

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.

Chemotherapy and SUV in Colorectal Cancer

In an article published in the May issue of *Gut and Liver* (2014;8:254–264), Lee et al. from Seoul National University Hospital and College of Medicine (Korea) reported on a retrospective study designed to assess associations between recent chemotherapy and maximum standardized uptake values (SUV_{max}) on ¹⁸F-FDG PET/CT in patients with colorectal cancer. The study included the records of 509 patients (401 not treated with chemotherapy before surgery and 108 treated with chemotherapy within 6 mo before surgery). Average SUV_{max} was found to be significantly lower in patients treated with chemotherapy than in those not treated, with this association also holding true within groups with the same pathologic staging of disease. The difference in sensitivity with and without chemotherapy was greatest using an SUV_{max} cutoff value of 6.4. SUV_{max} in primary tumor was not found to be an independent predictor of lymph node metastasis. The authors concluded that information about previous chemotherapy should be

taken into account in ¹⁸F-FDG PET imaging interpretation in colorectal cancer.

Gut and Liver

Pretherapy ¹²⁴I PET and Prediction in DTC

Khorjekar et al. from MedStar Washington Hospital Center (DC) reported on May 12 ahead of print in *Thyroid* on a retrospective study on management in differentiated thyroid cancer (DTC) designed to determine whether negative ¹²³I pretherapy PET imaging in patients with elevated thyroglobulin levels after negative ¹³¹I or ¹²³I imaging can successfully predict negative ¹³¹I posttherapy imaging results. The authors used data from an existing database comparing ¹²⁴I PET and ¹³¹I planar imaging in patients with proven DTC, who were suspected of having metastatic DTC on the basis of laboratory and clinical findings and who underwent both ¹³¹I planar and ¹²⁴I PET imaging. A subgroup of 12 patients was identified who had elevated thyroglobulin, negative diagnostic ¹³¹I/¹²³I scan and ¹²⁴I PET imaging, radioiodine therapy, a posttherapy ¹³¹I scan, and previous ¹³¹I therapy with a subsequent positive post-¹³¹I therapy scan. Foci of uptake were categorized by experienced readers as positive for thyroid tissue/metastases or physiologic. Ten (83%) patients had positive foci on ¹³¹I posttherapy imaging, leading the authors to note that ¹³¹I posttherapy scans are often positive in patients with elevated serum thyroglobulin levels, despite negative diagnostic ¹³¹I or ¹²³I scan and negative ¹²⁴I PET imaging. They concluded that a “negative ¹²⁴I PET scan in a patient with elevated serum thyroglobulin level, negative diagnostic ¹³¹I planar scan, and whose prior post ¹³¹I therapy scan was positive will have a low predictive value for a negative post ¹³¹I therapy scan and should not be used to exclude the option of a ‘blind’ ¹³¹I therapy.”

Thyroid

PET/CT-Guided Biopsies in Skull Base Lesions

In an article e-published on May 12 ahead of print in *Head & Neck*, Dubach et al. from the University of Bern (Switzerland) and the University of Leipzig (Germany) reported on the use of an optically tracked navigation system for multimodal image-guided biopsies in follow-up of difficult-to-evaluate but PET-positive lesions. The focus of the study was in 7 patients with suspected persistence or recurrence of skull base carcinoma, including sinonasal ($n = 3$), nasopharyngeal ($n = 1$) adenocarcinoma ($n = 2$), and carcinoma of unknown primary origin ($n = 1$). Histologic studies on resected material confirmed local persistent or recurrent malignant disease ($n = 5$), radioosteonecrosis ($n = 1$), and super infection ($n = 1$). The authors concluded that ¹⁸F-FDG PET/CT-navigated biopsies may be useful, especially “if functional anomalous areas in FDG PET/CT do not cause structural alterations in MRI/CT and if endoscopic visualization is impossible because of posttreatment alterations.”

Head & Neck

Isthmocervical SLN Labeling and SPECT/CT

Mücke et al. from the Hannover Medical School (Germany) reported on May 10 ahead of print in *Gynecologic Oncology* on the clinical feasibility of transcervical subepithelial injection into the isthmocervical region of the myometrium, a novel injection technique for sentinel lymph node (SLN) detection in endometrial carcinoma. The authors compared SLN detection using this technique with SPECT/CT and with lymphoscintigraphy. The study included 31 women with endometrial carcinoma. Each patient received a transcervical injection of 10 MBq ^{99m}Tc-nanocolloid into the isthmocervical myometrium (with no anesthesia), followed 30–60 min later by lymphoscintigraphy and SPECT/CT imaging. Patent blue was administered before surgery. The

number and location of SLNs detected on imaging were compared with intraoperative and histopathologic results. The transcervical injection technique resulted in high intraoperative detection rates (90.3%), with 57% of identified SLNs being pelvic bilateral and 25% para-aortic. SPECT/CT was significantly better at identifying SLNs than lymphoscintigraphy. In those cases in which SLNs were identified in 1 hemipelvis, histologic evaluation of the SLN correctly predicted lymph node metastases for this basin (sensitivity, 100%; negative predictive value, 100%; false-negatives, 0%). The authors noted that transcervical SLN marking in combination with SPECT/CT is easily applicable and, for SLN dissection, “may be a safe and feasible staging technique for clinical routine in endometrial cancer.”

Gynecologic Oncology

SPECT/CT SUVs in Sacroiliac Joint Dysfunction

In an article e-published on May 17 ahead of print in the *European Spine Journal*, Tofuku et al. from the Imakiire General Hospital (Kagoshima, Japan) evaluated the utility of SPECT/CT in the diagnosis of sacroiliac joint dysfunction. The study included 32 patients (10 men, 22 women) with severe dysfunction who had failed to respond to 1 y of conservative treatment and who scored >4 points on a 10-cm visual analog scale. Each patient underwent separate ^{99m}Tc -methylene diphosphonate SPECT and CT imaging. The imaging sets were coregistered, and CT attenuation correction was applied. All patients with severe sacroiliac dysfunction were found to have tracer accumulation, with standardized uptake values (SUVs) >2.2 (mean SUV = 4.7). Nineteen patients' symptoms were lateralized, and in these patients mean SUVs in the symptomatic side were significantly higher than those on the less or nonsymptomatic side. In patients with no lateralization, differences in SUVs between sides were minimal. In addition, patients with higher levels of tracer accumulation had greater symptom severity and progressed to more advanced treatments. The authors concluded that

“SPECT/CT may be a suitable supplementary diagnostic modality for sacroiliac joint dysfunction as well as a useful technique for predicting the prognosis of this condition.”

European Spine Journal

^{15}O - H_2O PET and Myocardial Perfusion Impairment

Danad et al. from the VU University Medical Center (Amsterdam, The Netherlands) reported on April 29 ahead of print in the *European Heart Journal* on subendocardial perfusion measurement and quantification of the transmural perfusion gradient (TPG) in myocardial ischemia using ^{15}O - H_2O PET as a means for characterizing coronary artery disease. The study included 66 patients with chest pain who underwent ^{15}O - H_2O PET imaging and determination of fractional flow reserve in all coronary arteries, followed by invasive coronary angiography. A total of 30 (45%) patients had fractional flow reserve ≤ 0.80 and were diagnosed with coronary artery disease. Out of 198 individual vessels analyzed, 53 (27%) showed a positive fractional flow reserve. Transmural hyperemic myocardial blood flow was $3.09 \pm 1.16 \text{ mL min}^{-1} \text{ g}^{-1}$ in non-ischemic myocardium and $1.67 \pm 0.57 \text{ mL min}^{-1} \text{ g}^{-1}$ in ischemic myocardium. The average TPG decreased during hyperemia and was lower in arteries with a positive fractional flow reserve. A TPG threshold of 0.94 yielded an accuracy to detect CAD of 59%, which was inferior to the 85% accuracy of transmural myocardial blood flow, with an optimal cutoff of $2.20 \text{ mL min}^{-1} \text{ g}^{-1}$. The diagnostic accuracy of subendocardial perfusion measurements was comparable with that of transmural myocardial blood flow. The authors concluded that because cardiac ^{15}O - H_2O PET imaging can distinguish subendocardial from subepicardial perfusion in myocardium of normal dimensions and because hyperemic TPG is significantly lower in ischemic myocardium, this technique “can potentially be employed to study subendocardial perfusion impairment in more detail.” They cautioned that the diagnostic accuracy of subendocardial hyperemic perfusion and TPG “appears

to be limited” compared with that of quantitative transmural myocardial blood flow.

European Heart Journal

^{18}F -FDG PET in Obstructive Sleep Apnea

In an article e-published on April 29 ahead of print in the *American Journal of Respiratory and Critical Care Medicine*, Kim et al. from the University of Pittsburgh (PA) used ^{18}F -FDG PET and MR imaging to evaluate metabolic activity in the tongue in patients with sleep apnea. The study was initiated on the basis of observations indicating that tongue electromyographic activity is increased in apneics and might be associated with a change in glucose uptake. The study included 30 obese control individuals and 72 obese individuals with sleep apnea. Each participant underwent ^{18}F -FDG PET imaging, MR imaging, and a standard overnight sleep study to determine an apnea-hypopnea index (AHI) value. Glucose uptake on PET was assessed as standardized uptake value (SUV) in upper airway tissues. The control participants had average AHI values of 4.7 ± 3.1 events/h. The corresponding figure for the participants with sleep apnea was 43.5 ± 2.8 events/h. The group with apnea had significantly less glucose uptake in the genioglossus than did controls, but no differences were found in SUVs in controls and apnea patients in the masseter, pterygoid, or in neck or submental fat deposits. The authors concluded that the reduction in glucose uptake in the tongue in patients with apnea was “likely secondary to alterations in tongue muscle fiber type or to chronic denervation” and “argues against the neuromuscular compensation hypothesis explaining the increase in tongue electromyographic activity in apneics.

American Journal of Respiratory and Critical Care Medicine

PET/MR Imaging in Cervical Cancer

Gruneisen et al. from University Hospital Essen, University Hospital

Duesseldorf, and University Duisburg-Essen (all in Germany) reported on May 7 in *PLoS One* (2014;9:e96751) on a study assessing the correlation of maximum standardized uptake value (SUV_{max}) from PET and minimum apparent diffusion coefficient (ADC_{min}) from MR in integrated imaging in primary and recurrent cervical cancer. The study included 19 women (mean age, 51.6 y; range, 30–72 y) with histopathologically confirmed primary cervical cancer ($n = 9$) or suspected tumor recurrence ($n = 10$), each of whom underwent integrated PET/MR imaging. Regions of interest were drawn in the images to assess SUV_{max} , and ADC parameter maps were constructed to determine ADC_{min} values. A total of 54 lesions (12 cervical cancer lesions, 42 lymph node metastases) were identified in 15 patients. Mean SUV_{max} (12.5 ± 6.5) and ADC_{min} ($644.5 \pm 179.7 \times 10^{-5}$ mm²/s) values for all assessed lesions showed a significant but weak inverse correlation. However, when lesions were categorized as either primary or recurrent tumors, SUV_{max} and ADC_{min} in primary tumors and associated primary lymph node metastases were found to have a strong and inverse correlation. No such correlation was found in recurrent lesions. The authors concluded that these initial results demonstrate “the high diagnostic potential of simultaneous PET/MR imaging for the assessment of functional biomarkers, revealing a significant and strong correlation of tumor metabolism and higher cellularity in cervical cancer lesions.”

PLoS One

PET/CT and Chemotherapy Outcomes in TNBC

In an article e-published on May 16 ahead of print in the *European Journal of Cancer*, Groheux and colleagues from the Saint-Louis Hospital (Paris), the Institut Curie (Paris), the University of Bordeaux, and INSERM (Brest) (all in France) reported on a study assessing the ability of ¹⁸F-FDG PET/CT to predict pathologic outcomes after neoadjuvant chemotherapy in women with triple-negative

breast cancer. The study included 50 such patients without distant metastases who underwent PET/CT imaging at baseline and after 2 courses of neoadjuvant chemotherapy. Changes in maximum standardized uptake values (SUV_{max}) were assessed between the 2 scans in primary tumor and lymph nodes, and these changes were correlated with pathologic response and event-free survival over a mean follow-up of 30.3 mo. After chemotherapy, results at surgery showed that 19 patients had experienced a pathologic complete response and 31 had residual tumor. Of these 31, 13 experienced relapse during follow-up. Change between PET scans in SUV_{max} in the primary tumor was the most predictive pathologic variable. A threshold of 42% decrease in SUV offered the most accurate prediction of event-free survival. Using this cut-off, 32 patients were metabolic responders and 18 were nonresponders. The pathologic complete response rates for responders and nonresponders were 59% and 0%, respectively. The corresponding 3-y event-free survival percentages were 77.5% and 47.1%, respectively. The authors concluded that “interim ¹⁸F-FDG can early predict the inefficacy of neoadjuvant chemotherapy in triple-negative breast cancer patients” and “shows promise as a potential contributory biomarker in these patients.”

European Journal of Cancer

General Neurology Diagnosis of PD

Joutsa et al. from the University of Turku and Turku University Hospital (Finland) reported on April 26 ahead of print in *Parkinsonism and Related Disorders* on the accuracy of general neurologists in diagnosing parkinsonism syndromes. The retrospective study included postmortem records of 111 patients who had received a clinical parkinsonism diagnosis during life and 122 patients who received a neuropathologic diagnosis of a parkinsonism syndrome after death, including 11 incidental cases. Of the 77 individuals who had received diagnoses of Parkinson disease, only 55 (75.3%) had such

diagnoses confirmed after death, yielding a sensitivity of clinical diagnosis for idiopathic Parkinson disease of 89.2% and specificity of 57.8%. For progressive supranuclear palsy the corresponding figures were 52.9% and 100%, respectively, and for multiple system atrophy were 64.3% and 99.0%, respectively. The authors concluded that despite significant improvements in diagnostic criteria and techniques, Parkinson disease is “heavily overdiagnosed by general neurologists, whereas parkinsonism plus syndromes are underdiagnosed,” and that the diagnostic accuracy for Parkinson disease remains relatively low, with as many as one-fourth of diagnoses being incorrect.

Parkinsonism and Related Disorders

PET and Treatment Response in Rectal Cancer

In an article e-published on May 7 ahead of print in *Annals of Surgical Oncology*, Memon et al. from the University of Melbourne (Parkville, Australia) reported on a systematic review of the literature on clinical studies assessing the role of ¹⁸F-FDG PET imaging in prediction of pathologic complete response in patients with resectable locally advanced rectal cancer. The inclusion criteria yielded 17 clinical studies for systematic review, including 7 that assessed postchemoradiation maximum standardized uptake values (SUV_{max}), 9 that assessed the response index for SUV_{max} , and 13 that looked at the correlation between PET assessment of treatment response and prediction of survival. The authors found that metabolic complete response assessed by SUV_{max} or visual response and response index for SUV_{max} was strongly correlated with with disease-free and overall survival. They concluded that SUV_{max} and response index for SUV_{max} appear to be useful ¹⁸F-FDG PET markers for prediction of response and survival and that ¹⁸F-FDG PET “may have a role in outcome prediction in patients with advanced rectal cancer.”

Annals of Surgical Oncology

PET/CT After Chemoimmunotherapy in Lymphoma

Martella, from Sapienza University (Rome, Italy) and a consortium of researchers from Italy, Switzerland, the UK, and Spain representing the International Extranodal Lymphoma Study Group, reported on May 5 ahead of print in the *Journal of Clinical Oncology* on a study designed to assess the role of ^{18}F -FDG PET/CT after rituximab and anthracycline-containing chemoimmunotherapy in patients with primary mediastinal large B-cell lymphoma. The study included 115 such patients who had undergone PET/CT at completion of standard chemoimmunotherapy. Of this group, 102 patients then underwent consolidation radiation therapy. A complete metabolic response (negative PET or low residual tracer activity) was achieved in 54 patients (47%). In the remaining 61 patients, residual tracer uptake was higher than mediastinal blood pool uptake but lower than liver uptake in 27 (23%), slightly higher than liver uptake in 24 (21%), and significantly higher in 10 (9%). Complete metabolic response on PET after chemoimmunotherapy successfully predicted higher 5-y progression-free survival. The authors found that using liver uptake as a cutoff for PET positivity (boundary of score, 3–4) offered the best discrimination between high and low risk of failure within 5 y. They concluded that because > 90% of patients with primary mediastinal large B-cell lymphoma are projected to be alive and progression free at 5 y despite a low complete metabolic response rate (47%) after chemoimmu-

notherapy, PET/CT provides valuable information in defining the role of consolidation radiation therapy in this setting.

Journal of Clinical Oncology

Also of interest:

- Kobe C, Kuhnert G, Kahraman D, et al. Assessment of tumor size reduction improves outcome prediction of positron emission tomography/computed tomography after chemotherapy in advanced-stage Hodgkin lymphoma. *J Clin Oncol*. 2014 May 5; e-published ahead of print.
- Eggers C, Schwarta F, Pedrosa DJ, Kracht L, Timmerman L. Parkinson's disease subtypes show a specific link between dopaminergic and glucose metabolism in the striatum. *PLoS One*. 2014;9:e96629.
- Gryglewski G, Lanzenberger R, Kranz GS, Cumming P. Meta-analysis of molecular imaging of serotonin transporters in major depression. *J Cereb Blood Flow Metab*. 2014 May 7; e-published ahead of print.
- Kim J, Ryu JK, Kim C, Paeng JC, Kim YT. Is there any role of positron emission tomography computed tomography for predicting resectability of gallbladder cancer? *J Korean Med Sci*. 2014;29:680–684.
- Brigo F, Matinella A, Erro R, Tinazzi M. ^{123}I -FP-CIT SPECT (DaTSCAN) may be a useful tool to differentiate between Parkinson's disease and vascular or drug-induced parkinsonisms: a meta-analysis. *Eur J Neurol*. 2014 April 30; e-published ahead of print.

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches by offering valuable summaries of pertinent literature. The Newsline editor recommends several reviews accessioned into the PubMed database in April and May. In an article e-published on May 16 ahead of print in *Epilepsia*, Dedeurwaerdere et al. from the University of Antwerp (Wilrijk, Belgium) provided an overview of a “Workshop on Neurobiology of Epilepsy appraisal: New systemic imaging

technologies to study the brain in experimental models of epilepsy.” Evangelista and Cervino from the Istituto Oncologico Veneto (Padua, Italy) summarized “Nuclear imaging and early breast cancer detection” on May 15 ahead of print in *Current Radiopharmaceuticals*. In an article e-published ahead of print in the *Journal of Neuroimmune Pharmacology*, de Paula Faria et al. from the University of Groningen (The Netherlands) reviewed “PET imaging in multiple sclerosis.” Cohen and Klunk from the University of Pittsburgh School of Medicine (PA) reported on “Early detection of Alzheimer's disease using PiB and FDG PET” on May 10 ahead of print in *Neurobiology of Disease*. In an article published on May 17 ahead of print in *Medecine et Maladies Infectieuses*, Revest et al. from Centre Hospitalier Universitaire de Rennes (France) described the “Contribution of ^{18}F fluorodeoxyglucose PET/CT for the diagnosis of infectious disease.” Lococo et al. from the Istituto di Ricovero e Cura a Carattere Scientifico–Arcispedale Santa Maria Nuova (Reggio Emilia, Italy) reviewed “PET/CT assessment of neuroendocrine tumors of the lung with special emphasis on bronchial carcinoids” on May 22 ahead of print in *Tumour Biology*. Foster et al. from the National Institutes of Health offered “A review on segmentation of positron emission tomography images” on April 28 ahead of print in *Computers in Biology and Medicine*. In an article in the May 15 issue of *Clinical Cancer Research*, van der Veldt and Lammertsma from the VU University Medical Center (Amsterdam, The Netherlands) provided perspective on “In vivo imaging as a pharmacodynamics marker.”