



Each month the editor of *Newsline* selects articles on therapeutic, diagnostic, research, and practice issues from a range of international publications. Most 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

SPECT and PET in Cerebral Infarction in Newborns

Kusaka et al. from Kagawa University (Japan) reported in the January issue of *Pediatric Neurology* (2005;32:46–49) on an observational study using SPECT and PET to evaluate rapid changes in regional cerebral blood flow (rCBF) and glucose metabolism during acute and subacute stages of cerebral infarction in 2 newborn infants. Other imaging modalities sometimes used in such circumstances do not convey information about CBF or metabolic activity. The authors noted subacute increases in blood flow and metabolic rate in the infarcted area of a newborn with multiple apneic episodes within 2 days after birth and acute increases in the infarcted area in an infant with acute clonic seizures within 24 hours after birth. Follow-up studies for both infants showed decreases in blood flow and metabolic rate in the infarcted ar-

reas. The authors suggest that these results and similar uses of SPECT and PET “should contribute to an understanding of the relationship between blood flow and metabolic rate changes after neonatal infarction as well as to improvement of diagnosis of neurologic impairments in neonates.”

Pediatric Neurology

PET vs. PET/CT in Lymphoma Staging

The incremental value added by hybrid PET/CT imaging over PET alone in staging patients with Hodgkin’s disease and non-Hodgkin’s lymphoma (NHL) was reported by researchers from the David Geffen School of Medicine at the University of California, Los Angeles, in the November/December issue of *Molecular Imaging and Biology* (2004;6:411–416). The study by Allen-Auerbach et al. included 73 patients (37 women, 36 men; 20 with Hodgkin’s disease, 53 with NHL) who were imaged with PET/CT as part of staging. Image findings were verified by clinical follow-up, additional imaging, and, when available, histology. The results were compared with readouts of only the PET portion of each study. PET and PET/CT did not agree in 7 patients, of whom PET/CT correctly upstaged 2 and downstaged 5. Overall staging was accurate with PET/CT in 93% of patients and with PET in 84% of patients. The authors concluded that “lymphoma is staged with higher accuracy using PET/CT than PET alone.”

Molecular Imaging and Biology

Rest GIK MIBI vs. ²⁰¹Tl Reinjection for Assessment of Myocardial Viability

Orea et al. from the Instituto Nacional de Ciencias Medicas y Nutri-

cion Salvador Zubiran (Mexico City) reported in 2004 in the *Revista de Investigacion Clinica* (2004;56:321–326) on a study of the comparative values of ^{99m}Tc-sestamibi (MIBI) imaging preceded by an injection of glucose-insulin-potassium (GIK) solution and the reinjection ²⁰¹Tl technique in detection of myocardial viability in patients after myocardial infarction. The study included 74 patients (52 men, 22 women) who had experienced myocardial infarctions within the previous 1–7 months. Each patient underwent pharmacologic stress (dipyridamole), rest redistribution, and reinjection ²⁰¹Tl imaging as well rest/stress MIBI imaging after GIK injection. The severity of perfusion defects on ²⁰¹Tl rest reinjection and GIK MIBI imaging were compared. The results from analysis of more than 1,400 involved segments indicated that the GIK MIBI protocol was safe and effective and improved the detection of perfusion reversible defects compared with the thallium reinjection technique. The authors noted that the GIK MIBI protocol obtained “better information regarding myocardial viability, with lower acquisition time and less cost.”

Revista de Investigacion Clinica

^{99m}Tc-Labeled Interleukin in Pulmonary Infections

Rennen et al. from the University Medical Center Nijmegen (The Netherlands) reported in the December issue of *Chest* (2004;126:1954–1961) on a study designed to assess the potential of ^{99m}Tc-labeled interleukin-8 (a cytokine with roles in angiogenesis, tumorigenesis, and metastasis) for scintigraphic imaging of several pulmonary infections in a rabbit model. The experimental design, built on pre-

vious studies by the group, included 4 immunocompromised rabbits with aspergillosis, 4 rabbits with pneumococcal (gram-positive) pneumonia, and 4 immunocompetent rabbits with *Escherichia coli*-induced (gram-negative) pneumonia. Distribution of the ^{99m}Tc interleukin-8 was assessed both by imaging and counting dissected tissues. The authors found that the technique allowed early (within 2 hours after injection) and excellent localization and identification of the extent of pulmonary infection in each of the 3 models. They concluded that the ^{99m}Tc -labeled interleukin-8 “offers many advantages over the conventionally used radiopharmaceuticals to image pulmonary infection. . . i.e., rapid and easy preparation, short time span between injection and imaging, low radiation burden and, most importantly, clear delineation of the infectious foci.”

Chest

^{99m}Tc -L-Methionine Brain SPECT for Recurrent Tumor

Building on previous work using ^{99m}Tc SPECT to differentiate between recurrent brain tumor and postradiation reactive gliosis, Barai et al. from the All India Institute of Medical Sciences (New Delhi) reported in the October issue of *Acta Radiologica* (2004;45: 649–657) on a study assessing ^{99m}Tc -labeled L-methionine as a tracer. The study included 42 patients with primary brain tumors who underwent ^{99m}Tc -L-methionine SPECT, which was correlated with additional radiologic and histopathologic findings. The tracer showed localized increased uptake in the 40 patients with tumor recurrence, but no accumulation in the 2 patients with postradiation gliosis. In addition, the mean differential uptake rate in high-grade tumors was significantly higher than in low-grade tumors. The authors concluded that “ ^{99m}Tc -L-methionine can be used as a SPECT tracer to differentiate tumor recurrence from postradiation gliosis.”

Acta Radiologica

PET/CT in Management of Hepatic Metastases from Colorectal Cancer

Selzner et al. from University Hospital Zurich (Switzerland) reported in the December issue of *Annals of Surgery* (2004;240:1027–1034) on a study comparing the value of contrast-enhanced CT and ^{18}F -FDG PET/CT in providing useful information that altered management strategies for patients with liver metastases from colorectal cancer. The study included 76 patients evaluated for resection of such liver metastases. Each patient received a contrast-enhanced CT and a PET/CT scan, and the sensitivity and specificity of the 2 modalities were compared for detection of intrahepatic tumor load, extrahepatic metastases, and local recurrence at the colorectal site. Although CT and PET/CT showed similar sensitivities (95% and 91%, respectively) for detecting intrahepatic metastases, PET/CT was better able than CT to diagnose intrahepatic recurrences in patients with previous hepatectomy (100% and 50%, respectively), to detect local recurrences at the primary colorectal resection site (93% and 53%, respectively), and to detect extrahepatic disease (89% and 64%, respectively). Findings resulting from PET/CT alone resulted in a change in therapeutic strategy for 21% of patients in the study. The authors concluded that although PET/CT and contrast-enhanced CT provide similar information about hepatic metastases from colorectal cancer, PET/CT is superior in detecting both extra- and intrahepatic recurrences and local recurrence at the site of the original colorectal surgery. They noted that at their institution all patients being evaluated for liver resection for metastatic colorectal cancer now routinely undergo PET/CT.

Annals of Surgery

PET Assesses Response to Therapy in High-Grade Soft Tissue Sarcoma

Schuetze et al. from the University of Washington Medical Center (Seattle) reported in an article e-published

ahead of print on December 1 in *Cancer* on a study designed to assess the ability of ^{18}F -FDG PET to detect histopathologic response to therapy and predict tumor progression in patients with high-grade soft tissue sarcomas. The study included 46 patients with high-grade localized sarcomas in whom PET imaging was performed before neoadjuvant chemotherapy (baseline) and later before surgery. Resected specimens were examined for residual viable tumor, and patients were followed up for disease recurrence and survival. Patients with a baseline tumor maximum standardized uptake value (SUV) ≥ 6 and a $< 40\%$ decrease in ^{18}F -FDG uptake after chemotherapy were at high risk of systemic disease recurrence (estimated at 90% by 4 years from original diagnosis). Patients with a $\geq 40\%$ decline in the maximum SUV after chemotherapy were at significantly lower risk of recurrent disease and/or death. The authors concluded that ^{18}F -FDG PET showed “promise as a tool to identify the patients with sarcoma who are most likely to benefit from chemotherapy.”

Cancer

PET in Adenocarcinoma of Esophagus and Esophagogastric Junction

Sihvo et al. from the Helsinki University Central Hospital (Finland), the University of Turku (Finland), and the Pajjat-Hame Central Hospital (Lahti, Finland) reported in the December issue of the *Journal of Gastrointestinal Surgery* (2004;8:988–996) on the use of PET imaging in staging, management, and prediction of survival in patients with adenocarcinoma of the esophagus and esophagogastric junction. The study included 55 patients identified for radical esophageal resection who were imaged for staging with PET, spiral CT, and endoscopic ultrasonography. Results were compared with histopathology and survival data. PET, CT, and ultrasound showed similar accuracy in detecting locoregional lymph node metastases (60%, 58%,

and 72%, respectively), and adding PET to standard staging did not improve N stage accuracy. In M staging, however, the respective accuracies of CT (75%) and PET (76%) were improved by combining PET and CT (87%) and PET, CT, and ultrasound (91%). Of the 55 patients, 19 (35%) had metastatic lesions. CT and ultrasound identified 8 of 19 patients with metastatic lesions, and the addition of PET to these 2 modalities identified 14 of these patients. Although PET did not improve the prediction of survival in nodal disease without distant metastases, positive PET for distant metastases that were also identified by either positive ultrasound or CT proved an accurate predictor of poor survival. The authors concluded that despite the fact that the staging value of PET by itself in adenocarcinoma of the esophagus is limited, "adding PET to standard staging does, however, improve detection of stage IV disease and its associated poor survival."

Journal of Gastrointestinal Surgery

PET in RT Planning for Esophageal Carcinoma

In the December issue of *Radiotherapy and Oncology* (2004;73:269–275), Vrieze et al. from the University Hospital Gasthuisberg (Leuven, Belgium) reported on a comparative study assessing whether incremental information could be provided by ^{18}F -FDG PET in delineation of clinical target volumes in patients undergoing radiation therapy (RT) for advanced esophageal carcinoma. The study analyzed imaging and RT data from 30 patients. The results of ^{18}F -FDG imaging were compared with those of CT and endoscopic ultrasound for 14 defined regions of potential lymph node involvement. In 14 of the 30 patients (47%), CT and ultrasound findings differed from those of PET imaging. In 8 of these patients, 9 lymph node regions were found with pathologic nodes only on conventional imaging, and the influence of ^{18}F -FDG PET would have led to a decrease in the irradiation volumes in 3 of these pa-

tients. In 6 patients, 8 lymph node regions were identified as normal on CT and ultrasound but pathologic on PET. In 3 of these patients (10%), ^{18}F -FDG PET would have led to enlargement of the irradiated volume. The authors concluded that the significant chance of a false-negative result with ^{18}F -FDG imaging indicates that irradiated volumes should not be reduced based on this method alone. However, the high specificity of positive PET in enlarging irradiated volumes in regions without suspected lymph nodes on CT and/or ultrasound "indicates a role for ^{18}F -FDG-PET in radiotherapy planning for esophageal cancer."

Radiotherapy and Oncology

^{11}C -Methionine PET and Regional Salivary Gland Function

Buus et al. from the Aarhus University Hospital (Denmark) reported in the December issue of *Radiotherapy and Oncology* (2004;73:289–296) on a study evaluating the utility of ^{11}C -methionine PET for measuring regional salivary gland function after radiotherapy (RT) for head and neck cancer. The study included 8 patients with head and neck cancer, 2 of whom underwent ^{11}C -methionine PET imaging before RT and 6 after parotid-sparing RT. The authors outlined a kinetic model of salivary gland ^{11}C -methionine metabolism, in which salivary gland function was quantified by net metabolic clearance of the tracer, yielding a K value. They found that parotid gland K values correlated positively with parotid gland salivary flow, indicating that this metric can be used as an index of salivary gland function. Ks of parotid and submandibular glands were reduced depending on the median radiation dose. The authors concluded that salivary gland function can be measured by dynamic ^{11}C -methionine PET, which is a promising method for studying individual responses of major salivary glands to irradiation.

Radiotherapy and Oncology

PET/CT Simulation in RT Planning

Heron et al. from the University of Pittsburgh School of Medicine (PA) reported in the December issue of the *International Journal of Radiation Oncology, Biology, Physics* (2004; 60:1410–1424) on a prospective study of the effect of PET/CT planning simulation on tumor and normal tissue delineation in radiation therapy (RT) planning in patients with head and neck cancer. The study included simulations of 21 patients imaged in treatment position on a PET/CT scanner and transferred to an RT planning system. Abnormal areas of ^{18}F -FDG uptake on PET were compared with gross tumor volumes and abnormal nodal regions defined on CT. The authors found that PET imaging identified the primary tumor in all cases, whereas CT missed the primary in 3 simulations. Volumes for the primaries were significantly larger on CT than on PET, but this was not true for nodal regions. The authors concluded that "hybrid PET/CT simulation is feasible and provides valuable information that results in greater delineation of normal tissues from tumor-bearing areas at high risk for recurrence."

International Journal of Radiation Oncology, Biology, Physics

PET in Cartilaginous Tumors of Bone

In a study reported in the December issue of the *Journal of Bone and Joint Surgery* (American volume) (2004;6-A:2677–2685), Lee et al. from the College of Physicians and Surgeons of Columbia University (New York, NY) reported on an investigation on the preoperative utility of PET in assessing the glucose metabolism of cartilaginous tumors of the bone. The study included 27 patients with a total of 35 biopsy-proven cartilaginous tumors imaged by plain radiography, conventional bone scanning, MR imaging, and PET.

The glucose metabolism as maximal standardized uptake values (maxSUVs) on PET was compared with histopathologic grade, tumor size, recurrence, and metastasis. The mean maxSUV in 13 benign bone tumors was 1.147 ± 0.751 , in 12 grade I chondrosarcomas was 0.898 ± 0.908 , and in 10 high-grade (grade II or III) chondrosarcomas was 6.903 ± 5.581 . Metastasis but not tumor size or recurrence was associated with a higher SUV. Grade II and III chondrosarcomas had higher glucose metabolism than low-grade cartilage tumors on PET, but PET could not distinguish between benign and grade I malignant cartilaginous tumors. The authors concluded that although PET has limitations, "it may be useful for predicting high-grade chondrosarcomas."

Journal of Bone and Joint Surgery
(American volume)

Case Study of PET in MS Evaluation

In a study published in the November/December issue of the *Japan Journal of Ophthalmology* (2004;48:591–593), Murai et al. from the Tokyo Medical and Dental University (Japan) reported on a case study in which PET was used to evaluate multiple sclerosis (MS)-associated hemianopia in a 20-year-old man. After MR imaging revealed a mass in the temporoparietal lobe and subsequent biopsy led to a diagnosis of MS, the patient underwent ^{18}F -FDG imaging and ^{11}C -flumazenyl imaging. ^{18}F -FDG PET showed low glucose metabolism in the lesion, and ^{11}C -flumazenyl showed significantly reduced uptake in the demyelinated optic radiation but only slight reduction of uptake in the primary visual cortex. At 2-year follow-up, the patient's visual field had recovered to normal. The authors concluded that "PET can be a useful tool for estimating the visual outcome of patients with hemianopia in MS."

Japan Journal of Ophthalmology

Therapy

Radioisotope Contribution to Activity and Toxicity in RIT

The contribution of the radioisotope to the activity and toxicity of radioimmunotherapy (RIT) was assessed by Davis et al. from Stanford University (CA) and other medical centers and reported in the December issue of *Clinical Cancer Research* (2004;10:7792–7798). The authors first determined the single-agent activity of tositumomab and assessed the contribution of ^{131}I radiolabeling by retrospectively comparing treatment outcomes for the tositumomab and ^{131}I -tositumomab regimen with outcomes from equivalent total doses of unlabeled tositumomab. The study included 78 patients with refractory/relapsed non-Hodgkin's lymphoma assigned to either radiolabeled or unlabeled tositumomab treatment (with crossover treatment provisions for those progressing in the unlabeled group). After a median follow-up of 42.6 months, a comparison of the groups showed significantly greater overall and complete responses in those who received the labeled regimen than in those who did not. The 19 patients who crossed over to labeled therapy also experienced greater overall and complete responses than did those who remained in the unlabeled group. At the same time, hematologic toxicity was more severe and other adverse events were more frequent after ^{131}I -tositumomab than after tositumomab alone. The authors concluded that although unlabeled tositumomab showed single-agent activity, in this direct comparison, "all of the therapeutic outcome measures were significantly enhanced by the conjugation of ^{131}I to tositumomab."

Clinical Cancer Research

Are Whole-Body Scans Before ^{131}I Ablation Necessary?

Salvatori et al. from the Catholic University of the Sacred Heart (Rome,

Italy) reported in the December issue of *Clinical Endocrinology* (Oxford) (2004;61:704–710) on a retrospective study designed to evaluate whether preliminary diagnostic whole-body ^{131}I scans are necessary before performing ^{131}I ablative therapies for thyroid carcinoma in patients lacking thyroid remnants or metastases. The study included 875 patients with previous total or near-total thyroidectomy who underwent ^{131}I ablative therapy with no preliminary diagnostic whole-body scan. Patients underwent whole-body scans at 2–5 days after radioiodine treatment to identify thyroid remnants and metastases. Most patients (94%) were found to have thyroid remnants or metastases on scans after therapy, and most (91.2%) were also found to have detectable thyroglobulin off L-T4 and positive 24-hour neck uptake. In an additional 30 patients (3.6%) faint positive scans after therapy were classified as false-positive because of negative 24-hour neck uptake and undetectable thyroglobulin measures. Fourteen patients (1.6%) with very small lymph node metastases positive on scans after therapy showed undetectable thyroglobulin off L-T4. The authors concluded that because most patients have residual thyroid tissue after total thyroidectomy, "it seems reasonable to omit routine diagnostic whole-body scans before ^{131}I treatment" and cited the clinical, administrative, and economic advantages of omitting the scan.

Clinical Endocrinology (Oxford)

Serum Tg Levels at Remnant Ablation Predict Thyroid Carcinoma Recurrence

In an article e-published ahead of print on December 21 in the *Journal of Clinical Endocrinology and Metabolism*, Kim et al. from the Ulsan University Hospital and the Ulsan College of Medicine (Seoul, Korea) reported on an investigation designed to determine