Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. 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. We have recently added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of both diagnostic and therapeutic progress in this area. The selection also highlights the growing transition of molecular imaging research techniques into routine clinical practice.

MOLECULAR IMAGING

Imaging Early-Stage Diabetes Changes

Medarova et al. from the Athinoula A. Martinos Center for Biomedical Imaging and the Massachusetts General Hospital (Boston, MA) reported on August 6 ahead of print in *Diabetes* on a study of MR imaging of microvascular changes in type 1 diabetes in a mouse model. The study included mice with and without type 1 diabetes that were monitored by MR imaging after injection with the long-circulating paramagnetic contrast agent gadolinium-diethylenetriaminepentaacetic acid labeled with fluorescin. The authors found significantly greater accumulation of the tracer in the pancreas of diabetic animals than in controls. In both groups, MR imaging allowed in vivo semiquantitative assessment and direct visualization of distribution. At histology, tracer in the diabetic animals was found well distributed throughout the vascular compartment of the pancreas and was found to have leaked into the islet interstitium. In the control animals, the tracer was restricted to the pancreatic vasculature at the islet periphery. These results indicated that changes in vascular volume and permeability associated with early stages of diabetes can be monitored noninvasively and semiquantitatively using MR imaging. The authors concluded that the ability to noninvasively monitor the dynamics of pancreatic microvasculature "would aid in early diagnosis and permit the assessment, design, and optimization of individualized therapeutic intervention strategies."

Diabetes

Dual-Modality MR and Fluorescence Tracer

Xu and a cooperative research group from the National Cancer Institute (Bethesda, MD), and the Howard Hughes Medical Institute (Chevy Chase, MD) reported on August 21 ahead of print in *Bioconjugate Chemistry* on the preparation and preliminary evaluation of a biotin- and lectin-targeted dendrimer-based probe for use in dual-modality MR and fluorescence imaging. The authors described their approach for the preparation of a novel MR agent that features a well-defined dendron structure and a unique biotin functionality that combines with fluorescently labeled avidin to yield a supramolecular avidin-biotin-dendrimer-gadolinium complex. In preliminary imaging studies in mice bearing ovarian tumors, they found that the probe efficiently targeted the tumors and delivered sufficient amounts of chelated gadolinium and fluorophores to produce images that could be visually assessed by MR and optical imaging, respectively. They concluded that "the avidin-biotin-dendrimer complex may be used as a tumor-targeted probe for dual-modality MR and fluorescence imaging."

Bioconjugate Chemistry

Noninvasive Optical Evaluation of Bone Mineral

Kozloff et al. from the Massachusetts General Hospital and Harvard Medical School (Boston) reported in the August issue of the *Journal of Bone and Mineral Research* (2007;22:1208–1216) on a study assessing the ability of a far-red fluorescently labeled pamidronate (FRFP) probe to bind to regions of bone formation and resorption for 3D fluorescence molecular tomographic imaging in both in vitro and in vivo studies. The ability of the FRFP probe to bind to mineral was assessed using intact and demineralized dentine slices. Binding was studied in vivo in 3 types of mouse models: developing neonates, bone healing after injury, and metastasis-induced osteolysis and fracture. In vitro studies indicated that the probe binds to bone in direct correlation with the quantity of mineral present. In vivo, FRFP was found to bind to surfaces of actively forming bone, surfaces undergoing active resorption, and quiescent surfaces not involved in formation or resorption. The authors noted that binding is probably modulated by vascular delivery of the imaging agent to the exposed mineral surface and by the total quantity of surface exposed. Like conventional bone scans, this approach can visualize regions of bone formation with a large volume of labeled surface but cannot discriminate pure osteolysis caused by metastasis. They concluded that "FRFP may function as a local biomarker of bisphosphonate deposition to assess interplay between drug and cellular environment or may be combined with other imaging agents or fluorescent cells for the noninvasive assessment of local bone metabolism in vivo."

Journal of Bone and Mineral Research

BRET in Single Cells In Vivo

Continuing their groundbreaking work in molecular imaging, researchers from Stanford University (CA) reported in the August 1 issue of *Cancer Research* (2007;67:7175–7183) on an improved bioluminescence resonance energy transfer (BRET) strategy for imaging intracellular events in single cells and living subjects. De et al. reported on the generation of a novel BRET vector that fuses a green fluorescent acceptor protein with a novel mutant Renilla luciferase donor selected for higher quantum yield. This new vector showed an overall 5.5-fold improvement in the BRET ratio, greatly improving the dynamic range of the BRET signal. The authors noted that this new BRET strategy "provides a unique platform to assay protein functions from both single live cells and cells located deep within small living subjects" and that applications will include anticancer therapy screening in cell culture and in small living animals.

Cancer Research

THERAPY

Coregistered PET and CT in RT Planning

Macmanus et al. reported in the August issue of *Australasian Radiology* (2007;51:386–393) on a method for obtaining CT and PET images at separate acquisitions for radiotherapy (RT) planning in non–small cell lung cancer (NSCLC) and compared the results with those obtained using CT alone. The study included 10 patients diagnosed with NSCLC who underwent imaging for planned radical RT. Separate CT and PET images were acquired and coregistered using dedicated software and fiducial markers. The resulting data were uploaded in the RT planning systems. Treatment plans were prepared for CT alone and for the coregistered images. PET influenced the treatment plan in all 10 patients. In 3 patients, significant tumor areas would have been outside the planning target had PET not been used. In 3 other cases, PET improved the marginal coverage of the planning target volumes. In 4 patients (3 with atelectasis), significant reductions in percentage of total lung volume receiving 20 Gy or more were achieved by the addition of PET. The authors concluded that "use of coregistered PET/CT images significantly altered treatment plans in a majority of cases" and that their technique "could be used in routine practice at centers without access to a combined PET/CT scanner."

Australasian Radiology

Radioguided Neurosurgery

Bhanot et al. from the Manipal Institute for Neurological Disorders (Bangalore, India) reported in the August issue of the *British Journal of Neurosurgery* (2007;21:382–388) on initial experiences with radioguided neurosurgery in patients with brain tumors. The study included 19 patients scheduled to undergo surgery. The researchers first used fused SPECT and CT images to confirm a high degree of ^{99m}Tc-sestamibi uptake in all patients. A gamma probe was used intraoperatively to distinguish tumor from normal brain and check for residual lesions after excision of visually identifiable tumor. Their results, although not compared with a control group of patients undergoing conventional nonradioguided surgery, were excellent. They concluded that the use of radioguided neurosurgery "enhances the neurosurgeon's confidence with tumors in or near eloquent [speech] areas and provides reliable proof of the completeness of excision in real time."

British Journal of Neurosurgery

SPECT/CT in Advanced Pancreatic Cancer

In a study e-published on August 21 ahead of print in *Cardiovascular and Interventional Radiology*, Ikeda et al. from the Kumamoto University Graduate School of Medical and Pharmaceutical Sciences (Japan) reported on a study comparing images of intrahepatic and pancreatic perfusion acquired with a combined SPECT/CT system and evaluating the efficacy of combined continuous transcatheter arterial infusion (CTAI) and systemic chemotherapy in the treatment of advanced pancreatic carcinoma. The study included 33 patients (22 men, 11 women) with stage IV pancreatic cancer and liver metastases who underwent CTAI. After reservoir creation, gemcitabine administration was combined with 5-fluorouracil infusion. All patients underwent SPECT/CT, and pancreatic perfusion was assessed. Tumor response was assessed by CT imaging at 3 months using World Health Organization criteria. Patients (n = 45) with tracer uptake noted in the pancreatic tumor and homogeneous perfusion distribution in the liver showed better treatment results. Of these, patients with uptake both in the pancreatic cancer and in the liver survived longer than those with no uptake in the pancreatic cancer and heterogeneous distribution in the liver. The authors concluded that in patients with advanced pancreatic cancer, CTAI with systemic chemotherapy appeared to be effective and may prolong survival. They added that "a reservoir port system allowing for the homogeneous distribution of anticancer drugs is necessary to improve the prognosis of patients with advanced pancreatic cancer." The utility of SPECT/CT in assessing and characterizing early perfusion was also noted.

Cardiovascular and Interventional Radiology

RIT Complications and At-Risk Patients

In a study e-published on August 20 ahead of print in the *Journal of Clinical Oncology*, Czuczman et al. from the Roswell Park Cancer Institute (Buffalo, NY), University of California at Los Angeles, Biogen Idec (San Diego, CA), Mayo Clinic (Rochester, MN), and Northwestern University (Chicago, IL) reported on the incidence of treatment-related myelodysplastic syndrome (t-MDS) and treatment-related acute myelogenous leukemia

(t-AML) in patients after ibritumomab tiuxetan radioimmunotherapy (RIT). The study analyzed data on t-MDS and t-AML in 746 patients with non-Hodgkin's lymphoma (NHL) treated with the ibritumomab tiuxetan regimen in registration and compassionate-use trials. At a median follow-up of 4.4 years, 19 patients (2.5%) had developed t-MDS or t-AML. These malignancies were diagnosed at a median of 5.6 years (range, 1.4–13.9 years) after the initial diagnosis of NHL and 1.9 years (range, 0.4–6.3 years) after RIT. The authors found that most patients with t-MDS or t-AML had multiple cytogenetic aberrations, usually on chromosomes 5 and 7, suggesting previous exposure to chemotherapy. The annualized incidences of t-MDS and t-AML after RIT were found to be consistent with those expected in patients with NHL who have undergone extensive previous chemotherapy treatment and did not appear to be increased by RIT. The authors concluded by suggesting that cytogenetic testing before treatment with RIT may identify "existing chromosomal abnormalities in previously treated patients, particularly those who have been treated with alkylating agents and purine nucleoside analogs and would be at higher risk for t-MDS or t-AML."

Journal of Clinical Oncology

DIAGNOSIS

PET and Aggressive Thyroid Cancer

In a study e-published on August 23 ahead of print in the *Annals of Surgical Oncology*, Are et al. from the University of Nebraska Medical Center (Omaha) reported on research designed to determine whether thyroid malignancies incidentally detected by ^{18}F-FDG PET represent a more aggressive variant of primary thyroid cancer. The retrospective study began with a database of 11,500 patients who had undergone a total of 17,250 PET scans for various indications. Of these, PET findings were positive for thyroid abnormality in 377 patients, 32 of whom progressed to operative intervention. Twenty-two of these patients had final diagnoses of primary thyroid cancer. Twelve (54%) of these 22 patients were found to have variants of primary thyroid carcinoma (tall-cell, 11 patients; poorly differentiated thyroid carcinoma, 1 patient) with poor prognoses, and extrathyroidal extension was noted in 14 of these 22 (63%) patients. Among the 11 patients with tall-cell variant, the rate of extrathyroidal extension was 90%. The authors concluded that "thyroid malignancies incidentally detected on FDG PET scan harbor a high rate of unfavorable prognostic features and may represent a more aggressive variant of primary thyroid carcinoma." They cautioned that patients identified with incidental thyroid abnormalities on PET should be "be subjected to further investigation with a view to possible operative intervention."

Annals of Surgical Oncology

PET/CT in IBD

Meisner et al. from the University of Wisconsin Hospital and Clinics (Madison) reported in the August issue of *Inflammatory Bowel Disease* (2007;13:993–1000) on a pilot study designed to explore the ability of PET/CT to identify regions of active inflammation in both ulcerative colitis and Crohn's disease. The study included 12 patients (7 with Crohn's disease, 5 with ulcerative colitis) who underwent PET/CT for evaluation of exacerbations of inflammatory bowel disease and 20 control patients undergoing PET/CT for solitary pulmonary nodules. PET activity scores were assigned to the small bowel and 4 colon regions based on the amount of ^{18}F-FDG uptake (with the liver as the reference organ). PET activity was seen in 13 of 24 (52%) regions in patients with ulcerative colitis, with a high (95.8%) correlation between PET activity and disease activity as verified by conventional colonoscopy, disease activity indices, and radiology. PET activity was seen in 19 of 32 (59.4%) regions in patients with Crohn's disease, with an 81.3% correlation between PET activity and clinically verified disease activity. PET activity was seen in only 2 of 100 regions in the 20 control patients. The authors concluded that these results suggested that PET/CT "may be a noninvasive method of identifying disease activity in patients with inflammatory bowel disease."

Inflammatory Bowel Disease

Gated SPECT in Progressive Coronary Occlusion

In an article e-published on August 17 ahead of print in the *International Journal of Cardiovascular Imaging*, Christian et al. from the Mayo Clinic and Foundation (Rochester, MN) reported on a study designed to determine whether gated ^{99m}Tc-sestamibi SPECT imaging can track small changes in myocardial blood flow in a model of progressive ischemia. The study included 8 pigs that underwent lateral thoracotomy for placement of an ameroid constrictor on the left circumflex coronary artery and indwelling femoral and left atrial catheters for serial microsphere determinations of absolute myocardial blood flow. Over a study period of 6 weeks, animals underwent concurrent left atrial microsphere and radiotracer injections every 7 days, followed by gated SPECT imaging with high-resolution collimation and standard processing. The authors found that myocardial blood flow decreased progressively (27% below resting values) but with a clear and significant partial recovery by day 42 (13% improvement from peak ischemia). SPECT perfusion and calculations of gated regional wall motion closely paralleled the dynamic pattern of myocardial blood flow caused by the ameroid constrictor. SPECT mean contrast ratios decreased 21% from baseline scans in the left circumflex artery territory and improved 11% from peak ischemia, whereas the gated regional wall motion peaked at 1.36 and improved to 1.13 by day 42. The authors concluded that "gated SPECT—a technique readily available—tracks dynamic changes in myocardial blood flow closely with both perfusion and regional wall motion" and that these findings have direct

implications for measuring the efficacy of new therapies for the alleviation of chronic ischemia.

International Journal of Cardiovascular Imaging

PET and Cerebral Amyloid Burden

Johnson et al. from the Massachusetts General Hospital (Boston, MA) reported on August 7 ahead of print in the *Annals of Neurology* on a study investigating the potential of PET imaging with Pittsburgh Compound B in the detection of cerebrovascular deposition of β-amyloid (cerebral amyloid angiopathy [CAA]), a major cause of hemorrhagic stroke. The study included 6 nondemented individuals diagnosed with probable CAA, 9 patients with probable Alzheimer's disease (AD), and 15 healthy controls, all of whom underwent PET imaging with Pittsburgh Compound B. Tracer uptake was positive in all individiuals with CAA and AD, as assessed both by distribution volume ratio measurements and by visual inspection of PET images. Global cortical tracer retention was significantly increased in patients with CAA compared with control participants but was lower in CAA participants than in those with AD. The occipital-to-global tracer ratio, however, was significantly greater in CAA participants than in those with AD. The authors concluded that Pittsburgh Compound B-PET "can detect cerebrovascular β-amyloid and may serve as a method for identifying the extent of CAA in living subjects."

Annals of Neurology

Novel PET Radioligand for Neuroimaging

Boutin et al. from the Laboratoire d'Imagerie Moléculaire Expérimentale (Orsay, France) reported in the August 6 issue of *Glia* (2007;55:1459–1468) on a new peripheral benzodiazepine receptor (PBR) as an alternative to PK11195 for PET imaging of neuroinflammation. The researchers studied the in vitro properties of ^{11}C-CLINME and evaluated in vivo imaging of local acute neuroinflammation using the tracer in a rat model and compared the results with those using ^{11}C-PK11195. The novel tracer showed a higher contrast between the PBR-expressing lesion site and the intact side of the same rat brain than did ^{11}C-PK11195. Although uptake levels in lesions were similar for the 2 tracers, ^{11}C-CLINME uptake was lower in the noninflamed part of the brain. ^{11}C-CLINME localization correlated well with activated microglial cells, as verified by immunohistochemistry and autoradiography. The authors concluded that these promising results suggest that "further studies of this new compound should be carried out to better define its capacity to overcome the limitations of ^{11}C-PK11195 for PBR PET imaging."

Glia

PET and Adult ADHD

Volkow et al. from the National Institute on Drug Abuse (Bethesda, MD) and the Brookhaven National Laboratory (Upton, NY) reported in the August issue of the *Archives of General Psychiatry* (2007;64:932–940) on a study using PET imaging to test the hypothesis that striatal dopamine activity is depressed in adults with attention-deficit/hyperactivity disorder (ADHD) and that this contributes to symptoms of inattention. The study included 19 medication-naïve adults with ADHD and 24 healthy controls, each of whom underwent ^{11}C-raclopride PET imaging after placebo and after intravenous methylphenidate hydrochloride, a stimulant that increases extracellular dopamine by blocking dopamine transporters. Differences in tracer binding before and after methylphenidate administration were compared with symptoms assessed using an adult ADHD rating scale. At placebo imaging, levels of D2/D3 receptor availability were lower in the left caudate in individuals with ADHD than in controls. Methylphenidate administration induced smaller decrements in ^{11}C-raclopride binding in left and right caudate (blunted DA increases) and higher scores on self-reports of "drug liking" in ADHD individuals than in control subjects. This blunted response to methylphenidate in the caudate regions was associated with symptoms of inattention and with higher self-reports of drug liking. Methylphenidate was also found to decrease ^{11}C-raclopride binding in hippocampus and amygdala in all patients, and these decrements were smaller in individuals with ADHD. The authors concluded that this depressed dopamine activity in caudate and limbic regions in adults with ADHD was associated with inattention and with enhanced reinforcing responses to intravenous methylphenidate, adding that "this suggests that dopamine dysfunction is involved with symptoms of inattention but may also contribute to substance abuse comorbidity in ADHD."

Archives of General Psychiatry

PET and PTSD

In an article e-published on July 31 ahead of print in *Molecular Psychiatry*, Geuze et al. from The Netherlands Ministry of Defense (Utrecht) and the Utrecht University Medical Centre reported on an ^{11}C-flumazenil PET study assessing benzodiazepine γ-aminobutyric acid (GABA[A]) receptors in the prefrontal cortices of veterans with and without posttraumatic stress disorder (PTSD). These receptors are believed to play a role in modulating central nervous system responses to stress. The study included 9 drug-naïve male veterans with deployment-related PTSD and 7 veterans without PTSD matched for age, sex, and region and year of deployment. Each participant underwent dynamic 3D ^{11}C-flumazenil PET imaging and MR imaging. Region of interest (ROI) analyses using both template-based and manual ROIs showed significantly reduced tracer binding throughout the cortex, hippocampus, and thalamus in individuals with PTSD. The authors concluded that this observed global reduction in tracer binding in patients with PTSD "provides circumstantial evidence for the role of the benzodiazepine-GABA(A) receptor in the pathophysiology of PTSD and is consistent with

previous animal research and clinical psychopharmacological studies."

Molecular Psychiatry

Thalidomide and Thyroid Cancer

Ain et al. from the Veterans Affairs Medical Center (Lexington, KY) and the University of Kentucky (Lexington) reported in the August issue of *Thyroid* (2007;17:663–670) on the results of a phase II trial of thalidomide for therapy of radioiodine-unresponsive and rapidly progressive thyroid carcinomas. The study included 36 patients with follicular, papillary, insular, or medullary thyroid carcinomas and distant, radioiodine-unresponsive metastases (defined as volumes increasing at a rate ≥30% per year before entry into the study). Daily thalidomide was initiated at 200 mg, increasing over 6 weeks to 800 mg or maximum tolerated dose. Toxicities and responses, including tumor volumes, were assessed at 8-week intervals throughout the study. Of the 28 patients who were evaluable for inclusion in results analysis, 5 (18%) had partial responses (median duration, 4 months) and 9 (32%) had stable disease (median duration, 6 months). Median survival for responders was 23.5 months and for nonresponders was 11 months. The most frequent toxicity-associated complication was fatigue (77%). Four patients had grade 3–4 infections (without neutropenia), 1 had pericardial effusion, and 1 had pulmonary embolus. The authors concluded that "thalidomide confers therapeutic benefit in subsets of thyroid cancer patients with rapidly progressive, distantly metastatic disease."

Thyroid

Viral-Derived Peptide for Cancer Imaging

Hausner et al. from the University of California, Davis and the Queen Mary's School of Medicine and Dentistry (London, UK) reported in the August 15 issue of *Cancer Research* (2007;67:7833–7840) on the use of a peptide derived from the foot-and-mouth disease virus for PET imaging of $\alpha_v\beta_6$ expression in human cancers. The authors previously identified this peptide as a potent and highly selective inhibitor of $\alpha_v\beta_6$ expression. In vitro and in vivo studies in cancer xenografts in mice reported in this article provide supportive data. In the mouse studies, viral-derived peptide was found to have rapid uptake and selective retention (>5 hours) in $\alpha_v\beta_6$-positive but not in $\alpha_v\beta_6$-negative tumors, as well as fast renal elimination. Specific imaging of $\alpha_v\beta_6$-positive tumors was achieved, and the peptide was described as "an important new tool for early detection and improved management of many types of cancers."

Cancer Research

(Continued from page 26N)

telephone survey recorded the responses of more than 6,300 people in 2003 and more than 5,500 people in 2005.

Use of the Internet as a source for cancer-specific information remained relatively unchanged during the study period. However, the number of people using the Internet to communicate with their health care providers or providers' offices through a Web site (including e-mailing questions and scheduling appointments) increased from 7% in 2003 to 10% in 2005. Use of the Internet to gather health information about topics other than cancer increased from 2003 to 2005. In 2003, 51% of respondents reported looking for health information for themselves and 46% for someone else. In 2005, these respective percentages were 58% and 60%. Women were more likely to search for cancer information from all sources than men, and people aged 50–64 years were most likely to search for cancer-specific information.

"The survey is not only a surveillance tool but can be used to study relationships of how knowledge about health care is dependent on channels of communication," said Bradford Hesse, PhD, chief of NCI's Health Communication and Informatics Research Branch.

The researchers also looked at changes in cancer knowledge and beliefs and worked with statisticians and geographic information systems specialists to create maps to visualize regional geographic variation, much like a weather map. These maps are created by using information from neighboring states to provide information for areas with relatively small sample sizes. The maps in the report will allow researchers and health care providers to visually identify areas of the country in need of improved or targeted health communication. The maps also illustrate knowledge about breast and colorectal cancer screening recommendations, as well as general knowledge about the human papillomavirus, cervical cancer, and lung cancer. The maps, as well as data from both the 2003 and 2005 HINTS surveys, are available to researchers and health care providers throughout the country for their own programs and planning.

"Population-based surveys such as HINTS give us a rich source of knowledge about the awareness of the American public," said NCI Director John E. Niederhuber, MD. "Our next step must be to research how best to translate newfound understandings of patterns and preferences into better ways of educating and serving all of our patients through cancer prevention, screening, treatment, and survivorship."

For more information about HINTS, see http://cancercontrol.cancer.gov/hints.

National Cancer Institute

FDA Approves NDA for ^{13}N-Ammonia Injection

On August 23, the U.S. Food and Drug Administration (FDA) approved a new drug application (NDA) for a ^{13}N-ammonia injection product, under the title "Ammonia N 13 Injection." The approved NDA reference number

is NDA 22-119. Thomas Chaly, PhD, submitted the NDA on behalf of the Feinstein Institute for Medical Research/North Shore/LIJ Health System, New York University Medical College (Manhasset, NY). The Feinstein Institute for Medical Research is the first institution in the United States to secure NDA approval for a ^{13}N-ammonia injection. The product is manufactured in a class 100000 clean room environment and a class 100 biological cabinet for the preparation of the container closure vial. ^{13}N-ammonia has shown extraordinary promise as a PET radiotracer in imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing coronary artery disease.

The Feinstein Institute for Medical Research/North Shore/LIJ Health System also received FDA approval for the drug "Fludeoxyglucose F 18 Injection" (^{18}F-FDG injection) on August 19, 2005 (NDA 21-870). The FDA has implemented new Structured Product Labeling (SPL) as a mandatory standard for the exchange of product labeling along with any NDA. Dr. Chaly and his group have completed this new requirement for the ^{13}N-ammonia injection, and the same format will be used for preparing the SPL/Physician Labeling Rule XML document for the ^{18}F-labeled injection.

The Feinstein Institute for Medical Research/North Shore/ LIJ Health System

NIDA's Rice Receives Smissman Award

Kenner C. Rice, PhD, whose research led to the development of compounds or medications that have the potential to treat, prevent, or image drug addiction, was presented on August 20 with the 2007 Smissman Award at the American Chemical Society (ACS) national meeting in Boston, MA. Rice is chief of the Chemical Biology Research Branch of the National Institute on Drug Abuse (NIDA; Bethesda, MD). Among his contributions recognized by the ACS is the discovery of cyclofoxy, an ^{18}F-labeled opioid antagonist used as a PET imaging agent to study opioid effects in the brain. Rice also developed the National Institutes of Health (NIH) Opiate Total Synthesis, which allows medical opiates to be produced synthetically in any quantity, offering opiate researchers independence from foreign sources of opium.

"Dr. Rice is indeed deserving of this prestigious honor," said NIH Director Elias A. Zerhouni, MD. "During his tenure at NIH he has designed and directed the synthesis of many drugs and research tools that have helped identify and characterize different drug effects and interactions. His fellowship programs have helped to create a whole new generation of scientists producing exciting research in the fields of organic and medicinal chemistry."

The Bristol–Myers Squibb Smissman Award is given to a living scientist whose research, teaching, or service has had a substantial impact on the intellectual and theoretical development of the field of medicinal chemistry.

American Chemical Society