



Each month the editor of *Newslines* 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 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. 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

### “Positherapy”: $^{18}\text{F}$ -FDG in Breast Cancer

Moadel et al. from the Albert Einstein College of Medicine (Bronx, NY) reported in the February 1 issue of *Cancer Research* (2005;65:698–702) on continued research into targeted breast cancer therapy with  $^{18}\text{F}$ -FDG, a technique the group has termed “positherapy.” In previous work, the authors demonstrated the therapeutic potential of positrons in malignancy at the cellular level (*Breast Cancer Res.* 2003;5:R199–R205). The current article reports on tumor growth rate and survival after  $^{18}\text{F}$ -FDG therapy in a mouse breast cancer model. Tumor-bearing mice were treated with a dose of the radiotracer equivalent to the maximum tolerated dose for humans. The treatment resulted in significant prolongation of survival and decrease in tumor growth rate in comparison with nontreated controls. Substantial differences in distribution of glucose transporters (GLUT) 1, 4, and 8 in tumor masses were ob-

served, with GLUT1 localizing mainly in necrotic areas and expressed mostly at the cell membrane, indicating that GLUT1 was probably the most responsible for cellular uptake. The authors concluded that “these results are important for the development of positherapy with  $^{18}\text{F}$ -FDG for refractory metastatic breast and other cancers.”

*Cancer Research*

### Initial Treatment with $^{131}\text{I}$ -Tositumomab

Evidence of the effectiveness of  $^{131}\text{I}$ -tositumomab therapy continues to accrue, as the results of clinical trials are assessed and as elapsed time provides perspective on survival and quality of life. Results of a multi-institutional study were published in 2 journals in February. In the February 3 edition of the *New England Journal of Medicine* (2005;352:441–449), an article by Kaminski from the University of Michigan Medical Center (Ann Arbor) and other authors detailed a trial in which a single course of  $^{131}\text{I}$ -tositumomab therapy was used as initial treatment for patients with stage III or IV follicular B-cell lymphoma. The study included 76 patients who received a dosimetric administration of tositumomab and  $^{131}\text{I}$ -labeled tositumomab and 1 week later received the therapeutic dose. Of these patients, 75% (57) showed a complete response, with 40 of these responders remaining in remission for 4.3–7.7 years. Some response was noted in all but 5% of patients treated, and the 5-year progression-free survival for all patients was 59%, with a median progression-free survival of 6.1 years. Hematologic toxicity was moderate, but no transfusions or hematopoietic growth factors were required, and no cases of myelodysplastic syndrome were reported. The authors concluded that “a

single 1-week course of  $^{131}\text{I}$ -tositumomab therapy as initial treatment can induce prolonged clinical and molecular remissions in patients with advanced follicular lymphoma.” The editors of *The New England Journal of Medicine* hailed the treatment in a separate commentary as a “hot new treatment for lymphoma.”

In an article e-published ahead of print on February 24 in *Blood*, many of the same authors reported on the occurrence of treatment-related myelodysplastic syndromes and acute myeloid leukemia after initial therapy with  $^{131}\text{I}$ -tositumomab in patients with non-Hodgkin’s lymphoma (NHL) and compared these results with those from patients with NHL who had previously undergone treatment(s) with other regimens. Bennett from the University of Rochester School of Medicine (NY) and others outlined the aggregated results from 7 studies including 1,071 patients (995 with relapsed/refractory low-grade NHL with a median of 3 prior treatment regimens) and 76 patients with previously untreated low-grade follicular NHL. A single dose of tositumomab, followed 1 week later by the radiolabeled tositumomab, was administered. Median follow-up was 6 years after diagnosis and 2 years after radioimmunotherapy (RIT) in previously treated patients and 4.6 years after RIT for previously untreated patients. Treatment-related myelodysplastic syndromes and/or acute myeloid leukemia were reported in 35 of the 995 previously treated patients, but only 13 of these were confirmed to have developed these conditions after RIT, an incidence consistent with the prior chemotherapy regimens of these patients. During a median follow-up period of almost 5 years, no cases of treatment-related myelodysplastic syndromes or acute myeloid leukemia were re-

ported in the group of 76 patients receiving the  $^{131}\text{I}$ -tositumomab as initial therapy for NHL.

*The New England Journal of Medicine Blood*

## Long-Circulating Liposomes as Delivery Agents

Oku and Namba from the University of Shizuoka (Japan) reported in the February issue of *Methods in Enzymology* (2005;391:145–162) on the use of glucuronate-modified, long-circulating liposomes as effective antitumor drug carriers in therapy. The survey article included data previously reported by the authors' research group on antineovascular therapy by use of radiotargeted long-circulating liposomes (*J Control Release*. 2004; 100:41–52) and noted the benefits of monitoring localization and accumulation using PET techniques. The focus of the current article was on characteristics, in vivo trafficking, and usage in cancer therapy of glucuronate-modified liposomes, which bind to macrophage-like cells in vitro and passively accumulate in tumor tissue. This technique carries significant promise of reducing many of the side effects usually associated with the delivery of some anticancer agents.

*Methods in Enzymology*

## PET in Follow-Up of Hepatic Tumor Ablation

Blokhuis et al. from the VU Medical Center (Amsterdam, The Netherlands) reported in a late-year supplement to the *Scandinavian Journal of Gastroenterology* (2004; 241[suppl]:93–97) on the use of  $^{18}\text{F}$ -FDG PET and CT in long-term follow-up of patients who had undergone radiofrequency ablation of primary and secondary liver tumors. The study included 15 patients, of whom 1 had been diagnosed with primary liver tumor and the remaining 14 had been diagnosed with hepatic metastases from breast (1), ovary (1), renal cell (1), and colorectal (11) car-

cinoma. Each patient underwent CT imaging before and after ablation and at regular intervals, and 11 patients underwent PET scanning at regular intervals. The mean follow-up period was 16.8 months. Positive uptake, which defined tumor recurrence in the study, was seen in 4 of the 11 patients evaluated with PET at a mean period of 6.8 months. At CT evaluation, tumor recurrence was observed in these patients but at a mean time of 9.8 months. The authors concluded that "the use of PET in combination with CT scan at follow-up may lead to earlier detection of tumor recurrence than contrast-enhanced CT alone."

*Scandinavian Journal of Gastroenterology*

## Diagnosis

### PET and Aspects of Cerebral Blood Volume

Ito et al. from the Akita Research Institute of Brain and Blood Vessels (Japan) and Tohoku University (Sendai, Japan) recently published 2 reports in the *Journal of Cerebral Blood Flow and Metabolism* on the use of PET to measure aspects of cerebral blood volume (CBV). In the first, e-published ahead of print on February 16, the group described  $\text{H}_2^{15}\text{O}$  and  $^{11}\text{C}$  PET assessment of changes in the arterial fraction of human CBV during hypercapnia and hypocapnia. Their results indicated that alterations in CBV during these conditions are caused by changes in arterial blood volume with no accompanying changes in venous or capillary blood volumes. In the March issue of the same journal (2005;25: 371–377), the authors compared PET measurement of changes in cerebral blood flow and oxygen metabolism during neural activation with blood oxygenation level-dependent (BOLD) contrast measured by functional MRI.  $\text{C}^{15}\text{O}$ ,  $^{15}\text{O}_2$ , and  $\text{H}_2^{15}\text{O}$  PET studies were performed on volunteers both while executing a right-hand motor task and at rest, followed by functional MRI

studies to measure the BOLD signal under the same 2 conditions. A significant positive correlation was seen between changes in the cerebral blood flow and the BOLD signal, and a significant negative correlation was observed between changes in the cerebral oxygen extraction fraction and the BOLD signal. The authors concluded that "this supports the assumption on which BOLD contrast studies during neural activation are based."

*Journal of Cerebral Blood Flow and Metabolism*

### PET/CT in RT Planning for Non-Small Cell Lung Cancer

$^{18}\text{F}$ -FDG PET/CT and CT alone were compared in modeling of radiotherapy planning for patients with CT-staged N2–N3M0 non-small cell lung cancer (NSCLC) in a study by van der Wel et al. from the Maastricht Clinic (Maastricht, The Netherlands) published in the March 1 issue of the *International Journal of Radiation Oncology, Biology, Physics* (2005;61: 649–655). The study included 21 patients. Two 3-dimensional conformal treatment plans were devised for each patient, one with CT-based and the other with PET-based planning target volumes, both designed to deliver 60 Gy in 30 fractions. Dosimetric factors were calculated, and tumor control probabilities were estimated. The authors found that the average gross tumor volume of nodes was lower on PET/CT than on CT ( $9.9 \pm 4.0$  and  $13.7 \pm 3.8$  cm, respectively) and that all dose-volume characteristics for the esophagus and lungs decreased in favor of PET/CT. For the same toxicity levels of the lung, esophagus, and spinal cord, the dose could be increased from  $56.0 \pm 5.4$  Gy with CT planning to  $71.0 \pm 13.7$  Gy with PET planning. Because the information provided by PET/CT not only reduced the risk of volume and location error but also allowed significant radiation dose escalation, the tumor control probability was raised. The authors concluded that "the results of

this modeling study support clinical trials investigating incorporation of FDG-PET information in CT-based radiotherapy planning.”

*International Journal of Radiation Oncology, Biology, Physics*

### Novel Analogs for PET- and SPECT-Aided RT

Ginjt et al. from the University Hospital Basel (Switzerland) reported in the February 1 issue of *Clinical Cancer Research* (2005;11:1136–1145) on preclinical evaluation of novel octreotide analogs with broad human somatostatin receptor (sstr) profiles for PET and SPECT imaging to refine targets in radiotherapy. The authors studied 2 promising synthetic octreotides: [1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA),1-Nal<sup>3</sup>,Thr<sup>8</sup>] octreotide (DOTA-NOC-ATE) and [DOTA,BzThi<sup>3</sup>,Thr<sup>8</sup>]-octreotide (DOTA-BOC-ATE), each labeled with both “cold” and radioactive <sup>111</sup>In. The properties of these analogs were compared with those of the more familiar <sup>111</sup>In-DOTA-TOC, which shows affinity only to human sstr2. The authors found that both analogs showed high affinity to human sstr2, sstr3, and sstr5, with lesser but notable affinity to sstr4, and were internalized much more efficiently than was <sup>111</sup>In-DOTA-TOC. Biodistribution studies in rats showed high (twice that of <sup>111</sup>In-DOTA-TOC) and specific uptake of both novel analogs in tumor and in sstr-expressing normal tissue, with significantly lower renal uptake. The authors concluded “these data suggest that the novel radiopeptides are superior to <sup>111</sup>In/<sup>90</sup>Y-DOTA-TOC and show great promise for the clinical application in the imaging of sstr-positive tumors and their targeted radiotherapy.”

*Clinical Cancer Research*

### PET Assesses Function in Vegetative States

In an article published in the March issue of the *Journal of Neurology, Neurosurgery, and Psychia-*

*try* (2005;76:432–434), Coleman et al. from Addenbrooke’s Hospital (Cambridge, UK) reported on continued research with PET to identify and differentiate the neurologic characteristics of patients in vegetative and minimally conscious states. The focus in this study was on the relationship between neuronal electrical function in 10 patients (6 in the vegetative state and 4 minimally conscious) who underwent simultaneous electroencephalography and PET imaging. The authors found that homeostatic coupling between neuronal electrical activity and regional glucose metabolism was preserved in all the minimally conscious patients but was absent in all the vegetative state patients. These results, they concluded, suggest that “patients in the vegetative state may endure an impaired coupling relation between neuronal electrical function and cerebral energy metabolism.”

*Journal of Neurology, Neurosurgery, and Psychiatry*

### PET in Parkinson’s Response to Apomorphine

Hosey et al. from the National Institutes of Health (Bethesda, MD) and scientists from Rush University Medical Center (Chicago, IL) and the University of Amsterdam (The Netherlands) reported in the January/February issue of *Clinical Neuropharmacology* (2005;28:18–27) on the use of H<sub>2</sub><sup>15</sup>O PET to explore the time course of central nervous system responses to apomorphine in patients with idiopathic Parkinson’s disease (PD) and in healthy volunteers. After baseline imaging, agonist-induced changes in regional cerebral blood flow (rCBF) were evaluated both in and outside areas usually associated with PD changes. Administration of apomorphine reversed the increased rCBF in PD patients in subcortical regions, including the basal ganglia and cerebellum, and produced widespread effects throughout the brain. Because these effects were seen out-

side the areas usually associated with changes in patients with PD, the authors discussed the implications of the results for a revised model of apomorphine effects.

*Journal of Neurology, Neurosurgery, and Psychiatry*

### PET and Cardiac Hemodynamics in Adenosine Infusion

In an article published in the February 15 issue of the *Journal of the American College of Cardiology* (2005;45:553–558), Mishra et al. from the Harvard Medical School (Boston, MA) reported on the use of <sup>13</sup>N-ammonia PET to elucidate the relationship between myocardial blood flow and peripheral hemodynamic effects during intravenous adenosine infusion. The study included 348 individuals with no evidence of obstructive coronary artery disease. Each patient underwent <sup>13</sup>N-ammonia PET imaging at rest and during a 6-minute adenosine infusion. The authors found that during the infusion, heart rate increased and mean arterial pressure decreased, and that neither of these measures correlated well with hyperemic myocardial blood flow or coronary vascular resistance. They concluded that changes in cardiac hemodynamics during intravenous adenosine infusion are generally poor predictors of changes in myocardial blood flow or coronary vascular resistance during peak hyperemia and “should not be used to assess the effectiveness of vasodilator stress in myocardial perfusion imaging.”

*Journal of the American College of Cardiology*

### <sup>18</sup>F-FDG PET and Depression in Early Alzheimer’s

Holthoff et al. from the Dresden University of Technology (Germany) reported in the February 15 issue of *Biological Psychology* (2005;57:412–421) on PET measures of altered cerebral glucose metabolism in patients

with early Alzheimer's disease (AD). The study included 53 patients with early AD (17 with apathy; 10 with clinical depression; and 26 with neither of these symptoms) who underwent  $^{18}\text{F}$ -FDG imaging. Apathy was found to be associated with significant decreases in left orbitofrontal regions when compared with patients free of apathy. Depression was associated with hypometabolism in dorsolateral prefrontal regions. The authors concluded that "these findings support the notion that different functional circuits underlie apathy and depression in early AD."

*Biological Psychology*

### **PET Identifies Spinal Cord Compression in Melanoma**

In the March issue of the *European Journal of Surgical Oncology* (2005;31:197–204), Francken et al. from the Royal Prince Alfred Hospital (Camperdown, Australia) described a study designed to evaluate the utility of  $^{18}\text{F}$ -FDG PET in identifying spinal cord compression in patients with metastatic melanoma. The study included records of 1,365 PET studies from patients with melanoma. Of these, 50 were identified as being at risk of spinal cord compression, and 35 of these were reviewed with MR imaging and CT to confirm or refute the diagnoses. In 9 patients, compression of the spinal cord or adjacent neurologic structures was confirmed, with 8 patients undergoing immediate treatment. The authors concluded that PET can detect imminent, unsuspected spinal cord compression in patients with metastatic melanoma and that "immediate anatomical imaging of the spine is recommended in patients who have evidence of spinal cord compression on PET."

*European Journal of Surgical Oncology*

### **PET, PET/CT, and MR Imaging in Charcot Neuroarthropathy**

PET, hybrid PET/CT, and MR imaging were compared in the preop-

erative evaluation of diabetics with Charcot foot deformities in a study published in the December issue of *Foot and Ankle International* (2004;25:890–895) by Hopfner et al. from the Justus-Liebig University of Gießen (Germany). The study included 16 patients with type 2 diabetes with previous clinical and radiologic diagnoses of Charcot neuroarthropathy. Out of a total of 39 Charcot lesions confirmed at surgery, 37 were detected by dedicated PET, 30 by PET/CT, and 31 by MR imaging. The authors pointed out that PET carries several advantages over MR imaging in the diabetic foot. Not only can PET aid in differentiating between osteomyelitis and Charcot neuroarthropathy, but it is more accurate in patients in whom metal implants may compromise MR findings. They concluded "because it provides important additional data, ring PET may be preferable to radiography and MRI in the preoperative evaluation of patients with Charcot neuroarthropathy of the foot. Hybrid PET, because of its poorer resolution compared to ring PET, appears less suitable for routine clinical application."

*Foot and Ankle International*

### **$^{99\text{m}}\text{Tc}$ -MDP and Bone Mineral Density Measurements**

Campbell et al. from the Royal Perth Hospital (Australia) reported in the spring issue of the *Journal of Clinical Densitometry* (2005;8:14–17) on the effect of  $^{99\text{m}}\text{Tc}$ -methylene diphosphonate ( $^{99\text{m}}\text{Tc}$ -MDP) on bone mineral density (BMD) measurements in the lumbar spine and neck of the femur. The study included 20 patients who underwent dual-energy X-ray absorptiometry with a Hologic QDR4500 scanner before and after injection of the radiotracer. A group of 30 volunteers underwent similar sequential imaging and assessment with the injection of the radioisotope. No significant change in BMD measures were detected after  $^{99\text{m}}\text{Tc}$ -MDP injection for either measurement site, and compari-

son with the control group showed that the precision of the readings was similar in both groups. The authors concluded that "this study has shown that any effect produced by a typical bone scan dose of  $^{99\text{m}}\text{Tc}$ -MDP is small in comparison with the intrasubject variance when estimating BMD" and when using the scanner in this study.

*Journal of Clinical Densitometry*

### **$^{99\text{m}}\text{Tc}$ -Sestamibi in Radioguided Parathyroidectomy**

In the March issue of the *European Journal of Surgical Oncology* (2005;31:191–196), Rubello et al. from the Istituto Oncologico Veneto (Rovigo, Italy) evaluated the efficacy of low-dose  $^{99\text{m}}\text{Tc}$ -sestamibi administration for radioguided parathyroid surgery in patients with primary hyperparathyroidism. The study included 300 such patients, who underwent preoperative  $^{99\text{m}}\text{Tc}$ -sestamibi subtraction scintigraphy and high-resolution ultrasonography. Of these patients, 211 were scheduled for minimally invasive radioguided parathyroidectomy and 89 were scheduled for traditional bilateral neck exploration.  $^{99\text{m}}\text{Tc}$ -sestamibi was injected 10 minutes before intraoperative radiolocalization, and rapid parathyroid hormone assays were performed. Of the patients who underwent minimally invasive radioguided parathyroidectomy, 207 were successfully treated for a solitary parathyroid adenoma (PA) through a 2–2.5-cm skin incision. Radioguided surgery was less successful in the second group, especially in patients with  $^{99\text{m}}\text{Tc}$ -sestamibi-avid nodules. Even in these patients, however, the combination of radioguided surgery and rapid parathyroid hormone assay was helpful in the management of multigland disease. The authors concluded that "low-dose  $^{99\text{m}}\text{Tc}$ -sestamibi administered a few minutes before surgery is sufficient for minimally invasive radioguided parathyroidectomy in patients with high likelihood of a solitary

PA and without concomitant  $^{99m}\text{Tc}$ -sestamibi-avid thyroid nodules.”

*European Journal of Surgical Oncology*

## **$^{11}\text{C}$ -WAY PET and Chronic Fatigue Syndrome**

Cleare et al. from the Institute of Psychiatry and Guy's, King's and St. Thomas' School of Medicine (London, UK) reported in the February

issue of *Biological Psychiatry* (2005; 57:239–246) on a study assessing brain 5-HT<sub>1A</sub> receptor binding potential using PET  $^{11}\text{C}$ -WAY-100635 in patients with chronic fatigue syndrome (CFS). The study included 10 medication-free patients, who fulfilled consensus criteria for CFS and had no diagnosed psychiatric illness, and 10 healthy individuals. The authors found that the patients with CFS showed a marked reduction in

5-HT<sub>1A</sub> receptor binding potential compared with control individuals, a difference that was especially visible in the hippocampus. They noted that this decrease is not necessarily a primary feature of CFS but may be related to underlying pathophysiology or may be secondary to other processes, such as previous depression or biological changes associated with CFS.

*Biological Psychiatry*

## **NOTIFICATION OF PROPOSED BYLAWS CHANGE**

March 15, 2005

Members of the Society of Nuclear Medicine:

The following Item represents a proposed amendment to the SNM Bylaws based on the request of SNM members and the House of Delegates. This change was presented to the House of Delegates at the recent mid-winter meeting in Tampa and is now being distributed to the membership. Its approval will be voted on by the House of Delegates in June 2005.

The proposal would add a new section to Article III (Membership) to create an additional designation for members, i.e. Life Member. This designation would not replace the existing membership classifications but would rather give special recognition to members who have met certain criteria, determined by the Board of Directors.

Sincerely,

*Warren H. Moore, MD*

Warren Moore, MD  
Chair, Committee on Bylaws

### **ITEM 1**

#### **ADD to ARTICLE III**

#### **Section 2: Life Membership**

**Members of the Society in any membership classification who have made special contributions and commitments to the Society may be designated by the Board of Directors as Life Members. Criteria for eligibility and selection procedures shall be determined by the Board. Life Members shall retain all rights, privileges, and responsibilities of their membership classification and shall have such additional privileges and recognition as are granted by the Board, consistent with the Bylaws.**

**RATIONALE:** A mechanism is desired to recognize and reward individuals who have made specific contributions to the Society including monetary contributions and a commitment to be involved in the furtherance of the mission of the Society. Life membership may have a different dues structure and certain limited privileges, such as VIP registration, as determined by the Board. Life Membership is an additional designation, which members may seek in addition to their primary membership classification.

Existing Sections 2 and 3 of Article III would be renumbered as Sections 3 and 4 respectively but would not be changed in any other way.