NRC Seeks ACMUI Nominations

The Nuclear Regulatory Commission (NRC) announced in December a request for nominations for the position of interventional cardiology physician on the Advisory Committee on the Medical Uses of Isotopes (ACMUI). The official call for nominations appeared in the *Federal Register* on December 9 (2003;68:68652). Nominees should be interventional cardiologist physicians with experience in intravascular brachytherapy use of radiation sources. Committee members serve a 3-year term, with possible reappointment to an additional 3-year term. The ACMUI advises NRC on policy and technical issues related to the regulation of the medical use of radioactive material. Responsibilities include providing comments on changes to NRC rules, regulations, and guidance documents; evaluating certain nonroutine uses of radioactive material; providing technical assistance in licensing, inspection, and enforcement cases; and bringing key issues to the attention of the NRC for appropriate action. The current committee membership includes the following professionals: nuclear medicine physician, nuclear cardiologist, medical physicist in nuclear medicine (unsealed byproduct material), therapy physicist, radiation safety officer, nuclear pharmacist, 2 radiation oncologists, patients' rights advocate, FDA representative, state government representative, and health care administrator. Nominees must be U.S. citizens and be able to devote approximately 80 hours per year to committee business. Members who are not federal employees are compensated for their service and reimbursed for expenses. Nominees will undergo a security background check and will be required to complete financial disclosure statements to avoid possible conflicts of interest. Interested candidates should submit 4 copies of a resumé to the Office of Human Resources, attn: Ms. Joyce Riner, 301-415-5030, arw@nrc.gov, Mail Stop T2D32, U.S. Nuclear Regulatory Commission, Washington DC 20555. Applications will be accepted until March 8. For more information, contact Angela R. Williamson, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington DC 20555.

U.S. Nuclear Regulatory Commission

NRC Seeks Comment on Changes to Certification Criteria

The Nuclear Regulatory Commission (NRC) is requesting public comment on proposed changes to criteria used to recognize certifications conferred by professional specialty boards on applicants for various medical radiation safety positions. In a proposed rule announced on December 9 in the *Federal Register (2003; 68:*68549–68563), the NRC listed several proposed changes to 10 CFR Part 35, "Medical Use of Byproduct Material," based on recommendations by the NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI). According to a commission press release, the proposed rule is designed to make the process of recognizing boards by the NRC or Agreement States more efficient. These proposed changes, developed by the NRC and Agreement States in consultation with the ACMUI, would remove some of the prescriptive requirements for recognition of board certifications. The proposed rule would provide boards more latitude in making the determination that an individual is fully trained and capable of performing duties related to radiation safety. The revised requirements would include a degree from an accredited college or university, professional experience, passing an examination conducted by the specialty board, and specialized training. The specific degree level and amount of training and experience required would vary depending on the position. A public comment period will remain open until February 23. Comments may be submitted by post to Secretary, U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, ATTN: Rulemakings and Adjudications Staff; by fax to (301) 415-1101; or by e-mail to SECY@nrc.gov. Comments may also be submitted online via the NRC's rulemaking Web site at http://ruleforum.llnl-.gov. All comments should include "RIN 3150-AH19" in the subject line.

U.S. Nuclear Regulatory Commission

New Grant.gov Web Site

The U.S. Department of Health and Human Service (HHS) unveiled on December 9 a single, comprehensive Web site on finding and applying for all federal grant programs. The Web site, Grants.gov, is designed to make it easier for organizations to learn about and apply for federal grants. "For the first time, there will be a single government-wide source for information about grants programs across the federal government," said HHS Secretary Tommy Thompson. "By putting relevant information in one place, we're helping to level the playing field for organizations less familiar with federal grant programs so that they too can identify and apply for appropriate grants." HHS led the development of the cross-agency Web site, which now has information about more than 800 available grant programs involving all 26 federal grant-making agencies. These agencies together award more than $360 billion in grant funds. The site provides information in a standardized format across agencies and includes a "Find Grant Opportunities" feature to help applicants identify potential funding. The site also contains an "Apply for Grants" feature that simplifies the application process by allowing applicants to download, complete, and submit applications for specific grant opportunities from any federal grant-making agency. As of January 1, application packages had been posted to the

Grants.gov Web site by 5 U.S. Departments: Commerce, Education, Energy, Justice, and HHS. This section will be expanded in the coming months as federal agencies continue to post application information about additional grant opportunities. The site was developed with extensive input from organizations that apply for and receive federal grants. Grants.gov is a collaborative effort involving HHS and the Departments of Agriculture, Commerce, Defense, Education, Homeland Security, Housing and Urban Development, Justice, Labor and Transportation, as well as the National Science Foundation. More information is available at www.grants.gov.

U.S Department of Health and Human Services

NIH Issues RFA on Interdisciplinary Training

A new request for applications (RFA), intended to stimulate the development of interdisciplinary training programs, was issued on December 23 as part of the National Institutes of Health (NIH) Roadmap activities. The purpose of this RFA is to encourage and enable the development of an interdisciplinary workforce by ensuring that undergraduate, predoctoral, and postdoctoral students receive the didactic and research experiences necessary to lead and/or engage in integrative and team approaches to solve complex biomedical and health problems. To accomplish this aim, the NIH is inviting applications for developing and implementing novel training programs focused on new interdisciplinary science. This solicitation has several unique features: (1) undergraduate students may be supported in these programs; (2) support is not limited to U.S. citizens and permanent residents; and (3) support is provided for up to 10% faculty release time for course or curriculum development. Additional information about this program, including application criteria and guidelines, can be found in the announcement, which can be accessed at http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-015.html. Applications for this RFA are due at NIH by March 10, 2004.

National Institutes of Health

News from NIBIB

New Deputy Director. Roderic I. Pettigrew, MD, director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the National Institutes of Health (NIH), named Belinda Seto, PhD, as deputy director of NIBIB on December 16. In this position, she will work directly with Pettigrew to oversee all aspects of the institute's operations. Seto assumed this position after a nearly 1-year tenure as acting deputy director for extramural research at the NIH, where she served as advisor to the NIH director on extramural policy issues and was responsible for developing and implementing policies and procedures for extramural research and training programs funded by the NIH. She has also served as deputy director of the Office of Extramural Research (OER) and director of the Office of Reports and Analysis in the OER. She received her doctorate in biochemistry from Purdue University and has been with NIH for almost 30 years

Workshop on Biomedical Industry Research and Training. NIBIB conducted a workshop to explore new avenues for partnering and interacting with industry on December 16 and 17 in Bethesda, MD. The goals of the workshop were to obtain input from biomedical industry representatives on (1) specific research needs or problems that need to be solved to provide significant improvements in healthcare and (2) ways that the NIBIB and industry can collaborate to effectively translate research results to patient care and to address anticipated manpower needs. Participants included representatives from 23 companies that encompassed a broad range of commercial biomedical endeavors, representatives from NIH and other federal agencies, and extramural observers. Specific topics discussed during the meeting included industry research needs that will result in significant health care improvements, federal government–biomedical industry interactions, and future personnel needs and associated training opportunities. Research discussion focused on topics that industry currently would not or could not support as part of research agendas. Additional information on the workshop is available at www.nibib.nih.gov. A report detailing the results of the workshop will be prepared and posted on the site.

Grant application resource. NIBIB staff announced on December 16 the development of a new resource designed to assist applicants in the grant writing process. A checklist for grant applicants using the PHS 398 has been developed. This checklist is primarily for use in writing R01 and R21 applications, but many of the items on the list apply to other grant mechanisms. Applicants are encouraged to review this list and make sure that all items have been addressed before submitting completed applications. The checklist can be accessed on the NIBIB Web site at www.nibib.nih.gov/about/Applicant_Checklist.pdf.

National Institute of Biomedical Imaging and Bioengineering

"Nuclear Forensics" Highlighted by IAEA

The extension of radiotracers to crime solving was highlighted at a fall meeting at the International Atomic Energy Agency (IAEA) in Vienna, Austria. Experts from Argentina, Australia, Germany, Italy, and Turkey met in November 2003 at the IAEA to review the use of nuclear techniques in forensic applications. These techniques include but are not limited to neutron activation analysis, x-ray fluorescence, proton-induced x-ray emission, ^{14}C "bomb pulse" recent dating, and γ spectrometry. As a complimentary tool to conventional

investigation methods, nuclear analytical techniques can provide additional evidence to clarify criminal cases. The IAEA is working to share experience and improve analytical capabilities in the field, particularly in developing countries. Drawing on reported cases worldwide, the IAEA is now documenting experience in the field, including case studies highlighting the use of nuclear techniques. The November meeting was initiated to compile information for updating where and how nuclear and related techniques are being used for police investigations of criminal cases as well as antiterrorism activities. This work is in addition to the IAEA's activities in other areas of the emerging field of nuclear forensics, including a focus on analyzing the nature, use, and origin of nuclear materials through determination of radioisotopes, isotopic and mass ratios, material age, impurity content, chemical form, and physical parameters. Analytical methods developed for nuclear forensic applications are used in international safeguards and for preventing illicit nuclear trafficking.

International Atomic Energy Agency

Positrons, Antimatter, and Cancer

The European Organisation for Nuclear Research (CERN; Geneva, Switzerland) and PBar Labs (Newport Beach, CA) announced on November 25 the completion of the first experiments designed to reveal the biologic effectiveness of antiproton radiation in cells. The international collaboration, initiated by PBar, relied on CERN's accelerator technologies. "We are grateful that CERN agreed to host and give support to the experiments," said Larry Welch, PBar CEO. "CERN is the only research facility in the world providing an antiproton beam with the characteristics needed for such experiments." Dr. Rolf Landua from CERN added, "The study of biological effects of antiprotons on cells is of great interest for potential future therapeutical applications. We at CERN are very happy to take part in this pioneering and fundamental research." Dr. Rodney Withers, chair of the Radiation Oncology Department at the UCLA Medical Center and a senior member of the PBar collaboration stated, "The measured results to date indicate that for a narrow dose peak at the end of their path the antiprotons deliver an effective dose which is about 10 times higher than at the surface where the beam entered." Researchers on the project speculated on the tissue-sparing possibilities of antiproton therapy and the possibility that the number of treatment sessions might be reduced for many patients. The collaboration included researchers from CERN and University Hospital Geneva, the UCLA Medical Center, the University of Aarhus and Aarhus University Hospital in Denmark, British Columbia Cancer Research Center in Canada and the University of Maastricht in The Netherlands. Publication of preliminary results is expected in early 2004.

European Organisation for Nuclear Research

PBar Labs

DOE-Funded Scientists Decode DNA of Clean-Up Bacterium

Department of Energy (DOE)-funded researchers have decoded and analyzed the genome of a bacterium with the potential to bioremediate radioactive metals and generate electricity, according to a DOE press release issued in mid-December and an article published in the December 12 issue of *Science* (2003;302:1967–1969). Researchers at The Institute for Genomic Research (TIGR; Rockville, MD) and the University of Massachusetts, Amherst, reported that *Geobacter sulfurreducens* possesses "extraordinary" capabilities to transport electrons and reduce metal ions as part of its energy-generating metabolism. These researchers had previously found that *Geobacter* species can precipitate a wide range of radionuclides and metals (including uranium, technetium and chromium) from groundwater, preventing them from migrating to wells or rivers. The analysis of the genome sequence revealed a number of capacities that had not been previously suspected. "We've provided a comprehensive picture that has led to fundamental changes in how scientists evaluate this microbe," said Barbara Methé, the TIGR researcher who led the genome project. "Research based on genome data has shown that this microbe can sense and move towards metallic substances, and, in some cases, can survive in environments with oxygen." *Geobacter* reduces metal ions in a chemical process during which electrons are added to the ions. As a result, the metals become less soluble in water and precipitate into solids, which are more easily removed. Small charges of electricity are also created through the reduction process. The latter process interests the DOE because of the potential to create a *Geobacter* "bio-battery." *Geobacter* microbes are widely distributed in nature and are commonly found in subsurface environments contaminated with radionuclides and metals. Researchers have demonstrated that if they "feed" the microbes simple carbon sources, such as acetate, they grow faster and precipitate more radionuclides and metals. These findings are now serving as the basis for a test of a bioremediation strategy aimed at removing uranium from groundwater at a Uranium Mill Tailings Remedial Action site in Colorado. The Natural and Accelerated Bioremediation Research (NABIR) and Microbial Genome Programs in the DOE's Office of Science funded the $800,000 *G. sulfurreducens* sequencing project. More information on NABIR is available at www.lbl.gov/NABIR and on the Microbial Genome Program at http://doegenomes.org.

U.S. Department of Energy

Newsbriefs from the Literature

Diagnosis

Abnormalities Visible with PET Decades Before Alzheimer's Onset

Two studies widely covered in the popular media in December indicated promising results in the use of ^{18}F-FDG PET in the identification of functional brain abnormalities in persons at genetic risk for late-onset Alzheimer's disease (AD). A study by Reiman et al. from the Banner Good Samaritan Medical Center (Phoenix, AZ) was e-published on December 19 ahead of print in the *Proceedings of the National Academy of Sciences.* The authors had previously reported that cognitively normal, late-middle-aged carriers of the apolipoprotein E ϵ4 allele, a common susceptibility gene for late-onset AD, have abnormally low rates of glucose metabolism in the same brain regions as patients with probable AD. The current study was designed to assess whether ϵ4 carriers show the same abnormalities as young adults. Apolipoprotein E genotypes were established in normal volunteers between the ages of 20 and 39. Clinical ratings, neuropsychologic tests, MR imaging, and PET imaging were performed in 12 ϵ4 heterozygotes, all with the ϵ3/ϵ4 genotype, and 15 noncarriers of the ϵ4 allele, 12 of whom were individually matched for sex, age, and educational level. An automated algorithm was used to generate an aggregate surface-projection map that compared regional PET measurements in the 2 groups. The young adult ϵ4 carriers and noncarriers did not differ significantly in clinical ratings or neuropsychologic test scores. However, the young ϵ4 carriers had abnormally low rates of glucose metabolism bilaterally in the posterior cingulate, parietal, temporal, and prefrontal cortex. The authors concluded that "carriers of a common Alzheimer's susceptibility gene have functional brain abnormalities in young adulthood, several decades before the possible onset of dementia."

Haier et al. from the University of California, Irvine, reported in the December 23 issue of *Neurology (*2003; 61:1673–1679) on a study using ^{18}F-FDG PET to assess the origin and sequence of predementia brain changes in middle-aged individuals with Down syndrome, a group identified as at risk for dementia. The study included 17 individuals with Down syndrome, 10 individuals with moderate Alzheimer's disease, and 24 age-matched control subjects. Regional cerebral glucose metabolic rates (GMRs) were measured during the performance of a cognitive task. Statistical parametric mapping conjunction analyses showed that both the Down syndrome and Alzheimer's groups had lower GMRs (primarily in the posterior cingulate) than the controls. Compared with controls, the Down syndrome group had higher GMRs in the same areas of inferior temporal/entorhinal cortex in which the individuals with Alzheimer's disease had lower GMRs. Results were similar when remeasured after 1 year. The authors concluded that hypermetabolism in the temporal/entorhinal cortex in Down syndrome patients may reflect a compensatory response early in disease progression. They suggested that these compensatory responses may subsequently fail, leading to neurodegenerative processes that would be "detectable in vivo as future GMR decreases in inferior temporal/entorhinal cortex" and accompanied by clinical signs of dementia.

Proceedings of the National Academy of Sciences

Neurology

Whole-Body PET/CT vs. MRI in Tumor Staging

In the December 23 issue of *Journal of the American Medical Association* (2003;24:3199–3206), Antoch et al. from University Hospital Essen (Germany) reported on a definitive study to determine the staging accuracies of both whole-body PET/CT and whole-body MRI for different malignant diseases. The prospective study included 98 patients (mean age, 58 years old; range, 27–94 years) with various oncologic diseases who underwent back-to-back whole-body ^{18}F-FDG PET/CT and whole-body MRI for tumor staging. The mean follow-up period for these patients was 273 days (range, 75–515 days). Images were evaluated by 2 blinded reader teams, and diagnostic accuracies of PET/CT and MRI were compared. The authors found that PET/CT correctly determined the overall TNM stage in 75 (77%) patients, whereas MRI determined overall TNM stage in 53 patients (54%). PET/CT had a direct impact on patient management in 12 patients, and MRI changed the therapy regimen in only 2 patients. Separate assessment of T stage (with pathologic verification) in 46 patients showed PET/CT to be accurate in 37 (80%) and MRI to be accurate in 24 (52%). N stage was correctly determined in 91 patients (93%) with PET/CT and in 77 patients (79%) with MRI. The 2 procedures showed nearly equal abilities in detecting distant metastases. The authors concluded that "superior performance in overall TNM staging suggests the use of ^{18}F-FDG PET/CT as a possible first-line modality for whole-body tumor staging."

Journal of the American Medical Association

Coregistration of Cardiac Ultrasound and SPECT

Walimbe et al. from the Cleveland Clinic Foundation (OH) reported in the December issue of the *International Journal of Cardiovascular Imaging* (2003;19:483–494) on a study demonstrating the feasibility of multimodality registration of anatomic information from 2D and 3D cardiac ultrasound images with perfusion data from cardiac SPECT images. For 9 sets of cardiac ultrasound and SPECT cine loops, the authors

performed temporal alignment by interpolation of existing SPECT images at cardiac phases corresponding to available ultrasound images images. Spatial registration was performed in 3D image space using a mutual information-based approach. Experts from both echocardiography and nuclear medicine rated the clinical utility of each registration using a scale of 1–5, with a rating of 3 or higher indicating clinical utility. Five examples of 2D ultrasound–SPECT registration received an average rating of 4.2, and 4 cases of 3D ultrasound–SPECT registration received an average rating of 2.85. The overall average evaluation (3.58) was greater than the predetermined level of 3 likely to indicate clinical utility. The authors concluded that coregistration of SPECT and ultrasound is not only feasible but "has the potential to provide a more accurate and powerful tool for diagnosing coronary artery disease."

International Journal of Cardiovascular Imaging

^{99m}Tc-MAG3 Renography in Short-Term Hypothyroidism

In an article e-published ahead of print in the December 17 issue of the *American Journal of Nephrology*, Karanikas et al. from the University of Vienna (Austria) reported on a study using ^{99m}Tc-mercaptoacetyltriglycine (^{99m}Tc-MAG3) renography to investigate possible changes in renal tubular function in severe short-term hypothyroidism. The study included 27 patients (7 men, 20 women; ages, 19–79 years) who had undergone thyroidectomy and, subsequently, ^{99m}Tc-MAG3 renography both before and after thyroid hormone replacement therapy. As part of the study, ^{51}Cr-ethylenediaminetetraacetic acid (^{51}Cr-EDTA) clearance and serum creatinine concentrations were determined. The authors found that serum creatinine concentrations were significantly higher in hypothyroidism (1.30 ± 0.44 mg/dL) than after thyroxine substitution (1.04 ± 0.32 mg/dL). ^{51}Cr-EDTA clearance showed that the glomerular filtration rate was significantly lower in hypothyroidism (61 ± 18 mL/min) than after treatment (75 ± 23 mL/min). However, the authors found no influence of thyroid hormones on the outcomes of ^{99m}Tc-MAG3 renography, with no significant differences in total excreted activities and other parameters. These findings suggested that renal hemodynamic changes in severe hypothyroidism mainly affect glomerular function and that, in general, "the glomerular filtration rate reduction seems to be reversible after hormone substitution therapy." The authors added that care should be taken in patients with renal insufficiency.

American Journal of Nephrology

Comparative Costs of SLN Biopsy

Ronka et al. from Helsinki University Hospital (Finland) reported in the January issue of the *Annals of Oncology* (2004;15:88–94) on a study comparing total hospital costs of 3 different sentinel lymph node (SLN) biopsy protocols with those of diagnostic axillary lymph node dissection (ALND) in breast cancer. The study included 237 patients with breast cancer who underwent SLN biopsy with frozen-section diagnosis. The sequences of treatment procedures for each patient were evaluated using 3 hypothetical scenarios: diagnostic ALND, SLN biopsy without frozen-section diagnosis, and SLN biopsy as out-patient surgery before breast surgery (if any). The actual hospital costs per patient were €3,750. The costs per patient would have been €3,020 with the ALND model, €4,087 if the frozen section had not been performed, and €4,573 with the SLN biopsy on an outpatient basis before surgery. The costs with or without frozen-section diagnosis would have been approximately equal at a threshold false-negative rate of 35%. The authors concluded that the SLN procedure was associated with higher hospital costs than diagnostic ALND, but that frozen-section diagnosis "seems to be worthwhile" as long as the false-negative rate is <35%.

Annals of Oncology

Respiration Effects in PET/CT

In an article e-published ahead of print on December 16 in *European Radiology*, De Juan et al. from the University Hospital Zurich (Switzerland) reported on a study assessing the frequency and severity of respiration-induced curvilinear respiration artifacts (RICAs) on PET/CT images with varying CT respiration protocols. The retrospective study included 2 groups of 100 patients each. One group had been imaged with PET/CT before and the other after the implementation of a protocol with breath hold in the normal expiration position for the CT acquisition. In both groups, CT data were used for attenuation mapping and image coregistration, and RICAs were consensus ranked by 2 observers on a scale of 0 (no visible RICAs) to 3. A significant difference was noted between the 2 groups, with a 45% decrease in artifact frequency and a 68% decrease in grade-2 and -3 artifacts in the group using the normal expiration breath-hold protocol. The authors concluded that these results suggest that "breath hold during the normal expiration position for CT scanning can be recommended to reduce the occurrence and the severity of RICA on PET/CT."

European Radiology

PET Predicts Survival in Pancreatic Carcinoma

Sperti et al. from the University of Padova (Italy) and Castelfranco Veneto (Venice, Italy) reported in the December issue of the *Journal of Gastrointestinal Surgery* (2003;7:593–560) on a study evaluating the role of ^{18}F-FDG PET in predicting survival in patients with pancreatic cancer.

The retrospective study began with 118 patients who underwent ^{18}F-FDG PET for staging of pancreatic cancer. Standardized uptake values (SUVs) were calculated for 60 of these patients. This group was divided into high- (SUV $>$ 4; 29 patients) and low- (SUV $\leq$ 4; 31 patients) uptake groups, and individual TNM status was determined, along with tumor grade, medical or surgical treatment, and other parameters. The authors found that survival was significantly and inversely influenced by tumor stage, tumor grade, and SUV but that only stage and SUV were independent predictors of survival. When patients who were analyzed for SUV were stratified according to other variables, ^{18}F-FDG uptake also correlated with survival when any of the following factors was considered: stage III–IVa, stage IVb, tumor resection, moderately differentiated tumors, age $<$ 65 years, CA19-9 levels $>$ 300 kU/L, and absence of diabetes. The authors concluded that "SUV calculated with ^{18}F-FDG PET is an important prognostic factor for patients with pancreatic cancer and may be useful in selecting patients for therapeutic management."

Journal of Gastrointestinal Surgery

^{99m}Tc-Pertechnetate-Labeled Antigranulocyte Antibodies in Splenic Atrophy

Huic et al. from Zagreb University (Croatia) reported in the December issue of the *Croatian Medical Journal* (2003;44:767–768) on the use of ^{99m}Tc-pertechnetate-labeled antigranulocyte antibodies (anti-NCA-95) in scintigraphy to assess the spread and activity of disease in a patient with poorly controlled ulcerative colitis. The 14-year-old boy had a 7-year history of the disease, with suspected disturbance of splenic function. Scintigraphy showed high anti-NCA-95 uptake in the rectum and sigmoid and descending colon, indicating an active inflammatory process. The spleen was not visible on the scans, although it had been noted on ultrasound examination in a previous year. In a subsequent colectomy, no spleen was found. The authors noted that many of the benefits of anti-NCA-95 scintigraphy as a diagnostic tool were shown in this patient: "With a single injection, we were able to show the spread and activity of the intestinal disease, distribution and function of the granulopoietic bone marrow, and absence of the spleen."

Croatian Medical Journal

Radiolabeled mAb J591 in Metastatic Prostate Cancer

Bander et al. from the New York-Presbyterian Hospital/Weill Medical College of Cornell University (New York, NY) reported in the November issue of the *Journal of Urology* (2003;170:1717–1721) on an interim analysis of imaging data collected in 2 phase I radioimmunotherapy (RIT) trials to assess the ability of radiolabeled monoclonal antibody (mAb) J591 directed to the extracellular domain of prostate specific membrane antigen (PSMA) to target sites of known metastatic prostate cancer. The trials were designed to evaluate dose-limiting toxicity, maximum tolerated dose, pharmacokinetics, and organ dosimetry in patients with progressing hormone-independent prostate cancer. In trial 1, 29 patients received In-labeled J591 for imaging and ^{90}Y-labeled J591 for therapy. In trial 2, 24 patients were treated with ^{177}Lu-labeled J591, which can be imaged. In the present study, planar gamma camera imaging studies on these 2 groups of patients were reviewed and compared with sites of metastatic prostate cancer seen on bone scan, CT, and/or MRI. Bone scan, CT, or MRI showed evidence of metastatic disease in 46 (87%) of 53 patients. In the 43 patients who were evaluable with radiolabeled J591, bone and/or soft tissue lesions were targeted accurately in 42 (98%). The authors concluded that "radiolabeled J591 accurately targets bone and soft tissue metastatic prostate cancer sites and may be useful for targeting therapeutic and/or diagnostic imaging agents."

Journal of Urology

^{18}F-FDG Uptake in Malignant Pleural Mesothelioma

Researchers from the Brigham and Women's Hospital and Harvard Medical School (Boston, MA) reported in the December issue of *Thorax* (2003;48:1077–1082) on a study evaluating the significance of the pattern, intensity, and kinetics of ^{18}F-FDG uptake in patients with malignant pleural mesothelioma. The study by Gerbaudo et al. included 16 patients who had been diagnosed with pleural disease after undergoing CT and who subsequently underwent ^{18}F-FDG imaging with a dual-detector gamma camera operating in coincidence mode. Resulting ^{18}F-FDG uptake index and increment of ^{18}F-FDG lesion uptake over time (malignant metabolic potential index [MMPi]) were calculated, and the results compared with histology findings. On histology, 12 patients were found to have malignant mesotheliomas (10 epithelial, 2 sarcomatoid), with a total of 32 positive lesions. Patterns of uptake matched observations on extent of disease from both surgery and CT. Extrathoracic spread and metastases were found to have higher ^{18}F-FDG uptake indices than primary or nodal lesions. No correlation was found between histologic grade and stage. Although the intensity of lesion uptake was poorly correlated with histologic grade, good correlation was noted with surgical stage. ^{18}F-FDG lesion uptake increased over time at a higher rate in patients with more advanced disease. The MMPi was a better predictor of disease aggressiveness than histologic grade. The authors concluded

that these results suggested that "the pattern, intensity, and kinetics of ^{18}F-FDG uptake in mesothelioma are good indicators of tumor aggressiveness and are superior to the histological grade in this regard."

Thorax

Prediction of Cardiac Events in "Normal" MPS

Abidov et al., from the Cedars-Sinai Medical Center (Los Angeles, CA) reported in the November 19 issue of the *Journal of the American College of Cardiology* (2003;42:1818–1825) on a study evaluating the prognostic value of transient ischemic dilation (TID) of the left ventricle (LV) in patients with normal stress myocardial perfusion SPECT (MPS). The study included 1,560 patients (group 1) with normal stress MPS (436 vasodilator and 1,124 exercise stress) findings and no rest LV enlargement, who were followed for 2.30 ± 0.67 years for cardiac death or myocardial infarction (hard events [HE]) and revascularizations (soft events [SE]). Such events were also analyzed in a broader group of 2,037 patients with normal stress MPS (group 2, including patients with minimal defects). Events for patients in group 1 totaled 42 (13 HE, 36 SE). Patients in the highest TID quartile (TID ≥ 1.21) had a higher total event rate than others, regardless of the type of stress test. Other independent predictors of total events were age, typical angina, and diabetes. In group 2, TID was also predictive of total events. The authors concluded that "in patients with otherwise normal MPS, TID is an independent and incremental prognostic marker of total events, even after significant clinical variables—age, typical angina, and diabetes—are accounted for." They noted that their findings also appear to apply to the broader population of "normal" MPS, which included patients with minimal perfusion defects.

Journal of the American College of Cardiology

^{111}In-Pentetreotide SPECT/CT in Neuroendocrine Tumors

Krausz et al. from the Hadassah University Hospital (Jerusalem, Israel) reported in the November issue of *Clinical Endocrinology* (Oxford) (2003;59:565–573) on a study evaluating the effect of sequentially performed ^{111}In-pentetreotide SPECT/CT fusion on somatostatin receptor (SR) study interpretation and the clinical management of neuroendocrine tumors. The study included 72 patients who were imaged with routine SR scintigraphy and SPECT/CT at 4, 24, and 48 hours after injection of 222 MBq ^{111}In-pentetreotide. Imaging was performed for evaluation of carcinoid (45 patients), islet cell tumor (15 patients), metastatic neuroendocrine tumor (7 patients), medullary thyroid carcinoma (4 patients), and ophthalmopathy (1 patient). The authors found that SR scintigraphy was negative in 28 patients and positive in 44 patients. In 48 patients (including all 28 negative studies), SPECT/CT provided no additional information. However, SPECT/CT improved localization of scintigraphy-detected lesions in 23 of the 44 positive studies, defined extent of disease in 17, showed unsuspected bone involvement in 3, and differentiated physiologic from tumor uptake in 3. SPECT/CT changed clinical management in 10 patients, altered the surgical approach in 6, spared unnecessary surgery in 2, and modified the therapeutic modality in 2 patients. The authors summarized the results: "SPECT/CT affected the diagnostic interpretation of SRS in 32% of the patients and induced changes in management in 14% of the patients."

Clinical Endocrinology (Oxford)

Therapy

^{131}I-MIBG Treatment in Pheochromocytoma and Paraganglioma

Safford et al. from Duke University (Durham, NC) reported in the December issue of *Surgery* (2003;134: 956–962) on a retrospective review of their institution's experience with the use of ^{131}I-metaiodobenzylguanidine (^{131}I-MIBG) in the palliative treatment of metastatic pheochromocytoma and paraganglioma. The study included 22 patients with metastatic pheochromocytoma and 11 patients with paraganglioma treated with ^{131}I-MIBG during a 10-year period at Duke. The mean dose received by patients was 388 ± 131 mCi ^{131}I-MIBG, and median survival after treatment was 4.7 years. The authors noted that most patients experienced a symptomatic response leading to an improved survival (4.7 years with ^{131}I-MIBG and 1.8 years without). Increased survival was noted in patients who showed measurable hormone response (4.7 years with measurable response and 2.6 years with no response). Patients who received an initial high dose (>500 mCi) also lived longer than those receiving a lower dose (3.8 and 2.8 years, respectively). The authors concluded that these results "support ^{131}I-MIBG treatment for select patients with metastatic pheochromocytoma" and that an initial dose of 500 mCi may be optimal. They noted that prolonged survival was best predicted by symptomatic and hormone response to ^{131}I-MIBG treatment, but cautioned that the benefits of ^{131}I-MIBG treatment for metastatic pheochromocytoma should be weighed against its side effects.

Surgery

Calculating Site-Delivered Dosages in Restenosis Prevention

Camenzind et al., from the University of Geneva (Switzerland) and University Hospital Dijkzigt (Rotterdam, The Netherlands) reported in the January issue of the *Journal of Cardiovascular Pharmacology* (2004; 43:133–139) on a method for determining the required theoretical dose of a site-delivered, γ-labeled somatostatin analog in the prevention of

restenosis after coronary angioplasty in humans. The study included 7 patients in whom small amounts of ^{111}In-octreotide were infused after angioplasty at the site of dilatation through a coil balloon and quantified using a radioisotopic technique. The efficiency of delivery ranged from 0.1% to 2.7% of the total infused dose of 0.18 μg, corresponding to a mean peak delivered amount of 1.8 ± 1.9 ng. Total locally bioavailable ^{111}In-octreotide reached 2.2 ± 2.15 ng/h. Based on current in vitro bioavailability and peak concentration data about amounts needed to inhibit proliferation and thymidine incorporation in human coronary smooth muscle cells, it was calculated that a dose 4,000 times higher (approximately 700 μg) would be needed to obtain biologic efficacy in 50% of treated patients. This method of quantification of regional pharmacokinetics enables the determination of a theoretical site-specific dose for achieving appropriate bioavailablility above the therapeutic threshold concentration for smooth muscle cell inhibition. The authors suggested this approach as a viable method for the determination of appropriate site-specific coronary infusion doses for the inhibition of restenosis after balloon angioplasty.

Journal of Cardiovascular Pharmacology

^{111}In-Pentetreotide in Bone Metastases from Neuroendocrine Tumor of Pancreas

Van der Hiel et al. from the Leiden University Medical Center (The Netherlands) reported in the December issue of the *European Journal of Endocrinology* (2003;149:479–483) on results of therapy with high doses of ^{111}In-pentetreotide in a single patient with bone metastases from a neuroendocrine tumor of the pancreas. The 55-year-old man had initially been diagnosed with a neuroendocrine tumor of the pancreas and liver metastases. After surgery and chemotherapy, a tumor regression of 30% was achieved. In long-term follow-up, bone scintigraphy showed multiple metastases. The patient then underwent 8 cycles of ^{111}In-pentetreotide (each separated by 5 weeks and consisting of 6 GBq ^{111}In-pentetreotide). Scintigraphy was performed before initiation of this therapy and at its completion. Comparison of the scans showed a lessening in the intensity of uptake in the lesions, a regression in the number of lesions, and similar results in skeletal lesions. Radiographic, CT, and chromogranin-A levels showed stable disease. The authors concluded that these results suggest that the use of "high-dose radiolabeled somatostatin analogs could be of significant use, even in the case of bone metastases."

European Journal of Endocrinology

Localized Cancer Therapy with Radiolabeled Biotin

In the November issue of *European Urology* (2003;44:556–559), Chinol et al. from the European Institute of Oncology (Milan, Italy) reported on a potential new approach to radionuclide therapy using native avidin bound with ^{99m}Tc-labeled biotin administered intravesically in superficial bladder cancer. The study included 15 patients with transitional cell bladder cancer who were instilled intravesically with radiolabeled avidin. Biopsies were obtained from macroscopically normal and tumor tissues before transurethral resection, and radioactivity in the samples was measured. The authors found increased accumulation of radiolabeled avidin in tumor tissue compared with normal bladder tissue. In some individuals, they noted "remarkably high quotients of uptake" in tissues. The authors concluded that this initial study "indicated that intravesical administration of radiolabeled avidin resulted in a preferential accumulation in tumor tissue compared with normal urothelium." They noted that additional exploration would be necessary to assess the possible efficacy of treating superficial bladder neoplasms locally by replacing ^{99m}Tc with high-energy β-emitting radionuclides associated with biotin.

European Urology

Anaerobic Bacteria in Radiation Therapy

In a study published in the December 9 issue of the *Proceedings of the National Academy of Sciences* (2003;100:15083–15088), Bettegowda et al. from the Howard Hughes Medical Institute (Chevy Chase, MD) and the Johns Hopkins Medical Institutes (Baltimore, MD) reported on an experiment designed to test a hypothesis that anaerobic bacteria that can selectively destroy hypoxic regions in tumors could enhance the effects of radiation. The authors used spores of *Clostridium novyi*-NT to treat transplanted tumors in several mouse models. The bacteria improved the efficacy of radiotherapy with external beam radiation from a ^{137}Cs source, with systemic radioimmunotherapy with a ^{131}I-conjugated monoclonal antibody, and with a previously undescribed form of experimental brachytherapy using plaques loaded with ^{125}I seeds. The authors noted that the *C. novyi*-NT spores added little toxicity to any of the 3 radiotherapeutic regimens, and the combination of spores and radiation resulted in "long-term remissions in a significant fraction of animals."

Proceedings of the National Academy of Sciences