

BRIEF REPORTS

Free Access to *JNM* CE Articles

Continuing education (CE) articles appearing in *The Journal of Nuclear Medicine (JNM)* will now be made available without charge through Highwire Press, the journal's online publisher. *JNM* Editor in Chief Heinrich Schelbert, MD, PhD, made the announcement in April.

In addition to access to the full text of CE articles, jnm@snmjournals.org also links physician visitors to online examinations (free to SNM members, \$15 for nonmembers). Successful completion of each exam confers American Medical Association Physician's Recognition Award credit. Many *JNM* CE articles are also available for technologist Verification of Involvement in Continuing Education credit and/or American Council on Pharmaceutical Education credit. The first CE article to appear without charge, "Brain ^{18}F -FDG PET in the Diagnosis of Neurodegenerative Dementias: Comparison with Perfusion SPECT and with Clinical Evaluations Lacking Nuclear Imaging," was made available on April 20.

GE Completes Amersham Acquisition

General Electric (GE) Company announced on April 8 that it had acquired all outstanding shares of Amersham plc. Under the umbrella of GE Healthcare, the combination of GE Medical Systems and Amersham interests is projected to generate \$16 billion in revenues in 2005. GE Healthcare will be headquartered in Chalfont St. Giles (UK), with GE Healthcare Technologies in Waukesha, WI, and GE Healthcare BioSciences in Little Chalfont (UK). Among the stated goals of the acquisition were to "accelerate the development of molecular imaging and personalized medicine by more rapidly developing and bringing to market new targeted imaging agents and

diagnostics that will enable our customers to diagnose, treat, and monitor diseases at an earlier stage than ever before." Even before the acquisition, GE and Amersham had been collaborating on research and development of ^{18}F -fluorothymidine and its applications in PET imaging. Industry analysts have expressed interest in the company's plans for marketing both imaging apparatus and radiopharmaceuticals to the same customers.

GE Healthcare

Idle or Accessible? PET Problems in Canada

Newspapers across North America reported disputes between Canadian government officials and the PET community in early May. On April 28, physicians at the public-supported Hotel Dieu Hospital were ordered by Health Minister Philippe Couillard to stop renting access to their PET scanner to private clinics. On the surface, the move seemed a judicious example of fair allotment of medical care. If many Quebec citizens must wait for weeks or even months for PET scans under the government health plan, why should such scans be available on demand to private payers at as much as \$2,500 (Canadian) per examination?

The answer is not so simple but will be familiar to almost any nuclear medicine practitioner who has introduced new technology under stringent reimbursement rules: because of restricted funding, the scanner had been sitting idle for 18 hours per day. The hospital introduced a 2-tiered system in the hopes of maximizing revenues while better utilizing the new technology. The machine was installed in January 2003. In its first year, about 1,200 patients were scanned, only 60 of whom were private patients. The hospital collected approximately \$100,000 (Canadian) in rental fees. On Couillard's orders, the hospital immediately

stopped the rental arrangements on its scanners. In response to news of the unused scanner time, the Quebec Health Department announced it would set aside \$3.5 million per year so that 5,000 additional government-supported examinations can be performed on Quebec's 4 PET units. Diagnostic imaging under the government plan is free to Canadian citizens.

In London, Ontario, SNM member and University of Western Ontario Chair of Nuclear Medicine Jean-Luc Urbain, MD, was experiencing similar difficulties at St. Joseph's Hospital with his new PET/CT scanner, one of only 8 hybrid units in the entire country. Cancer Care Ontario, the government agency that makes reimbursement decisions, refused to pay for clinical imaging with PET/CT. Current research funding covers imaging of no more than 6 patients per week. "It is extremely embarrassing," Urbain told the local press. "It is pitiful to have a situation like this, where an instrument has been demonstrated to be extremely useful throughout the world and patients are being denied access to it." Despite the backlog of patients waiting to be imaged, Cancer Care Ontario insisted that both PET and the hybrid technology are unproven and called for additional clinical trials to assess their clinical effectiveness. "It is going backwards in time," said Urbain, citing the extensive U.S. FDA reviews and approvals in growing numbers of indications. "The government of Ontario is asking us to reinvent the wheel."

Joint Symposium on Biomedical Informatics

Registration is now open for the joint National Institutes of Health (NIH) Bioengineering Consortium and Biomedical Information Science and Technology Initiative Consortium symposium, to be held on the NIH campus in Bethesda, MD, June

21–22. Titled “Biomedical Informatics for Clinical Decision Support: A Vision for the 21st Century,” the symposium will focus on clinician decision support, including software tools and approaches needed to deliver biomedical information technologies to clinicians and patients at the time and place where decisions are made about risk, diagnosis, treatment, and follow-up. For more information about the symposium, including the agenda, scientific poster session, and online registration, see www.becon.nih.gov/symposium2004.htm.

National Institute for Biomedical Imaging and Bioengineering

Neuroscience Informatics Conference

Physicians and researchers met on April 26 and 27 on the National Institutes of Health (NIH) campus in Bethesda, MD, for a conference commemorating the 10th anniversary of the Human Brain Project (HBP). The conference was titled, “A Decade of Neuroscience Informatics: Looking Ahead,” and specialists reviewed the field’s achievements and predicted the direction of future technological, scientific, and social challenges and opportunities.

“The explosion of data about the brain is overwhelming conventional ways of making sense of it,” said Elias A. Zerhouni, MD, director of NIH. “Like the Human Genome Project, the HBP is building shared databases in standardized digital form, integrating information from the level of the gene to the level of behavior. These resources will ultimately help us better understand the connection between brain function and human health.”

The HBP is coordinated and sponsored by 4 federal agencies: NIH, the National Science Foundation, the National Aeronautics and Space Administration, and the U.S. Department of Energy. During its first 10 years, 241 investigators have been funded through the program for

a total of approximately \$100 million.

A complete copy of the program and links to specific aspects of the meeting can be accessed at: www.nimh.nih.gov/neuroinformatics/anmeeting.cfm.

National Institute of Mental Health

Unusual Patient, Top-Notch Care

The nuclear medicine staff at Martin Memorial Diagnostic Center in Stuart, FL, saw an unusual patient on April 28. Hutch, a 100-pound loggerhead turtle with an unidentified infection, underwent a ^{99m}Tc bone scan. “For Martin Memorial Health Systems or any other facility down here, it’s not a normal occurrence,” hospital representative Judy LeRose told a local TV station. Hutch had been undergoing rehabilitation at nearby Marinelifelife Center in Juno Beach. He had originally been found on the grounds of the St. Lucie Power Plant and brought to the center to recuperate before release into the wild. When he stopped eating, blood tests revealed an infection that could not be localized.

Randy Presley, a nuclear medicine technologist at Martin Memorial, responded to a request from Marinelifelife veterinarian Nancy Mettee by organizing an all-volunteer, after-hours special imaging session at the hospital. The patient was placed on his back under the camera, while staff held his flippers and rubbed his head during injection of the tracer and initial imaging. Four hours later, Hutch underwent a second round of imaging. “This was an interesting procedure,” said Presley. “I x-rayed a horse in the past but never a turtle.”

Results were pending at Newline press time, but Marineland staff hope to release Hutch in the near future.

From the Literature

Each month the editor of Newline selects articles on therapeutic, diagnostic, research, and practice issues in

nuclear medicine 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.

Therapy

RIT in Pneumococcal Infection

Researchers from Albert Einstein College of Medicine (Bronx, NY), the Institute for Transuranium Elements (Heidelberg, Germany), and the National Cancer Institute (Bethesda, MD) published promising results on the application of radioimmunotherapy (RIT) in the treatment of *streptococcus pneumoniae* in a mouse model and in vitro. Dadachova et al. reported their findings in the May issue of *Antimicrobial Agents and Chemotherapy* (2004;48:1624–1629). Some members of the group most recently reported on studies suggesting the feasibility of RIT for fungal infections (*J Nucl Med.* 2004; 45:313–320). In the current study, the authors evaluated the susceptibility of *S. pneumoniae* to human monoclonal antibody D11, which binds to pneumococcal capsular polysaccharide 8, conjugated with ^{213}Bi . Incubation of serotype 8 *S. pneumoniae* with ^{213}Bi -D11 resulted in dose-dependent killing of bacteria. Sixty percent more mice in the group treated with 80 μCi ^{213}Bi -D11 survived than in the untreated control group. No toxicities were noted. The authors concluded that the study “establishes that RIT can be applied to the treatment of bacterial infections.” They also noted the importance of developing non-drug-dependent methods of treating *S. pneumoniae*, for which new antibiotics must continually be developed to counteract evolving resistance.

Antimicrobial Agents and Chemotherapy

Ultrasound and Radionuclide Tumor Therapy

A study published in the April issue of *Ultrasonics* (2004;42:903–906) suggests that the expanding applications of radionuclides in diagnosis and therapy may reach to ultrasound. Van Wamel et al. from the Erasmus Medical College (Rotterdam, The Netherlands) reported on “adjunctive ultrasound contrast microbubble treatment,” a process that involves permeabilizing cells by sonoporation with a goal of increasing the antitumor efficacy of radionuclide treatment. The authors incubated rat pancreatic CA20948 tumor cells with 2 dyes labeled with ^{111}In -DOTA-Tyr(3)-octreotate. Uptake levels were compared for different ultrasound settings in cells treated with ultrasound and contrast microbubbles. They determined optimal microbubble-to-cell ratios and ultrasound settings that resulted in 160% higher internalization of the tracer than in untreated cells. They concluded that “these results show that adjunctive tumour treatment with the radionuclide ^{111}In -DOTA-Tyr(3)-octreotate and ultrasound contrast microbubbles may be feasible.” They suggested that with this technique, lower radionuclide doses would be required than those used in conventional radionuclide therapy to achieve the same antitumor effect.

Ultrasonics

^{131}I -Labeled mAbs for NHL

In a report e-published on April 20 ahead of print in *Blood*, Rizzieri et al. from Duke University Medical Center (Durham, NC) detailed the results of a phase I study of the pharmacokinetics, dosimetry, and toxicity of ^{131}I -antitennascin chimeric 81C6 for the treatment of non-Hodgkin’s lymphoma. The study included 9 patients, who received a dosimetric dose of 370 MBq. Of these, 3 received an administered activity of 1,480 MBq (2 of these patients developed toxicity requiring stem cell infusion) and 6 received an adminis-

tered activity of 1,110 MBq (2 developed toxicity requiring stem cell infusion). The mean effective half-life was 110 hours, and mean effective whole-body residence time was 159 hours. Uptake was rapid in the viscera but slower in tumor. Clearance was slower in tumor as well. The mean absorbed dose to the whole body was 67 cGy but was 963 (up to 1,517) cGy at tumor sites. One patient attained complete remission, and 1 attained partial remission. The authors concluded that, “These data demonstrate this radiopharmaceutical to be an encouraging agent for the treatment of lymphoma, particularly if methods to protect the normal viscera are developed.”

Blood

^{125}I -Labeled mAbs in Thyroid Tumor Xenografts

An investigation of the potential application of radiolabeled monoclonal antibodies (mAbs) to human thyroglobulin in tumor targeting in patients with differentiated thyroid carcinoma was reported in the April issue of the *Indian Journal of Experimental Biology* (2004;42:354–360) by Damle et al. from Bhabha Atomic Research Center (Mumbai, India). ^{125}I -labeled mAbs D5I and F9I were used in an immunosuppressed animal model bearing xenografts of human thyroid tumor tissue. Maximum tumor uptake was obtained at 72 hours after antibody injection. The absolute tumor uptake and tumor-to-blood ratio with mAb D5I were significantly higher than those for F9I or controls. The authors concluded that the results held promise for clinical applications, particularly for tumor targeting in patients whose metastases do not concentrate radioiodine.

Indian Journal of Experimental Biology

^{131}I Dose in Thyroid Remnant Ablation

Bal et al. from the All India Institute of Medical Sciences (New

Delhi) reported in the April issue of the *Journal of Clinical Endocrinology and Metabolism* (2004;89:1666–1673) on a large study designed to identify an optimal dose for ^{131}I remnant ablation therapy in differentiated thyroid cancer. The study included 509 patients, who were randomized into groups according to ^{131}I administered activity (15, 20, 25, 30, 35, 40, 45, and 50 mCi as a single dose). These patients had undergone total/near-total thyroidectomy (72%) or subtotal or hemithyroidectomy (28%). Remnant ablation was achieved in 59.6% (15-mCi group), 63.6% (20 mCi), 81.4% (25 mCi), 83.6% (30 mCi), 79.4% (35 mCi), 78.3% (40 mCi), 84.4% (45 mCi), and 81.8% (50 mCi) of patients, with an overall average of 77.6% (overall ablation rate, 77.6%). A significant difference was noted between ablation rates of those receiving less than 25 mCi and those receiving more, but no significant difference was noted among the groups receiving 25 mCi or more. The authors found that patients receiving at least 25 mCi of ^{131}I had a 3 times better chance of achieving remnant ablation than those receiving lower activities. The authors concluded that any administered activity of ^{131}I between 25 and 50 mCi appeared to be adequate for remnant ablation.

Journal of Clinical Endocrinology and Metabolism

Diagnosis

PET in SLE Assessment

Nowak et al. from the National Institute of Arthritis and Musculoskeletal Disease (Bethesda, MD) reported in the April issue of *Arthritis and Rheumatism* (2004;50:1233–1238) on a pilot study to evaluate the utility of ^{18}F -FDG PET in the assessment of distribution of activated lymphocytes in patients with systemic lupus erythematosus (SLE). The study included 10 patients with active SLE and 9 with inactive SLE in whom PET images were obtained from the inguinal region to above the ears, beginning 1 hour

after injection of the tracer. Imaging results and standard uptake values (SUVs) were compared. Increased ^{18}F -FDG uptake was noted in lymph nodes in both groups, although no statistical differences were noted between the 2 groups when compared with results in healthy volunteers. Thymic uptake was seen in 5 of 10 patients with active lupus but in none of the 9 patients with inactive disease. The authors concluded that "increased FDG uptake in lymph nodes of both patients with active SLE and patients with inactive SLE suggests that metabolic, and probably immunologic, activity is enhanced not only in active, but also in clinically quiescent, disease." They also concluded that the increased thymic uptake observed only in patients with active disease suggests that the thymus plays an important role during periods of disease activity.

Arthritis and Rheumatism

Scintigraphic Monitoring of Catheter Ports in Diabetics

Current methods of assessing the level of function in percutaneous catheter-port systems for continuous insulin therapy are invasive and carry the risk of infection. In the March issue of *Experimental and Clinical Endocrinology and Diabetes* (2004;112:148–152), Lindner et al. from the Institute of Molecular Biophysics, Radiopharmacy, and Nuclear Medicine (Bad Oeynhausen, Germany) reported on a noninvasive scintigraphic procedure to evaluate function in such systems and compared the absorption kinetics of intraperitoneal and umbilical catheter ports. The study included 10 patients with intraperitoneal catheter-port systems and 12 patients with umbilical catheter-port systems implanted into the partially redilated umbilical vein. In each group, 3 patients were experiencing catheter port dysfunction as confirmed by imaging or laparoscopy. $^{99\text{m}}\text{TcO}_4^-$ was injected into each patient's port, and a region of interest was drawn around the activity at the tip of each catheter. The half-life of tracer

absorption was calculated. No significant differences were noted in the absorption half-lives of the 2 groups with normal port system function (an average of 6.7 ± 3.2 min). These values differed significantly from those of the 2 dysfunctional catheter-port groups (19.3 ± 6.7 min). The authors calculated an upper threshold half-life value of 11.8 min to assess function. They concluded that imaging with $^{99\text{m}}\text{TcO}_4^-$ is "an accurate, noninvasive, and quick method to assess the function of both umbilical and intraperitoneal insulin catheter ports and that a half-life value > 11.8 min is indicative of a catheter dysfunction."

Experimental and Clinical Endocrinology and Diabetes

^{18}F -FLT and ^{18}F -FDG in Pulmonary Lesions

In a study published in the April issue of the *Journal of Thoracic and Cardiovascular Surgery* (2004;127:1093–1099), Halter et al. from the University of Ulm (Germany) reported on a prospective study comparing ^{18}F -FDG PET and 3-deoxy-3- ^{18}F -fluorothymidine (^{18}F -FLT) PET in the preoperative workup of central pulmonary focal lesions. The study included 20 patients with histologically confirmed bronchial carcinoma, 7 patients with benign lesions, and 1 patient with an atypical carcinoid. All underwent both ^{18}F -FDG and ^{18}F -FLT PET imaging before surgery, and results were compared with pathologic findings. Sensitivity and specificity for staging of the primary tumor were 86% and 100%, respectively, for ^{18}F -FLT PET and 95% and 73%, respectively, for ^{18}F -FDG PET. The sensitivity and specificity of ^{18}F -FLT PET for N stage assessment were 57% and 100%, respectively, and 86% and 100%, respectively, for ^{18}F -FDG PET. The authors concluded that these findings suggest that "the number of false-positive findings in FDG PET might be reduced with FLT PET" and that "PET imaging with FLT represents a useful supplement to FDG in assessing the

malignancy of central pulmonary focal lesions."

Journal of Thoracic and Cardiovascular Surgery

New Agents for Amyloid Plaque Imaging

Cai et al. from the National Institute of Mental Health (Bethesda, MD) reported in the April 22 issue of the *Journal of Medical Chemistry* (2004; 47:2208–2218) on a study evaluating ^{18}F -labeled 6-iodo-2-(4'-N,N-dimethylamino)phenylimidazo[1,2- α]pyridine (IMPY) derivatives as prospective agents for PET imaging of β -amyloid plaque in Alzheimer's disease. The authors described the synthesis process in detail, including the substitution of either a 3-fluoropropyl or a 2-fluoroethyl (^{18}F -FEM-IMPY) group for 1 of the 2 N-methyl groups of IMPY. In experimental PET imaging in mice, high uptake in the brain was observed with both tracers. Washouts of brain activity for the 2 analogs were biphasic, with an initial rapid phase over 20 minutes and a subsequent much slower phase. ^{18}F -FEM-IMPY autoradiography of postmortem brain sections from individuals with Alzheimer's disease showed high displaceable uptake in gray matter and low nonspecific binding in white matter. The authors concluded that "IMPY derivatives have favorable in vivo brain pharmacokinetics and a moderate affinity for imaging β -amyloid plaques; however, further improvements are needed to reduce radioactive metabolites, increase binding affinity, and reduce lipophilicity."

Journal of Medical Chemistry

HIV Infection Imaging

Venneti et al. from the University of Pittsburgh School of Medicine (PA) reported in the April issue of the *Journal of Clinical Investigation* (2004;113:981–989) on the use of PET to image brain macrophages in simian immunodeficiency virus (SIV)-infected macaques. Encephalitis, resulting from infiltration of the brain with infected and activated macrophages, is a common phenomenon in

both HIV infection in humans and SIV infection. Two authors of this study, Bissel and Wiley, reported earlier this year on productive and nonproductive infections of specific cell types in the brains of HIV-infected patients with and without HIV encephalitis (*Brain Pathol.* 2004;14:97–108). In the current study, ^{11}C -labeled PK11195, a ligand for peripheral benzodiazepine receptors, was injected into 11 SIV-infected macaques, each of which underwent PET imaging. Six animals showed increased binding in vivo. At post mortem, all 6 showed signs of encephalitis, whereas the macaques that showed no increase in tracer binding did not have encephalitis. The authors concluded that these results “suggest that PET ^{11}C -PK11195 imaging can detect the presence of macrophages in SIV encephalitis in vivo and may be useful to predict the development of HIV encephalitis and in studies of the pathogenesis and treatment of HIV dementia.” Of special note was the promise of the technique in early identification of encephalitis, facilitating faster initiation of treatment.

Journal of Clinical Investigation

Fast 3-D PET Image Reconstruction

Brasse et al. from the University of Pittsburgh reported in the April issue of *IEEE Transactions on Medical Imaging* (2004;23:413–425) on a method for performing fast and accurate 3-dimensional (3-D) backprojection using only a sequence of Fourier transform operations for line-integral data acquired by planar detector arrays in PET. Using software-based Fourier transform calculations, the authors compared their planogram backprojection with standard 3-D backprojection and showed that the novel approach resulted in a reduction in computation time by a factor of approximately 15.

IEEE Transactions on Medical Imaging

PET Imaging in Asia

Despite significant obstacles in availability of apparatus, radiophar-

maceuticals, and trained personnel, the routine use of clinical PET is spreading around the world. Ho, from the Hong Kong Sanatorium and Hospital (China), summarized the technology's advances in Asia in a survey article in the March issue of the *Annals of the Academy of Medicine, Singapore* (2004;33:155–165). The author pointed out that Asian and Western populations have distinct and characteristic disease spectrums and cancer incidences that call for different allocations of imaging resources. Some of the cancer types for which ^{18}F -FDG is less sensitive (hepatocellular carcinoma, urological carcinoma, gastric malignancy, mucinous and clear-cell gastrointestinal tumours, neuroendocrine tumours, and well-differentiated thyroid cancers) are more prevalent in Asia than in Europe or the Americas, leading to a higher false-negative rate. Conversely, with the greater prevalence of tuberculosis, more false-positive PET results in chest imaging are seen in Asia. The author lauded the strides that PET has made in Asia and called for a stronger emphasis on research into new radiopharmaceuticals that can address the specific needs of the populations being served.

Annals of the Academy of Medicine, Singapore

MIBI SPECT Alone Before Parathyroidectomy

Researchers from Tel Aviv University (Israel) reported in the April issue of *Archives of Surgery* (2004; 139:433–437) on a study designed to assess early postinjection $^{99\text{m}}\text{Tc}$ -sestamibi (MIBI) SPECT as the sole localizing procedure before focused parathyroidectomy in patients with primary hyperparathyroidism. The study by Schachter et al. included 82 consecutive patients with primary hyperparathyroidism who underwent a standard double-tracer subtraction planar scan for preoperative localization. Patients were scheduled for minimally invasive radioguided surgery. On the morning of scheduled

surgery, each patient received $^{99\text{m}}\text{Tc}$ -MIBI and underwent an early, postinjection SPECT study. Results verified at surgery indicated that the sensitivity of the SPECT studies averaged 96% versus 78% for the planar studies. The SPECT study was helpful in locating adenomas in 10 patients with multinodular goiter disease. No recurrent or persistent hyperparathyroidism was reported during a follow-up period of more than 6 months. The authors suggested that the use of preoperative SPECT as the only localizing study on the morning of the operation lowers costs and provides accurate 3-dimensional information on deeply seated or ectopic adenomas. In addition, the intraoperative gamma probe technique enables the surgeon to focus the search, provides instant feedback regarding the progress of the operation, reduces surgical trauma and complications, and yields better cosmetic results.

Archives of Surgery

PET and Management of Aggressive Lymphomas

PET is becoming a mainstay of management in a number of disease states, from diagnosis to staging to outcomes prediction. In the March issue of *Current Opinions in Oncology* (2004;16:100–105), Kasaman et al. from the Johns Hopkins Medical Institutions reviewed recent findings on PET contributions to risk assessment in patients. They found that PET has emerged as a strong prognostic tool in patients with aggressive lymphomas, accurately predicting relapse risk after only a few cycles of chemotherapy and providing important outcomes information. They concluded that “early identification of high-risk patients through the combination of PET and existing prognostic indices could lead to earlier implementation of intensive therapies and improved clinical outcomes.”

Current Opinions in Oncology