NCI, FDA Announce New Initiatives in Strategic Partnership

At a Friends of Cancer Research meeting in Washington, DC, on November 12, National Cancer Institute (NCI) Director Andrew C. von Eschenbach, MD, and FDA Commissioner Mark McClellan, MD, PhD, announced 2 new collaborative initiatives to facilitate the development and use of better cancer treatments. The initiatives include a new system for submitting investigational new drug (IND) applications electronically under the Cancer Biomedical Informatics Grid (caBIG) project. "In taking these important concrete steps, we are moving the NCI–FDA partnership from an idea to a working reality that will make a difference for patients," said von Eschenbach. McClellan said, "We are working to get safe and effective cancer therapies to patients as quickly and inexpensively as possible. Using modern information technologies to make our processes more efficient is a key approach to achieving this goal."

Information released by the NCI and FDA indicated that the new initiatives will:

- Link cancer researchers around the United States electronically to the FDA to reduce the time it takes for promising new drugs to be reviewed for testing in clinical trials. Electronic submission of data should allow patients earlier access to clinical trials as a result of shorter FDA processing time of IND applications; and
- Initiate cancer fellowship training programs aimed at developing a corps of physicians and scientists who are expert in clinical research, the regulatory approval process, and translation of research breakthroughs into clinical practice.

These initiatives result from ongoing work from the 2 organizations' Interagency Oncology Task Force, which was established in May 2003 to improve the efficiency of all aspects of cancer drug development and regulatory review.

The FDA has agreed to work with NCI to develop clinical trial management software that makes it easier for cancer research groups and the FDA to work collaboratively. The 2 organizations will work to coordinate standards and develop tools to streamline regulatory interactions and accelerate the overall review process for new cancer drugs. These activities will become part of the NCI's caBIG, in which the FDA has agreed to participate.

Under the new cancer fellowship training programs initiative, fellows will work in clinical oncology programs at NCI and in the technical and regulatory review programs at the FDA. As a result, fellows will bring state-of-the-art knowledge and technology to bear on the design, conduct, and review of clinical trials.

National Cancer Institute
FDA

ASNC to Host Symposium on Cardiovascular Molecular Imaging

The American Society of Nuclear Cardiology (ASNC) is planning a symposium on cardiovascular molecular imaging at the National Institutes of Health in Bethesda, MD, May 3–4. Educational sponsors of the symposium include the SNM, ASNC, and the American College of Radiology.

Program objectives include educating the scientific community about the potential of targeted cardiovascular molecular imaging, providing an overview of critical issues related to the development of targeted radiolabeled tracers and tracer imaging technology, reviewing the imaging of cardiac reporter genes and gene expression, defining the potential of imaging in cardiac receptors and metabolism, promoting basic science research in and clinical applications of cardiovascular molecular imaging, and offering an overview of the potential of molecular imaging for improving the understanding and management of critical cardiovascular pathophysiologic processes.

A call for abstracts has been issued. Abstracts must be received by January 16. Young Investigator Awards, including a $500 travel grant, complementary registration, and certificate, will be given for the 7 best abstracts submitted by physicians or scientists who are currently in residency or fellowship training programs or are younger than 35. In addition, the registration fee will be waived for residents and fellows whose abstracts are selected for presentation. Program co-chairs include James Caldwell, MD, University of Washington (Seattle); Robert Gropler, MD, Washington University (St. Louis, MO); Lynne Johnson, MD, Brown University (Providence, RI); Leslie Leinwand, PhD, University of Colorado (Boulder); Albert Sinusas, MD, Yale University School of Medicine (New Haven, CT); and Heinrich Schelbert, MD, PhD, University of California at Los Angeles School of Medicine. For more information see www.asnc.org.

American Society of
Nuclear Cardiology

NIH Expands Long-Distance Clinical Learning

The National Institutes of Health (NIH) Clinical Center announced on November 26 that in 2003 it had extended clinical research training programs to reach more than 1,400 physicians and other health professionals in locations as far away as Peru and Puerto Rico.

"Proper training of clinical researchers is critical to advancing medical science," said Dr. John I. Gallin, director of the NIH Clinical Center. "In the past, researchers have relied on mentors to teach them how to conduct clinical trials. We have established a formalized training pro-

gram to fill this critical gap and we're extending it worldwide."

In 2003, 1,426 students were enrolled in 3 core courses: Introduction to the Principles and Practice of Clinical Research, Principles of Clinical Pharmacology, and Ethical and Regulatory Aspects of Clinical Research. These courses are available not only to NIH researchers but are transmitted by satellite or Web videocast to remote locations.

The program also expanded its diversity outreach in 2003. The Introduction to Principles course, for example, included 69 registrants at Meharry Medical College in Nashville, TN; 11 students at Morehouse School of Medicine in Atlanta, GA; and 60 students at the University of Puerto Rico in San Juan. Other locations participating in the course in 2003 were the Children's National Medical Center, George Washington University Medical Center, and Georgetown University Medical Center in Washington, DC; the State University of New York in Syracuse; the University of Texas Southwestern Medical Center in Dallas; and the U. S. Naval Medical Research Center Detachment in Lima, Peru.

Complementing these programs are 2 formal Clinical Center partnerships, 1 with Duke University and the other with the University of Pittsburgh, that lead to master's degrees in clinical research.

Additional information on these courses can be obtained from the Clinical Center Office of Clinical Research Training and Medical Education at 301-496-9425.

National Institutes of Health

HHS Announces Medical Reserve Corps Grants

On October 30 Health and Human Services Secretary Tommy G. Thompson announced 167 grants totaling more than $8 million to agencies in 40 states to help community-based organizations develop local volunteer medical emergency and public health response capabilities through the Medical Reserve Corps (MRC) program. "These awards will continue to support our communities in planning and establishing local, citizen-centered volunteer MRC units, which will include physicians, nurses and others with a broad range of skills in health and other support fields," said Thompson.

MRC units include local citizen volunteers trained to respond to health and medical situations in support of established, local public health and emergency medical response systems. Volunteers' responsibilities may include emergency medical care and triage, logistic or backup support for trauma units and hospitals in the event of a disaster, immunization campaigns, or public health awareness programs.

The MRC program is headquartered in the Office of the Surgeon General, which administers the grant funds and offers technical assistance to all MRC communities. For more information and a complete list of grantee agencies, go to www.medicalreservecorps.gov.

Department of Health and Human Services

Hospital Spending Increased, Nursing Shortage Temporarily Eased

The Federation of American Hospitals has released the results of 2 studies indicating that future spending for hospital services will increase substantially (despite widespread predictions that increases would be only moderate) and that the number of nurses employed by hospitals and the wages they earned grew dramatically in 2002. The results were discussed at a symposium on future demand for hospital services and supply of nursing personnel on November 12.

The data on hospital spending reported by economist Stuart Altman and colleagues from Brandeis University indicated that total real hospital spending per capita between 2000 and 2012 could increase by 75%, reflecting a predicted average annual increase of 4.8% and a substantially increased demand for hospital beds. They also found that hospital spending by baby boomers grew more rapidly than that by older individuals, a trend that indicates increased spending as now middle-aged individuals grow older. Results of the study were published in the November–December issue of *Health Affairs* (2003;22: 12–26).

Peter Buerhaus, senior associate dean for research at Vanderbilt University School of Nursing, reported that employment of registered nurses (RNs) grew by nearly 10% between 2000 and 2002 and that RN earnings in 2002 increased substantially compared with previous years, suggesting that the shortage of nurses may be easing. Two thirds of the increase in employment came from older RNs, with the remainder supplied by RNs born in other countries. The authors noted, however, that the numbers of young nurses entering the profession is still not high and that the supply of older nurses is finite. They predicted that the number of young people enrolling in nursing programs would have to increase at an unprecedented rate—by at least 40% per year—to make up for the number of nurses expected to retire. Results of the study were published in the November–December issue of *Health Affairs* (2003;22:191–198).

Advocates Call for More PET in UK

At a news conference held in London on November 17, heads of health charities and medical personnel called for the British government to provide more PET facilities. They focused their comments on the effects of the current shortage on more than 38,000 UK patients diagnosed with lung cancer each year. Only 5 PET scanners are available in National Health Service hospitals in England and Wales. Charities including Macmillan Cancer Relief, the British

Lung Foundation, and CancerBACUP joined forces to urge the British government to acquire at least 10 new PET scanners in England and Wales within 5 years.

At the news conference, retired surgeon Jules Dussek, MD, said: "I would be very unhappy if I would be forced to operate on someone with lung cancer without a PET scan. I would feel naked and defenseless." Patients reported waits as long as 8 weeks and journeys of up to 3 hours for PET services.

Several participants in the news conference suggested that lung cancer patients have received scant attention because of the stigma attached to the disease and because many patients do not survive long enough to effectively protest the quality of their care.

Professor Mike Richards, the UK's national cancer director, was later quoted by the BBC as saying that the government was determined to prevent lung cancer through programs aimed at smoking cessation and at improving services for patients. He said as yet there was "no conclusive proof that widespread early screening was necessarily an effective use of resources" but added that a framework for PET scanning in the UK was under development.

BBC

Newsbriefs from the Literature

Dean Steps Down at NIBIB

On November 24, Donna J. Dean, PhD, deputy director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the National Institutes of Health (NIH), announced that she would leave her position to become senior scholar in residence at the National Academy of Engineering (NAE). In her new capacity, she will work with the National Academies, federal agencies, academic institutions, and the private sector on issues at the interface of engineering and the life and health sciences. She will join the NAE in January.

"It was my great privilege to work with a stellar group of staff who built a firm foundation for NIBIB's future," she said. "I will always be proud of the pivotal role that I played in creating a new institute at NIH that has unlimited potential to foster new arenas of research. I have never had so much fun in my career, nor worked so hard, as in the past 3 years. With supportive colleagues across the NIH, in the Institute, and in the extramural community, it truly was a stimulating and exciting endeavor."

Before becoming NIBIB deputy director in September 2002, Dean served as the NIBIB acting director during the formation and development stages of the new Institute from its beginnings in January 2001, in addition to serving as the senior scientific advisor to the NIH acting director.

National Institute of Biomedical Imaging and Bioengineering

Diagnosis

Nuclear Medicine and the Cognitive Processes of Spirituality

In 1896, when interest in the newly introduced x-ray reached a fevered pitch, a number of respected medical practitioners speculated on the possibility that the new technology might be able to visualize the human soul. For more than 100 years, these and similar efforts were cited as risible examples of early, unfettered enthusiasm. Today, however, nuclear medicine techniques promise to provide images, not of the soul, but of qualities often referred to as spiritual and previously deemed unquantifiable.

In a study published in the October issue of *Perceptual and Motor Skills* (2003;97:625–630), Newberg et al. from the Hospital of the University of Pennsylvania (Philadelphia) reported on the use of ^{99m}Tc-hexamethylpropyleneamine oxime SPECT to measure cerebral blood flow changes during meditative prayer. The study included 3 Franciscan nuns who were experienced practitioners of "verbal-based" meditation involving internal (nonspoken) repetition of specific phrases. The volunteers were scanned before and after 50 minutes of meditation. Postmeditation scans showed increased blood flow in the prefrontal cortex (7.1%), inferior parietal lobes (6.8%), and inferior frontal lobes (9.0%) compared with premeditation (baseline) scans. A strong inverse correlation was noted between blood flow changes in the prefrontal cortex and ipsilateral superior parietal lobe. The authors also compared these results with those from a previous study of 8 Buddhist volunteers who used a different meditation technique (*Psychiatry Res.* 2001;106: 113–122). The authors concluded that this study on a limited number of subjects "demonstrated the feasibility of studying different types of meditation with neuroimaging techniques, suggested that several coordinated cognitive processes occur during meditation, and also raised important methodological issues."

In the November issue of the *American Journal of Psychiatry* (2003; 160:1965–1969), Borg et al. from the Karolinska Institute and Hospital (Stockholm, Sweden) reported on the use of ^{11}C-WAY100635 PET in assessing the relationship between serotonin-receptor density and spiritual experiences. The study included 15 healthy male volunteers who underwent PET imaging as well as assessment with the Swedish version of the Temperament and Character Inventory self-report questionnaire. As an index of 5-HT1A receptor density, binding potential was calculated for the dorsal raphe nuclei, hippocampal formation, and neocortex, and the results were correlated with responses for each of the 7 aspects, or dimensions, of the personality questionnaire. A significant inverse correlation was found in only 1 of these aspects, the "self-transcendence" di-

mension, which described personality traits including religious behavior and attitudes. Additional analysis showed that binding potential correlated with only 1 of the subscales of this dimension: "spiritual acceptance." The authors concluded that this finding suggested that "the serotonin system may serve as a biological basis for spiritual experiences" and that a "several-fold variability in 5-HT1A receptor density may explain why people vary greatly in spiritual zeal."

Perceptual and Motor Skills
American Journal of Psychiatry

SPECT and Hashimoto's Encephalitis

Zettinig et al. from the University of Vienna (Austria) reported in the November issue of *Clinical Endocrinology* (Oxford) (2003;59:637–643) on a study using ^{99m}Tc-ethylcystein dimer (ECD) SPECT to evaluate brain perfusion in euthyroid patients with autoimmune thyroiditis. In part the study was designed to assess whether the encephalopathy (often referred to as Hashimoto's encephalitis) associated with the condition actually constitutes a distinct clinical entity. The study included 41 euthyroid patients with autoimmune thyroiditis and 35 matched healthy individuals. Participants were screened for significant neurologic histories, morphologic brain abnormalities, depression, and mood disorders. All participants underwent ^{99m}Tc-SPECT imaging. Brain perfusion was quantified automatically with both a voxel-based analysis and a volume-of-interest (VOI)–based analysis of 46 predefined cortical and subcortical regions. The authors found a significant difference between patients and controls in the mean volume of perfusion defects deviating 2 SD below normal values in the voxel-based analysis. Hyperperfused areas did not differ significantly in the 2 groups. In the group of euthyroid patients, perfusion defects correlated significantly with the amount of time since diagnosis of autoimmune thyroiditis. VOI-based analysis showed that abnormal regions of perfusion were more frequent in the patient group than in the healthy volunteers, but no pattern of regional involvement emerged. Although scores on depression and mood disorder assessment instruments varied greatly between the 2 groups, these results did not correlate with perfusion patterns or abnormalities. The authors concluded that these findings of impaired brain perfusion in patients "further strengthen the hypothesis of a possible cerebral involvement in autoimmune thyroiditis in individual cases" and that "the presence of cerebral hypoperfusion suggests a cerebral vasculitis as the most likely pathogenetic model."

Clinical Endocrinology (Oxford)

^{99m}Tc-MIBI Parathyroid Scintigraphy

In a study e-published ahead of print on November 26 in the *World Journal of Surgery*, Gotthardt et al. from the Philipps-University of Marburg (Germany) reported on a meta-analysis of their institution's experience and the literature on ^{99m}Tc-methoxyisobutylisonitrile (MIBI) parathyroid scintigraphy, with special attention to previously noted discrepancies in reports on the sensitivity of the procedure. The institutional study included 139 patients who underwent parathyroid scintigraphy and subsequent surgery between 1991 and 1999. Of these, 109 were found at surgery to have primary hyperparathyroidism and 30 to have secondary parathyroidism. The sensitivity and specificity of parathyroid scintigraphy were 45% and 94%, respectively, in patients with primary hyperparathyroidism and 39% and 40%, respectively, in patients with secondary parathyroidism. These results were compared with the results of a nonstatistical systematic meta-analysis of the 52 published studies about parathyroid scintigraphy. Sensitivities reported varied from 39% to 90%. The authors concluded that differing scintigraphic techniques did not account for the wide differences in reported sensitivity. Their own data and "partially unpublished" data from a number of university hospitals suggested that the sensitivity of the procedure in clinical routine may be lower than that predicted in much of the literature. They concluded that "a well-designed and properly conducted prospective study is necessary to evaluate the reasons for the differences observed."

World Journal of Surgery

Postradiation PET Predicts Early Tumor Regrowth

Researchers from Japan reported in the December issue of the *International Journal of Radiation Oncology, Biology, Physics* (2003;57:1231–1238) that ^{18}F-FDG PET performed immediately after radiation therapy can predict early tumor regrowth. The study by Koike et al. from the Yokohama City University School of Medicine (Japan) included 20 patients who received radiation for a variety of malignant tumors and who underwent PET image before and within 10 days of completing radiation therapy. Standardized uptake values (SUVs) were calculated for 26 lesions imaged in the 20 patients before and after treatment, and these were correlated with outcomes at 3 months after radiation. Retention indices (RIs) were calculated as the SUV on the posttherapy image minus that on the pretherapy image. RIs were significantly different between patients with and without residual tumor at 3 months after irradiation. All 9 lesions in 6 patients with residual tumors showed RIs >0.1, whereas none of the lesions with RIs <0.1 showed residual tumors. The authors concluded that "dual-time FDG PET imaging just after irradiation is potentially useful for predicting early regrowth of malignant tumors."

International Journal of Radiation Oncology, Biology, Physics

Phantom Dose Measurements in SLN Lymphoscintigraphy

Researchers from Hong Kong reported in the *British Journal of Radiology* (2003;76:818–823) on a phantom study designed to assess the total dose to patients undergoing sentinel lymph node (SLN) lymphoscintigraphy. Law et al. from Queen Mary Hospital used an adult female phantom and a set of thermoluminescent dosimeters to measure both the transmission scan and the internal emission dose. They duplicated the protocol used in their institution, with an external transmission ^{57}Co flood source irradiating the phantom in the posterior, left lateral, left posterior oblique, right lateral, and right posterior oblique positions. Four ^{99m}Tc deposits as internal emission sources were used to simulate peritumoral injection. After measuring the results, the authors calculated that in their protocol, the patient with breast cancer undergoing SLN lymphoscintigraphy received a maximum effective dose of 52 μSv for a 1-day protocol (18 MBq injection) and 204 μSv for a 2-day protocol (74 MBq injection) when only the SLN was excised. The patient effective dose was reduced if other radioactive tissues were removed in the procedure. The authors concluded that "although the doses are low compared with other radiological examinations, the results are informative for patients concerned about radiation exposure for this new imaging technique."

British Journal of Radiology

Intradermal Injection in SNL Mapping

Fleming et al. from St. Vincent's University Hospital and University College Dublin (Ireland) reported in the December issue of the *European Journal of Surgical Oncology* (2003; 29:835–838) on a study comparing the efficacies of intraparenchymal and intradermal isotope injections in sentinel lymph node (SLN) mapping in 125 patients with histologically confirmed breast cancer. Each of 80 patients was administered radioisotope in 4 intraparenchymal injections around the tumor. Each of 45 patients received an intradermal injection at a single site over the tumor. In both groups, isosulphan blue dye was injected around tumors. Sentinel nodes were identified using a combination of lymphoscintigraphy, blue dye, and an intraoperative hand-held gamma probe. A combination of blue dye and isotope successfully located the SLN in 96% of the intraparenchymally injected group and 100% of the intradermally injected group. The authors concluded that "intradermal isotope injection in combination with intraparenchymal blue dye optimizes the localization of the SLN in breast cancer."

European Journal of Surgical Oncology

^{123}I-BMIPP SPECT and Prediction of Cardiac Death

In a study published in the November issue of *Circulation Journal* (2003;67:918–924), Sasaki et al. from the Fujisawa Municipal Hospital (Japan) reported on a study assessing the effectiveness of ^{123}I-β-methyliodophenyl pentadecanoic acid (BMIPP) SPECT in predicting cardiac death in patients with chronic heart failure. The study included 74 patients with chronic heart failure and left ventricular ejection fractions (LVEFs) <45%. All patients underwent both ^{201}Tl SPECT and BMIPP SPECT. Tracer uptake was scored in numerous cardiac segments, and heart-count-to-mediastinum (H/M) ratios were calculated. During a mean follow-up period of 660 days, 17 patients died of cardiac causes. Multivariate analysis identified H/Ms and LVEFs as independent predictors of cardiac death. The authors concluded that "analysis of the myocardial metabolism by BMIPP SPECT can predict high-risk patients with chronic heart failure."

Circulation Journal

Gated Blood-Pool SPECT and Right Ventricular Function

Slart et al. from University Hospital Groningen (The Netherlands) reported in the October issue of the *International Journal of Cardiovascular Imaging* (2003;19:401–407) on a study designed to compare gated blood-pool SPECT using NuSMUGA calculation software (Northwestern University, Chicago, IL) and first-pass radionuclide angiography (FPRNA) in evaluating right ventricular ejection fraction (RVEF). The study included 22 patients in whom FPRNA and gated blood-pool SPECT acquisition were performed. RVEF calculations were performed manually and with the software, using all gated short-axis slices of the right ventricle. The authors found that the software-calculated RVEF from gated blood-pool SPECT did not correlate with that of conventional FPRNA. Mean FPRNA RVEF was 55% ± 10%, and mean gated blood-pool SPECT RVEF calculated with NuSMUGA was 32% ± 8%. Manual gated blood-pool SPECT RVEFs also did not correlate with conventional FPRNA, although they did correlate well with the software-calculated values. The authors concluded that "FPRNA and gated blood-pool SPECT calculations cannot be considered to be equivalent. Therefore, the NuSMUGA program cannot be used to calculate RVEF."

International Journal of Cardiovascular Imaging

^{123}I-β-CIT SPECT and 5-Year Progression in Parkinson's Disease

Researchers from the University of Vienna (Austria) reported in the November issue of *Movement Disorders* (2003;18:1266–1272) on a study of the effectiveness of ^{123}I-2β-carbomethoxy-3β(4-iodophenyl)tropane (^{123}I-β-CIT) SPECT in assessing the decline of striatal dopamine transporter binding over a period of 5 years in a group of patients diagnosed

with early Parkinson's disease (PD). The study by Pirker et al. included 21 patients imaged after diagnosis at 3 intervals over a 5-year period. The authors found that when the period from the initial scanning to 26 ± 11 months (scan 2) after was compared with the period from scan 2 to 38 ± 15 months after, there was no significant difference in the rate of decline of striatal binding. The authors concluded that these data do not suggest "substantial change in the course of dopaminergic degeneration in PD within the first 5–7 years after symptom onset," a finding that is contrary to a current assumption of rapid decline in binding capacity during early stages of the disease.

Movement Disorders

Therapy

Long-Term Survival in Differentiated Thyroid Cancer

The prognostic factors relevant for long-term survival in differentiated thyroid cancer were investigated retrospectively in a large patient group by Eichhorn et al., of the Johannes Gutenberg-Universitat Mainz (Germany), and reported in the October issue of *Thyroid* (2003;13:949–958). The study included 484 patients (358 women; 126 men) with differentiated thyroid cancer (330 papillary; 154 follicular) who had been treated after thyroidectomy with at least 2 ^{131}I therapies and followed-up for a median of 7.6 years at the same institution. The authors found corrected cause-specific 5-, 10-, and 20-year survival rates in the whole cohort to be 0.95, 0.90, 0.83, respectively (low-risk papillary cancer: 0.99, 0.97, 0.89, respectively; low-risk follicular cancer: 0.98, 0.89, 0.89, respectively; high-risk papillary cancer: 0.89, 0.85, 0.85, respectively; high-risk follicular cancer: 0.88, 0.73, 0.52, respectively). Variables with significant negative influence on survival included distant metastases, persisting elevated human thyroglobulin levels after 1 ^{131}I therapy, age 45 years, and, in follicular cancer, sex. Locoregional external radiotherapy did not improve survival but was associated with comorbidity. The aggressiveness of the initial lymph node resection was not a prognostic factor for survival.

Thyroid

Electroporation and Radioiodine Uptake

A novel approach to enhance radioiodine uptake in a human thyroid cancer cell line was reported by Gopal et al. from the Bhabha Atomic Research Center (Mumbai, India) in the November issue of *Applied Radiation and Isotopes* (2003;59:305–310). The authors used electroporation, a process that involves the application of short, high-voltage electric pulses that briefly render plasma membrane permeable, to incorporate radioiodine into a noniodine-concentrating human thyroid cancer cell line (WRO). The cultured WRO cells, which usually do not incorporate iodine because of a lack of a specific transporter protein, incorporated significant amounts of radioiodine after electroporation. Factors affecting the extent of uptake by electroporation included the strength of the electric field, external concentrations of iodine, length of time of electroporation, and temperature of incubation. The incorporated radioiodine was retained over a period of 24 hours. The authors noted the promising implications of these results for thyroid cancer if validated in in vivo studies.

Applied Radiation and Isotopes

Expanding ^{188}Re Applications in Therapy and Treatment

The advent of in-house ^{188}Re generators has provided additional momentum to research on a growing number of radiopharmaceuticals that apply its advantageous physical and chemical properties to radiotargeted therapy and treatment of various cancers and diseases. The range of radiopharmaceuticals and potential clinical applications was surveyed in the October issue of *Cancer Biotherapy and Radiopharmaceuticals* (2003;18:707–717) by Jeong and Chung from Seoul National University College of Medicine (Korea). ^{188}Re is in use in various agents aimed at the reversal of restenosis in coronary arteries, palliation of metastatic bone pain, and treatment of liver cancer, solid tumors, and rheumatoid arthritis. The authors called for research in the development of new ^{188}Re-labeled radiopharmaceuticals to target cancer-specific monoclonal antibodies and peptides.

In the same issue of the journal (2003;18:719–726), Zhang et al. from Gunma University School of Medicine (Japan) reported on the use of ^{188}Re-hydroxyethylidine diphosphonate (HEDP) for the palliation of bone pain in lung cancer patients. The study included 30 patients with painful osseous metastases from lung cancer who were administered ^{188}Re-HEDP in activities ranging from 1.15 to 4.6 GBq and then followed clinically for up to 1 year. Prompt and significant relief of bone pain occurred in 80% of patients, with no significant side effects or toxicity, and 46% of patients discontinued analgesics after administration of the radiopharmaceutical.

Cancer Biotherapy and Radiopharmaceuticals

RIT in Head and Neck Squamous Cell Carcinoma

Colnot et al. from the VU University Medical Center (Amsterdam, The Netherlands) reported in the September issue of *Cancer Immunology and Immunotherapy* (2003;52:576–582) on the safety and other characteristics of ^{99m}Tc-labeled humanized monoclonal antibody (mAb) BIWA 4 (bivatuzumab) for radioimmunotherapy (RIT) in patients with squamous cell carcinoma of the head and neck (HNSCC). The authors evaluated the safety, tumor-targeting potential,

pharmacokinetics, and immunogenicity of ^{99m}Tc-labeled BIWA 4 in 10 patients undergoing operations for primary HNSCC, who were treated first with doses of 25 (3 patients), 50 (4 patients), and 100 mg (3 patients). Radioimmunoscintigraphy was performed within 1 hour and after 21 hours, and patients underwent surgery at 48 hours after injection. Imaging showed targeting of primary tumors in 8 of 10 patients and lymph node metastases in 1 of 5 patients. The highest tumor uptake and tumor-to-nontumor ratios were observed in the 50-mg dose group. Tumor uptakes were 12.9 ± 5.9, 26.2 ± 3.1, and 15.4 ± 1.9 percentages of the injected dose (%ID)/kg for the 25-, 50-, and 100-mg dose groups, respectively, and the tumor-to-bone marrow ratios for these groups were 1.7 ± 0.5, 3.2 ± 1.1, and 2.0 ± 0.6% ID, respectively. The administration of ^{99m}Tc-BIWA 4 was well tolerated by all patients, and no human antihuman antibody responses were observed. The authors concluded that ^{99m}Tc-BIWA 4 can safely be administered to patients with HNSCC and that "these findings support the use of BIWA 4 for RIT studies in patients with HNSCC."

Cancer Immunology and Immunotherapy

^{64}Cu and Cytotoxicity in Targeted Radiotherapy

In a study published in the October 15 issue of *Cancer Research* (2003; 63:6864–6869), Wang et al. from the Washington University School of Medicine (St. Louis, MO) reported on a study of subcellular distribution of somatostatin analogue ^{64}Cu-labeled 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid-octreotide (TETA-OC) and ^{111}In-labeled diethylenetriaminepentaacetic acid-octreotide (DTPA-OC) in somatostatin receptor-positive AR42J rat pancreatic tumor cells in vitro. The purpose of the study was to investigate the mechanisms of ^{64}Cu cytotoxicity. Cell uptake and organelle isolation studies were conducted and compared in ^{64}Cu-TETA-OC and ^{111}In-DTPA-OC. Nuclear localization of each radioisotope increased over time, 19.5% ± 1.4% of the ^{64}Cu and 6.0% ± 1.0% of the ^{111}In in the cell nucleus at 24 hours. When ^{64}Cu-TETA-OC was incubated in pulse-chase experiments with AR42J cells for 4 hours, the nuclear localization of ^{64}Cu increased significantly over the next 20 hours (from 9.8% ± 1.0% to 26.3 ± 5.4%). A separate control pulse-chase experiment showed that the redistribution mechanisms of ^{64}Cu from ^{64}Cu-TETA-OC were different from those of the same isotope in ^{64}Cu-cupric acetate. The amount of ^{64}Cu from ^{64}Cu-TETA-OC also increased in the mitochondria over the 24 hours after administration. The authors concluded that these results suggested that "localization of substantial quantities of ^{64}Cu to the cell nucleus and mitochondria may contribute to cell killing with ^{64}Cu radiopharmaceuticals."

Cancer Research

Hyperthermia, Ultrasound, and MicroPET

Singh et al. from the Washington University School of Medicine (St. Louis, MO) reported in the January–February issue of the *International Journal of Hyperthermia* (2004;20; 32–44) on the development of a microPET-compatible small animal hyperthermia ultrasound system for the heating of subcutaneously implanted tumors in studies of tumor hypoxia. They described the device and presented data from phantom and in vivo experiments indicating that the ultrasound system could produce hyperthermia to a target temperature of 41.5°C in tumors that were 8 ± 2 mm in diameter in mice. This temperature could be maintained within a narrow range for up to 4 h without affecting the core temperature of the animals.

International Journal of Hyperthermia