



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. Note that although we have divided the articles into therapeutic and diagnostic 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. At the same time, research in molecular chemistry and biology has increasing relevance to nuclear medicine investigations. 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

Laparoscopic SLN Dissection in Prostate Cancer

Jeschke et al. from the Elisabethinen Hospital (Linz, Austria) reported in the June issue of the *Journal of Urology* (2005;173:1943–1946) on a technique that allows radioisotope-guided sentinel lymph node (SLN) dissection by laparoscopy in conjunction with laparoscopic radical prostatectomy. The study included 71 consecutive patients with a mean operative prostate specific antigen of 8.88 ng/mL who were scheduled for laparoscopic radical prostatectomy. Each patient was administered 200 MBq technetium-labeled human albumin colloid as an injection in the prostate gland under transrectal ultrasound guidance 24 hours before surgery. Using a custom-designed laparoscopic gamma probe during

surgery, SLNs were identified and removed for frozen section analysis. If analysis revealed metastases, extended pelvic lymph node dissection was performed. The procedure detected radioactivity on 2 sites in 50 patients (70.4%), 1 site in 19 patients (26.7%), and no sites in 2 patients (2.8%). In 81 of the 142 pelvic side walls (54.7%), SLNs were exclusively outside of the obturator fossa. Eight of the 11 total detected metastases were outside of the obturator fossa. The authors concluded that SLN dissection by laparoscopy is feasible and that it detects micrometastases outside of the obturator fossa in a significant number of patients.

Journal of Urology

PET in Preoperative Staging of Gastric Adenocarcinoma

In an article e-published ahead of print on April 26 in *Cancer*, Chen et al. from the Yonsei University College of Medicine (Seoul, Korea) reported on the use of ^{18}F -FDG PET in preoperative staging of gastric adenocarcinoma. The study included 68 patients with gastric adenocarcinoma who were referred for preoperative PET scans and who also underwent spiral CT imaging. Results of PET and combined PET and CT were compared with histologic findings at surgery. PET showed increased uptake in primary tumor in 64 of 68 patients (sensitivity, 94%), with a mean standard uptake value of 7.0. Significant association was noted between ^{18}F -FDG uptake and macroscopic type, tumor size, lymph node metastasis, histologic type, and TNM stage. PET was similar in accuracy to CT in diagnosing local and distant lymph node metastases and peritoneal status but had a higher specificity in assessing local lymph node status. PET showed additional diag-

nostic value in 10 (15%) of 68 patients by upstaging 4 and downstaging 6 patients. PET results combined with those of CT were more accurate for preoperative staging than either modality alone. The authors concluded that ^{18}F -FDG PET “improves the preoperative TNM staging of gastric adenocarcinoma” and can “facilitate the selection of patients for a curative resection by confirming a nodal status identified by CT.”

Cancer

PET and Cervical Carcinoma of Unknown Primary Tumor

Freudenberg et al. from the University Hospital Essen (Germany) reported in the May/June issue of *Medical Principles and Practice* (2005;14:155–160) on a study designed to evaluate an optimized PET/CT protocol for head and neck cancer and assess the usefulness of the technique in identifying unknown primary tumors in patients with biopsy-proven cervical lymph node metastases. The study included 21 patients with cervical lymph node metastases of unknown primary tumors who underwent staging with ^{18}F -FDG PET/CT. Results from PET alone, CT alone, PET and CT read side by side, and fused PET/CT were evaluated separately and correlated with history or clinical follow-up. Primary tumors were identified in 12 patients (57%) by fused PET/CT, in 11 patients (52%) by both PET alone and side-by-side PET and CT, and in 5 patients (23%) by CT alone. The authors concluded that although accurate fusion of functional and morphologic data by PET/CT is a promising imaging modality in the clinical workup of patients with cervical cancers of unknown primary tumors, the data in this study indicate that fused PET and CT images increased the sensitivity of detection

compared with CT alone but not with PET alone or PET and CT read side by side.

Medical Principles and Practice

Digital Fusion of PET and CT in Rectal Cancer Recurrence

In a study e-published ahead of print on May 9 in the *Annals of Surgical Oncology*, Fukunaga et al. from Osaka University (Japan) evaluated the clinical and therapeutic value of digital fusion of ¹⁸F-PET and CT images in patients with suspected local recurrence of rectal cancer. The study included 42 patients referred for suspicion of local recurrence after curative resection of rectal cancer. Each patient underwent PET and CT imaging, and the fusion image was reconstructed with a commercially available digital software program. PET and CT alone were compared with the fusion results. Fusion provided a correct diagnosis in 39 (93%) patients; CT alone provided a correct diagnosis in 33 patients (79%); and PET alone did so in 37 patients (88%). Fusion altered patient management in 11 (26.2%) patients, including differentiation of tumor from postoperative scar and/or identification of exact anatomic location. The authors concluded that digital fusion imaging “has a potential clinical value in the treatment of suspected local recurrence of rectal cancer.”

Annals of Surgical Oncology

MR vs. PET in Cervical Cancer Metastases

In an article e-published ahead of print on May 10 in the *Japanese Journal of Clinical Oncology*, Park et al. from the Sungkyunkwan University School of Medicine (Seoul, Korea) reported on a study comparing the efficacies of PET and MR imaging in detection of parametrial involvement and lymph node metastases in patients with cervical cancer. The study included 36 patients with cervical cancer who underwent MR and PET imaging within the week

prior to radical surgery. Extent of tumor on surgical findings was compared with International Federation of Gynecology and Obstetrics (FIGO) staging and MR and PET results. The accuracy of FIGO staging was 67% and of MR staging was 84.4%. PET showed a greater ability to detect pelvic lymph node metastases than did MR imaging (75% and 67%). All nodes showing uptake on PET were confirmed as metastatic by pathologic analysis. The authors concluded that PET is more useful for the evaluation of pelvic lymph nodes but that MR imaging provides an improved evaluation of local tumor extension. They noted that PET still misses microscopic disease and suggested that additional studies should evaluate the utility of PET/CT in a similar study of disease extension to provide data on the comparative cost effectiveness of MR, PET, and PET/CT imaging in patients with cervical cancer.

Japanese Journal of Clinical Oncology

Whole-Body PET in Skin Cancer Staging

Cho et al. from the Yonsei University College of Medicine (Seoul, Korea) reported in the April issue of *Dermatologic Surgery* (2005;31:442–446) on a study of the use of ¹⁸F-FDG PET as part of baseline staging in patients with cutaneous squamous cell carcinoma (SCC). The study included 12 patients with SCC, 9 of whom were classified as at high risk. Whole-body ¹⁸F-FDG PET imaging was performed on 11 patients for staging and in 1 patient for restaging 1 year after excision. Primary lesions were detected in 9 patients (83.3%), with lymph node involvement identified in 3 patients (25.0%), and distant organ (lung) involvement identified in 1 patient (8.3%). In 1 patient with a primary positive lesion, stomach cancer with involvement of adrenal glands, omentum, and lymph nodes was also detected. All the patients classified as high risk showed uptake in primary lesions. The authors noted the dearth

of studies comparing the cost effectiveness or utility of sentinel lymph node biopsy and PET imaging in patients with SCC. They concluded that “considering the noninvasiveness and thoroughness in checking the whole body, including distant organs, FDG PET may have clinical value as a baseline workup study for patients with high-risk SCC.”

Dermatologic Surgery

PET as Outcome Metric in Prostate Cancer

In a study published in the May 1 issue of *Clinical Cancer Research* (2005;11:3210–3216), Morris et al. from the Memorial Sloan-Kettering Cancer Center (New York, NY) reported on the use of ¹⁸F-FDG PET as a measure of progression in patients being treated for castrate metastatic prostate cancer. The study included 22 patients who underwent PET imaging at baseline and at 4 weeks and 12 weeks (only 18 patients were imaged at 12 weeks) during antimicrotubule chemotherapy. In each patient, the average maximum standardized uptake value (SUV) was measured in 5 lesions and taken as the quantitative PET outcome measure. This was compared against the conventional measures of prostate-specific antigen (PSA) at 4 weeks and PSA, bone scan, and soft tissue imaging at 12 weeks, using a criterion that a 25% increase in PSA indicated progression. PET correctly identified the clinical status of 20 (91%) at 4 weeks and 17 (of 18; 94%) patients at 12 weeks. When a >33% increase in both PSA and maximum ¹⁸F-FDG SUV was used to define progression, the utility of PET was even greater. The authors noted that ¹⁸F-FDG PET “is promising as an outcome measure in prostate cancer,” and that, as a single modality, “it can show treatment effects that are usually described by a combination of PSA, bone scintigraphy, and soft tissue imaging.”

Clinical Cancer Research

PET and Prognosis in Aggressive Lymphoma

In an article e-published ahead of print on April 28 in *Blood*, Haioun et al. from Paris XII University (Creteil, France) reported on the utility of PET in predicting treatment outcomes in patients with newly diagnosed aggressive lymphoma. The study included 90 patients (37 classified as lower risk and 53 classified as high risk) who were imaged with ^{18}F -FDG PET before induction chemotherapy, after 2 cycles of treatment, and after the completion of treatment. These results were compared with CT imaging after 4 cycles. At the 2-week point in treatment, PET imaging was negative in 54 patients and positive in 36. After completion of treatment, 83% of these PET-negative patients had achieved complete remission, but only 58% of PET-positive patients had done so. Longer-term outcomes differed significantly between PET-negative and PET-positive groups: 2-year event-free survival for these groups was 82% and 43%, respectively, and the 2-year overall survival was 90% and 61%, respectively. The authors noted that the predictive value of PET was valid in both lower- and higher-risk groups and that PET should be used as an early guide in first-line strategies in aggressive lymphoma.

Blood

PET Distinguishes Bone Infection from Postsurgical Inflammation

In an article e-published ahead of print in the May 13 issue of the *Journal of Orthopaedic Research*, Jones-Jackson et al. from the University of Arkansas for Medical Sciences (Little Rock) reported on a study designed to assess the ability of ^{18}F -FDG PET to identify infection in a postoperative rabbit osteomyelitis model. *Staphylococcus aureus* infection was initiated at the time of surgery in 1 group of rabbits, whereas the other group underwent surgery without initiation of infection. Animals underwent

PET imaging and conventional radiography at 1 day and at 1, 2, 3, and 4 weeks after surgery and were killed at 4 weeks for histologic and bacteriologic analyses. Tracer uptake was visible in bone in all rabbits 1 day after surgery. Visual interpretation of PET scans detected a significant difference between infected and uninfected groups as early as day 8, although standard uptake value comparisons at the surgical site were not significant until after the first week (in part because of regional lymph node uptake in the animals). The authors concluded that PET is a promising method for distinguishing between bone infection and routine inflammation after surgery.

Journal of Orthopaedic Research

PET and Residual Disease vs. Scar in Idiopathic Retroperitoneal Fibrosis

Vaglio et al. from the University of Parma (Italy) reported in the March/April issue of *Clinical and Experimental Rheumatology* (2005; 23:231–234) on a study of the ability of PET to evaluate the metabolic activity of residual masses in patients treated for idiopathic retroperitoneal fibrosis (IRF). Residual masses are common after treatment in such patients, and conventional imaging cannot reliably differentiate between active disease and scarring. The study included 7 patients treated for IRF, all of whom reported constitutional symptoms and/or pain and showed high acute-phase reactant levels. CT showed a periaortoiliac mass in each patient. Three patients underwent surgical ureterolysis and 2 received ureteral stents. All patients received pharmacologic treatment and underwent ^{18}F -FDG PET imaging at varying times after the end of treatment. Symptoms and reactant levels improved in all patients, and CT showed significant reductions in IRF. However, all patients had residual retroperitoneal mass. PET showed very slight aortoiliac ^{18}F -FDG uptake in only a single patient, and no patient relapsed during follow-up. The authors

concluded that although posttreatment residual masses are common in patients treated for IRF, in most cases these probably represent metabolically inactive tissue. However, PET provides a viable method for distinguishing metabolically active tissue from scar.

Clinical and Experimental Rheumatology

Technologist Dose in PET

In the second in a series of articles in *Medical Physics* (2005;32:861–865) on radiation exposure in PET imaging, Zeff and Yester from the University of Alabama at Birmingham tracked daily doses received by PET technologists. In previous work, the authors' data indicated that, despite high patient self-attenuation, shielding, and standard precautionary measures, PET technologist occupational doses can remain quite high (approximately 12 mSv/year). In the current study, observations of methods and routine procedures indicated that close technologist-patient interaction both during and after tracer administration (as much as 20 minutes per study) is the prime contributor to such high doses. The authors recommended the development of a more innovative approach to radiation protection for PET technologists.

Medical Physics

PET in Transplant Gene Therapy

Dharmarajan et al. from the Washington University School of Medicine (St. Louis, MO) reported in the June issue of the *American Journal of Transplantation* (2005;5:1216–1225) on PET as a means of performing molecular imaging in rodent models to assess the success of experimental gene therapy in preventing ischemia/reperfusion (I/R) injury and allograft rejection after lung transplantation. Rats were initially transfected with adenovirus encoding a fusion gene of a mutant Herpes simplex virus-1 thymidine kinase and the green fluorescent protein. After 24 hours, lungs were transplanted in 3 groups representing

normal transplant, I/R injury, and acute rejection. After imaging, lungs were excised and analyzed for thymidine kinase activity. PET detected transgene expression in transplanted lungs even in the presence of acute rejection or I/R injury, and uptake correlated with lung tissue assays of thymidine kinase activity. The authors concluded that “noninvasive molecular imaging with PET is a feasible, sensitive, and quantitative method for characterizing pulmonary transgene expression in experimental lung transplantation” and noted the importance of this finding for clinical applications of gene therapy in transplantation.

American Journal of Transplantation

Exercise MPI After Stenting

In an article published in the March issue of the *American Heart Journal* (2005;149:534–540), Rajagopal et al. from the Cleveland Clinic Foundation (OH) reported on a study designed to determine whether exercise myocardial perfusion imaging can provide independent prognostic information in patients who have undergone coronary stenting. In a retrospective study, the authors analyzed the outcomes of 370 patients who had undergone dual-isotope exercise nuclear scintigraphy at least 1 month after coronary stenting. Patients were classified by presence or absence of ischemia, and endpoints were mortality from any cause or myocardial infarction (MI) during a median of 30 months of follow-up. A total of 86 patients (23%) had ischemia and 284 (77%) did not. Patients with ischemia had a 30-month event rate of 17%, whereas those without had a rate of 9.1%. After adjusting for a number of factors, the authors concluded that scintigraphic evidence of ischemia independently predicted death or MI in both symptomatic and asymptomatic patients.

American Heart Journal

PET in Isotretinoin Brain Changes

In a study receiving wide media coverage and appearing in the May issue of the *American Journal of Psychiatry* (2005;162:983–991), Bremner et al. from Emory University (Atlanta, GA) used ¹⁸F-FDG PET to assess brain function before and after treatment with isotretinoin, a widely prescribed but controversial acne medication. Case reports have suggested a relationship between isotretinoin administration and depression and suicide. The study included 30 adults with acne who were divided into 2 groups and treated for 4 months with either isotretinoin or an antibiotic. Patients were imaged with PET before and after treatment. Isotretinoin was associated with decreased brain metabolism in the orbitofrontal cortex (–21% activity versus +2% change for antibiotic). No differences in the severity of depressive symptoms were noted in the 2 groups before or after treatment. The authors concluded that this study suggests that isotretinoin treatment is associated with changes in brain functioning and that these findings warrant additional study.

American Journal of Psychiatry

Therapy

Controlling Individual Molecular Dynamics

In an article published in the May 13 issue of *Science* (2005;308:1000–1003), Lastapis et al. from the Université Paris-Sud (Orsay, France) reported on continuing inroads in controlling the inner workings of individual molecules. They reported on picometer-scale electronic control of molecular dynamics inside a single molecule. Tunneling electrons from a low-temperature scanning tunneling microscope were used to control, through resonant electronic excitation, the molecular dynamics of an individual biphenyl molecule adsorbed on a silicon surface. Different reversible molecular movements

were selectively activated by tuning the electron energy and by selecting precise locations for excitation inside the molecule. The authors concluded that, “these experiments demonstrate the feasibility of controlling the molecular dynamics of a single molecule through the localization of the electronic excitation inside the molecule.”

Science

Single-Cell Microdosimetry in RIT of B-Cell Lymphoma

In a study published in the April issue of *Cancer Biotherapy and Radiopharmaceuticals* (2005;20:224–230), Hindorf et al. from Lund University (Sweden) and the Royal Marsden Hospital and Institute of Cancer Research (Sutton, UK) reported on a study of the variation in energy deposition in experimental spheres simulating single-cell microdosimetry. The authors began their theoretical preparation by noting the wide variations in particle energy of different electron-emitting radionuclides used for radioimmunotherapy of B-cell lymphoma and questioning whether conventional mean absorbed dose is a relevant parameter for use in single-cell dosimetry. They performed Monte Carlo simulations of uniform energy deposition from 1,000, 300, 100, and 10 electrons in a sphere with a radius of 7.7 μm . The simulated electrons were monoenergetic (18, 28, 141, or 935 keV). Absorbed dose per emitted electron, absorbed fraction, fraction of cellular volume in which energy was deposited, and dose/volume histograms were calculated. They found that absorbed fractions varied between 0.60 (18 keV) and 0.001 (935 keV), and absorbed dose to the cell per electron emitted varied by a factor of 10, from 0.898 mGy (18 keV) to 0.096 mGy (935 keV). They also noted that the non-uniformity of the absorbed dose to a cell increased with increasing electron energy and decreased with the number of decays inside the studied

(Continued on page 33N)

(Continued from page 30N)

volume. These data suggest the consideration of a more stochastic approach to RIT dosimetry, and the authors concluded that “the wide distribution of energy deposition should be taken into account when analyzing and designing trials for targeted radionuclide therapy.”

Cancer Biotherapy and Radiopharmaceuticals

Nanopharmaceuticals and RIT in Ovarian Cancer

In the February 10 issue of the *Journal of Pharmacy and Pharma-*

ceutical Sciences (2005;7:29–34), McQuarrie et al. from the University of Alberta (Edmonton, Alberta) reported on a multistep radioimmunotherapeutic (RIT) approach to late-stage ovarian cancer, using a combination of a bispecific monoclonal antibody (bsmAb) with ^{90}Y -labeled biotinylated long-circulating liposomes as a potential adjuvant treatment. In the small animal trial, a bsmAb with anti-CA 125 and antibiotin epitopes was engineered for use with liposomes coated with biotin to deliver the ^{90}Y to xenografted NIH:OVCAR-3 (CA 125+) human ovarian cancer cell tumor sites in Balb/c nude mice. One group of mice received a radiolabeled bsmAb,

and the other group received sequential intraperitoneal administration of the targeting and therapy moieties. Median tumor growth delay in the single administration group was 77.7 days and in the combination therapy group was 91 days. The authors noted that this approach, designed to increase the amount of radioactivity delivered to the tumor site compared with conventional mAb radionuclide delivery, “indicated an appreciable delay in progress of tumor and ascites development in treated vs. control populations.”

Journal of Pharmacy and Pharmaceutical Sciences

