zone, and 5 in both zones. In 18 patients (44%), ^{18}F-FDG uptake was present along with prostatic calcification. The authors concluded that although incidental prostate ^{18}F-FDG uptake does not usually indicate prostate cancer, "FDG uptake not coexisting with calcification indicates the possibility of prostate cancer and should be included in the differential diagnosis for performing other clinical examinations."

Oncology Reports

PET/CT and Burkitt Lymphoma

In an article e-published on February 12 in the *European Journal of Haematology*, Carrillo-Cruz et al. from the Instituto de Biomedicina de Sevilla/CSIC/Universidad de Sevilla (Spain) reported on the role of ^{18}F-FDG PET/CT in the management of newly diagnosed Burkitt lymphoma and in evaluation of disease after first-line chemotherapy. The retrospective study included images acquired in 32 patients (a total of 52 images: 20 at diagnosis, 27 after treatment, 5 to monitor residual disease). PET/CT results were compared with those from contrast-enhanced CT, and in the 17 patients for whom both imaging studies were acquired at diagnosis, discrepancies (the majority in extranodal sites) were found in 64.7%. In the 13 patients who underwent both imaging studies for treatment response, 38% had residual masses detected by CT with negative PET/CT. In the 27 patients who underwent posttreatment PET/CT, 22 had complete responses, with 1 true-positive and 4 false-negative findings. Over a median follow-up of 27 months, no relapses were seen in the patients with negative PET/CT findings (negative predictive value, 100%). For 4 patients with false-positive lesions after treatment, mean maximum standardized uptake values (SUV_{max}) at nodal sites posttreatment averaged 4.1 compared with 14.9 at diagnosis and at extranodal sites averaged 3.8 at posttreatment compared with 12.1 at

diagnosis (positive predictive value of 100% with a cutoff value <66% of SUV_{max} at diagnosis). The authors concluded that in patients with Burkitt lymphoma "more accurate staging can be achieved by using PET/CT," pointing to the high negative and positive predictive values.

European Journal of Haematology

PET in Neurofibromatosis Complication

Combemale et al. from the Léon Bérard Comprehensive Cancer Center (Lyon, France), Henri Mondor Hospital (Créteil, France), and Saint Eloi University Hospital (Montpellier, France) reported on February 6 in the online journal *PLoS One* (2014;9:e85954) on evaluation of a semiquantitative index for ^{18}F-FDG PET diagnosis of malignant peripheral nerve sheath tumors in neurofibromatosis type 1. The retrospective study included 113 such patients (63 men, 50 women) with 145 tumors imaged over a period from 2000 to 2012. Prior to 2004, a semiquantitative metric (uptake ratio between tumor and normal liver [T/L]) was used. When maximum standardized uptake values (SUV_{max}) from dedicated PET became available, both the T/L and SUV_{max} were documented. A total of 65 suspected lesions had T/L $\geq$ 1.5; of these, 40 were found to be malignant peripheral nerve sheath tumors and 25 were benign. A total of 80 tumors had T/L <1.5; of these, 79 were found to be benign neurofibromas at pathology or follow-up. The 1.5 T/L cutoff yielded negative and positive predictive values of 98.8% and 61.5%, with 97% sensitivity and 76% specificity. No significant correlation was found between malignancy and absolute tumor SUV_{max} in the dedicated PET/CT data acquired on later patients. The authors concluded that the semiquantitative T/L index with a cutoff of 1.5 allowed more sensitive and specific differentiation of malignant from benign tumors than did SUV_{max} and also was more reproducible and not as user dependent.

PLoS One

Choline PET and Prostate Cancer Nodal Relapse

In an article e-published on February 8 ahead of print in the *Journal of Urology*, Jilg et al. from the University of Freiburg (Germany) and University Ulm (Germany) reported on a study evaluating the diagnostic accuracy of choline-tracer PET/CT for nodal relapse of prostate cancer, with a focus on location and size of tumor infiltration in lymph nodes. The study included 72 men with nodal prostate cancer relapse after primary therapy who underwent pelvic and/or retroperitoneal salvage lymph node dissection after ^{11}C-choline or ^{18}F-fluoroethylcholine whole-body PET/CT imaging with results indicating lymph node disease but no other metastases. The accuracy of PET/CT was compared with postdissection analyses for 160 dissected lymph node regions (pelvic left/right, retroperitoneal), 498 subregions (common external and internal iliac, obturatoria, presacral, aortic bifurcation, aorta, caval, and interaortocaval), and 2,122 lymph nodes. Metastases were found in 32% of resected lymph nodes (238 positive subregions and 111 positive regions). PET/CT was positive for 209 subregions and 110 regions, with resulting region-based sensitivity, specificity, positive and negative predictive values, and accuracy of 91.9%, 83.7%, 92.7%, 82.0%, and 89.4%, respectively. The respective subregion-based figures were 80.7%, 93.5%, 91.9%, 84.1%, and 87.3%, and lesion-based figures were 57.0%, 98.4%, 94.5%, 82.6%, and 84.9%, respectively. More than 70% (278/393) of true-positive metastases detected by PET/CT were located in lymph nodes with a short-axis diameter <10 mm. The sensitivity of choline-tracer PET/CT was 13.3%, 57.4%, and 82.8% for tumor infiltration depths of $\geq$2–<3, $\geq$5–<6, and $\geq$10–<11 mm, respectively. The location of lymph node metastases and choice of ^{11}C- or ^{18}F-labeled radiotracer had no significant effect on diagnostic accuracy. The authors concluded that choline-tracer PET/CT "detects affected lymph node regions...in prostate cancer relapse with high accuracy and seems helpful for guiding salvage lymph node dissection." They added that the sensitivity of this imaging approach appears to decrease with the size of metastatic infiltration in lymph nodes and also that the approach detects metastases in a significant fraction of lymph nodes that are not enlarged on CT.

Journal of Urology

REM Sleep Behavior Disorder and DLB

Chiba et al. from the Juntendo Tokyo Koto Geriatric Medical Center (Japan) and Yokohama City University School of Medicine (Japan) reported in the February issue of *Psychiatry and Clinical Neurosciences* (2014;68:137–144) on a study using PET to assess the association between patterns of glucose hypometabolism in the primary visual cortex and clinical variables in dementia with Lewy bodies (DLB). The study included 27 DLB patients who underwent ^{18}F-FDG PET imaging. The researchers compared demographic and clinical data between patients with and without glucose hypometabolism in the primary visual cortex. The only distinguishing factor between the 2 groups was onset age of probable rapid eye movement sleep behavior disorder, with earlier onset seen in patients with hypometabolism. The authors concluded that glucose hypometabolism in the primary visual cortex provides a potential mechanism for the link between antecedent rapid eye movement sleep behavior disorder and subsequent development of clinical symptoms in DLB patients. They added that this metabolic pattern may represent the effect of the pathophysiologic process of DLB on the sleep disorder rather than a distinct condition in DLB disease progression.

Psychiatry and Clinical Neurosciences

PET and Sensitivity to Stress

In an article e-published on February 3 in *Frontiers in Human Neuroscience*, Mirrione et al. from the Brookhaven National Laboratory (Upton, NY), Stony

Brook University (NY), and the Icahn School of Medicine (New York, NY) reported on a study in rats in which PET assessment of metabolic activity in uncontrollable stress was correlated with subsequent ability to respond effectively to stressful situations. The authors used ^{18}F-FDG PET imaging to assess metabolic activity in wild-type Sprague Dawley rats during "uncontrollable, inescapable, unpredictable foot-shock stress." Rats were subsequently reimaged during controllable, escapable, predictable foot-shock stress. When the 2 sets of images were correlated, the degree to which rats failed to escape shocks in the retest was correlated with increased metabolic activity in the lateral septum and habenula. This metabolic activity in the habenula correlated with activity in the lateral septum, hypothalamus, medial thalamus, mammillary nuclei, ventral tegmental area, central gray, interpeduncular nuclei, periaqueductal gray, dorsal raphe, and rostromedial tegmental nucleus, caudal linear raphe, and subiculum transition area. Activity in the lateral septum correlated with metabolic activity in the preoptic area, medial thalamus, habenula, interpeduncular nuclei, periaqueductal gray, dorsal raphe, and caudal linear raphe. The authors concluded that these data "suggest a group of brain regions involved in sensitivity to uncontrollable stress involving the lateral septum and habenula" and discussed the potential relevance of these findings for other "learned helplessness" behaviors.

Frontiers in Human Neuroscience

PET in Carotid and Femoral Plaques

Shaikh et al. from the University of Aberdeen/Aberdeen Royal Infirmary (UK) reported in the March issue of the *British Journal of Surgery* (2014;101:363–370) on a comparison of ^{18}F-FDG uptake on PET in carotid plaques in patients who had experienced a recent thromboembolic cerebrovascular event with similar uptake in femoral artery plaques from patients with leg ischemia and to investigate the correlation of tracer uptake with M1 and M2 macrophages present in the plaques. The study included patients who underwent carotid endarterectomy for significant symptomatic carotid stenosis and patients with severe leg ischemia and significant stenosis of the common femoral artery. All patients underwent ^{18}F-FDG PET imaging, and resected tissues underwent histologic analyses. A total of 29 carotid and 25 femoral artery plaques were included in the study. The maximum dynamic uptake was similar in carotid and femoral plaques, whereas CD68 macrophage counts were significantly increased in carotid plaques, as were M1 proinflammatory macrophages. The extent of carotid stenosis was correlated with maximum dynamic ^{18}F-FDG uptake. The authors added that in patients on statin therapy, tracer uptake was seen in areas of significant arterial stenosis, regardless of degree of inflammation.

British Journal of Surgery

Patient Interests and PET in Routine Surveillance

In an article e-published on February 18 ahead of print in *Cancer Epidemiology, Biomarkers, and Prevention*, Tan et al. from the University of Pennsylvania and the Hospital of the University of Pennsylvania (Philadelphia), the Dana–Farber Cancer Institute (Boston, MA), and the Massachusetts General Hospital (Boston) reported on a study looking at the connection between information seeking by patients with colorectal, breast, and prostate cancers and utilization of PET imaging for routine surveillance. A total of 944 patients with nonmetastatic disease were surveyed about their experience with PET for routine surveillance and the extent to which they had sought cancer-related information from both nonmedical sources and from providers. Over a 12-mo period several years after diagnosis, 11% of patients reported having undergone PET imaging at least once. The process of consulting nonmedical sources for cancer-related information was associated with more reported PET imaging. Patient interactions with physicians, including queries about cancer-related information, were not significant predictors of PET imaging during this period. The authors concluded that "exposure to cancer-related information through mass media and lay interpersonal sources may be driving inappropriate utilization of high-cost advanced imaging procedures."

Cancer Epidemiology, Biomarkers, and Prevention

PET/CT and SPECT/CT in Osteomalacia

Jadhav et al. from the KEM Hospital (Mumbai, India) reported on February 14 ahead of print in *Clinical Endocrinology* on a retrospective study assessing the relative performance of 3 imaging approaches (^{18} F-FDG PET/CT, ^{99m}Tc-labeled hydrazinonicotinyl-Tyr3-octreotide [^{99m}Tc-HYNIC-TOC] SPECT/CT, and ^{68}Ga-DOTATATE PET/CT) in tumor localization in patients with primary tumor–induced osteomalacia. The study included the records of 9 patients, each of whom had undergone imaging with at least 2 of the approaches under analysis. Positive findings were noted in 50% of patients with ^{18}F-FDG PET/CT (8 patients imaged), 100% with ^{99m}Tc-HYNIC-TOC SPECT/CT (6 patients imaged), and 100% with ^{68}Ga-DOTATATE PET/CT (7 patients imaged). Six patients underwent both ^{99m}Tc-HYNIC-TOC SPECT/CT and ^{68}Ga-DOTATATE PET/CT, and coregistered imaging results correlated closely. The authors concluding observation, based on this small-group study, was that somatostatin receptor–based functional scans performed better than ^{18}F-FDG PET/CT in tumor localization in primary tumor–induced osteomalacia.

Clinical Endocrinology

Pancreatic Metabolism and Obesity

In an article e-published on February 14 ahead of print in the *Journal of Clinical Endocrinology and Metabolism*, Honka et al. from the University of Turku (Finland), the University of Kagawa (Japan), the University of Tampere (Finland), and the National Research Council (Padua and Pisa, Italy) reported on a 2-part PET study

designed to determine whether pancreatic metabolism and blood flow are altered in obesity. In translational studies, PET and MR imaging using ^{18}F-FDG, a palmitate analog (^{18}F-FTHA), and ^{15}O-H_2O were performed in rodents and pigs to validate assessment of pancreatic metabolism. The subsequent clinical study included 52 morbidly obese and 25 healthy age-matched individuals in whom pancreatic glucose/fatty acid uptake, fat accumulation, and blood flow were assessed along with markers of β-cell function. Obese individuals were found to have elevated pancreatic fatty acid uptake, more fat accumulation, lower glucose uptake both during fasting and euglycemic hyperinsulinemia, and blunted blood flow in the pancreas compared with healthy participants. Blood flow, fatty acid uptake, and fat accumulation were negatively associated with multiple markers of β-cell function. In addition to concluding that PET is a feasible method for measuring pancreatic metabolism, the authors concluded that "obesity leads to change in pancreatic energy metabolism with a substrate shift from glucose to fatty acids." They added that in morbidly obese individuals, "impaired pancreatic blood flow may contribute to β-cell dysfunction and in the pathogenesis of type 2 diabetes."

Journal of Clinical Endocrinology and Metabolism

RIT, NHL, and ASCT

Gopal et al. from the University of Washington and the Fred Hutchinson Cancer Research Center (Seattle) reported on February 11 ahead of print in *Biology of Blood and Marrow Transplantation* on a study of augmentation of myeloablative doses of ^{131}I-tositumomab radioimmunotherapy with concurrent fludarabine and autologous stem cell transplantation (ASCT) in older patients with B-cell non-Hodgkin lymphoma (NHL). The study included 36 patients (median age, 65 y) with high-risk, refractory, or relapsed NHL and an average of 2 (range, 1–9) previous regimens (12 patients had chemoresistant disease). Per standards of care, infusions of ^{131}I-tositumomab were derived from individualized organ-specific absorbed dose estimates delivering ≤27 Gy to critical organs. Fludarabine was initiated 72 h after infusion, followed by ASCT. Dose-limiting organs in this patient group included lung (n = 30), kidney (n = 4), and liver (n = 2), with median administered ^{131}I activity of 471 mCi (range, 260–1,620 mCi). After determining tolerance, fludarabine was escalated to 30 mg/m^2 for 7 d. The researchers found that engraftment was prompt, with no early treatment-related deaths, and only 2 patients with ≥grade 4 nonhematologic toxicities. Over a median follow-up of 3.9 y, estimated overall survival, progression-free survival, and nonrelapse mortality were 54%, 53%, and 7%, respectively. The authors concluded that "fludarabine up to 210 mg/m^2 can be safely delivered with myeloablative ^{131}I-tositumomab and ASCT in older adults with B-cell NHL."

Biology of Blood and Marrow Transplantation

PET/CT in Low-Grade Serous Ovarian Cancer

In an article e-published on February 14 ahead of print in *Gynecologic Oncology*, Takeuchi et al. from the University of Texas MD Anderson Cancer Center (Houston, TX) reported on the usefulness of ^{18}F-FDG PET/CT monitoring after initial treatment in patients with low-grade serous ovarian carcinoma. The retrospective study included 48 such patients (39 with recurrent disease, 9 without) who had undergone a total of 91 ^{18}F-FDG PET/CT scans during follow-up after primary treatment. Twenty-seven of these scans (30%) had an effect on management planning. Sensitivity, specificity, and accuracy in detection of disease recurrence were 94%, 100%, and 97%, respectively, for ^{18}F-FDG PET/CT. The respective figures were 89%, 95%, and 93% for CT imaging and 68%, 89%, and 73% for serum CA-125 tests. Survival after recurrence was poorer in patients with total lesion glycolysis values >67.7 g. The authors concluded that "^{18}F-FDG PET/CT may provide useful information during the follow-up of patients with low-grade serous ovarian carcinoma after initial treatment" and that total lesion glycolysis may be a useful predictor of survival after recurrence.

Gynecologic Oncology

Thyroglossal Tract Thyroid Tissue and ^{131}I Ablation Therapy

Barber et al. from Monash University (Melbourne, Australia) reported on January 31 ahead of print in *Clinical Endocrinology* on a study of the incidence of thyroglossal tract thyroid tissue on SPECT/CT after ^{131}I ablation therapy and total thyroidectomy for thyroid cancer. The study included 83 patients after total thyroidectomy and initial ^{131}I ablation who underwent whole-body planar and SPECT/CT imaging of the neck. Thyroglossal tract thyroid tissue was defined as radioactive tissue in the anterior neck, superior to the thyroid bed and in close proximity to the midline without evidence of localization to lymph nodes. After localization by SPECT/CT, neck regional activity was quantified on planar imaging. On review of both images for each patient, results were categorized as positive, negative, or equivocal. Thyroglossal tract thyroid tissue was identified in 39 (47%) patients on SPECT/CT. In these patients, this tissue contributed to a median of 49% of total neck activity. The authors concluded that "given the high prevalence of this tissue, our results suggest that total neck ^{131}I activity on planar imaging may not be suitable to assess the completeness of thyroid bed surgery."

Clinical Endocrinology

Calcium Score vs. CT Angiography

In an article in the March issue of *Atherosclerosis* (2014;233:190–195), Hulten et al. from the Brigham and Women's Hospital (Boston, MA), Walter Reed National Military Medical Center (Bethesda, MD), Massachusetts General Hospital (Boston), and Baptist Health South Florida (Miami) reported on a study designed to compare the prognostic value of coronary artery calcium (CAC) scoring and coronary CT angiography in identification

of obstructive coronary artery disease (CAD) in symptomatic patients. The study included 1,145 patients (mean age, 55 ± 12 y) without prior CAD who underwent both CCTA and CAC scoring, and accuracy and prognostic value for major adverse cardiac events were compared. A total of 406 (35%) patients were normal on CCTA, 454 (40%) had <50% stenosis, and 285 (25%) had ≥50% stenosis. CAC was zero in 483 (42%), 395 (82%) of whom had normal CCTA, 81 (17%) <50% stenosis, and 7 (1.5%) ≥50% stenosis. Two (0.4%) of these 7 patients had ≥70% stenosis. No major adverse cardiac events were noted in these 7 patients over a follow-up of 2 y. For diagnosis of ≥50% stenosis CAC was found to have a sensitivity of 98% and specificity of 55%. The authors summarized their findings that "among symptomatic patients with CAC zero, a 1%–2% prevalence of potentially obstructive CAD occurs, although this finding was not associated with future coronary revascularization or adverse prognosis within 2 years."

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in January and February. In an article e-published on February 10 ahead of print in *Laryngoscope*, Johnson and Branstetter from the University of Pittsburgh School of Medicine (PA) summarized "PET/CT in head and neck oncology: state-of-the-art 2013." Mehta et al. from the Yale School of Medicine (New Haven, CT) reported on February 10 ahead of print in *Thyroid* on "Improving the quality of thyroid cancer care: how does the Thyroid Cancer Care Collaborative cross the Institute of Medicine's quality chasm?" Shindo et al. from Oregon Health and Science University (Portland) provided on January 28 ahead of print in *Head and Neck* an overview of "Management of invasive well-differentiated thyroid cancer: an American Head and Neck Society consensus statement." In an article in the February issue of *Anticancer Research* (2014;34:585–592), Nogami et al. from Keio University (Tokyo, Japan) reviewed the "Application of FDG-PET in cervical cancer and endometrial cancer: utility and future prospects." Navarro-Pelayo Láinez et al. from Hospital Universitario Virgen de las Nieves (Granada, Spain) discussed "The role of positron emission tomography/computed tomography imaging with radiolabeled choline analogues in prostate cancer" in an article e-published on February 15 ahead of print in *Actas Urologicas Españolas.* In an article in the February issue of *Alzheimer's & Dementia* (2014;10:S55–S61), Femminella and Edison from the Imperial College London (UK) provided a detailed "Evaluation of neuroprotective effect of glucagon-like peptide 1 analogs using neuroimaging."