

# Nuclear Medicine Makes News at SNM Annual Meeting



An insider's look at SNM 2004 in Philadelphia.

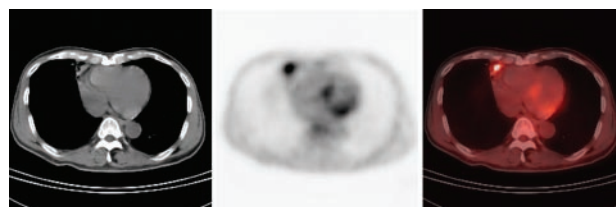
World attention was directed toward the 51st Annual Meeting of the SNM, June 19–23, at the Pennsylvania Convention Center in Philadelphia. More than 4,000 nuclear medicine physicians, scientists, physicists, pharmacists, technologists, and industry representatives attended the 4 days of special programs, educational sessions, scientific presentations, and auxiliary events. In the exhibition hall, more than 2,000 exhibitors and vendors showed their products and discussed their work with attendees.

Working with a list of presenters prepared by the SNM Program Committee, Society staff and consultants prepared a series of scientific press releases for distribution at the meeting. Extensive coverage followed, including synopses on major broadcast networks and cable news channels, in newspapers around the world, and on radio news. Among the foci of especially intense interest were the potential benefits of new technologies; techniques for the early diagnosis of Alzheimer's disease (AD); advanced imaging for the diagnosis, staging, and treatment of cancer; nuclear cardiology; and growing collaboration between nuclear medicine and bioengineering. This month, Newsline looks at a few of the presentations that received international notice.

## The Discriminating Power of PET/CT

Antoch et al. from University Hospital Essen (Germany) reported in a session on June 20 on the accuracy of

$^{18}\text{F}$ -FDG PET/CT in tumor staging in 260 patients with a range of oncologic disease (Fig. 1). All patients underwent PET/CT for staging, and designated reader teams subsequently evaluated (using the TNM system) CT images alone, PET images alone, and CT plus PET viewed separately. The results were compared with the results of fused imaging and with baseline references of histopathology and clinical follow-up. The authors found that 218 patients (84%) were correctly staged with PET/CT, 197 (76%) with side-by-side CT and PET, 163 (63%) with CT alone, and 166 (64%) with PET alone. Sensitivity and specificity for PET/CT were 92% and 93%, respectively, better than for any of the separate or side-by-side



**Figure 1.** Sixty-eight-year old male with hepatocellular carcinoma. On CT alone (left) a small lesion of the pericardium was not determined to represent thoracic disease. PET alone (center) demonstrated an area of increased glucose metabolism falsely diagnosed as a pulmonary metastasis. Fused PET/CT datasets (right) accurately pointed the area of increased glucose metabolism to the small pericardial lesion. The pericardial metastasis was verified on follow-up.

modality interpretations. The authors concluded that tumor staging with PET/CT is significantly more accurate than PET or CT alone or side-by-side display of images, a diagnostic advantage that in this study translated into beneficial changes in management for a number of patients. Antoch noted, "We are ecstatic with the results. Obviously, when dealing with all types of cancers, the sooner we can get to the treatment the better. The new tumor imaging method using the integrated PET/CT will now allow doctors and patients to get an earlier jump on the disease."

On June 22, Namdar et al. from University Hospital (Zurich, Switzerland) presented an evaluation of PET/CT image quality in coronary lesion anatomy and pathophysiologic severity in a group of 25 patients with previously documented coronary artery disease (Fig. 2). The addition of PET integrated with CT angiography was significant. Of the 15 false-positive coronary segments identified by angiography, 13 were correctly labeled as normal by PET. In the 14 lesions without patent bypass graft, PET revealed stress-induced ischemia in 7 lesions in 6 patients, thus relieving the 8 remaining patients of the financial and physical burden of unnecessary revascularization. According to Namdar, "In the medical community, we are always looking for new ways to approach old problems. Any time you can avoid invasive procedures without sacrificing accuracy or increasing risk, you're doing a great service to the patient. In the case of the combined PET/CT scanner, we have found a very accurate method of diagnosing potential heart risks that is much easier on the patient."

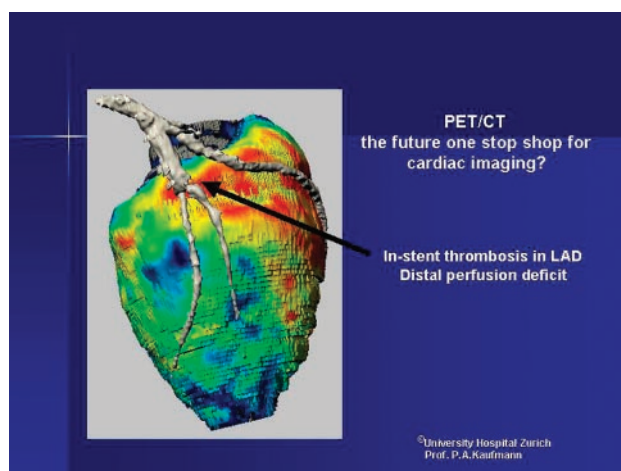
While PET/CT applications in oncology continue to expand, the fused modality is also gaining ground in imaging infection. Keidar et al. from the Rambam Medical Center presented results on June 21 on the use of  $^{18}\text{F}$ -FDG PET/CT for the evaluation and differentiation of localized osteomyelitis adjacent to pedal soft-tissue infec-

tion in diabetic patients. Osteomyelitis occurs in up to one third of diabetic foot infections, often as a result of direct contamination from a soft-tissue lesion. Early diagnosis and initiation of antibiotic therapy are essential in sparing the limb. The study included 13 patients with diabetes who underwent PET/CT imaging for suspected osteomyelitis of the foot. PET/CT images were evaluated, as were separate PET and CT images, and the results were compared with definitive diagnoses at surgery or clinical follow-up.  $^{18}\text{F}$ -FDG uptake on PET imaging alone proved effective in correctly identifying 8 patients with infection. PET/CT helped to refine these diagnoses in 5 patients with uptake in bone (indicating osteomyelitis), as well as to identify the 3 patients in whom infection was confined to soft tissue. The authors concluded that PET is helpful in imaging diabetes-related infection and that PET/CT adds a level of precise anatomic localization that can prove crucial in initiating early and effective therapy. Keidar told the press, "If we can detect the precise location of infection, the treatment strategy will be easier to define. Our study shows how advances in imaging technology can directly affect patient care and make a big difference for patients with complications of diabetes."

### Wide Range of PET Topics

Infection was also the focus of a study reported in a poster session by Fukuchi and Ishida from The National Cardiovascular Center (Osaka, Japan). The team investigated the use of  $^{18}\text{F}$ -FDG PET in the differentiation of infected from noninfected vascular grafts. The study included 15 patients, some with suspected infected grafts and others with stable, noninfected grafts. Diagnoses based on PET were compared with final diagnoses based on surgical results or clinical follow-up. PET successfully identified inflammatory foci in all 7 patients with infection. Fukuchi noted, "Infection of vascular prosthetic grafts remains a major surgical challenge, because it can be reduced but not eradicated by avoiding risk factors and by applying antibiotic therapy." PET studies appear to accurately, safely, and specifically diagnose graft infection and facilitate the timely initiation of appropriate therapy.

In a report that received the international media coverage at the SNM annual meeting, Wang et al. of the U.S. Department of Energy's Brookhaven National Laboratory (Upton, NY) reported on the use of  $^{18}\text{F}$ -FDG PET to elucidate the functional neurologic connections between hunger and the stimulating presence of food. The study included 12 healthy individuals, in whom brain response was measured in 3 different situations: food stimulation, neutral stimulation, and no stimulation. Before each situational testing (on separate days), participants were food deprived for 18 hours. Participants' regional brain metabolic activities were assessed by PET when presented with food (visual, olfactory, auditory, and gustatory display of food), when presented with non-food-related

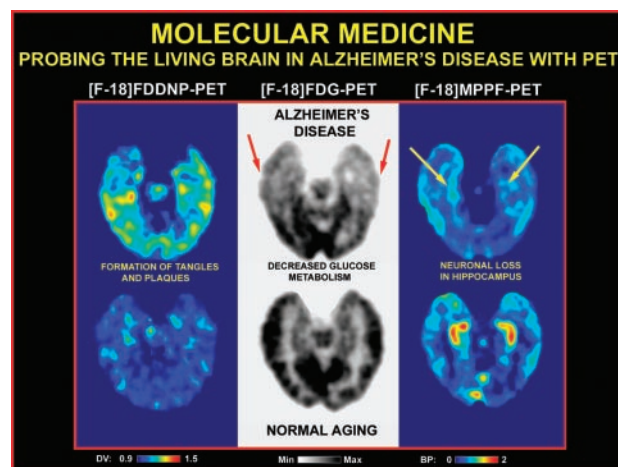


**Figure 2.** Visualizing the coronary artery tree with PET/CT. The narrowed coronary artery indicated is reducing blood flow to the heart muscle it serves, demonstrated by areas of reduced perfusion shown in blue.

items, and at baseline with no stimulation. Restraint, disinhibition, and hunger factors were scored separately and correlated with metabolic activity. The authors found that food stimulation significantly increased brain metabolic activity. According to Wang, “individuals for whom food is more reinforcing have to rely more on cognitive control to not eat when they have the desire to eat. Our results showed that people who have higher metabolic changes in the left ventral striatum of the brain during food stimulation need more cognitive restraint; in other words, for those who are more sensitive to food stimulation, it is more difficult and takes more effort to diet.” He added, “if we know how the brain reacts to food and hunger, we can figure out what occurs chemically during perceived abnormal responses. The hope is that, if we understand the brain’s chemical response to food, then we will be able to manage things like eating disorders and find new and innovative treatment options.”

On June 22, Tawakol et al. from Massachusetts General Hospital (Boston, MA) reported on the use of  $^{18}\text{F}$ -FDG PET in imaging carotid plaque and providing a noninvasive index of inflammation. The study included 9 patients with moderate-to-high-grade carotid stenosis who underwent PET imaging that was coregistered with carotid MR studies. In each patient, standard uptake values (SUVs) were assessed for assigned quadrants every 2.5 mm along the length of the carotid plaque. Plaque tracer uptake was reported as a ratio of plaque to separately measured blood SUV. Results were compared with histologic examination of carotid specimens collected during endarterectomy within 1 month of imaging. The results revealed a high correlation of  $^{18}\text{F}$ -FDG uptake on PET with the degree of plaque inflammation. “This is the first time FDG PET imaging has been used to provide an index of vascular inflammation in human subjects,” said Tawakol. “The potential applications of the study are numerous. Obviously, early detection and better characterization of carotid plaque could enhance our ability to combat stroke. We also anticipate that the FDG-PET method could be used to test plaque-stabilizing drugs. Moreover, we hope that a similar method might be developed to detect coronary artery disease in the future.”

PET continues to be a focus of efforts assessing methods to definitively detect and quantify progression in AD (Fig. 3). On June 22, Kepe et al. from the University of California at Los Angeles–David Geffen School of Medicine reported on PET studies to establish patterns of binding distribution of  $^{18}\text{F}$ -FDDNP as an *in vivo* measure of AD pathology progression. The study included 13 patients diagnosed with AD and 10 control subjects. All individuals underwent both  $^{18}\text{F}$ -FDDNP PET and  $^{18}\text{F}$ -FDG PET imaging. Regional SUVs for  $^{18}\text{F}$ -FDDNP were found to be elevated in the medial temporal lobe, parietal lobe, and prefrontal area in patients with AD compared with control participants.  $^{18}\text{F}$ -FDG PET imaging for the AD patients showed parallel decreases in glucose metab-



**Figure 3.** Representative examples of 3 PET scans performed in a patient with Alzheimer’s disease (AD) (upper row) and in a cognitively normal control subject (lower row). The patient with AD has decreased glucose metabolic rate (~20%) in the temporal lobe (middle column) and decreased serotonin 1A receptor density (50%–60%) in the hippocampi indicative of significant level of cell loss in those regions (right column); in contrast,  $^{18}\text{F}$ -FDDNP binding is elevated in all cortical areas demonstrating presence of neurofibrillary tangles and senile plaques (left column).

olism in temporoparietal regions and correlated well with the increased global  $^{18}\text{F}$ -FDDNP binding also observed in these patients. These observations were in agreement with known patterns of post mortem pathology reported in the literature. The authors concluded that “All tested measures of  $^{18}\text{F}$ -FDDNP binding very well separate AD and control populations, which, together with the pattern of the binding distribution, gives a very good indication of disease involvement.” Kepe told the press, “This opens opportunities for the use of PET with  $^{18}\text{F}$ -FDDNP, not only for possible diagnosis in early stages of the disease but also for testing the effects of future experimental drugs developed to prevent lesion formation and for monitoring the effects of the drugs aimed at removing the lesions.”

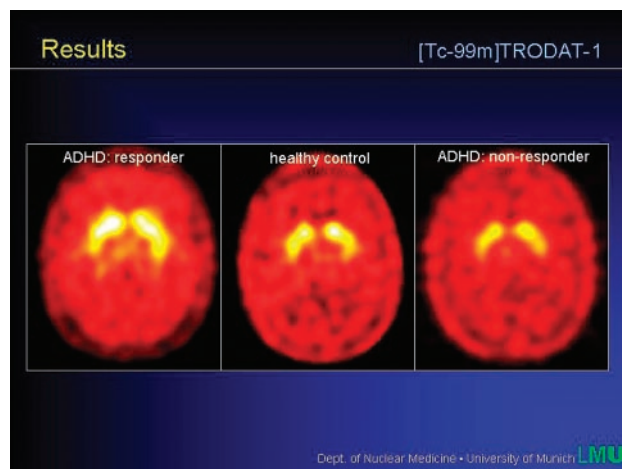
### Predicting Outcomes

The ability of nuclear imaging to accurately stage oncologic disease is being rapidly expanded to include the prediction of outcomes after surgery and to a range of potential therapies. Outlining what some press coverage described as “crystal ball” capabilities, Eschmann et al. from the University of Tübingen (Germany) reported on June 21 on the prognostic effect of  $^{18}\text{F}$ -fluoromisonidazol ( $^{18}\text{F}$ -MISO) PET in the management of patients with non-small cell lung cancer (NSCLC) and head and neck cancer (HNC). The study included 31 patients (NSCLC = 20; HNC = 11) who underwent both dynamic and static PET scans at 2 and 4 hours after injection of 400 MBq  $^{18}\text{F}$ -MISO. All patients were scheduled for curative radiotherapy. PET data were correlated with clinical follow-up



(available on 19 patients only). The authors found that uptake values for the tracer were nondiagnostic at 2 hours after injection but that uptake values at 4 hours after injection clearly separated those patients who would experience local recurrence from those who would not. Tumor-to-muscle ratios (TMRs) assessed at 4 hours after injection also correlated with the risk of relapse. No patient with a TMR < 1.4 ( $n = 3$ ) presented with tumor recurrence, whereas 50% of patients with TMRs of 1.4–2 ( $n = 6$ ) and 90% of patients with TMRs > 10 ( $n = 10$ ) experienced recurrence. The authors concluded that the results of radiotherapy can be predicted in this group of patients on the basis of the kinetic behavior of  $^{18}\text{F}$ -MISO in tumor tissue and that accumulation, high uptake, and high TMR are highly suggestive for an incomplete response to treatment. Eschmann said, “Should this technique become standard practice—using  $^{18}\text{F}$ -MISO PET images to predict the possible recurrence of tumor—then treatment methods can correspond to prognosis. We believe that  $^{18}\text{F}$ -MISO PET represents a valuable tool for patient discrimination. Patients with increased risk of relapse may be introduced to an intensified therapeutic regimen.”

SPECT was featured in a study to predict clinical response of adult patients with attention deficit hyperactivity disorder (ADHD) to methylphenidate (MPH; Ritalin) treatment (Fig. 4). On June 22, la Fougère et al. from the University of Munich (Germany) reported on a study designed to determine whether the degree of binding of  $^{99\text{m}}\text{Tc}$ -TRODAT-1 to striatal dopamine transporters could predict response to MPH as measured by the Clinical Global Impressions (CGI) scale before and after treatment. Because 20%–30% of patients with ADHD do



**Figure 4.** Attention deficit hyperactivity disorder (ADHD) patients who demonstrated high levels of dopamine transporter molecules in the brain responded better to therapy with methylphenidate, a dopamine transporter-blocking drug, than those with low binding values. Measurement of dopamine transporter levels may be useful in predicting which ADHD patients will respond to treatment with methylphenidate.

not respond to MPH therapy, a method of predicting therapeutic response would eliminate unnecessary medication and facilitate the initiation of alternative therapies. The study included 18 adult patients, 13 of whom showed high levels of dopamine transporter binding. Of these, 12 showed significant improvement of symptoms after initiation of MPH therapy. None of the 5 patients who showed reduced uptake was seen to improve with MPH. According to la Fougère, “Our results indicate that measurement of dopamine transporter may be an important prognostic predictor for therapeutic response to Ritalin. If we can determine who will respond to the drug and who will not respond, then only those patients who will benefit will be treated.”

### Targeted and Genetic Therapies

The role of external radiation beam therapy in mantle cell lymphoma has been limited by the systemic nature of the disease. Radioimmunotherapy (RIT) offers a promising alternative, but one that must be carefully coordinated with chemotherapeutic regimens. On June 22, Divgi et al. from the Memorial Sloan-Kettering Cancer Center (New York, NY) reported on a sequential regimen using tositumomab (Bexxar) RIT for cytoreduction (to provide optimal crossfire) followed by CHOP chemotherapy. The study included 13 patients with untreated mantle cell lymphoma who showed measurable disease with less than 25% bone marrow involvement. Each patient underwent a tositumomab/ $^{131}\text{I}$ -tositumomab regimen followed 13–16 weeks later by 6 cycles of CHOP. After all sequential treatments were completed, the overall response rate was 75%. Of the 10 participants who finished all treatments, 9 achieved a complete response. Side effects and toxicities were within acceptable limits. According to Divgi, “although further follow-up is necessary to determine if this novel therapeutic approach represents a treatment advance in mantle cell lymphoma, the results of this particular study—a 90% complete remission rate—were outstanding.”

A reversed sequential use of Bexxar was reported by Kostakoglu et al. from the Weill Cornell Medical Center and the Center for Lymphoma and Myeloma (New York, NY) and the Corixa Corporation (San Francisco, CA) on June 22. This group looked at the efficacy of sequential administration of fludarabine followed by RIT with the tositumomab/ $^{131}\text{I}$ -tositumomab regimen in patients with untreated non-Hodgkin’s lymphoma (NHL). The study included 38 patients with NHL (51% follicular mixed and 49% follicular small cleaved). All but 1 patient were categorized as having stage III or IV disease. All patients underwent 3 cycles of fludarabine therapy (3 patients dropped out of the study during this phase). The response to fludarabine among the remaining patients was 89% (3 complete responses, 28 partial responses). After

*(Continued on page 52N)*

studies using VEGF inhibitors in patients with von Hippel-Landau syndrome and RCC.

*Urologic Oncology*

## Functional Imaging and Radiotherapy Planning

In a study published in the June issue of *Medical Physics* (2004;31:1452–1461), Das et al. from Duke University (Durham, NC) reported on an investigation of the dosimetric feasibility of delivering radiotherapy doses to lung tumors in proportion to  $^{18}\text{F}$ -FDG activity measured in tumors on PET. The fact that FDG uptake is correlated with tumor cell proliferation rate, the authors reasoned, implies that this dose delivery strategy

is theoretically capable of providing the same duration of local control at all voxels in tumor. Preliminary work with target dose-delivery calculations based on SPECT maps of normal lung perfusion was outlined and additional considerations described. An intensity modulation optimization methodology was developed to deliver the calculated doses and applied to 2 patients with lung cancer. Dosimetric feasibility was assessed by comparing spatially normalized dose-volume histograms from the nonuniform dose prescription ( $^{18}\text{F}$ -FDG PET derived) with those from a uniform dose prescription with equivalent tumor integral dose. Although the optimization methodology was capable

of delivering the nonuniform target prescription as easily as the uniform target prescription, in 1 patient the critical structure dosage from the nonuniform dose prescription exceeded dose-volume/function limits and greatly exceeded that from the uniform dose prescription. Adhering to these limits in practice would theoretically entail reduction of the duration of local control. The authors concluded that “even though it appears feasible to tailor lung tumor dose to the FDG-PET activity distribution. . . strict adherence to dose-volume/function limits could compromise the effectiveness of functional image guided radiotherapy.”

*Medical Physics*

*From the SNM Annual Meeting (Continued from page 16N)*  
Bexxar therapy, all patients showed a response, with 83% showing a complete response. Seventy-two percent of all patients treated are still in complete remission 4.4 years later. Kostakoglu noted that “the results are very encouraging. We feel that further evaluation of the addition of RIT to chemotherapeutic regimens for patients with follicular lymphoma is warranted. This may be the future of treatment with radiolabeled antibodies.”

The use of radiotracers in gene therapy is among the most rapidly growing areas in medical research. Lee et al. from the Case Western Reserve University (Cleveland, OH), the Thomas Jefferson National Accelerator Facility (Newport News, VA) and the University of Virginia (Charlottesville) reported on small animal  $^{125}\text{I}$ -FIAU

imaging of the expression of the HSV1-tk delivered into cystic fibrosis (CF) knockout mice. The authors had previously reported on in vivo imaging of radiolabeled DNA complexes containing the therapeutic CF transmembrane conductance regulator gene and monitored its distribution in transgenic CF mice. The HSV1-tk in the current study was delivered in the same fashion. In this study, a custom-built imaging system included both x-ray and planar gamma scintigraphy. The authors found that x-ray images of the mice were readily aligned with scintigraphic images and that radioactivities detected on day 2 indicated that new genetic material was being expressed in the lungs of the mice. According to Lee, “Although the results are preliminary, they are extremely encouraging.” ❁

*de Hevesy Award (Continued from page 36N)*

Alavi’s contributions to nuclear medicine extend well beyond his own research. He and his wife, Dr. Jane Alavi, have been long-time supporters of educational and research opportunities for students in nuclear medicine. Their names are associated with the Alavi–Mandell Awards, which recognize trainees and young scientists who publish articles as senior authors in *The Journal of Nuclear Medicine*. Their generosity also supports the Pilot Research Grants and the Bradley–Alavi Student Fellowship Awards funded by the Education and Research Foundation (ERF) of the SNM. The Alavis not only continue to contribute to the foundation but are

active in persuading other colleagues to join them in their support of these important endeavors. Most recently, Abass donated time, energy, and funds to his country of origin, Iran, by assisting physicians and scientists from that country in developing a PET center. He is similarly generous with his time: he serves on the Society’s ERF board of directors and is also involved in numerous SNM activities.

“I am honored that I was selected by the Society of Nuclear Medicine for such a distinction,” said Alavi. “I share this recognition with my family, my mentors, and with so many students with whom I have worked over the past 3 decades. This is truly a highlight of my career.” ❁