Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Many selections come from outside the standard canon of nuclear medicine and radiology journals. Note that although we have divided the articles into diagnostic and therapeutic categories, these lines are increasingly blurred as nuclear medicine capabilities rapidly expand. Many diagnostic capabilities are now enlisted in direct support of and, often, in real-time conjunction with therapies. 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.

Diagnosis

PET Assessment of Optimal Dosage

In a study e-published ahead of print on November 17 in the *International Journal of Neuropsychopharmacology*, Takano et al. from the National Institute of Radiological Sciences (Chiba, Japan) reported on the use of PET imaging of dopamine D2 receptor occupancy to determine optimal doses of 2 conventional antipsychotic medications. The authors noted that previous receptor binding studies have indicated that 70%–80% of dopamine D2 receptor occupancy induces the desired antipsychotic effects without provoking unwanted side effects. PET was used to measure receptor occupancy with sulpiride and sultopride, which are usually prescribed at similar doses (300–1,200 mg). However, the doses of these benzamide antipsychotics required to reach and remain within the 70%–80% occupancy level were quite different: 1,010–1,730 mg for sulpiride but only 20–35 mg for sultopride. Based on D2 receptor occupancy, sultopride was found to be more than 50 times more potent than sulpiride, leading the authors to conclude that sultopride is routinely overdosed in the clinical setting. They pointed to the extraordinary possibilities for PET imaging in determining optimal levels of medication in psychiatric and neurologic applications, both in preventing chronic overdosage and allowing clinicians to maximize the effects of medications that fail to produce desired effects in lower doses.

International Journal of Neuropsychopharmacology

Imaging Chronic Osteomyelitis

Termaat et al. from the VU University Medical Center (Amsterdam, The Netherlands) reported in the November issue of the *Journal of Bone and Joint Surgery* (American vol; 2005;87:2464–2471) on a systematic review and metaanalysis of the literature to determine the most suitable imaging techniques for excluding or confirming chronic osteomyelitis. The authors' search yielded 23 clinical studies covering a wide range of imaging and assessed the published data on sensitivity and specificity compared with results of histologic analyses, findings on culture, and clinical follow-up longer than 6 months. The modalities included in these studies (some of which compared several imaging techniques) were leukocyte scintigraphy (13), bone scintigraphy (7), combined bone and leukocyte scintigraphy (6), MR imaging (5), ^{18}F-FDG PET (4), combined bone and gallium scintigraphy (3), plain radiography (2), CT (1), and gallium scintigraphy (1). PET was found to be the most sensitive, with 96% sensitivity, a level approached only by MR imaging at 84% and bone scintigraphy at 82%. PET also had the highest specificity at 91%, with combined bone and leukocyte scintigraphy the next highest at 84%. Bone scintigraphy had the lowest specificity at 25%. The authors noted that although the sensitivity and specificity of leukocyte scintigraphy in detecting chronic osteomyelitis in the peripheral skeleton were relatively high at 84% and 80%, respectively, it achieved corresponding figures of only 21% and 60% in the axial skeleton. The aggregated metadata led the authors to conclude that ^{18}F-FDG PET has the highest diagnostic accuracy for confirming or excluding the diagnosis of chronic osteomyelitis and that although leukocyte scintigraphy provides an "appropriate" diagnostic accuracy in the peripheral skeleton, ^{18}F-FDG PET is superior for detecting chronic osteomyelitis in the axial skeleton.

Journal of Bone and Joint Surgery

PET and MR Imaging in TIAs

In the December issue of *Stroke* (2005;36:2642–2647), Davies et al. from Addenbrooke's Hospital (Cambridge, UK) reported on the utility of combined ^{18}F-FDG PET and high-resolution MR imaging in the identification of lesions after transient ischemic attacks (TIAs). The authors quantified plaque inflammation before endarterectomy using the combined technique in 12 patients who had experienced recent TIAs. In 7 patients, uptake on PET was highest in the lesion already targeted by angiography for endarterectomy. In 5 patients, however, uptake was low in the targeted lesion. Of this group, 3 had nonstenotic lesions identified on MR imaging that also showed high ^{18}F-FDG uptake. In each of these 3 patients, the inflamed nonstenotic lesions correlated closely with the patients' presenting symptoms. The authors noted that although selection of stenotic lesions for carotid endarterectomy is usually guided by

angiographic appearance, the nature of plaque and degree of inflammation may be better indicators of lesions from which future embolic events will occur. They concluded that, "our data suggest that angiography may not always identify the culprit lesion" and that the combination of PET and high-resolution MR imaging "can assess the degree of inflammation in stenotic and nonstenotic plaques and could potentially be used to identify lesions responsible for embolic events."

Stroke

PET: Total Tracking in Stem Cell Gene Therapy

Hung et al. from the Academia Sinica (Nankang, China) reported in the November 1 issue of *Clinical Cancer Research* (2005;11:7749–7756) on a study using ^{18}F-fluorohydroxymethylbutylguanine (^{18}F-FHBG) to assess the efficacy of human mesenchymal stem cells (hMSC) for targeting microscopic tumors and monitoring suicide gene or cytokine gene therapy in a mouse model. In the study, human colon cancer cells were transplanted into immunodeficient mice. Three to 4 days later, "tracer" hMSCs expressing herpes simplex virus type 1 thymidine kinase (HSV1-TK) and enhanced green fluorescent protein reporter genes were administered. ^{18}F-FHBG PET images at 4 weeks showed the presence of HSV1-TK+ tumor stroma. The accuracy of these imaging results was compared with histochemical, immunofluorescent, and cytometric analyses, which indicated that hMSCs can target microscopic tumors and then proliferate and differentiate to contribute to formation of a significant portion of tumor stroma. The authors concluded that PET imaging "should facilitate clinical translation of stem cell-based anticancer gene therapeutic approaches by providing the means for in vivo noninvasive whole-body monitoring of trafficking, tumor targeting, and proliferation of HSV1-tk–expressing tracer hMSCs in tumor stroma."

Clinical Cancer Research

Bronchoscopy and PET in Pulmonary Nodules

In the November issue of *Chest* (2005;128:3558–3564), Chhajed et al. from University Hospital Basel (Switzerland) reported on a study in which bronchoscopy and ^{18}F-FDG PET were used in an integrated approach to diagnosis of noncalcified lesions identified on chest radiography as ≤3 cm in diameter. The study included 74 patients who underwent both bronchoscopy and PET after such a diagnosis. Bronchoscopy alone provided what proved to be accurate diagnoses in 39 patients (35 with cancer, 4 benign). In the remaining 35 patients in whom bronchoscopy was nondiagnostic, PET imaging was positive in 19 patients. Of these, 14 were found to have malignant lesions and 5 were found to have benign lesions. The authors concluded that "combining bronchoscopy and PET scanning has a useful role in the diagnosis of noncalcified chest radiologic lesions ≤3 cm in size," adding that "if bronchoscopy is nondiagnostic, a PET scan should be performed."

Chest

^{11}C-Acetate PET for Lung Adenocarcinomas

Nomori et al. from the Saiseikai Central Hospital, the National Cancer Center, and the Nishidai Clinic (Tokyo, Japan) reported in the December issue of the *Annals of Thoracic Surgery* (2005;80:2020–2025) on the use of ^{11}C-acetate as an alternative to ^{18}F-FDG for PET detection of well-differentiated adenocarcinomas of the lung. They compared PET imaging with both tracers in 54 pulmonary nodules (1–3 cm) that showed ground-glass opacities on CT. Post-imaging analyses showed that 37 of the nodules were lung adenocarcinomas and 17 were the result of inflammation. Nineteen (51%) of the adenocarcinomas were identified by ^{11}C-acetate PET, and 14 (38%) were identified by ^{18}F-FDG PET. Of the 23 adenocarcinomas not identified by ^{18}F-FDG PET, 8 (35%) were identified by ^{11}C-acetate, and all of these 8 were well-differentiated adenocarcinomas. The authors concluded that ^{11}C-acetate PET "could be useful to diagnose pulmonary nodules with ground-glass opacity images which were not identified by ^{18}F-FDG-PET."

Annals of Thoracic Surgery

PET and CT in Aortic Graft Infection

The results of a study comparing ^{18}F-FDG PET and CT imaging in the detection of aortic graft infection were reported in the November issue of the *Journal of Vascular Surgery* (2005;42:919–925) by Fukuchi et al. from the Osaka Medical Center for Cancer and Cardiovascular Diseases (Japan). The study included 33 patients who underwent PET imaging after referral for evaluation of suspected arterial prosthetic graft infection. PET images were assessed visually for density of uptake and patterns of accumulation. Patients also underwent CT imaging, and the results of the 2 studies were compared in each patient and correlated with surgical, microbiologic, and clinical follow-up findings. The sensitivity of PET was higher than that of CT (91% and 64%, respectively). The specificity of CT was higher than that of PET (86% and 64%, respectively). When the authors took focal uptake as the positive PET criterion for aortic graft infection, the specificity and positive predictive values of PET improved significantly to 95% and 95%. They concluded that, although both CT and PET are useful, that with focal uptake as the criterion the efficacy of ^{18}F-FDG PET was "superior to that of CT in the diagnostic assessment of patients with suspected aortic graft infection."

Journal of Vascular Surgery

PET and CT in GIST Therapy Monitoring

Goldstein et al. from the Prince of Wales Hospital and University of New South Wales (Sydney, Australia) reported in the November 16 issue of

Oncology (2005;69:326–332) on a comparison of the relative utilities of gamma camera–based PET and CT in the assessment of imatinib treatment response in patients with gastrointestinal stromal tumors (GISTs). The study included 18 patients with biopsy-proven malignant GIST who were being treated with imatinib as part of much larger clinical trials comparing the efficacies of imatinib doses. Serial CT imaging was performed to monitor tumor response, and gamma camera–based ^{18}F-FDG PET studies were performed within 2–3 days of each CT scan. The patients were found to have a total of 74 lesions. Of the 47 liver lesions, only 31 (63%) were identified on PET imaging. Initial PET imaging identified 9 of 10 primary lesions (4 stomach, 4 duodenal, 2 small bowel) and 15 of 17 extrahepatic metastatic sites. Significantly, ^{18}F-FDG PET demonstrated changes before CT in all 8 patients who showed subsequent improvement on both modalities. The authors concluded that although PET had a relatively reduced sensitivity when compared with CT for the detection of lesions, especially in the liver, that gamma camera–based PET changes were in several instances visible before those on CT scanning. They added, that gamma camera–based PET "has the potential to influence clinical decision making and should be considered as part of the standard care of patients on imatinib."

Oncology

PET Clarifies FUO

PET is increasingly reported as the "tipping" diagnostic factor in case studies in the medical literature. One example was a study e-published ahead of print on November 3 in *Clinical Rheumatology* by Obermeier et al. from the University of Regensburg (Germany). The patient was a 77-year-old male with a 3-week history of fever, general malaise, and an admitting diagnosis of fever of unknown origin (FUO), a set of symptoms that had recurred 5–7 times over the past 30 years with no resulting diagnoses. Physical examination showed no signs of infection, although laboratory results indicated an active inflammatory process. Rheumatologic parameters showed nonspecific changes. The authors referred the patient for ^{18}F-FDG PET imaging, which showed marked enhanced glucose uptake in the ascending aorta and the cardiac valves. The patient's diagnosis was changed to vasculitis, he was started on a treatment course of corticosteroids, and his fever disappeared in 5 days. Blood chemistry values returned to normal as well.

Clinical Rheumatology

SPECT in Assessment of MCI/AD

In an article published in the January issue of *Neurobiology of Aging* (2006;27:24–31), Borroni et al. from the University of Brescia (Italy) evaluated the combined roles of ^{99m}Tc-ECD SPECT and memory scores in predicting conversion to Alzheimer's disease (AD) in individuals with mild cognitive impairment (MCI). The study included 31 patients with MCI who underwent clinical and neuropsychological examinations and regional cerebral blood flow (rCBF) SPECT scans at baseline. All individuals were followed for 2 years. Combined neuropsychological assessment of memory deficits and rCBF SPECT images identified preclinical AD with a combined sensitivity and specificity of 77.8%. The authors concluded that "the patterns of hypoperfusion ^{99m}Tc-ECD SPECT and the severity of memory deficits predict the risk of progression to probable AD dementia in MCI subjects" and noted the added significance of such diagnostic approaches as effective treatments for AD are developed.

Neurobiology of Aging

^{99m}Tc-MIBI Scintigraphy in Multiple Myeloma

Villa et al. from the University of Genoa Medical School (Italy) reported in the September issue of the *Journal of Experimental and Clinical Cancer Research* (2005;24:355–361) on a study assessing the diagnostic value of ^{99m}Tc-sestamibi (MIBI) in the detection and monitoring of bone marrow involvement in patients with multiple myeloma. The study included 42 patients with monoclonal gammopathy of undetermined significance (MGUS) and 68 patients with multiple myeloma (51 with active disease, 11 in complete remission, and 6 in partial remission) after chemotherapy. All patients underwent ^{99m}Tc-MIBI imaging. Scans were negative in all MGUS patients. Among patients with multiple myeloma, 54 patients (49%) had positive scans (active disease, 48; partial remission, 5; complete remission, 1). Scans were negative in 14 (complete remission, 10; partial remission, 1; active disease, 3), yielding an overall sensitivity and specificity for ^{99m}Tc-MIBI scintigraphy of 92% and 96%, respectively. In follow-up, additional scanning results continued to closely reflect disease activity. The authors concluded that "a negative ^{99m}Tc-MIBI scan in patients with suspected multiple myeloma clearly, though not absolutely, indicates absence of disease or clinical remission." They added that this suggests both the diagnostic value of ^{99m}Tc-MIBI in this application and its potential role in monitoring of disease progress.

Journal of Experimental and Clinical Cancer Research

SPECT in NSCLC RT Planning

A role for SPECT lung imaging combined with CT imaging in planning for radiotherapy (RT) of non–small cell lung cancer (NSCLC) was outlined by Christian et al. from the Royal Marsden National Health Service Foundation Trust (Sutton, UK) in an article e-published ahead of print in the November 3 issue of *Radiotherapy and Oncology.* Six patients with localized NSCLC underwent both CT and SPECT imaging that was coregistered in the RT planning system. SPECT images were used to define a volume of perfused functioning lung (FL). Inverse planning software created 3D-conformal therapy plans, with a goal of

minimizing dose to whole lung and/or dose to functioning lung. Four plans were created for each patient. Mean differences in whole lung and functioning lung were calculated. The results led the authors to conclude that "SPECT perfusion images can be accurately coregistered with RT-planning CT scans and may be helpful in creating treatment plans for patients with large perfusion deficits."

Radiotherapy and Oncology

PET and Prognoses for Metastatic Thyroid Carcinoma

Robbins et al. from the Memorial Sloan–Kettering Cancer Center (New York, NY) reported ahead of print in the November 22 issue of the *Journal of Clinical Endocrinology and Metabolism* on the use of ^{18}F-FDG PET in providing real-time predictions at initial imaging in metastatic thyroid cancer. The study included scans from 400 patients who had been diagnosed with thyroid cancer. All scans were reviewed and compared with overall survival over a median follow-up of approximately 8 years. The prognostic value of additional clinical information (gender, age, serum thyroglobulin, tumor stage, histology, and radioiodine avidity) were recorded along with PET results. The authors found that age, initial stage, histology, thyroglobulin, radioiodine uptake, and PET outcomes all correlated with survival by univariate analysis. Only age and PET results remained as strong predictors under multivariate analysis. The authors concluded that ^{18}F-FDG PET is a "simple, expensive, but powerful means to restage thyroid cancer patients who develop subsequent metastases, assigning them to groups that are either at low (FDG-negative) or high (FDG-positive) risk of cancer-associated mortality."

Journal of Clinical Endocrinology and Metabolism

Therapy

^{90}Y-Anti-CD22 mAb RIT

In the November 1 issue of *Clinical Cancer Research* (2005;11:7920–7928), Vallera et al. from the University of Minnesota Cancer Clinic (Minneapolis) reported on the efficacy of a high-affinity, rapidly internalizing anti-CD22 monoclonal antibody (mAb) to deliver ^{90}Y radioactivity to B lymphoma cells in a mouse model. In a line of mice with CD22(+) Burkitt's lymphoma, the therapeutic effect of ^{90}Y-labeled anti-CD22 was found to be dose dependent and irreversible. Treated mice showed a significantly better antitumor response than control mice and survived more than 200 days with no evidence of tumor. The authors noted that tumor-bearing mice treated with ^{90}Y-labeled anti-CD22 had no radiologic bone marrow damage, whereas a control tumor-bearing group of mice showed significant damage. This suggested that the presence of CD22(+) tumor protected mice from bone marrow damage. The authors concluded that anti-CD22 radioimmunotherapy with ^{90}Y-labeled anti-CD22 is "highly effective in vivo against CD22-expressing malignancies and may be a useful therapy for drug-refractory B cell leukemia patients."

Clinical Cancer Research

Review of Postsurgical ^{131}I in Thyroid Cancer

Pacini et al. from the University of Siena (Italy) reported in the November issue of the *European Journal of Endocrinology* (2005;153:651–659) on a literature review and expert panel consensus report on postsurgical use of ^{131}I in patients with papillary and follicular thyroid cancer. The panel noted general agreement that (1) patients with unifocal microcarcinomas <1 cm in diameter and no node or distant metastases have a $<2\%$ recurrence rate after surgery alone and that (2) postsurgical ^{131}I offers cause-specific survival benefits in patients suspected of having persistent disease or known to have tumor in the neck or distant sites. Evidence was limited that postsurgical radioiodine could reduce recurrence or mortality after complete thyroidectomy and adequate lymph node dissection, but the authors noted that when there was uncertainty about the completeness of surgery, evidence suggests that radioiodine can reduce recurrences. They concluded that postsurgical radioiodine should be used selectively but is definitely indicated in patients with distant metastases, incomplete tumor resection, or complete tumor resection but high risk of recurrence and mortality.

European Journal of Endocrinology